Achilles Tendinopathy – Sonographic Features, Correlation with Clinical Outcomes and Injection Therapy

Daniel M Walkley

A thesis submitted for the degree of
Doctor of Philosophy
Charles Sturt University

July 2017
Certificate of Authorship

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, understand that it contains no material previously published or written by another person, nor material which to a substantial extent has been accepted for the award of any other degree of diploma at Charles Sturt University or any other educational institution, except where due acknowledgement is made in the thesis. Any contribution made to the research by colleagues with whom I have worked at Charles Sturt University or elsewhere during my candidature is fully acknowledged.

I agree that this thesis be accessible for the purpose of study and research in accordance with normal conditions established by the Executive Director, Library Services, Charles Sturt University or nominee, for the care, loan and reproduction of thesis, subject to confidentiality provisions as approved by the university.

Daniel Walkley

27th July 2017
Abstract

Introduction
Achilles tendinopathy refers to the clinical disease characterised by tendon pain and swelling that results in impaired performance. Chronic tendinopathy can be a significant problem, especially in the sporting population. Even though sonographic investigation is commonly used to assess the structural integrity of the Achilles tendon, there is variability within the literature on how to accurately and reliably assess the Achilles tendon using ultrasound. This has led to a general lack of consistency in defining tendinopathic changes. Previous studies have cited a lack of a gold standard as a major limitation to Achilles tendinopathy assessment and research. There is an inconsistent and often weak relationship between sonographic findings and severity of clinical symptoms. To date, there have been no studies quantitatively assessing tendon grey-scale and Doppler sonographic appearances and comparing these to a validated outcome measure of symptomology.

The primary goal in the management of Achilles tendon disease is to return patients to their desired level of activity without significant residual pain. When conservative treatment fails, injection therapy is often offered. There are various injectable therapies currently being employed for the treatment of recalcitrant Achilles tendinopathy, yet only sparse scientific evidence exists to support any specific injection treatment. High-volume peritendinous glucocorticoid injections are one such injection method growing in popularity, with early studies showing promising results. The aim of these injections are to mechanically disrupt (by stretching, breaking or occluding) the neurovascular bundles growing from the paratenon into the tendon. Additional to injection therapy, appropriate load management of the tendon has been shown to be the most successful long-term intervention. Therefore, it was hypothesised that the combination of a large-volume peritendinous glucocorticoid injection with a graded functional loading program from a
physiotherapist would lead to an improvement in outcomes for patients with recalcitrant Achilles tendinopathy.

**Methodology**

An expert panel of professionals (Delphi panel) was formed with extensive knowledge and experience in the assessment of tendinopathy using ultrasound. This combined with a thorough literature review led to the development of the Achilles ultrasound assessment tool (AUAT). The AUAT is a numeric scoresheet that holistically assesses the entire spectrum of sonographic changes present within the tendinopathic tendon and peritendinous tissues, allowing semi-quantification of the appearance of these structures.

The construct validity, reliability and repeatability of the AUAT were assessed by evaluating the level of agreement between 6 sonographers and 6 radiologists assessing the same sonographic images from 4 different patients. Whilst, sonographic correlation with clinical outcomes was assessed by exploring the relationship between AUAT scores with a validated index for the clinical severity of Achilles tendinopathy, the Victorian Institute of Sport assessment – Achilles (VISA-A) questionnaire. A cohort of 43 participants with chronic Achilles tendinopathy elected to undergo a single high-volume peritendinous glucocorticoid injection in combination with a supervised rehabilitation program. Patients were injected with 1mL celestone chronodose combined with 2mL xylocaine and 20mL of cold normal saline. Blinded assessors evaluated participants pre-intervention and at 24-week follow-up sonographically using the AUAT and clinically with the VISA-A.

**Results**

The AUAT was able to differentiate sonographically normal tendons from abnormal ($\kappa = 0.481$, $p < 0.001$), even in tendons with only mild sonographic changes. Inter-observer reliability showed almost perfect levels of agreement between both sonographer and radiologist groups ($\kappa = 0.949$, $p < 0.001$), while intra-observer
reliability showed no significant difference between initial and subsequent AUAT assessments ($p > 0.05$).

The results of the correlation of the AUAT with clinical findings are conflicting, with no association at initial presentation ($r_s = -0.04$, $p > 0.05$) between AUAT score and the clinical score of symptomology, the VISA-A. Yet at 24-week follow-up of the same patient cohort after intervention, a significant moderate strength relationship existed ($r_s = -0.56$, $p > 0.001$).

For the management of recalcitrant Achilles tendinopathy, a single high-volume ultrasound guided peritendinous injection significantly reduced pain and improved function when combined with exercise therapy. This clinical improvement assessed by the VISA-A ($p > 0.001$) coincided with a sonographic improvement in tendon morphology as assessed by the AUAT ($p > 0.001$).

**Conclusion**

The AUAT is a valid and reliable tool to define and represent the sonographic changes involved in Achilles tendinopathy and possesses the potential to be a useful instrument when evaluating the status and progress of Achilles tendon disorders. The construct validity of the AUAT via its Delphi formation along with its high levels of inter and intra observer reliability demonstrate the strengths and clinical applicability of this tool. The relationship of the AUAT to clinical symptoms is variable, with this study contributing to the growing body of evidence that there is a disconnect between structure and pain. In recalcitrant Achilles tendinopathy, a single high-volume peritendinous glucocorticoid injection leads to a significant reduction in pain and improvements in both function and tendon sonographic appearance.
I could not have completed this work without the help and encouragement of a number of people. My gratitude and appreciation go to you all.

My beautiful wife Jess, thank you so much for all of the love and support that you have given me throughout this process. You know that I could not have done this without you.

Zara, thank you for being such a good little girl and sleeping whilst Daddy works on the computer.

Thank you to my primary supervisor Associate Professor Paul Tinley and secondary supervisor Dr Rod McGregor, for your continual guidance, encouragement and motivation. Without your mentorship, I would not have been able to pursue this goal. Despite our geographical separation, we were able to overcome this with ease thanks to the many teleconferences and track changes. Thank you so much for everything that you both have done.

Dr Wes Cormick, thank you for your constant inspiration and drive, pushing me to become the best Sonographer and patient advocate that I can be.

My gratitude also goes to Ben Rohrlach who enabled my statistical processing and for your ability to translate these results into practical terms.

Thank you to all of the staff at Fowler Simmons Radiology and Canberra Specialist Ultrasound for providing me the time and access to your facilities.

Finally, I am indebted to all the participants who have given freely of their time and experience, I have learnt a lot from you.
“I know how to solve every problem that has ever been solved”

Richard Feynman
Prologue

I call my next patient’s name from the waiting room. Hesitantly following me into the ultrasound consulting room is Michael, a 32-year-old podiatrist and runner. I read his referral letter and begin to listen to his story about his Achilles pain. His story is a common tale, involving a history of relative tendon overload and well-meaning but misguided advice based on previous suboptimal imaging reports.

In his younger years, Michael was an elite track athlete; eight-months ago he was enticed to return to the sport of middle distance running. During this time, his weekly running mileage has increased from 15kms to an average of 50kms, and intensity even more so. With this dramatic increase in load, Michael developed mid-substance Achilles pain that initially presented as stiffness in the morning and at the beginning of exercise which would resolve as activity continued. This pain then evolved to be present throughout the day and continual throughout exercise. This was beginning to affect his training and limit performance, as well as interfering with his daily life.

Michael then consulted with a sports physician who referred him for a diagnostic ultrasound to determine the extent and stage of his tendon disease. The ultrasound report merely confirmed a ‘hypoechoic change in the mid-belly of the Achilles consistent with tendinopathy’. This imaging examination provided no additional information that was not already clinically apparent, and as such, Michael continued running at current levels, whilst commencing conservative treatment through a physiotherapist consisting of massage, dry needling, biomechanical alteration, stretching, kinesio-taping, and an eccentric exercise program.

After three-months of conservative treatment, Michael had not made significant progress and was unable to compete in a local 1500m running event that he had been attempting to train for. At this point he decided this management approach
was not suitable for his needs and after discussing with his treating clinician, presented at my clinic for a diagnostic ultrasound and injection therapy as deemed appropriate.

The ultrasound imaging today revealed mid-substance Achilles tendinopathy presenting with a thickened Achilles that was diffusely hypoechoic with internal fibrillar heterogenicity and neovascularity as seen with Doppler ultrasound. Additionally, there were signs of paratendinopathy, fat pad inflammation and plantaris tendon involvement. On discussing the new and detailed findings with Michael, it was discovered that several of the management interventions previously applied were potentially having a negative effect on his recovery from injury.

Michael’s story is not unique. Often medical imaging is variable and operator dependant leading to variations in the reporting of findings. The aim of musculoskeletal diagnostic imaging is to confirm the treating clinician's diagnosis and give an accurate account regarding the status of tissues that cannot be readily assessed clinically. Imaging should assist in not only making the diagnosis, but also the guidance of management and treatment strategies. This prompted my desire to pursue further research in the area of Achilles tendinopathy, as this seemingly simple process is often inadequately assessed and often recalcitrant to treatment. This body of work attempts to assist both medical imaging professionals and clinicians to better utilise ultrasound imaging to advance the health of their patients.
Table of Contents

Certificate of Authorship ........................................................................................................ ii
Abstract ..................................................................................................................................... iii
Acknowledgements ..................................................................................................................... vi
Prologue .................................................................................................................................... viii
Table of Contents ....................................................................................................................... x
List of Tables ............................................................................................................................... xv
List of Figures, Images and Charts ............................................................................................ xvi
List of Appendices ..................................................................................................................... xvii
List of Symbols, Abbreviations and Nomenclature .................................................................... xviii

Chapter One: Introduction ........................................................................................................ 1
  1.1 Objective and Research Questions .................................................................................. 6
  1.2 Dissertation Format ......................................................................................................... 6

Chapter Two: Review of the Literature ..................................................................................... 8
  2.1 Search Strategy and Study Selection .............................................................................. 8
  2.2 Introduction .................................................................................................................... 9
  2.3 Anatomy of the Achilles Tendon .................................................................................... 10
  2.4 Histology of the Normal Achilles Tendon ....................................................................... 12
  2.5 Biomechanics and Mechanotransduction of the Achilles Tendon ................................. 15
  2.6 Aetiology of Tendinopathy ............................................................................................. 18
  2.7 Pathophysiology of Achilles Tendinopathy .................................................................... 20
  2.8 Diagnosis and Imaging .................................................................................................... 28
  2.9 Sonographic Presentation of Achilles Tendinopathy ...................................................... 35
    2.9.1 Tendon changes ....................................................................................................... 35
    2.9.2 Mid-portion Tendinopathy ...................................................................................... 37
    2.9.3 Enthesis Pathology ................................................................................................. 38
    2.9.4 Neovascularity ....................................................................................................... 39
    2.9.5 Paratendinopathy ................................................................................................. 41
  2.10 Complications, Barriers to Treatment and Associated Findings ................................. 43
# Table of Contents

3.3.2 Research Aims.................................................................................................................. 102
3.3.3 Hypothesis.......................................................................................................................... 103

3.4 Study 2: The Reliability and Construct Validity of the AUAT............................................. 103
3.4.1 Identified Knowledge Gaps............................................................................................... 103
3.4.2 Research Questions............................................................................................................ 103
3.4.3 Hypothesis.......................................................................................................................... 103

3.5 Study 3: High-Volume Injection Therapy – A Novel Adjunct in the Management of Achilles Tendinopathy.................................................. 103
3.5.1 Identified Knowledge Gaps............................................................................................... 103
3.5.2 Research Questions............................................................................................................ 104
3.5.3 Hypothesis.......................................................................................................................... 104

3.6 Study 4: AUAT and Correlation with Patient Symptoms....................................................... 104
3.6.1 Identified Knowledge Gaps............................................................................................... 104
3.6.2 Research Questions............................................................................................................ 105
3.6.3 Hypothesis.......................................................................................................................... 105

Chapter Four: Formation of the Achilles Ultrasound Assessment Tool (AUAT)....... 106
4.1 Introduction ............................................................................................................................. 106
4.2 Rationale ............................................................................................................................... 108
4.3 Aim........................................................................................................................................ 109
4.4 Methodology.......................................................................................................................... 109

4.5 Formulation of the Achilles Ultrasound Assessment Tool.................................................... 110
4.5.1 Literature Review .............................................................................................................. 110
4.5.2 Previous Holistic Assessment Formats............................................................................. 114

4.6 Delphi Procedure.................................................................................................................... 115
4.6.1 Delphi – Round 1: Expert Group Formation and Item Generation ......................... 115
4.6.2 Delphi – Round 1: Results............................................................................................... 117
4.6.3 Delphi – Round 2: Scoresheet Formation ................................................................. 117
4.6.4 Delphi – Round 2: Discussion and Formation of the AUAT ...................................... 118
4.6.5 Delphi – Round 2: Results............................................................................................... 119
4.6.6 Delphi – Round 3: Clinimetric Testing .......................................................................... 124
4.6.7 Delphi – Round 3: Results ............................................................................................. 125
Chapter Five: The Reliability and Construct Validity of the AUAT ......................... 126
  5.1 Introduction .................................................................................................. 126
  5.2 Aim .......................................................................................................... 127
  5.3 Methodology ............................................................................................. 128
    5.3.1 Observers ............................................................................................ 128
    5.3.2 Patients ............................................................................................... 129
    5.3.3 Sonographic Evaluation ...................................................................... 130
  5.4 Ethics ......................................................................................................... 133
  5.5 Statistical Analysis .................................................................................... 133
  5.6 Results ....................................................................................................... 135
    5.6.1 Validity .................................................................................................. 135
    5.6.2 Blinded Inter-Observer Reliability ...................................................... 136
    5.6.3 Defined Inter-Observer Reliability ...................................................... 136
    5.6.4 Longitudinal Intra-Observer Reliability ............................................. 136
  5.7 Discussion .................................................................................................. 137
  5.8 Limitations and Future Directions ............................................................. 139
  5.9 Conclusion ................................................................................................ 141

Chapter Six: High-Volume Injection Therapy - A Novel Adjunct in the Management of Achilles Tendinopathy ................................................................. 142
  6.1 Introduction ................................................................................................ 142
  6.2 Injection Therapy ...................................................................................... 143
  6.3 A New Technique for High-Volume Injection Therapy ............................ 146
  6.4 Aim .......................................................................................................... 147
  6.5 Methodology ............................................................................................. 148
    6.5.1 Patients ................................................................................................ 148
    6.5.2 Sonographic Evaluation ..................................................................... 149
    6.5.3 Clinical Outcome Measures .............................................................. 149
    6.5.4 Intervention ....................................................................................... 150
    6.5.5 Follow-up ........................................................................................... 153
  6.6 Ethics ......................................................................................................... 153
  6.7 Statistical Analysis .................................................................................... 153
# Table of Contents

## Chapter Seven: AUAT and Correlation with Clinical Outcomes

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.1 Introduction</td>
<td>169</td>
</tr>
<tr>
<td>7.2 Aim</td>
<td>172</td>
</tr>
<tr>
<td>7.3 Methodology</td>
<td>172</td>
</tr>
<tr>
<td>7.3.1 Patients</td>
<td>172</td>
</tr>
<tr>
<td>7.3.2 Sonographic Evaluation</td>
<td>172</td>
</tr>
<tr>
<td>7.3.3 Clinical Outcome Measure</td>
<td>173</td>
</tr>
<tr>
<td>7.3.4 Intervention</td>
<td>173</td>
</tr>
<tr>
<td>7.3.5 Follow-up</td>
<td>173</td>
</tr>
<tr>
<td>7.4 Ethics</td>
<td>174</td>
</tr>
<tr>
<td>7.5 Statistical Analysis</td>
<td>174</td>
</tr>
<tr>
<td>7.6 Results</td>
<td>174</td>
</tr>
<tr>
<td>7.7 Discussion</td>
<td>179</td>
</tr>
<tr>
<td>7.8 Conclusion</td>
<td>185</td>
</tr>
</tbody>
</table>

## Chapter Eight: Discussion and Conclusion

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1 Summary of Findings</td>
<td>188</td>
</tr>
<tr>
<td>8.2 Implications of Findings</td>
<td>191</td>
</tr>
<tr>
<td>8.3 Thesis Limitations</td>
<td>194</td>
</tr>
<tr>
<td>8.4 Further Areas of Research</td>
<td>196</td>
</tr>
<tr>
<td>8.5 Conclusion</td>
<td>198</td>
</tr>
</tbody>
</table>

Epilogue | 199

References | 200

Appendices | 220
## List of Tables

Table 1: Delphi Panel Demographics ................................................................. 116
Table 2: Delphi – Round 1: Results ................................................................. 117
Table 3: Delphi – Round 3: Results ................................................................. 125
Table 4: Observer Demographics and Experience ........................................ 129
Table 5: AUAT Reliability Results ................................................................. 135
Table 6: Participant Demographics and Results .......................................... 155
Table 7: Pre-intervention Results ................................................................. 175
Table 8: Frequency of Individual AUAT Variable Occurrence .................... 176
Table 9: Post-Intervention Results ............................................................... 177
List of Figures, Images and Charts

Figure 1: Normal tendon histology (H&E stain, 100x) ................................................. 13
Figure 2: Schematic representation of collagen synthesis and degradation with regard to time ........................................................................................................... 17
Figure 3: Degenerative tendon histopathology (H&E stain, 100x) ...................... 22
Figure 4: Pathology continuum ................................................................................. 48

Image 1: High-volume peritendinous injection procedure demonstrating patient positioning, probe orientation and injection technique ........................................... 151
Image 2: Needle introduction ....................................................................................... 152
Image 3: Needle repositioning .................................................................................... 152
Image 4: Pre high-volume injection ........................................................................... 161
Image 5: Post high-volume injection ........................................................................ 161

Histogram 1: Distribution of AUAT scores pre and post intervention....................... 156
Histogram 2: Distribution of VISA-A scores pre and post intervention .................... 158
Line Chart 1: AUAT response to intervention ............................................................ 157
Line Chart 2: VISA-A response to intervention ........................................................ 159
Scatter Plot 1: Relationship between VISA-A and tendon thickness ...................... 177
Scatter Plot 2: Relationship between VISA-A and AUAT score ......................... 178
List of Appendices

Appendix 1: AUAT ........................................................................................................ 220
Appendix 2: VISA-A.................................................................................................... 221
Appendix 3: AUAT Technical Briefing...................................................................... 224
Appendix 4: Standardised Warm-up........................................................................ 236
Appendix 5: Sonographic Evaluation....................................................................... 237
Appendix 6: Observer Information Sheet ................................................................. 239
Appendix 7: Observer Consent Form...................................................................... 242
Appendix 8: Patient Information Sheet ................................................................... 243
Appendix 9: Patient Consent Form ......................................................................... 246
Appendix 10: Patient Information Sheet .................................................................. 247
Appendix 11: Patient Consent Form ....................................................................... 250
## List of Symbols, Abbreviations and Nomenclature

<table>
<thead>
<tr>
<th>Symbol or Phrase</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achillodynia</td>
<td>Pain in the Achilles region.</td>
</tr>
<tr>
<td>Tendinopathy</td>
<td>Degenerative change in a tendon due to a failed healing response.</td>
</tr>
<tr>
<td>Achilles Tendinopathy</td>
<td>The clinical disease characterised by tendon pain, swelling, and impaired performance.</td>
</tr>
<tr>
<td>Tenocyte</td>
<td>Tendon cell.</td>
</tr>
<tr>
<td>Collagen</td>
<td>A structural protein.</td>
</tr>
<tr>
<td>Extracellular Matrix</td>
<td>A scaffold of connective tissue (primarily collagen and proteoglycans), that links tissues of the body together, playing an important role in force transmission and tissue maintenance.</td>
</tr>
<tr>
<td>Mid-substance</td>
<td>The region of the Achilles tendon, 2-6cm from the calcaneal insertion.</td>
</tr>
<tr>
<td>Enthesis</td>
<td>The fibrous connective tissue connecting tendon into bone.</td>
</tr>
<tr>
<td>Achilles Enthesopathy</td>
<td>Pathological change resulting in pain at or around the most distal portion of the Achilles at its attachment on the calcaneal tuberosity.</td>
</tr>
<tr>
<td>Paratenon</td>
<td>A loose areola envelope of connective tissue containing nerves and blood vessels that surrounds the tendon</td>
</tr>
<tr>
<td>Bursae</td>
<td>Small fluid filled spaces that lie between the tendon and an overlying structure that lubricate and reduce friction.</td>
</tr>
<tr>
<td>Fat pad</td>
<td>A richly innervated and vascularised adipose deposit that supports and provides a biomechanical advantage to tendons.</td>
</tr>
<tr>
<td>Echogenicity</td>
<td>The ability of a tissue to reflect an ultrasound beam and produce echoes.</td>
</tr>
<tr>
<td>Hypoechoic</td>
<td>Reduced echogenicity due to tissues reflecting relatively few ultrasound beams, usually due to a pathological change in the tissue.</td>
</tr>
<tr>
<td>------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Neovascularisation</td>
<td>An angiogenic activity involving the formation of new blood vessels and associated nerves.</td>
</tr>
<tr>
<td>Doppler Ultrasound</td>
<td>Diagnostic ultrasound machines have the ability to utilise their ultrasound beams to employ and interpret a Doppler effect. This can be used to assess whether structures (usually blood) are moving towards or away from the transducer, and their relative velocity.</td>
</tr>
<tr>
<td>Mechanotransduction</td>
<td>The physiological process whereby cells sense and respond to mechanical load.</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>A class of corticosteroids that are a part of the feedback mechanism of the immune system. These substances have the ability to reduce certain functions of the immune response, such as metabolism and inflammation.</td>
</tr>
<tr>
<td>VISA-A</td>
<td>Victorian Institute of Sport Assessment – Achilles questionnaire, is an Achilles specific pain and disability patient reported outcome measure, to serve as an index of severity for Achilles tendinopathy.</td>
</tr>
</tbody>
</table>
Achilles tendinopathy refers to the clinical condition characterised by tendon pain, swelling, localised tenderness and impaired performance (Maffulli, Khan, & Puddu, 1998). Achilles tendinopathy occurs most frequently in the mid-portion of the tendon (2-6cm proximal to the calcaneus) and is the most common lower limb complaint in athletes (Woo, Arnoczky & Renström, 2008). Mid-portion Achilles tendinopathy notoriously develops into a recalcitrant condition, being longstanding in nature and often difficult to manage (Boesen, Hansen, Boesen, Malliaras, & Langberg, 2017). The exact aetiology and pathophysiology of this condition are not fully understood; however, it is known that tendon overload is the main causative stimulus of this pathological process (Abate et al., 2009; Barker-Davies et al., 2017; Cook & Purdam, 2009). Although traditionally considered an inflammatory condition, histopathology studies of mid-portion Achilles tendinopathy have shown degenerative changes within the tendon due to a failed healing response (Cook & Purdam, 2009). This state of dysrepair within the tendon involves a haphazard proliferation of tenocytes, associated abnormalities within tenocytes, and also a disruption of collagen fibres along with an increase in the non-collagenous matrix (Maffulli, Longo, & Denaro, 2010). This results in a tendon that is less capable of sustaining repeated tensile load, more susceptible to damage and commonly painful (Maffulli et al., 2010). Intrinsic and extrinsic factors may play a part in the development of mid-portion tendinopathy, which can progress in isolation, or be associated with complications that can impact on prognosis and management. These potential complications include paratenon changes, fat pad and bursal inflammation, synovio-entheseal complex pathology, intra-tendinous calcifications and involvement of the plantaris tendon (Bianchi & Martinoli, 2007; Wijesekera, Calder, & Lee, 2011).
The imaging of tendons with ultrasound is commonly used in the clinical setting to assist in the diagnosis of tendinopathy, direct treatments, monitor the efficiency of interventions and assess the risk of developing symptoms (Scott et al., 2013). Ultrasound is now the most common imaging modality employed to assess the structural integrity of the Achilles tendon; being fast, easily accessible and affordable (Nadeau, Desrochers, Lamontagne, Lariviere, & Gagnon, 2016; Wijesekera et al., 2011). Tendinopathy on ultrasound imaging may demonstrate tendon thickening, collagen fascicle disorganisation and irregularity, tendon hypoechogenicity and neovascularity within the tendon substance as observed with colour or power Doppler (Cook & Purdam, 2009). Even though ultrasound is the preferred diagnostic method for assessing Achilles tendinopathy, limited reliability of this modality is often cited due to operator dependency and a lack of standardised assessment and grading protocols (Sunding, Fahlström, Werner, Forssblad, & Willberg, 2016). In musculoskeletal practice, there is clearly a need to understand where these potential errors exist, in an attempt to improve the reliability and repeatability of assessments made by imaging professionals (Sim & Wright, 2005).

Ultrasound demonstrates both grey-scale and Doppler changes within pathological tendinopathic tendons (Archambault et al., 1998; Ohberg, Lorentzon, & Alfredson, 2001). While a number of different scales have been described to assess and quantify the degree of tendon heterogeneity or neovascularisation, there is no uniform categorisation for assessing the Achilles tendon using ultrasound imaging, making comparisons between studies difficult (Bianchi & Martinoli, 2007). What defines a significant hypoechoic area, diffuse thickening or significant vascularity is often not well defined in most studies. Additionally, the reliability of the various measurement and evaluation techniques employed are seldom reported (Cook, Khan, Kiss, & Griffiths, 2000; Sengkerij, de Vos, Weir, van Weelde, & Tol, 2009; Sunding et al., 2016). Compounding the lack of confidence within the research, current literature makes little mention regarding the diagnostic criteria of complications to management that are associated with Achilles tendinopathy; however, there is significant evidence documenting the relationship of these
complications with poor outcomes (Hutchison et al., 2013). Previous studies have cited the lack of a ‘gold standard’ in the categorisation of imaging assessment as a major limitation to Achilles tendinopathy assessment and research (Khan & Maffulli, 1998). This lack of consistency has the potential to lead to incorrect treatment rationales and subsequently poorer patient outcomes. There is a need within the medical imaging community for the standardisation of a more encompassing sonographic assessment criteria to enable the accurate and reliable assessment of the Achilles tendon using ultrasound.

Various sonographic changes are associated with Achilles tendon pain, including grey-scale abnormalities, change in shape and neovascularity; yet their relationship to symptoms is unclear (Gibbon, Cooper, & Radcliffe, 2000; Khan et al., 2003; Malliaras, Voss, Garau, Richards, & Maffulli, 2012; Ohberg et al., 2001). Many studies assessing the relationship between sonographic findings and the severity of clinical symptoms have shown an inconsistent and often weak association between clinical symptoms and imaging assessment (Bakkegaard, Johannsen, Hojgaard, & Langberg, 2015; de Jonge et al., 2014; Emerson, Morrissey, Perry, & Jalan, 2010; Malliaras, Purdam, Maffulli, & Cook, 2010; Ohberg et al., 2001; Ooi, Schneider, Malliaras, Chadwick, & Connell, 2015). A criticism of the literature is that these comparative studies use varying sonographic imaging techniques and assessments that are then paired to variable outcome measurements. To date, there have been no studies on the relationship between an all-encompassing assessment of the sonographic appearance of the tendon and clinical symptoms using a validated outcome measure.

The goal in management of Achilles tendinopathy is to return patients to their desired level of activity without significant residual pain. This is often achieved with modification of training loads and strength-based rehabilitation programs that enable most people to return to previous activity levels (Bedi, Jowett, Ristanis, Docking, & Cook, 2016). While no gold standard treatment schedule exists for the management of Achilles tendinopathy, it appears that progressive loading exercises
are integral to reach successful outcomes (Boesen et al., 2017). Additional treatment modalities including; rest, cryotherapy, non-steroidal anti-inflammatory drugs, manual therapy, biomechanical corrections and extracorporeal shockwave therapy are often utilised with variable levels of success (Wijesekera et al., 2011).

The literature suggests that up to 25% of patients fail these conservative management techniques; with others finding that the relatively slow recuperation of tendon injuries exceeds desired timeframes (Kader, Saxena, Movin, & Maffulli, 2002). When conservative treatment fails, injection therapy is often offered, but only sparse scientific evidence exists supporting any specific injection treatment (Boesen et al., 2014; Scott et al., 2013). There are a variety of different injectable therapies currently being employed for the treatment of tendinopathy, including glucocorticoids, prolotherapy, sclerotherapy, protease inhibitor injections, autologous blood, platelet rich plasma and tenocytes (Scott et al., 2013). Currently, glucocorticoids remain the most widely used injectable therapy for a variety of tendinopathies (Scott et al., 2013). These are usually administered with local anaesthetic and best practice dictates that ultrasound be used to guide needle placement to the desired area (Fredberg et al., 2004). The mechanism of action of glucocorticoids is by inhibiting inflammation-associated molecules including cytokines, chemokines and arachidonic acid metabolites, along with a reduction in angiogenesis and an inhibition of adhesion molecules involved in nociceptive pathways (Burke & Adler, 2016).

Despite much debate, there is still no consensus regarding the best injectable therapy to use in patients with recalcitrant tendinopathy that have failed conservative treatment (Kearney, Parsons, Metcalfe, & Costa, 2015). High-volume peritendinous glucocorticoid injections are one such injection technique growing in popularity, and early studies have demonstrated promising results (Boesen et al., 2017). This technique involves a large volume of saline, steroid and local anaesthetic injected into the interface between the Achilles and peritendinous tissues. The aim of this technique, in theory, is to mechanically disrupt, by stretching, breaking or
occluding the neurovascular bundles growing from the peritendinous tissues into the tendon, effectively de-innervating the tendon. This has the potential to reduce the proliferation of fibroblasts, angiogenesis, vascular activation and pain transmission within the tendon; the core components for the pathogenesis of tendinopathy (Chan et al., 2008). Small studies on high-volume peritendinous glucocorticoid injections have been shown to reduce pain and improve function in both the short and long-term, making it a valuable technique in musculoskeletal therapy (Boesen et al., 2017; Chan et al., 2008; Humphrey et al., 2010; Maffulli, Spiezia, Longo, Denaro, & Maffulli, 2013; Resteghini & Yeoh, 2012; Wheeler, 2014). Despite these findings, there remains no consensus within the literature as to what volume this entails, and variations of injection technique exist. Additionally, as different case series utilise different protocols, with differing injection regimens, medications, follow-up periods and protocols; direct comparison between methods is difficult and no technique has demonstrated superiority.

Due to the multifactorial aetiology of Achilles tendinopathy, clinicians often resort to multiple approaches to rehabilitate the patient and the utilisation of concurrent therapies (Iversen, Bartels, & Langberg, 2012). There is no ‘one size fits all’ approach and clinical reasoning becomes important to reach successful outcomes. Whilst appropriate load management for the tendon has been shown to be the most successful intervention, with graded loading exercises giving the best long-term outcomes for Achilles tendinopathy, injection therapy may be useful to progress the recalcitrant patient (Alfredson & Cook, 2007; Magnusson, Bartels, & Langberg, 2010). It was hypothesised that the combination of large-volume peritendinous glucocorticoid injection with a graded, functional loading program from a physiotherapist, should deliver optimum outcomes. Additionally, the loading program should be based on an accurate sonographic description of the health of the tendon, dictating the site and stage of tendinopathy along with the identification of potential complications of treatment. This holistic management approach aims to achieve the complex process of tendon healing by addressing both the mechanical and chemical factors involved in tendinopathy.
1.1 Objective and Research Questions

From the discussion above, it is clear that there is value in the development of a quantifiable method to assess the Achilles tendon using ultrasound that can be utilised as an assessment tool in both everyday practice and within the research setting. An improved assessment technique has the potential to facilitate increased accuracy and efficiency in diagnostic imaging. Additionally, the applicability of this tool may be used to influence clinical management and treatment of Achilles tendinopathy.

The primary research aim for this study was therefore to:

- Develop a standardised, objective sonographic tool to allow reliable and repeatable assessment of the Achilles tendon using ultrasound.

The primary research questions of the study are:

1. Is this newly formed tool a valid, reliable and repeatable method for the assessment of Achilles tendinopathy when used by radiologists and sonographers?

2. When using this semi-quantifiable method to assess pathological Achilles tendons using ultrasound, is there a relationship between ultrasound findings and clinical symptoms in patients with mid-portion Achilles tendinopathy?

3. For adults with clinically diagnosed recalcitrant Achilles tendinopathy, is there an improvement in pain and function as assessed by the VISA-A score and/or change in sonographic findings after a single ultrasound guided high-volume peritendinous injection of 1mL celestone chronodose, 2mL xylocaine and 20mL of cold normal saline in conjunction with a physiotherapist based loading program after 24-weeks?

1.2 Dissertation Format

This thesis consists of a collection of four main studies detailing the sonographic assessment of the Achilles tendon, management of Achilles tendinopathy and the relationship between sonographic imaging and symptoms. These studies are as follows:
• Chapter Four describes the formation of a semi-quantitative measurement tool to assess the sonographic changes associated with Achilles tendinopathy via a Delphi process.

• Chapter Five details a construct validity, reliability and repeatability study of the newly formed Achilles Ultrasound Assessment Tool (AUAT).

• Chapter Six is a prospective case series exploring the efficiency of an ultrasound guided high-volume peritendinous glucocorticoid injection in conjunction with a physiotherapist-based loading program for patients with recalcitrant Achilles tendinopathy at 24-week follow-up.

• Chapter Seven examines the relationship between the thorough sonographic assessment technique of the AUAT and patients pain and function levels using the Victorian Institute of Sport Assessment – Achilles (VISA-A) score on this same cohort of patients.

These studies are supported by a comprehensive review of the literature (Chapter Two), a description of the conceptual framework on which the research was based (Chapter Three) and a summary of the findings with future research directions (Chapter Eight). Additional information, including consent and information forms, the VISA-A, the AUAT, and associated technical briefing are included in the appendices for completeness; allowing for a clear and precise judgment to be made of the importance and originality of the research reported in this dissertation.
Chapter Two: Review of the Literature

The purpose of this literature review is to highlight the histopathological and sonographic changes seen as the pathological Achilles tendon progresses through the tendinopathy spectrum. This review was used to inform and provide background materials for the development of a new sonographic assessment tool for the Achilles tendon. Additionally, this review evaluates and discusses the various rehabilitation and interventional techniques used in the management of Achilles tendon disease, with this background knowledge used to situate a new treatment protocol for the management of recalcitrant Achilles tendinopathy.

2.1 Search Strategy and Study Selection

The search for original articles published in the English language between January 1985 and May 2017, and referring to Achilles tendinopathy and sonography was carried out in PUBMED and EMBASE databases. Abstracts from scientific conferences were not included. The search was performed using the following key words; Achilles AND tendinopathy OR tendinitis OR tendinosis OR injection AND ultrasound OR sonography OR ultrasonography OR Doppler. The key words refer to Mesh Terms or, if not available, to key words present in the title/abstract.

Only references with available abstracts were assessed. Titles, abstracts and full reports of the articles identified were systematically screened by the principal author for relevance, with articles then being selected if they addressed the previously mentioned research questions, listed in Chapter One. A discussion of the discovered relevant literature and critical appraisal follows.
2.2 Introduction

The Achilles tendon is the thickest and strongest tendon in the body and is subject to some of the highest loads. These tensile loads can be up to 10-times body weight during running, jumping, hopping and skipping (Soma & Mandelbaum, 1994).

The Dutch surgeon, Philip Verheyen, was the first in 1693 to actually name the Achilles tendon after the Greek hero Achilles, prior to that it was known as ‘tendo magnus of Hippocrates’ (van Dijk, van Sterkenburg, Wiegerinck, Karlsson, & Maffulli, 2011). In Greek mythology, Achilles was the greatest and most central character of Homer’s *Iliad*. When Achilles was a baby, it was foretold that he would die young. To prevent his death, his mother held him by the heel and dipped him into the river Styx that offered powers of invulnerability. This magical water covered his body but not his heel. Achilles, who despite displaying dominance on the battlefield, had his death come from a single arrow to the heel; his only unprotected area. From this point in time, the Achilles tendon was considered a weak point of the human body. Throughout the years, mid-portion Achilles pain has been a topic of much research and remains one of the most injured tendon regions of the body (Woo et al., 2008). Achilles tendon injuries can be caused by a variety of traumatic and overuse conditions and are one of the most frequent clinical presentations seen within sports medicine clinics (Yang, Pugh, Coleman, & Nokes, 2010).

Pain in the Achilles tendon region (achillodynia) is the most common lower limb complaint of athletes (Woo et al., 2008). Although its prevalence appears to be higher in recreational and professional athletes, achillodynia is also frequent in the non-athletic population, noted to occur in up to one third of sedentary patients (Longo, Ronga, & Maffulli, 2009). Achilles tendinopathy is the most frequent pathological process associated with achillodynia and is most common in middle-aged men (35-45 years of age) involved in running and jumping sports (Longo et al., 2009). The poor regenerative capability of tendons plays a major role in this chronic disease. Achilles tendinopathy is extremely common in runners, with an estimated
annual incidence of 9%, a lifetime risk of 23.9% for athletes and has been reported as high as 5.9% for the general population (Kujala, Sarna, & Kaprio, 2005).

Acute Achilles tendon ruptures are common in young athletes and middle-aged people participating in recreational activities, with an incidence rate ranging from 6-18 per 100,000 per year (Longo, Petrillo, Maffulli, & Denaro, 2013). Although an acute rupture appears to occur due to a traumatic injury in a healthy tendon, in reality, it is caused by an excessive eccentric contraction on a pathological asymptomatic tendon (Hattrup & Johnson, 1985).

To understand the injury biomechanics and stress forces associated with the Achilles tendon, we first need to consider the gross anatomy.

2.3 Anatomy of the Achilles Tendon

Tendons are specialised connective tissue structures interposed between muscles and bones that transfer forces created by contractile cells in muscles to bone to make joint movement possible (Jozsa & Kannus, 1997). The Achilles tendon is the distal insertion of the triceps surae muscle (gastrocnemius-soleus musculotendinous unit) onto the postero-superior margin of the calcaneus and its unique structure of parallel collagen fibres allow it to store and release substantial amounts of tensile energy (Woo et al., 2008).

The gastrocnemius muscle originates from the posterior lateral and medial femoral condyles, crossing the knee, ankle and subtalar joints to insert onto the calcaneus. The gastrocnemius muscle consists mainly of fast twitch type II fibres and when it plantar flexes the foot on the ankle, and flexes the knee, the body is propelled forward (O’Brien, 2005). The soleus muscle lies anterior to the gastrocnemius muscle and originates form the proximal tibia, fibula and interosseous membrane and crosses the ankle and subtalar joints. The soleus is a postural muscle that acts only on the ankle joint and assists in plantar flexion for toe-off during propulsion (O’Brien, 2005). The soleus contracts to counteract the tendency for the body to tilt
forward at the ankle when the centre of gravity passes in front of the axis of movement of the knee joint. The soleus also acts as a peripheral vascular pump, and is composed primarily of slow twitch type I fibres (O’Brien, 2005).

Distally, both the gastrocnemius and soleus muscles form an aponeurosis, from which a tendon originates. Once the soleus contributes fibres to the Achilles tendon, the tendon begins to rotate, allowing the gastrocnemius fibres to be positioned laterally, whilst the soleus fibres are positioned medially towards their insertion (van Sterkenburg & van Dijk, 2011). This 90-degree rotation produces stress within the tendon that is greatest 2 to 6cm above the calcaneal insertion, a common site for tendinopathy (Wijesekera et al., 2011). The Achilles tendon is not encased in a synovial sheath, but is surrounded by a paratenon consisting of single layer cells. This tissue is richly vascularised and is responsible for much of the blood supply to the tendon (Maffulli, Sharma, & Luscombe, 2004).

The osteotendinous junction ( enthesis) is comprised of a structurally continuous gradient of tissue types consisting of four areas; dense fibrous connective tissue, uncalcified fibrocartilage, mineralised fibrocartilage and bone. This specialised interface that transitions tendon to bone dissipates forces preventing collagen fibre bending, fraying, sheering and ultimately failure (Benjamin & McGonagle, 2001).

Two bursal ( fluid-filled) sacs are associated with the Achilles tendon insertion. These bursae cushion and support the tendon along with acting as a lubricant between the tendon as it passes over bone, and superficially between the tendon and the skin. Located anterior (deep) to the Achilles tendon is the retrocalcaneal (subtendinous) bursa, between the insertion of the tendon and the tuberosity of the posterior surface of the calcaneus. Whilst the superficial or subcutaneous bursa is located between the posterior (superficial) distal tendon and the skin (O’Brien, 2005).
The plantaris tendon is present in most, but not all patients. The plantaris muscle originates from the inferior aspect of the lateral supracondylar ridge of the femur and the posterolateral aspect of the knee joint capsule, superior and medial to the lateral head of gastrocnemius. After a small, variable sized muscle belly, it then quickly forms a long distal tendon that runs under the medial gastrocnemius, along the medial aspect of the Achilles tendon before having a variable insertion, either becoming confluent with the medial Achilles, inserting into the paratenon or having its own separate insertion on the medial side of the posterior surface of the calcaneus (Olewnik, Wysiadecki, Polguj, & Topol, 2017; Spina, 2007). The Achilles and plantaris tendons are collectively surrounded by a paratenon, which may or may not have a dividing membrane of paratenon between the two tendons (Spina, 2007). This vestigial structure is absent in 7-20% of the population with pathology of this tendon being an important differential diagnosis in achillodynia (Olewnik et al., 2017; Spina, 2007).

An accessory soleus muscle is also an anatomical variant that may be present in 0.5-6% of the population (Rubio, Franco, Montero, Ugarte, & Valero, 2015). When present this accessory muscle may insert directly on the anterior margin of the Achilles tendon or via a separate tendon on the calcaneus, anteromedial to the Achilles (Wijesekera et al., 2011). This muscle may present as a soft tissue mass bulging medial to the distal Achilles tendon and may be a source of extrinsic compression onto the Achilles tendon or neurovascular bundle (Rubio et al., 2015).

The presence of a plantaris tendon or an accessory soleus muscle may impact on the health of the Achilles tendon leading to pathological change. The identification of the presence and effect of these structures may have a significant impact on clinical management (Wijesekera et al., 2011).

2.4 Histology of the Normal Achilles Tendon

The basic composition of tendon is ground substance (or extracellular matrix), a viscous substance rich in proteoglycans, and cells interspersed between collagen
bundles (Khan, Cook, Bonar, Harcourt, & Astrom, 1999). The collagen provides the tendon with tensile strength; whilst the ground substance provides structural support for the collagen fibres, regulates the extracellular activity and is involved in the development, organisation and growth control of the tendon (Khan et al., 1999; Magnusson et al., 2010). Tendon cells (tenocytes), are flat tapered cells that are sparingly embedded within the extracellular matrix amongst the collagen fibrils (Figure 1). These are responsible for synthesising both ground substance and pro-collagen building blocks of protein (Ganderton et al., 2015).

**Figure 1:** Normal tendon histology (H&E stain, 100x). Demonstrating dense, clearly defined parallel and slightly wavy collagen bundles (pink). Between collagen bundles is a fairly even sparse distribution of cells (tenocytes) with thin wavy nuclei (stained blue). (Ganderton et al., 2015, p. 12)

The Achilles is formed primarily by type I collagen fibrils and these are held in place by small proteoglycan molecules, organised into parallel groups. Large diameter
fibrils are grouped with smaller sized fibrils to create tightly packed primary fascicles, which are then grouped into secondary fascicles and finally tertiary bundles. The connective tissue layer, the endotenon, surrounds the fascicles and contains the vascular, lymphatic and nerve supply that is peripherally covered by a fine, smooth, loose connective tissue sheath; the epitenon. A loose, areolar soft tissue layer, the paratenon, then covers the tendon externally, consisting of primarily type I and type III collagen fibrils, some elastic fibrils and an inner lining of synovial cells (Khan et al., 1999). The paratenon can be further divided into deep visceral (continuous with the epitenon) and parietal (peritenon) layers. The space between the visceral and parietal layers is called the mesotenon. This space carries and delivers the lymphatic, vascular and neural supply to the Achilles, with its layers allowing gliding movements to occur under the crural fascia; acting with the function of a synovial sheath (Paavola & Jarvinen, 2005). Although the paratenon acts a synovial sheath, it is less well organised. The paratenon does not have a complete epithelium, but does have fasciacyte cells that produce hyaluronan, a substance that exists where gliding surfaces are present and assists in the better management of mechanical stress (Stecco et al., 2014).

The tendon consists predominantly of extracellular tissue, hence has low metabolic requirements. This relatively bradytrophic characteristic enables the tendon to remain under tension for long periods without the risk of necrosis or ischemia. The Achilles receives its vascular supply from three sources; the perimyseal vessels at the musculotendinous junction, the periosteal vessels at the osteotendinous junction and the majority intrinsically from the vessels around the tendon within the paratenon (in particular the ventral mesotendon). These three sources form a capillary loop system to adequately supply the tendon (van Sterkenburg & van Dijk, 2011).

The neural supply to the Achilles is provided through three main sources; nerves from the attaching muscles derived from the tibial nerve, peritendinous nerve trunks from the surrounding paratenon and by small fasciculi from cutaneous
nerves, in particular the sural nerve (Paavola & Jarvinen, 2005). These nerve fibres follow the vascular channels, forming a rich plexus in the paratenon, before penetrating the epitenon and terminating as nerve endings on the tendon surface, with only a limited number actually penetrating the tendon (Wijesekera et al., 2011). The number of nerves and nerve endings around the Achilles is relatively low, leading to the tendon proper being relatively aneuronal (van Sterkenburg & van Dijk, 2011). Despite the scarcity of intratendinous nerves, pain receptors are abundant in the paratenon (Maffulli et al., 2004). Nerve endings of myelinated fibres act as mechanoreceptors to detect changes in pressure or tension, while unmyelinated nerve endings act as nociceptors, responding to and transmitting pain signals (Maffulli et al., 2004). Along with these nerve endings, both sympathetic and parasympathetic nerve fibres have also been identified in the Achilles tendon (Maffulli et al., 2004).

2.5 Biomechanics and Mechanotransduction of the Achilles Tendon

Actin and myosin are present in tenocytes, with tendons being stiff and resilient (Kader et al., 2002). These are ideal mechanical properties for the transmission of force from muscle to bone, with this high tensile strength allowing stretch up to 4% before structural damage (Kader et al., 2002). When an Achilles tendon is stretched more than 2%, the collagen fibres lose their wavy configuration, yet will return to normal if the strain placed on it remains at less than 4%. At strain levels greater than 8%, macroscopic rupture will occur (Jozsa & Kannus, 1997). These high tensile properties allow the Achilles tendon to withstand loads of 6.1 - 8.2 x bodyweight during running, undergoing tensile forces of up to 9kN (Jozsa & Kannus, 1997).

