87078278

The Role of Nuclear Medicine in Imaging Companion Animals

Peer Reviewed Paper

Geoffrey M. Currie, M MedRadSc, M AppMngt, CNMT
Janelle M. Wheat, B AppSc, M MedRadSc

School of Clinical Sciences, Charles Sturt University, Wagga Wagga, Australia.

Correspondence:
Geoff Currie
School of Clinical Sciences
Locked Bag 588
Charles Sturt University
Wagga Wagga 2678
Australia
Telephone: +61 2 6933 2822
Facsimile: +61 2 6933 2866
Email: gcurrie@csu.edu.au

Foot line: Nuclear Scintigraphy in Companion Animals

Introduction:

The role of equine nuclear medicine in Australia has been previously described in this journal[1] and more recently, Lyall et al.[2] provided a general overview of demographics of veterinary nuclear medicine departments in Australia. Lyall et al.[2] discuss the main clinical applications of nuclear medicine scintigraphy in companion animals; dogs and cats. The aim of this article is to discuss in brief the applications of commonly performed nuclear medicine procedures in humans with respect to veterinary applications. More detailed discussion will also be offered for investigation of pathologies unique to veterinary nuclear medicine or which are more common in animals than humans.

Companion animals are living longer today due to advances in both veterinary and human medicine.[3] The problem is, like humans, longevity brings higher incidence of old age morbidity.[3] As a pet owner, one might be initially motivated to extend life expectancy which is followed by the realisation that one also demands quality of life for pets. Early detection through advanced diagnostic tools, like nuclear medicine scintigraphy, allows greater efficacy in veterinary disease.

There are limited veterinary nuclear medicine facilities in Australia[2] due to cost and demand. Not surprisingly then, the growth of veterinary nuclear medicine in Australia, and overseas, has been integrally coupled to evaluation of race horses. While these facilities are generally specifically designed for race horses, racing greyhounds, lame family horses and companion animals are being investigated more frequently.

In the USA, the American College of Veterinary Radiology (ACVC) is very active clinically and in research. The ACVC journal, Journal of Veterinary Radiology and Ultrasound, is published quarterly and includes a Nuclear Medicine section. Within the ACVR is the Society of Veterinary Nuclear Medicine. Proliferation of veterinary nuclear medicine centres in the USA has been associated with insurance and lifestyle changes.

In Australia one can now obtain health insurance for pets, for example on home contents insurance policies. Lifestyle changes have seen greater pressure being placed on veterinarians to better prevent and manage serious illness in our pets and to give us a little more information than, for example, 'he's old now, it might be time to put him down'. The veterinarians, then, need access to advanced diagnostic tools to provide improved animal care, health management and answers for pet owners.

Bone Scintigraphy

The three phase bone scan is the most commonly performed veterinary procedure.[4] The most common use of bone scintigraphy is poorly localised lameness which is often accompanied by normal xrays until the condition is advanced. Myhre et al.[5] indicate that bone scintigraphy allows refinement of the lameness diagnosis which facilitates more accurate treatment and improved prognosis. Localisation of the source of lameness may be more difficult to determine in animals because of communication barriers. Causes of lameness are best treated early to avoid associated complications (eg. arthritis).

Osteosarcoma is the most common bone tumour in dogs and has a tendency toward leg bones (75-85% occur in limbs), larger breeds and middle age to older dogs.[6] Not only is it the most common bone tumour in dogs (85% of bone malignancies), but it is also the fastest growing making early diagnosis essential. Dogs tend to present with lameness and swelling, xrays are often normal early and the treatment includes amputation with or without chemotherapy.

Other applications of canine bone scintigraphy include:

- Trauma, infection and metastatic disease. Full skeletal survey is helpful following major trauma (e.g. car accident) and in undiagnosed fever because communication barriers are prohibitive of detailed clinical assessment. Prostate cancer is common in both dogs and cats.[6] Bone scintigraphy will demonstrate skeletal metastases sooner than xray.[7]
- Discospondylitis is spinal osteomyelitis that, in dogs, is generally the result of staphylococcus aureus.[6] This infection may manifest post operatively following disc fenestration, fusion or chord decompression.[6] On occasion, this problem has also been reported in cats.[6]
- Total hip replacements are regularly performed in dogs in order to resolve pain and dysfunction secondary to coxofemoral arthritis.[8] Evaluation of prosthetic joints to differentiate loosening from infection is a role for scintigraphy.
- Legg-Calve-Perthes disease is typical in the hip joints of female small breeds of dog including the terrier breeds, miniature pinscher and poodles.[6,9] The dog generally presents with single limb painful lameness in the first four to 11 months of life.[9] Dogs generally will go on to develop osteoarthritis of the coxal joint.[6]

