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CARDIOLOGY Rounds™

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Stress Cardiolite Imaging

Do The Results in Clinical Practice Meet Our Expectations?

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Stress myocardial perfusion imaging fulfills an important role in the physician's assessment of patients with known or suspected coronary artery disease. In the past several years, the performance of perfusion imaging utilizing technetium-99m sestamibi or Cardiolite has progressively increased. This increase in utilization is based on comparable sensitivity and specificity to thallium scintigraphy[1,2] and the additional ability to assess ventricular function either with first pass techniques[3] or with gated acquisition of the perfusion data.[4] In addition, Cardiolite imaging results in a clearer definition of myocardial perfusion defects, reduction of tissue attenuation, and an increase in myocardial counts due to the shorter half life and higher energy of technetium as compared to thallium. With the higher counts in the myocardium gated studies of the perfusion images are possible for the assessment of both global and segmental left ventricular function. This report will substantiate the validity of Cardiolite imaging by assessing the value of this technique in our own nuclear cardiology laboratory at St. Michael's Hospital.

Diagnostic Value of Cardiolite

The diagnostic and prognostic value of cardiolite have been confirmed by several investigators utilizing exercise or dipyridamole forms of stress.[1,2,5,6] We retrospectively reviewed over 600 studies in our laboratory and found 72 consecutive patients who had either dipyridamole (n=22) or treadmill exercise (n=50) with rest and stress Cardiolite scans and coronary angiography performed within three months without an intervening cardiac event. Many of these patients had studies to identify the significance of borderline angiographic lesions. The standard rest-stress one day protocol for performance of Cardiolite imaging was performed with data acquired 360° in 4° steps with 15 seconds per stop, thirty minutes after the stress injection and 18 seconds per stop 1 hour following the rest injection. The stress images were acquired with ECG gating of eight frames per cardiac cycle. With standard back projection processing of the data utilizing both the 360° or the 180° data from 45° RAO to

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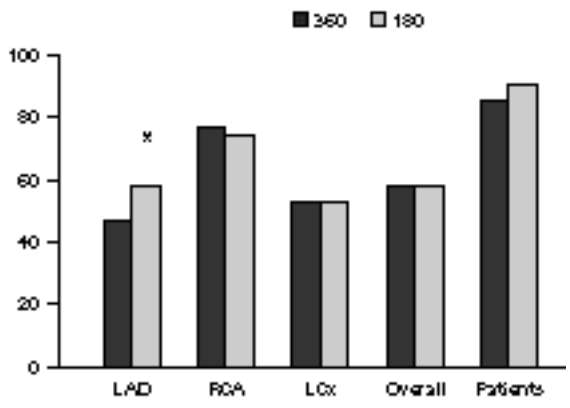
45° LPO we created the standard short axis, vertical long axis and horizontal long axis stress and rest images.

To assess inter-observer reproducibility, three observers blindly interpreted the studies and scored 13 segments per patient and localized defects to the left anterior descending (LAD), right coronary artery (RCA) or left circumflex (LCX) territories. The coronary angiograms are interpreted by two observers and ≥50% stenosis was considered significant.

There was excellent reproducibility of myocardial perfusion imaging with a kappa of 0.58 for stress 360° data and 0.63 for the stress 180° data. Both of these measures of reproducibility were highly significant with $p < .05$, but the stress 180° reproducibility was superior to the 360° reproducibility. Similar reproducibility was demonstrated with rest imaging.

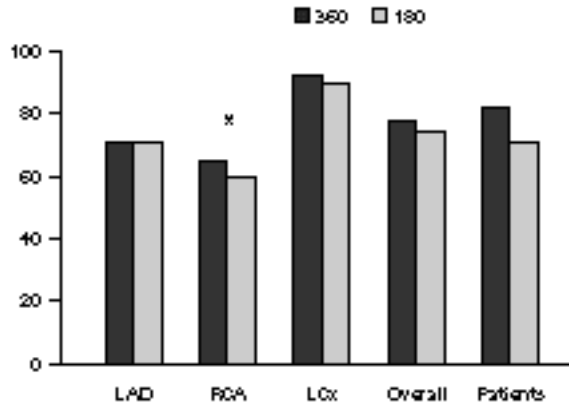
The sensitivity and specificity are summarized in Figures 1 and 2. There was excellent sensitivity and high specificity for coronary artery disease in individual patients. Overall the ability to detect individual stenoses was similar to that reported in the literature for thallium scintigraphy. The sensitivity for LAD disease is somewhat less than expected, but is likely related to the low exercise HR and patient selection criteria of this population. Of note, the sensitivity for LAD disease was superior with 180° of data as compared to 360° of data,

Figure 1: Sensitivity for Stenosis ≥ 50%



*p<0.05

Figure 2: Specificity for Stenosis < 50%



*p<0.05

but specificity for RCA disease better with 360° acquisition.