The muscles that form the Achilles tendon act mainly to plantarflex the ankle, with the gastrocnemius muscle also flexing the knee joint (Wijesekera et al., 2011). Although the Achilles tendon may be regarded as a single force transmitting structure, it remains unknown if stress and strain forces are homogeneously transmitted throughout the tendon (Magnusson et al., 2010). Tendon is a mechanosensitive tissue and as such undergoes the process of
mechanotransduction when exposed to load. This process describes the phenomenon whereby during tensile loading, fibroblasts and their cell nuclei that are located between fibrils within the intrafascicular space, undergo deformation, which is important in the mechanical signal transduction of the tissue (Magnusson et al., 2010). These fibroblasts (tenocytes) are responsible for the production of collagen and other matrix proteins that can induce a 2-3-fold increase in collagen formation that peaks around 24-hours after exercise and can remain elevated for up to 70-80 hours (Langberg, Skovgaard, Karamouzis, Bülow, & Kjaer, 1999). There is also a degradation of proteins, which increases as a result of exercise, earlier and to a greater extent than collagen synthesis (Langberg et al., 1999). Therefore, after cessation of exercise and up to 18-36 hours thereafter, there is a negative net balance in collagen levels (Figure 2). However, the balance becomes positive in terms of net collagen levels for up to 72-hours after exercise (Figure 2). From this finding, Magnusson et al. (2010) concluded that a net increase in collagen requires a restitution period, and without sufficient rest, a continuous loss of collagen is likely to occur. This may render the tendon vulnerable to overuse injuries and tendinopathy may result due to an imbalance between the synthesis and breakdown of collagen.
**Figure 2:** Schematic representation of collagen synthesis and degradation with regard to time (h = hours) (Magnusson et al., 2010, p. 264).

Within the literature, the true pathoetiología of tendinopathy is still not well understood, although tendon tensile overload is postulated as the most probable cause (Boesen et al., 2017). Some overload models conclude that tensile overload ‘micro-tears’ are the main causative factor, yet there is emerging evidence that a cell-led response to load is the primary driver in tendinopathy (Cook & Purdam, 2012). Almekinders, Weinhold, and Maffulli (2003) raised the possibility that compression, or a differential in tensile loads, may be a causative drive in the aetiology of Achilles tendon pathology. Almekinders et al. (2003) suggested that strain at the tendon insertion was not uniform and proposed that the joint side of the tendon (anterior aspect) was exposed to less tensile load (stress shielded) and may be subjected to compressive loads. Additionally, internal shear forces may be present due to the differential contribution of the gastrocnemius and soleus fibres to the tendon (Cook & Purdam, 2012). There is also emerging evidence to suggest that the plantaris tendon may also apply an external compressive force on the tendon that may initiate tendinopathy of either or both the Achilles and plantaris tendons (Alfredson, 2011; Olewnik et al., 2017). Finally, there is also evidence that a
potential source of external compression may arise from the fascial aponeurosis that extends from the superior peroneal retinaculum and encapsulates the posterior aspect of the tendon (Alfredson, 2017, Cook & Purdam, 2012).

2.6 Aetiology of Tendinopathy

Although tendinopathies have a multifactorial origin, the primary stimulus for degenerative change is mechanical loading (Cook & Purdam, 2009). Along with load, there are other contributing factors involved including a complex interaction of intrinsic and extrinsic factors that may be crucial in the initiation and propagation of injury (Cook & Purdam, 2009). Know intrinsic factors associated with mid-portion Achilles tendinopathy include age, genes, cytokine production, gender, biomechanics, body composition and the presence of systemic diseases (diabetes mellitus, systemic lupus erythematosus, chronic renal failure, rheumatoid arthritis, thyroid disorders, parathyroid disorders, collagen deficiencies and infectious diseases) (Cook & Purdam, 2009; Maffulli, Via, & Oliva, 2014; Rees, Wilson, & Wolman, 2006). Studies have also reported an increased incidence of Achilles tendinopathy in patients who possess the gene alpha 1 type V collagen (COL5A1), which encodes for a structural protein found in tendons (McGarvey, Singh, & Trevino, 1996; Mokone, Schwellnus, Noakes, & Collins, 2006).

The incidence of tendinopathy is lower in women than in men, with women showing lower levels of tendinopathy during pre-menopausal years, but an increase after menopause (Bryant et al., 2008). Post-menopausal estrogen deficiency seems to down-regulate collagen turnover and decrease the elastic properties of tendons; with increasing age also having an effect on tendon metabolism and healing (Maffulli et al., 2014). Connective tissue ageing is associated with compromised tissue function, increased susceptibility to injury and reduced healing capacity (Maffulli et al., 2014). This occurs due to a decrease in overall cellularity and an increase in collagen cross-linking with advanced glycation end products (AGEs) that accumulate with age (Maffulli et al., 2014). The ageing tendon loses its elastic properties, causing the muscle to work more. These changes in stress distribution
alter the internal mechanics of the musculo-tendinous unit, and along with the subsequent tendon changes, cause an increase in the risk of the development of tendinopathy (Magnan, Bondi, Pierantoni, & Samaila, 2014). Increased AGE formation is also associated with diabetes mellitus and has been shown to affect the interactions between collagen fibres, extracellular matrix protein and tenocytes (Gautieri, Redaelli, Buehler, & Vesentini, 2014). This results in the diabetic tendon having both reduced healing capacity and altered mechanical properties (Gautieri et al., 2014).

Obesity has been shown to be associated with an increased risk in the development of tendinopathy, yet the physiopathology of this relationship is yet to be understood. In obese patients, the deforming forces on rear foot position are increased and may lead to overuse of the Achilles tendon (Magnan et al., 2014). Animal studies on obesity have observed histologic changes in the extracellular matrix with lipid drops accumulating within the matrix along with disorganised collagen fibrils (Biancalana Veloso, & Gomes, 2010). Additionally, obesity is frequently associated with other diseases such as diabetes mellitus and insulin resistance, both of which are known to be associated with poor tendon health (Maffulli et al., 2014). These factors may play a role in regeneration and reduce the tendon’s ability to heal (Maffulli et al., 2014).

The common potential extrinsic factors associated with tendinopathy development include environmental factors (equipment, footwear, working environment), changes in training pattern, poor technique and previous injury (Rees et al., 2006). Additionally, those patients with fluoroquinolone antibiotic usage have a higher incidence rate of tendinopathies as the fluoroquinolone ciprofloxacin, causes enhanced interleukin-1β-mediated matrix metalloproteinase 3 (MMP3) release, which inhibits tenocyte proliferation and reduces collagen and matrix synthesis (Maffulli et al., 2014).
2.7 Pathophysiology of Achilles Tendinopathy

Maffulli et al. (1998) first proposed the term Achilles “tendinopathy” for the clinical syndrome characterised by a combination of tendon pain, localised tenderness and swelling that impaired performance. This resulting in a tendon that is less capable of sustaining repeated tensile load. An excess in total load volume or too much training that utilises the elastic function of the Achilles tendon are the key elements that induce tendon overload and are important in the onset of tendon degeneration (Barker-Davies et al., 2017; Cook & Purdam, 2012).

There is no widely accepted criteria to determine whether an overuse tendon injury is acute or chronic, however Hawary, Stanish, and Curwin (1997) suggest that if the symptoms have been experienced for less than 2 weeks, the Achilles disorder should be classified as acute tendinopathy; if the symptoms have been 2-6 weeks, it should be classified as sub-acute tendinopathy; and if the symptoms have persisted more than 6 weeks, the term chronic tendinopathy should be used. Acute, sub-acute and chronic tendon changes are merely descriptive terms, only referring to the duration of symptoms and do not represent the underlying pathology that may be present.

The underlying cause of Achilles tendinopathy is multifactorial and as a result it can be recalcitrant to treatment (Maffulli et al., 2004). Epidemiological observations clearly show tendon overload being the main pathological stimulus of Achilles tendinopathy, yet the causative drive remains elusive (Abate et al., 2009; Kader et al., 2002). Although traditionally considered an inflammatory condition, histopathological studies of mid-portion Achilles tendinopathy have shown degenerative changes within the tendon due to a failed healing response (Cook & Purdam, 2009). These histological evaluations have been performed by assessing Achilles tendon biopsies, intratendinous microdialysis, and contemporary molecular biology techniques (cDNA-arrays, real-time quantitative PCR) of appropriately prepared biopsy tissue, with all analysis techniques failing to show evidence of prostaglandin-mediated inflammation (Alfredson & Cook, 2007). However, it has been shown that there is often a combination of tendon pathologies occurring,
including hypoxic, hyaline, mucoid, fibrinoid and lipoid degeneration (Cook & Khan, 2008). A review of histopathological studies of symptomatic Achilles tendons by Khan et al. (1999) reported that the degeneration involved is usually ‘mucoid’ or ‘lipoid’ in nature. Mucoid degeneration often results from overuse and causes the affected region to soften, lose its normal glistening white appearance and become grey or brown. Whilst lipoid degeneration refers to an abnormal accumulation of lipid within the tendon tissue, along with the presence of abnormal collagen fibres and a loss of the classical hierarchical tendon structure, which is primarily a product of aging (Khan et al., 1999).

Using light microscopy, similar studies by Astrom and Raising (1995) and Khan et al. (1999) demonstrated that symptomatic tendons reveal an obvious change in collagen fibre structure. Collagen fibres that are thinner than normal were shown to be present along with the loss of the normal parallel bundles; with collagen being more diffuse and bundles coalesced (Astrom & Raising, 1995; Khan et al., 1999). Both authors noted the presence of large mucoid patches and vacuoles between fibres, along with an increase in Alcian-blue-staining ground substance (Figure 3). It was also noted that neovascularisation and an increase in the number of cells with rounded nuclei were present (Figure 3). Within these symptomatic Achilles tendons, the increase in vascularity resulted in blood vessels being randomly orientated, sometimes at right angles to the collagen fibres, yet inflammatory lesions and granulation tissue were infrequently found (Astrom & Raising, 1995; Khan et al., 1999).
Figure 3: Degenerative tendon histopathology (H&E stain, 100x). Islands of degenerative tendon (wavy irregular collagen-pink; multiple cells – blue) are interspersed between other stages of pathology, including vacuoles between fibres and normal tendon. (Ganderton et al., 2015, p. 13)

The different types of degeneration present often overlap and cannot always be precisely differentiated, with some histopathological studies showing up to 90% of symptomatic tendons have differing types of degeneration occurring within the same tendon (Syha et al., 2013). Whether the underlying process is mucoid, lipoid, hypoxic, hyaline, or fibrinoid within the tendinopathic Achilles; this degenerative process causes general degeneration and disorganisation of collagen fibres, increased vascularisation and irregular cellularity, with a lack of classical inflammatory cells (Cook & Khan, 2008).
There are several main theories on the causes of tendon degeneration. Mechanical, vascular, thermal, neural and cellular driven theories have all been proposed. The supporting arguments and basis to each of these theories will now be discussed.

The mechanical theory is a collagen-driven model of tendinopathy. This theory implies that damage to the tendon can occur even if it is stressed within its physiological limits, due to cumulative microtrauma being applied and not leaving enough time for repair (Kader et al., 2002). This leads to a tendon that is unable to endure further tension and stress, causing its structure to disrupt microscopically with inflammation, oedema and pain resulting (Paavola et al., 2002). There are two main thought processes behind the mechanical theory for tendinopathy. In the first proposed process, Jozsa and Kannus (1997) claim that mechanical tendon injuries are derived from repetitive strain of the tendon resulting in an overuse injury where the ability of the tenoblasts and tenocytes to repair the fibre damage is exceeded. The second, alternative hypothesis within the mechanical theory for the causation of mid-portion tendinopathy is that this microtrauma may arise from non-uniform stress within the Achilles tendon due to different force contributions from the gastrocnemius and soleus units. This theoretically leads to abnormal load concentrations within the tendon and frictional forces within the fibrils (Arndt Komi, Bruggemann, & Lukkariniemi, 1998). This theory of tendon overload may lead to collagen fibres excessively sliding past one-another, causing damage to their crosslinks and tissue denaturation. The cumulative micro-trauma postulated in this theory then not only causes weakening of tendon cross-linking, but also affects the non-collagenous matrix and the vascular elements of the tendon; with this tissue injury leading to the formation of tendinopathy (Abate et al., 2009).

Whichever subgroup of mechanical causative theory is subscribed to, they both note that the majority of collagen in healthy tendons is type I in nature, whilst there is significantly less type I and more type III collagen in the degenerative tendon (Malliaras et al., 2010). Since type III collagen is a major collagen type synthesised during tendon healing after injury, it would appear that tendon degeneration is
perhaps the result of an incomplete repair process (Paavola et al., 2002). This
theory gives an explanation on how chronic repetitive damage to a tendon
accumulates over time and why tendinopathy is degenerative rather than
inflammatory in nature (Paavola et al., 2002). However, this mechanical theory does
not adequately explain why exercise can improve diseased tendons, why certain
tendons are more susceptible than others or why tendinopathy and ruptures can
occur in patients of a sedentary nature (Rees et al., 2006).

Another postulated theory involves hyperthermia. As the tendon is submitted to
strenuous exercise, very high temperatures develop, with failure to control this
exercise-induced hyperthermia leading to cell apoptosis due to a thermal insult
(Rees et al., 2006). Studies by Li et al. (2004) have shown that peaks of 43-45°C can
be reached inside the tendon and that temperatures above 42.5°C can result in
fibroblast death. Therefore, there is the possibility that exercise-induced
hyperthermia may be detrimental to tendon cells and be a component responsible
for the formation of tendinopathy. Yet this theory doesn’t explain why exercise can
improve the health of the tendon and why many people develop tendinopathy when
exercising at levels below that capable of inducing tissue hyperthermia (Rees et al.,
2006).

The vascular theory suggests that tendons, or parts of tendons, have poor blood
supply and are prone to vascular insufficiency (Rees et al., 2006). This theory
postulates that if tendons with a poor blood supply undergo heavy loading or
functional overload then a vascular ischemic injury may result. This offers an
explanation as to why the mid-portion of the Achilles tendon appears to be the most
susceptible to degenerative change due to its watershed vascular supply (Alfredson,
2005). This theory still doesn’t explain why loading exercise can structurally
improve tendons and there remains no convincing evidence of vascular compromise
in healthy individuals (Rees et al., 2006). The vascular theory was also contradicted
by Fukuda, Hamada, and Yamanaka (1990) who noticed that within partial
thickness tears of rotator cuff tendons, the critical zone (watershed area)
demonstrated relative hyper-perfusion when compared with the proximal stump and a hyperaemic response existed at the edge of the tear.

The neural theory has been formulated from a number of observations on the neural supply of tendons and the neural changes associated with tendinopathy. Observations contributing to the neural theory include tissue hypoxia and consequent changes in tendon induced free radicles due to ischemia-reperfusion injury and exercise induced hyperthermia (Wilson & Goodship, 1994). There is also a close relationship in tendons between nerve cell endings and mast cells, raising the possibility of neurally mediated mast cell degranulation and release of neural mediators (Rees et al., 2006). Other studies have found the neuropeptide, substance P nerves and Neurokinin-1 receptors in the vascular wall with calcitonin gene related peptide nerves close to the vascular wall; all of which have been implicated as pro-inflammatory mediators (Alfredson et al., 2001). Finally, glutamate, a common excitatory neurotransmitter and modulator of pain, is found in high levels within painful tendons, but not in pain free tendons (Alfredson et al., 2001). All of these observations suggest that tendons receive nociceptive innervation and alterations to neural homeostasis may lead to tendon pathology. However, this theory provides no insight as to why not all pathological tendons are painful.

The cellular model of tendinopathy takes into account many factors from the above theories to describe this failed healing response and is currently the preferred theory for the pathogenesis of tendinopathy. The cellular model places emphasis on the tenocyte being primarily responsible for maintaining the extracellular matrix in response to its environment (Cook, Rio, Purdam, & Docking, 2016). Healthy tendons are ‘plastic’ structures that are capable of adapting to their load requirements and biochemical environment by altering structure and changing mechanical properties (Cook et al., 2016; Killian, Cavinatto, Galatz, & Thomopoulos, 2012). Tendon cells respond to mechanical loading with biochemical signals, resulting in a cascade of responses (cell activation, proteoglycan expression and changes within collagen type) which are important for tissue development, homeostasis, healing and
degeneration (Killian et al., 2012). These biochemical signals, cytokines, enzymes and growth factors maintain tendon homeostasis by either creating a catabolic environment (leading to decreased tendon mechanical properties) or an anabolic environment (leading to an increase in these mechanical properties) within the tendon (Killian et al., 2012).

Excess training volume or too much training utilising the elastic function of tendons are the key aspects to inducing tendon overload (Cook & Purdam, 2012). When load requirements become too great for the tendon to adequately adapt, it then becomes pathological (Cook & Purdam, 2009). The cellular driven model of tendinopathy has recently been described as a continuum, with stages of reactive tendinopathy, tendon dysrepair and degenerative tendinopathy (Cook & Purdam, 2009). This model explains the tendons positive response to appropriate loading exercises and the detrimental effects to the tendon as a result of chronic overload and compressive loads; along with having successful correlations to clinical findings (Cook & Purdam, 2009). Further elaboration of the cellular driven model of tendinopathy and its relation to sonographic presentation is described later in this literature review under the section ‘2.10 tendinopathy continuum and sonographic presentation’.

Despite the fact that there are various models proposed for the pathogenesis of tendinopathy, there are specific cellular responses that occur throughout this process. Given the low metabolic rate of tendons, the optimal conditions for healing overloaded tendons are adequate recovery time, along with suitable metabolism and blood supply. When these conditions are not met, the healing mechanisms fail and tendinopathy prevails (Abate et al., 2009). It is well known that chronic Achilles tendinopathy is difficult to treat with the source of pain and the background to the pain mechanisms associated with mid-portion Achilles tendinopathy yet to be fully understood (van Sterkenburg & van Dijk, 2011).
Although tendinopathy is a degenerative process with a lack of classical inflammatory cells, there are however signs of neurogenic inflammation due to the presence of neuropeptides such as substance P and calcitonin gene-related peptide within the tendinopathic tendon (Scott, Khan, Roberts, Cook, & Duronio, 2004). These biochemical mediators have been implicated as pro-inflammatory mediators and are significantly expressed in chronic tendinopathy (Rees, Stride, & Scott, 2014). These substances not only exert a proliferative effect on tenocytes, with substance P also increasing the ratio of type III: type I collagen mRNA, which may contribute to the formation of smaller collagen fibres seen in tendinopathic tendons (Fong et al., 2013). Substance P also leads tenocytes to adopt a myofibroblast-like phenotype, with increased smooth muscle Actin expression and increased contractile activity. Therefore, the more proliferative and active phenotype of tenocyte observed in chronic tendinopathy may result from the local production of inflammatory mediators (Fong et al., 2013).

The molecule vascular endothelial growth factor (VGEF) is prominent within tendinopathic tendons (Rees et al., 2014). This is produced by the large quantities of macrophages and is thought to be responsible for the formation of neovascularity and neoinnervation (Rees et al., 2014). Angiogenesis is believed to be one of the key components in the pathogenesis of tendinopathy (Vasta et al., 2016). Therefore, chronic tendinopathy should be regarded as a process of degradation, which appears to involve many aspects of the chronic injury-repair response (Rees et al., 2014).

In summary, the underlying causative aetiology for Achilles tendinopathy is multifactorial, with current theories suggesting that this degenerative process is primarily driven by a cellular response to tendon overload (Abate et al., 2009; Cook & Purdam, 2009; Kader et al., 2002; Maffulli et al., 2004). The changes that occur to the tendon during this pathological process are readily seen using various medical imaging modalities (Scott et al., 2013). Sonographic examinations have become routine in clinical practice for the imaging of pathological tendons and should be the
first imaging modality of choice due to being inexpensive, readily available, clearly
defining the pathology at hand and can be used for the evaluation of therapy
(Davies, Baudouin, King, & Perry, 1991; Risch et al., 2016). To date however, no
standardised, all-inclusive sonographic evaluation method exists to assess both
tendon structure and associated complications of tendinopathy.

2.8 Diagnosis and Imaging

This literature review has found that there is no single, specific test for Achilles
tendinopathy. The diagnosis is primarily performed clinically; involving a patient
history of tendon pain and a physical examination demonstrating focal thickening.
Fredberg et al. (2004) reported a high level of misdiagnosis of Achilles tendinopathy
and the role of palpation has been questioned, as it is highly sensitive (84%) in
reproducing symptoms, yet is non-specific in accurately determining the
pathological process involved (73%) (Hutchison et al., 2013). If a clinical diagnosis
is not clear, diagnostic imaging may reveal the pathology present within the tendon.
Imaging techniques involving plain radiography, ultrasound and magnetic
resonance imaging (MRI) are used in the clinical setting to confirm the presence and
location of intratendinous tendon pathology, identify other structural changes and
associated findings, and to act as an adjunct to the clinical picture. Historically, soft
tissue radiography provided useful information on the involved Achilles tendon, but
this technique has been superseded by other imaging techniques (Kader et al.,
2002). Although plain radiography is no longer the imaging modality of choice, it
often still plays a role in diagnosing associated or incidental bony abnormalities.
Nowadays the imaging of tendons with MRI and ultrasound is commonly used in the
clinical setting to assist in the diagnosis of tendinopathy, monitor the efficiency of
treatments and assess the risk of developing symptoms (Chang & Millar, 2009; Cook
& Purdam 2009; Scott et al., 2013). However, while imaging shows the presence and
extent of structural change within tendons, this information requires clinical
interpretation of the images and correlation with pain and aggravating factors to
make an accurate diagnosis, as there is often a disconnect between structure and
pain (Docking, Ooi, & Connell, 2015).
Magnetic resonance imaging has excellent soft tissue contrast detail and multi-planar imaging capabilities with excellent reproducibility (Bleakney & White, 2005). Despite this benefit, MRI is costly and is limited in its availability and accessibility to the general public (Docking et al., 2015). Recent advances in ultrasound system technologies and improvements in the sensitivity of Doppler imaging have increased the utility and accessibility of ultrasound imaging. Ultrasound imaging can focus on an area of pain or clinical suspicion of pathology, with rapid correlation to clinical palpation, whereas MRI provides a global assessment of the area of concern (Docking et al., 2015). Additionally, with modern high-frequency transducers, ultrasound can achieve a higher spatial resolution than routine MRI (Sunding et al., 2016).

Ultrasound has increasingly been used to assess pathological changes seen within tendinopathic tendons, including tendon thickening and changes to tendon echogenicity (Archambault et al., 1998). In addition to grey-scale changes, Doppler ultrasound can assess the degree of neovascularity within and around tendons (Ohberg et al., 2001). Ultrasound has risen in popularity amongst musculoskeletal practitioners as it is quick, minimally invasive and affordable (Scott et al., 2013). Ultrasound imaging of tendons is used in the clinical setting to assist in the diagnosis of tendinopathy, monitor the efficiency of treatments and assess the risk of developing symptoms (McAuliffe, McCreesh, Culloty, Purtill, & O'Sullivan, 2016; Scott et al., 2013).

The examination of validity and specificity of all imaging modalities has shown variable results (Docking et al., 2015). Due to ethical issues associated with collecting tissues from appropriate controls, the majority of studies have compared the various imaging modalities to clinical diagnosis as the gold standard form of assessment. There exist only a few studies comparing imaging assessment to surgical or histological findings (Docking et al., 2015). One such study by Astrom et al. (1996) found that ultrasound had excellent accuracy when correlated with surgical findings in approximately 80% of cases. However, there has been a
limitation in conventional imaging modalities of all types in differentiating between tendinosis and partial tears, with the diagnosis often made by clinical history (sudden versus slow onset of symptoms) (Paavola, Paakkala, Kannus, & Jarvinen, 1998). Additionally, there is the complication of identifying the presence of asymptomatic imaging findings (Paavola et al., 1998). Hence imaging in association with clinical assessment and thorough history taking is paramount in making the correct diagnosis.

Although abnormalities detected by imaging are likely to be associated with pain and symptoms, it is possible that these morphological changes are painless and that the symptoms may be arising from another source, hence clinical correlation with imaging has been advocated (Alfredson & Cook, 2007). Ultrasound has been shown to be accurate and sensitive in the diagnosis of clinical Achilles tendinopathy with high levels of reproducibility and reliability, independent of the examiner’s experience (Khan et al., 2003; Risch et al., 2016). Khan et al. (2003) also noted that ultrasound, in trained hands, is more accurate than MRI and is able to give a more specific diagnosis due to superior spatial resolution. Fine structures like secondary fibre bundles of a tendon can be depicted on ultrasound, but not on routine MRI (Sunding et al., 2016). With ultrasound better assessing the internal architecture of the tendon than MRI, it also provides the additional benefit of dynamic imaging; allowing the region of concern to undergo active and passive movements that may provide further information and aid in diagnosis (Docking et al., 2015). Ultrasound is advantageous as it can be used to localise the area of interest and allow for palpation with the transducer, allowing for correlation of imaging findings with clinical findings. Along with the dynamic nature and correlation abilities of ultrasound, it is also useful to facilitate the accurate guidance of needle-based interventional procedures (Wijesekera et al., 2011).

Ultrasound has been used diagnostically in tendinopathy since its inception into musculoskeletal imaging in the eighties, with the majority of this research being focused on the Achilles and patellar tendons. This relationship of diagnostic
ultrasound and tendinopathy has formed because tendons, being superficial structures, are depicted in high resolution on ultrasound imaging as they are well suited to today’s modern, high-frequency transducers (10-21MHz). On the negative side of ultrasound imaging, there is a limited field of view with linear transducers and a decrease in penetration when using high frequencies (Sunding et al., 2016). This can make it difficult to survey important adjacent structures and assess structures that lay at depth. These factors however are negligible when imaging superficial tendons such as the Achilles because of the tendons’ location and the ease of access to adjacent structures. Another drawback often mentioned is the dependence on the technical skills and experience of the operator, along with a long learning curve to become proficient, which is often time consuming (Sunding et al., 2016). Although the difficulties of operator experience and technical proficiency are difficult to overcome; it is hoped that the development and use of a standardised, semi-quantitative assessment tool will result in improved reliability and reduced inter-operator variability for the sonographic assessment of the Achilles tendon.

Sonographically, the normal healthy Achilles tendon demonstrates an echogenic pattern of parallel fibrillar lines representing tendon fascicles in the longitudinal plane and an echogenic ovoid shape in the transverse plane. Whereas the tendinopathic tendon exhibits a spindle shaped/fusiform thickening of the tendon with ill-defined hypoechoic areas within the tendon substance and may or may not demonstrate increased vascularity on Doppler imaging (Wijesekera et al., 2011).

Colour and power Doppler have both been used to investigate the presence and role of neovascularity within tendons over the last 20 years, with normal tendons being relatively avascular (Yang et al., 2010). Real-time colour Doppler imaging utilises two separate ultrasound beams to image tissue structure (grey-scale) and blood flow (Doppler) information simultaneously with the resultant Doppler information superimposed on the grey-scale image. Moving reflectors within blood vessels, mainly red blood cells, create a frequency shift in the returning Doppler ultrasound signal that is analysed via autocorrelation to produce colour flow images. In colour
Doppler imaging, both the frequency shift and the phase from the autocorrelation are analysed to form the image, giving information on both flow direction and frequency shift. This frequency shift can be interpreted as blood flow velocity. Power Doppler differs from colour Doppler in that calculation of the flow velocity and flow direction are not performed, in place of this, the Doppler signal power (related to the signal amplitude) is obtained and displayed. These two different forms of Doppler have different strengths and weaknesses. Power Doppler has improved flow sensitivity in the detection of small vessels over colour and is less susceptible to noise artefact, however it has the disadvantage of not giving information on flow direction or velocity (Yang et al., 2010). In the setting of tendon assessment, direction and velocity criteria are not required, with power Doppler being preferential over colour Doppler as it can demonstrate a greater number and extent of neovessels, as well as a more detailed visualisation of vessel progression (Risch et al., 2016). Settings should be optimised for low blood-flow to improve the sensitivity to visualisation of intra-tendinous vessels, such as reducing wall filters, using high Doppler frequency to improve spatial resolution, having low pulse repetition frequency (PRF) and adequate colour gain (Risch et al., 2016; Yang et al., 2010). Also, it is assumed that with evolving technology, the general sensitivity of Doppler ultrasound will increase; therefore, the most current ultrasound systems should be used (Risch et al., 2016).

Besides conventional grey-scale and Doppler ultrasound, there are other categories of ultrasound imaging that are used in the clinical and research setting including sonoelasticity and ultrasound tissue characterisation. Sonoelasticity is an ultrasound-based method that provides evaluation of the mechanical properties of tendons by estimating the tissue elasticity or ‘hardness’. Studies have shown that healthy tendons are ‘hard’ whilst diseased tendons are ‘soft’ (Ooi, Schneider, Malliaras, Counsel, & Connell, 2015). Both axial-strain and shear-wave elastography technologies exist, with both techniques identifying pathological areas within the tendon and displaying these in the softer tissue spectrum (McCreesh & Lewis, 2013). Axial-strain sonoelastography requires manual compression and displays the
subjective distribution of strain data on an elastogram caused by tissue compression, whereas shear-wave elastography provides a more objective quantitative measure of the intrinsic tissue elasticity using a focussed acoustic push-pulse (Ooi, Malliaras, Schneider, & Connell, 2014). De Zordo et al. (2009) showed that sonoelastography is highly sensitive and specific in identifying regions of pathology in common extensor tendons of the elbow in patients with lateral epicondylalgia. Additionally, Drakonaki, Allen, and Wilson (2009) have shown that elastography is a feasible and reliable method to objectively evaluate the Achilles tendon. This work was further supported by De Zordo et al. (2010) who found that tendon softening observed using elastography was comparable to a clinical diagnosis of symptomatic Achilles tendinopathy. The elastography and grey-scale sonographic findings showed excellent levels of agreement (97% and 93% respectively) (De Zordo et al., 2010). With Klauser et al. (2013) finding similar levels of agreement between strain elastography and grey-scale assessment, with the addition of positive histological confirmation on 13 cadaveric Achilles tendons. Ooi et al. (2015) assessed the Achilles tendons of marathon runners finding similar levels of agreement between strain elastography and grey-scale ultrasound as well as Doppler assessment. These findings suggest that elastography is sensitive to small strain alterations in early Achilles tendon degeneration and may have the ability to identify early pathological changes before they become clinically apparent (Ooi et al. 2015).

It is recommended however, that elastography should not be used as a stand-alone imaging modality, but should be used in conjunction with, and as a supplementary tool to grey-scale and Doppler assessment (Ooi et al., 2015). As this technology becomes more widely available and routinely used, the addition of sonoelastography to existing morphological ultrasound assessments may further enhance the sensitivity and accuracy for diagnosis and categorisation of tendinopathy.
Recently, ultrasonic tissue characterisation (UTC) has been introduced as a reliable method for the quantification of tendon structure in the research literature (van Schie et al., 2010). This method uses conventional ultrasound to semi-quantify tendon structure (Bedi et al., 2016). A 3-dimensional stability reconstruction of the grey-scale echo pattern is rendered from continuous cross-sectional images of the tendon. From this, the stability of pixel brightness over 25 consecutive transverse images (4.8mm) is calculated and categorised into 4 echo types dependant on the degree of structural homogenicity (Bedi et al., 2016). This mechanism was initially evaluated with equine tendons and showed excellent correlation with histopathology changes. This technique on human tendons has been shown to have good intra and inter-observer reliability, and in a small study on chronic Achilles tendinopathy, it has been shown to discriminate against symptomatic and asymptomatic tendons (van Schie et al., 2010). This imaging technique may be useful in the research setting as a computer quantifies the grey-scale ultrasound signal of tendon echogenicity into one of four echo patterns. However, the setback of this technique in clinical practice is that it requires a specific UTC unit to be used that produces a relatively poor grey scale assessment of the tendon and reduces the dynamic nature of musculoskeletal ultrasound. The purchase and usage of a specific piece of equipment specifically for Achilles and patellar tendon assessment is unlikely to have widespread implementation throughout the medical imaging community, and as such, UTC has had a limited utilisation within the clinical setting, remaining only a novel research tool.

A criticism of all conventional imaging modalities is their reliance on subjective interpretation of images, with research often being limited to classifying tendons as either normal or abnormal, or to use a subjective rating based pathological features and their perceived severity. Objective quantification of tendon structure has been limited to measurements relating to tendon dimensions (diameter or cross-sectional area) and the percentage of the pathological area within the normal tendon (Docking et al., 2015). Grey-scale and Doppler ultrasound is the norm in current imaging practices with excellent accuracy at detecting structural abnormalities.
within tendinopathic tendons (Paavola et al., 1998). Therefore, protocols for standard ultrasound assessment covering all facets of tendinopathy with numeric quantification will have a greater and more widespread applicability.

Ultrasound traditionally has been a radiologist’s domain, however recently its affordability and accessibility has expanded with an increase in usage by rheumatologists, sports medicine physicians and physiotherapists (Yim & Corrado, 2012). Since tendinopathy is associated with latent symptoms developed from aggravating activities, the inclusion of ultrasound findings to a thorough clinical examination is advantageous in correctly managing tendon pathology (McCreesh & Lewis, 2013). There is the potential to enhance diagnosis with clinicians performing their own ultrasound examinations and correlating findings with their clinical diagnosis. Imaging is useful as an adjunct to the clinical picture as it shows the presence and extent of structural changes, yet needs clinical context due to the disconnect between structure and pain. However, caution is advised, with the potential for misinterpretation of imaging findings in this setting due to the experience of the operator. This may potentially confuse the clinical diagnosis and lead to poor outcomes due to technical and operator insufficiencies. Adequate training and a standardised assessment technique will reduce the risk of these potential barriers to reaching an accurate diagnosis.

2.9  Sonographic Presentation of Achilles Tendinopathy
There are distinct changes seen in the tendon tissue during the tendinopathy process when viewed using grey-scale ultrasound. Diffuse tendon thickening and an associated reduction in echogenicity have been reported, along with focal hypoechoic regions of change (Malliaras, Cook, Ptasznik, & Thomas, 2006).

2.9.1  Tendon changes
Diffusely abnormal tendons present with an overall reduction in echogenicity and a loss of the normal fascicular pattern. This presentation may be an indication of tendon overload, leading to a proliferative cellular response within the tissue, with a
shift in proteoglycan content from small leucine-rich proteoglycans (e.g. decorin) to larger hydrophilic proteoglycans (e.g. aggrecan) (Corps et al., 2006). Associated with this is an increase in bound water and ground substance accumulation, whist the tendon still maintains a healthy collagen matrix (Cook & Purdam, 2009). It has been proposed by Malliaras et al. (2010) that an increase in ground substance and bound water molecules cause the tendon to appear hypoechoic on ultrasound, as ground substance is less echogenic than collagen. However, human biopsy studies are required to confirm the association between this proliferative response and the changes seen sonographically, as the literature to date has only been performed on animal models (Malliaras et al., 2010). Tendons may then continue to thicken and become focally abnormal due to continual overload, progressing to focal areas of degenerative tendinopathy. These focal areas of reduced echogenicity and fascicle disorganisation represent continued ground substance accumulation, breakdown of the collagen matrix and neurovascular ingrowth (Cook & Purdam, 2009). As the collagen fascicles change from type I to type III, these larger fibres with their haphazard arrangement cause the ultrasound beam to generate multiple reflections and shadowing. This results in hypoechogenicity and focal hypoechoic areas on ultrasound imaging due to the lack of parallel-aligned fibres and the subsequent lack of uniform reflection from the ultrasound beam (Docking et al., 2015).

Pathological tendons have been shown to increase their anterior-posterior diameter. This finding has been reflected in work by Richards, Win, and Jones (2005) who found sonographically abnormal Achilles tendons to have an anterior-posterior thickness greater than 5.9mm and that the average tendinopathic tendon was 11.1mm in thickness. This increase in size is likely due to the accumulation of ground substance and neurovascular ingrowth associated with tendon pathology. Richards et al. (2005) also found that Doppler ultrasound signal was present only in tendons greater than 6.5mm in thickness, indicating that larger tendons may contain more abnormal vessels. This was further supported by Malliaras and Cook (2011) who demonstrated an ordinal relationship between symptoms and grey-scale ultrasound changes along with increasing anterior-posterior tendon thickness.
The changes seen within a tendinopathic tendon tend to follow an expected pattern. Malliaras et al. (2010) demonstrated that patellar tendons follow a predictable sequence, developing diffuse changes in echogenicity (associated with reactive tendinopathy) before progressing to focal areas of pathology (degenerative tendinopathy). Additionally, there is the development of diffuse changes prior to the return to a normal sonographic appearance in tendons with previously identified focal hypoechoic lesions (Malliaras et al., 2010). This supports the pathology continuum model for tendinopathy and demonstrates how sonographic imaging can reflect the status of the tendon within this continuum, however, no studies have yet attempted to reproduce these results in the Achilles tendon.

Ultrasound assessment of both tendon thickness and echogenicity has been shown to be sensitive to change; with a study among athletes showing that changes in both can be identified within short time periods (Malliaras et al., 2010). In a later study, Malliaras and Cook (2011) demonstrated that patellar tendons can change up to 3mm in anterior-posterior thickness within only one month and that focal changes within tendons can develop and be seen sonographically within this timeframe.

### 2.9.2 Mid-portion Tendinopathy

The Achilles mid-portion is classified as the portion of tendon between 2 and 6cm from the calcaneal insertion, whilst the insertional Achilles is classified as the portion of tendon less than 2cm from the calcaneus (Clain & Baxter, 1992). The mid-portion of the Achilles has been shown to contain distinct fascicles from the deriving musculature that remain separate from one another (Szaro, Witkowski, Smigielski, Krajewski, & Ciszek, 2009). Within the mid-belly of the Achilles, the medial gastrocnemius fascicles primarily form the posterolateral as well as part of the posteromedial Achilles, the lateral gastrocnemius fascicles form the anterolateral and a portion of the anteromedial Achilles, and the soleus fascicles form the central and medial part of the tendon (Szaro et al., 2009). This rotation and fascicle separation has been shown in cadaveric studies along with being readily identifiable during sonographic assessment (Counsel, Comin, Davenport, & Connell, 2015).
When visualised with ultrasound, this fascicular involvement pattern in mid-portion Achilles tendinopathy has been shown to most commonly involve fibres from the medial head of gastrocnemius and/or soleus (Counsel et al., 2015).

Mid-portion Achilles tendinopathy is a syndrome characterised by pain, swelling and impaired performance (Maffulli et al., 1998). The swelling of this mid-portion disease can be either diffuse or focal, and typically nodular in nature. This involves pathology of the tendon proper and may or may not involve tendinosis (a failed healing response of tendon degeneration without histological intratendinous inflammation) resulting in either focal or diffuse hypoechoic changes to the tendon on ultrasound imaging (van Dijk et al., 2011). The mid-portion of the Achilles tendon has been shown to be statistically thicker in anterior-posterior diameter in chronically symptomatic tendons than their asymptomatic counterparts (Leung & Griffith, 2008).

2.9.3 Enthesis Pathology

The insertion of the tendon into bone or osteotendinous junction is referred to as the ‘enthesis’ and involves a gradual transition from tendon to cartilage to lamellar bone. Pathology of where the Achilles tendon inserts into the posterior aspect of the calcaneus or ‘Achilles enthesopathy’ can be considered a separate condition to that of mid-portion tendinopathy (Cook & Purdam, 2012). The enthesis is structurally and histologically different from the tendon proper. There are large differences between the mechanical properties of tendon and bone; hence large stress concentrations arise here (Killian et al., 2012). The enthesis has four transitional zones from bone to tendon, ranging from mineralised to unmineralised fibrocartilage with several changes in collagen type and proteoglycans (Benjamin & McGonagle, 2001). This layering allows the enthesis to bear all types of load and evenly distribute stress forces. Along with these different layers of composition, the enthesis organ also distributes stress by utilising a shallow attachment angle at the tendon insertion as well as via the interdigitation of transitional tissue with bone (Killian et al., 2012). The enthesis is richly innervated with C, A-delta and substance
P sensory and nociceptive nerve fibres, whilst being relatively avascular as vessels from the bone can reach, but not breach, the bone-tendon interface or ‘tide mark’ (Benjamin & McGonagle, 2001). The fibrocartilage is reactive to compressive and sheer forces, with pathology of the enthesis being termed enthesopathy and is similar to that of the tendon with fatty, hyaline, cystic, calcific or mucoid degeneration able to occur (Killian et al., 2012).

Enthesopathy, demonstrated sonographically, can display a spectrum of pathology, ranging from thickening of the hypoechoic unmineralised fibrocartilage to irregularity of the echogenic bone margin with demonstrable enthesophytes (bony spurs) or subcortical cysts (Syha et al., 2013). Since these changes involve the bone-tendon junction, pathology that involves structural changes to the enthesis are often permanent in nature. Therefore, structural changes in this region often remain even after symptoms resolve. These changes may occur due to a stress shielding response or may be due to excessive compressive or frictional forces (Almekinders et al., 2003). Regardless of the causative drive, changes to the enthesis are representative of the Achilles tendons’ adaptation to its load requirements (Benjamin & McGonagle, 2001). This explains why asymptomatic changes to the enthesis are regularly seen; with a study by Leung and Griffith (2008) showing up to 63% of asymptomatic normal tendons have irregularity of the enthesis, involving cortical irregularity and bony spurring. In the symptomatic enthesis however, grey-scale ultrasound often demonstrates thickening of the hypoechoic insertional fibres, thickening of the superficial paratenon, oedema within the fat pad and fluid within the bursa. Doppler ultrasound may show increased vascularity within the paratenon, superficial bursa and insertional fibres and may demonstrate vessels breaching through the bone-tendon interface (Syha et al., 2013).

2.9.4 Neovascularity

Normal tendons have low vascularity, but sufficient for their metabolic needs. This normal amount of vascularity is not identifiable sonographically with Doppler ultrasound (Longo et al., 2009). In the 1990’s blood flow was demonstrated in
symptomatic tendons using power Doppler ultrasound, subsequently Ohberg and Alfredson (2002) defined this blood flow as neovascularisation. These tortuous, small lumen vessels infiltrate the tendon, primarily from the anterior aspect of the tendinopathic area and from the paratenon, invaginating and spreading diffusely throughout the tendon (Longo et al., 2009). There is a relationship between Doppler identifiable neovascularisation seen in abnormal tendons with pain, symptoms and outcome that has been demonstrated in many studies, yet this association is not absolute (Yang et al., 2010).

In asymptomatic tendons, there may be pathological blood flow that cannot be detected with Doppler ultrasound due to the slow flow and small size of the vessels, whereas in the tendinopathic tendon, the increased blood flow is readily identified (Longo et al., 2009; Risch et al., 2016; Tol, Spiezia, & Maffulli, 2012). It has been reported that up to 47-88% of patients with symptomatic tendinopathy can present with sonographically identifiable neovascularity (de Vos, Weir, Cobben, & Tol, 2007; Tol et al., 2012). However, neovascularity in the absence of pain is not necessarily pathological, as Longo et al. (2009) demonstrated that this may indicate a physiological response to training in athletes, with some studies reporting observable vascularity in 29-35% of asymptomatic patients (Sengkerij et al., 2009). The significance and clinical relevance of neovessels in chronic mid portion Achilles tendinopathy is the subject of debate, with the relationship between neovascularisation and symptoms showing conflicting results, yet is routinely requested, examined and reported within medical imaging practices (de Vos et al., 2007). De Jonge et al. (2013) examined 141 symptomatic Achilles tendons and found a weak association between neovascularity and the VISA-A score, particularly the function domain of the VISA-A. Overall however, studies and clinical experience suggest that abnormal tendons with detectable vascularity are more likely to be symptomatic than those without (Cook et al., 2004).

Alfredson (2005) performed immunohistochemical analyses of tendon biopsies and showed that neural and vascular ingrowth (neovascularity) occurred within painful
tendinopathic tendons. This ingrowth was associated with an increase in pain signal substances of substance P, catecholamines, acetylcholine and glutamate (a potent pain modulator in the central nervous system) and their receptors. These receptors can lead to cell proliferation, interfere with pain sensation, influence collagen production, take part in vasoregulation and promote cell degeneration and apoptosis (Danielson, Alfredson, & Forsgren, 2007). It is believed that a combination of neovascularity (nerve and vessel ingrowth) and an increase in signal substances combine to produce tendon pain as well as advancing the tendinopathy process.

Neovascularisation is an angiogenic process whereby new blood vessels and accompanying nerves grow into and invade the tendon. These blood vessels and nerves run together and use similar chemical signals for growth and navigation towards the target area. These two systems are inextricably linked and should be thought of as neoneurovascularisation (Webborn, 2008).

2.9.5 Paratendinopathy
Paratendinopathy involves acute or chronic inflammation and/or degeneration of the paratenon; a loose areolar and adipose envelope surrounding the tendon. The paratenon consists of straight bundles of type I and type III collagen fibrils with a straight microfibrillar arrangement and a variable diameter (van Sterkenburg & van Dijk, 2011). These fibres form an outer parietal and inner visceral layer, which is lined with synovial cells. The space between these, the mesotenon, allows blood vessels, lymphatics and nerve pedicles to enter the tendon substance and reduce friction during movement (Bianchi & Martinoli, 2007).

Acute paratendinopathy involves oedema and hyperaemia of the paratenon, histopathologically showing inflammatory cells and may involve the production of a fibrin exudate in the space between the tendon and paratenon (van Dijk et al., 2011). This fibrin exudate causes the crepitus that may be felt with palpation during the clinical examination. Chronic paratendinopathy involves thickening of the paratenon due to mucoid degeneration, increased fibrin exudate, prominent and
widespread proliferation of fibroblasts and vascular proliferation with a slight inflammatory infiltrate (Khan et al., 1999). This thickening and formation of connective tissue, results in adhesions between the tendon, paratenon and skin, preventing smooth gliding movements (Paavola & Jarvinen, 2005). There is also a strong presence of myofibroblasts. These are fibroblasts with stress fibres composed of α-smooth muscle within their cytoplasm, and thus, are capable of creating forces required for wound contraction (Ehrlich et al., 1994). These cells are in abundance (around 20%) within the chronically pathological paratenon and synthesize type I and III collagen (Jarvinen et al., 1997). The activity of these cells has been hypothesised by Jarvinen et al. (1997) to be responsible for scarring and contraction within adhesions resulting in external constriction around the tendon. This in turn may lead to constriction of the vascular channels, leading to impaired circulation, which may further contribute to the pathogenesis of Achilles tendinopathy (Jarvinen et al., 1997). Since the paratenon is highly vascularised and innervated, it may be a significant pain source in Achilles tendinopathy (Stecco et al., 2014). Novel surgical treatments targeting the nerve and blood vessel-rich peritendinous tissues on the ventral side of the Achilles tendon (minimally invasive scraping procedures) have shown promising results in improving symptoms in patients with chronic Achilles tendinopathy (Ruergard & Alfredson, 2014). This contributes further evidence towards the concept that chronic paratendinopathy is a significant complication associated with Achilles pathology.

The normal paratenon appears as a thin line surrounding the Achilles tendon, isoechoic or slightly hypoechoic to the adjacent tendon (Stecco et al., 2014). In acute paratendinopathy, ultrasound reveals an increase in fluid beneath the peritendinous layer surrounding the tendon, giving the tendon a thin hypoechoic halo. However, in the chronic phase, the paratenon becomes thickened, hypoechoic with ill-defined borders and may show neovascularity on Doppler ultrasound (Paavola & Jarvinen, 2005). Stecco et al. (2014) has shown that a paratenon more than 1.35mm in thickness is predictive of paratendinopathy, even before alterations in tendon echotexture exist. Sonographically, this visualised paratenon thickening is often
associated with chronic Achilles tendinopathy and the presence of this thickening is often helpful in confirming the diagnosis (Leung & Griffith, 2008).

This review of current imaging studies has demonstrated that diffuse and focal tendon changes, neovascularity, mid-portion tendinopathy, enthesis pathology and paratendinopathy, if present, are all visible when the Achilles tendon is imaged using ultrasound (Bianchi & Martinoli, 2007). Individuals with Achilles tendinopathy are a non-homogeneous group; experiencing a wide variety of pathologies that are often grouped together under this umbrella term. There is a gap within the literature regarding a consensus on how to grade and report these sonographic changes, with a wide variety of methodologies used and only selected components currently included. These changes are rarely commented on within the sports imaging literature, yet may severely impact patients' outcome and response to therapy (Sunding et al., 2016).