Canine panosteitis is a pathology readily evaluated with bone scintigraphy despite it having no counterpart in humans.[10] Canine panosteitis is a spontaneous, self-limiting disease of young, large breed dogs most often the German shepherd but also the Bassett hound, Scottish terrier, great Dane, St. Bernard, Doberman pinscher, German shorthaired pointer, Irish setter, Airedale, golden retriever, Labrador retriever, Samoyed and miniature schnauzer.[9,10] There is also a predilection to male dogs.[9,10] The dog generally presents with obscure, intermittent lameness without a history of trauma and may have one or more limbs affected simultaneously or sequentially.[10] Xray changes tend to be subtle, however, the endosteal and subperiosteal new bone formation allow the bone scan to demonstrate striking abnormalities that resemble Paget's disease or fibrous dysplasia in the long bones of the limbs.

Endocrine Scintigraphy

By far the most common reason for thyroid scintigraphy in veterinary medicine is the evaluation of cats with hyperthyroidism. Thyroid scintigraphy is particularly useful in cats without palpable thyroid enlargement. Nap et al.[11] determined 60 minutes post intravenous administration of ^{99m}Tc pertechnetate as the peak thyroid uptake and the ideal time to quantitated thyroid uptake. The normal range has been determined to be 0.3% to 3.9% with values in excess of 5% correlating with hyperthyroidism.[11] Alternatively, thyroid to salivary gland ratios can be calculated with euthyroid cats represented by values lower than 1.5.[12] ^{131}I therapy is the treatment of choice for feline hyperthyroidism (over surgery or antithyroid medication).[13]

Hyperthyroidism is the most common endocrine disease in cats and affects older cats more commonly[6,14,15] and was first recognised in 1979.[14] While there is no tendency toward breeds or gender.[6] Kass et. al.[16] showed a three fold increase in risk associated with the use of cat litter, a weak increased risk associated with use of topical ectoparasite preparations, a two to three fold increase in risk associated with commercially produced canned food and a decreased risk for Siamese and Himalayan breeds. While diagnosis is often made using serum assay for T4 or T3 levels, these levels may be normal in 30% of cats with hyperthyroidism (particularly old cats).[15,17]

Scintigraphy of thyroid tumours in dogs can provide information regarding both functional status and extent of disease and have important implications for treatment and prognosis. In contrast to cats, most thyroid tumours in dogs are malignant (85%) and most affected dogs remain euthyroid.[6] Thyroid tumours represent 1% to 4% of all canine neoplasms[6,18] and 15% of canine head and neck tumours.[18] Thyroid cancer is especially prevalent in older dogs and beagles, boxer and golden retriever breeds.[6] Canine thyroid cancer is locally invasive with a tendency for locoregional and pulmonary metastases[18] and, unfortunately, more than 50% of dogs with thyroid carcinoma have detectable metastasis at the time of diagnosis. This prevents a surgical cure for these patients so ^{131}I ablation is the treatment of choice. Prognosis is generally poor because metastases occur early and tend to be widespread.[6] This highlights the importance of the thyroid scan in improving outcomes by early diagnosis.

Canine hypothyroidism can be difficult to diagnose due to the breadth of symptoms that may seem contradictory at times. Diagnosis is important because treatment is simple (hormone supplementation) and the associated conditions are serious including mega-oesophagus, ruptured knee ligaments, testicular atrophy, cardiomyopathy, excessive bleeding and corneal ulcers.[3] The inherited disease is known as autoimmune lymphocytic thyroiditis and is of particular concern to breeders of the golden retriever, great Dane, beagle, borzoi, Shetland sheepdog, American cocker spaniel, Labrador retriever, Rottweiler, boxer, Doberman pinscher, German shepherd, Akita, old English sheepdog and Irish setter.[3]

Thyroid uptake calculations in the canine thyroid scan can be performed at 20 minutes or 1 hour post intravenous administration of ^{99m}Tc pertechnetate without variation.[19] The normal range for canine thyroid uptake is 0.3% to 0.9%.[19]

Congenital hypothyroidism has been reported in cats with an underlying cause of either thyroid dysgenesis or inherited iodination defects. Thyroid scintigraphy with quantitation can be utilised to differentiate between the two pathologies.