From these data we conclude that 180° of data acquisition is sufficient for excellent sensitivity and specificity for coronary artery disease and reasonable sensitivity for individual coronary lesions. The Cardiolite images have excellent reproducibility which is related to the consistent excellent image quality and clearly defined myocardial perfusion defects. Careful differentiation of reduced inferior wall uptake due to diaphragmatic attenuation from inferior infarction is necessary to improve specificity.

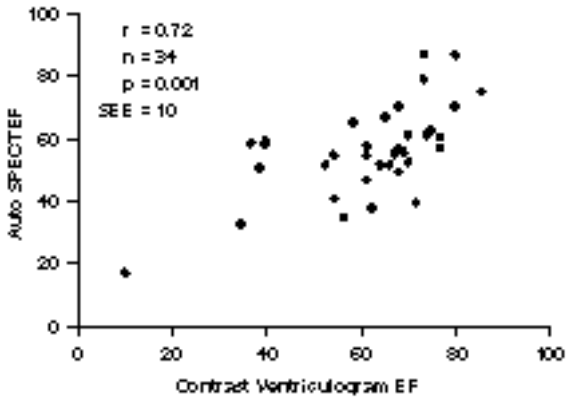
Assessment of left ventricular function

The knowledge of ventricular function has prognostic importance and impacts upon medical therapy, the decision for intervention and requirement for additional testing in patients with known or suspected coronary artery disease. Since gated Cardiolite images have been reported to accurately assess segmental and global left ventricular function,[4] we felt it imperative to document our ability to assess ventricular function.

We compared our visual assessment of global left ventricular function of gated SPECT Cardiolite images versus contrast ventriculography in sixty-two patients. There was agreement within one score of global left ventricular function in 90% of the patients. However, in

assessment of segmental wall motion there was agreement in 67% of segments. In segments with normal myocardial perfusion hypokinesis by contrast ventriculography was underestimated, and in segments with severe perfusion defects ventricular segmental wall motion was frequently considered abnormal, but was normal by contrast ventriculography. A possible explanation for this discordance is the presence of myocardial stunning which may occur following exercise, but had resolved by the time of performing the contrast ventriculogram. The quantitative assessment of ejection

Figure 3: Automatic Gated SPECT EF vs Contrast Ventriculography EF



fraction using a completely automated program correlated highly with contrast ventriculography as shown in Figure 3.

We conclude that segmental wall motion assessment with gated SPECT is accurate but care must be taken in assessing ventricular function in segments with severe perfusion abnormalities. Apparent inferior defects due to diaphragmatic attenuation can easily be identified by the observation of normal wall motion and thickening on the gated images. The automatic determination of ejection fraction by gated SPECT is accurate as compared to both contrast ventriculography and echocardiography.

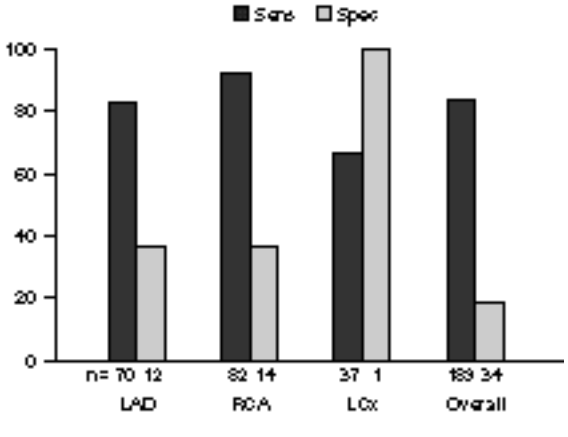
Cardiolite imaging post myocardial infarction

Exercise thallium scintigraphy in the pre-thrombolytic era predicted prognosis[7] early following myocardial infarction, but was not sensitive in detecting stenoses outside of the infarct related territory.[8,9] To evaluate Cardiolite imaging in this population we performed dipyridamole Cardiolite studies in 223 consecutive patients, 56+ 11 years of age, 87% male, with 125 patients receiving thrombolytic therapy, 4 weeks following myocardial infarction. We evaluated the frequency of dipyridamole Cardiolite perfusion defects in the territory of the infarct related artery and as well in the non-infarct related artery with stenoses a > 50% which were definited at coronary angiography performed within twenty-four hours of the perfusion study.