2.10 Complications, Barriers to Treatment and Associated Findings

Imaging of painful tendons, however useful in providing important information on structure and state of disease, is not a necessity for the correct diagnosis or appropriate management of Achilles tendinopathy (Hutchison et al., 2013). Imaging is paramount however in the detection and identification of differential diagnosis for tendinopathy, where treatment may need to be altered to address the specific condition (Docking et al., 2015). Within this review of the literature, the following structures, when pathological, may become complications or potential barriers to treatment in patients with Achilles tendinopathy. The impact on the Achilles tendon along with the pathological and sonographic changes of these structures will now be explored.

2.10.1 Plantaris

The plantaris tendon is present in most, but not all patients, running medial to the distal Achilles tendon (Spina, 2007). Isolated ruptures of the plantaris tendon have been reported in the literature and are associated with a sudden acute onset of
symptoms, usually in the upper to mid-calf (Spina, 2007). Besides traumatic rupture of the plantaris tendon, it may be involved in the pathogenesis and aetiology of mid-portion Achilles tendinopathy, along with having isolated tendinopathy of its own tendon (Alfredson, 2017). These concepts have been reinforced by a recent review of cadaveric, histological and clinical/surgical studies by Masci, Spang, van Schie, and Alfredson (2016) which support the theory of the plantaris tendon contributing to persistent pain in patients who present with mid-portion Achilles tendinopathy. There are at least nine different relations between the plantaris and Achilles tendons, leading to different interactions, potential pathology and subsequent presentation (Alfredson, 2017).

A surgical study by Olewnik et al. (2017) found the most common variant of plantaris insertion onto the calcaneal tuberosity to be a fan shaped insertion on the medial side of the Achilles tendon. Alfredson (2011) found excised pathological plantaris tendons to be macroscopically thicker than the normal plantaris tendon and histologically demonstrated tendinosis like changes with similar matrix degradation to that shown in mid-portion Achilles tendinopathy. The plantaris may also play a role in extrinsic compression and/or sheering forces on the Achilles when it is pathological, as it is stronger, stiffer and less extensible than the Achilles tendon (Steenstra & van Dijk, 2006). Due to the plantaris crossing the knee and ankle joints, there is a differential movement between it and the Achilles that may lead to friction, inflammation and adhesions between the plantaris and Achilles tendons (Bedi et al., 2016). A surgical study by Bedi et al. (2016) on 17 athletes with focal Achilles tendinopathy found in all cases, the plantaris tendon to be invaginated or adherent to the medial Achilles. A series of 73 patients undergoing surgical treatment for mid-portion Achilles tendinopathy, found 58 to have an invaginated or closely related plantaris tendon (Alfredson, 2011). While a surgical and clinical study by Ruergard and Alfredson (2014) found that patients with persistent medial Achilles pain who had failed previous surgical intervention, who then underwent surgical excision of the plantaris tendon, had improved outcomes.
Even though plantaris involvement in mid-portion Achilles tendinopathy is common, there is sparse information regarding the diagnosis of plantaris involvement using ultrasound or colour Doppler (Alfredson, 2017; Masci et al., 2016). Olewnik et al. (2017) recommended ultrasound imaging be performed in patients with Achilles tendinopathy to examine whether the plantaris tendon is contributing to symptoms. Sonographically the pathological plantaris tendon has a variable appearance due to the many anatomical variations, but commonly appears enlarged, hypoechoic and may have a hypoechoic layer of paratendinopathy towards its insertion, similar to Achilles tendinopathy. This tendon, including its associated paratenon, may demonstrate increased signal on Doppler ultrasound (Alfredson, 2017; Masci et al., 2016).

2.10.2 Fat pad
In Kager’s triangle, the anatomical region anterior to the Achilles tendon, a mass of adipose known as Kager’s fat pad is commonly pathological in both tendinopathy and enthesopathy of the Achilles tendon. There are fibrous connections between the Achilles tendon and the fat pad via the paratenon that anchor and stabilise the adipose, leading to associated movement of the fat pad and the Achilles with dorsiflexion and plantarflexion (Theobald et al., 2006). When Kager’s fat pad is irritated it becomes oedematous with a higher water content. This sonographically presents as an increase in echogenicity and becomes heterogeneous in appearance. The echogenicity of Kager’s fat pad should be relatively hypoechoic to that of the adjacent tendon and if uncertainty arises, it may be compared to the contralateral fat pad for assessment (Leung & Griffith, 2008).

2.10.3 Calcification
Although a relatively rare entity, calcification may occur within the body of the Achilles tendon (Leung & Griffith, 2008). Calcification within any tendon is often referred as calcific tendinopathy or calcific tendinosis. The most commonly affected tendon in the body for calcific tendinopathy is the supraspinatus tendon in the shoulder, which is often found as an incidental finding during x-ray or ultrasound
Calcification in peripheral tendons is significantly less common, yet more frequently symptomatic; however, reliable figures on incidence and prevalence are difficult to obtain (Rees et al., 2006).

The histopathological process involved in calcific tendinopathy is unknown, along with the clinical significance and prognosis. It is believed to be as a result of an ongoing degenerative process involving calcium hydroxyapatite deposition, whilst other theories suggest it is the result of chondrogenic metaplasia, or a self-limiting cell-mediated process (Rees et al., 2006; Syha et al., 2013). Although the aetiology is unknown and the process relatively rare, it is often clinically significant and should not be overlooked (Syha et al., 2013). Sonographically these focal calcifications within the tendon form a highly reflective interface between the surrounding tendon and the outer shell of the calcium, resulting in the deposit appearing extremely echogenic. This highly reflective deposit may reduce through transmission of the ultrasound beam, which in turn, may or may not result in posterior acoustic shadowing depending on its concentration (Bianchi & Martinoli, 2007; Chang & Miller, 2009).

2.10.4 Retrocalcaneal Bursa
The main synovial bursa of the ankle is the retrocalcaneal bursa, located between the Achilles tendon and the upper face of the calcaneus. In normal conditions this synovial-lined pouch contains a small amount of fluid that decreases friction between the anterior tendon and the calcaneus (Bianchi, Martinoli, Gaignot, de Gautard, & Meyer, 2005). This normal small pouch of fluid may be present sonographically as a 2-3mm thick hypoechoic structure adjacent the normal asymptomatic tendon (Leung & Griffith, 2008). The retrocalcaneal bursa is directly related to the paratenon and Kager’s fat pad, and is often affected in tendinopathy and enthesopathy processes (Syha et al., 2013). In these cases, the bursa histologically exhibits degeneration of its fibro-cartilaginous walls, often with calcification or hypertrophy. Along with this, the synovial infoldings hypertrophy whilst intraluminal fluid increases and may contain fibrin bands as it thickens (Syha
et al., 2013). Sonographically this finding presents as a well-encapsulated hypoechoic structure anterior to the tendon and may show increased vascularity on Doppler ultrasound.

2.10.5 Superficial Bursa
The superficial or subcutaneous bursa lies between the subcutaneous tissues posterior to the tendon and reduces friction between the posterior aspect of the tendon and the skin. When the superficial bursa becomes inflamed, there is often a painful, solid swelling on the posterolateral aspect of the calcaneus, and often discoloration of the skin. It is frequently associated with shoes with a rigid posterior portion (van Dijk et al., 2011). The superficial bursa is an adventitious bursa that develops as a response to friction and undergoes the same pathological process as the retrocalcaneal bursa when pathological, including hypertrophic synovial tissue formation and fluid accumulation (van Dijk et al., 2011). This finding presents sonographically as an elongated hypoechoic structure posterior to the tendon insertion and is often associated with thickening of the dermis (Syha et al., 2013).

2.11 Tendinopathy Continuum and Sonographic Presentation
Historically, research, assessment and treatment of tendon pathology was focused around an inflammatory model of pathology. This view then progressed to the opinion of ‘failed healing’ being the main pathology (McCreesh & Lewis, 2013). However, more recently the perspective has been that of a cellular driven, primarily degenerative pathology with minimal inflammatory influence (Maffulli et al., 1998). In 2009, Cook and Purdam (2009) proposed a continuum of pathology to describe the tendinopathy spectrum to include 3 overlapping stages within the continuum, reactive, dysrepair and degenerative tendinopathy (Figure 4). These stages have increasing degrees of pathology with a decreasing capacity of the pathological area to recover. This model is highly clinically applicable, with a framework describing how treatments may be best aligned with the stage of tendinopathy present, along with the clinical presentation of each stage (McCreesh & Lewis, 2013).
Figure 4. Pathology continuum. This model embraces the transition from normal through to degenerative tendinopathy and highlights the potential for reversibility early in the continuum. Reversibility of pathology is unlikely in the degenerative stage. (Cook & Purdam, 2009, p. 410)

Reactive tendinopathy describes a non-inflammatory proliferative response within the cells and the matrix, resulting in a homogeneous fusiform thickening of the tendon in response to acute overload. This results in reduced stress on tendon fibres
by increasing cross-sectional area and increased stiffness, decreasing the force per unit area (Cook & Purdam, 2009). The tenocytes become rounded and produce large proteoglycans (e.g. aggrecan and versican). These large proteins attract water that changes the matrix and can cause some separation of tendon fibres (Cook & Purdam, 2009). This change in the proteoglycan content alters the extracellular matrix, but results in minimal change to the collagen (Ganderton et al., 2015). Sonographically this results in a tendon with an increased diameter that shows fusiform thickening, is homogeneous, but has a decreased echogenicity due to increased water content between tendon fibres and no sonographic evidence of neovascularity (Cook & Purdam, 2009).

Tendon dysrepair describes attempted tendon healing, similar to reactive tendinopathy but with greater matrix breakdown. There is a general increase in the number of chondrocytic cells as well as the presence of myofibroblasts. This results in an increase in production of both proteoglycans and collagen. This greater increase of water attracting proteins results in greater separation of the matrix, allowing for vascular and associated neural ingrowth into the tendon matrix (Cook & Purdam, 2009). Work by Murchison et al. (2007) on the scleraxis gene showed an increase in expression during the repair and remodelling phase. This attempt to restore the normal phenotype is frequently imperfect and leads to metaplastic or fibrotic change to the tendon. Sonographic imaging shows a swollen tendon with increased diameter and collagen disorganisation. There are areas of heterogenicity with some collagen fascicle discontinuity represented as focal areas of hypoechogenicity. Colour and power Doppler may reveal neovascularity within the tendon substance (Cook & Purdam, 2009).

Degenerative tendinopathy describes the progression of matrix and cell changes, involving areas of cell death due to apoptosis, trauma or tenocyte exhaustion. There may be areas of acellularity, while the matrix is disordered, filled with vessels, ground substance, matrix breakdown products and little collagen. There is a lack of intact type I collagen fascicles and their replacement with thinner, poorly organised
Proteoglycans binded with water further cleave apart collagen and cause greater disorganisation of the matrix allowing for marked vessel ingrowth. At this stage, there is general heterogenicity of the tendon, with islands of degenerative tendinopathy surrounded by other stages of tendinopathy and normal tendon tissue (Cook & Purdam, 2009). Sonographically these tendons are diffusely heterogeneous with hypoechoic regions displaying few reflections from collagen bundles. Colour and power Doppler show numerous large vessels within the tendon substance, often in numerous regions (Cook & Purdam, 2009).

Overall, tendinopathy presents as a mixture of pathology, with the tendon showing discrete regions of normal tendon, interspersed with areas of tendinopathy in various stages. The most common clinical presentation is reactive on degenerative tendinopathy, where an island of degenerative tendinopathy is surrounded by reactive pathology, within the remaining tendon (Ganderton et al., 2015). This allows for heterogeneous pathology within a single tendon and accurate imaging and documentation are paramount to facilitate appropriate treatment and the timing of intervention, as different stages of pathology require different rehabilitation strategies (Ganderton et al., 2015).

Partial tears are a rare occurrence, however micro tears may occur in the advanced degenerative tendon (Cook & Purdam, 2009). These appear sonographically as hypoechoic defects in the tendon, free of collagen material. These are often difficult to detect with normal imaging, however are frequently seen when intra-tendinous injections are performed as the injectate acts as a contrast medium, outlining the extent of the tear. These micro-tears are of little clinical importance and are managed as part of a tendinopathic tendon (Cook & Purdam, 2009).

2.12 Quantification of Sonographic Assessment
Research on the sonographic assessment of tendons has primarily been performed on Achilles and patellar tendons. These superficial tendons are easily assessed by both ultrasound and MRI, along with having similar causative factors when
pathological (Chang & Miller, 2009). It has been postulated that because these tendons undergo similar histopathological changes throughout the tendinopathy spectrum and the imaging findings associated are similar, that imaging studies are applicable from one tendon to the other (Cook & Purdam, 2009). This assumption has been broadly applied across the research literature and is yet to be disputed.

Tendinopathy on ultrasound imaging may demonstrate tendon thickening, collagen fascicle disorganisation and irregularity, tendon hypoechogenicity and neovascularity within the tendon substance as observed with colour or power Doppler (Cook & Purdam, 2009). These ultrasound appearances are well known to occur throughout the tendinopathy spectrum, yet the inclusion, classification and quantification of these sonographic occurrences are rarely performed. A common criticism of imaging is the lack of objective quantifiable assessment, with reliance on subjective interpretation of images and the grading of these features based on perceived severity (Docking et al., 2015). A commonly used simple method of grading tendinopathy is that developed by Archambault et al. (1998) and describes grade 1 a normal tendon; grade 2 an enlarged tendon; and grade 3 a tendon containing a hypoechoic area with or without tendon enlargement. This simple grading system does not distinguish between normal and pathological tendons or assesses neovascularity, along with not including related changes that may occur in the surrounding tissues.

Additionally, the identification of hypoechoic areas within tendons requires a degree of caution due to the potential artefact of anisotropy. Anisotropy is a property of highly ordered structures, such as tendons, whereby the reflective echogenicity of the structure is dependent on the angle of insonation of the interrogating sound beam (Chang & Millar, 2009). The sonographic beam needs to be orientated perpendicular to the tendon structure, as a non-orthogonal beam may make the tendon appear artefactually hypoechoic, mimicking tendinosis or a tear (Chang & Millar, 2009).
Overall, within medical imaging research studies there is a lack of consistency and
generalised confusion regarding the sonographic appearances of tendinopathy. A
recent review by Burke and Adler (2016, p. 495) described the sonographic features
of tendinopathy and detailed inclusion criteria involving abnormalities of the
‘adjacent cortical bone at the tendon attachment, demonstrating irregularity, pitting
and enthesophyte formation’. Yet these findings are clearly describing irregularities
and pathology at the enthesis, or bone tendon junction, and may often not be
associated with tendinopathy. As the enthesis organ is a histopathologically
different structure to tendon, it withstands different stresses and undergoes
pathological changes under differing conditions to that of the tendon proper. As
such, it should be considered as a different clinical entity to that of tendinopathy.

A study by Bakkergaard et al. (2015, p. 459) describing the sonographic changes associated with Achilles tendinopathy as
objective parameters entailed inclusion criterion of ‘tenosynovitis on grey-scale
imaging, as hyper or hypo-echoic changes to the paratenon with poorly defined
borders’. Yet the Achilles tendon doesn’t have a synovial sheath, hence can never
undergo tenosynovitic change. These two recent studies emphasise the current lack
of understanding within the imaging community of anatomy, histopathology and
associated sonographic changes in Achilles tendinopathy. This misleading literature
continues to facilitate the documentation and reporting of sonographic findings that
do not adequately represent the true pathology present.

This ambiguity in literature is no more prevalent than in the description and
quantification of intratendinous blood flow. A number of measurement scales have
been suggested as tools by which the degree of neovascularisation present may be
graded (Resteghini & Yeoh, 2012). Within the clinical setting, quantification of
neovascularity is sparsely used, often described as mild, moderate, or florid, with no
degree of standardisation. In other settings the mere presence of Doppler signal is
reported, with no attempt to quantify the degree. The first quantitative scoring
system of neovascularity was defined by Ohberg, Alfredson, and Khan (2002),
grading the appearance of vessels inside of a tendon. Subsequently this scoring
system has been modified and adapted by numerous authors including Boesen, Boesen, Koenig, Bliddal, and Torp-Pedersen (2006), de Vos et al. (2007), Sengkerij et al. (2009), Hirschmuller et al. (2012), Sunding et al. (2016) and Risch et al. (2016). Whilst the Ohberg scoring system has been modified by each of the above authors, agreement has not been reached concerning the most suitable variant, with no direct comparison between the differing interpretations of the original score. The Ohberg measurement technique consists of a simple 5-point scale and although having a high degree of subjectivity, it has been demonstrated to have excellent inter-observer reliability (Sengkerij et al., 2009). Another method used by Cook, Kiss, Ptasznik, and Malliaras (2005) and Malliaras et al. (2006) is to determine the total vessel length of intra-tendinous blood flow, while an alternative approach employed by Boesen et al. (2012) and Malliaras et al. (2012) involved the use software to analyse the amount of colour pixels within the tendon. This lack of consensus and knowledge about the reliability of these differing scoring systems along with the absence of the best method for assessment of neovascularity itself makes it difficult to compare and interpret study results.

Within the rheumatology profession, there have been numerous attempts to quantify sonographic assessment and reach consensus for the assessment of the enthesis in patients with spondyloarthritis. Balint, Kane, Wilson, McInnes and Sturrock (2002) are one such group who formulated an enthesis score for the lower-limb based on ultrasound findings in the rheumatology population. The Achilles component of their score included tendon thickening, bursitis, bony erosions and enthesophyte formation; with one point being scored for each abnormality present and representing a pathological enthesis. However, their methodology did not include hypoechoic change to the tendon as this important feature was deemed too subjective (Balint et al. 2002). D’Agostino, Said-Nahal, Hacquard-Bouder, Brasseur, Dougados and Breban (2003) utilised the basis of the previously mentioned assessment technique and combined this with unpublished observations to formulate their own method combining both grey-scale and Doppler changes. In this method the enthesis was assessed and graded either as being stage
1, 2a, 3a, 2b or 3b according to pre-defined sonographic criteria. These studies led Terslev et al. (2014) to highlight the lack of consensus regarding which elementary structures of the enthesis should be examined with ultrasound and how to define any abnormality found. It is clear from these rheumatological studies that the inconsistent use of various and differing assessment methodologies is not isolated only to tendinopathy.

The quantification of sonographic changes within a pathological tendon, both grey-scale and Doppler, is required to allow accurate screening, assessment and evaluation of tendon injuries to take place. Even though many methods exist to evaluate individual components of tendinopathy and diagnostic imaging plays an important role in this assessment, a common criticism of all imaging techniques is the disconnect between imaging findings and symptoms (Malliaras & Cook, 2006). Hirschmuller et al. (2010) showed that Achilles tendons in runners that are currently or have previously been symptomatic are significantly thicker than a normal tendon, as well as there being an increase in the presence of hypoechoic lesions and neovascularity. Yet grey-scale abnormalities were rarely found in asymptomatic runners’ tendons. These findings replicate research into other soft tissue structures (i.e. intervertebral discs in low back pain, knee and hip cartilage loss, shoulder rotator cuff tears), where pathological anatomy is more likely associated with symptoms, yet there is no direct or linear relationship between imaging abnormalities and clinically significant symptoms (Cook et al., 1998; McAuliffe et al., 2016). However, studies on the Achilles tendon have only compared one or two imaging variables with clinical outcome (e.g. tendon thickness, echogenicity, and/or neovascularity). There has been no research to date, which attempts to summarise the entire sonographic spectrum of tendinopathy and compare its relationship to clinical outcomes.

Current theories suggest that pain in tendinopathy arises from biochemical irritants, peritendinous tissues or neurovascular ingrowth (Fredberg & Stengaard-Pedersen, 2008, Lian et al., 2006; van Sterkenberg & van Dijk, 2011). However, none of these
factors have been correlated directly to the subjective measure of pain, for example neovascularisation has been shown to have little correlation with clinical outcomes, and can be present in pain free tendons (Tol et al., 2012). When the tendon is thoroughly assessed, individual components are only a part of the picture involved in the tendinopathy process and each does not necessarily correspond directly with pain. Pain is multifactorial and can be present in patients with normal imaging (Longo et al., 2009). The complex nature of pain is of great significance, therefore the pathoaeiology of Achilles pain will now be discussed.

2.13 Achillodynia
The aetiology of the origin of pain and associated pain mechanisms in patients with Achilles tendinopathy (achillodynia) is yet to be entirely clarified and appears to be somewhat independent of underlying tendon pathology (van Sterkenburg & van Dijk, 2011). Pain is frequently associated with pathological tendons, however tendon pain in apparently normal tendons has been described, along with the phenomenon where pathological tendons can be clinically asymptomatic (Cook et al., 2000; Malliaras & Cook, 2006).

Pain is the most common symptom of Achilles tendinopathy (Yang et al., 2010). In the active patient, pain occurs at the beginning of initial loading and persists for a short while after the end of an exercise activity, with a period of diminished discomfort in between. As the pathologic process progresses and the condition becomes chronic, pain may occur during the entire exercise session leading to reduced performance, activity curtailment or cessation, and in severe cases, may interfere with activities of daily living (Maffulli et al., 2014).

The Achilles tendon is surrounded by richly innovated mechanoreceptors, including Ruffini corpuscles, Pacinian corpuscles and free nerve endings. All of these may play a part in both proprioception and nociception (Scott et al., 2013). There are also many autonomic fibres surrounding the tendon, which can be involved in regulating tendon blood flow, along with tenocyte metabolism and pain signalling.
Microdialysis studies along with immunohistochemical and gene expression analysis have shown that glutamate, a well-known neurotransmitter and very potent modulator of pain in the central nervous system, is found in high-levels in painful tendons, but not in normal tendons (Alfredson et al., 2001). These high levels of glutamate were also associated with an increase in the presence of glutamate receptors in close vicinity to nerves, along with an up-regulation of vascular endothelial growth factor (VEGF) in patients with painful Achilles tendinopathy (Alfredson, Ohberg, & Forsgren, 2003). Also, the identification of neovascularisation (neural and vascular ingrowth) within tendinopathic tendons has raised suspicions of local neural pathways being associated with achillodynia (Ohberg & Alfredson, 2002). Biopsies taken from areas of tendon with tendinosis and neovascularisation showed neural structures in close association with the vessels; with substance P nerves in the vascular wall and calcitonin gene related peptide nerves close to the vascular wall (Bjur, Alfredson, & Forsgren, 2005). These studies indicate that nociceptive nerve fibres accompany the neovascularisation seen in Achilles tendinopathy, and that these systems are inextricably linked during this angiogenic response (Alfredson et al., 2003; Webborn, 2008). In fact, there are studies that suggest blood vessels arise later than nerves, implying that the neural component is the primary factor for the development of neovascularity (Webborn, 2008). In the clinical setting neovascularity which is commonly seen sonographically using Doppler ultrasound, is associated with the site of maximal tenderness and maximal thickening of the abnormal tendon (Alfredson, 2003).

There have been conflicting results between studies aimed at reducing Achilles pain by treating the neurovascular ingrowth with sclerosing injections. Initial studies by Ohberg and Alfredson (2002) injected a sclerosing agent into the neovascularised area outside the ventral part of the tendon and reported excellent pain relief. This study suggested that neovascularisation (neo-vessels and accompanying nerves) might be the sole source of pain. However further studies by the same authors along with others have failed to achieve the same outcomes, indicating that there is more to achillodynia than just neovascularity (de Jonge et al., 2014).
Since tendinosis involves structural degeneration of the load-bearing matrix, with tenocytes producing nociceptive as well as catabolic substances and an absence or minimal presence of inflammatory cells; the pathogenesis of tendon pain is unclear (Scott et al., 2013). Sensory afferent fibres are present both within the tendon, but particularly within the peritendinous tissues. Since these nerves possess receptors for nociceptive substances, they may sensitise the nerves and augment pain signalling (Scott et al., 2013). Diffuse pathological changes within the peritendinous tissues are frequently associated with intra-tendinous changes during the tendinopathy process and in many cases, thickening of the paratenon may predate tendon damage (Stecco et al., 2014). As the paratenon is highly vascularised and innervated, this may be a significant source of tendon pain in achillodynia.

Recent pain physiology research suggests that musculoskeletal pain is multifactorial, and an increased emphasis has been placed on the consideration of central sensitisation as well as psychosocial factors (Moseley et al., 2003). Central sensitisation describes a pain sensation that is driven or enhanced by central neurological factors rather than a peripheral nociceptive source (Mosley et al., 2003). A study of common extensor tendinopathy in the elbow by Coombes, Bisset, and Vicenzino (2009) demonstrated the presence of mechanical hyperalgesia, both locally and on the contralateral side, indicating the presence of central sensitisation. Similarly lowered mechanical pain thresholds have been shown elsewhere within the body (McCreesh & Lewis, 2013). Along with these central sensitivity components, psychosocial factors may be important in prognosis and the development of chronicity (McCreesh & Lewis, 2013). Therefore, chronic tendon pain may be a representation of the complex interplay between local and central up-regulated factors. This explains the phenomenon whereby measurable structural change may not necessary correlate with a therapeutic outcome, due to the many processes that can be involved in achillodynia, including neural, biochemical and myogenic changes (Drew et al., 2012).
2.14 Imaging and Correlation with Symptoms

Grey-scale ultrasound abnormalities and changes in MRI signals tend to precede tendon pain for a variable period of time (Malliaras et al., 2006). One of the biggest challenges in terms of the use of imaging in tendinopathy is the prevalence of asymptomatic structural changes (Malliaras et al., 2006). Similar to the use of diagnostic radiology in spinal and knee pain, it is not yet possible to differentiate between symptomatic and asymptomatic tendons using any form of imaging, with correlation to clinical examination recommended (McCreesh & Lewis, 2013). Due to the latency of symptom presentation after aggravating activities in tendinopathy, it has been proposed that the development of imaging protocols to assess the relative changes in tendon properties in response to loading may be useful in identifying tendons at risk of becoming symptomatic (Shalabi, Kristoffersen-Wiberg, Aspelin, & Movin, 2004). While a number of different scales have been described to quantify the degree of neovascularisation or tendon heterogenicity, there is no generally accepted gold standard for assessing Achilles tendinopathy. Previous studies have cited this lack of a gold standard as a major limitation to Achilles tendinopathy research (Khan & Maffulli, 1998).

Within the literature for grey-scale sonographic changes to tendons, a study by Malliaras et al. (2010) on patellar tendons of volleyball players showed that when tendons are sonographically classified, there is a correlation between these findings and pain. They found that there is a greater probability of tendon pain in tendons with focal hypoechoic regions and diffusely thickened changes, than those that appear sonographically normal. This supports the results previously shown by Myllymaki, Bondestam, Suramo, Cederberg, and Peltokallio (1990) that longstanding pain tends to be associated with a hypoechoic region within the tendon.

Astrom et al. (1996) investigated histological agreement with grey-scale ultrasound assessment of the Achilles tendon, with ultrasound identifying 21 of 26 (80.8%) cases containing histological degeneration. This research implies that grey-scale
ultrasound can be used for locating Achilles tendon abnormalities, however this method alone is not completely reliable for the diagnosis of Achilles tendon disorders. Ooi et al. (2015) used the 3-point grading scale as described by Archambault et al. (1998) to assess 120 symptomatic Achilles tendons and 120 age and sex matched controls, finding that this assessment technique yielded a sensitivity of 99.1%, specificity of 78.9% and overall accuracy of 94.7% in confirming clinically symptomatic tendinopathy. Bakkegaard et al. (2015) demonstrated that an increase in tendon thickness and hypoechoic change within the tendon both had associations with increased pain at palpation, morning pain and pain at function when assessed using a visual analogue scale. Whereas an observational study of elite gymnasts by Emerson et al. (2010) reported that ultrasound overestimates the prevalence of Achilles tendinopathy. Their study found that only one third (35%) of those with ultrasound abnormalities were associated with clinical symptoms (Emerson et al., 2010). However, when ultrasound is used in conjunction with clinical assessment, it has the ability to detect pathological symptomatic change within a tendon (Malliaras et al., 2010).

Within the literature on Doppler ultrasound, a recent prospective study of tendinopathic Achilles tendons by de Jonge et al. (2014) found that when looking at neovascularity alone, there was a weak association with clinical severity as assessed by the VISA-A. Throughout the literature, a variable relationship has been established between neovascularity in abnormal tendons shown by Doppler ultrasound and patient symptoms and outcomes. Some studies have shown an absolute association, whilst in other studies the relationship has been less clear, with only 47-88% of symptomatic tendons demonstrating neovascularity on Doppler ultrasound (Cook et al., 2005; de Jonge et al., 2014; Ohberg et al., 2001; Peers, Brys, & Lysens, 2003). Ooi et al. (2015) found when using the method described by Gisslen, Gyulai, Soderman, and Alfredson (2005) to assess Doppler signal, that Doppler ultrasound alone was 68.2% sensitive, 91.4% specific and 82.5% accurate in categorising patients according to clinical diagnosis. Ohberg et al. (2001) and Malliaras et al. (2010) have both found that Doppler flow was more
common among tendons containing a focal hypoechoic region when compared to those with diffuse thickening. Additionally, they found that Doppler signal was absent among sonographically normal, asymptomatic tendons. Bakkergaard et al. (2015) found that increased Doppler flow was suggestive for the severity of Achilles tendinopathy as measured using a visual analogue scale for morning, functional and palpation pain. When neovascularity and structural changes are present together, there is a much stronger likelihood of the tendon being symptomatic (Ohberg et al., 2001). Overall, these studies have shown a general consensus that indicates abnormal tendons with detectable vascularity seem to be more painful than those without (Cook et al., 2005). Reviewing the above mentioned studies, the rationale behind this variable relationship between neovascularity and patient symptoms may lie with the variable use of outcome measures used and the lack of standardisation in imaging techniques. Particularly, the lack of standardisation in the assessment of neovascularisation is of concern; with multiple varying methodologies being utilised between studies (Cook et al., 2005; de Jonge et al., 2014; Ohberg et al., 2001; Ooi et al. 2015, Peers, Brys, & Lysens, 2003).

There has been evidence that symptomatic tendons may contain neovascularity that may not be identifiable with Doppler imaging (Cook et al., 2005). This may be a potential cause for the discrepancy within the literature on the presence of neo-vessels identified with Doppler imaging. However, technological advancements have improved the sensitivity to low-level vascular flow, implying that if current market-leading machines were used in previous studies, their results may differ. A strong emphasis also needs to be placed on proper ultrasound system operation including the appropriate setting of pulse repetition frequency, baseline filter settings, Doppler gain and operating frequency; as these factors may play a significant role in the identification of vessels. Yang et al. (2010) performed a review of Doppler settings in studies of the Achilles tendon and found that there was gross heterogeneity in the reporting and the standardisation of these settings. From this review, even though the majority of studies used colour Doppler, Yang et al. (2010) recommends the use of power Doppler over colour Doppler as it is independent of
the angle of incidence of the beam and is more sensitive in the detection of flow within vessels, even as small as 0.3mm in diameter. Other recommendations to demonstrate a greater number and extent of vessels include having pulse repetition frequency set as low as possible where ‘flash’ artefacts are eliminated, colour gain on the threshold of noise and Doppler frequency set as high as possible to maximise spatial resolution (Yang et al., 2010).

The detection of vascularity is also sensitive to tendon and muscle stretch and contraction, both of which can occlude neo-vessels. Examiners must ensure a relaxed tendon to maximise sensitivity of Doppler ultrasound, however many studies have used various foot positioning, not documented positioning or used a position of neutral dorsi-plantar flexion, that in some patients will actually impede Doppler signal identification (Cook et al., 2005).

Cook et al. (2005) indicated that moderate exercise significantly enhances the detection of tendon blood flow and Risch et al. (2016) recommends the standardisation and control of physical activity prior to sonographic examination to prevent variability in Doppler assessment. Although there are several articles on tendon vascularity, a limited number of studies reported the activity of the person before imaging, with some authors even restricting patients from exercise prior to assessment (Risch et al., 2016). This methodology involving an absence of activity prior to examination may in fact reduce the amount of visible blood flow able to be detected, potentially reducing the sensitivity of these studies (Cook et al., 2005). Despite these findings and recommendations, there is currently no literature describing a standardised warm-up before imaging. Therefore, painful tendons need to be exercised to fully evaluate tendon vascularity and improve standardisation and sensitivity of assessment. However, the degree of exercise that is required to standardise a vascularity protocol is yet to be established (Cook et al., 2005).

It has been demonstrated that abnormal tendons on ultrasound, showing hypoechoic regions and diffuse thickening, have been reported among athletes
without pain (Cook et al., 1998). Additionally, associated Doppler flow may increase the risk of pain and pain may even be present in tendons with normal imaging (Cook et al., 1998; Malliaras et al., 2010; Ohberg et al., 2001). This supports the hypothesis by Syha et al. (2013) that relative changes within the tendon are more likely to be reflective of patient symptoms, and there is a need for quantitative parameters to characterise the intratendinous structure of the tendon, as this may be more sensitive to change than purely tendon diameter. As discussed previously, studies have shown that biochemical substances (including glutamate, substance P and calcitonin gene-related peptide) associated with neurovascular ingrowth may have a role in tendon pain and that these substances are also present in sonographically normal, asymptomatic tendons (Scott et al., 2013). This provides a potential pain mechanism for tendons that do not demonstrate any abnormality on grey-scale and/or Doppler ultrasound imaging (Malliaras et al., 2010).

The conflicting results on the relationship between sonographic grey-scale and Doppler findings with patient symptoms and/or outcomes are probably a result of a number of factors. Firstly, many of the studies have been performed on athletes from various sports, hence having different demands on their tendons and different rates of incidence. Secondly, what defines a significant hypoechoic area, diffuse thickening or significant neovascularity is not well defined, nor is it graded, or quantified. These highly variable methods of evaluation utilise subjective interpretation of the sonographic features. Finally, what constitutes significant symptoms is also subjective, with some studies using inability to compete, with others using clinical testing or questionnaires. Therefore, a standardised method for grading sonographic abnormalities needs to be developed and utilised, along with its association to a valid outcome measurement needs to be established to fill this gap in the literature.

In symptomatic tendons, ultrasound will almost always reveal structural abnormalities. These typically include localised tendon thickening with hypoechoic areas and increased vascularity, yet the relationship between these findings and
pain is not linear (Comin et al., 2013). Even though sonographic changes do not exactly correlate to symptoms, this is probably of little clinical importance, as once tendon-related pain has developed, patient symptoms and activity tolerance, not sonographic features, guide management. However, Drew et al. (2012) has suggested that imaging is useful in identifying diagnostic subtypes within tendinopathy and can lead to better targeting of treatment.

2.15 Imaging as a Predictor of Outcome

The use of ultrasound as a prognostic indicator for tendon symptomology and duration of symptoms has been a topic of debate (Comin et al., 2013). Studies within the literature investigating tendon structure are of cross-sectional design, meaning that it is unclear as to whether structural abnormalities on imaging predict future symptoms, or whether they are simply a normal physiological response to sporting load and not indicative of future complaints (McAuliffe et al., 2016).

When ultrasound is used as a predictive measure of symptoms, there is a weak association between sonographic abnormalities and the development of tendon pain. A longitudinal study of asymptomatic ballet dancers concluded that the presence of hypoechoic defects within the patellar or Achilles tendon was a weak predictor of tendon related pain and disability (Comin et al., 2013). This is consistent with Fredberg and Bolvig’s (2002) study on soccer players which found that only players with sonographically abnormal patellar tendons went on to develop symptoms during the season, whilst there was no occurrence of pain in players that were sonographically normal at the beginning of the season. Archambault et al. (1998) used a simple grading system to retrospectively grade Achilles tendinopathy on 33 patients with Achillodynia. This study concluded that patients with minimal sonographic change at initial presentation were more likely to recover fully and in a shorter period of time than patients with abnormal appearing tendons that were enlarged with hypoechoic areas. Bakkegaard et al. (2015) found that heterogeneous Achilles tendons (hyper and/or hypo-echoic changes) were a prognostic marker for poor outcome at 6-months following a
conservative strengthening management program. A recent systematic review and meta-analysis by McAuliffe et al. (2016) found asymptomatic Achilles tendons with abnormalities visualised using ultrasound hold a four-fold risk of developing tendinopathy in the future. Therefore, using ultrasound as a screening tool may identify athletes at risk of future symptoms, allowing activity modification and preventative programs to be implemented that may prevent occurrence (Comin et al., 2013). However, the evidence to support such strategies are lacking at this time (McAuliffe et al., 2016).

Since tendon abnormalities have been identified in a large percentage of asymptomatic individuals, it may not be warranted to intervene in all cases (Fredberg & Bolvig, 2002). Studies suggest that within certain subgroups, asymptomatic tendon abnormalities may be present in up to 59% of the population, particularly with increasing age and sporting endeavours (Docking et al., 2015). In fact, a study by Fredberg, Bolvig, and Andersen (2008) on elite soccer players found that prophylactic eccentric exercises in athletes with normal imaging did not reduce the risk of developing symptomatic patellar tendinopathy. Whilst in patients who presented with abnormal imaging at the start of the season, there was in fact an increased risk of developing symptoms after prophylactic exercises (Fredberg et al., 2008).

Inconsistencies between studies make it difficult to assess prognosis due to the lack of a uniform standard in the reporting of imaging findings. It has been postulated that tendon abnormalities in asymptomatic populations may simply indicate physiological structural adaptations to the loads placed on the tendon (McAuliffe et al., 2016). Within the literature, a poor correlation between sonographic findings and symptoms has been demonstrated, yet abnormal tendons, regardless of defining criteria used, are more likely to be symptomatic and are predictive of an increase in the incidence of future symptomatic tendinopathy (McAuliffe et al., 2016). Since structurally abnormal tendons have an increased incidence, but are not solely predictive, they should be treated as just one of many risk factors in the
development of symptomatic tendinopathy similar to load, anthropometric factors and genetics, rather than solely as a diagnostic feature (McAuliffe et al., 2016).

2.16 Healing Processes and Management
Although Achilles tendinopathy was originally considered an inflammatory process, many studies have conclusively shown that the degenerative pathology found is more akin to a failed healing response (Cook & Purdam, 2009). The most common form of tendon healing is by scarring, which is inferior to the tendon healing via regenerative processes (Jozsa & Kannus, 1997). Tendons heal in a similar manner to other soft tissues, which heal through three phases; inflammatory (1-7 days), proliferative (7-21 days), and remodelling (three weeks to one year) (Kader et al., 2002). Tendons however, are metabolically less active than bone and muscle, hence may take a longer time period to heal (Kader et al., 2002).

During the healing process, connective tissues rely on the proliferation of new blood vessels and fibroblasts to form granulation tissue. As the fibroblasts migrate into the wound, they undergo a period of intense mitotic activity with the secretion of extracellular matrix products, in particular type I and type III collagen and glycosaminoglycans (Jozsa & Kannus, 1997). This newly produced granulation tissue slowly develops into mature scar, with collagen maturation and remodelling occurring as the wound heals. This is a prolonged process in tendons due to fibroblasts synthesising type III collagen that is then slowly replaced by type 1 collagen over a period of several weeks as the tensile strength slowly increases (Jozsa & Kannus, 1997).

A feature and criticism of the use of imaging in individuals with tendinopathy is the poor correlation between abnormal imaging and symptoms (Docking et al., 2015). Due to the limited understanding and complex nature of tendon pain as previously mentioned, there is often a disconnect between pathological changes and pain. This also rings true for the imaging of healing tendons, as once a tendon undergoes degenerative tendinopathy, cell dysfunction and death results in the matrix being
unable to regain full structural integrity. Histopathologically this means that the tendon loses its capacity to fully recover; yet patients can often become asymptomatic and reach a full functional recovery (Cook & Purdam, 2009). Ohberg, Lorentzon, Alfredson, and Maffulli (2004) demonstrated that once Achilles tendon pain improved, the sonographic structure and vascularity improved to an extent, but some characteristics remain abnormal for several years. Shalabi, Kristoffersen-Wilberg, Svensson, Aspelin, and Movin (2004) reported a significant decrease in Achilles tendon volume and intratendinous signal on MRI in 25 patients following a 3-month eccentric loading program. However, while improvements in tendon structure were observed, the tendons did not return to normal on imaging. Similarly, a long-term follow-up on 20 patients from the same cohort reported no significant difference in tendon volume compared to baseline measures, despite improvements in pain and function (Gardin, Movin, Svensson, & Shalabi, 2010). A systematic review by Drew, Smith, Littlewood, and Sturrock (2014) found improvements in pain and function after exercise therapy were not mediated by changes in tendon structure. Importantly, these studies suggest that improvements in tendon structure, although associated with improved outcomes, are not a necessity for clinical improvements.

Research on pathological Achilles and patellar tendons using ultrasound tissue characterisation demonstrated an increase in the mean cross-sectional area of aligned fibrillar structure compared to structurally normal tendons (Docking & Cook, 2015). This has led the researchers to hypothesise that pathological tendons increase their size as a method to maintain aligned fibrillar structure to still tolerate load. They have also implied that this is an adaptation to load and that relative stability in tendon structure, rather than change towards normalisation, is linked to improved outcomes (Docking & Cook, 2015). Therefore, appropriate imaging should be used if clinically indicated to confirm the diagnosis of Achilles tendinopathy, however the applicability of imaging in grading clinical severity, assessing the response to therapy, or influencing management, is to be used with caution.
Management of tendinopathy is often trial and error based, usually involving controlled motion and exercise along with behaviour modification and correction of predisposing factors. These are the pinnacles of treatment, since the response of tendon tissue to mechanical loading is to increase metabolic and circulatory activity, as well as to increase extracellular matrix synthesis (Woo et al., 2008). The literature suggests that almost a quarter of Achilles tendinopathy patients fail conservative management requiring either significant activity modification or surgical intervention (Kader et al., 2002). However, new research in the realm of non-surgical treatment options and a better understanding of the pathophysiology of tendinopathy has significantly reduced this likelihood (Woo et al., 2008).

Benjamin (2002) has shown that loading a tendon is both anabolic and catabolic to the tendon on a cellular level and that repair and remodelling is slow. Work by Magnusson et al. (2010) has shown that tendons are metabolically active and that mechanical loading stimulates fibroblast activation that results in an acute collagen expression and stimulates collagen protein synthesis. This process has been termed mechanotransduction (Magnusson et al., 2010). Interestingly, it has been shown that the rate of collagen synthesis increases up to a certain point after appropriate tendon loading, and then levels off with increasing workload, indicating that there is a ceiling effect as to how much collagen can be synthesised (Magnusson et al., 2010). Habitual loading results in higher rates of collagen synthesis, both at rest and at the basal state due to the constant effect of loading from the previous 24-48 hours, resulting in tendon hypertrophy (Couppe et al., 2008).

Cook and Purdam (2009) recommend that interventions should be tailored to the pathology at hand and that applying a single intervention to all presentations is unlikely to be successful. Therefore, detailed sonographic assessment and reporting of Achilles pathology and potential complications to rehabilitation are essential to guide the type and timing of intervention to allow successful management of the patient. A discussion of the therapeutic management strategies used in Achilles tendinopathy will now be explored.
2.17 Passive Treatments
There are many conservative treatment options available for the management of Achilles tendinopathy, however the evidential basis for many of these therapies remains sparse. Even though conservative management is recommended in the preliminary stages, this has rarely been compared in randomised, prospective studies. Recent advancements in the treatment approaches and management of Achilles tendinopathy have in a large part come from studies that have correlated basic science principles with clinical observation (Brukner & Khan, 2009). The numerous conservative management options used by sports medicine practitioners include rest (complete or modified activity), orthotic therapy, pharmacological agents, and various electro-physical agents (therapeutic ultrasound, interferential, laser therapy), which are all aimed at controlling symptoms (Wijesekera et al., 2011). The goal of these treatments along with correcting etiological factors is to reduce inflammation and promote healing, however there is limited evidence to their effectiveness in humans as the majority of studies have been on animal models (Brukner & Khan, 2009). Since tendon loading stimulates collagen repair and remodelling, complete rest of an injured tendon can be detrimental (Maffulli et al., 2004). Therefore, modified rest, reducing activity at the injured site but allowing activity elsewhere has been recommended with a gradual return to full activity.

There are many passive or adjunct treatments advocated in the literature for the management of Achilles tendinopathy and a summary of the proposed mechanism of action and supporting evidence for each will now be presented. Due to the limited evidence supporting these therapies and the fact that no randomised controlled trials have been performed on these passive therapies; the following adjunct treatments (cryotherapy, biomechanical alterations, NSAIDs, ESWT and GTN) are listed below according to their potential impact to the tendon tissue.

2.17.1 Cryotherapy
Cryotherapy has been deemed a useful adjunct in the management of acute tendinopathy, due to it having an analgesic effect, reducing the metabolic rate of the
tendon and decreasing extravasation of blood and protein from the new capillaries found in tendon injuries (Jozsa & Kannus, 1997).

2.17.2 Biomechanical Alterations
Modification of foot posture in some patients can reduce pain and increase the load capacity of the tendon (McCrory et al., 1999). Manual therapies aimed at increasing joint range can result in a temporary increase of joint mobility and reduction in pain, whilst an orthosis that places the hindfoot in a neutral position may be beneficial (McCrory et al., 1999). A heel lift of 15mm or greater is classically used as an adjunct to the management of Achilles tendon pain by de-loading the tendon (Maffulli et al., 2014).

2.17.3 Non-Steroidal Anti-Inflammatory Drugs
Non-steroidal anti-inflammatory drugs (NSAIDs) are often used in the management of acute athletic injuries for analgesic purposes. On theoretical grounds, one would predict that the anti-inflammatory action of NSAIDs would have no therapeutic effect in tendinopathy due to the lack of inflammatory cells. Furthermore, the analgesic effect of NSAIDs may permit patients to ignore early symptoms, allowing further damage to the tendon to occur, thus delay healing. Although short-term symptomatic relief has been seen in acute tendinopathy, there is however no evidence to support that NSAIDs have any effect in chronic Achilles tendinopathy and may even impair tendon healing by inhibiting cell migration and proliferation (Tsai et al., 2007). It is believed that the small positive (short term) effect may only be due to the analgesic effect of NSAIDs (Zwiers, Wiegerinck, & Dijk, 2016).

2.17.4 Extracorporeal Shock Wave Therapy
Extracorporeal shock wave therapy (ESWT) is a treatment where acoustic shock waves are directed through the skin to the affected area, sometimes using ultrasound to detect the region of interest and optimally position the device. The mechanism of action is unknown, but it is speculated that the energy delivered may promote diffusion of cytokines across vessel walls, resulting in stimulation of the
healing cascade (Wijesekera et al., 2011). ESWT also has potential analgesic effects by disturbing sensory nerve fibres and creating changes in the dorsal root ganglia that potentially can induce a reduction in pain sensation (Zwiers et al., 2016). A randomised controlled trial by Rompe, Nafe, Furia, and Maffulli (2007) of 75 patients compared ESWT to eccentric loading and a wait-and-see policy for the treatment of mid-portion Achilles tendinopathy. This study found at 4-month follow-up that there was no difference in clinical outcome between those treated by ESWT and eccentric loading (Rompe et al., 2007). There was however, a significant benefit found in both of the therapy groups over the wait-and-see group. A subsequent study by Rompe, Furia, and Maffulli (2009) investigating the adjunctive use of ESWT in combination with eccentric loading found at 4-month follow-up, a greater improvement using ESWT with exercise over eccentric loading alone. Further studies have failed to show ESWT being equally beneficial to exercise therapy and other studies have shown no significant benefit using a longer-term follow-up (Scott et al., 2013).