^{99m}Tc sestamibi may have an important role to play in identifying parathyroid adenomas and parathyroid hyperplasia in dogs with persistent hypercalcaemia. Currently, ultrasound is generally used for this assessment.[6]

Endocrine Radionuclide Therapy

^{131}I therapy for feline hyperthyroidism is safe and effective with a success rate of 90%.[15] ^{131}I therapy represents the 'gold standard' in treatment of feline hyperthyroidism[13] with therapy success (euthyroid outcome) in 85% of cases and hypothyroidism in another 10%.[6] Subcutaneous administration of ^{131}I is the recommended route of therapy administration based on safety and effectiveness.[20,21] ^{131}I therapy in cats can cause significant decreases in renal function.[6,22] Slater et. al.[23] showed age and gender of cats were predictors of survival (higher survival for younger cats and female cats).

^{131}I therapy of canine thyroid carcinoma has been shown to increase post surgical survival from three months (no radionuclide therapy) to 34 months.[24] Invasive canine thyroid carcinoma is effectively treated with radionuclide therapy in isolation or as an adjunct to surgery.[24] There are, however, issues relating to individual doses, animal hospitalisation, waste management and radiation safety that require careful consideration and compliance with relevant state licensing authorities.

Gastrointestinal Scintigraphy

There are three main types of hepatic imaging in companion animals:

- ^{99m}Tc sulphur colloid is employed to assess reticuloendothelial function for hepatic and/or splenic morphology (size and shape) and space occupying lesion (cyst, haematoma, abscess or tumour).
- ^{99m}Tc IDA derivatives are employed for hepatobiliary scanning to assess biliary tract patency and acute or chronic cholecystitis.
- ^{99m}Tc pertechnetate is employed for porto-systemic shunt assessment. Scintigraphy is very sensitive in determining the presence of communication between portal and systemic veins and quantitating the shunt index.

A porto-systemic shunt is an abnormal communication between the portal circulation and the systemic circulation.[25] It is usually congenital but may develop secondary to liver disease.[25] A porto-systemic shunt can be intra or extra hepatic. The shunt allows the blood from the gastro-intestinal tract to bypass the liver and go directly into the systemic circulation. This can cause the liver to be malnourished due to a lack of nutrients and the rest of the body is subjected to potentially high levels of toxins that would normally have been filtered out or been inactivated by the liver. In dogs, congenital shunts are most common in the miniature schnauzer, Yorkshire terrier, Irish wolfhound, Cairn terrier and old English sheepdog although it can occur in any breed of dog.[25]

Transcolonic portal scintigraphy involves placement of ^{99m}Tc pertechnetate into the intestine (rectum) of a dog or cat and imaging transit. In a normal animal the radiopharmaceutical is absorbed into the portal circulation and rapidly transported to the liver. In an animal with a porto-systemic shunt, the radiopharmaceutical bypasses the liver and appears in the heart first. While porto-systemic shunts can be diagnosed with a blood test, scintigraphy allows:[6]

- confirmation of diagnosis,
- localisation of shunt,
- quantitation of shunt (shunt index),
- post operative evaluation (shunt ligation),
- accuracy and safety.

A number of other gastrointestinal abnormalities and disease can be detected using a variety of studies currently employed in human nuclear medicine. Koblik and Hornof[26] identify oesophageal and gastric motility problems, gastro-oesophageal reflux, abnormal gastric secretion, gastrointestinal haemorrhage and inflammatory diseases as the main gastrointestinal application of nuclear medicine. Scintigraphy is recognised as the 'gold standard' for evaluation of gastric emptying in animals.[27]

Renal Scintigraphy

Renal disease is common in cats and dogs and may include infection, tumours, cysts, stones, toxic injury and a number of inflammatory processes. Management of renal disease in companion animals often requires functional evaluation pre and post treatment. Renal scintigraphy employs both ^{99m}Tc DMSA for differential function and ^{99m}Tc DTPA for renography.

