Left Ventricular Ejection Fraction Determination in Gated Single Photon Emission Computed Tomography: 8 Versus 16 Bin Data

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Foot line: 8 versus 16 bin gated SPECT

SUMMARY
While Quantitative Gated SPECT (QGS) determined gated single photon emission computed tomography (SPECT) functional parameters have been previously validated, acquisition and processing parameters consistent with those utilised in validation studies are adhered to infrequently. The aim of this investigation was to determine the impact on left ventricular ejection fraction (LVEF) determination of 8 versus 16 bin data in post stress data.

The gated stress studies of 160 patient files were examined. Each gated study was acquired using a 16 bin gated SPECT acquisition. On completion of the acquisition, the 16 bin data was reconstructed to produce short axis slices. The short axis slices were re-binned to produce 8 bin data which, with the 16 bin data, used QGS to generate functional data.

The mean LVEF for the 16 bin data was 64.0% (95% CI 61.9-66.1%) and for the 8 bin data was 59.9% (95% CI 57.8-62.0%). Excellent correlation was demonstrated with a correlation coefficient of 0.99. The mean difference between matched pairs of 16 and 8 bin LVEF data was 4.1% (95% CI 3.8-4.5%). The matched pair t test demonstrated a statistically significant difference (P < 0.0001) and a statistically significant difference was shown between the means (P = 0.0002).

The impact of performing 8 bin data collection results in a 4.1% underestimation of the stress LVEF due to temporal under-sampling. This approximates the 3.7% underestimation widely reported in the literature for post-filtered resting data although there is a statistically significant difference between matched pairs (P = 0.02). Using stress data does, however, require the same 4% LVEF correction recommended for rest data.

Key words: QGS, underestimation, functional, gate interval, ejection fraction

INTRODUCTION
Gated myocardial perfusion SPECT was initially developed to aid in differentiating artefact from pathology (Go et al., 2004). The superior imaging characteristics of 99mTc over 201TI allow 99mTc based radiopharmaceuticals to be synchronised to the patient’s electrocardiogram (gated) while maintaining adequate count density in individual cardiac frames (intervals). The advantage of gated SPECT in myocardial perfusion studies is that it allows simultaneous assessment of myocardial perfusion and ventricular function (Zaret & Bellar, 1999).

It is widely acknowledged that 8 bin gated SPECT studies underestimate the LVEF and volumes by smoothing of time-volume curve (Germano & Berman, 1999). The under sampling in 8 bin gated studies smooths the end systole measurement and influences LVEF measurement (Manrique et al., 2000). An increase in temporal sampling to 16 bins should result in increased accuracy of volumes, especially the end systolic volume (ESV) (Navare et al., 2003) since early sampling of the time volume curve is more accurate for end systole with increased bin number. The majority of nuclear medicine departments, however, perform gated SPECT studies with 8 bins (Germano & Berman, 1999; Manrique et al., 2000; Navare et al., 2003; Wheat et al., 2005). Wheat, Currie and Adams (2005) reported that 91.0% of nuclear medicine departments in Australia employ 8 bin gated myocardial perfusion SPECT.

Historically, 8 bin gated SPECT studies have been preferred due to limitations in computer processing power, computer storage and count density (counts per pixel) (Germano & Berman, 1999; Navare et al., 2000). Processing time and storage space required is doubled in 16 bin
gated SPECT studies compared to the same acquisition parameters in an 8 bin study. These increases are not particularly problematic with current generation computing, however, count density remains an issue. Gating a SPECT acquisition reduces the counts per pixel by a factor equal to the number of gate intervals and, thus, a 16 bin gated study halves the counts per pixel compared to an 8 bin study. This translates to pixel noise 1.4 times higher for 16 bin data compared to 8 bin data. Decreasing the count density by increasing the gated bin number can cause a subsequent decrease in image quality which may cause suboptimal left ventricular edge definition (Navare et al., 2003) and, thus, inaccuracies in LVEF determination (Nichols et al., 1996). A solution might be to increase the acquisition time to yield the same pixel counts as a 16 bin gated SPECT study; however, the time taken for a gated SPECT should be no longer than that of a non-gated SPECT (Germano & Berman, 1999). An increase in acquisition time may decrease patient tolerance and increase patient motion causing artefact introduction (Wheat & Currie, 2004; Currie & Wheat, 2004).