2.17.5 Glyceryl Trinitrate

Topical glyceryl trinitrate (GTN), a prodrug of nitric oxide, is thought to induce tendon healing by stimulating collagen synthesis in fibroblasts (Langberg et al., 2007). Traditionally these transdermal patches are used for the management of ischemic heart disease for their vasodilatory effects, however the use of GTN transdermal patches has been suggested as an appropriate intervention for the management of Achilles tendinopathy (Alfredson & Cook, 2007). A double blind randomised trial by Paoloni, Appleyard, Nelson, and Murrell (2004) of 65 patients with chronic Achilles tendinopathy, compared the continuous application of a GTN patch to the tendon and eccentric training, with a placebo patch combined with eccentric training. At 6-month follow-up, they found a significant reduction in activity pain (VAS scores) in the GTN group compared to the placebo group. A similar study by Kane, Ismail, and Calder (2008) who randomised 40 patients to either GTN patch and daily exercises or sham patch and exercises, found at 6-months a significant improvement in pain and disability scores using the VAS.
ratings of the Ankle Osteoarthritis Scale. There was however, no significant
difference between groups in ether pain or disability scores. In addition, histological
examination of Achilles tendons of participants that failed treatment and required
surgery showed no difference between groups in either neovascularisation, collagen
synthesis or tenocyte stimulation after GTN therapy (Kane et al., 2008).

A known complication of GTN therapy is the side effect of headaches due to the
vasodilation of peripheral arteries and veins. Several subjects in both Paoloni et al.
(2004) and Kane et al. (2008)'s studies had to cease treatment due to these
'unacceptable' side effects. Given the lack of statistical benefit and risk of adverse
events and interactions with other medications, the use of topical glyceryl trinitrate
for the treatment of chronic tendinopathy is not recommended (Scott et al., 2013).

2.18 Exercise Therapy
Treatment for Achilles tendinopathy requires complex clinical reasoning with
reference to the pathoanatomical diagnosis, which ultrasound can readily make
(Scott et al., 2013). The rehabilitation for tendon pathology will vary considerably
depending on the site of pathology, stage of tendinopathy, functional assessment,
activity status of the person, contributing issues of the kinetic chain and co-
morbidities (Scott et al., 2013). Rehabilitation should be evidence based and
accurate ultrasound imaging can form an important part of the clinical decision-
making process.

Tendons are a mechanosensitive tissue, with recent literature reviews confirming
that the most important treatment modality is appropriate loading (Killian et al.,
2012; Magnusson et al., 2010). Published efficiency studies indicate that exercise
therapy alone results in improvement in 60-90% of cases, however this high success
rate cannot be expected in the usual clinical practice (Wetke, Johannsen, &
Langberg, 2015). Many of the studies involved elite athletes and motivated
researchers seeking high compliance rates. In the everyday clinical environment,
these ideal settings are unlikely to be met and often the percentage of patients
reaching complete resolution of symptoms is at the lower end of the range (Wetke et al., 2015).

Although tendon overload and overuse are commonly thought of as the primary driver for tendinopathy, exercise therapy can be used as a therapeutic measure to rehabilitate and help normalise the injured tendon (Scott et al., 2013). Tendon overload causes repetitive strain to the tendon, which overwhelms the tendons ability to cope and adapt to its stress and tension load environment, becoming pathological (Magnan et al., 2014). Management between load and load capacity is important in the prevention and management of tendinopathies (Cook & Purdam, 2009). In vivo studies on rat patellar tendons undergoing cyclic loading by Sun et al. (2008) have shown that lower strain levels produced a more favourable tissue deformation pattern than moderate or high strain along with the suppression of pro-inflammatory mediators and an increase in these substances in the higher strain groups. These in vivo models provide further histopathological and biochemical evidence to support different exercise loading interventions in various stages of tendinopathy.

It is well known that well-structured, long-term exercise, within a physiological range does not harm the tendon, but in fact reinforces it by stimulating production of new collagen fibres (Abate et al., 2009). A study by Langberg et al. (2007) showed that after exercise, both synthesis and deregulation of collagen are increased, but collagen synthesis prevails and persists longer than collagen degradation. This leads to tendon tissue becoming larger, having an increase in its tensile strength and elastic stiffness, hence becoming more resistant to injury (Abate et al., 2009). There is also the release of inflammatory and growth substances, along with enzymes that are important in regulating cell activity and matrix degradation, with roles in fibre growth and development (Abate et al., 2009).

Exercise therapy has been shown to have an analgesic effect on the tendinopathic tendon, with a recent study by Rio et al. (2015) demonstrating that isometric
exercise can immediately reduce patellar tendon pain and increase maximal voluntary isometric contraction, with the effect sustained for at least 45-minutes. It is believed that cortical changes and motor neurons pool recruitment, and/or changes at a tissue level are the underlying mechanisms responsible for the changes in pain (Rio et al., 2015).

Historically, eccentric exercise therapy has been based on the recommendation by Curwin and Stanish (1984) who stressed the importance of eccentric training as part of the rehabilitation process for tendon injuries and demonstrated positive outcomes from a 6-week program of progressive tendon load. From this framework, Alfredson, Pietila, Jonsson, and Lorentzon (1998) adapted this program and scientifically evaluated eccentric calf muscle training for mid-portion Achilles tendinopathy. Since the development of Alfredson’s program, this model has been the most widely used exercise intervention with the most evidence of benefit of any of the conservative management options (Wheeler, 2014). The benefits associated with exercise therapy have been seen in both athletic and non-athletic populations and can lead to both a decrease in the abnormal thickening and a degree of normalisation of the tendon architecture visible on ultrasound (Ohberg et al., 2004). Eccentric exercises have been proposed to promote collagen fibre cross-link formation and facilitate tendon remodelling at a greater rate than concentric loading. In the Alfredson program, patients have to perform eccentric heel drops on the affected leg and use the non-effected leg to concentrically return to the starting position. The exercise is repeated for three sets of 15 repetitions and is performed with both the knee bent and knee straight. This is performed twice a day for a period of 12 weeks, with load being increased, guided by the pain response during exercise. This program is effective when other conservative treatments have failed (rest, NSAID’s, orthoses, physical therapy) and has a reported success rate of approximately 90% in patients who are compliant with the program (Alfredson et al., 1998).
However, a recent review by Habets and van Cingel (2014) could not draw a conclusion as to the most effective exercise prescription for Achilles tendinopathy. This was due to the various studies assessed lacking detail on the methodology used for training parameters and compliance, along with heterogeneity in study populations (Habets & van Cingel, 2014). Also protocols other than those of Alfredson et al. (1998) have achieved similar results, but have not been as rigorously evaluated (Habets & van Cingel, 2014). Eccentric exercises may have important implications for tendinopathy including modulation of the neurological stretch response, perturbations of tendon force, increased shear force between the tendon and peritendinous tissues, pain modulation and adaption of mechanotransduction signalling in passive tendon structures (Ganderton et al., 2015).

Although load-based exercise training has shown favourable results; the optimum training regime to deliver the ideal dosage remains unknown. While there exists evidence for the use of eccentric exercise, it is not recommended in isolation as it fails to address strength and kinetic chain deficits (Ganderton et al., 2015). In general, a fine balance must be met between under stimulating and overloading the healing tendon (Killian et al., 2012). Generic rehabilitation prescriptions based solely on evidence-based medicine are unlikely to achieve best results due to the various inter and intra-tendinous pathologies that may be present and can leave the individual vulnerable to reoccurrence. In view of this, research by Magnusson et al. (2010) confirms that appropriate loading is the most important modality in tendon rehabilitation and is the only stimulus with the capacity to positively affect the tendon matrix. Treatment should therefore be individualised, with practitioners choosing exercises and progressions based on the patient’s capability to allow for an optimal exercise load setting without exacerbating pain (Coombs et al., 2013).

Exercise prescription can target matrix reorganisation and collagen synthesis, reduce tenocyte activity, effect tendon compliance and have an analgesic effect (Scott et al., 2013). Cook and Purdam’s (2009) tendinopathy continuum model
provides a reasoned basis for applying targeted rehabilitation and ultrasound can help to establish the clinical staging. This rehabilitation program should be tailored to address identified impairments including muscle bulk asymmetries, kinetic chain dysfunction, tolerance of energy storage and release loads in the Achilles, then progress towards movements and activities relevant to the individual’s sport or daily activities (Ganderton et al., 2015). Whilst exercise is the cornerstone of rehabilitation for all stages of tendinopathy, it should be individually applied according to presentation and stage. For example, reactive tendinopathy requires relative rest from high tendon load activities. In contrast dysrepair and degenerative tendinopathy require progressive loading to moderate cell response and address functional deficits (Ganderton et al., 2015). Hence an individualised holistic program based on tendon load management should be applied to optimise tendon remodelling and recovery, with accurate ultrasound imaging being able to assist in staging treatment.

2.19 Injection Therapy
Injection therapy is often offered when conservative treatment fails, but only sparse scientific evidence exists for any specific injection treatment (Boesen et al., 2014). There are a variety of different injectable therapies currently being employed for the treatment of tendinopathy, including glucocorticoid, prolotherapy, sclerotherapy, protease inhibitor injections, autologous blood, platelet rich plasma and tenocytes. Some study protocols for injection therapy opt for a single injection while others require a series of injections, separated by a defined time period with little evidential basis as to the rationale behind these differing methodologies (Scott et al., 2013). A recent systematic review by Kearney et al. (2015) on all injection therapies for the management of Achilles tendinopathy found insufficient evidence to recommend any specific individual therapy. Despite this, glucocorticoids remain the most widely used injectable therapy for a variety of tendinopathies (Scott et al., 2013). The injections are usually administered with local anaesthetic and best practice dictates that ultrasound be used to guide needle placement to the desired area; be that either intratendinously, peritendinously or into bursa (Fredberg et al.,
If repeat glucocorticoid injections are required, it has been recommended that a 4-week interval between subsequent injections be maintained due to the long-acting effects of glucocorticoid, giving the risk of over-treating by providing a potentially unnecessary intervention (Fredberg et al., 2004). For other injection therapies that may require repeat injections, there are no guidelines as to the recommended time interval between subsequent injections and this is left to the discretion of the treating clinician (Longo et al., 2009).

2.20 Glucocorticoid Injections

Controversy exists regarding the use of glucocorticoid steroidal injections in the management of tendinopathy (Scott et al., 2013). In other regions of the body, glucocorticoid injections have been shown to have the potential to reduce tensile strength and healing properties of tendons (Wong et al., 2004). While glucocorticoid injections have been shown to have short-term pain-relieving effects, commonly little or no improvements are seen in the longer-term. (Burke & Adler, 2016; Smidt et al., 2002). In the Achilles, this short-term improvement has been demonstrated by Fredberg et al. (2004) as a reduction in walking pain along with a reduction in the anterior-posterior thickness of the tendon shown sonographically. Even though these controversies exist, glucocorticoid injections are the most common, non-surgical intervention used in the management of recalcitrant tendinopathies (Scott et al., 2013).

The mechanism of action of glucocorticoids is through the inhibition of inflammation-associated molecules, including cytokines, chemokines and arachidonic acid metabolites, along with a reduction of adhesion molecules involved in nociceptive pathways (Burke & Adler, 2016). A histological study of rotator cuff tears by Matthews, Hand, Rees, Athanasou, and Carr (2006) suggests that the use of intra-tendinous cortisone injections for small rotator cuff tears might in fact be detrimental, potentially reducing their ability to heal. There is evidence that intratendinous injections into the common extensor tendon of the elbow can lead to cell death and atrophy via a reduction in collagen synthesis (Nirschl, 1992). Hugate,
Pennypacker, Saunders, and Juliano (2004) found intra-tendinous injections of glucocorticoid into rabbit Achilles tendons can cause up to a 20% reduction in the tensile strength of the tendon, seven weeks after injection. There are numerous in vitro animal studies that have commented on the reduction of the mechanical tensile strength of collagen fibres, however these studies have mainly been conducted on whole tendon and mostly address cellular responses, therefore are not necessarily applicable to the tensile bearing unit of the tendon (Haraldsson et al., 2006). Additionally, some studies have failed to show this loss of mechanical strength in animal studies (Haraldsson et al., 2006). Finally, many studies incubate animal sections in a bath of corticosteroid for up to 7-days, making the translation of these results to human studies involving injection therapy being questionable at best (Haraldsson et al., 2006).

There have been limited human studies on the cellular and mechanical effects of glucocorticoids. Small in vitro studies suggest glucocorticoids can reportedly affect tenocyte proliferation and viability, collagen production and deposition, scar formation, and synthesis of extracellular matrix products (Wong, Tang, Fu, Lee, & Chan, 2004). This has the potential to reduce tendinous tissue strength (Wong et al., 2004). Conversely, a study by Kongsgaard et al. (2009) showed that injections peritendinously and in moderate concentrations, did not affect patellar tendon mechanical properties, with an absence of deleterious effects on the tendinous tissues. The anti-inflammatory effects of steroids are also potentially advantageous in reducing paratendinous abnormalities (Kongsgaard et al., 2009).

A systematic review on glucocorticoid injections and tendons of both humans and animals by Dean et al. (2014) concluded that the local administration of glucocorticoids has a significant negative effect on tendon cells in vitro, with a reduction in the mechanical properties of the tendon. Yet most of the 14 human studies that were included in the review were not radiologically guided, which is inconsistent with current-day best practice. There were gross discrepancies of the type and dose of injectate and a limited description as to whether the injection was
placed inter or peri-tendinously, limiting the applicability of these results. Dean et al. (2014) also noted that there is a clear role for glucocorticoid injections in the treatment for tendinopathy, but it is important to consider the potential negative effects of these injections and this must be made on a case-by-case basis. Consideration must be given regarding the individual patient characteristics and pathogenesis of the disease as to whether this treatment choice is appropriate for the stage and type of tendinopathy present (Dean et al., 2014).

Previous studies have shown that the outcome associated with glucocorticoid injections elsewhere in the body, either into bursa or joint space, are dependent on the correct placement of the needle (Fredberg et al., 2004). Many studies do not dictate whether injections are performed blind or radiologically guided to confirm needle placement, yet results are often compared (Dean et al., 2014). Ultrasound is an ideally suited tool to guide injection therapy and the most frequently used in current practice. There have been no studies to compare blind versus image-guided injections into or around the Achilles tendon, yet one would argue that the positioning of the injectate would affect outcome (Fredberg et al., 2004). This restricts the ability to compare image-guided versus non-guided injection studies.

The debate regarding glucocorticoid injections for the management of Achilles tendinopathy continues, with conflicting results demonstrated within the literature. A randomised controlled trial by Fredberg et al. (2004) demonstrated positive results. However, previous literature by DaCruz, Geeson, Allen, and Phair (1998) concluded that an unguided ‘peritendinous’ glucocorticoid injection made no difference compared to placebo in palpation squeeze test or return to activity at 12-weeks and advocated invasive surgical intervention. An earlier literature review by Shrier, Matheson, and Kohl (1996) found only two rigorous studies on peritendinous Achilles injections, concluding that there was no significant benefit over placebo in preventing recurrence, yet cited the alarming lack of literature and small sample sizes. These studies demonstrate poor methodology and outcome measures, limited detailed diagnosis with potential sub-groups not being identified...
and accounted for, along with injection therapy not being standardised nor image
guided. To date, there has been limited further research in this field and further
studies need to be performed to explore and justify the use of glucocorticoids in the
management of Achilles tendinopathy.

Many clinicians advise against injection of glucocorticoid in or around the Achilles
tendon due to the risk of rupture, even though this risk has not been substantiated
in large studies (Speed, 2007). This belief of potential rupture probably has its
origins from case reports on non-guided injections and case series studies of oral
corticosteroid use. Clinical literature consistently shows this rupture hypothesis to
be false, yet this theory continues to be perpetuated within current literature
(Shrier et al., 1996, Speed, 2007). To what extent the few documented tendon
ruptures post injection can be attributed to the steroid treatment itself and/or
progression of the tendinopathy disease remains unknown (Haraldson et al., 1994).
The other risks associated with glucocorticoid injections including fat atrophy and
skin discolouration are well recognised (Speed, 2007). There is however, no
scientific data to suggest that a peritendinous injection of steroid would harm the
tendon if correct indication and correct technique are used (Fredberg et al., 2004).
Animal studies have shown that peritendinous injections have no effect on tendon
strength and prevent peritendinous adhesions (Shrier et al., 1996). In fact,
peritendinous corticosteroid injection to the Achilles tendon has been advocated by
Alfredson and Cook (2007) as a worthwhile adjunct to a considered management
program, used to relieve pain, allowing the patient to undertake and progress in a
loading exercise program.

It is well accepted that tendinopathy is a degenerative process (Kader et al., 2002).
However, it is likely that elements of the inflammatory response play a role in the
progression and continuation of tendon dysrepair (Rees et al., 2014). Schubert,
Weidler, Lerch, Hofstadter, and Straub (2005) demonstrated the presence of
macrophages and T and B lymphocytes in chronic Achilles tendinopathy using
primary monoclonal antibodies. Whilst a review by Rees et al. (2014) using
advanced immunohistochemistry and gene expression analysis demonstrated increased levels of macrophage-derived interleukin-1, cyclo-oxygenase, isoforms of transforming growth factor-B and increased substance P, along with extensive inflammatory changes in the peritendinous tissues of chronically pathological tendons. These studies confirm the presence of inflammatory cells associated with chronic tendinopathy, which has led to an increased emphasis being placed on treatments that address these inflammatory elements.

Although inflammation is not the dominant pathology in all cases, anti-inflammatory strategies may be therapeutic to the chronically pathological tendon, especially to the peritendinous tissues (Burke & Adler, 2016). Glucocorticoid is known to suppress inflammation by reducing macrophage activity and reducing angiogenesis (Burke & Adler, 2016; Rhen & Cidlowski, 2005). This catabolic action of glucocorticoids can also induce a direct vasoconstrictor effect on smooth muscle cells, suppress the production of vasodilators (e.g. nitric oxide) and affect tenocyte production and phagocytic activity of various extracellular matrix components (Wong et al., 2004). These characteristics of glucocorticoid on tendon tissue have the ability to reduce the haphazard proliferation of tenocytes and disorganisation of collagen, reducing tendon abnormalities (Rees et al., 2014). This concept was postulated by Fredberg et al. (2004) who claimed that the changes involved in tendinopathy could be both inflammatory and degenerative in nature, and that glucocorticoid could have a role to play in reducing both of these components. Their study found that sonographically guided peritendinous injections of steroid around chronically pathological Achilles and patellar tendons led to an effective reduction of pain along with reducing thickness and sonographic intra-tendinous abnormalities (Fredberg et al., 2004).

There is substantial evidence that glucocorticoids can be effective in chronic tendinopathy by relieving pain, reducing swelling and improving function in the short-term, although this comes at greater risk of reoccurrence in the long-term (Rees et al., 2014). This evidence of reoccurrence is based on the findings of Bisset
et al. (2006) in the lateral epicondylalgia population on patients who received a cortisone injection as the sole intervention, having a higher risk of relapse (72%) versus a wait-and-see control group (9%). Similarly, a single glucocorticoid injection for lateral epicondylalgia did not provide a significant long-term benefit when compared to placebo, non-steroidal anti-inflammatory drugs or physiotherapy, in a randomised controlled trial by Smidt et al. (2002). This is consistent with findings observed by Kongsgaard et al. (2009) on patellar tendons comparing cortisone injection to eccentric decline squat training and heavy slow resistance training, finding that cortisone has good short-term but poorer long-term effects in patellar tendinopathy patients when used as the sole therapy. Coombs et al. (2013) compared corticosteroid injection to placebo (saline injection) in conjunction with physiotherapy exercises for patients with a clinical diagnosis of lateral epicondylalgia. This study concluded that the use of corticosteroid injection versus placebo injection resulted in worse clinical outcomes after 1-year, with physiotherapy not resulting in any significant differences. These patients had no imaging to confirm the diagnosis or identification of potential confounding factors; along with all injections being performed blind (without image guidance) by five different general practitioners at the site of maximal palpable tenderness. This unguided method of injection technique is against current day best practice as there is no way of knowing if the injections were placed at the site of maximal structural changes, intra-tendinously, peri-tendinously, intra-articularly or subcutaneously.

The issues that some clinicians have related to corticosteroid injections are therefore less that they do not work, but more that the benefits are generally of short duration and that there is the hypothetical risk of weakening of the structural integrity of the tendon in the long-term (Rees et al., 2014). Fredberg et al. (2004) reported that the greatest ‘risk’ of glucocorticoid injections is that an athlete with chronic pain, after an injury period of several months, may be pain-free after a few weeks. It has been postulated that the often-seen relapse of symptoms in patients is due to the combination of steroids with too aggressive rehabilitation or too early
return to full activity on a relatively deconditioned tendon (van Ark, Zwerver, & van Den Akker-Scheek, 2011).

Despite the widespread use of glucocorticoid injection therapy, the evidence supporting this method remains uncertain and the actual physiology of treatment, unclear (Scott et al., 2013). Many of the studies on the efficiency of glucocorticoid injections for Achilles, rotator cuff, patellar and common extensor tendinopathy have been limited by the actual methodology of the interventional treatment, quantity of injectate, heterogeneity of patient cohorts and the timing and type of outcome measures used. Despite the heterogeneity in the quality of research available, the overall consensus suggests that the majority of patients experience short-term improvement in pain and or function, however, remain at higher risk of relapse in the medium to long-term (Scott et al., 2013).

2.21 Local Anaesthetics

Peritendinous injections of local anaesthetics are often combined with glucocorticoid steroid injections for the treatment and management of tendinopathies (Piper et al., 2012). Although this technique is commonly employed to manage and reduce the potential acute ‘flare’ of symptoms associated with injection therapies, there is little knowledge regarding the long-term safety and efficiency of this technique (Piper et al., 2012). Local anaesthetic toxicity has been established for many types of cells including neurons, myocytes and chondrocytes, with damage to cells being shown to occur with anaesthetic agents alone or in combination with corticosteroids (Nuelle, Cook, Stoker, Cook, & Sherman, 2017). While there have been many recent investigations demonstrating toxicity of local anaesthetics and glucocorticoids in other cell types, there have been a limited number of studies on the effects to tenocytes and tendons (Nuelle et al., 2017). In vitro studies suggest there is a dose-dependent relationship between local anaesthetic concentration and tenocyte toxicity for all common local anaesthetics (lidocaine, ropivacaine, bupivacaine) (Nuelle et al., 2017; Piper et al., 2012).
Although there are conflicting results regarding glucocorticoids and the potential detrimental effects on tendons and tenocytes, glucocorticoids may potentiate the deleterious effects of local anaesthetics to tendons (Piper et al., 2012; Wong et al., 2004). This is important clinically as most injections are performed as a combination of local anaesthetic and steroid. Therefore, glucocorticoid injections should be combined (if necessary) with the lowest concentration of local anaesthetics to reduce any potential negative effects on tenocyte cell proliferation and viability.

2.22 High-volume Injections

While the source of achillodynia is yet to be clearly established, some authors have hypothesised that the main cause of pain originates from the peritendinous tissues rather than the tendon itself (Scott et al., 2013). Neovascularity is often present in tendinopathic tendons, causing the ingrowth of sensory and sympathetic nerves from the paratenon to accompany these neovessels. Since these nerves can release nociceptive substances, they may be one of the primary sources of pain (van Sterkenburg & van Dijk, 2011). There is also supporting evidence that there is nerve-mediated dysregulation of tendon metabolism, with immunohistochemical and gene expression analysis studies showing a marked increase in expression of vascular endothelial growth factor (VEGF) within tendinopathic tendons. VGEF is one of the key molecules involved in driving vascular hyperplasia and this angiofibroblastic change has been highlighted as the main feature in tendinopathy (Vasta et al., 2016). There is evidence of neurotransmitters such as substance P, nitric oxide and calcitonin gene-related peptide (CGRP) having a role in continuing the pathogenesis of tendinopathy (Vasta et al., 2016). Additionally, during the tendinopathy process, the paratenon often becomes thickened and fibrotic. This can be a source of extrinsic compression, further negatively impacting on the tendon and advancing the tendinopathy process (Cook & Purdam, 2012).

Despite continual debate and a number of interventional trials and reviews, it is still unclear which injectable therapy is best to use in patients with recalcitrant Achilles
tendinopathy. There is however, emerging evidence from small trials that high-volume injections are a superior option (Barker-Davies et al., 2017). The aim of high-volume injections is to mechanically disrupt, by stretching, breaking or occluding the neurovascular bundles growing from the paratenon into the tendon; effectively de-innervating the tendon. This has the potential to reduce the proliferation of fibroblasts, angiogenesis, vascular activation and pain transmission within the tendon; the core components for the pathogenesis of tendinopathy (Boesen et al., 2017; Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013; Resteghini & Yeoh 2012; Wheeler, 2014). Along with this the tendon is effectively decompressed from the constraints of paratenon constriction on an already enlarged tendon. Doppler ultrasound consistently shows the immediate disappearance of neovascularisation after high-volume injection; however a component of this effect may be the result of the extrinsic compressive effect of the volume of injectate collapsing the small vessels (van Ark et al., 2011).

A range of high-volume image-guided injection therapies have been reported, using a large overall volume of injectate, typically between 30-50mL (Wheeler, Mahadevan, Bhatt, & Bhatia, 2016). The injectate mixture is composed of local anaesthetic, sterile saline and glucocorticoid, with several small case studies showing promising results for mid-portion Achilles tendinopathy. A case series by Chan et al. (2008) and preliminary studies by Humphrey et al. (2010) have shown that high-volume peritendinous injections decrease pain and improve function in both the short and long-term. In these studies, a mixture of 10mL 0.5% bupivacaine hydrochloride and 25mg of hydrocortisone acetate was injected. This was then immediately followed by 40mL of normal saline. A study by Boesen et al. (2014) using the same technique found a significant improvement in VISA-A score at both 12 and 24-week follow-up along with a decrease in tendon thickness. These improvements were significantly greater than both a control group and comparative platelet-rich plasma injection group when combined with an eccentric loading program. Another study by Maffulli et al. (2013) substituted hydrocortisone for aprotinin, a broad-spectrum serine protease inhibitor. At 1-year follow up, there
was a statistically significant and clinically relevant improvement in VISA-A score. However, in recent times aprotinin has been withdrawn worldwide following concerns about postoperative thrombosis and organ dysfunctions. The author promoting this therapy has now changed to using hydrocortisone acetate in their day-to-day practice (Maffulli et al., 2013).

Given several studies have resulted in comparative effects of high-volume injections, regardless of the substance injected; either aprotinin or hydrocortisone acetate, it has been proposed by Maffulli et al. (2013) that the positive results from high-volume injections possibly arise from the mechanical effect of the injectate, rather than the drugs used. A small case series by Wheeler (2014) followed 14 patients whom were injected with 10mL 1% lidocaine and 40mL saline but without corticosteroid or aprotinin. This study observed an improvement in VISA-A and pain rating with benefit continuing or increasing over the early and medium periods, which was sustained for most patients at a year or more (Wheeler, 2014). This adds further support to the theory that high-volume injections, regardless of injectate and volume used, are an effective procedure for the management of recalcitrant Achilles tendinopathy. However, due to different case series using different protocols, with differing injection regimens, medications, follow-up periods and protocols; direct comparison between methods is difficult and no technique has demonstrated superiority. To date, only one randomised controlled trial has subjected this interventional technique to comparison with sham injection and exercise therapy, finding high-volume injection therapy to be superior to eccentric exercise alone (Boesen et al., 2017).

2.23 Concurrent Therapies
Although the research literature suggests that between 60-90% of patients will respond positively to exercise therapy, none of the efficacy studies offer solutions as how to manage the non-responding patient (Wetke et al., 2015). In the clinical situation, many clinicians opt for glucocorticoid injections as an adjunct to
treatment programs to allow patients to progress with rehabilitation (Alfredson & Cook, 2007).

Many studies solely reporting on injection therapy are of low quality. There are very few randomised controlled trials and even fewer studies comparing injection therapies to placebo or a control group within the Achilles tendinopathy population (van Ark et al., 2011). The studies that have used a control group, use a variable control, ranging from no treatment, local anaesthetic injection, to exercise therapy of various forms including loading exercises, paced walking and exercise classes (van Ark et al., 2011). This heterogeneity of a control group leaves one to speculate the authenticity of a true control. Many studies also incorporate concurrent therapies as this is proposed to be a useful adjunct to injection therapy and makes clinical sense (Alfredson & Cook, 2007). If the underlying biomechanical and extrinsic factors are not corrected along with appropriate load management, then the same driving forces that created tendinopathy will remain and symptoms will reoccur. As tendon healing requires a complex interaction, where mechanical and chemical factors work together, a multimodal intervention involving glucocorticoid injection and exercise therapy is recommended in patients with recalcitrant tendinopathy (van Ark et al., 2011). Fredberg et al. (2004) recommends 3-6 months of rehabilitation after local steroid injection for chronic Achilles tendinopathy to achieve optimal results.

In reviewing the literature where concurrent therapies (injection therapy and loading exercises) have been used, it is questionable as to whether the possible effects can be ascribed to the injection or physical therapy (van Ark et al., 2011). No studies were found where an injection technique used in conjunction with physical therapy is compared to physical therapy alone in the management of Achilles tendinopathy. However, most patients seek injection therapy when their symptoms have failed to improve after conservative management including exercise therapy. Therefore, injection therapy in conjunction with exercise therapy may be beneficial in these patients, potentially leading to improved outcomes (van Ark et al., 2011). A
study by Boesen et al. (2014) compared the effect of high-volume injections or platelet rich plasma in combination with eccentric training to placebo treatment (sham injections and exercise training) finding both active intervention groups had greater efficiency in improving activity and reducing symptoms than the control group. In the lateral epicondylalgia population, Coombes, Bisset, Brooks, Khan, and Vicenzino (2013) found glucocorticoid injections resulted in inferior long-term effects when compared to exercise or wait and see grouping. At long-term follow-up, no difference in outcome was seen regarding whether or not physiotherapy exercises were performed concurrently with the glucocorticoid injection (Coombes et al., 2013). This study, with its randomised controlled clinical design, left no option for individualised treatment options, including offering injection therapy for patients who had failed conservative uni-modal management (Coombes et al., 2013). A study by Wetke et al. (2015) on symptomatic Achilles tendinopathy followed 93 subjects as they undertook a concentric/eccentric exercise program with slow and cautious progression. If the patients were unable to commence or progress with the exercise program due to pain they were offered a peritendinous glucocorticoid injection (between the anterior tendon and fat-pad at site of maximum sonographic pathology) to assist in progressing their rehabilitation. Patients were offered injection and not required to partake in injection therapy if they declined, but were still invited to continue with the study. Patients were offered up to 3 injections with an interval of at least 4 weeks between injections. They found highly significant short-term improvements after injection therapy when used for selected patients who did not respond to conservative therapy alone, as well as good long-term effects at 6-month follow up (94% improved and 77% reported an excellent or good result). These results led the authors to recommend the use of glucocorticoid injections in Achilles tendinopathy patients if exercise therapy alone doesn’t lead to improvements in pain and function (Wetke et al., 2015).

Although multiple studies have prescribed exercise therapy programs in conjunction with injection therapy, large differences exist between the types and
volume of exercise prescribed (van Ark et al., 2011). Exercise therapy should be evidence-based, targeted and patient specific (Magnusson et al., 2010). There is no ‘one size fits all’ approach to load based exercise rehabilitation, as the mechanical requirements of a tendon will vary greatly from a sedentary patient to an elite athlete.

2.24 Other Injection Therapies
Proliferative therapy (prolotherapy), involves injecting hypertonic glucose and local anaesthetic within the tendon substance. The aim of prolotherapy is to promote a local inflammatory repair response and it has evidence of a moderate-level improvement in Achilles tendon pain in the medium-term (Coombes, Bisset, & Vicenzino, 2010). This method of treatment utilises ultrasound to guide irritating agents into the abnormal areas within the tendon. This is thought to initiate an inflammatory response causing fibroblast proliferation and subsequent collagen production, resulting in increased tendon strength (Coombes et al., 2010).

The injectate, hypertonic glucose, acts by causing an osmotic shock to cells leading to the release of pro-inflammatory substances (Zwiers et al., 2016). This creates a similar cellular response to dry needling of the tendon where repeated lancing of the tendon aimed to incite internal haemorrhage, a consequent inflammatory reaction and formation of granulation tissue (Wijesekera et al., 2011). Prolotherapy injections into the Achilles tendon have been shown to be no more effective than eccentric exercise alone (Coombes et al., 2010). The level of evidence for prolotherapy is similar to that of sclerotherapy, which involves using colour or power Doppler ultrasound to guide polidocanol (aethoxysklerol) injections into areas of the tendon that have increased Doppler signal. This treatment modality is based on the presence of tendon neovascularity on Doppler ultrasound, which is a common feature of painful Achilles tendons but not of those that are pain free (Ohberg & Alfredson, 2002). Some studies have implicated neovascularisation as a possible indirect cause of symptoms of Achilles tendinopathy and have hypothesised that the destruction of these vessels and accompanying nerves may
lead to a reduction in symptoms (Zwiers et al., 2016). Ohberg and Alfredson (2002) performed a series of studies using Doppler ultrasound to guide polidocanol (a sclerosing agent) into areas of increased Doppler signal, just outside the ventral tendon. These areas of increased Doppler signal represent regions of neovascularity and the aim of this intervention is to cause vascular sclerosis and neurolysis of these abnormally proliferative structures. These studies have shown moderate short to medium-term benefits in small patient groups (Coombes et al., 2010).

Subsequently, Alfredson and Ohberg (2005) performed a randomised controlled, double-blind trial to evaluate whether there was a difference in effect between sclerosing injections and local anaesthetic injections alone. After a 3-month follow-up, 5 out of 10 patients treated with a maximum of two polidocanol injections were satisfied with treatment with a significant reduction in pain, while no patients in the control group (local anaesthetic alone) were satisfied. Upon completion of the study, further treatment with additional polidocanol injections elicited a successful outcome in 10 out of 10 participants in the polidocanol group, and after cross-over into the polidocanol treatment group, 9 out of 10 in the control group were satisfied with outcomes.

Although there are no evidence-based studies discouraging these injection techniques, in recent times within the clinical setting, both sclerosing and prolotherapy interventional techniques have lost favour due to the inflammatory reaction that they cause, leading to worsening of the patient’s symptoms and reducing function in the short-term, without any significant benefit in the long-term (Scott et al., 2013). These injection techniques usually require repeat treatments and have shown to have no advantage over other injection therapies in either the short or long-term, with a review by Coombes et al. (2010) finding prolotherapy injection therapy to be no more effective than a placebo injection of saline.

Biological therapies have gathered popularity in recent times, including autologous blood and especially platelet-rich plasma (PRP) injections. Autologous blood
injections are principally composed of the patient’s own red blood cells and aim to enhance tendon healing via collagen regeneration and stimulation through a fibroblastic response (Scott et al., 2013). Whereas PRP is prepared from autologous whole blood, which is centrifuged to selectively remove red blood cells and only the platelet rich component is used. PRP with a platelet concentration of at least 1,000,000/uL in 5mL of plasma is associated with enhancement of healing within in vitro studies and is suggested, in theory, to be superior to autologous blood (Foster, Puskas, Mandelbaum, Gerhardt, & Rodeo, 2009). The aim of both methods of biotherapy is to deliver a wide array of bioactive substances to the tendinopathic area. The theory of this is similar to that of prolotherapy, however the mechanism of healing is via the body’s normal physiological pathways, involving platelets and growth factors, rather than via an inflammatory response to a noxious stimulus (Scott et al., 2013).

The proposed beneficial physiology behind biological injectates is to heal the tendon via the typical wound-healing course, by inducing an inflammatory phase, that will be followed by proliferative and then remodelling phases (Killian et al., 2012). The introduction of bioactive agents aims to create a controlled inflammatory response via the introduction of platelets, macrophages, monocytes and neutrophils, which in turn, causes the release of chemotactic agents that recruit blood vessels, fibroblasts and intrinsic tenocytes. This then leads to the proliferative phase where fibroblasts multiply and begin to produce collagen. After this, during the remodelling phase, cellularity decreases and collagen is cross-linked and orientated parallel to the direction of muscle force and ultimately an improvement in tissue function may occur (Killian et al., 2012). The precise role of the ‘cocktail’ of growth factors that are introduced with the application of PRP is not yet clear, although it seems that among other growth factors, platelet-derived growth factor (PDGF), transforming growth factor β (TGF-β) and vascular endothelial growth factor (VEGF) promote tissue healing (van Ark et al., 2011).
The goal of biological injectates is to enhance tissue healing and have this occur at a faster rate. Although commonly used in clinical practice, there is however conflicting evidence and no general consensus in the literature for support of biological therapies in tendinopathy (Scott et al., 2013). A double-blind randomised placebo controlled trial showed no difference between 54 chronic Achilles tendinopathy patients who were treated with an eccentric strengthening protocol plus either PRP or saline injection at either 24-week or 1-year follow up (de Jonge et al., 2011; de Vos et al., 2010). However, at both 24-week and 1-year follow-up, both groups had significant improvements in pain, function and structure following a single PRP injection, yet there was no significant difference between PRP and saline groups. These results led the authors to conclude that any intervention resulted in long-term improvements (de Jonge et al., 2011; de Vos et al., 2010). A smaller randomised controlled trial by Pearson, Rowlands, and Higet (2012) compared eccentric strength training to blind intra-tendinous autologous blood injections in addition to eccentric training and found no significant benefit. When autologous blood is injected unguided into the peritendinous tissues in conjunction with eccentric exercise therapy, it has been shown by Bell, Fulcher, Rowlands, and Kerse (2014) to have no additional benefit. However, studies by others on regenerative therapies have found variable outcomes, ranging from improvements in function and structure to a gross reduction in both of these entities (Scott et al., 2013).

This lack of supporting evidence for the use of biological injectates in the management of Achilles tendinopathy is conceivably due to the lack of standardisation in the quantification and methodology of the preparation of the product along with the various administration techniques. Several studies use differing follow-up periods and outcome measurements, yet comparisons are often made on studies using these differing methodologies (Burke & Adler, 2016). There are differing methods to prepare PRP that are used in clinical practice, resulting in different volumes and concentrations of platelets, white blood cells and red blood cells, with no method claiming superiority in the clinical setting (Burke & Adler, 2016). Along with this, the literature is of high risk of potential bias, with variability
of comparators and many of the outcome measures used in the studies being of low quality (Moraes, Lenza, Tamaoki, Faloppa, & Belloti, 2014).

There is a school of thought indicating that the needling of the tendon during the injection process may be an influential process in the outcomes for biological therapies (de Jonge et al., 2011). The repeated laceration used in some studies can initiate a healing response due to trauma and bleeding. Additionally, it is not known if the injected volume remains intratendinous for a sustained period, or leaks into the peritendinous tissues (de Jonge et al., 2011).

An alternative regenerative medicine technology exists consisting of the usage of stem cells or differentiated cells such as tenocytes. This form of regenerative medicine seeks to harness the potential of cell biology for the re-establishment of lost tissue functionality (Andia & Maffulli, 2017). Tissue specific biopsies are performed to harvest cells and these are implanted after 3-4 weeks of growth in vitro. The harvest tissue may consist of either adipose, bone marrow, tendon or skin fibroblasts, and when these are injected into the affected tendon, it is assumed that the introduced cells differentiate and replace injured cells due to the presence of environmental molecular cues (Andia & Maffulli, 2017). There is a sizeable amount of work on animal studies suggesting that stem cells and tenocyte injections seem to have some degree of effect on remodelling the pathological tendon, however translation work in human medicine is lacking (Andia & Maffulli, 2017).

There have been numerous reviews on biological therapies, reaching different conclusions on the degree of efficiency, and it is accepted that there is a limited number of high-quality studies showing a beneficial effect with autologous blood, PRP or stem cell therapy (Burke & Adler, 2016). Whilst biological therapy may not be appropriate for the majority of Achilles tendinopathy patients, these interventions may be appropriate for certain individuals. Future research is needed to better identify and subgroup individuals that may benefit from this form of regenerative medicine.
2.25 Minimally Invasive Surgery

The mainstay of Achilles tendinopathy management is conservative therapy orientated around load management and exercise-based rehabilitation. As a general rule, if this treatment method fails, orthopaedic surgeons allow patients to consider surgical intervention after exhausting appropriate conservative management for greater than six months (Kader et al., 2002). One method of surgical intervention used in the management of tendinopathy is described as a minimally invasive surgical technique. This technique is that of percutaneous ultrasound guided needle fenestration, also known as percutaneous tenotomy or dry needling (Burke & Adler, 2016). The technique involves using ultrasound to identify the pathological tendon, then guiding a needle to the affected area and repeatedly fenestrating or lancing the abnormal tendon. The aim of this treatment is to traumatise and selectively lacerate the tissue to encourage localised bleeding and fibroblastic proliferation, ideally promoting ordered collagen and ultimately tendon healing (Housner, Jacobson, & Misko, 2009).

Reports from authors promoting this intervention, indicate positive results from small case series using patient-reported outcome measures (Housner et al., 2009). However, the studies advise that the treatment is not suitable for patients with diffuse or multinodular tendinopathy or paratendinopathy, advising a formal surgical exploration be performed (Housner et al., 2009). To date, there have been only small case series with high potential bias and no randomised controlled trials on the technique of minimally invasive surgery for the management of Achilles tendinopathy.

2.26 Surgical Intervention

There are numerous surgical techniques described within the orthopaedic literature for the treatment of chronic Achilles tendinopathy and there is evidence supporting this approach as an appropriate treatment option when other treatments have failed (Kader et al., 2002). In general, these surgical procedures can be broadly grouped into four categories: open tenotomy, with removal of the abnormal tissue
and the paratenon not stripped; open tenotomy, with removal of the abnormal tissue and the paratenon stripped; open tenotomy, with longitudinal tenotomy with or without paratenon stripping; percutaneous longitudinal tenotomy (Kader et al., 2002). The various differing techniques all share the same goals; to excise fibrotic adhesions, remove degenerative nodules, make longitudinal incisions into the tendon to detect intratendinous lesions, restore vascularity to the tendon, and to initiate a cellular matrix response with an attempt to promote healing (Maffulli et al., 2004). These techniques are associated with relatively long postoperative rehabilitation and delays of up to 6-months before patients are back in full tendon loading activities (Bedi et al., 2016).

The mechanism as to why surgery promotes healing of the tendon is not understood (Maffulli et al., 2004). It has been argued that the postoperative healing response and careful progression of rehabilitation with excellent compliance after surgery, rather than the surgery itself, causes the improvement in patient symptoms (Sandmeier & Renstrom, 1997). The multiple longitudinal tenotomies have been shown in rabbit Achilles tendons to improve neuroangiogenesis within the tendon; increasing blood flow and potentially providing a better environment for healing (Friedrich, Schmidt, Jungmichel, Horn, & Josten, 2001).

A systematic review of surgical techniques by Tallon, Coleman, Khan, and Maffulli (2001) showed many authors reported good to excellent results in up to 85% of cases, yet many of these high success rates were not reproduced by subsequent studies. This review also found that there was an inverse relationship between the reported success rate and the quality of the scientific methodology used in the study (Tallon et al., 2001). Kader et al. (2002) commented on how it was remarkable that most studies did not report their assessment procedure, yet most authors reported good or excellent results. This may explain why many of the reported success rates are not reproduced in the clinical setting (Kader et al., 2002). It is difficult to compare studies and surgical techniques as most researchers do not report their assessment technique, or when they do, used poor quality outcome measures.
Also of note, there are currently no prospective randomised trials and limited use of controls, with many studies being case or descriptive studies. Therefore, the reported success rate of surgical intervention for Achilles tendinopathy should be viewed with caution.

Inflammation and degeneration are not mutually exclusive, but work together in the pathogenic cascade of Achilles tendinopathy (Abate et al., 2009). This can explain why different therapies achieve differing results and are more appropriately applicable to different patient subgroups. However, exercise therapy has been a suggested form of management in tendinopathies since the 1980’s and has been shown to be the superior treatment choice for Achilles tendinopathy, giving the best short and long-term outcomes (Scott et al., 2013). The effectiveness of an intervention needs to be evaluated by an appropriate valid and reliable outcome measure. The various outcome measures and scales that are used for the clinical grading of Achilles tendinopathy will now be discussed.

2.27 Outcome Assessment

While the treatment options for Achilles tendinopathy vary, so do the outcome measures and scales used to assess their effectiveness. A systematic review by Kearney et al. (2015) examining the effectiveness of injection therapy for Achilles tendinopathy noted a gross heterogenicity in outcome measures used. Their review discovered that the most commonly employed outcome measure was the VISA-A, however authors had utilised alternatives including; patient-reported quality of life, pain scales, return to previous activities, adverse events, patient rating of satisfaction and non-validated patient reported outcomes (Kearney et al., 2015).

Achilles tendinopathy describes a clinical syndrome where both pain and reduced function are the cardinal signs (Maffulli et al., 1998). Interventions concerned primarily with pain have often used outcome measures like the visual analogue scale (VAS) or numeric rating scale (NRS) (Robinson et al., 2001). Other studies that have incorporated both pain and function into their assessment criteria have used a
performance measure such as strength, range of motion or return to activity (Robinson et al., 2001). Examples of lower limb outcome measures that include both pain and function into their assessment methodology include the Foot and Ankle Outcome Score (FAOS) and the Achilles specific Victorian Institute of Sport Assessment – Achilles (VISA-A) questionnaire (Robinson et al., 2001).

Since non-standardised outcome measures with limited reliability and validity testing have been used throughout various Achilles tendon studies, the comparison between studies and evaluation of effectiveness of treatment is therefore difficult (Iversen et al., 2012). Studies require an assessment system where participants are not influenced by the investigator, provide accurate feedback on relevant change and show significance of the output for each outcome measure (Robinson et al., 2001). Subjective measures such as the VAS and NRS when used as a primary outcome measure can introduce bias into a study, with little being known about the significance of change relating to pain from musculoskeletal disease (Breivik, Bjornsson, & Skovlund, 2000). Performance tests, return to sport and muscle measurements are not globally applicable and may not be comparable between subject groups (Robinson et al., 2001). The use of a global measure of assessment as the evaluation tool specific to the Achilles tendon is the ideal standard. The VISA-A is a patient-reported outcome measure that involves a short questionnaire that is self-reported and aims to capture a person’s perceptions of specified aspects of their health status (Mallows, Littlewood, & Malliaras, 2017). Such questionnaires are ideally suited to areas such as tendinopathy where structural change does not consistently correlate with clinical symptoms.

The VISA-A is comprised of eight questions that assess the domains of pain, function in daily living, and sporting activity; with results ranging from 0-100, where 100 represents an asymptomatic fully functional subject (Robinson et al., 2001). The content of each question was developed through a review of the literature and consultations from individuals with expertise in the area of Achilles tendinopathy. Since the visual analogue scale has been found to be more accurate and sensitive
than categorical verbal scales, the first six questions of the VISA-A utilise the VAS to allow patients to report the magnitude of subjective symptoms on a continuum. The founders of this tool determined that activity is best measured using a categorical rating system based on an incremental range of values; therefore, the final two questions use this method (Robinson et al., 2001).