There are a number of considerations when interpreting canine and feline renal scans including kidney size. Normal kidney size is measured proportionally to the second lumbar vertebrae (L2) with dogs being 2.5 to 3.5 times the length of L2 and cats being 2.4 to 3.0 times L2.[6] The reproductive status of cats will also influence kidney size with neutered cats having smaller kidneys.[6]

Kerl and Cook[28] report that it is difficult to evaluate renal dysfunction in animals and recommend glomerular filtration rate (GFR) as the most accurate assessment of renal function in animals. The GFR has also been shown to be useful in pre treatment risk stratification for renal failure of cats undergoing ^{131}I treatment for hyperthyroidism.[22] The normal GFR value for dogs is greater than 3ml/min/kg and in cats is greater than 2.5 ml/min/kg.[29] Interpretation of ^{99m}Tc DTPA renograms, however, are also useful with normal renal transit times being similar to those in humans.[30]

Renal scintigraphy with diuretic challenge has been used widely to evaluate obstructive uropathy.[6,29] Sonography has been used widely to evaluate renal transplant rejection in dogs,[6] however, renal scintigraphy may provide a tool to address its limitations. The ratio of the slope of the arterial curve to the slope of the transplanted kidney curve is used to assess renal transplant rejection with a ratio of 1.03 being normal.[29]

Quantitative ^{99m}Tc DMSA renal scintigraphy is a valuable tool to assess the renal function that will remain following surgical procedures. The knowledge of how each individual kidney is functioning (differential function) can dramatically affect the plans to surgically remove a kidney stone or remove an entire kidney damaged by infection or tumour. Compensatory renal hypertrophy refers to a remaining kidney enlarging post nephrectomy and this can be by as much as 40% within three weeks.[6]

Brain Scintigraphy

Canine brain scintigraphy is undertaken using conventional radiopharmaceuticals (^{99m}Tc DTPA, ^{99m}Tc pertechnetate and ^{201}Tl chloride) for assessment of intracranial lesions (e.g. tumours, cysts, haemorrhage.

abscess and trauma) and ^{99m}Tc HMPAO for assessment of cerebral blood flow abnormalities (e.g. seizures, epilepsy, cognitive dysfunction and behavioural changes).

Brain tumours in dogs can occur at any age but usually after 5 years and are the most common cause of seizures after the age of 5 when toxins, trauma and diabetes have been eliminated as the cause.[6,25] Any breed can have brain tumours but some are at higher risk including the boxer, golden retriever and Doberman pincher.[25] The approximate incidence of brain tumours in dogs is 15 per 100000.[6] Symptoms may occur gradually or suddenly and include seizures, changes in behaviour and neurological deficits. Diagnosis is crucial because the 'wait and see' approach allows the tumour to grow and decreases the efficacy of any treatment.[25] Meningiomas are one of the more common canine brain tumours and tend to be slow growing, benign lesions.[6]

As dogs age, some will develop cognitive deficits, not unlike humans. Dogs that demonstrate geriatric behavioural changes not attributable to general pathologies (e.g. tumour) are covered by the term canine cognitive dysfunction.[31,32] There are four general categories of behaviour in canine cognitive dysfunction including, loss of cognition/recognition, loss of housetraining, disorientation and changes to the sleep-wake cycle.[32] Nuclear medicine plays a useful role in eliminating other causes of symptoms and in evaluating progress and response to treatment of behavioural changes using cerebral perfusion SPECT. This role mirrors that of cerebral perfusion SPECT in the aging human.

Cardiac Scintigraphy

Cardiac imaging includes using ^{99m}Tc sestamibi to assess myocardial perfusion in coronary artery disease in dogs. More commonly, rest gated heart pool scanning (RGHPS) using ^{99m}Tc RBCs are used to assess cardiac function pre chemotherapy to monitor the impact of chemotherapy agents on myocardial function. Dilated cardiomyopathy is a frequent occurrence in dogs, particularly the Irish wolfhound and Doberman pinscher, and these may also benefit from RGHPS.[6]

First pass studies have been performed to detect and quantitated left to right shunts. Bahr, Miller and Gordon[33] reported first pass QP:QS as a reliable non invasive procedure to accurately quantitate a patent ductus arteriosus in dogs before and after shunt occlusion. ^{99m}Tc MAA has been used to diagnose right to left cardiac shunts in dogs because it is quick, easy and accurate while providing shunt quantitation.[34] Moreover, the scintigraphic appearances permit easy differentiation of normality, tetralogy of fallot and reverse patent ductus arteriosus.