While 8 bin gated SPECT acquisitions are widely accepted, there is some discrepancy in the literature regarding the magnitude of LVEF underestimation. Fore resting studies, Germano et al. (1995) report a 3.7% underestimation of LVEF on 8 bin gated SPECT studies compared to the validated 16 bin data recommending an addition of 4% to QGS software (Cedars Sinai Medical Centre, Los Angeles, CA) determined 8 bin LVEFs. This 4% underestimation in resting studies has been supported by other investigators (Germano & Berman, 1999; Manrique et al., 2000; Kumita et al., 2001; Wright et al. 2001).

The American Society of Nuclear Cardiology (ASNC) recommends that gated SPECT be performed on both stress and rest studies due to the potential impact of stress induced stunning (Wheat & Currie, 2005). Despite this, 64.4% of departments perform gating on the stress study only and, more significantly in the context of this discussion, only 4.4% of nuclear medicine departments perform gating on the rest study only (Wheat et al. 2005). In stress studies, Navare et al. (2003) determined a 6.3% underestimation of LVEF comparing 8 bin gated data to 16 bin. Intuitively, stress induced stunning would impact on both 8 and 16 bin data. While differences are expected between rest and stress functional parameters in stress induced stunning, there is no clear reason for a difference in magnitude in this effect between 8 and 16 bin data. More rapid heart rates during post stress imaging may have an impact on this discrepancy due to steeper time-activity curves and, thus, greater impact of temporal undersampling.

This study aimed to investigate the relationship between 8 bin and 16 bin stress gated SPECT LVEFs.

**Methodology**

This clinical investigation employed a retrospective repeat-measures design which allowed a single clinical data set to act as both the control group (16 bins) and the experimental group (8 bins). Patients were excluded if the electrocardiogram (ECG) was not amenable to gating (i.e. non sinus rhythm). A total of 160 patient files were included in this study, each with a gated stress study only (rest not gated).

All patients in the study population followed a one day rest/stress protocol using a 300 MBq (8 mCi) rest dose and 1110 MBq (30 mCi) stress dose of $^{99m}$Tc sestamibi (DuPont Pharma, City). A triple detector gantry was used to acquire all patient data. All data acquisitions employed low energy, high resolution collimation with step and shoot mode, elliptical orbits, 15% energy window and a 64x64 matrix. The zoom was 1.42 (4.4 mm pixel size) and projections were acquired at three degree intervals for 17 seconds per projection to provide a total acquisition time of 11 minutes. All patients were positioned supine with their feet into the gantry and arms hyperextended out of the field of view for a 16 interval gated SPECT acquisition.

The gated SPECT data for both 8 and 16 bin gated data sets were reconstructed using 180 degree filtered backprojection and a three dimensional (3D) Butterworth low pass filter (order 4.0 and cut-off 0.21 cycles/cm) followed by reconstruction and reorientation of gated short axis slices. The 16 bin gated short axis slices were re-binned to 8 bin and both the 8 and 16 bin data was processed using QGS.

Statistical significance was calculated using the Student’s $t$ test with a $P$ value less than 0.05 being considered significant. The differences between independent means and proportions was calculated with a 95% confidence interval (CI). Correlation was evaluated with Chi-Square analysis and reliability measured using Cohen’s Kappa coefficient. Bland-Altman analysis (Bland & Altman, 1995) and the matched pairs $t$ test were used to assess agreement between paired data.

Approval for this study was granted by the Charles Sturt University Ethics in Human Research Committee for the retrospective manipulation of the de-identified patient data.

**Results**

All 160 clinical gated stress studies had both 16 and 8 bin data analysed with QGS software following reconstruction. The sample included 47.5% females and 52.5% males. The mean patient age was 59.1 years with a range of 36 years to 95 years. No statistically significant difference was noted between the mean age of females (60.7 years) and males (57.7 years) ($P = 0.10$).

The mean LVEF for the 16 bin data was 64.0% (95% CI 61.9 to 66.1%) and for the 8 bin data was 59.9% (95% CI 57.8 to 62.0%). Excellent correlation was demonstrated between the 16 and 8 bin LVEFs with a correlation coefficient of 0.99 (Fig. 1). The Bland-Altman analysis provided a deeper insight into the differences between 16 and 8 bin LVEFs (Fig. 2) and indicated that the 95% limits of agreement included 95.6% of data points, supporting a strong agreement between data. The mean difference between matched pairs of 16 and 8 bin LVEF data (deltaEF) was 4.1% (95% CI 3.8 to 4.5%) where a positive difference indicates that the 16 bin LVEF is greater than the 8 bin LVEF.