The VISA-A questionnaire has been shown to be an accurate index of severity for Achilles tendinopathy, which has undergone reliability and construct validity testing as well as cross cultural adaptations (Iversen et al., 2012). Robinson et al. (2001) showed strong evidence for test-retest reliability with no difference in scores between tests at one week apart. Construct validity was confirmed by comparing the VISA-A to the Percy and Gonochie grading system, the Curwin and Stanish grading system, and by comparing the score among groups of participants where the severity of the score could be clinically determined with favourable results (Robinson et al., 2001). The median VISA-A score in non-surgical patients presenting at primary care clinics has been reported to lie between 24 and 63 points (Iversen et al., 2012; Robinson et al., 2001). With studies following successful treatments showing improvements in score to means of 11 to 72 points and a score of 90 or higher being reported to represent full recovery following Achilles tendinopathy (Iversen et al., 2012; McCormack, Underwood, Slaven, & Cappaert, 2015). While there is no definitive minimally clinical important difference established for the VISA-A score, several authors have claimed that it lies somewhere between 6.5 and 12 points (Iversen et al., 2012; McCormack et al., 2015). This is comparable to other scales in musculoskeletal medicine defining an improvement of 10-15% to have clinical significance (Ostelo et al., 2008).

Evaluative scales must be able to differentiate patients who have changed clinically from those who have not, and must be designed and evaluated for reproducibility, validity and responsiveness. Currently the VISA-A is the only specific Achilles scale to assess pain and activity level; as such this self-administered questionnaire is currently considered the first choice in outcome measurement for the Achilles
tendon (Iversen et al., 2012; Robinson et al., 2001). This has resulted in the majority of current-day studies on the Achilles tendon utilising the VISA-A as their primary outcome measurement tool, yet some exceptions still remain.
3.1 Summary of the Literature Review

From the extensive literature review, the following conclusions can be made:

- Chronic tendinopathy is a significant problem, particularly in active and sporting populations (Barker-Davies et al., 2017; Woo et al., 2008).
- Mid-portion Achilles tendinopathy is a degenerative process with mechanical overload being the primary driver (Abate et al., 2009; Barker-Davies et al., 2017; Cook & Purdam, 2009; Rees et al., 2014). Although degenerative in nature, this process with a lack of classical inflammatory cells, has signs of neurogenic inflammation (Scott et al., 2004).
- Tendinopathy on ultrasound imaging may demonstrate tendon thickening, collagen fascicle disorganisation and irregularity, tendon hypoechoogenicity and neovascularity within the tendon substance (Cook & Purdam, 2009).
- Potential complications to the management of Achilles tendinopathy include paratenon changes, fat pad and bursal inflammation, synovio-entheseal complex pathology, intra-tendinous calcifications and involvement of the plantaris tendon (Bianchi & Martinoli, 2007; Wijesekera et al., 2011).
- A common criticism of ultrasound imaging is a lack of objective quantifiable assessment, with reliance on subjective interpretation of images and the grading of these features based on perceived severity (Docking et al., 2015). This has led to significant variance when evaluating tendons and subsequently poor reliability and repeatability of testing (McAuliffe et al., 2016; Sunding et al., 2016).
- There is no gold standard technique for assessing the Achilles tendon with ultrasound (Sunding et al., 2016).
- Various sonographic changes are associated with Achilles tendon pain, yet their relationship to symptoms is unclear (Gibbon et al., 2000; Khan et al., 2003; Malliaras et al., 2012; Ohberg et al., 2001). Many studies assessing this
relationship have shown an inconsistent and often weak association between clinical symptoms and ultrasound assessment (Bakkegaard et al., 2015; de Jonge et al., 2014; Emerson et al., 2010; Malliaras et al., 2010; Ohberg et al., 2001; Ooi et al., 2015).

• The goal in management of Achilles tendinopathy is to return patients to their desired level of activity without significant residual pain. While no gold standard treatment schedule exists for the management of Achilles tendinopathy, it appears that progressive loading exercises are integral to reach successful outcomes (Boesen et al., 2017).

• When conservative treatment fails, injection therapy is often offered (Scott et al., 2013). Despite much debate, there is still no consensus regarding the best injectable therapy to use in patients with recalcitrant tendinopathy (Kearney et al., 2015).

• High-volume peritendinous glucocorticoid injections are one such injection technique growing in popularity which involve a large volume of saline, steroid and local anaesthetic to be injected into the interface between the Achilles and peritendinous tissues (Boesen et al., 2017). Small studies on high-volume peritendinous glucocorticoid injections have been shown to reduce pain and improve function in both the short and long-term (Boesen et al., 2017; Chan et al., 2008; Humphrey et al., 2010; Maffulli, Spiezia, Longo, Denaro, & Maffulli, 2013; Resteghini & Yeoh, 2012; Wheeler, 2014).

• There remains no consensus within the literature as to the optimal volume required for high-volume peritendinous glucocorticoid injections and variations of injection technique currently exist. Additionally, as different case series utilise different protocols, with differing injection regimens, medications, follow-up periods and protocols; direct comparison between methods is difficult and no technique has demonstrated superiority (Boesen et al., 2017).

• Various surgical techniques have been employed for the management of recalcitrant Achilles tendinopathy (Kader et al., 2002). The literature
reporting high success rates from surgery generally utilise poor scientific methodology (Tallon et al., 2001).

3.2 Rationale for the Studies

From the summary of the literature review detailed above, it is clear that there is value in the development of a quantifiable method to assess the Achilles tendon using ultrasound. This tool should be valid and reliable allowing it to be utilised as a sonographic tool to assess tendon response following intervention. Additionally, with the increased employment of high-volume peritendinous glucocorticoid injections for the management of chronic Achilles tendinopathy, further research is required to detail the optimal injection technique and type, along with the resulting clinical and sonographic benefits. Finally, the association between clinical status and the sonographic appearance of tendinopathic tendons is often described as ambiguous (Gibbon et al., 2000; Khan et al., 2003; Malliaras et al., 2012; Ohberg et al., 2001). This uncertain relationship may be due to differing assessment techniques in both clinical and sonographic outcome.

Using the foundation of the previously detailed literature review and rational for the studies, the conceptual framework that underpins the development of the Achilles Ultrasound Assessment Tool (AUAT) and proposed treatment regime is detailed below. Due to the nature of the studies being orientated around the development of a new sonographic tool for the assessment of the Achilles tendon based on observer interpretation of ultrasound imaging, a mixed method paradigm with quasi-experimental design was utilised. This integrated way of conducting research involves bringing together a number of related concepts and perspectives to address each individual research problem (Imenda, 2014; Johnson, Onwuegbuzie & Turner, 2007). As mixed methods research is an intellectual and practical synthesis, based on qualitative and quantitative research and recognises the importance of traditional research methods but also offers a powerful third paradigm choice that often will provide the most informative, complete, balanced and useful research results (Johnson et al., 2007).
The construction of the conceptual framework details the formation of each study based on experimental knowledge, existing concepts and research, experimental research and details the subsequent hypothesis for each following study (Maxwell, 2005). This conceptual framework provided guidance to the individual studies as questions were fine-tuned, methods for measuring variables were selected and analysis were planned (Imenda, 2014).

3.3 Study 1: Formation of the Achilles Ultrasound Assessment Tool (AUAT)

3.3.1 Identified Knowledge Gaps

Previous authors have assessed individual components of Achilles tendinopathy, however, to date, there has been no attempt to holistically summarise the entire spectrum of sonographic changes present within the tendinopathic tendon or peritendinous tissues (Malliaras & Cook, 2011). The variability within the literature makes interpreting and comparing studies difficult and there have been calls for the formation of a uniform assessment method (Wijesekera et al., 2011).

3.3.2 Research Aims

The purpose of this study is to:

- Identify the known sonographic changes associated with Achilles tendinopathy involving both the tendon and surrounding tissues.
- Develop a standardised, objective sonographic tool to allow reliable and repeatable assessment of the Achilles tendon using ultrasound.
- This sonographic tool should be able to differentiate between normal and abnormal tendons, define tendon changes, identify potential complications or barriers to treatment, and be sensitive to detect small sonographic changes and trends over time.
- This sonographic tool should be applicable in both everyday clinical practice and within the research setting.
3.3.3 **Hypothesis**

It was hypothesised that a standardised, objective sonographic tool that can be easily performed, would allow for the reliable and reproducible assessment of the symptomatic Achilles. This would lead to the development of a clinically applicable tool when studying tendon response after different treatment interventions.

3.4 **Study 2: The Reliability and Construct Validity of the AUAT**

3.4.1 **Identified Knowledge Gaps**

The AUAT is a new sonographic tool designed to fill the void found within the imaging literature; attempting to standardise the assessment of the Achilles tendon using ultrasound imaging. The AUAT has been formulated through a Delphi process, however for this to be a clinically applicable tool, the construct validity, inter and intra-observer reliability of this new tool need to be assessed.

3.4.2 **Research Questions**

- Is the AUAT a valid, reliable and repeatable method of assessing clinically symptomatic Achilles tendons?
- Is the AUAT reliable when used by different assessor groups, consisting of sonographers and radiologists?

3.4.3 **Hypothesis**

The AUAT is a valid and reliable tool to assess the Achilles tendon using ultrasound.

3.5 **Study 3: High-Volume Injection Therapy – A Novel Adjunct in the Management of Achilles Tendinopathy.**

3.5.1 **Identified Knowledge Gaps**

There are a variety of different injectable therapies currently being employed for the treatment of recalcitrant tendinopathy; yet only sparse scientific evidence exists supporting any specific injection treatment (Kearney et al., 2015; Scott et al., 2013). Along with injection therapy, concurrent exercise therapy is often employed to
optimise outcomes (Magnusson et al., 2010; van Ark et al., 2011). High-volume peritendinous glucocorticoid injections are one such injection technique growing in popularity, with a limited amount of evidence demonstrating positive short-term outcomes (Boesen et al., 2017). The effect that this injection technique has on the tendon and surrounding structures sonographically is unknown (Boesen et al., 2014; Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013). Additionally, many studies use the term ‘high-volume injection’ to describe large volume peritendinous injections, yet there is no consensus within the literature as to what volume this entails nor details regarding the injection technique associated with its administration (Boesen et al., 2014; Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013).

3.5.2 Research Questions

- What is the benefit, both clinically and sonographically, of a single high-volume peritendinous glucocorticoid injection in combination with a load-based exercise program for the treatment of recalcitrant mid-portion Achilles tendinopathy?

3.5.3 Hypothesis

A single high-volume peritendinous glucocorticoid injection, combined with a load-based exercise program, results in a significant clinical improvement in patient rated pain and function. This clinical improvement is associated with a sonographic improvement.

3.6 Study 4: AUAT and Correlation with Patient Symptoms

3.6.1 Identified Knowledge Gaps

Various differing methodologies for assessing tendinopathy have shown an inconsistent and often weak relationship with clinical severity (Bakkegaard et al., 2015; de Jonge et al., 2014; Emerson et al., 2010; Malliaras et al., 2010; Ohberg et al., 2001; Ooi et al., 2015). A criticism of the literature is that these comparative studies apply varying sonographic imaging techniques and assessment methodologies that
are then paired to variable outcome measurements. To date there has been no studies on the holistic tendon sonographic appearance and the relationship to symptoms using a validated outcome measure. There is a need to determine if the AUAT carries qualities that allow it to correlate with symptomology of Achilles tendinopathy.

3.6.2 Research Questions
Does a relationship exist between the clinical features of Achilles tendinopathy and the sonographic appearance of the tendon as defined by the AUAT?

3.6.3 Hypothesis
There is a relationship between ultrasound findings as assessed by the AUAT and the VISA-A questionnaire of symptomology in patients with mid-portion Achilles tendinopathy.

3.7 Summary
The aforementioned knowledge gaps, research questions and hypothesis are thoroughly explored in the following four chapters with a summary of findings and future research directions elaborated in Chapter Eight.
Chapter Four:
Formation of the Achilles Ultrasound Assessment Tool (AUAT)

4.1 Introduction
Achilles tendinopathy is a common condition however the exact aetiology and pathogenesis is not fully understood (Cook & Purdam, 2009; Barker-Davies et al., 2017; Jozna & Kannus, 1997). Sonographic investigation is commonly used to assess the structural integrity of the Achilles tendon, yet there are inconsistencies within the literature as to how best assess the Achilles tendon. One of the most frequently cited criticisms of ultrasound imaging is in relation to its reliability, as it is perceived to have considerable risk of errors as well as significant variance when evaluating tendons due to operator experience, non-standard imaging protocols, variations in transducer positioning and variability in defining the pathology present (Docking et al., 2015; McAuliffe et al., 2016; Scott et al., 2013; Sunding et al., 2016). Although several published studies have highlighted the role of ultrasound in the assessment and grading of Achilles tendinopathy, a lack of consensus on which elementary structures should be examined and how to define any abnormality found has remained. Therefore, there is a need for a quantitative index of sonographic changes that may be present in the tendinopathic Achilles tendon.

A number of investigators have described tendon pathology on ultrasound as focal or diffuse thickening with areas hypoechoogenicity representing fibrillar disorganisation (Astrom et al., 1996; Cook & Purdam, 2009; Leung & Griffith, 2006). However, within the medical imaging community there is a lack of consistency regarding the reporting of tendon pathology, limited to subjective interpretation with little ability to quantify tendon structure (Bedi et al., 2016). Additionally, there is non-uniformity, both in the definitions being applied and the technical parameters and scanning methods being used (Bakkegaard et al., 2015; Bedi et al., 2016; Sunding et al., 2016). Interpretation of ultrasound imaging is often descriptive in nature based on either the different echotexture observed (e.g. homogeneous or
heterogeneous), echogenicity (e.g. hyperechoic or hypoechoic) or the maximum thickness of the tendon often measured with little relation to significance (Nadeau et al., 2016). The interpretation of imaging findings is largely influenced by the examiners experience in both performing the imaging and their ability to interpret the findings. This lack of consistency and consensus was demonstrated in a recent systematic review by McAuliffe et al. (2016) investigating ultrasound assessment of Achilles tendinopathy and its relationship with predicting symptoms. They described within the literature a wide variety of criteria used to describe tendon abnormalities, with the authors settling on the criteria of “any deviation in tendon structure” (McAuliffe et al., 2016, p. 1517). The majority of the studies assessed in this systematic review used either tendon thickness, hypoechogenicity or an increase in vascularity as seen on Doppler ultrasound to be indicative of tendon abnormality, either as a stand-alone criterion or as a combination of the above three parameters. Yet in assessing these studies, the definition of an increase in tendon thickness is often undefined, criteria for the presence of hypoechogenicity elusive and vascularity was often assessed using differing methods (McAuliffe et al., 2016). This demonstrated variety in terminology and lack of quantification will inhibit ultrasound being used reliably as a screening tool, outcome measure or to assess effectiveness of treatment.

Besides the grey-scale and Doppler changes known to occur within the tendon, abnormalities of the plantaris tendon along with pathology of the paratenon, fat pad, bursa and enthesis have all been broadly associated with Achilles tendinopathy (McAuliffe et al., 2016; Wijesekera et al., 2011). These findings are readily apparent using ultrasound imaging, but are seldom included in medical imaging reporting (Wijesekera et al., 2011). Along with the lack of consistency in reporting abnormalities, there is also a lack of quantification of the sonographic change within the tendon, surrounding structures and associated neovascularity. Often non-specific subjective terms such as absent, mild, moderate and severe are used to report findings, which some authors propose adequately defines tendon abnormalities (Comin et al., 2013). These arbitrary distinctions lack consistency,
which in turn leads to poor reproducibility of testing (McAuliffe et al., 2016). This lack of reliable quantification has had a flow-on effect to the research community with authors using a range of definitions as to what constitutes Achilles tendinopathy sonographically.

4.2 Rationale

Previous authors have assessed individual components of Achilles tendinopathy, however, to date, there has been no attempt to holistically summarise the entire spectrum of sonographic changes present within the tendinopathic tendon or peritendinous tissues (Malliaras & Cook, 2011). The variability within the literature makes interpreting and comparing studies difficult and there have been calls for the formation of a uniform assessment method (Wijesekera et al., 2011). This current study hypothesised that a standardised, objective sonographic tool that can be easily performed, would allow for the reliable and reproducible assessment of the symptomatic Achilles. This may lead to improved patient outcomes by giving the treating clinician additional information regarding the health of the tendon, stage and extent of tendinopathy. Furthermore, with the identification of any complications to management, clinical reasoning may change which may ultimately affect treatment and outcome. This ultrasound assessment should be able to differentiate between normal and abnormal tendons, but also define the tendon changes, identify potential complications or barriers to treatment, whilst being sufficiently sensitive to detect small sonographic changes and trends over time. This research study also hypothesised that if the ultrasound assessment is performed in an educated, uniform manner, then sonographic findings should be more repeatable and reliable. Improved correlation with patient symptoms may occur and this would lead to the development of a clinically applicable sonographic tool when studying the tendon response after different treatment interventions.
4.3 Aim

The goal of this study is to create a standardised and validated, easily reproducible sonographic scoresheet to assess the structural changes associated with tendinopathy as seen on ultrasound.

4.4 Methodology

A Delphi process was undertaken to define sonographically detected Achilles tendinopathy and its core components. The utilisation of the Delphi process assisted in establishing construct validity of this questionnaire through the validation of content, language and structure of the associated identifying scoresheet. The Delphi process was chosen as it has been described to be the most appropriate method of establishing relevance, flow and validity of content inclusion (Kerr, 2001). This systematic expert opinion approach is used across numerous disciplines to ascertain consensus on issues; especially in the diagnosis of health and medicine conditions (Diamond, Grant, Feldman, Pencharz, Ling, Moore & Wales, 2014; Fink, Kosecoff, Chassin, & Brook, 1984). As this predefined decision method uses standardised criteria and controlled feedback to evaluate agreement, the Delphi process is therefore considered more valuable than less formalised consensus approaches (Diamond et al., 2014).

A modified Delphi technique was chosen to synthesise accumulated expert opinion on this topic, whereby a combination of self-administered questionnaires and a physical meeting of the experts occurred between Delphi rounds to discuss the results (Boulkedid, Abdoul, Loustau, Sibony & Alberti, 2011). The aims and rounds of the modified Delphi technique were designed to formulate a questionnaire that possessed strong content, convergent and divergent validity. For the purpose of this study consensus was achieved by a decrease in variance in group responses until the majority of participants agreed to a particular viewpoint. Rounds of the Delphi would continue until an achievement of consensus was reached, which was determined as > 80% of Delphi participants agreeing on the format and content of the sonographic tool.
4.5 Formulation of the Achilles Ultrasound Assessment Tool

A review of the literature relating to the pathological changes associated with Achilles tendinopathy and their sonographic appearance involving both the tendon and paratendinous tissues was undertaken by a single reviewer; the principal author. The references selected were reviewed and judged on their contribution to the body of knowledge to this topic. The construct and validity of any clinical studies was carefully considered, and the outcomes of management protocols were scrutinised. The main findings of this review have been previously documented in Chapter Two, however a summary of the relevant literature regarding sonographic imaging of Achilles tendinopathy and assessment methodologies that was provided to the Delphi panel members is detailed below:

4.5.1 Literature Review

A widely referenced study by Fredberg and Bolvig (2002) assessed the significance of sonographically detected tendinosis in elite soccer players, yet their assessment criteria simply included the presence of spindle-shaped thickening to classify tendons as abnormal. No comments were made on tendon echogenicity or the status of peritendinous structures, only tendon thickness. Bakkegaard et al. (2015) assessed tendons for tendinopathic change by identifying any of the following: tendinosis (hyper/hypoechoic areas within the tendon), bursitis, calcifications within the tendon, tenosynovitis, calcaneal spurs, tendon thickening or increased peri or intra-tendinous blood flow; yet provided little information regarding the diagnostic inclusion criteria for these findings. Additionally, any of the aforementioned abnormalities were classified as tendinopathic change to the tendon (Bakkegaard et al., 2015). Balint et al. (2002) formulated an enthesis score for the lower limb based on ultrasound findings in the rheumatology population. The Achilles component included tendon thickening, bursitis, bony erosions and enthesophyte formation; with one point being scored for each abnormality present and representing a pathological enthesis. In the tendinopathy population, a similar approach was used by Emerson et al. (2010) when assessing elite gymnasts, determining that a tendon was abnormal if there was the existence of any one
ultrasound finding including either neovascularity, focal thickening, hypoechoic areas or blurring of the paratenon. Looking for and identifying more than one type of abnormality within the tendon is important to maximise sensitivity of diagnosis, whilst grading the degree of severity of change will enable the exploration of relationships between sonographic findings with symptoms and clinical outcome (Emerson et al., 2010).

Sonographic changes seen within a pathological tendon have shown to correlate well with histopathological changes. Archambault et al. (1998) used a simple sonographic grading scheme for patients with Achilles tendinopathy defined as grade 1 – normal appearing tendon (parallel margins with homogeneous echotexture), grade 2 – enlarged tendon (bowed margins with homogeneous echotexture), grade 3 – hypoechoic area with or without tendon enlargement (dark area within tendon, with or without bowed margins). Later this grading system was used by Movin et al. (1998) to assess the histopathological state of the tendon. The visualised hypoechoic regions that presented either as nodular, diffuse or multifocal hypoechoic areas were then biopsied under ultrasound guidance. The histopathological results of this study demonstrated that the focal hypoechoic areas contained very abnormal tendon structure including an increased number of proteoglycans. However, moderate pathology was also found in the neighbouring areas within the same tendon, indicating a more generalised disorder (Movin et al., 1998). This gives further support to the theory that ultrasound diagnosis needs to do more than just describe a focal hypoechoic area to accurately represent the histopathology present within a tendinopathic tendon (Sunding et al., 2016).

The aforementioned basic sonographic assessments, or versions of them, are still used in many research reports, yet there have only been limited studies on the reliability and validity of this type of assessment (Kader et al., 2002). It is unlikely that a 3-point grading system will be able to accurately represent the extent of pathology present and without quantification for normality, cannot differentiate between normal and abnormal tendons. Additionally, the lack of inclusion and
consideration of the status of the peritendinous tissues or identification of neovascularity may further reduce sensitivity. These restrictions and noted variability, may be potential reasons behind the lack of consistency and operator dependency reported by some authors (Docking et al., 2015; McAuliffe et al., 2016; Sunding et al., 2016).

A well-respected study by Kongsgaard et al. (2009) for the treatment of patellar tendinopathy simply used anterior-posterior tendon thickness to assess the grey-scale appearance of tendons. This measurement was used along with the assessment of colour Doppler flow within the tendon as an appropriate sonographic assessment parameter for the tendon at both initial and follow-up assessments. This primitive method of sonographic assessment is grossly limited, as it does not represent the changes that are apparent within the tendon or peritendinous tissues. Therefore, this method of assessment will not reflect the grey-scale changes that are readily seen clinically and may have a limited association to clinical outcome. Many studies have used tendon thickening to describe sonographic abnormalities, yet the exact measurement which defines thickening is often not stated (McAuliffe et al. 2016). An earlier study by Leung and Griffith (2008) described the diagnostic sonographic appearances of Achilles tendinopathy, establishing that not only tendon enlargement and an increase in vascularity indicated tendon pathology, but also disruption of the fibrillar pattern, increased Kager’s fat pad echogenicity and paratenon thickening were common representative findings. Therefore, the assessment of Achilles tendinopathy should involve not only tendon thickness and Doppler changes, but should include a more all-encompassing approach when assessing the tendon and peritendinous tissues.

Poltawski, Ali, Jayaram, and Watson (2012) formulated a method to assess common extensor tendons in people with tennis elbow using sonographic scales to quantify the extent of pathology and hyperaemia within the tendon. Grey-scale assessment consisted of identifying and rating tendon thickening, hypoechoic areas, fibrillar disruption and calcification using an ordinal four-point scale, where 0=normal,
1=mild, 2=moderate, 3=severe. These components were assessed individually as well as cumulatively to give a score out of 12. Additionally, Doppler ultrasound was assessed using a 5-point scale (0-4) using the researchers pre-determined criteria. Their results showed moderate to excellent reliability and repeatability, providing support for the use of sonographic grading of tendinopathy in the research environment that may be of value in the clinical realm (Poltawski et al., 2012). This gives potential for a similar score to be formulated for the Achilles tendon that also possesses high levels of reliability and validity.

The variability within the literature on how to accurately and reliability assess the Achilles tendon using ultrasound has led to a general lack of consistency in defining grey-scale characteristics and even more apparent is the lack of standardisation in documenting neovascularity identified on Doppler ultrasound. There is a need within the medical imaging community for standardisation of a more descriptive and encompassing sonographic assessment for Achilles tendinopathy. It is paramount to use imaging in association with clinical assessment to accurately distinguish the cause of achillodynia, as treatment, management and ultimately patient outcomes will be affected (Wijesekera et al., 2011).

There have been variations within the literature for the reliability of ultrasound assessment in tendinopathy, with results from Risch et al. (2016) on Doppler ultrasound showing considerably lower inter-observer reliability than previously reported in previous studies. For the reliable sonographic assessment of a tendon, 2 tasks require the investigators skills. First the investigator has to manually perform the examination; detecting and identifying the pathology at hand whilst optimising equipment settings to enable them to do so. Secondly, they have to evaluate and score the images appropriately. Nadeau et al. (2016) specified that an imperative emphasis needed to be placed on adhering to a rigorous and standardised assessment protocol when assessing an Achilles tendon with ultrasound to reach an acceptable level of reliability and accuracy.
4.5.2 Previous Holistic Assessment Formats

Within the magnetic resonance imaging (MRI) literature there have been several attempts to create an all-encompassing imaging assessment technique for the Achilles tendon. Schweitzer and Karasick (2000) differentiated Achilles tendon pathology into 7 different clinical groups, including a total of 11 subgroups with different imaging in an attempt to characterise and standardise findings. These groups differ with respect to location (insertional, peritendinous and intratendinous changes), morphology (rupture, calcification, hypoxic and mucoid degeneration), and chronicity (acute versus chronic). A further study by Weber et al. (2011), aimed to develop quantitative and qualitative MRI criteria to differentiate pathological tendons by reducing these to 4 different clinical groups based on morphological MRI findings and the correlation with histopathology. These were described as (1) peritendinous change, (2) increase in the size of the Achilles tendon with focal intratendinous changes, (3) visible morphological changes in the case of mucoid degeneration, and (4) ruptures. From this information Syha et al. (2013) concluded that clinical and morphological imaging should include location (peritendinous, intratendinous insertional, or intratendinous non-insertional), morphology (increase in calibre versus generalised structural changes), and chronicity (acute versus chronic tendinopathy).

Ultrasound has been shown to be as sensitive and accurate as MRI in the assessment of tendinopathy (Scott et al., 2013). Additionally, with modern high-frequency transducers, ultrasound can achieve a higher spatial resolution than routine MRI (Sunding et al., 2016). Ultrasound is seen as the imaging modality of choice for assessing Achilles tendons as it is quick, minimally invasive, accessible and affordable (Scott et al., 2013). Ultrasound imaging of the Achilles tendon is currently used in the clinical setting to assist in the diagnosis of tendinopathy, monitor the efficiency of treatments and to assess the risk of developing symptoms (McAuliffe et al., 2016; Scott et al., 2013). Additionally, ultrasound machines are becoming more affordable and accessible. No longer are they solely found in radiology practices, nowadays they are commonly being utilised in many sports medicine clinics.
Studies on ultrasound assessment criteria of the Achilles tendon have been limited in number, and to date there has been a limited attempt to classify these findings. A study of sonographic findings by Leung and Griffith (2008) found changes in tendon calibre, echogenicity, echotexture and intratendinous vascularity are indicative of Achilles tendinopathy, with additional signs being changes of the paratendinous tissues including increased Kager’s fat pad echogenicity and paratenon thickening. However, to-date there has been no attempt made to quantify and classify these known findings. The above-mentioned MRI classification, along with the known sonographic findings and a thorough literature review was used as the basis for the formulation of a scoresheet for the sonographic assessment of the Achilles tendon.

4.6 Delphi Procedure

4.6.1 Delphi – Round 1: Expert Group Formation and Item Generation

A focus group of professional experts was established to form a Delphi panel consisting of the principal scoresheet developer, a sonologist, a radiologist, a sonographer and two experienced physiotherapists. Details of the panel demographics and experience are detailed in Table 1. These members were invited and consented to participate; ensuring representation of different specialities, stakeholders and opinions from professionals who have an interest in the outcome of this study. Where possible, members were chosen who had previously published or considered clinical experts on the topics of Achilles tendinopathy or tendon sonographic imaging. The experts did not represent any specific organisations.
Table 1: Delphi Panel Demographics

<table>
<thead>
<tr>
<th>Expert</th>
<th>Speciality</th>
<th>Age</th>
<th>Years of Experience</th>
<th>Gender</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sonographer</td>
<td>32</td>
<td>7</td>
<td>Male</td>
<td>ACT</td>
</tr>
<tr>
<td>2</td>
<td>Sonologist</td>
<td>52</td>
<td>23</td>
<td>Male</td>
<td>ACT</td>
</tr>
<tr>
<td>3</td>
<td>Radiologist</td>
<td>46</td>
<td>18</td>
<td>Male</td>
<td>SA</td>
</tr>
<tr>
<td>4</td>
<td>Sonographer</td>
<td>43</td>
<td>18</td>
<td>Male</td>
<td>SA</td>
</tr>
<tr>
<td>5</td>
<td>Physiotherapist</td>
<td>51</td>
<td>28</td>
<td>Male</td>
<td>ACT</td>
</tr>
<tr>
<td>6</td>
<td>Physiotherapist</td>
<td>47</td>
<td>23</td>
<td>Female</td>
<td>VIC</td>
</tr>
</tbody>
</table>

The first round of the exploration phase of the Delphi involved generating items for potential inclusion in an assessment scoresheet for Achilles tendinopathy. Relevant items from the literature review (Chapter Two) were selected for inclusion and a summary of the relevant literature (4.5.1 Literature Review) was circulated to members. In addition, colleagues were consulted to find unpublished items used in clinical practice. A direct approach was used initially to discuss with colleagues with an expertise in lower limb disorders, tendinopathy or radiology regarding topics that they felt worthy of inclusion within the scoresheet.

The principal researcher acted as the coordinator who distributed the aforementioned summary of relevant literature and formulated a questionnaire asking the members to generate items for potential inclusion into the scoresheet. The results were returned to the coordinator, with the members being blinded to each other’s answers. These items were amalgamated with the existing items from the literature review and peer consultation. A summary of these results is listed in Table 2, with this being circulated to all members.
4.6.2 Delphi – Round 1: Results

Table 2: Delphi – Round 1: Results.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Tendon thickness</td>
</tr>
<tr>
<td>2.</td>
<td>Grey-scale characteristics</td>
</tr>
<tr>
<td>3.</td>
<td>Region of tendinopathy</td>
</tr>
<tr>
<td>4.</td>
<td>Focal or diffuse changes</td>
</tr>
<tr>
<td>5.</td>
<td>Tendon thinning</td>
</tr>
<tr>
<td>6.</td>
<td>Tendon tears</td>
</tr>
<tr>
<td>7.</td>
<td>Enthesis pathology</td>
</tr>
<tr>
<td>8.</td>
<td>Neovascularity</td>
</tr>
<tr>
<td>9.</td>
<td>Paratendinopathy</td>
</tr>
<tr>
<td>10.</td>
<td>Calcification</td>
</tr>
<tr>
<td>11.</td>
<td>Plantaris pathology</td>
</tr>
<tr>
<td>12.</td>
<td>Superficial bursa changes</td>
</tr>
</tbody>
</table>

4.6.3 Delphi – Round 2: Scoresheet Formation

The results of the first round of the Delphi procedure confirmed the disparity in current terminology and assessment criteria. From the topics listed in Table 2, participants of the Delphi panel were asked to review the items and during a meeting, work to develop an assessment methodology based on the previously detailed literature to evaluate the extent of pathology present within these components and express this as a numerical value. Prior to the meeting, all members were given the opportunity to present the use of preferred terms and assessment systems. At the commencement of the meeting, the principal researcher gave a short presentation to the group highlighting key points in the research literature and presented data of the currently used terminology and assessment criteria for the sonographic appearance of Achilles tendinopathy. A discussion followed and based on the opinion and responses of the Delphi panel after the second round, led to the development of the scoresheet and the division into a
primary tendinopathy component and a secondary complications component involving the contents listed in Table 2. A summary of the discussion follows.

4.6.4 Delphi – Round 2: Discussion and Formation of the AUAT
Several methods of grey-scale tendon assessment have been identified within the sonographic literature ranging from tendon thickness, comparison to the asymptomatic side and comparison to a ‘normalised’ portion of the same tendon. Terminology to describe these changes is also variable, with some examiners commenting on echogenicity without a stated reference, stating the observed changes as mild, moderate or severe, or some combination of the above mentioned subjective methods (Alfredson, 2003; Cook, Khan, Kiss, Purdam, & Griffiths, 2000; Cook & Purdam, 2009; Malliaras et al., 2010; Sunding et al., 2016; Wijesekera et al., 2011). This variation within the current literature on the methodology of how to assess tendons was seen as one of the major reasons why such a variation exists within sonographic tendon assessment. This variability directly effects the reliability of ultrasound as a diagnostic tool and outcome measure, whilst limiting comparisons between studies. The formation and utilisation of a standardised and quantitative methodological tool would help to resolve these shortfalls.

Many studies evaluating the grey-scale appearance of tendons often only evaluate and discuss the reliability of differentiating between normal and pathological findings (Sunding et al., 2016). This has limited usefulness clinically along with within the quantitative research setting, as the evaluation of the extent of pathology along with sensitivity to change is restricted when only using a dichotomised scale. Research has shown that condition specific numerical scales tend to have greater sensitivity and specificity than general-purpose scales (Kitaoka & Patzer, 1997). Hence the goal of this study arose; to create a method to objectively and numerically evaluate Achilles tendinopathy with ultrasound to fill the gap within the research literature.
4.6.5 Delphi – Round 2: Results

Following the second round of the Delphi, it was unanimously decided that the assessment scoresheet would be divided into a primary tendinopathy component and a complications or barriers to treatment component. Within the tendinopathy component it was decided to include tendon size (anterior-posterior diameter), as this has consistently shown to increase when pathology is present (Malliaras et al., 2006). Although some studies have used cross-sectional area to measure tendon size, tendon thickness has been the most commonly employed method within the literature, showing excellent inter-rater reliability regardless of operator experience (McAuliffe et al., 2016). Richards et al. (2005) has shown that morphologically abnormal tendons have an anterior-posterior diameter greater than 5.9mm. A recent systematic review by McAuliffe et al. (2016) has shown that diagnostic ultrasound measures of tendon size are reliable, both in terms of relative and absolute reliability. Differences between symptomatic and asymptomatic tendons of 2.4mm in anterior-posterior diameter have been reported for the Achilles tendon (Syha et al., 2013). The chosen increments for classifying tendon thickness were less than 6mm, 6-8mm, 8.1-10mm and greater than 10mm. The rationale behind choosing these increments was to reduce the significance of potential errors in measurement, yet still allowing sensitivity to variation, making the tool more applicable to interval change. In obtaining the tendon measurement, the ultrasound beam was required to be strictly orthogonal to the tendon, as obliquity of the scan plane may cause an overestimation of the tendon calibre (Leung & Griffith, 2008). However, although measurement of tendon calibre is useful for cross-sectional or longitudinal studies, there is a wide normal range and an overlap between normal and tendinopathic values exist (Leung & Griffith, 2008). Therefore, tendon thickness needs to be associated with other additional signs such as tendon echogenicity, paratenon thickening and vascularity to accurately represent the diagnosis of Achilles tendinopathy.

The mid-portion of the Achilles has been shown to contain distinct fascicles from the deriving musculature that remain separate from one another (Counsel et al., 2015;
Szaro et al., 2009). This rotation and separation is readily identifiable during sonographic assessment; hence an attempt was made to differentiate global tendinopathy from tendinopathy derived from a single muscle group (Szaro et al., 2009). Additionally, the current pathophysiological model of tendinopathy represents a continuum of pathological change, with diffuse thickening thought to represent a pre-pathological reactive state of ground substance deposition (Comin et al., 2013). This has been based on the work by Malliaras et al. (2010) showing that patellar tendons follow a predictable sequence, with diffuse thickening preceding the development of focal hypoechoic areas in previously normal tendons. Additionally, this diffuse thickening is present prior to a return to normal appearance in previously focally hypoechoic tendons (Malliaras et al., 2010). Therefore, it was decided to discriminate between tendons with globally diffuse pathology and those with focal pathology that may involve fibres solely from a singular muscle group, or represent focal areas or islands of degeneration.

Diffuse changes were divided into greater or less than 50% of the tendon being involved. Diffuse changes identified as being greater than 50% of the tendon, indicating that the entire tendon is involved, whilst less than 50% of the tendon involvement usually implies that a single muscle group, commonly from either the medial head of gastrocnemius and/or soleus components is involved (Counsel et al., 2015).

Focal changes were incorporated and divided into small (less than 5mm) regions usually representing focal areas of tendinosis and myxoid degeneration, or larger (greater than 5mm) regions often incorporating partial tendon tendinosis and responsible for the rare event of tendon thinning. The 5mm size division was based solely on the researchers’ clinical experience as a method to separate small from large areas that may behave differently in the clinical setting. Under the continuum tendinopathy model, these regions histologically may represent areas of degeneration involving tissue apoptosis and deterioration (Comin et al., 2013).
The subgroup of tendon tears did not receive a majority agreement from the Delphi panel and as such was excluded from the scoresheet. This phenomenon clinically presents differently, is often diagnosed in the clinical setting and results in completely different management strategies than that of tendinopathy. The term partial tear should be reserved for acute partial tendinous lesions. In fact, this term may be questioned altogether as to whether it exists (van Dijk et al., 2011). Additionally, tendon thinning was excluded, as it was determined that describing focal tendon changes in which this process occurs adequately represented this phenomenon.

Neovascularisation scores have been shown to alter during treatment of Achilles tendinopathy, although the interpretation of this and its application as an objective measure remains unclear (Malliaras & Cook, 2006). Several similar scoring systems have been formulated to categorise neovascularity in the Achilles and patellar tendons, however there is no one uniform gold standard (Alfredson, 2002; Alfredson & Ohberg, 2005; Boesen et al., 2006; de Vos et al., 2007; Hirschmuller et al., 2012; Richards et al., 2005; Sengkerij et al., 2009; Sunding et al., 2016).

The first original categorical scoring method described by Ohberg involved a 5-grade scale (0-4+) and involved the counting and estimation of visible vessels. Its creators have rightly described this technique as investigator dependant, only estimating the degree of neovascularity (Ohberg & Alfredson, 2002). Along with this operator variability, when using current day Doppler technology with its increased sensitivity and improved visualisation of low-flow micro-vessels, this method of assessment may incorrectly skew results towards the higher end of the scale. Sengkerij et al. (2009) modified this score, yet still involved the counting of vessels, grading 0-3 vessels as “0” to “3+” and more than 3 vessels as “4+”. This still possessed the same disadvantages as the original Ohberg score. Throughout the literature many authors use the ‘modified Ohberg score’ yet some authors have modified it differently, with some displaying a range from 0-3, with others 0-4 (Cook et al., 2005; Hoksrud et al., 2008; Sengkerij et al., 2009; Ooi et al., 2015). Richards et
al. (2005) detailed a time consuming and potentially erroneous approach of simply counting the number of vessels seen using Doppler ultrasound as a method for assessing neovascularity. Cook et al. (2005) showed excellent reliability results of re-scoring the same image using their method of measuring the total length of the largest vessel. This method was chosen, as the authors believed that this was the simplest way to measure change in vascularity, however it has not been shown to correlate with symptoms and has the ability to under or overestimate the degree of neovascularity within a tendon by simply choosing to measure one single vessel. The relevance and practical applicability of this method remains debatable and to date no other author has replicated this method of assessment. De Vos et al. (2007) and Sunding et al. (2016) presented similar methods for their versions of the modified Ohberg score with a version comparable to that used in rheumatology, using a 4-point score to grade vascularity into no, mild, moderate and severe flow. This method does not require the time consuming and potentially erroneous task of counting vessels and is clinically highly applicable. Sengkerij et al. (2009) demonstrated excellent levels of inter-observer reliability (interclass correlation coefficient of 0.85) using a modified Ohberg score for neovascularity in both symptomatic and asymptomatic Achilles tendons, with similar high-levels of reliability reproduced by Risch et al. (2016).

For the reasons mentioned above, it was considered that the more commonly used neovascularity score, the modified Ohberg scale would be chosen as adapted from de Vos et al. (2007) and Sunding et al. (2016), which divides tendons in to 4 categories, ranked by the degree of visible neovascularity. The Delphi panel uniformly chose this method of assessment due to its sensitivity, reliability, ease of use and high clinical applicability (Hoksrud et al., 2008). In this version of the modified Ohberg score 0 represents no visible blood vessels, 1 represents 1-2 blood vessels (mild blood flow), 2 represents several blood vessels (moderate blood flow), and 3 represents many blood vessels (florid blood flow).
In the initial study by Ohberg and Alfredson (2002) colour Doppler was used, however since this study, other authors have chosen to use power Doppler due to its superior sensitivity in low flow states, along with being non-dependant on the angle of insonation (Reiter, Ulreich, Dirisamer, Ts cholakoff, & Bucek, 2004). The Delphi panel elected to use power Doppler and this decision was supported by literature from Richards et al. (2005) who found higher sensitivity in the identification of neovascularity of the Achilles tendon when using power Doppler. In their study power Doppler identified intra-tendinous blood flow in all 45 patients, whereas colour Doppler only identified flow within 24 of these tendons (Richards et al., 2005).

Commonly held opinions within the musculoskeletal ultrasound community would suggest that when it comes to evaluating neovascularisation within a tendon, it is not just the amount and intensity of visible high blood flow that should be of interest, but also the extent of spread within and along the tendon tissue (Risch et al., 2016). An example of this is how the Achilles tendon with mid-portion tendinopathy shows a predictable presentation for neurovascular ingrowth. Firstly, the neovascularity initially appears from the anterior paratenon and Kager’s fat pad invading into the ventral tendon, with this common sonographic presentation correlating with what is consistently seen in histo-anatomical studies (Longo et al., 2009; Ohberg & Alfredson, 2002). Secondly, progression of the neurovascular ingrowth extends into additional regions, either superior or inferior to the main area of tendinopathy, but still from the ventral tendon. Finally, in gross neovascularity, a third region of vessel origin can be identified as the vessels spread around the paratenon and then invade the tendon through its posterior aspect (Sunding et al., 2016). For these reasons, the Delphi panel decided that not only the amount of vessels visible but also the number of regions of neovascularity should be included into the scoresheet to better represent and quantify the neovascularity present.
The complications associated with Achilles tendinopathy deemed worthy of inclusion by the expert panel as additions to the scoresheet included the presence of calcifications, paratendinopathy, plantaris pathology, and enthesopathy. The enthesopathy component was further broken down to include pathology of the retro-calcaneal bursa, superficial bursa and Kager’s fat pad, as some or all of these components may be present during active symptomatic enthesopathy, and the management of these complications is dependent on an accurate diagnosis.

From here the items were listed and weighting given according to their perceived relevance. The tendinopathy component was divided into tendon thickness and heterogenicity components along with a neovascularity component encompassing a modified Ohberg score including the identification of the number of regions involved. This gave a total of 13 points for the tendinopathy component. The following 7 potential complications identified were listed and scored in either a no (0) or yes (1) fashion giving a total score of 20 points.

4.6.6 Delphi – Round 3: Clinimetric Testing
The working version of the scoresheet was trialled among the focus group. Anonymous feedback was sought regarding content validation, ease of use, order of topics and practicality. The principal researcher collated the results of this feedback and this information was sent back to the group for review (Table 3).
### Table 3: Delphi – Round 3: Results

<table>
<thead>
<tr>
<th>Question</th>
<th>Summary of Delphi panel responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Able to identify pathological and normal tendons?</td>
<td>• Yes.</td>
</tr>
<tr>
<td></td>
<td>• Appropriate.</td>
</tr>
<tr>
<td>Encompasses all pathologies?</td>
<td>• Yes.</td>
</tr>
<tr>
<td>Presence of unnecessary topics?</td>
<td>• No.</td>
</tr>
<tr>
<td></td>
<td>• None included.</td>
</tr>
<tr>
<td>Appropriate order of topics?</td>
<td>• Separate into tendinopathy and complications components.</td>
</tr>
<tr>
<td></td>
<td>• Tendon thickness should be the first criteria assessed.</td>
</tr>
<tr>
<td>Numerical quantification.</td>
<td>• Appropriate.</td>
</tr>
<tr>
<td>Ease of use?</td>
<td>• Change size of scoring squares.</td>
</tr>
<tr>
<td></td>
<td>• Grammatical changes.</td>
</tr>
<tr>
<td></td>
<td>• Develop instruction brief with examples.</td>
</tr>
<tr>
<td></td>
<td>• Include descriptive terms in neovascularity and echotexture.</td>
</tr>
</tbody>
</table>

### 4.6.7 Delphi – Round 3: Results

Table 3 provides a summary of the feedback given by the expert panel. All panellists agreed with the tool content, appropriateness, validity and numerical quantification, and as such the Delphi process was concluded. Several suggestions were made to make the tool more user-friendly, including the formation of a descriptive instruction brief with examples. This was developed and constructed by the expert panel and is presented as the AUAT Technical Briefing (Appendix 3). This scoresheet with uniform Delphi consensus was deemed appropriate in its content and structure to enable accuracy, reliability, validity and ease of use of the tool. The final version of the scoresheet was called the AUAT - Achilles Ultrasound Assessment Tool (Appendix 1).
Chapter Five:
The Reliability and Construct Validity of the AUAT

5.1 Introduction

Ultrasound has been used for clinical musculoskeletal examinations and tendon research since the 1980’s. Today it is seen as the preferred diagnostic imaging method to examine superficial tendons and other soft tissues, yet Sunding et al. (2016) would suggest that the technique is operator dependant and hence is prone to variability as an assessment tool.

Tendon research using ultrasound as either a diagnostic criterion, an observation or as a tool for outcome measurement, shows varying results due to the differing methodologies used and a lack of standardised protocols. Assessment criteria regarding tendon thickness, structural abnormalities and neovascularisation are commonly used, however, the reliability of these measurements and qualitative evaluations are seldom reported (Sunding et al., 2016). This is of concern in an ever-increasing ‘evidence based’ diagnostic medical field where ultrasound imaging is frequently used as a key diagnostic criterion for Achilles tendinopathy and often directs treatment options (Nadeau et al., 2016).

There has been limited research into the inter-observer reliability of ultrasound when evaluating tendon disease within the current literature. Further compounding the issue, different authors use several different subjective, qualitative and quantitative measures to assess tendinopathy, making comparisons between studies difficult (Cook et al., 2000; Sengkerij et al., 2009; Sunding et al., 2016). Many studies evaluating the grey-scale appearance of tendons often only evaluate and discuss the reliability of differentiating between normal and pathological findings (Sunding et al., 2016). It is widely accepted that ultrasound can identify and evaluate the structural changes seen in tendinopathy, however there is no general consensus within the literature regarding the most reliable method to assess the grey-scale
The AUAT is a numeric scoresheet that rates the health of an Achilles tendon as seen using diagnostic ultrasound. The AUAT gives a numeric rating from 0 (normal) to 20 (pathological), on the features of the Achilles tendon that can be seen using ultrasound. The AUAT has been developed by an expert panel of professionals with expertise in the assessment of tendinopathy using imaging (a sonologist, a radiologist, two physiotherapists and two sonographers) and was formulated, along with having its validity confirmed via a Delphi process. The AUAT is therefore a new tool that is designed to fill the void found within the imaging literature. The AUAT attempts to standardise the assessment of Achilles tendon ultrasound imaging, whilst classifying the entire spectrum of pathologies that may be encountered during this examination.