Extent of coronary artery disease

Defects were common in the territory of the infarct related artery as shown in Figure 4, but the sensitivity of a defect in the non-infarct related artery was poor ie. <40% for the LAD and left circumflex and only 60% for the right coronary artery (Figure 5). There was however excellent specificity of >80% in the LAD and left circumflex and 60% in the right coronary artery

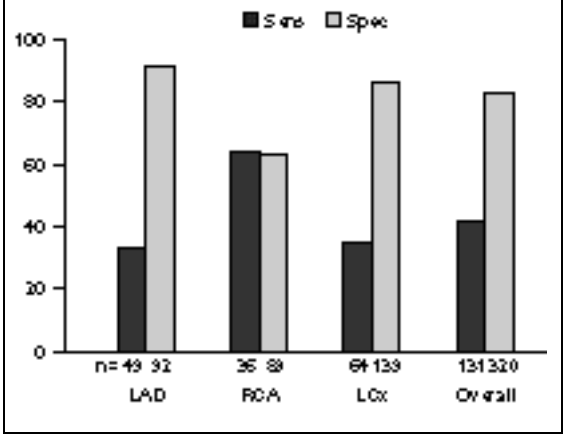
Figure 4: Dypyridamole Sestamibi Defects in Infarct Related Arteries with ≥ 50% Stenosis



(Figure 5). In the 130 patients with single vessel disease a single defect was present in 81% of the subjects. However, in the 93 patients with multivessel disease, only 50% had defects in two or more territories.[10]

Thus, even with the improved imaging techniques of Cardiolite as compared to thallium, we have a similar lack of sensitivity for detecting coronary stenoses away from the infarction territory. These are similar to the data we have previously described with thallium scintigraphy and also reported by Haber et al.[9]

Figure 5: Dypyridamole Sestamibi Defects in Non-Infarct Related Arteries with ≥ 50% Stenosis



Myocardial Viability

There continues to be discussion as to the most appropriate method for assessment of myocardial viability with single photon perfusion agents. In 125 of these patients with recent myocardial infarction, we performed rest thallium imaging as well as rest Cardiolite imaging. The frequency of reversible defects when comparing the rest studies with the dipyridamole Cardiolite images are shown in Figure 6.

Figure 6: Reversibility of Stress MIBI Defects
Rest MIBI vs Rest Thallium

Rest Thallium	Rest MIBI			
	Normal	Reversible	Nonrevers	Worsening
Normal	**21**	**0**	**0**	**0**
Reversible	**0**	**49**	**22**	**3**
Nonrevers	**0**	**3**	**25**	**1**
Worsening	**3**	**0**	**1**	**3**

With rest thallium there was significantly more reversible defects as compared to rest cardiolite imaging. Thus, there is almost 50% greater reversibility with thallium imaging as compared to Cardiolite imaging. However, the prognostic value and clinical relevance of these differences requires further evaluation.

Summary

From this clinical evaluation of cardiolite imaging in our nuclear cardiology laboratory we conclude that:

- Stress Cardiolite imaging accurately detects the presence or absence of coronary artery disease.
- Stress Cardiolite imaging, as is the case with thallium-201 imaging, is less than ideal in detecting individual coronary lesions, particularly in patients with recent myocardial infarction.
- Reversibility of perfusion defects is more common with thallium as opposed to rest Cardiolite imaging.
- Segmental and global ventricular function can be assessed with gated imaging of Cardiolite images and improves specificity of perfusion imaging.
- 180° of data acquisition is superior to 360° acquisition.