Heartworm is pathology with nuclear medicine applications unique to companion animals. Heartworm (dirofilaria immitis) is a parasite affecting dogs and cats worldwide (with the exception of Antarctica).[3] The parasite is usually transferred between animals by mosquito. While an animal can have the parasite in both blood and lungs, the disease may not manifest.[3] The worm number needs to exceed a critical value based on the animals size and activity level before the worms move to the heart and the animal becomes symptomatic.[3] Adult worms can grow to 30 cm.[3] The treatment of heartworm can cause pulmonary embolism requiring perfusion scintigraphy evaluation.[6] RGHPS may be useful in assessing the functional status of right sided cardiac enlargement caused by dirofilariasis.[6] Pulmonary angiography has been used to evaluate pulmonary arteries infected with heartworm and found a correlation between the number of heartworms infecting a dog and the type and severity of arterial abnormality.[6] ^{99m}Tc MAA perfusion scintigraphy may follow the same principle to provide a useful tool in stratifying severity of disease in infected dogs. The main application of nuclear medicine to this point has been the use of dirofilaria immitis specific monoclonal antibodies to diagnose heartworm in dogs.[35]

Lung Scintigraphy

Ventilation studies may be limited due to patient compliance and risks of contamination due to lack of compliance. Perfusion studies have been used to assess pulmonary embolism (particularly post joint replacement), chronic obstructive airways disease and severity of lung symptoms due to heartworm. Pulmonary embolism is more common in dogs than cats.[6] Middle age to older dogs with one or more venous stasis causing co-morbidities are the typical patient.[6]

Koblik et. al.[36] concluded that V/Q scanning was superior to pulmonary angiography and digital subtraction angiography in suspected PE in dogs. It may be particularly beneficial in dogs after total hip replacement. Pulmonary embolism is a cause of mortality related to total hip replacement and also has significant morbidity although the exact incidence of mortality is unknown.[8] Poteet & Liska[8] reported 100% incidence of pulmonary embolism in asymptomatic dogs post total hip replacement noting that while death associated with the hip replacement procedure is rare, pulmonary embolism is a potential cause of mortality in these dogs.

Oncology and Inflammation

Inflammatory conditions in companion animals investigated with nuclear medicine include multi-system infections, inflammatory bowel disease, osteomyelitis, septic arthritis, rheumatoid arthritis, post surgical infection, orthopaedic implant assessment and discospondylitis. ^{67}Ga and ^{99m}Tc WBC has been used for localisation of a septic focus, pyrexia of unknown origin, osteomyelitis, inflammatory bowel disease, assessment of surgical sites and orthopaedic implants.

Robben et al.[37] used ^{111}In octreotide for localisation of primary and metastatic insulomas in dogs and have found it to be at least equal to ultrasound and computed tomography. The use of ^{111}In octreotide in detection of pancreatic insulomas has also been reported.[38] In dogs, most insulomas are malignant and 45% show visible metastases during surgery.[6]

Steyn and Ogilvie[39] reported positively on the use of ^{99m}Tc sestamibi in the evaluation of malignant canine lymphoma and, in particular, staging of disease and evaluating the response to treatment. ^{123}I MIBG has been reported in the diagnosis of canine pheochromocytoma[40] while bone scintigraphy is useful for assessment of skeletal metastases.[7] ^{89}Sr metastron has also been used for palliation of metastatic bone pain in dogs.

CONCLUSION

While veterinary nuclear medicine focussing on companion animals in Australia is in its infancy, there is an expanding demand for services. There is, however, a foundation of suitably qualified practitioners to work in conjunction with veterinary expertise. There is an opportunity to build and expand on infrastructure currently in place for equine nuclear medicine to establish dedicated facilities for companion animals. Dedicated facilities are crucial since the requirements of gantry configurations for small animals differs significantly from that of large animals. Companion animals can be accommodated on standard current generation gamma cameras without hardware customisation.

POST SCRIPT

Veterinary nuclear medicine offers an interesting and challenging variation to normal technologist duties. The Charles Sturt University (CSU) nuclear medicine laboratory is equipped to offer the full gamut of services for companion animals and it is hoped that, in collaboration with the recent commencement veterinary science at CSU, that dedicated companion animal scintigraphy will be offered in the Riverina soon.