Within the radiology profession, both sonographers and radiologists routinely dually assess patients with musculoskeletal problems when referred for a diagnostic medical ultrasound, with the radiologist providing the final written report. The level of agreement between these two groups of professionals is paramount to improving patient outcomes, along with increasing efficiency within a radiology practice. The utilisation of a standardised sonographic outcome measure such as the AUAT should assist in improving agreement between these two professional groups.

5.2 Aim
The aim of this study was to assess the construct validity, reliability and repeatability (test-retest reliability) of the AUAT by assessing the level of agreement
between sonographers and radiologists using the AUAT to assess Achilles tendons (inter-observer reliability) and their ability to reach the same conclusion on repeated testing (intra-observer testing). The levels of validity, reliability and repeatability were assessed by evaluating the levels of agreement of the overall AUAT score (the numeric total of its individual components) including the quantitative measure of tendon thickness, qualitative evaluation of both tendon structure and grading of neovascularisation along with the identification of potential complications to treatment.

To assess the score’s construct validity, radiologists and sonographers tested the AUAT to determine if the tool could differentiate sonographically normal tendons from pathological tendons.

Three methods of reliability were then tested.

- The first was a blinded inter-observer reliability test in which the agreement of a complete comparison between two sonographers performing an AUAT assessment on the same set of images from four different patients was assessed.
- Secondly, a defined inter-observer reliability test was performed, involving a comparison between the twelve different observers using the AUAT to assess the same tendon images from four different patients.
- Thirdly, a longitudinal intra-observer reliability test comparing the same twelve observers performing repeated AUAT assessments on the same image set on two different occasions, two weeks apart.

5.3 Methodology

5.3.1 Observers

Through a local medical imaging information session, expressions of interest were sought from radiologists and sonographers to participate in this study. Twelve observers were recruited and participated in this reliability testing.
demographics and experience of these observers are listed in Table 4. The volunteer observers were supplied with an observer information form (Appendix 6) and provided written, informed consent (Appendix 7). The invited consenting observer group included six radiologists and six sonographers from two different private imaging companies with no associations or commercial interests to this study. Prior to the commencement of the study, the investigators were given a written explanatory technical briefing developed by the principal researcher that outlined the process of using the AUAT and gave examples of how to interpret the AUAT results to arrive at an accurate diagnosis (Appendix 3). The observers were encouraged to ask questions of the principal researcher to seek clarification on any parts of the AUAT that they did not understand.

Table 4: Observer Demographics and Experience

<table>
<thead>
<tr>
<th>Observer</th>
<th>Qualification</th>
<th>Gender</th>
<th>Years MSK Ultrasound Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Radiologist</td>
<td>Male</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>Radiologist</td>
<td>Male</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>Radiologist</td>
<td>Male</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Radiologist</td>
<td>Male</td>
<td>23</td>
</tr>
<tr>
<td>5</td>
<td>Radiologist</td>
<td>Male</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Radiologist</td>
<td>Female</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>Sonographer</td>
<td>Male</td>
<td>7</td>
</tr>
<tr>
<td>8</td>
<td>Sonographer</td>
<td>Male</td>
<td>18</td>
</tr>
<tr>
<td>9</td>
<td>Sonographer</td>
<td>Male</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>Sonographer</td>
<td>Female</td>
<td>23</td>
</tr>
<tr>
<td>11</td>
<td>Sonographer</td>
<td>Male</td>
<td>16</td>
</tr>
<tr>
<td>12</td>
<td>Sonographer</td>
<td>Female</td>
<td>1</td>
</tr>
</tbody>
</table>

5.3.2 Patients

Four participants were invited to participate in this study, consisting of three patients who were referred for diagnostic imaging to a specialist musculoskeletal
imaging practice suffering from pain, swelling or tenderness in the Achilles region, along with one asymptomatic control subject with a sonographically normal Achilles tendon. Participants were selected by the principal researcher using a convenience sampling method and represented the spectrum of tendinopathy that is observed sonographically in the clinical setting. These participants subjectively represented mild, moderate and severe tendinopathic change. The patient with mild changes demonstrated minimal echotexture intratendinous change involving a minor increase in tendon diameter, fusiform thickening, homogeneous decreased echogenicity and no neovascularity of the Achilles tendon. Moderate changes were observed as an increase in tendon diameter with associated fibre disorganisation, heterogeneous hypoechoic regions and a minor increase in Doppler signal. Whereas the patient with a severely tendinopathic tendon displayed a grossly thickened and heterogeneous tendon with a loss of normal echogenicity, disorganised tendon fibres and florid intratendinous blood flow.

Invited participants were provided with a patient information form (Appendix 8) and informed written consent was gained (Appendix 9) to utilise de-identified ultrasound images and short video clips of the ultrasound acquired during the participant’s medically requested ultrasound examination by the principal researcher. The images represented a full range and accurate distribution of the sonographic changes seen in the Achilles tendon that would be encountered in the symptomatic population, from the normal age and sex matched subject with no clinical disease through to a severely diseased state. In addition, all patients received a formal ultrasound examination and consultation from an experienced musculoskeletal sonologist to formally confirm the clinical diagnosis of Achilles tendinopathy and exclusion of other pathology.

5.3.3 Sonographic Evaluation

Following a standard clinical examination, participants underwent a routine warm-up (Appendix 4) and sonographic examination according to the regular clinical protocol developed by the principal researcher (Appendix 5).
Sufficient images were recorded by the principal researcher to demonstrate grey-scale appearances and power Doppler findings in both the transverse and longitudinal plane to allow the accurate identification of pathology within the Achilles or surrounding tissues. Along with still images, three sets of 12-second-long video clips were acquired, demonstrating the grey-scale appearance of the Achilles tendon in longitudinal and transverse planes, and with the power Doppler box overriding the grey-scale image, highlighting any identifiable blood flow. The video clips were used as an adjunct to the static images, showing the entire tendon and areas of interest; enabling an initial impression to be verified or amended.

These images and video clips were de-identified on the ultrasound machine and electronically transferred to a picture archiving and communication system, Inteleviewer (Intelerad medical systems incorporated, Canada). All data sets were kept in a locked environment, only accessible by the principal researcher and his supervisors. The de-identified images from the four participants were labelled as either patient A, B, C or D by the principal researcher to maintain confidentiality and blind the observers to the participants. Each of the twelve observers assessed each of the four participants’ images through the Inteleviewer software on a EIZO RadiForce RX430 monitor (EIZO, Japan) and scored them using the AUAT on two occasions, two weeks apart (to reduce possible recall bias). The observers were numbered 1-12, blinding them to the principal researcher along with being blinded to the other observer’s results.

The measurement data obtained from using the AUAT was as follows:

- Tendon thickness was measured in millimetres by assessing the tendon in its maximal anterior-posterior diameter, from outer-edge to outer-edge of the paratenon. The ultrasound beam was deemed to be strictly orthogonal to the tendon, as obliquity of the scan plane may cause and overestimation of the tendon calibre.
The tendon was then assessed as to whether it had undergone diffuse and/or focal changes in comparison to the sonographically normal regions of either the ipsilateral or contralateral Achilles tendon. Diffuse changes were determined if there was a loss of echotexture and echogenicity of the tendon in a global setting, whereas focal changes were isolated in nature.

If diffuse changes were present, the amount of affected tendon was estimated in cross-section and scored as being either less than 50% of the tendon or greater than 50%.

If focal changes were present, representing intratendinous islands of myxoid degeneration, intratendinous cysts or degenerative tendinopathy, the largest area was measured and scored as to whether it was between 1 and 5mm, or greater than 5mm in maximal length.

The degree of vascularity was assessed using the modified Ohberg scale, where 0 represents no visible blood vessels, 1 represents 1-2 blood vessels (mild blood flow), 2 represents several blood vessels (moderate blood flow), and 3 represents many blood vessels (florid blood flow) (de Vos et al., 2007; Sunding et al., 2016). The region of vessels was also assessed as to whether there was 1 group (commonly in the ventral tendon), 2 groups (also commonly in the ventral tendon) or 3 groups (often an additional group from the posterior paratenon extending into the tendon).

The tendon was then assessed for any potential complications involved with tendinopathy and scored in either a yes/no manner. These results contributed to the final AUAT score.

- Calcifications, presenting as echogenic foci with or without posterior enhancement.
- Paratendinopathy, demonstrated by blurring, thickening and hypoechogenicity of the paratenon of the Achilles.
- Plantaris involvement in either tendinopathy or paratendinopathy, shown as focal thickening or change in echotexture of the plantaris tendon if present.
• Active enthesopathy that is likely to be contributing to symptoms, ranging from insertional tendinopathy to thickening of the fibrocartilage layer, subcortical erosions or cysts and bony spur formation with neovascularity.

• Retrocalcaneal bursa inflammation, identified as thickened bursal walls and or hypoechoic fluid within the bursa.

• Inflammation of Kager’s fat pad, showing increased echogenicity of the fat pad or vascularity compared to the contralateral side

• Superficial bursa, presenting as either fluid or thickening within the soft tissues between the posterior Achilles and the dermis.

5.4 Ethics
The research was reviewed and accepted by the Charles Sturt University ethics committee who approved this study; with protocol number 400/2016/10.

5.5 Statistical Analysis
Statistical analysis was performed using SPSS (IBM SPSS Statistics, Version 22.0) and R (R Core Team, 2014) with kappa2 function in the irr package (Gamer et al., 2012). Significance level was assumed for all measures when \( p \) values were less than 0.05. For sample description, ordinal data is presented as mean score and standard deviation (SD).

Analysis of construct validity (differentiating normal from pathological) and defined interobserver reliability analysis was performed using Fleiss’ Kappa statistic, as this is the only method for which we can compare more than two raters (Fleiss, 1971). Although this method is not designed for ordinal qualitative data, the results remain valid and present a far more conservative result. Fleiss’ Kappa coefficients are interpreted according to Landis and Koch (1977) as ‘poor’ (<0.0), ‘slight’ (0.0-0.20), ‘fair’ (0.21-0.40), ‘moderate’ (0.41-0.60), ‘substantial’ (0.61-0.80) and ‘almost perfect’ (0.81-1.00).
To investigate the consistence of the blinded inter-observer reliability (complete comparison between two raters) and defined inter-observer reliability (comparison between twelve different raters), Cohen's Kappa was used (Cohen, 1968). Cohen's Kappa has the striking advantage of taking into account the ordinal qualitative nature of this data, and as such, a squared rating was used (as suggested) to take into account for the ordinal nature (Cohen, 1968). Cohen’s kappa coefficients are interpreted according to McHugh (2012) as ‘none’ (0-0.20), ‘minimal’ (0.21-0.39), ‘weak’ (0.40-0.59), ‘moderate’ (0.60-0.79), ‘strong’ (0.80-0.90) and ‘almost perfect’ (> 0.90). The null hypothesis for both of these tests is that the level of agreement observed is simply by chance (‘coincidence’), that there is no agreement between observers.

Longitudinal intra-observer reliability was assessed using the Cochran-Mantel-Haenszel test (Mantel & Haenszel, 1959). Since all observers scored patient A and AUAT score of 0 for both initial and review assessments (Table 5), patient A was not included in this section of analysis. Additionally, as no observers varied their score by more than 1 point, analysis of agreement was performed by assessing the relative change in AUAT score. Hence data was interpreted as ‘-’ if the observers score decreased by one, ‘0’ if the score did not change, and ‘+’ if the score increased by one. Note that a $p$-value > 0.05 indicates that the change in rating is just random noise. Hence a $p$-value > 0.05 means that increasing or decreasing AUAT scores between initial and review assessments is equally likely for any observer assessing any of patient B, C, or D ultrasounds. Because of the small sample size, equal $M^2$ statistics and hence $p$-values are possible. The null hypothesis for this test is that any change in AUAT score is independent of the rater, and the individual being rated.
5.6 Results

Table 5: AUAT Reliability Results

<table>
<thead>
<tr>
<th>Patient</th>
<th>Descriptor</th>
<th>Median</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Initial</td>
<td>Normal</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A Review</td>
<td>Normal</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B Initial</td>
<td>Mild</td>
<td>3.5</td>
<td>3.25</td>
<td>0.87</td>
</tr>
<tr>
<td>B Review</td>
<td>Mild</td>
<td>3</td>
<td>3.17</td>
<td>0.83</td>
</tr>
<tr>
<td>C Initial</td>
<td>Moderate</td>
<td>10.5</td>
<td>10.58</td>
<td>0.67</td>
</tr>
<tr>
<td>C Review</td>
<td>Moderate</td>
<td>10.5</td>
<td>10.58</td>
<td>0.67</td>
</tr>
<tr>
<td>D Initial</td>
<td>Severe</td>
<td>13</td>
<td>12.92</td>
<td>0.67</td>
</tr>
<tr>
<td>D Review</td>
<td>Severe</td>
<td>13</td>
<td>13.08</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Initial = initial assessment; Review = subsequent assessment. Patient A – asymptomatic normal control; B - mild sonographic changes; C – moderate sonographic changes; D – severe sonographic changes. SD = standard deviation.

5.6.1 Validity

The four patients in this study had a range of demonstrable pathology as interpreted by the AUAT, with mean scores from all observers ranging from 0 to 13.08 (Table 5). At initial assessment, mean AUAT scores for the asymptomatic normal control patient was 0, whilst the patient with mild sonographic changes was 3.25 ± 0.87. These patients and occasions of assessment were chosen to assess the construct validity of the AUAT for differentiating normal from mild tendinopathic changes during the initial assessment. Reliability of validity assessment was $\kappa = 0.481$, with $Z$-score = 8.71 and $p$-value $\approx 0$. Hence, we conclude that the sonographers’ and radiologists’ agreement on AUAT assessment is not by chance and that the observers agree on a significant difference between sonographically normal and abnormal tendons.
5.6.2 Blinded Inter-Observer Reliability
Two observers were chosen by chance (by drawing 2 marbles from a bag of 12, numbered 1-12, representing each observer). The results from Observer 11 and Observer 12 were randomly selected and a complete comparison of the observers’ assessments on the same set of images from all 4 patients yielded inter-observer reliability of $\kappa = 0.917$, with Z-score $= 2.73$ and $p$-value $= 0.00636$. Hence the null hypothesis is rejected with the observers’ agreement of AUAT scores not being by chance, with almost perfect levels of agreement (McHugh, 2012). This blinded inter-observer reliability test indicates that both assessors reached the same AUAT score on nearly all occasions, highlighting the value of this clinical tool.

5.6.3 Defined Inter-Observer Reliability
The inter-observer reliability between all 12 observers at initial assessment on all four patients gave $\kappa = 0.439$, with Z-score $= 18.2$ and $p$-value $\approx 0$. Hence, we conclude that both radiologists’ and sonographers’ agreement on AUAT assessment is not by chance, demonstrating a moderate level of agreement. When the observers were further divided into only sonographer or radiologist groups there were similar levels of agreement with sonographers giving $\kappa = 0.398$, with Z-score $= 7.85$ and $p$-value $\approx 4 \times 10^{-15}$ and radiologists $\kappa = 0.395$, with Z-score $= 7.71$ and $p$-value $\approx 1.27 \times 10^{-14}$. However, when assessing for differences between groups, when data is pooled and AUAT scores are grouped as either from sonographers or radiologists, the weighted kappa gives $\kappa = 0.949$, with Z-score $= 4.66$ and $p$-value $\approx 3.22 \times 10^{-6}$. Therefore, the null hypothesis is rejected, as during initial assessment there was almost perfect agreement between sonographer and radiologist groups, highlighting the strong levels of consistency between assessors with different training backgrounds (McHugh, 2012).

5.6.4 Longitudinal Intra-Observer Reliability
Assessing for differences between initial and two-week repeated AUAT assessments for all 12 observers gave $M^2 = 3$ with $p$-value $= 0.5578$. Therefore, there is no significant difference between initial and review AUAT scores for pathological
tendons, hence the observers were consistent. When the observers were divided into only sonographer or radiologist groups, there was similar levels of consistency, with sonographers giving $M^2 = 4$ with $p$-value = 0.4046 and radiologists $M^2 = 3$ with $p$-value = 0.5578. Therefore, a minor, non-significant change in score was no more likely for either sonographer or radiologist groups during subsequent AUAT assessments. When assessing for differences between groups in longitudinal intra-observer reliability, pooled AUAT scores into either sonographer or radiologist groups yielded $M^2 = 2.9137$ with $p$-value = 0.5724. Hence the two groups were equally consistent, with no significant difference identified between initial and review AUAT assessments.

5.7 Discussion

The imaging of tendons with ultrasound is commonly used in the clinical setting to assist in the diagnosis of tendinopathy, monitor the efficiency of treatments and assess the risk of developing symptoms (Scott et al., 2013). In musculoskeletal practice and research, there is a need to determine the reliability of measurements and assessments made by imaging professionals (Sim & Wright, 2005). Ultrasound has increasingly been used to assess pathological changes seen within tendinopathic tendons including tendon thickening and changes in tendon echogenicity (Archambault et al., 1998). In addition to grey-scale changes, Doppler ultrasound can assess the degree of neovascularity within and around tendons (Ohberg et al., 2001). The AUAT is a tool designed to comprehensively assess all components of tendinopathy seen using ultrasound.

A criticism of imaging modalities is their reliance on subjective interpretation of images based on operator experience, with research often being limited to classifying tendons as either normal or abnormal, or using an arbitrary subjective rating (Docking et al., 2015). Objective quantification of tendon structure is often not achievable in many areas of musculoskeletal imaging, being limited to measurements relating to tendon dimensions and size of pathological area (Docking et al., 2015). The use of semi-quantitative rather than subjective assessment
methods has greater objectification and will more likely represent the present pathology. The AUAT uses the sonographic assessment of Achilles and allows this information to be interpreted as ordinal categorical data, giving a semi-quantitative score for its outcome.

The ability of the AUAT to differentiate sonographically normal tendons from abnormal, even with only mild sonographic changes, highlights the strengths and potential clinical applicability of this tool. Previous studies have failed to show a link between sonographic imaging and tendon pain, with Malliaras and Cook (2006) describing the clinical occurrence of normal imaging in patients with tendon pain. This could however reflect the lack of standardisation and sensitivity in their ultrasound assessment criteria. Clinically, we rarely experience the phenomenon where a patient with tendon-derived pain has normal imaging results when appropriate imaging and technique are used. This current study was developed to highlight the ability of the AUAT to consistently differentiate normal from mild, subtle tendon changes, confirming the validity of this tool for the assessment of Achilles tendinopathy.

The establishment of the AUAT though a Delphi panel consensus along with the construct validity shown in this study highlights the clinical applicability of the AUAT. The almost perfect levels of agreement between sonographer and radiologist groups ($\kappa = 0.949$) supports the use of this tool in both the clinical and research environment, giving the assessor confidence that despite the background of the observer, they will reach near the same score when using this tool. The strong levels of agreement shown in the longitudinal intra-observer reliability study give confidence in consistence of repeatability when using this tool. The fact that no observer varied their score by more than 1 point on the AUAT between initial and review assessments on pathological tendons highlights the level of consistency that can be achieved when using this sonographic tool. These results support the use of the AUAT within user populations who most frequently utilise ultrasound to assess tendon pathology.
5.8 Limitations and Future Directions

Ideal validation of the AUAT scoring system would require comparison with histological analysis of the tendons. However, tissue samples are normally only acquired during surgery for advanced tendinopathy that has failed conservative treatment (Docking et al., 2015). There are several ethical considerations involved in acquiring tissue samples from asymptomatic patients along with patients with mild and moderate grades of tendinopathy. Hence acquiring tendon samples for a histopathological correlation study is problematic. Our study was comparative with other studies found in the research literature where the clinical diagnosis was used as the gold standard of assessment, rather than invasive histological analysis (Docking et al., 2015).

Although ultrasound is the preferred method for imaging the Achilles tendon, some studies have looked at magnetic resonance imaging (MRI) for the diagnosis and assessment of tendinopathy (Bleakney & White, 2005). Even though ultrasound can achieve higher spatial resolution than routine MRI, ultrasound is perceived to carry a higher risk of variance due to an increased reliance on operator dependency (Sunding et al., 2016). Therefore, future studies should correlate the AUAT assessment with MRI of the Achilles tendon to assess for any differences in reliability between these two techniques.

This study utilised similar methodology to comparable studies testing the reliability of sonographic scoring systems (Cook et al. 2000; Sengkerij et al. 2009; Sunding et al. 2016). However, as per previous studies, the acquisition of ultrasound images is another potential variable that was not tested in the current study. Ultrasound image acquisition requires technical knowledge and skills to enable accurate machine optimisation, probe manipulation and subsequent image acquisition. The variability in the image acquisition phase of sonography may influence the interpretation and hence reliability of the AUAT as an assessment tool. Future studies should assess the reliability of assessors interpreting and applying the AUAT on independently acquired ultrasound images of pathological tendons. Clinical
experience suggests that live scanning is the preferable method to assess a tendon as assessors can be dynamic with their imaging, focus on and interrogate regions of interest of their choosing, whilst using comparisons to other areas of the tendon or the contralateral side if required. This method allowing for interpretation whilst live scanning the patient, rather than viewing images and recordings, may potentially further enhance the reliability of the assessment protocol used in our study.

Although sonographers and radiologists are the main groups of professionals who utilise ultrasound to diagnose and assess musculoskeletal problems, there are an increasing number of other health professionals incorporating this skill into their daily practice. This group includes rheumatologists, sports medicine physicians, physiotherapists and podiatrists (Yim & Corrado, 2012). Future studies may involve assessing the reliability of the AUAT between non-radiology observer groups.

As discussed previously, the aggregate rating of the morphological sonographic tendon changes seen when using the AUAT has not been validated as a measure of pathological severity. Although this assessment technique has faced validity as an indicator of the extent of abnormality within the tendon and can differentiate between symptomatic and asymptomatic normal controls. Therefore, these findings provide support for the use of the AUAT as a sonographic grading of Achilles tendinopathy in the research and clinical context. Cross-sectional and longitudinal studies of the AUAT with clinically observed variables and histological comparison may potentially further enhance its clinical significance. The AUAT has established itself as a valid and reliable sonographic measurement tool that is ideally positioned to be the leading outcome technique for the sonographic assessment of the Achilles tendon in future research projects. As more data and analysis of the AUAT accumulates including its association with clinical symptoms and outcomes, it may become increasingly valuable as a clinical tool in the decision making, evaluation and management of Achilles tendinopathy. At present, some medical imaging centres within Australia are already utilising the AUAT as an assessment tool to assist both sonographers and radiologists to accurately identify all components of
Achilles tendinopathy seen during a routine diagnostic ultrasound examination with positive consistent outcomes.

5.9 Conclusion
There is a need for a quantitative index of sonographic changes that may be present in the tendinopathic Achilles tendon. With a rigorous method of how to assess the Achilles tendon for sonographically evident structural change, the amount and distribution of neovascularity, along with the identification of potential complications or barriers to treatment, the AUAT is a valid, reliable and easy to administer tool that defines and represents these changes. The AUAT demonstrates high levels of inter and intra-observer reliability as well as construct validity between differing assessor groups. The utilisation of the AUAT may lead to improved assessment, clinical reasoning and clinical diagnosis, and ultimately through these channels the AUAT may improve patient outcomes. The AUAT fills the current void in musculoskeletal medicine literature as a valid and reliable sonographic outcome measurement tool, possessing qualifications to be a useful instrument when evaluating the status and progress of Achilles tendon disorders, both clinically and in quantitative research.
6.1 Introduction

The goal in management of Achilles tendinopathy is to return patients to their desired level of activity without significant residual pain. Because achillodynia is often multi-factorial and can involve multiple pathologies, treatment needs to be individualised to the patient, based on the pathology present, using current evidence based rehabilitation techniques (Alfredson & Cook, 2007). This is often considered more of an art than science. Non-operative management remains the mainstay for treatment of Achilles tendinopathy with modification of training loads and strength-based rehabilitation being shown to enable most people to return to previous activity (Bedi et al., 2016).

The Achilles tendon is made up of collagen fibrils (primary, secondary and tertiary fibres), each wrapped in endotenon, which in turn is enveloped by an epitenon forming the actual tendon (Abate et al., 2009). The Achilles tendon does not have a true synovial sheath, instead the epitenon is surrounded by a paratenon, with the space between the tendon and this thin layer of tissue containing fluids rich in mucopolysaccharides that provide nutrients and lubrication, prevent friction and protect the tendon (Kjaer, Langberg, & Magnusson, 2003).

Depending on the extent of pathology at hand, tendinopathy may involve structural damage to the tendon including disruption of the load-bearing matrix, which may require healing timeframes that are longer than desired by the patient (Cook & Purdam, 2009). During sporting pursuits, the Achilles tendon may transmit forces up to 10-times body weight, yet has a slow metabolic rate evidenced by having only 13% of the oxygen uptake of muscle and requiring more than 100 days to synthesise new collagen (Vailas, Tipton, Laughlin, Tcheng, & Matthes, 1978). Leadbetter (1992)
postulated that tissue damage is already advanced when an athlete first notices tendon pain. This explains the common clinical phenomenon where once a patient first notices symptoms, their pathology may already be advanced, requiring relative rest in the short term and the process of repair to the tendon taking months rather than weeks. This extended duration of symptoms may have a profound effect on an individual's sporting pursuits, physical and psychosocial well-being, and quality of life (Bedi et al., 2016).

6.2 Injection Therapy

Injection therapy is often offered when conservative treatment fails (Boesen et al., 2014). There are a variety of different injectable therapies currently being employed for the treatment of recalcitrant tendinopathy, including glucocorticoids, prolotherapy, sclerotherapy, autologous blood, platelet rich plasma and tenocytes; yet only sparse scientific evidence exists supporting any specific injection treatment (Kearney et al., 2015; Scott et al., 2013). These different injection therapies have differing potential methods of action, with some having an anabolic effect on the tendon, whilst others are catabolic.

Since the aim of injection therapies is to reduce symptoms and improve patient function, therapies need to be appropriately targeted and consideration given to their potential action with respect to the underlying pathology within the tendon. Along with injection therapy, concurrent exercise therapy is often employed utilising the mechanosensitive properties of tendons to assist in collagen regeneration, matrix reorganisation and tendon healing (Magnusson et al., 2010; van Ark et al., 2011).

Glucocorticoid injections, although lacking supporting evidence for their role in treating tendinopathy, are the most commonly used injectate and are one of the most common forms of intervention in recalcitrant tendinopathy (Scott et al., 2013). There is evidence that glucocorticoids can be effective in the management chronic tendinopathy by relieving pain, reducing swelling and improving function in the
short-term, although this comes at greater risk of reoccurrence in the long-term (Rees et al., 2014; Scott et al., 2013). The mechanism of action of glucocorticoids is by inhibiting inflammation-associated molecules including cytokines, chemokines and arachidonic acid metabolites, along with a reduction in angiogenesis and an inhibition of adhesion molecules involved in nociceptive pathways (Burke & Adler, 2016).

It is well accepted that tendinopathy is a degenerative process, however it is likely that elements of the inflammatory response play a role in the pathogenic cascade of Achilles tendinopathy (Abate et al., 2009; Kader et al., 2002; Rees et al., 2014). Although inflammation is not the dominant pathology in all cases, anti-inflammatory strategies may be therapeutic in the chronically pathological tendon, especially in the peritendinous tissues (Burke & Adler, 2016). The paratenon is highly vascularised with more innervation than the tendon; this provides the basis for a theory that the paratenon is a significant source of symptoms for patients with Achilles tendinopathy (Stecco et al., 2014). Paratenon thickening and inflammation associated with Achilles tendinopathy can cause extrinsic compression on the tendon, vascular compromise and a reduction of the normal gliding movements between the tendon and paratenon; factors that may advance the tendinopathy continuum (Paavola & Jarvinen, 2005; Stecco et al., 2014). Therefore, the introduction of a catabolic agent such as glucocorticoid may reduce the effects of the pathological paratenon, leading to a reduction of pain and improvements in function.

High-volume peritendinous glucocorticoid injections aim to mechanically disrupt, by stretching, breaking or occluding the neurovascular bundles growing from the paratenon into the tendon; effectively de-innervating the tendon. This has the potential to reduce the proliferation of fibroblasts, angiogenesis, vascular activation and pain transmission within the tendon; the core components for the pathogenesis of tendinopathy. Additionally, high-volume injections into the peritendinous space act to mechanically stretch the constricting paratenon, effectively decompressing
the already enlarged pathological tendon. Small studies on high-volume peritendinous injections have demonstrated reduced pain levels, symptoms and improved function in both the short and long-term (Boesen et al., 2017; Chan et al., 2008; Humphrey et al., 2010; Mafulli et al., 2013; Resteghini & Yeoh, 2012; Wheeler, 2014).

There is no gold standard treatment regimen for the treatment of Achilles tendinopathy (Boesen et al., 2017). Although appropriate load management of the tendon has been shown to be the most successful intervention, with graded loading exercises giving the best long-term outcomes for Achilles tendinopathy, not all patients will achieve a successful outcome from loading exercises alone (Magnusson et al., 2010). The literature suggests that up to 25% of patients fail conservative management; with others finding that the relatively slow recuperation of tendon injuries exceeds desired timeframes (Kader et al., 2002). Yet, glucocorticoids have the ability to reduce pain and improve function in the short-term with a limited effect on tendon structure, whilst exercise therapy can alter the tendon both metabolically and mechanically. The employment of concurrent therapies is often utilised in the management of tendinopathy and one of the most commonly utilised combinations is injection therapy and exercise therapy (Alfredson & Cook, 2007). Anecdotally, many clinicians find the use of multimodal therapy achieves superior results to those of a unimodal intervention due to the ability to target multiple causative facets and address pre-disposing factors (Boaz, Baeza, & Fraser, 2011).

Therefore, this study hypothesised that the combination of large-volume peritendinous glucocorticoid injection with a graded, functional loading program from a physiotherapist, should deliver optimum outcomes. Additionally, the loading program should be based on an accurate sonographic description of the health of the tendon, dictating the site and stage of tendinopathy along with the identification of potential complications of treatment. This holistic management approach aims to achieve the complex process of tendon healing by addressing both the mechanical and chemical factors involved in tendinopathy.
6.3 A New Technique for High-Volume Injection Therapy

Many studies use the term ‘high-volume injection’ to describe large volume peritendinous injections, yet there is no consensus within the literature as to what volume this entails (Boesen et al., 2014; Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013). For the current study this research used a combined injectate mixture of 1mL celestone chronodose (5.7 mg/mL betamethasone) with 2mL xylocaine (lidocaine [1%] 20mg in 2mL) and 20mL of cold normal saline (sodium chloride 180mg in 20mL).

The betamethasone is used for its catabolic nature, to reduce hypertrophy of the pathological paratenon and to prevent the acute mechanical inflammatory reaction produced by the large amount of fluid injected around the tendon and the stretching of the paratenon layer (Boesen et al., 2017; Burke & Adler, 2016). The lidocaine was used to provide a temporary analgesic effect (Piper et al., 2012). The methodology used in this study utilised a lower volume than other authors due to the rare but potential cardiovascular complications from large doses of lidocaine due to its function as a sodium channel blocker and found that this 2mL dosage in conjunction with the cold saline provided adequate analgesia (Piper et al., 2012). Additionally, local anaesthetics have shown to have a dose-dependent deleterious effect on tenocytes in vitro, which may be potentiated when used in combination with glucocorticoids (Piper et al., 2012). Therefore, this smaller dose of local anaesthetic was adequate to reduce the acute ‘flare’ of symptoms after injection therapy with a minimal potential negative effect to the tendon.

The volume of normal saline used was 20mL, rather than 40-50mL used by other authors (Boesen et al., 2014; Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013) as we found that this volume was adequate to dissect the paratenon away from the tendon; allowing for circumferential separation of the pathological paratenon from the tendon by the introduced fluid. Volume in addition to this 20mL only extravasated into the surrounding subcutaneous tissues, which was perceived to be unnecessary, with no additional advantage. Finally, the normal saline was
cooled to +3°C. This provided three benefits; firstly, the cold saline creates a local vasoconstrictive effect, decreasing the extravasation of blood and protein from new vessel growth associated with tendinopathy; secondly the vasoconstriction reduces any potential bleeding due to mechanical forces associated with the injection; and thirdly a cryogenic effect to further aid in analgesia (Jozsa & Kannus, 1997).

Studies by previous authors have aimed for needle placement only on the anterior surface of the tendon, between the ventral Achilles tendon and Kager’s fat pad (Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013; Resteghini & Yeoh, 2012; Wheeler, 2014). An alternative injection technique developed by the principal researcher and his colleagues based on the high-volume injection techniques previously described by other authors, was formulated and utilised in this study. This technique involves both the dorsal and ventral aspects of the tendon being injected and is the preferred injection method at their clinic; allowing circumferential stripping of the paratenon. Utilising this method, the needle was initially positioned on the ventral tendon. As the injectate solution was introduced, the needle was manoeuvred both medially and laterally, and superiorly and inferiorly, to allow the injectate to cover the entire surface of the anterior tendon. Once this result was satisfactory achieved, the needle was then partially retracted and repositioned, placed between the dorsal aspect of the tendon and paratenon. Again, as the injectate was introduced, the needle was manoeuvred to allow circumferential coverage of the tendon. This technique allows for the entire visualised section of paratenon to be separated and dissected from the pathological portion of the Achilles tendon; allowing the injectate to fully bathe the periphery of the tendon. Guiding the needle within this small space requires both excellent needle guidance skills and high-quality equipment.

6.4 Aim
The aim of this study was to assess the benefit, both clinically and sonographically, of a single high-volume peritendinous glucocorticoid injection in combination with a
load-based exercise program for the treatment of recalcitrant mid-portion Achilles tendinopathy.

Additionally, the AUAT has shown to be valid and reliable method to assess the Achilles tendon using ultrasound on pre-acquired images. The subsequent aim of this study was to assess the overall inter-rater reliability of the AUAT when applied during both the image acquisition and interpretation phases.

6.5 Methodology

6.5.1 Patients

Utilising a sample of convenience, over a period of six months, 43 patients who were referred for diagnostic imaging to a specialist musculoskeletal imaging practice suffering from pain, swelling or tenderness in the Achilles region were invited to participate in this study. All patients met the inclusion criteria of a clinical diagnosis of mid-portion Achilles tendinopathy of any duration, with a request for diagnostic imaging and/or injection-based intervention. Patients were excluded from participating in this study if they had a primary diagnosis of an insertional disorder or enthesopathy, history or suspicion of tendon rupture or known presence of a systemic illness. Invited participants were provided with a patient information form (Appendix 10) and informed written consent was gained (Appendix 11). All patients received a formal ultrasound examination and consultation from an experienced musculoskeletal sonologist to formally confirm the clinical diagnosis of Achilles tendinopathy and exclusion of other pathology. Injection therapy was only offered when clinically appropriate and after patients had attempted conservative management. All 43 patients included in this study had experienced symptoms for greater than three months and had previously undertaken and failed a physiotherapist-guided rehabilitation routine.
6.5.2 **Sonographic Evaluation**

Following a standard clinical examination, participants underwent a routine warm-up (Appendix 4) and sonographic examination according to the regular clinical protocol by the principal researcher (Appendix 5).

The sonographic examination was performed independently by two assessors (Assessor A – sonologist, Assessor B - sonographer) who were blinded to each other’s assessment along with being blinded to the participant’s VISA score of symptomology. Sufficient images were recorded to demonstrate grey-scale appearances and power Doppler findings in both the transverse and longitudinal plane to accurately identify any pathology seen in the Achilles or surrounding tissues. This sonographic data was compiled by the assessors and used to independently complete the Achilles Ultrasound Assessment Tool (AUAT) (Appendix 1), a valid and reliable method to define and represent the sonographic changes involved in Achilles tendinopathy. This blinded AUAT score from each assessor (labelled Assessor A or Assessor B), ranging from 0 (normal) to 20 (pathological), was de-identified of patient details and linked to the participant only by the numeric value allocated for identification purposes.

6.5.3 **Clinical Outcome Measures**

The primary clinical outcome measure was the Victorian Institute of Sports Assessment – Achilles (VISA-A) score (Appendix 2), a validated questionnaire for clinical outcome in Achilles tendinopathy. The scores can range from 0-100, where 100 represents no symptoms and perfect function. The VISA-A incorporates elements of symptom ratings in various loaded states, amount of activity possible and ratings of participation. It has undergone clinimetric testing in terms of reliability, construct validity, discrimination and sensitivity to change, and has been determined as an appropriate outcome measure specific for Achilles tendinopathy (Robinson et al., 2001). Participants were requested to complete this questionnaire prior to the ultrasound investigation. The assessors were blinded to the participants VISA-A score.
6.5.4 Intervention

Prior to injection, the procedure was discussed with the participants where they were advised of the aims and potential risks of injection therapy and informed consent was gained (Appendix 11). Participants were positioned prone, with their feet off the end of the plinth. Using a sterile technique, both skin and probe were cleaned with betadine (povidone-iodine 10% w/v). 1mL celestone chronodose (5.7 mg/mL betamethasone) was mixed with 2mL xylocaine (lidocaine 20mg) and 20mL of cold normal saline (sodium chloride 180mg) in a 20mL luer lock syringe. The saline was kept at +3 degrees centigrade. A 22-guage (0.7x50mm) needle was attached and used to deliver the injectate mixture. The tendon was scanned in a short-axis/transverse manner at the level of maximal tendinopathy and real-time ultrasound was used to guide the needle both anteriorly and posteriorly to the tendon. The needle was positioned between the epitenon and the surrounding paratenon under direct ultrasound visualisation (Image 1). The injectate was introduced between the Achilles tendon and paratenon with the needle being re-positioned as required to ensure that the affected area of the tendon was adequately circumferentially bathed (Image 2, Image 3). The injection was performed by a qualified sonologist under constant sonographic visualisation ensuring that optimal needle placement was achieved at all times, with the needle bevel abutting, but not entering the tendon.
Image 1. High-volume peritendinous injection procedure demonstrating patient positioning, probe orientation and injection technique.
**Image 2.** Needle introduction. Achilles tendon in short axis. Note the needle placed on the anterior aspect of the tendon and injectate introduced between the anterior aspect of the Achilles tendon and the fat pad.

**Image 3.** Needle repositioning. Achilles tendon in short axis. Note that the needle has been repositioned to the posterior aspect of the Achilles tendon between the epitenon and the surrounding paratenon.
Post procedure participants are allowed to walk on the injected limb immediately, but are advised to refrain from high impact activity for 72-hours. After this period, they were advised to commence physiotherapy for an individualised graded loading program.

6.5.5 Follow-up
The 24-week mark was chosen as the primary follow-up endpoint for this study as the reported potential relapse in symptoms after glucocorticoid injection has been shown to occur at or before 6-months (Fredberg et al., 2004). Participants were contacted at 24-weeks after intervention and requested to re-present to the clinic by the principal researcher. Follow-up VISA-A and ultrasound assessment, including AUAT assessment was performed as per the baseline assessment protocol by both assessors, who were blinded to each other’s sonographic assessment along with the participant’s clinical outcome.

6.6 Ethics
Since the study involved high-volume injections that are considered a standard treatment technique in specialist radiology practices within Australia; no participant had any treatment withheld and there was no additional treatment given to any participant within the trial. The research was reviewed and accepted by the Charles Sturt University ethics committee who approved this study; with protocol number 414/2013/02 and all participants provided written informed consent.

6.7 Statistical Analysis
Statistical analysis was performed using SPSS (IBM SPSS Statistics, Version 22.0) and R (R Core Team, 2014) with kappa2 function in the irr package (Gamer et al., 2012). A p value of 0.05 defined statistical significance. For sample description, ordinal data is presented as mean score and standard deviation with variation range.
Inter-rater reliability between the two blinded assessors using the AUAT to assess the participants’ tendons using ultrasound was analysed using Cohen’s Kappa (Cohen, 1960). Cohen’s Kappa coefficients are interpreted according to Fleiss (1971) as poor (<0.4), fair to good (0.4-0.75) and excellent agreement (0.75-1). The null hypothesis for this test is that the level of agreement observed is simply by chance (‘coincidence’).

For analysis of outcome, the results from the AUAT and VISA-A consisted of ordinal categorical variables (that are paired). As the data is semi-quantitative and is not normally distributed, the Wilcoxon signed-rank (non-parametric) test was used to compare differences between baseline and follow-up sonographic AUAT scores from Assessor A along with the participants’ VISA-A scores.

6.8 Results

6.8.1 Participants
Mean participant age was 49.47 ± 9.43 (range 28-71) with an even distribution between male and female participants (Table 6). 43 participants underwent high-volume injection therapy for recalcitrant Achilles tendinopathy in conjunction with an individualised physiotherapist-guided rehabilitation program. All participants demonstrated sonographically abnormal Achilles tendons prior to intervention, confirming the diagnosis of Achilles tendinopathy. No participants reported any adverse effects from the intervention. Six participants were lost to follow-up (three moved interstate and were unavailable for follow-up and three did not re-present at subsequent appointments) giving a total of 37 subjects with a complete dataset. When contacted, all three interstate participants who were lost to follow-up subjectively reported a positive improvement in symptoms.
Table 6: Participant Demographics and Results

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Median</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participant age</td>
<td>43</td>
<td>47</td>
<td>49.47</td>
<td>9.43</td>
<td>28-71</td>
</tr>
<tr>
<td>Gender</td>
<td>19(M)</td>
<td>24(F)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUAT (pre-intervention)</td>
<td>43</td>
<td>10</td>
<td>9.79</td>
<td>3.16</td>
<td>2-17</td>
</tr>
<tr>
<td>AUAT (post-intervention)</td>
<td>37</td>
<td>7</td>
<td>7</td>
<td>4.17</td>
<td>2-16</td>
</tr>
<tr>
<td>VISA-A (pre-intervention)</td>
<td>43</td>
<td>45</td>
<td>45.21</td>
<td>19.76</td>
<td>11-82</td>
</tr>
<tr>
<td>VISA-A (post-intervention)</td>
<td>37</td>
<td>71</td>
<td>68.35</td>
<td>22.44</td>
<td>16-100</td>
</tr>
</tbody>
</table>

6.8.2 Inter-Observer Reliability

During both baseline and follow-up sonographic assessment using the AUAT, the blinded assessors had excellent agreement with $\kappa = 0.887$ and $\kappa = 0.955$ respectively. When the level of agreement was assessed on the cumulative baseline and follow-up AUAT assessments totalling 80 participants, Cohen’s Kappa returned $\kappa = 0.848$, again demonstrating excellent levels of agreement (Fleiss, 1971). Hence, the null hypothesis that the agreement between observers is simply by chance was rejected as these results indicate that both assessors reached the same AUAT score on nearly all occasions.

6.8.3 Sonographic Outcome

There was a statistically significant difference between baseline and 24-week follow-up AUAT assessments after intervention ($p$-value = $2.57 \times 10^{-5}$). The mean AUAT score at baseline (n=43) reduced from $9.79 \pm 3.16$ (range 2 - 17) to $7 \pm 4.17$ (range 2 - 16) at follow-up (n=37). Histogram 1 demonstrates how initial, pre-intervention scores (green) are generally distributed towards higher AUAT scores of sonographic pathology, whilst the follow-up, post intervention scores (red) are largely positioned at the lower end of the scale. When these results are analysed at the individual participant level, Line Chart 1 reflects the general reduction in participant AUAT score from baseline to 24-week follow-up and hence, a general reduction in sonographic abnormality. This significant reduction in sonographically
demonstrated pathology using the AUAT has a median difference in score of -3 (Table 6).

**Histogram 1:** Distribution of AUAT scores pre and post intervention. AUAT score represents the numeric quantification of sonographic Achilles changes. Frequency indicates the number of participants with this representative score.
**Line Chart 1:** AUAT response to intervention. Individual participant AUAT score tracked from baseline (pre-intervention) to 24-week follow-up (post-intervention).

### 6.8.4 Clinical Outcome

A statistically significant reduction in VISA-A scores occurred at 24-week follow-up after intervention \((p\text{-value} = 1.586 \times 10^{-5})\). The mean VISA-A score \((n=43)\) improved from \(45.21 \pm 19.76\) (range 11 - 82) at baseline to \(68.35 \pm 24.44\) (range 16 - 100) at follow-up \((n=37)\). Histogram 2 demonstrates the distribution of the initial presentation, pre-intervention VISA-A scores (green) occurring more commonly towards the lower, more symptomatic end of the VISA-A scale, while follow-up, post intervention (red) scores are largely associated with higher, improved VISA-A scores. When these results are analysed at the individual participant level, Line Chart 2 reflects the general increase in participant VISA-A score from baseline to 24-week follow-up.
week follow-up and hence, the general improvement in clinical outcome. This significant improvement in patient reported symptoms after intervention, resulted in a median improvement of 26 points on the VISA-A (Table 6).

Histogram 2: Distribution of VISA-A scores pre and post intervention. VISA-A represents the clinical score of symptomatic severity of Achilles tendinopathy. Frequency indicates the number of participants with this representative score.
**Discussion**

Ultrasound is a cost-effective modality that can accurately confirm the clinical diagnosis of Achilles tendinopathy and its associated complications, along with monitoring the efficiency of treatments and assessing the risk of developing symptoms (McAuliffe et al., 2016; Scott et al., 2013). The AUAT has been shown to be a valid and reliable tool for assessing and quantifying the sonographic features of Achilles tendinopathy. In this study, the AUAT demonstrated excellent levels of inter-observer reliability when tested in both the image acquisition and interpretation phases, placing further weight behind the construct of the AUAT as an appropriate tool for the sonographic assessment of Achilles tendinopathy. The previously demonstrated validity of this tool indicates that the AUAT score is
representative of sonographically visualised pathology and the strong level of agreement between examiners in the current study also gives confidence that the use of the AUAT is an appropriate choice for the initial and subsequent follow-up sonographic assessments.

This study demonstrated that a single high-volume peritendinous glucocorticoid injection significantly improved the sonographic appearance of the Achilles tendon as assessed with the AUAT at 24-week follow-up ($p = 2.57 \times 10^{-5}$). This improvement in tendon structure and morphology occurred in almost all tendons with a median of three points on the AUAT scale. Whilst considering that the intervention was peritendinous in nature, this study adds further evidence that the peritendinous tissues are a significant contributing factor in the origin and progression of tendinopathy. Glucocorticoids, whilst controversial in their role within the management of tendinopathy, have been shown in this study to be advantageous when targeted and the appropriate methodology used, in normalising tendon structure with no adverse effects experienced.

High-volume injections mechanically break and disrupt the ingrowth of neurovascular bundles growing from the paratenon into the tendon. This is commonly observed when using Doppler ultrasound to image the tendon post procedure with the immediate disappearance of previously demonstrated neovascularity (Image 4, Image 5). Although some of this observed effect may be the result of an extrinsic compressive effect of the injectate volume collapsing small vessels, the amount of neovascularity seen sonographically often continues to stay reduced for extended periods following injection. This has the potential to reduce vascular activation and pain transmission within the tendon, along with reducing external constriction from the pathological paratenon. Hence, there is the capacity to reduce the core components responsible for the advancement of tendons along the pathological spectrum (van Ark et al., 2011). This study has shown that high-volume injections have a positive effect on tendon structure in the medium-term.
Image 4: Pre high-volume injection. Longitudinal view of the Achilles tendon with Doppler ultrasound. Note the neovascularity shown with Doppler ultrasound invading the tendon from both the anterior and posterior peritendinous tissues.