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Upcoming Scientific Meetings

3-5 April 97
Vascular Biology '97
New Orleans, Louisiana, USA
(American Heart Association)
Tel.: 214-706-1100

10-12 April 97
Cardiac Pacing – 1997: New Indications for Pacing, Rate Adaptive Pacing Updates, Updates on Cardioversion-Defibrillation
Bethesda, Maryland, USA
(American College of Cardiology)
Tel.: 301-897-5400

12 April 97
Cardiology for the Practitioner
Toronto, Ontario, Canada
(St. Michael's Hospital, Division of Cardiology)
Tel.: 416-864-5719

28-29 April 97
Contemporary Management of Cardiovascular Disease Conference
Toronto, Ontario, Canada
(Heart and Stroke Foundation of Ontario)
Tel.: 416-489-7100 X:431

Abstracts of Interest

Detecting Coronary Artery Disease: Value and Cost-effectiveness of Noninvasive Tests

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The goal of our study was to evaluate the capacity and cost-effectiveness of three noninvasive diagnostic strategies for detecting coronary artery disease. We reviewed records of all patients who underwent cardiac catheterization in the first quarter of 1994; 132 patients with exertional angina, without previous coronary events or invasive intervention, were included. All patients were evaluated by clinical examination and risk factor assessment; 110 underwent stress testing; 55 had thallium imaging. We used logistic regression to calculate sensitivity, positive predictive value (PPV), and false-positive rates of three models of noninvasive strategies for detecting coronary artery disease. Based on these results and a review of current literature, we assessed the cost-effectiveness of the models, using a hypothetical population of 1000 patients with demographic characteristics similar to our patients. Evaluation of the quality of chest pain with risk factor analysis (Model 1) yielded a sensitivity of 76.7% and positive predictive value of 72.7%. With addition of stress testing (Model 2), sensitivity increased to 83.6% and PPV to 76.1%. With addition of thallium imaging (Model 3), sensitivity was 90.3% and PPV was 77,8%. Analysis of costs for each model was adjusted by adding the costs of inappropriate coronary angiographies, calculated on the basis of false-positive rates. Analysis revealed that inappropriate angiographies were less costly than noninvasive tests performed to avoid them. We found that clinical examination with risk factor analysis is the most cost-effective and reasonably sensitive method of detecting coronary artery disease in patients with exertional angina pectoris.

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Is there Justification for Follow-Up Symptom Limited Exercise Myocardial Perfusion Studies Late Post Myocardial Infarction?

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It is common clinical practice to perform a pre-discharge low level (LL) myocardial perfusion study followed by a symptom-limited (SL) study, 4-8 weeks later, to risk stratify patients (pts) after myocardial infarction. The clinical utility of this practice was retrospectively evaluated by comparing pairs of LL and SL SPECT studies in 36 stable post-MI pts. Their age was 60 ± 10 years (mean ± SD) with 75% men. Time between studies was 54 ± 28 days (range 11-143) with non interval cardiac events or interventions. Thallium was used in 32 pairs and sestamibi in 4. SPECT studies were interpreted by two blinded observers using a 20 segment scoring system. Results:

	LL	SL	p<
% mphr achieved	64 ± 12	82 ± 13	0.001
Mets achieved	5.1 ± 1	8.5 ± 3	0.001
Total abnormal segments	185	194	NS
Mean abnormal segments/pt.	5.1 ± 2.9	5.4 ± 3.4	NS
# fixed defects	116 (63%)	82 (42%)	0.004
# reversible defects	64 (35%)	106 (55%)	0.002
# reverse redistribution	5 (2%)	6 (3%)	NS

There were no differences in ß-blocker use (86% Vs 75%), clinical or EKG response to exercise, or presence of transient ischemic dilatation. There were 106 reversible defects on SL: 48% were present and reversible on LL, 26% were present but fixed on LL and 26% were new. The 28 fixed defects on LL that became reversible on SL were mostly of moderate intensity (71%), whereas the 79 defects which were fixed on both studies were mostly severe (66%; p<0.01). Five perfusion patterns were observed: 1) normal or equivocal on both (4 pts); 2) mostly fixed defects on both (8 pts); 3 combined fixed and reversible defects on both with no interval change (9 pts); 4) combined fixed and reversible defects with less ischemia on SL (1 pt); and 5) combined fixed and reversible defects with more ischemia on SL (14 pts). Of those with pattern #5, 10 pts had 2 or more additional reversible segments on SL in the same coronary territory compared to LL; 4 other pts had at least two new reversible segments in a remote coronary territory, compared to LL. Thus 14/36 (39%) pts were identified with significantly more ischemia on SL than on LL. Conclusion: Late symptom-limited myocardial perfusion testing following low level pre-discharge testing was justified because it demonstrated new ischemia in remote coronary territories or territories initially showing predominantly fixed defects. These may indicate additional risk for future cardiac events.

Excerpted from Journal of the *American College of Cardiology*, 1997;29 (supplement A) 197A.