**Figure 1:** Bivariate analysis of the LVEF calculated for 8 bin pre filtered reconstruction versus 16 bin pre filtered reconstruction demonstrating excellent correlation (0.99), the regression line demonstrates the uniformity of the ‘add 4%’ strategy across the range of LVEFs.

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is higher than that of the 8 bin. The match pair t test demonstrated a statistically significant difference between matched pairs ($P < 0.0001$) and a statistically significant difference was shown between the means ($P = 0.0002$). No statistically significant difference was noted in deltaEF for gender ($P = 0.22$) or age ($P = 0.38$).

The 16 bin mean EDV was 109.8 ml (95% CI 102.4 to 117.0 ml) and 110.5 ml (95% CI 103.1 to 117.9 ml) for 8 bin data. A statistically significant difference was noted between matched pairs ($P = 0.006$). The mean difference between 16 bin and 8 bin EDV (deltaEDV) was -0.8 ml (95% CI -1.4 to -0.2 ml) indicating that the 8 bin EDV was higher than the 16 bin although no statistical significance was noted between the means ($P = 0.82$). No statistically significant difference was noted in deltaEDV for gender ($P = 0.52$) or age ($P = 0.21$).

The 16 bin mean ESV was 44.1 ml (95% CI 38.3 to 49.9 ml) and 48.8 (95% CI 42.8 to 54.8 ml) for 8 bin data. A statistically significant difference was noted between matched pairs ($P < 0.0001$). The mean difference between 16 and 8 bin ESV (deltaESV) was -4.7 ml (95% CI -5.3 to -4.0 ml) indicating that the 8 bin ESV was higher than the 16 bin although no statistical significance was noted between the means ($P = 0.12$). No statistically significant difference was noted in deltaESV for gender ($P = 0.06$), however, a statistically significant difference was noted for gender ($P < 0.0001$). The mean deltaESV for females was -3.34 (95% CI -3.9 to -2.8) while for males it was -5.0 (95% CI -5.6 to -4.5) (Fig. 3). This may be the result of temporal sampling inaccuracies for 8 bin gated studies in smaller hearts. This is supported by the statistically significant difference ($P < 0.0001$) in left ventricular stroke volumes for males (123.1 ml with a 95% CI 111.9 to 134.2 ml) and females (75.7 ml with 95% CI 70.9 to 80.5 ml). Moreover, a relationship between left ventricular stroke volume and deltaESV was noted ($R^2 = 0.23$) (Fig. 4).

**Discussion/Conclusion**

A limitation of this investigation arising due to software limitations was that conversion of 16 bin data to 8 bin data was performed by adding contiguous pairs of short axis slices rather than contiguous pairs of acquired projections. The advantage of this approach was the ability to eliminate count density as a source of discrepancy between 16 and 8 bin functional data. The disadvantage of this approach was that the noise in the 8 bin short axis slices would be greater than those reconstructed from 8 bin projections because reconstruction amplifies noise. The high count rate of the stress projections and the stronger noise suppression employed, however, ensured noise levels were acceptable.

Previous work has shown that using an 8 bin gated acquisition in resting studies underestimates the LVEF by 3.7% requiring interpreting physicians to add 4% to the calculated LVEF (Germano & Berman, 1999). This study showed a 4.1% under estimation of the stress LVEF which, despite a statistically significant difference from 3.7% ($P = 0.02$), is consistent with the add 4% strategy. Our results are not consistent with the 6.3% underestimation previously reported for stress studies ($P < 0.0001$) and this may be due to differences reported in the LVEF determination between algorithms (Navare et al., 2003) or differences in the method of producing 8 bin data from 16 bin data.

Perhaps there is a multi-factorial explanation for the discrepancy between the 6.3% stress data underestimation reported by Navare et al. (2003) and the approximately 4% published in four rest studies (Germano & Berman 1999a;...
A greater potential impact of arrhythmias on LVEF inaccuracies if gating is compared may, however, be overcome using 16 bin gated SPECT. New generation gamma cameras with dedicated cardiac SPECT gantry configurations may minimise some of the disadvantages of 16 bin gated SPECT. There may, however, be a greater potential impact of arrhythmias on LVEF inaccuracies if gating is undertaken without a rejected beats bin.

**References**


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