REFERENCES

1. Fulton, I & Anderson, B 2002, Scintigraphy in equine practice, *ANZ Nuc Med J*, vol. 33, no. 2, pp. 55-57.
2. Lyall, D, O'Neill, H, Reichel, R, Roach, D & Scouler, A 2004, Who performs veterinary nuclear medicine and what do they use?, *ANZ Nuc Med J*, vol. 35, no. 3, pp. 131-134.
3. Woolf, N 2005, Dog Owners Guide, accessed 23/6/2005, <http://www.canismajor.com>
4. Balogh, L, Andocs, G, Thuroczy, J, Nemeth, T, Lang, J, Bodoi, K & Janoki, G 1999, Veterinary Nuclear Medicine. scintigraphical examination: a review, *Acta Vet. Brno*, vol. 68, pp. 231-239.
5. Myhre, G, Boucher, N & Aiken, L 1998, Incidence and correlation of scintigraphy findings to referral lameness at a private hospital, accessed , New Eng J Large Animal Health, vol. 1, no. 1, <http://www.neahi.org>
6. Farrow, C 2003, Veterinary diagnostic imaging: the dog and cat, Mosby, St Louis.
7. Head, L & Daniel, G 2004, Scintigraphic diagnosis: an unusual presentation of metastatic pheochromocytoma in a dog, *Vet Radiol Ultrasound*, vol. 45, no. 6, pp. 574-576.
8. Poteet, B & Liska, W 2001. Pulmonary thromboembolism associated with canine total hip replacement, ACVR conference abstract, Honolulu.
9. Richards, M 2002, Encyclopaedia of canine veterinary medical information, accessed 23/6/2005, <http://www.vetinfo.com/cencyclopedia/>
10. Lenehan, T, Van Sickle, D & Biery, D 1985, Canine Panosteitis, in Textbook of Small Animal Orthopaedics, eds. C, Newton & D, Nunamaker, International veterinary Information Service, Ithaca, New York.
11. Nap, A, Pollak, Y van den Brom, W & Rijnberk, A 1994, Quantitative aspects of thyroid scintigraphy with pertechnetate in cats, *J Vet Intern Med*, vol. 8, no. 4, pp. 302-303.
12. Henrikson, T, Armbrust, L, Hoskinson, J, Wedekind, K, Kirk, C, Milliken, G & Nachreiner, R 2003, Thyroid to salivary ratios determined by 99m technetium pertechnetate imaging in 32 euthyroid cats, ACVR conference abstract, Chicago.
13. Miles, K, Simpson, S, Zimmerman, T, Evans, R & Armstrong, E 2004, determination of release criteria for 131I therapy cats, ACVR conference abstract, Montreal.
14. Chun, R, Garrett, L, Sherman, A, Sargeant, J & Hoskinson, J 1999, Correlation of thyroid scintigraphy with long term response to radioiodine therapy in hyperthyroid cats, ACVR conference abstract, Chicago.
15. Richards, M 2002, Encyclopaedia of feline veterinary medical information, accessed 23/6/2005, <http://www.vetinfo.com/cencyclopedia/>
16. Kass, P, Petersen, M, Levy, J, James, K, Becker, D & Cowgill, L 1999, Evaluation of environmental, nutritional and host factors in cats with hyperthyroidism, *J Vet Intern Med*, vol. 13, no. 4, pp. 323-329.
17. Gelatt-Nicholson, K & Neuwirth, L 1999, Feline hyperthyroidism in cats with normal T4 levels: the importance of scintigraphy, ACVR conference abstract, Chicago.
18. Adams, W, Daniel, G, Legendre, A & Lane, I 2001, Combined surgery, radioiodine and hormone suppression therapy in treatment of canine thyroid carcinoma, ACVR conference abstract, Honolulu.
19. Adams, W, Daniel, G, Petersen, M & Young, K1997, Quantitative Tc-99m-pertechnetate thyroid scintigraphy in normal beagles, *Vet Radiol Ultrasound*, vol. 38, no. 4, pp. 323-328.
20. Theon, A, van Vechten, M & Feldman, E 1994, Prospective randomised comparison of intravenous versus subcutaneous administration of radioiodine for treatment of hyperthyroidism in cats, *Am J Vet Res*, vol. 55, no. 12, pp. 1734-1738.
21. Peterson, M & Becker, D 1995, Radioiodine treatment of 524 cats with hyperthyroidism, *J Am Vet Med Assoc*, vol. 207, no. 11, pp. 1422-1428.
22. Adams, W, Daniel, G, Legendre, A, Gompf, R & Grove, C 1997, Changes in renal function in cats following treatment of hyperthyroidism using 131I, *Vet Radiol Ultrasound*, vol. 38, no. 3, pp. 231-238.
23. Slater, M, Geller, S & Rogers, K 2001, Long-term health and predictors of survival for hyperthyroid cats treated with iodine 131, *J Vet Intern Med*, vol. 15, no. 1, pp. 47-51.
24. Worth, A, Zuber, R & Hocking, M 2005, Radioiodide (131I) therapy for the treatment of canine thyroid carcinoma, *Aust Vet J*, vol. 83, no. 4, pp. 208-214.
25. Thomas, W 1999, Underlying causes of seizures, accessed 23/6/2005, <http://www.canine-epilepsy.com>
26. Koblik, P & Hornof, W 1985, Gastrointestinal nuclear medicine, *Vet Radiol*, vol. 26, no. 5, pp.