Image 5: Post high-volume injection. Longitudinal view of the Achilles tendon with Doppler ultrasound. Note the lack of Doppler flow within the Doppler box demonstrating the absence of any visualised neovascularity within the tendon or peritendinous tissues.
Paratendinopathy involves inflammatory infiltration within the paratenon along with mucoid degeneration, increased fibrin exudate and proliferation of fibroblasts. Glucocorticoids can induce a direct vasoconstrictor effect on smooth muscle cells, suppress the production of vasodilators and alter the phagocytic activity of various extracellular matrix components (Wong et al., 2004). For these reasons, the introduction of a catabolic agent such as glucocorticoid is a logical choice to reduce the inflammatory response within the paratenon. Although the peritendinous tissues often undergo inflammatory processes during tendinopathy, the tendon itself primarily undergoes degenerative change (Cook & Purdam, 2009).

Histologically within the tendinopathic tendon, sparse inflammatory cells exist, however this does not mean that inflammatory mediators are not present (Rees et al., 2014). Many histological studies have demonstrated tenocyte hypoplasia and hypertrophy, providing indirect evidence of up-regulated inflammatory mediators (Rees et al., 2014). Therefore, the catabolic action of glucocorticoids has the potential to positively influence tendon structure by reducing the haphazard proliferation of tenocytes and disorganisation of collagen. Hence, the peritendinous injections used in this study may have an advantageous effect both on the peritendinous tissues and on the tendon itself with the summation of both of these factors contributing to the sonographic improvement in tendon structure observed with the AUAT at follow-up.

Tendons are mechanosensitive tissues, with an important treatment modality being appropriate loading (Killian et al., 2012; Magnusson et al., 2010). The concurrent therapy used in this study of high-volume injection combined with an individualised physiotherapist-guided loading program has shown improvements in Achilles tendon structure (AUAT median improvement of 3 points) as well as tendon pain and function (VISA-A median improvement of 26 points). Well-structured exercise therapy within a physiological range has been shown to reduce tendon pain, along with stimulating the production of new collagen fibres, promote the release of inflammatory and growth substances and stimulate the release of enzymes that are important in regulating cell activity and matrix deregulation (Abate et al., 2009;
Langberg et al., 2007; Ohberg et al., 2004; Rio et al., 2015). Therefore, some of the improvement in tendon morphology as represented in this study as a reduction in AUAT score can potentially be attributed to the concurrent physiotherapist-guided loading program. However, it can be postulated that since all patients included in this study had previously failed conventional therapy, including exercise therapy programs, the high-volume injection not only had an advantageous effect on tendon morphology, but also reduced patient symptoms. This reduction in symptoms can allow rehabilitation to progress beyond the previously pain-limited restrictions, having the potential to further normalise the tendon.

Interestingly, 41 of 43 patients in this study who presented with mid-portion Achilles tendinopathy were identified as having paratenon abnormalities. Paratendinopathy has previously been shown to be associated with Achilles tendinopathy; however, in the present study and patient cohort, an almost direct relationship was demonstrated between sonographically abnormal Achilles tendons and paratenon abnormalities (Ruergard & Alfredson, 2014). Therefore, changes to the paratenon may be more common than originally thought, with identification and treatment methods directed towards the paratenon being of increased importance.

At the 24-week follow-up point in this study, sonographic changes remained in the paratenons of 33 of 37 patients. This is possibly due to the chronic degenerative changes known to be associated with paratendinopathy including mucoid degeneration, increased fibrin exudate, and the widespread proliferation of fibroblasts (Khan et al., 1999). The assessment method used in this study only stated whether changes in the paratenon were present or not. This may not accurately represent the potential improvement in the peritendinous tissues that can occur. At present, there is no established reliable method or descriptor available to sonographically assess changes to the paratenon that is sensitive to change. With the increased observed incidence of paratenon change and current research placing a highlighted emphasis on the peritendinous tissues, future research should be directed at developing methods to assess and grade these changes.
The finding in this study that all tendons remained sonographically abnormal with a mean positive AUAT score of 7 ± 4.17 at 24-week follow-up, yet had a significant clinical improvement in VISA-A scores (p = 1.586 x 10^{-5}), may further support the thoughts of Docking and Cook (2015), where relative stability in tendon structure results in improved clinical outcomes. This concept was proposed from Docking and Cook’s (2015) review of 66 Achilles tendons and 50 patellar tendons using ultrasound tissue classification (UTC). Their findings concluded that degenerative tendons appear abnormal on imaging, but maintain sufficient levels of aligned fibrillar structure and can still tolerate high tensile load, allowing these abnormal tendons to remain asymptomatic. Cook and Purdam’s (2009) tendinopathy model indicates that degenerative tendinopathy has a limited scope for repair. Once the tendon matrix has undergone structural change, it is incapable of fully normalising.

Malliaras et al. (2010) investigated changes in patellar tendons over the course of a volleyball season and reported that tendons could vary in appearance from normal to diffusely thickened and hypoechoic. They also found that patellar tendons with a hypoechoic area were likely to remain unchanged, with 81% of the hypoechoic tendons continuing to exhibit a hypoechoic area throughout the season. Even using this limited sonographic classification technique, the aforementioned literature supports the current study which demonstrates that a degenerative tendon can structurally improve only to a point and despite the presence of intra-tendinous pathology, reaches a level of tissue homeostasis that does not need to completely normalise to allow for pain-free function to return.

It is difficult to quantify the severity of a condition where pain and dysfunction are major symptoms due to the individualised perception of pain, however the VISA-A was formed to measure the severity of Achilles tendinopathy and since its inception, has been shown to be a valid and reliable measurement tool (Robinson et al., 2001). The overall figures from this study of a median VISA-A improvement of 26 points relate well to other case series involving high-volume injections, reporting an improvement in VISA-A of between 29 and 38 points (Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013; Resteghini & Yeoh 2012; Wheeler, 2014). The
previously cited case series have all shown the same promising results from high-volume injections in terms of reduction of pain, symptoms, function and improvements in sonographic tendon structure however, the quality of published evidence remains limited. The previously mentioned studies are all case series in nature with no control group and one of the five case series using retrospective data for some of its results asking patients to remember what their symptoms were like prior to the injection (Chan et al., 2008). Furthermore, differing injection routines were used in these studies, with differing injectates, quantities and techniques employed along with inconsistent follow-up periods (often intra-study) ranging from 2 weeks to 12 months. More than half of patients in one study received more than one injection procedure with differing injectates used within this single study (Maffulli et al., 2013). Our prospective study utilised a consistent injectate mixture and technique resulting in a statistically significant improvement in pain and function at 24-week follow-up.

While there is no definitive clinical important difference for the VISA-A score, comparable scales in musculoskeletal medicine define an improvement of 10-15% to have clinical significance (Iversen et al., 2012; Ostelo et al., 2008). De Vos et al. (2010) described a clinically relevant difference as 12 points on the VISA-A score as based on previous studies and this number falls within the minimal clinical important difference of 10-15%. A lower score of 6.5 points was identified in a small study by McCormack et al. (2015) as the minimal clinically important difference in patients with insertional Achilles tendinopathy. Therefore, when applying either author’s minimally clinically important difference to the findings from this current study, the mean difference of 26 VISA-A points observed at follow-up, suggests that the findings are not only statistically significant, but they also have clinical significance.

A randomised, double blinded prospective study by Boesen et al. (2017) found a lower mean improvement of 22.2 points on the VISA-A scale at 24-week follow-up after their interpretation of high-volume injection therapy in combination with
exercise therapy. The technique detailed in their study differed from the current study in terms of injection technique used, dosage of injectate, and type of glucocorticoid and local anaesthetic utilised. All of these factors potentially limit the comparison to the current study, however the study by Boesen et al. (2017) also included a control group of 19 patients undergoing placebo injection (a few drops of saline under the skin). In this study at 24-week follow-up, the control group who underwent placebo injection and exercise therapy only had a mean improvement in VISA-A score of 8.8 points, with lower levels of sonographic tendon normalisation than the active intervention group. This amount of improvement is similar to that of de Vos, Heijboer, Weinans, Verhaar, and van Schie (2012) who explored solely eccentric exercise therapy in chronic mid-portion Achilles tendinopathy finding a mean improvement in VISA-A score of 11.3 points at 24-week follow-up. These studies confirm the positive clinical effects of exercise therapy, but indicate combined therapy with high-volume injections are superior to exercise therapy alone in recalcitrant tendinopathy (Boesen et al., 2017). Additional studies comparing the technique detailed in the current study are required to assess against a placebo (sham injection) control group to establish if a similar relationship exists. Furthermore, future research comparing the high-volume injection technique used in the current study against that employed by Chan et al. (2008), Humphrey et al. (2010) and Boesen et al. (2017) is required to determine the clinical superiority of high-volume injection techniques.

A potential concern of high-volume injection therapy is the known dramatic short-term improvement in pain and function, that may lead to a faster than tolerated return to sporting activities (Chan et al., 2008). In some individuals, returning to athletic activity prior to adequate rehabilitation of the musculo-tendinous unit may lead to symptom provocation or further injury (Boesen et al., 2017). It should be noted that one patient who reported the lowest VISA-A score at follow-up had completed a marathon two-weeks prior to reassessment, suffering a ‘flare’ of symptoms during the race. Prior to this race, she was asymptomatic and training at
full capacity. If an earlier follow-up period for this patient was implemented, the results may further strengthen the median improvement in VISA-A score.

The role of steroids in the management of tendinopathy is still debated and we do not advocate their intra-tendinous injection. The results of this study are limited by the case series nature of this study and by overall patient numbers. Also lacking a randomised control group, however it should be noted that all our patients had been referred to us after having already failed other modalities of conservative management. High-volume ultrasound guided injections are now being performed in numerous musculoskeletal radiology practices around Australia. This potential patient cohort could be used for a larger randomised controlled trial. Another potential criticism is that the physiotherapy intervention was not uniform and standardised, however this is representative of real-world practice where treatment is individually tailored to the patient depending on numerous factors including personal goals, load management and activity standards.

Strengths of this study include the use of a single experienced sonologist and a single experienced musculoskeletal sonographer, its prospective nature, the blinding of the assessors, the use of a valid and reliable index for assessing Achilles tendinopathy (the VISA-A questionnaire) and the standardisation of the ultrasound assessment with the use of a semi-quantitative valid and reliable assessment tool (the AUAT). This is the largest case series reporting the use of high-volume injections for the treatment of Achilles tendinopathy and is one of the only studies with a consistent medium-term follow-up period.

6.10 Conclusion
High-volume ultrasound guided peritendinous injections significantly reduce pain and improve function when combined with exercise therapy in patients with chronic Achilles tendinopathy. This clinical improvement is associated with a sonographic improvement in tendon morphology at 24-week follow-up. High-
volume injections are a clinically applicable technique to improve patient outcomes when exercise therapy alone fails to progress the recalcitrant Achilles tendon.
Chapter Seven:
AUAT and Correlation with Patient Symptoms

7.1 Introduction

Achilles tendinopathy defines the clinical condition of mid-tendon pain, swelling, localised tenderness and impaired performance (Maffulli et al., 1998). Tendinopathy on ultrasound imaging may demonstrate tendon thickening, collagen fascicle disorganisation and irregularity, tendon hypoechogenicity and neovascularity within the tendon substance as observed with colour or power Doppler (Cook & Purdam, 2009). Additionally, potential complications or barriers to treatment including plantaris tendon involvement, enthesis pathology, paratenon changes, intratendinous calcification along with fat pad and bursal inflammation; may be associated with Achilles tendinopathy (Bianchi & Martinoli, 2007). All of these complications, if present, are readily identified using ultrasound imaging (Bianchi & Martinoli, 2007). These sonographic changes have been well known to occur throughout the tendinopathy spectrum, yet until recently have not been regularly included in the classification and quantification of tendinopathy by most practitioners. The AUAT has been shown to be a valuable method by which to achieve this and possesses qualities that enable it to be a valid and reliable tool to semi-quantify and represent the structural changes seen sonographically in Achilles tendinopathy.

Historically, various differing methodologies for assessing tendinopathy have shown an inconsistent and often weak relationship with clinical severity (Bakkegaard et al., 2015; de Jonge et al., 2014; Emerson et al., 2010; Malliaras et al., 2010; Ohberg et al., 2001; Ooi et al., 2015). A criticism of the literature is that these comparative studies use varying sonographic imaging techniques and assessment methodologies that are then paired to variable outcome measurements. To date there has been no studies on the holistic tendon sonographic appearance and the relationship to symptoms using a validated outcome measure. Tendon thickness has been shown to increase
as intra-tendinous pathology progresses due to the accumulation of ground substance and neurovascular ingrowth (Richards et al., 2005). This concept is further supported by Malliaras and Cook (2011) who demonstrated a relationship between symptoms and grey-scale ultrasound changes along with increasing anterior-posterior tendon thickness. Despite this, a direct relationship has not been established between either of these variables (Malliaras & Cook, 2011).

The changes seen within a tendinopathic tendon tend to follow an expected pattern, with Malliaras et al. (2010) demonstrating that tendons follow a predictable sequence on grey-scale ultrasound, developing diffuse changes in echogenicity (associated with reactive tendinopathy) before progressing to focal areas of pathology (degenerative tendinopathy). Previously, other authors have used a simple method of grading these grey-scale appearances of tendinopathy as developed by Archambault et al. (1998), describing grade 1 as a normal tendon, grade 2 an enlarged tendon, and grade 3 a tendon containing a hypoechoic area with or without tendon enlargement. This simple grading system does not distinguish between normal and pathological tendons or assess neovascularity. Additionally, this methodology does not assess changes that may occur in the peritendinous tissues, yet is frequently used in studies correlating sonographic findings and clinical symptoms (Bakkegaard et al., 2015; Docking et al., 2015; Emerson et al., 2010; Malliaras et al., 2010; Ooi et al., 2015).

When researchers have looked at neovascularity using Doppler ultrasound, it has often been assessed as a separate entity to the grey-scale changes, which is not representative of the sonographic changes that occur during tendinopathy. A number of measurement scales have been suggested as tools by which the degree of neovascularity present may be graded, with the most common being the modified Ohberg score (Ohberg & Alfredson, 2002; Resteghini & Yeoh, 2012). When this method has been utilised to assess symptomatic Achilles tendons, it has been shown to have a weak association with clinical symptoms (odds ratio Exp(B) = 1.017) (de Jonge et al., 2014).
The assessment and quantification of all sonographic changes within a pathological tendon requires both grey-scale and Doppler assessment to allow for an accurate representation of the pathology present. Many methods exist to evaluate individual components of tendinopathy with limited attempts at correlation with clinical severity. What defines a significant hypoechoic area, diffuse thickening or significant vascularity is often not well defined in most studies, with these factors being rarely addressed. The AUAT is the first assessment tool to summarise and semi-quantify the entire sonographic spectrum of pathology that may be present in the tendinopathic Achilles tendon and there is a clear need to determine its relationship with clinical symptoms. The evaluation of this relationship will add further strength to the construct validity of the contents of the AUAT by establishing whether the sonographic assessment of the Achilles tendon is relevant and representative to clinically symptomatic tendons. This will further explore the validity of the AUAT by assessing whether the AUAT behaves in a way that is consistent with clinical symptoms.

A number of authors have suggested that although abnormal tendons may possess hypoechoic regions, diffuse thickening and neovascularity, these findings may be present in patients without pain (Cook et al., 2001; Malliaras et al., 2010; Ohberg et al., 2001). However, having abnormal sonographic features increases the likelihood of having or developing symptoms. There is a recent thought paradigm that relative changes within the tendon are more likely to be reflective of patient symptoms and that relative stability of the morphology of the tendon relates to improved outcomes (Docking et al., 2015; Syha et al., 2013). Hence the utilisation of the AUAT with its semi-quantitative characteristics for characterising tendon structure may be more sensitive to change than purely tendon diameter or the presence of a hypoechoic area. Previously, no convincing results have been presented concerning the relationship between symptoms and sonographic findings in patients with Achilles tendinopathy. Clearly there is a need to determine if the AUAT carries qualities that allow for the correlation of this score with the symptomology associated with Achilles tendinopathy.
7.2 Aim

The aim of this study was to determine if a relationship exists between the clinical features of Achilles tendinopathy and the sonographic appearance of the tendon as defined by the AUAT.

7.3 Methodology

The same patient cohort and assessment methodology as used in the previous study (Chapter Six) was analysed for this study, however patients who declined injection therapy were also included in the initial correlation assessment.

7.3.1 Patients

49 patients who were referred for diagnostic imaging to a specialist musculoskeletal imaging practice and suffering from pain, swelling or tenderness in the Achilles region were invited to participate in this study. All patients met the inclusion criteria of a clinical diagnosis of mid-portion Achilles tendinopathy of any duration, with a request for diagnostic imaging and/or injection-based intervention. Patients were excluded from participating in this study if they had a primary diagnosis of an insertional disorder or enthesopathy, history or suspicion of tendon rupture or known presence of a systemic illness. Invited participants were provided with a patient information form (Appendix 10) and informed written consent was gained (Appendix 11). All patients received a formal ultrasound examination and consultation from an experienced musculoskeletal sonologist to formally confirm the clinical diagnosis of Achilles tendinopathy and exclusion of other pathology. Injection therapy was offered only when deemed clinically appropriate and after patients had previously trialled a range of other conservative therapies. 43 of 49 patients elected to undergo high-volume injection therapy.

7.3.2 Sonographic Evaluation

Following a standard clinical examination, participants underwent a routine warm-up (Appendix 4) and sonographic examination according to the regular clinical protocol by the principal researcher (Appendix 5). The sonographic examination
was performed by an experienced sonologist (Assessor A) who was blinded to the participant’s clinical status and VISA-A assessment. This sonographic assessment was used by the assessor to complete the Achilles Ultrasound Assessment Tool (AUAT) (Appendix 1), with results ranging from 0 (normal) to 20 (pathological). A component of the AUAT involves the assessment of maximal tendon thickness in anterior-posterior diameter. This component of the AUAT was recorded and paired to the patient’s identification number. For the purpose of this study, only the AUAT assessment and measurement of tendon thickness from Assessor A (sonologist) were utilised for correlation assessment, with the assessment results from Assessor B (as produced in Chapter Six) not analysed in the current study.

7.3.3 Clinical Outcome Measure
The primary clinical outcome measure was the Victorian Institute of Sports Assessment – Achilles (VISA-A) score (Appendix 2), a validated questionnaire for outcome in Achilles tendinopathy. The scores can range from 0-100, where 100 represents no symptoms and perfect function. The VISA-A incorporates elements of symptom ratings in various loaded states, amount of activity possible and ratings of participation. It has undergone clinimetric testing in terms of reliability, construct validity, discrimination and sensitivity to change, and has been determined as an appropriate outcome measure specific for Achilles tendinopathy (Robinson et al., 2001). Participants were requested to complete this questionnaire prior to the ultrasound investigation which was held blinded to the assessors.

7.3.4 Intervention
High-volume injection therapy was performed as per the methodology described in Chapter Six to consenting participants.

7.3.5 Follow-up
Participants who underwent injection therapy were contacted at 24-weeks after intervention and requested to re-present to the clinic by the principal researcher. Follow-up VISA-A and ultrasound assessment, including AUAT assessment, were
performed as per the baseline assessment protocol by Assessor A, who was blinded to the participant’s clinical VISA-A score.

7.4 Ethics
The research was reviewed and accepted by the Charles Sturt University ethics committee who approved this study; with protocol number 414/2013/02 and all participants provided written informed consent.

7.5 Statistical Analysis
Statistical analysis was performed using SPSS (IBM SPSS Statistics, Version 22.0) and R (R Core Team, 2014) with hmsic function (Harrell et al., 2014). A p value of 0.05 defined statistical significance. For sample description, ordinal data is presented as mean score and standard deviation with variation range.

Due to the ordered categorical nature of both the VISA-A and the AUAT, the spearman correlation coefficient was used to determine the relationship between clinical symptoms (VISA-A) and sonographic findings (AUAT and tendon thickness). A least-squares regression line was used to investigate and quantify the relationship for interest purposes only, as a linear regression is only true for quantitative variables. Correlation coefficients were interpreted according to Hinkle, Wiersma and Jurs (2003) as ‘negligible correlation’ (0.0-0.3), ‘low correlation’ (0.3-0.5), ‘moderate correlation’ (0.5-0.7), ‘high correlation’ (0.7-0.9) and ‘very high correlation’ (0.9-1.0). The null hypothesis for these tests is that the level of agreement observed is simply by chance (‘coincidence’).

7.6 Results
23 males and 26 females agreed to participate in this study with a mean age of 49 years. At initial presentation (n=49) the mean tendon thickness was 9.77mm ± 2.34 (range 4.8 - 14.8) and mean AUAT score 9.79 ± 3.16 (range 2 - 17) with mean VISA-A of 45.21 ± 19.76 (range 11 - 82) (Table 7). An analysis of the frequency of
occurrence for individual variables that compose the AUAT score are detailed in Table 8.

Table 7: Pre-intervention Results

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendon thickness</td>
<td>9.5</td>
<td>9.77</td>
<td>2.34</td>
</tr>
<tr>
<td>AUAT</td>
<td>10</td>
<td>9.79</td>
<td>3.16</td>
</tr>
<tr>
<td>VISA-A</td>
<td>45</td>
<td>45.21</td>
<td>19.76</td>
</tr>
</tbody>
</table>

The rank correlation between tendon thickness and VISA-A gave a spearman correlation coefficient of \( r_s = -0.15 \) (\( p \)-value = 0.3123). Hence, this study concludes that there is no significant relationship between tendon thickness (measured in millimetres) and the VISA-A score of symptomology. When assessing the relationship between the AUAT and the VISA-A, the spearman correlation coefficient was \( r_s = -0.04 \) (\( p \)-value = 0.7714). Therefore, even when using an all-encompassing method to assess the tendon, we conclude that there is no significant relationship between tendon pathology visualised sonographically and clinical symptoms at initial presentation.
Table 8: Frequency of Individual AUAT Variable Occurrence

<table>
<thead>
<tr>
<th>Individual AUAT variable</th>
<th>Frequency of Occurrence (n=49)</th>
<th>Frequency of Occurrence (n=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50% hypoechoic</td>
<td>67%</td>
<td>67%</td>
</tr>
<tr>
<td>&lt; 6mm</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>&gt; 10mm</td>
<td>35%</td>
<td>30%</td>
</tr>
<tr>
<td>6 – 8mm</td>
<td>20%</td>
<td>19%</td>
</tr>
<tr>
<td>8.1 – 10mm</td>
<td>39%</td>
<td>46%</td>
</tr>
<tr>
<td>Diffuse Changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>12%</td>
<td>21%</td>
</tr>
<tr>
<td>≥ 50% hypoechoic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tendon Thickness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>41%</td>
<td>75%</td>
</tr>
<tr>
<td>1 – 5mm</td>
<td>10%</td>
<td>9%</td>
</tr>
<tr>
<td>&gt; 5mm</td>
<td>49%</td>
<td>16%</td>
</tr>
<tr>
<td>Focal Changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Degree of Vascularity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 – None</td>
<td>10%</td>
<td>19%</td>
</tr>
<tr>
<td>1 – Mild</td>
<td>41%</td>
<td>49%</td>
</tr>
<tr>
<td>2 – Moderate</td>
<td>35%</td>
<td>21%</td>
</tr>
<tr>
<td>3 – Florid</td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td>Region of Vessels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10%</td>
<td>19%</td>
</tr>
<tr>
<td>1</td>
<td>26%</td>
<td>40%</td>
</tr>
<tr>
<td>2</td>
<td>29%</td>
<td>23%</td>
</tr>
<tr>
<td>3</td>
<td>35%</td>
<td>18%</td>
</tr>
<tr>
<td>Calcification</td>
<td>12%</td>
<td>7%</td>
</tr>
<tr>
<td>Paratendinopathy</td>
<td>94%</td>
<td>95%</td>
</tr>
<tr>
<td>Plantaris Pathology</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>Condition</td>
<td>Pre-Intervention (%)</td>
<td>Post-Intervention (%)</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Enthesopathy</td>
<td>31%</td>
<td>19%</td>
</tr>
<tr>
<td>RC Bursa</td>
<td>12%</td>
<td>9%</td>
</tr>
<tr>
<td>Fat Pad</td>
<td>35%</td>
<td>18%</td>
</tr>
<tr>
<td>Superficial Bursa</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Following high-volume peritendinous injection and physiotherapist-guided rehabilitation, at 24-week follow-up (n=37) the mean tendon thickness was 9.76mm ± 2.19 (range 5.8 - 13.4) and mean AUAT score 7 ± 4.17 (range 2 - 16) with mean VISA-A of 68.35 ± 22.44 (range 16 - 100) (Table 9).

Table 9: Post-Intervention Results

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendon thickness</td>
<td>9.7</td>
<td>9.76</td>
<td>2.19</td>
</tr>
<tr>
<td>AUAT</td>
<td>7</td>
<td>7</td>
<td>4.17</td>
</tr>
<tr>
<td>VISA-A</td>
<td>71</td>
<td>68.35</td>
<td>22.44</td>
</tr>
</tbody>
</table>

The rank correlation between tendon thickness and VISA-A after intervention gave a spearman correlation coefficient of $r_s = -0.38$ ($p$-value = 0.0124). Hence, this study concludes that there is a statistically significant low-level correlation between tendon thickness (measured in millimetres) and the VISA-A score of symptomology after intervention (Hinkle et al., 2003). Specifically, as tendon thickness decreases, symptoms decrease (See Scatter Plot 1). A line of best fit returns a slope of -4.217, which implies that when tendon thickness decreases by 1mm, the VISA-A score decreases by 4.21 on average.
Scatter Plot 1: Relationship between VISA-A and tendon thickness. Demonstrating correlation present between Victorian Institute of Sport Assessment - Achilles (VISA-A) score and tendon thickness (mm).

When assessing the relationship between the AUAT and the VISA-A after intervention, the spearman correlation coefficient gave $r_s = -0.56$ ($p$-value = 0.0001). Therefore, after intervention, when using an all-encompassing method to assess the tendon, this study concludes that there is a statistically significant moderate strength relationship between tendon pathology visualised sonographically and clinical symptoms (Hinkle et al., 2003). Specifically, as the AUAT score decreases, symptoms decrease (see Scatter Plot 2). A line of best fit returns a slope of -3.9674, which implies that when the AUAT score decreases by 1, the VISA-A score decreases by 3.97 on average. Hence, this study shows the null hypothesis to be false and there is a relationship between sonographic findings and clinical symptoms, with the AUAT having a stronger relationship to VISA-A scores than tendon thickness.
Scatter Plot 2: Relationship between VISA-A and AUAT score. Demonstrating correlation present between Victorian Institute of Sport Assessment – Achilles (VISA-A) and Achilles Ultrasound Assessment Tool (AUAT) scores.

7.7 Discussion

The results from this study are conflicting. At initial presentation, patients with recalcitrant Achilles tendinopathy had no association with either their AUAT score or tendon thickness with the clinical score of symptomology, the VISA-A. Yet at follow-up, a relationship with both of these sonographic assessment techniques existed. Various sonographic changes are associated with Achilles tendon pain; including grey-scale abnormalities, change in shape and neovascularity, yet their relationship to symptoms is unclear (Gibbon et al., 2000; Khan et al., 2003; Malliaras et al., 2012; Ohberg et al., 2001). The results of this study are representative of the literature exploring the relationship between imaging findings and clinical outcomes, with this study contributing to the growing body of evidence that there is a disconnect between structure and pain.
At initial presentation, there was no statistically significant relationship between sonographic findings as assessed by the AUAT and clinical symptoms ($p$-value = 0.7714). While there are studies declaring that no correlation between sonographic abnormalities and pain in chronic painful tendons exists, there appears in the clinical setting however to be a limited relationship between these two entities (Boesen et al., 2012; Drew et al., 2014; Peers et al., 2003). A prospective cohort study by de Vos et al. (2012) found that tendon structure as assessed by ultrasound tissue characterisation (UTC) is not related to the clinical severity of symptoms as measured by the VISA-A at a single point in time or in change over time. Limitations to other studies investigating the relationship between sonographic changes and clinical severity include the variable use of outcome measures and the inconsistent use of imaging techniques, including a lack of standardisation in assessing the degree of sonographic change present (de Vos et al., 2012; McAuliffe et al., 2016). This study uses both validated and reliable sonographic and clinical outcome measurement tools.

Some authors have claimed that there is a cohort of patients who present with tendon-derived pain that have normal sonographic imaging (Longo et al., 2009). In the clinical setting, we do not encounter this phenomenon and suggest that either the equipment quality or assessment criteria used to define pathology may be inadequate. A systematic review by McAuliffe et al. (2016) cited a limitation of previous studies using variable terminology to define what is abnormal on ultrasound, raising the possibility of misrepresentation of the relationship between structure and function. It should be noted that all symptomatic tendons assessed in our study displayed sonographic abnormalities (Table 8) indicating that the AUAT is a sensitive tool for the detection and identification of sonographically visualised pathology in chronic Achilles tendinopathy. The findings from the initial study align with the growing consensus that symptomatic tendons are associated with abnormal imaging findings, yet the degree of symptomology is not directly related to the severity of these changes (McAuliffe et al., 2016).
The results from our study showed that at 24-week follow-up of the same patient cohort, after high-volume peritendinous injection and physiotherapist-guided rehabilitation, there was a statistically significant relationship between sonographic findings and clinical symptoms. The potential reasoning behind these conflicting results from the same patient cohort at differing time periods is discussed below.

Ultrasound assessment of both tendon thickness and echogenicity have been shown to be sensitive to change; a study among athletes showed that changes in both can be identified within short time periods (Malliaras et al., 2010). In a later study, Malliaras and Cook (2011) showed that tendons can change up to 3mm in anterior-posterior thickness within only one month and that focal changes within tendons can develop and be seen sonographically within this timeframe. Yet until now correlation of each of these factors (tendon thickness and grey-scale changes) with symptoms has only occurred individually. Each of these individual sonographic findings have shown a variable relationship to clinical symptoms (Malliaras & Cook, 2011). Supporting evidence that some individual components of imaging have a relationship with symptoms, Khan et al. (2003) showed that the total volume of hypoechogenicity on ultrasound correlated with the severity of symptoms as measured by the VISA-A score ($r_s = -0.33, p < 0.01$). Similar findings have been reported with increasing neovascularity, tendon thickness and hypoechoic or heterogeneous change within a tendon having inverse relationships with tendon pain (Bakkergaard et al., 2015; Malliaras et al., 2012). De Jonge et al. (2014) established that when looking at neovascularity alone there is a weak association with clinical severity as assessed by the VISA-A (odds ratio $\text{Exp}(B) = 1.017$). When neovascularity and structural changes are present together there is a much stronger likelihood of the tendon being symptomatic, despite this finding, previous studies have only looked at individual components and explored their relationship to symptoms. (Ohberg et al., 2001). The current study found that when using an all-encompassing method to assess all components of Achilles tendinopathy, there is a moderate strength correlation with the VISA-A ($r_s = -0.56, p = 0.0001$).
An increase in Achilles tendon anterior-posterior diameter has been linked with the presence of intratendinous pathology, including the sonographic abnormalities of heterogeneous tendon echogenicity and the presence of intratendinous Doppler flow (Hirschmuller et al., 2010; Peers et al., 2003; Richards et al., 2005). A history of loading activity predisposes tendons to structural change, with Hirschmuller et al. (2010) demonstrating Achilles tendons in runners that are or have previously been symptomatic are significantly thicker than normal tendons. Additionally, these tendons have an increased incidence of sonographic hypoechoic lesions and intratendinous neovascularity (Hirschmuller et al., 2010). In the current study, there was no significant difference between tendon thickness at follow-up, with almost identical mean diameters, yet there was a significant difference in AUAT score along with a clinical improvement in VISA-A score (Table 7, Table 9). These results indicate that the AUAT is a more sensitive method to evaluate tendon change than solely the measurement of tendon thickness. Additionally, the AUAT has a moderate strength correlation with the VISA-A ($r_s = -0.56$, $p = 0.0001$), whereas tendon thickness only displayed a low-level relationship ($r_s = -0.38$, $p = 0.0124$), implying that the AUAT has a stronger relationship to clinical severity than tendon thickness (Hinkle et al., 2003).

There are studies declaring that there is no correlation between sonographic abnormalities and pain in tendons with chronic tendinopathic changes (Boesen et al., 2012; de Vos et al., 2012; Peers et al., 2003). When evaluating results after treatment, Alfredson, Zeisig, and Fahlström (2009) found no normalisation of tendon structure and thickness years after intratendinous surgery, despite successful clinical outcomes. Conversely, Ohberg et al. (2004) and Lind, Ohberg, and Alfredson (2006) found remodelling of the tendon towards normalisation, with decreased thickness and improved sonographic appearance associated with clinically successful outcomes after eccentric training and sclerosing injections respectively. These conflicting results may be due to the assessors using differing assessment techniques. A follow-up study evaluating treatment of patellar tendinopathy found a positive correlation between both neovascularity and
structural change and the visual analogue score for pain during activity (Sunding et al., 2016). This is supported by the results of the present study using reliable and valid sonographic assessment techniques and outcome measures, indicating that after intervention when symptoms improve, the Achilles tendon reverts towards a more normal sonographic appearance.

Although exercise therapy has been associated with the improvement of tendon structure, de Vos et al. (2012) demonstrated that clinical improvements in 23 patients with chronic mid-portion Achilles tendinopathy after a 16-week eccentric exercise program did not correlate with ultrasound imaging using ultrasound tissue characterisation (UTC). These patients had a significant increase in their VISA-A by a mean of 11.3 points at 24-week follow-up, yet there was no significant change in patients imaging assessed by UTC ($r_s = -0.2, p = 0.94$). Our study contradicts these findings with a significant relationship found between sonographic appearance and clinical severity, associated with a clinical improvement after an intervention. Results from the current study raise the hypothesis that the AUAT may be a more sensitive method to assess tendons than UTC, however future comparative studies are required to establish this potential status.

It is known that sonographic change and intratendinous abnormalities tend to precede tendon pain for a variable period of time with these changes also persisting after the resolution of symptoms (Malliaras et al., 2006). The most common form of tendon healing is by scarring, which is inferior to the tendon healing via regenerative pathways (Jozsa & Kannus, 1997). This healing method is a prolonged process with granulation tissue slowly developing into mature scar, whilst collagen maturation and remodelling occurs. However, once the tendon undergoes degenerative tendinopathy with resultant cell dysfunction and death, the matrix of the tendon is unable to fully regain its structural integrity (Cook & Purdam, 2009). Histopathologically, this results in the tendon losing its capacity to fully structurally repair; however, the requirement of full repair may be insignificant as patients can often become asymptomatic and reach a full functional recovery without a full
structural recovery (Cook & Purdam, 2009). This has previously been supported by Ohberg et al. (2004) demonstrating that once Achilles tendon pain improved, sonographic structure and vascularity improved to an extent, but some characteristics remained abnormal for a number of years. Similar findings have been shown after intervention implying that improvements in pain and function are not mediated by changes in tendon structure and do not correlate with VISA-A scores (Drew et al., 2014; Richards et al., 2010). Therefore, from this finding, it is accepted that complete normalisation of tendon structure is not required for resolution of symptoms, with only minor improvements or relative tendon morphological stability being associated with improved outcomes. However, it needs to be considered that the sonographic assessment techniques used in previous studies evaluating this relationship may not be sensitive enough to detect subtle improvements in tendon structure and the utilisation of a more comprehensive sonographic assessment such as the AUAT may have led the authors to reach differing results.

The reason for the discrepancy between initial and follow-up correlation assessments is not clear. These conflicting results may be due to a number of factors. Firstly, tendon pain can be multifactorial, arising from the tendon itself, biochemical irritants, peritendinous tissues, neurovascular ingrowth or central neurological factors (Drew et al., 2014; Fredberg & Stengaard-Pedersen, 2008; Lian et al., 2006; Mosley et al., 2003; van Sterkenberg & van Dijk, 2011). As only a select few of these multifactorial pain generators can be visualised sonographically, it is therefore likely that some of the discrepancy between pathology and symptoms exist due to the complex interplay of local and central up-regulated factors with potential pain mechanisms coming from cellular sources. Imaging can only assess the structural degeneration of the load-bearing matrix that may occur during tendinopathy and the AUAT adequately reflects these changes. Additionally, improvements in tendon structure, although associated with improved outcomes are not a necessity for clinical improvement (Drew et al., 2014). Research on pathological Achilles and patellar tendons using ultrasound tissue characterisation
demonstrated an increase in mean cross-sectional area of aligned fibrillar structure compared to structurally normal tendons (Docking & Cook, 2015). This increase in volume of normally visualised tendon fibres has led to the hypothesis that pathological tendons increase their size as a method to maintain aligned fibrillar structure to still tolerate load. This implies that tendon thickening and irregularity is an adaptation to load and that relative stability in tendon structure, rather than a change towards normalisation is linked to improved outcomes (Docking & Cook, 2015). Therefore, it is hypothesised that the tendons assessed at initial presentation were relatively volatile in structure as the tendinopathy disease process was evolving. Conversely at follow-up, although still sonographically abnormal these tendons may be in a relatively static state, with this relative stability rather than volatility having a potential stronger relationship with symptomology.

Limitations of this study include the methodological process where only patients who underwent intervention were followed-up. The study of a control cohort who did not receive intervention would add further weight to these findings. Additionally, since there was a change in relationship between sonographic presentation and symptoms between initial presentation and medium-term follow-up, future studies should determine what relationship exists at the short-term (12-weeks) and long term (12-months to 2-year) time points. Finally, future studies may compare the AUAT to other tendon assessment techniques that have previously been correlated with symptomology to determine superiority, such as the historical Archambault 3-point scale of tendon assessment, the Ohberg method of assessing neovascularisation, and the more modern techniques of elastography and ultrasound tissue characterisation (Archambault et al., 1998; de Vos et al., 2012; Khan et al., 2003; Ohberg et al., 2001; Ooi et al., 2015).

7.8 Conclusion
The results of this study are conflicting, however they are representative of the current literature and demonstrate that there is a disconnect between tendon structure and clinical symptoms. All tendons in this study displayed sonographic
abnormalities, confirming symptomatic tendons have structural changes that can be visualised sonographically when an appropriate assessment criteria such as the AUAT is used. However, this sonographic presentation and correlation with symptoms is variable.

When the follow-up or surveillance of symptomatic tendons is concerned, tendons that improve clinically have a stronger correlation with sonographic findings. This improved association between structure and symptoms may be due to reduced structural volatility as the tendon reverts towards a more normal state. When assessing this relationship, the AUAT has a stronger level of agreement to the VISA-A than the simple measurement of tendon thickness.

The clinical relevance of this study confirms the disconnect between structure and symptoms in tendinopathy. Additionally, due to the known phenomenon of asymptomatic tendons demonstrating sonographic pathology, diagnosis and management of Achilles tendinopathy should not be solely based on either sonographic appearance or clinical diagnosis, but should be in combination with patient history, clinical and sonographic evaluation.
Chapter Eight:
Discussion and Conclusion

This thesis set out to examine the pathological presentation of Achilles tendinopathy and its appearance using ultrasound imaging, the relationship of sonographic findings to clinical severity, and treatment regimes. The intention of this research was to assist in better understanding the sonographic changes associated with Achilles tendinopathy, to help improve reliability of ultrasound assessment using a newly developed tool and to evaluate the effectiveness of high-volume injection therapy in the management of Achilles tendinopathy. There were four specific aims to this research:

1. The development of a standardised, objective sonographic tool to allow reliable and repeatable assessment of the Achilles tendon using ultrasound.

2. To establish that this newly formed tool is a valid and reliable method for the assessment of Achilles tendinopathy when used by radiologists and sonographers.

3. To demonstrate the relationship between ultrasound findings and clinical symptoms in patients with mid-portion Achilles tendinopathy.

4. To explore the potential change in pain and function as assessed by the VISA-A score and directly compare it to changes in sonographic findings after a single ultrasound guided high-volume peritendinous glucocorticoid injection in conjunction with a physiotherapist based loading program at 24-weeks.

These aims were achieved through four studies involving, the formation of an expert panel and Delphi process, a construct validity and reliability study on ultrasound images from patients with selected variable degrees of tendinopathy, and a case series on subjects with diagnosed Achilles tendinopathy undergoing injection therapy.
The four studies were:

- Chapter Four: The Formation of the Achilles Ultrasound Assessment Tool (AUAT).
- Chapter Five: The Reliability and Construct Validity of the AUAT.
- Chapter Six: High-Volume Injection Therapy – A Novel Adjunct in the Management of Achilles Tendinopathy.
- Chapter Seven: AUAT and Correlation with Patient Symptoms.

8.1 Summary of Findings

A review of the literature confirmed the disparity in current terminology and assessment techniques for the sonographic assessment of the Achilles tendon. Based on this knowledge, a focus group of professional experts in lower limb disorders, tendinopathy and radiology collaborated via a Delphi process to formulate the Achilles ultrasound assessment tool (AUAT). This scoresheet allows for the holistic assessment of the entire spectrum of sonographic changes present within the tendinopathic tendon and peritendinous tissues and allows for the semi-quantification and grading of the appearance of these structures. This scoresheet was designed to be easily performed, sensitive to change, and to enable a standardised, objective, reliable assessment of the Achilles tendon. The AUAT has had its content, language and structure validated through this Delphi process.

The AUAT scoresheet is divided into a primary tendinopathy component and a complications or barriers to treatment component. The primary tendinopathy component encompasses tendon thickness, echogenicity and echotexture, along with a modified Ohberg score for the identification of neovascularisation and the identification of the number of regions involved. The complications associated with Achilles tendinopathy include the presence of calcifications, paratendinopathy, plantaris pathology, and enthesopathy. The enthesopathy component is further broken down to include pathology of the retro-calcaneal bursa, superficial bursa and Kager’s fat pad, as some or all of these components may be present with active
enthesopathy and may contribute to symptoms. The management of each of these complications are dependent on an accurate diagnosis, hence the inclusion of each into the AUAT.

The items are weighted according to their perceived relevance by the independent expert panel, with the tendinopathy and complications components scoring up to 13 and 7 points respectively, giving a total tendinopathy score of 20 points. Thus, allowing the AUAT to sonographically semi-quantify and grade an Achilles tendon between 0 (normal) and 20 (pathological). To supplement the AUAT, an associated technical briefing was developed based on clinical practice, to help guide and allow self-directed education on how to accurately apply the tool and grade the Achilles tendon using ultrasound.

The AUAT was then formally assessed for reliability and construct validity when applied by both sonographer and radiologist groups. The results shown within this thesis demonstrate the validity of the AUAT, with observers being able to agree on a significant difference between sonographically normal and abnormal tendons ($\kappa = 0.481, p \approx 0$). Additionally, blinded inter-observer levels of agreement between sonographers were almost perfect ($\kappa = 0.917, p = 0.00636$) and defined inter-observer reliability levels between radiologist and sonographer groups demonstrated similar excellent results ($\kappa = 0.949, p \approx 3.22 \times 10^{-6}$). The longitudinal intra-observer reliability of the AUAT on sonographically pathological Achilles tendons showed consistency between observers, with no significant change between assessments at a two-week time point ($p > 0.05$). These presented results support the use of the AUAT as a reliable, repeatable and reproducible tool to accurately represent the sonographic changes associated with Achilles tendinopathy in clinical practice.

The goal in management of Achilles tendinopathy is to return patients to their desired level of activity without significant residual pain. When Achilles tendon disease becomes recalcitrant to conservative treatment, injection therapy is often
employed (Boesen et al., 2014). High-volume peritendinous glucocorticoid injections are one such method of injection therapy that is growing in popularity. Many studies use the term 'high-volume injection' to describe large volume peritendinous injections, yet there is no consensus within the literature as to what volume this entails (Boesen et al., 2014; Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013). The technique utilised in this thesis used a combined injectate mixture of 1mL celestone chronodose (5.7 mg/mL betamethasone) with 2mL xylocaïne (lidocaine [1%] 20mg in 2mL) and 20mL of cold normal saline (sodium chloride 180mg in 20mL), injected in the peritendinous space, both anterior and posterior to the tendon.

43 patients underwent this method of injection therapy in conjunction with a physiotherapist guided load-based rehabilitation program. This research demonstrated that a single high-volume peritendinous glucocorticoid injection when combined with exercise therapy significantly improved the sonographic appearance of the Achilles tendon and improved pain and function at 24-week follow-up in patients with recalcitrant Achilles tendinopathy. These improvements had median reduction of -3 points on AUAT assessment ($p = 2.57 \times 10^{-5}$) and a median 26-point increase on the VISA-A scale ($p = 1.586 \times 10^{-5}$). These results compared favourably with smaller case series on high-volume injection therapy in regard to tendon structure and symptoms (Boesen et al., 2017; Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013; Resteghini & Yeoh, 2012; Wheeler, 2014). This prospective study utilised blinded assessors, a consistent injectate mixture and technique, with validated outcome measures and a consistent follow-up period; features that previous studies have failed to achieve. This is the largest case series reporting the positive effects of high-volume injections for the treatment of Achilles tendinopathy and is one of the only studies with a consistent medium-term follow-up period.

The relationship between sonographic findings and symptoms were then assessed with conflicting results. At initial presentation, patients with recalcitrant Achilles
tendinopathy had no association with either their AUAT score or tendon thickness with the clinical score of symptomology, the VISA-A ($p > 0.05$). Yet at follow-up after intervention, a relationship with both of these sonographic assessment techniques and symptoms existed. Tendon thickness delivered a low-level correlation to VISA-A score with spearman correlation coefficient of $r_s = -0.38$ ($p = 0.0124$), whilst the AUAT revealed a stronger relationship with VISA-A score of $r_s = -0.56$ ($p = 0.0001$). These conflicting results are representative of the current literature demonstrating that there is a disconnect between structure and symptoms. All tendons in this study demonstrated sonographic abnormalities confirming that symptomatic tendons have structural changes that can be visualised sonographically when an appropriate assessment criteria such as the AUAT is used, however, this sonographic presentation and correlation with symptoms is variable. Additionally, no significant difference between tendon thickness at 24-week follow-up was found, yet there was a significant difference in AUAT score along with a clinical improvement in VISA-A score. These results indicate that the AUAT is a more sensitive method to evaluate tendon change than solely the measurement of tendon thickness.

8.2 Implications of Findings
The formulation of the AUAT involved the establishment of the first all-encompassing assessment method for both greyscale and Doppler ultrasound on the Achilles tendon. The ability of the AUAT to differentiate and semi-quantify normal tendons from abnormal, even with only mild sonographic changes, highlights the strengths and potential clinical applicability of this tool. While previous authors have assessed individual components of Achilles tendinopathy and used these to assist in the diagnosis of tendinopathy, direct treatments, monitor the efficiency of interventions and assess the risk of developing symptoms; the use of variable and limited assessment techniques is flawed (Scott et al., 2013). Now, with the development of the AUAT, there is a new method which allows for the specific, repeatable and reliable identification of sonographic findings, thus, allowing the direct comparison between studies and the accurate monitoring of the effectiveness.
of treatments. Additionally, this may lead to improvements in patient outcomes by giving the treating clinician supplementary information regarding the health of the tendon, stage and extent of tendinopathy.

Within the radiology profession, both sonographers and radiologists routinely dually assess patients with musculoskeletal problems when referred for a diagnostic medical ultrasound. The level of agreement between professionals is paramount to improving patient outcomes, along with efficiency within a radiology practice. Given the previous limited research into the inter-observer reliability of ultrasound when evaluating tendon disease, the high levels of inter and intra-observer agreement demonstrated in this research supports the use of the AUAT both in the clinical and research environment (Sunding et al., 2016). This proven reliability gives the assessor confidence that despite the background of the observer, they will reach a near same score.

The identification of potential barriers or complications of management is of the utmost importance within medical imaging examinations as clinical reasoning may change, ultimately affecting treatment and prognosis. The AUAT can help to facilitate the identification of such restrictions. Already there have been treatment techniques directed towards the plantaris tendon if involved in the tendinopathy process, with some authors claiming the diagnosis of plantaris tendon involvement being difficult to make (Alfredson, 2017). The AUAT readily considers plantaris involvement, and if broadly applied as an assessment tool, the use of the AUAT may have a profound effect on the direction of treatment approaches applied in clinical practice.

Paratendinopathy has been shown to be associated with Achilles tendinopathy; however, in this study and patient cohort, an almost direct relationship was demonstrated between sonographically abnormal Achilles tendons and paratenon abnormalities (Ruergard & Alfredson, 2014). Therefore, changes to the paratenon
may be more common than originally thought, with identification and treatment methods directed towards the paratenon being of increased importance.

The finding that all tendons remained sonographically abnormal after treatment, yet improved clinically, contributes to the belief that a degenerative tendon can structurally improve only to a point, and despite the presence of intra-tendinous pathology, reaches a level of tissue homeostasis that allows for pain-free function to return (Drew et al., 2014). The findings from this research contribute to the growing body of evidence that there is a disconnect between structure and pain (McAuliffe et al., 2016). However, the AUAT has a stronger relationship to symptoms than the measurement of tendon thickness alone.

Some authors have claimed that there is a cohort of patients who present with tendon-derived pain that have normal sonographic imaging (Longo et al., 2009). It should be noted that all symptomatic tendons assessed in the course of this research displayed sonographic abnormalities indicating that the AUAT is a sensitive tool for the detection and identification of sonographically visualised pathology. The AUAT may be a more sensitive tool to assess sonographic tendon changes than those used by other authors and may be a more appropriate choice for monitoring the efficiency of treatments. The AUAT has established itself as a valid and reliable sonographic measurement tool that is ideally positioned to be the leading outcome assessment in the sonographic assessment of the Achilles tendon in future research projects.

Since Achilles tendinopathy is often multi-factorial and can involve multiple pathologies, treatment needs to be individualised to the patient, based on the pathology present, using current evidence based rehabilitation techniques (Alfredson & Cook, 2007). Research from this study has demonstrated that a single high-volume peritendinous glucocorticoid injection is a beneficial intervention when combined with exercise therapy in improving patient outcomes and assists in normalising tendon structure. The results of a median 26-point increase in VISA-A
score after intervention indicate that these findings are not only statistically significant, but they also have clinical significance.

Whilst considering that the intervention applied was peritendinous in nature, this research adds further evidence that the peritendinous tissues are a significant contributing factor in the origin and progression of tendinopathy. Glucocorticoids, whilst controversial in their role within the management of tendinopathies, have been shown in this study, when combined as part of a high-volume injection, to be beneficial. Additionally, high-volume peritendinous glucocorticoid injections are advantageous in Achilles tendinopathy when targeted and the appropriate methodology used, in progressing the tendon towards a more normal sonographic structure and improving function. This technique is already beginning to be implemented in the clinical setting for the management of recalcitrant Achilles tendinopathy. This research adds to the body of knowledge in the realm of injection therapy, assisting clinicians to make evidence-based clinical reasoning decisions and facilitating the better management of patients.

8.3 Thesis Limitations
There are several methodological limitations brought to light throughout the course of this thesis. The aggregate rating of the morphological sonographic tendon changes seen when using the AUAT has not been validated as a measure of pathological severity. Ideal validation of the AUAT would require comparison with histological analysis of the tendons and the process of acquiring tissue samples for correlation is problematic and poses several ethical dilemmas. This research is comparative with other studies where the clinical diagnosis was used as the gold standard to which validity assessment was compared, rather than histological agreement (Docking et al., 2015). Additionally, the reliability and validity of the AUAT demonstrated throughout these studies has been established using only experienced ultrasound clinicians from a limited geographical region. Expansion to assess these qualities using more encompassing populations should be performed.
High-volume peritendinous glucocorticoid injection therapy has shown to improve tendon morphology, however the holistic management methodology used in this study was such that injection therapy was combined with exercise therapy. The concurrent use of exercise therapy utilises the mechanosensitive properties of tissues which has previously been shown to stimulate the production of new collagen fibres, promote the release of growth substances and stimulate the release of enzymes that are important in regulating cell activity and matrix deregulation (Abate et al., 2009; Langberg et al., 2007; Ohberg et al., 2004; Rio et al., 2015). Therefore, some of the improvement in tendon morphology as represented as a reduction in AUAT score can potentially be attributed to the concurrent physiotherapist-guided loading program. It can however be postulated that since all patients included in this study had previously failed conventional therapy, including exercise therapy programs, the high-volume injection not only had an advantageous effect on tendon morphology, but also potentially reduced patient symptoms allowing them to further progress their rehabilitation programs.

Another limitation of the interventional study involved the concurrent physiotherapist guided exercise intervention applied in conjunction with injection therapy. This intervention was not uniform in nature nor standardised across participants. It was instead individualised to participants abilities, needs and requirements. This methodology, although not the preferred methodology in a pure research setting, is entirely representative of real-world clinical practice.

The methodology of the correlation study was such that only patients who underwent intervention were followed-up. Since the majority of patients had a successful outcome after intervention, this is a source of potential bias towards a positive correlation. The study of a control cohort who did not receive intervention would add further weight to these findings.
8.4 Further Areas of Research

There are a number of concepts brought to light during the course of this thesis that are avenues for future research initiatives. Firstly, although sonographers and radiologists are the main groups of professionals who utilise ultrasound to diagnose and assess musculoskeletal problems, there are an increasing number of other health professionals incorporating this skill into their daily practice. This group includes rheumatologists, sports medicine physicians, physiotherapists and podiatrists (Yim & Corrado, 2012). Future studies may involve assessing the reliability of the AUAT between non-radiology observer groups.

Another finding was that the assessment method used in the AUAT of assessing peritendinous changes only stated whether changes in the paratenon were present or not. This may not accurately represent the potential subtle changes in the peritendinous tissues that can occur. At present, there is no established reliable method or descriptor available to sonographically assess changes to the paratenon that is sensitive to change. With the increased observed incidence of paratenon change and research placing a highlighted emphasis on the peritendinous tissues, future research should be directed at developing methods to assess and grade these changes.

The Technical Briefing (Appendix 3) gives examples of the differing sonographic abnormalities that may be observed when assessing the Achilles tendon and how to score them using the AUAT. These images should be replaced with clearer, better optimised images as technology improves and as more clinical cases become available to the scoresheet developers.

Studies comparing the relationship between ultrasound findings and symptoms have utilised various methodologies with conflicting conclusions (Boesen et al., 2012; de Vos et al., 2012; Peers et al., 2003). Previously used techniques and methodologies include the Ohberg method of assessing vascularity, the Archambault method of grey-scale assessment, elastography, ultrasound tissue characterisation
and MRI assessment (Archambault et al., 1998; de Vos et al., 2012; Khan et al., 2003; Ohberg et al., 2001; Ooi et al., 2015). Therefore, future studies should compare the AUAT assessment technique with other assessment methods that have been previously used in the literature, and determine the relationship of each with symptoms as assessed by the VISA-A. These comparative studies have the potential to determine if any other method of assessment possesses characteristics which have a stronger relationship to clinical symptoms than the AUAT.

Since there was a change in the relationship between sonographic findings (AUAT score) and symptoms (VISA-A) between initial presentation and medium-term follow-up (24-weeks), future studies should determine what level of correlation exists at different time points. The relationship between AUAT and VISA-A assessments should be examined at both the short-term (12-weeks) and long term (12-months to 2-year) time points to determine when this correlation changes and if it continues to change with time. Finally, since the majority of tendons assessed through the course of this thesis were chronic and degenerative in nature, future studies should assess the applicability and clinical relationship of the AUAT with tendons in other pathological states, such as acute reactive Achilles tendinopathy.

The AUAT has been primarily developed as an assessment method for the Achilles tendon. Research on sonographic assessment and quantification of tendon pathology has often applied similar methodologies to both the Achilles and patellar tendons, as similar pathological processes occur with disease of these tendons (Cook & Purdam, 2009). Therefore, future research may involve the development of a similar valid and reliable assessment for the patellar tendon based on the structure of the AUAT. Previously, similar modifications of outcome measurements exist, with the VISA-A, being originally derived from the VISA-P (patellar tendon) questionnaire and more recently the VISA-G (greater trochanteric pain syndrome) questionnaire also being developed as an adaptation of the VISA-P (Fearon et al., 2015).
As researchers have utilised various methodologies for their versions of high-volume injection therapies, a direct comparison between the methodology employed in this research and alternative injection techniques should be performed to determine clinical superiority (Boesen et al., 2017; Chan et al., 2008; Humphrey et al., 2010; Maffulli et al., 2013; Resteghini & Yeoh, 2012; Wheeler, 2014). Ideally a randomised controlled trial should be performed to compare the various injection techniques with placebo (sham) injection groups, both with and without concurrent exercise therapy, on a large cohort of patients to determine if other techniques can deliver equally impressive outcomes.

8.5 Conclusion

The AUAT has been proven to be a valid and reliable tool to define and represent the sonographic changes involved in Achilles tendinopathy and possesses qualifications to be a useful instrument when evaluating the status and progress of Achilles tendon disease. The construct validity of the AUAT via its Delphi formation along with its high levels of inter and intra observer reliability demonstrate the strengths and clinical applicability of this tool. The relationship of the AUAT to clinical symptoms is variable, with this study contributing to the growing body of evidence that there is a disconnect between structure and pain.

This research has shown that in patients with recalcitrant Achilles tendinopathy, a single high-volume peritendinous glucocorticoid injection combined with a supervised rehabilitation program can lead to a significant reduction in pain and improvements in both function and tendon sonographic appearance.

This research adds important information to the body of work surrounding the diagnosis, diagnostic imaging criteria and treatment of Achilles tendinopathy. The findings from these studies have a valuable impact on both medical imaging and sports medicine groups with the underlying goals of improving the reliability of diagnostic imaging, influencing the clinical management and treatment of Achilles tendinopathy, while most importantly, improving patient outcomes.
Michael underwent a diagnostic ultrasound and interventional procedure involving the AUAT assessment and a high-volume peritendinous glucocorticoid injection. Information gained from the AUAT assessment regarding the status and health of his Achilles tendon and peritendinous tissues were given to his treating sports physician and physiotherapist. This information resulted in a modification of his rehabilitation program, and post injection therapy, a reduction of symptoms allowed him to progress with his load-based exercise program. Following this procedure and 5 months of rehabilitation, Michael went on to compete in a 10km run as part of the Gold Coast marathon running festival, finishing in 32:49; falling only 7 seconds short of his personal best that he set some 8 years ago.


Bisset, L., Beller, E., Jull, G., Brooks, P., Darnell, R., & Vicenzino, B. (2006). Mobilisation with movement and exercise, corticosteroid injection, or wait and


Coombes, B. K., Bisset, L., Brooks, P., Khan, A., & Vicenzino, B. (2013). Effect of corticosteroid injection, physiotherapy, or both on clinical outcomes in
patients with unilateral lateral epicondylalgia: A randomized controlled trial. 


Emerson, C., Morrissey, D., Perry, M., & Jalan, R. (2010). Ultrasonographically detected changes in Achilles tendons and self reported symptoms in elite


interrater reliability and agreement, R package version 0.84. URL http://CRAN.R-project.org/package=irr


Vasta, S., Di Martino, A., Zampogna, B., Torre, G., Papalia, R., & Denaro, V. (2016). Role of VEGF, nitric oxide, and sympathetic neurotransmitters in the


## Appendix 1: AUAT

### Tendon Size

<table>
<thead>
<tr>
<th>Lt / Rt</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendon Thickness - AP diameter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6mm</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>6-8mm</td>
<td>☒</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>8.1-10mm</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>&gt; 10mm</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### Echotexture – Diffuse vs Focal Changes

<table>
<thead>
<tr>
<th></th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendon Thickness - AP diameter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse Changes – Gross assessment of cross-sectional hypoechoic area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>&lt; 50% Hypoechoic</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>≥ 50% Hypoechoic</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Focal Changes – Largest measurement of focal hypoechoic area or cystic space</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1-5mm</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>&gt; 5mm</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### NeoVascularity

<table>
<thead>
<tr>
<th>Degree of Vascularity</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Mild</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Moderate</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Florid</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### Regions of Vessels

<table>
<thead>
<tr>
<th></th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>3</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### Complications

<table>
<thead>
<tr>
<th></th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcification</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Partendinopathy</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Plantaris Pathology</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Enthesopathy</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>RC Bursa</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Fat Pad</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Superficial Bursa</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### Tendinopathy Total

<table>
<thead>
<tr>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcification</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Partendinopathy</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Plantaris Pathology</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Enthesopathy</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>RC Bursa</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Fat Pad</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Superficial Bursa</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### Complications Total

<table>
<thead>
<tr>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcification</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Partendinopathy</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Plantaris Pathology</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Enthesopathy</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>RC Bursa</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Fat Pad</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Superficial Bursa</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### Assessor: Date: / /

### AUAT Score

<table>
<thead>
<tr>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
<th>☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcification</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Partendinopathy</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Plantaris Pathology</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Enthesopathy</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>RC Bursa</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Fat Pad</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Superficial Bursa</td>
<td>No</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
Appendix 2: VISA-A

IN THIS QUESTIONNAIRE, THE TERM PAIN REFERS SPECIFICALLY TO PAIN IN THE ACHILLES TENDON REGION

1. For how many minutes do you have stiffness in the Achilles region on first getting up?

<table>
<thead>
<tr>
<th>Points</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Once you are warmed up for the day, do you have pain when stretching the Achilles tendon fully over the edge of a step? (keeping knee straight)

<table>
<thead>
<tr>
<th>Points</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>strong severe pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>no pain</td>
</tr>
</tbody>
</table>

3. After walking on flat ground for 30 minutes, do you have pain within the next 2 hours? (If unable to walk on flat ground for 30 minutes because of pain, score 0 for this question).

<table>
<thead>
<tr>
<th>Points</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>strong severe pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>no pain</td>
</tr>
</tbody>
</table>

Figure 1: The VISA-A questionnaire. Eight questions are used to determine the VISA-A score (continued). The VISA-A questionnaire can be downloaded in full at http://bjsm.bmjjournals/cgi/content/full/35/5/336/DC1.
We administered the VISA-A questionnaire to four populations: group 1 (non-surgical patients; n = 45) attended a primary care sports medicine clinic; group 2 (presurgical patients; n = 14) had been referred to a sports orthopaedist for tendon surgery; group 3 (university students; n = 63) represented a convenience sample of young normally active people to serve as a control group; group 4 (members of a running club; n = 24) represented active, but non-injured people whose age matched the patient groups. As imaging does not provide a yardstick for tendon disorders, diagnosis was by assessment of two expert clinicians, as has been justified in other tendon studies. For inclusion in the study, subjects in all groups had to be older than 18 who were able to give written informed consent. For groups 1 and 2, subjects had to have a diagnosis of Achilles tendinosis, paratendinitis, or partial rupture with or without a retrocalcaneal or Achilles bursitis. For groups 3 and 4, subjects had to belong to the two groups as defined. Women who were pregnant or nursing were excluded, as were patients with a total rupture of the Achilles tendon. Subjects with previous or current Achilles tendon symptoms, but who were not currently undergoing treatment for the condition, were not excluded from the control groups as these groups were designed to reflect the populations.

We tested construct validity in two ways. Firstly, the 45 non-surgical patients in group 1 completed the VISA-A test and two other...
8. Please complete EITHER A, B or C in this question.

- If you have **no pain** while undertaking *Achilles tendon loading sports* please complete Q8A only.
- If you have **pain** while undertaking *Achilles tendon loading sports* but it does **not stop you from completing the activity**, please complete Q8B only.
- If you have **pain that stops you from completing *Achilles tendon loading sports***, please complete Q8C only.

A. If you have **no pain** while undertaking *Achilles tendon loading sports*, for how long can you train/practise?

<table>
<thead>
<tr>
<th>NIL</th>
<th>1–10 mins</th>
<th>11–20 mins</th>
<th>21–30 mins</th>
<th>&gt;30 mins</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7</td>
<td>14</td>
<td>21</td>
<td>30</td>
</tr>
</tbody>
</table>

B. If you have **some pain** while undertaking *Achilles tendon loading sports*, but it does not stop you from completing your training/practice, for how long can you train/practise?

<table>
<thead>
<tr>
<th>NIL</th>
<th>1–10 mins</th>
<th>11–20 mins</th>
<th>21–30 mins</th>
<th>&gt;30 mins</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4</td>
<td>10</td>
<td>14</td>
<td>20</td>
</tr>
</tbody>
</table>

C. If you have **pain that stops you** from completing your training/practice in *Achilles tendon loading sports*, for how long can you train/practise?

<table>
<thead>
<tr>
<th>NIL</th>
<th>1–10 mins</th>
<th>11–20 mins</th>
<th>21–30 mins</th>
<th>&gt;30 mins</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>10</td>
</tr>
</tbody>
</table>

**TOTAL SCORE ( /100)**
Appendix 3: AUAT Technical Briefing

Achilles Ultrasound Assessment Tool (AUAT)
Technical Briefing

User Information
The Achilles Ultrasound Assessment Tool (AUAT) is designed to be a valid and reliable numeric scoresheet that rates the health of the Achilles tendon as seen using diagnostic ultrasound. The AUAT aims to be an all-encompassing summary of the spectrum of sonographic changes present within a tendinopathic tendon. It includes tendon thickness, echotexture, neovascularity and complications; whilst grading these in a quantitative manner. This tool has been formulated to give a numeric rating from 0 (healthy) to 20 (pathological) based on the features of the Achilles tendon that can be seen on ultrasound.

The aim of this guide is to help the user identify the different components of Achilles tendinopathy and to determine how to grade them accordingly using the AUAT. Each component of the AUAT is explained below with descriptors and examples.

Warm up and patient positioning
To standardise tendon size and perfusion, a standard warm-up should be performed. We recommend asking the patient to perform 10 bilateral calf raises; to use 3 seconds for the concentric part of the raise, to use 5 seconds for the eccentric part, and to stop if it is too painful to continue.

Patients are to be positioned prone with their feet off the end of the plinth in neutral dorsiflexion/plantarflexion for grey-scale assessment. For Doppler assessment, the patient should be positioned sitting on the edge of the bed with their legs in a gravity dependent position and ankles in a relaxed position of plantar flexion. This gravity dependent, relaxed position puts the tendon in a loose-packed position enhancing Doppler sensitivity.
Tendon Size

Tendon thickness: Anterior-Posterior (AP)

- Measure the tendon at its thickest anterior-posterior diameter, from outer-edge to outer-edge of the paratendon.
- Ensure that the measurement is taken perpendicular to the tendon fibers and that the tendon is not obliquely orientated.
- Take care not to compress the tendon with transducer pressure.

Image 1: Calipers (crosshairs) demonstrate correct placement for measuring anterior-posterior thickness.

Echotexture - Diffuse vs Focal changes

- Determine if the changes within the tendon are focal, diffuse, or are there focal islands of degeneration within a diffusely abnormal tendon?
- Comparisons are made to either a sonographically normal portion of the tendon or the asymptomatic side.
- Note that changes can be both focal and diffuse, therefore if appropriate, both sections may be completed.

Diffuse changes:

- Diffuse changes are determined if there is a loss of echotexture and echogenicity of the tendon in a global setting.

< 50% hypoechoic

- The tendon is defined as being <50% hypoechoic if the changes are diffuse in nature and involve less than 50% of the affected tendon in cross-sectional area.

Image 2: Hypoechoic superficial portion of the tendon (arrows) when compared to the deeper aspect (stars).
Image 3: Hypoechoic superficial portion of the tendon (arrows), involving less than 50% of the tendon in short axis.

≥ 50% hypoechoic

- Changes are considered diffuse in nature if they involve more than 50% of the affected tendon appearing hypoechoic in cross-section.


Image 5. Diffusely hypoechoic tendon involving more than 50% of the tendon in short axis (arrows).
Focal changes:
Classified as Nil, 1-5mm or >5mm
- Focal changes represent intratendinous islands of myxoid degeneration, intratendinous cysts or focal regions of degenerative tendinopathy.
- If focal changes are present, measure the largest total length of intratendinous changes in any plane to quantify the extent of the changes.

1-5mm

Image 6. Small focal island of tendinopathy, as shown by calipers (crosshairs). This region measured 2.8mm in longest diameter.

>5mm

Image 7. Small focal island of degenerative tendinopathy (hypoechoic area – arrows) within a tendinopathic tendon.

Image 8. Large focal area of tendinopathy. The hypoechoic region identified by calipers (crosshairs) measures 24mm.
Image 9. Large anechoic area within the tendon as shown by calipers (crosshairs), representing intra-tendinous cyst formation.

**Neovascularity**

Power Doppler should now be used with sensitivity optimised for low-flow identification including reduced wall filters, high Doppler frequency and low PRF. Gain should be increased until a level just below where the ‘flash’ artifact is observed to optimize visualization of all small vessels present.

**Degree of Neovascularity:**

0 = none, 1 = mild, 2 = moderate, 3 = florid

Identify the degree of Doppler signal within the tendon where 0 represents no visible blood vessels, 1 represents 1-2 blood vessels (mild blood flow), 2 represents several blood vessels (moderate blood flow), and 3 represents many blood vessels (florid blood flow).

0 = none

Image 10. Power Doppler box showing no visible vascularity with the tendinopathic tendon.
Image 11. Power Doppler demonstrating 2 small vessels arising from the ventral tendon.

Image 12: Power Doppler demonstrating several blood vessels throughout the tendon and fat pad.

Image 13. Power Doppler demonstrating many blood vessels diffusely scattered throughout the tendon.
Regions of Vessels:
Identify the number of regions of vessels infiltrating the tendon:
- Nil - no vessels
- 1 group - commonly in the ventral tendon
- 2 groups - also commonly in the ventral tendon
- 3 groups - often an additional group from the posterior paratenon extending into the tendon

Nil Regions

Image 14. No blood vessels visible within the power Doppler box.

1 Region

Image 15. 1 blood vessel arising from the ventral tendon.

2 Regions

Image 16. 2 distinct groups of vessels entering the ventral tendon.
3 Regions

Image 17. Chaotic blood flow with vessels entering the tendon from multiple regions involving both the dorsal and ventral tendon.

Complications

The tendon is then assessed for any potential complications involved in tendinopathy and scored as either a **Yes** or **No**.

Calcification

- Echogenic foci, with or without posterior enhancement within the tendon or peritendinous tissues.

Image 18. Echogenic calcium within a tendon without posterior shadowing (arrows).

Image 19. Echogenic calcium within a tendon with posterior shadowing (crosshairs).
Paratendinopathy
- Thickening, blurring or hypoechogenicity of the paratenon that may or may not include vascularity of the paratenon.

Image 20. Thickened, hypoechoic and striated paratenon surrounding the tendinopathic tendon (arrows).

Image 21. Paratendinopathy demonstrating increased vascularity within the paratenon on power Doppler.
Plantaris Pathology
- Plantaris involvement in either tendinopathy or paratendinopathy, shown as focal thickening or change in echogenicity of the plantaris tendon, if present.

Image 22. Enlarged tendinopathic plantaris tendon to the right of the Achilles tendon, shown as an enlarged circular tendon in cross-section (arrows).

Image 23. Enlarged tendinopathic plantaris tendon to the right of the Achilles with associated plantaris paratendinopathy presenting as a hypoechoic halo surrounding the tendon (arrows).

Enthesopathy
- Pathology of the enthesis that is deemed active and likely to be contributing to symptoms.
- This may include thickening or disruption of the fibrocartilage layer (the hypoechoic line at the junction of tendon and bone), erosions or cysts, and bony spur formation with neovascularity.
- Additionally, there may be tendinopathy of the insertional fibers at the junction of tendon and bone (tendon thickening, focal/diffuse changes in echotexture, calcification, neovasularity and or paratendinopathy)
Image 24. Active enthesopathy showing tendon swelling at the enthesis (arrows), bony spur formation (star) and new vessel growth present at the bone-tendon junction on Doppler ultrasound.

**Retro-calcaneal (RC) Bursa**

- Retro-calcaneal bursa inflammation, identified as thickened bursa walls and or hypoechoic fluid within the bursa.

Image 25. Retro-calcaneal bursitis showing increased anechoic fluid in the Retro-calcaneal bursa (crosshairs).
Fat Pad
- Inflammation of Kager’s fat pad, showing increased echogenicity of the fat pad or vascularity compared to the contralateral side

Image 26. Fat pad inflammation showing increased echogenicity of Kager’s fat pad with an oedematous, mottled appearance of the fat layer anterior to the Achilles tendon (stars).

Image 27. Inflamed, echogenic fat pad on the left (stars) with comparison to the normal fatpad on the right side.

Superficial Bursa
- Presenting as either fluid or thickening within the soft tissues between the posterior Achilles and the dermis.

Image 28. Thickening of the tissues overlying the tendon in the superficial bursa identified by calipers (crosshairs).
Appendix 4: Standardised Warm-up

Grigg, Wearing, and Smeathers (2009) showed that eccentric exercise of a normal Achilles tendon resulted in a decreased diameter for the following 3 hours, however Shalabi et al. (2004) found that chronic tendinopathic tendons increased their volume over the following 30 minutes. Therefore, a standardised warm-up should assist in differentiating normal from pathological tendons by anterior-posterior thickness. Additionally, Cook et al. (2004) has demonstrated that the activity of the tendon before imaging may have a crucial effect on tendon vascularity when imaged with Doppler sonography. Their findings indicate that moderate exercise significantly enhances the detection of tendon blood flow and recommend a standardised warm-up procedure to accurately identify intratendinous neovascularity.

Participants in this study were asked to perform 10 bilateral calf raises and were to use 3 seconds for the concentric part of the raise, to use 5 seconds for the eccentric part, and to stop if it was too painful to continue. These calf raises were performed as a standardised warm-up in an attempt to standardise patient's tendon perfusion, size and to evaluate their level of Achilles tendon pain.
Appendix 5: Sonographic Evaluation

Tendon structure was evaluated using a Toshiba Aplio 500 with PLT-1204BX transducer (Toshiba medical systems corporation, Japan). The patient was placed in a prone position with their feet off the end of a plinth and their ankle in a relaxed (neither dorsiflexed/plantarflexed) position. If anisotropy artefact was present, the ankle was positioned at 90 degrees to elongate the tendon fibres. The tendon was scanned with optimised B-mode scanning parameters such as depth, frequency and focal zone, both in transverse and sagittal planes, from the distal enthesis to the proximal musculo-tendinous junction.

Neovascularity was assessed using a standardised protocol by positioning the patient sitting on the edge of the bed with their legs in a gravity dependant position and ankles in a relaxed position of plantar flexion. There has been research demonstrating that when structures (joints and enthesis) are positioned off tone, Doppler sensitivity is enhanced (Lee, Zayat & Wakefield, 2009; Zappia, Cuomo, Martino, Reginelli & Brunese, 2016). In clinical practice the researchers have found that this gravity dependent, relaxed position puts the tendon in a loose-packed position reducing compressive forces on vascular structures. This position also uses gravity to dilate vascular pathways via physiological vascular engorgement. The researchers have anecdotally found that this positioning grossly enhances Doppler sensitivity in mild to moderate vascular states. Power Doppler ultrasound examination was performed in both the longitudinal and transverse planes using a constant (very light) probe pressure to avoid obliterating vessels. To minimise the pressure on the tendons when scanned, we aimed to have a discernible thin layer of gel seen on the screen, between the transducer interface and the skin. Power Doppler settings were standardised with PRF set at 4.1cm/s, low wall filter settings and Doppler gain was increased to a level where artefactual ‘flash’ colour signal was present, then reduced to just below this level, to maximise sensitivity to low flow.
These settings were chosen because they represent settings sensitive to depict all identifiable vascularity without excessive artefact.

Sufficient images were recorded to demonstrate grey-scale appearances and power Doppler findings in both the transverse and longitudinal plane to accurately identify any pathology seen in the Achilles or surrounding tissues. Along with still images, three sets of 12-second-long video clips were acquired, demonstrating the grey-scale appearance of the Achilles tendon in longitudinal, transverse, and with the power Doppler box overriding the grey-scale image, highlighting any identifiable blood flow. The video clips were used as an adjunct to the static images, showing the entire tendon and areas of interest; enabling an initial impression to be verified or amended.
Appendix 6: Observer Information Sheet

SUBJECT INFORMATION SHEET

Achilles Ultrasound Assessment Tool – inter-rater and intra-rater reliability

Mr Daniel Walkley (Principal Researcher, PhD student),
Fowler Simmons Radiology, 100 Hutt St Adelaide, (08)8229 2100

Associate Professor Paul Tinley (Supervisor), Charles Sturt University, Albury/Wodonga, (02)6051 9248

Dr Rod McGregor (Supervisor), Charles Sturt University, Port Macquarie, 0488 587 220

You are invited to participate in a study to evaluate the ability of ultrasound to comprehensively assess Achilles tendinopathy and the relationship of ultrasound findings to clinical symptoms.

The study is being conducted by Daniel Walkley, Physiotherapist and Sonographer, at Fowler Simmons Radiology, Adelaide. This project forms part of Daniel’s PhD study through the Faculty of Science, Charles Sturt University, Wagga Wagga. Other researcher’s involved in the project are listed at the top of this sheet.

Before you decide whether to participate in this study, it is important that you understand why the research is being done and what it will involve for you. Please take time to read the information provided carefully and discuss with others, if you so wish.

1. What the purpose of this study?

To discover if a formulated worksheet can comprehensively assess Achilles tendinopathy. This worksheet, called the Achilles Ultrasound Assessment Tool (AUAT), will be tested for its reliability between Sonographers and Radiologists, along with its reproducibility.

2. Why have I been identified and invited to participate in this study?

You have been identified as either a Radiologist or Sonographer with an interest in tendon imaging.

3. What if I don’t want to participate in the study?

There is no obligation to participate in the study and no ramifications if you choose not to participate.

4. What does the study involve?

If you choose to participate in the study, you will be asked to sign a participant Informed Consent Form. Once the Informed Consent Form is signed and returned, you will be given a copy of the AUAT and asked to read an education article outlining how to use the AUAT. You will be given the opportunity to ask questions or seek clarification on how to use this tool. From here, you will be asked to assess non-identified ultrasound images from four different Achilles tendons and complete an AUAT on each. This process will be completed again in

www.csu.edu.au
CPBEST Provider Numbers for Charles Sturt University are 00055F (NSW), 01947G (VIC) and 02606B (ACT). ABN: 63 878 708 551

239
two weeks’ time. These results will then be analysed to see if all assessors reached the same conclusions in their assessment of the ultrasound images.

5. Am I free to withdraw from the study at any time and for whatever reason?
Yes, you may withdraw from the study, without consequence, by providing written or verbal notification to Daniel Walkley at any time before or during the study (danielwalkley@gmail.com). Once the results have been published you will no longer be able to withdraw your consent.

6. Are there costs associated with participating in the study?
No, there are no costs associated with this study.

7. What will be done to make sure the information is confidential?
Your confidentiality will be maintained at all times. You will be allocated a number which is placed on your AUAT forms.

All data and analysis documents will be stored in a locked area. We aim to publish the results of this study in a scientific journal as well as in the PhD thesis however these will display no references to the identity of individuals involved. The records dealing with your participation will be kept under safe storage for five years after publication before being shredded or securely deleted from the computer.

8. Is there likely to be a benefit to me?
The main benefit of this research is to provide a reliable tool for sonographers and radiologists to assess Achilles tendons. It is unlikely you will derive any direct initial benefit from your participation in this study.

9. What are the possible risks and/or discomforts for me?
There are no expected risks or discomforts for participants. We ask that you keep your decision to participate or not participate confidential so that it has no impact on your work relationships.

10. What are the likely things that could be an inconvenience for me?
It is estimated that your participation will take 15-20 minutes of your time.

11. What is I have a working relationship with the principal researcher?
There is no reason that your decision to participate, or not participate, should affect any relationships between yourself and the principal researcher. Your participation is voluntary and you are free to withdraw at any time. The principal researcher has no financial, supervisory or management conflicts of interest in undertaking this project.

12. What happens with the results of the study?
All results of the study are strictly confidential. We do request permission to be able to present the results and publish the results in a peer-reviewed journal and PhD thesis, while maintaining participant confidentiality and anonymity at all times.

13. Can I obtain a copy of the research?

Publications arising from this research will be made available to participants on request.

14. What should I do if I want to discuss the study further?

When you have read this information, the researcher can be contacted to discuss it with you and answer any questions that you may have – Mr Daniel Walkley (08) 8229 2100.

15. Note:

The Faculty of Sciences’ Human Ethics Low Risk Committee has approved this project. If you have any complaints or reservations about the ethical conduct of this project, you may contact the Committee through the Executive Officer:

Executive Officer
Faculty of Science Low Risk Human Ethics Committee
Charles Sturt University
Locked Bag 49
Dubbo NSW 2830
02 6885 7327
scienceHREC@csu.edu.au

Any issues you raise will be treated in confidence and investigated fully and you will be informed of the outcome.

Thank you for taking the time to read this information.
Appendix 7: Observer Consent Form

Radiologist/Sonographer Consent Form

Achilles Ultrasound Assessment Tool — inter-rater and intra-rater reliability

Mr Daniel Walkley (Principal Researcher, PhD student),

Fowler Simmons Radiology, 100 Hutt St Adelaide, (08)8229 2100

Associate Professor Paul Tinley (Supervisor), Charles Sturt University, Albury/Wodonga, (02)6051 9248

Dr Rod McGregor (Supervisor), Charles Sturt University, Port Macquarie, 0488 587 220

I, .................................................................................................................., have been invited to participate in the above study.

My agreement is based on the understanding that the research study looks at a new tool (Achilles Ultrasound Assessment Tool) for radiologists and sonographers to assess ultrasound images of Achilles tendons. I understand that I am agreeing to read an article supplied by the principal researcher and use the AUAT to assess four sets of Achilles tendon images. I further understand that I will be asked to re-assess the same four cases using the AUAT two weeks after my initial assessment.

I have received and read the ‘Subject Information Sheet’ and understand the general purposes, methods and demands of the study. I have been given the opportunity to ask questions about the research and any questions I had have been answered to my satisfaction. I understand that the project may not be of direct benefit to me.

- I have read and understand the sections in the ‘Subject Information Sheet’ describing the tasks that I may be required to perform, possible risks, inconveniences and discomforts, which have also been explained to me.
- I understand that I can refuse to consent or withdraw from the study at any time before or during the study without explanation, and that if I do I will not be subjected to any penalty or discriminatory treatment.
- I understand that once the results from the study have been published it will no longer be possible to withdraw from the study.
- I understand that any information or personal details gathered in the course of this research about me are confidential and that neither my name nor any other identifying information will be used or published without my written permission.
- I understand that the Faculty of Science Human Ethics Low Risk Committee has approved this study and that if I have any complaints or concerns about this research I can contact:

  Executive Officer
  Faculty of Science Low Risk Human Ethics Committee
  Charles Sturt University
  Locked Bag 49
  Dubbo NSW 2830
  02 68857327
  scienceHREC@csu.edu.au

Any issues you raise will be treated in confidence and investigated fully and you will be informed of the outcome.

I hereby voluntarily consent and offer to take part in this study.

Signed by: .................................................................................................

Print Name: ............................................................................................

Date: .........................................................................................................
Appendix 8: Patient Information Sheet

SUBJECT INFORMATION SHEET

Achilles Ultrasound Assessment Tool – inter-rater and intra-rater reliability

Mr Daniel Walkley (Principal Researcher, PhD Student),
Fowler Simmons Radiology, 100 Hutt St Adelaide, (08)8229 2100

Associate Professor Paul Tinley (Supervisor), Charles Sturt University, Albury/Wodonga, (02)6051 9248

Dr Rod McGregor (Supervisor), Charles Sturt University, Port Macquarie, 0488 587 220

You are invited to participate in a study to evaluate the ability of ultrasound to comprehensively assess Achilles tendinopathy and the relationship of ultrasound findings to clinical symptoms.

The study is being conducted by Daniel Walkley, Physiotherapist and Sonographer, at Fowler Simmons Radiology, Adelaide. This project forms part of Daniel’s PhD study through the Faculty of Science, Charles Sturt University, Wagga Wagga. Other researcher’s involved in the project are listed at the top of this sheet.

Before you decide whether to participate in this study, it is important that you understand why the research is being done and what it will involve for you. Please take time to read the information provided carefully and discuss with others, if you so wish.

1. What the purpose of this study?

To discover if a formulated worksheet can comprehensively assess Achilles tendinopathy. This worksheet is called the Achilles Ultrasound Assessment Tool (AUAT), and it will be tested for its reliability between Sonographers and Radiologists.

2. Why am I being invited to participate in this study?

You have been identified as an otherwise healthy individual with Achilles tendinopathy, as identified on an ultrasound examination.

3. What if I don’t want to participate in the study?

There is no obligation to participate in the study and no explanation is needed if you choose not to participate.

4. What does the study involve?

If you choose to participate in the study, you will be asked to sign a participant Informed Consent Form. Once the Informed Consent Form is signed and returned, the images from the ultrasound that you have had performed will be de-identified and stored on a computer. These images will then be used by a group of medical imaging professionals to assess using a worksheet called the AUAT to determine the degree of
changes present in your tendon. The results from these assessors will then be analysed to see if they all reached the same conclusions in their assessment of the ultrasound images.

5. Am I free to withdraw from the study at any time and for whatever reason?
Yes, you may withdraw from the study, without consequence, by providing written or verbal notification to Daniel Walkley at any time before or during the study (danielwalkley@gmail.com). Once the results have been published you will no longer be able to withdraw your consent.

6. Are there costs associated with participating in the study?
No, there are no costs associated with this study.

7. What will be done to make sure the information is confidential?
Your confidentiality will be maintained at all times, your name and any identifying information removed from your images once you have consented to participate.

All data and analysis documents will be stored in a locked area. We aim to publish the results of this study in a scientific journal as well as in the PhD thesis however these will display no references to the identity of individuals involved. The records dealing with your participation will be kept under safe storage for five years after publication before being shredded or securely deleted from the computer.

8. Is there likely to be a benefit to me?
The main benefit of this research is to provide a reliable tool for sonographers and radiologists to assess Achilles tendons. It is unlikely you will derive any direct benefit from your participation in this study.

9. What are the possible risks and/or discomforts for me?
There are no expected risks or discomforts for participants.

10. What are the likely things that could be an inconvenience for me?
Only the time you take reading this information sheet and making your decision about participation.

11. What happens with the results of the study?
All results of the study are strictly confidential and remain anonymous. We do request permission to be able to present the results and publish the results in a peer-reviewed journal and PhD thesis, while maintaining your confidentiality and anonymity at all times.

12. Can I obtain a copy of the research?
Publications arising from this research will be made available to participants on request.

13. What should I do if I want to discuss the study further?
When you have read this information, the researcher can be contacted to discuss it with you and answer any questions that you may have – Mr Daniel Walkley (08) 8229 2100.
14. Note:

The Faculty of Science Human Ethics Low Risk Committee has approved this project. If you have any complaints or reservations about the ethical conduct of this project, you may contact the Committee through the Executive Officer:

Executive Officer
Faculty of Science Low Risk Human Ethics Committee
Charles Sturt University
Locked Bag 49
Dubbo NSW 2830
02 68857327
sciencePHEC@csu.edu.au

Any issues you raise will be treated in confidence and investigated fully and you will be informed of the outcome.

Thank you for taking the time to read this information.
Appendix 9: Patient Consent Form

Consent Form

Achilles Ultrasound Assessment Tool – inter-rater and intra-rater reliability

Mr Daniel Walkley (Principal Researcher, PhD student),
Fowler Simmons Radiology, 100 Hutt St Adelaide, (08)8229 2100

Associate Professor Paul Tinley (Supervisor), Charles Sturt University, Albury/Wodonga, (02)6051 9248

Dr Rod McGregor (Supervisor), Charles Sturt University, Port Macquarie, 0488 587 220

I, ____________________________, have been invited to participate in the above study.

My agreement is based on the understanding that the research study looks at a new tool (Achilles Ultrasound Assessment Tool) for radiologists and sonographers to assess ultrasound images of Achilles tendons. I understand that I am agreeing to allow the researchers to use my ultrasound images to test the usefulness of this tool, and that none of my images will contain any information that could identify me.

- I have received and read the ‘Subject Information Sheet’ and understand the general purposes, methods and demands of the study. I have been given the opportunity to ask questions about the research and any questions I had have been answered to my satisfaction. I understand that the project may not be of direct benefit to me.
- I have read and understand the sections in the ‘Subject Information Sheet’ describing the tasks that I may be required to perform, possible risks, inconveniences and discomforts, which have also been explained to me.
- I understand that any information or personal details gathered in the course of this research about me are confidential and that neither my name nor any other identifying information will be used or published without my written permission.
- I understand that The Faculty of Science Human Ethics Low Risk Committee has approved this study and that if I have any complaints or concerns about this research I can contact:

  Executive Officer
  Faculty of Science Low Risk Human Ethics Committee
  Charles Sturt University
  Locked Bag 49
  Dubbo NSW 2830
  02 6885 7527
  scienceHREC@csu.edu.au

Any issues you raise will be treated in confidence and investigated fully and you will be informed of the outcome.

I hereby voluntarily consent and offer to take part in this study.

Signed by: ____________________________

Print Name: ____________________________

Date: ____________________________

www.csu.edu.au
CRICOS Provider Numbers for Charles Sturt University are 00005F (NSW), 01947G (VIC) and 02606B (ACT). ABN: 83 878 708 551
Appendix 10: Patient Information Sheet

SUBJECT INFORMATION SHEET

Achilles Tendinopathy – Ultrasound assessment scoring system and correlation with clinical outcomes

Daniel Walkley and Wes Cormick
Supervisor: Prof Rob Davidson

You are invited to participate in a study to evaluate the ability of ultrasound to comprehensively assess Achilles tendinopathy and the relationship of ultrasound findings to clinical symptoms.

The study is being conducted by Daniel Walkley, Physiotherapist and Sonographer, at Canberra Specialist Ultrasound, Barton. This project is also forms part of a Higher Degree by Research through the Faculty of Science, Charles Sturt University, Wagga Wagga.

Before you decide whether to participate in this study, it is important that you understand why the research is being done and what it will involve for you. Please take time to read the information provided carefully and discuss with others, if you so wish.

1. What is the purpose of this study?

   To discover if a formulated worksheet can comprehensively assess Achilles tendinopathy. This worksheet will then be correlated with an outcome measurement tool (the Victorian Institute of Sport Assessment – Achilles Questionnaire VISA-A), to see if there is a relationship between the ultrasound findings and your experience of Achilles pain.

2. Why have I been identified and invited to participate in this study?

   You have been identified as an otherwise healthy individual with Achilles tendinopathy, fulfilling the inclusion and exclusion criteria.

Inclusion criteria

- Achilles tendon pain in relation to activity and exercise
- Mid-substance Achilles Tendinopathy

Exclusion criteria

- Disease affecting the lowermost part of the tendon (primary enthesis pathology)
- Achilles Rupture
3. What if I don’t want to participate in the study?

There is no obligation to participate in the study.

4. What does the study involve?

If you choose to participate in the study, you will be asked to sign a participant Informed Consent Form. The study runs for 6 months and involves 2 visits to Canberra Specialist Ultrasound, Barton.

Subject Assessment

```
Baseline
US
VISA-A
```

```
24 weeks
US
VISA-A
```

US = Ultrasound

VISA-A = Victorian Institute of Sport Assessment – Achilles

Once the Informed Consent Form is signed and returned, you will be asked to fill out part of the Subject Data Sheet, the VISA-A questionnaire. An ultrasound will be done to assess the degree of injury to your tendon. Both a qualified Ultrasound technician and Doctor will perform the ultrasound on your Achilles. Twenty-four weeks after your first assessment, we will contact you to make an appointment for you to come back to the study centre to complete a VISA-A questionnaire and have a subsequent ultrasound scan performed.

5. Am I free to withdraw from the study at any time and for whatever reason?

Yes, you may withdraw from the study, by providing written notification to Daniel Walkley (danielwalkley@gmail.com)

6. Are there costs associated with participating in the study?

If your referring Doctor or Physiotherapist has asked us to provide a diagnostic ultrasound and/or provide intervention or injections in or around your Achilles tendon, then the usual costs associated with the scan will apply. However, our 24-week follow-up scan will be performed free of charge.

If you are participating in the study without a formal referral (ie. No diagnostic scan or injections have been requested) then there will be no cost to you.
7. What happens with the results of the study?

All results of the study are strictly confidential and remain anonymous outside of the study research team. We do request permission to be able to present the results and publish the results in a peer-reviewed journal, while maintaining patient confidentiality and anonymity at all times.

8. What should I do if I want to discuss the study further?

When you have read this information, the researcher can be contacted to discuss it with you and answer any questions that you may have – Mr Daniel Walkley (02) 6210 5600.

9. Note:

The School of Dentistry and Health Sciences’ Ethics Committee has approved this project. If you have any complaints or reservations about the ethical conduct of this project, you may contact the Committee through the Executive Officer:

Jessica Daley
Charles Sturt University
School of Dentistry and Health Sciences
Locked Bag 588
Wagga Wagga NSW 2678
Tel: (02) 69332874
Fax: (02) 69332835

Any issues you raise will be treated in confidence and investigated fully and you will be informed of the outcome.
Appendix 11: Patient Consent Form

Consent Form

Achilles Tendinopathy – Ultrasound assessment scoring system and correlation with clinical outcomes

Mr Daniel Walkley (Principal Researcher), Dr Wes Cormick (Assistant Supervisor)

Prof Rob Davidson (Supervisor)

I ........................................................................................................... consent to participate in the Achilles Tendinopathy study.

I understand that I am free to withdraw my participation in the research at anytime, and if I do, I will not be subject to any penalty or discriminatory treatment.

The purpose of the research has been explained to me and I have been given the opportunity to ask questions about the research and received satisfactory answers.

I consent to allowing the results of this study to be presented and published in a peer-reviewed journal, whilst maintaining patient confidentiality and anonymity at all times.

I understand that any information or personal details gathered in the course of this research about me are confidential and neither my name nor any other identifying information will be used or published without my written permission.

The School of Dentistry and Health Sciences' Ethics Committee has approved this project. If you have any complaints or reservations about the ethical conduct of this project, you may contact the Committee through the Executive Officer:

Jessica Daley
Charles Sturt University
School of Dentistry and Health Sciences
Locked Bag 588
Wagga Wagga NSW 2678
Tel: (02) 69332874
Fax: (02) 69332835

Any issues you raise will be treated in confidence and investigated fully and you will be informed of the outcome.

Signed by: .................................................................

Print Name: .................................................................

Date: .................................................................