138-142.
27. Lora-Michiels, M, Hoskinson, J & Foster, L 1999, In vitro evaluation of 99mTc disofenin as a label for different nutrients on gastric emptying, ACVR conference abstract, Chicago.
28. Kerl, M & Cook, C 2005, Glomerular filtration rate and renal scintigraphy, *Clin Tech Small Anim Pract*, vol. 20, no. 1, pp. 31-38.
29. Daniel, G & Mitchell, S 1999, Renal nuclear medicine: a review, *Vet Radiol Ultrasound*, vol. 40, pp. 572-587.
30. Barthez, P & Wisner, E 1999, Renal transit time of 99mTc DTPA in normal dogs, *Vet Radiol Ultrasound*, vol. 40, pp. 649-656.
31. Overall, K 2000, Natural animal models of human psychiatric conditions: assessment of mechanism and validity, *Prog Neuro Psychopharmacol Biol Psychiatry*, vol. 24, pp. 727-776.
32. Ruehl, W & Hart, B 1998, *Canine cognitive dysfunction, in Psychopharmacology of animal behaviour disorders, Blackwell Science.*
33. Bahr, A, Miller, M & Gordon, S 1999, Evaluation of patent ductus arteriosus in dogs using first-pass nuclear angiocardiography, ACVR conference abstract, Chicago.
34. Morandi, F, Daniel, G, Gompf, R & Bahr, A 2002, Diagnosis of congenital cardiac right to left shunt with 99mTc MAA, ACVR conference abstract, Chicago.
35. Daniel, G & Allhands, R 1989, In-vivo testing of technetium-99m-labelled monoclonal antibodies specific for dirofilaria immitis, *Vet Radiol Ultrasound*, vol. 30, no. 2, pp. 74-79.
36. Koblik, P, Hornof, W, Harnagel, S & Fisher, P 1989, A comparison of pulmonary angiography, digital subtraction angiography and Tc-99mDTPA MAA ventilation perfusion scintigraphy for detection of experimental pulmonary emboli in the dog, *Vet Radio Ultrasound l*, vol. 30, no.4, pp. 159-168.
37. Robben, J, Pollak, Y, Kirpensteijn, J, Boroffka, S, van den Ingh, T, Teske, E & Voorhout, G 2005, comparison of ultrasonography, computed tomography and single photon emission computed tomography for the detection and localisation of canine insuloma, *J Vet Intern Med*, vol. 19, no. 1, pp. 15-22.
38. Lester, N & Newell, S 1999, Scintigraphic diagnosis of insuloma in a dog, *Vet Radiol Ultrasound*, vol. 40, no. 2, pp. 174-178.
39. Steyn, P & Ogilvie, G 1995, Tc-99m-methoxy-isobutyl-isonitrile (sestamibi) imaging of malignant canine lymphoma, *Vet Radiol Ultrasound*, vol. 36, no. 5, pp. 411-416.
40. Berry, C, Wright, K, Breitschwerdt, E & Feldman, J 1993, Use of iodine-123 metaiodobenzylguanidine scintigraphy for the diagnosis of pheochromocytoma in a dog, *Vet Radiol Ultrasound*, vol. 34, no. 1, pp. 52-55.