



UNIVERSITÀ  
DEGLI STUDI  
FIRENZE

## FLORE

# Repository istituzionale dell'Università degli Studi di Firenze

### **Gated single-photon emission computed tomography. The present-day "one-stop-shop" for cardiac imaging.**

Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

*Original Citation:*

Gated single-photon emission computed tomography. The present-day "one-stop-shop" for cardiac imaging / R. SCIAGRA'; LEONCINI M.. - In: THE QUARTERLY JOURNAL OF NUCLEAR MEDICINE AND MOLECULAR IMAGING. - ISSN 1824-4785. - STAMPA. - 49:(2005), pp. 19-29.

*Availability:*

This version is available at: 2158/222322 since: 2019-10-09T14:19:42Z

*Terms of use:*

Open Access

La pubblicazione è resa disponibile sotto le norme e i termini della licenza di deposito, secondo quanto stabilito dalla Policy per l'accesso aperto dell'Università degli Studi di Firenze (<https://www.sba.unifi.it/upload/policy-oa-2016-1.pdf>)

*Publisher copyright claim:*

(Article begins on next page)

# Gated single-photon emission computed tomography

The present-day “one-stop-shop” for cardiac imaging

R. SCIAGRÀ<sup>1</sup>, M. LEONCINI<sup>2</sup>

**Gated single-photon emission computed tomography (SPECT) is the current state-of-the-art approach to myocardial perfusion imaging. Initially, major emphasis was given to the improvement in diagnostic accuracy of myocardial perfusion imaging for the detection of coronary artery disease, because the evaluation of wall motion and thickening allows the recognition of attenuation artifacts and increases the observer's confidence. Different processing algorithms make possible to perform a reproducible and reliable assessment of left ventricular (LV) function, which has been extensively validated against various reference methods. Several articles report the additional value of functional data derived from gated SPECT to increase the accuracy of myocardial perfusion imaging in particular patient groups, such as women, to enhance the detection of multivessel coronary artery disease, and to permit the recognition of severe stenosis. An extensive literature indicates that gated SPECT allows a more accurate and reliable prognostic stratification of patients with known coronary artery disease. More recently, the peculiar contribution of gated SPECT in the assessment of myocardial viability has been demonstrated, with the possibility to evaluate in a single myocardial perfusion study the presence of preserved tracer uptake and the amount of contractile reserve through the acquisition of gated SPECT during inotropic stimulation with dobutamine. The most recent advance in the application of gated SPECT is the use of this technique for the reproducible assessment of LV functional changes, at follow-up or during inotropic stimulation, with perfusion data in the background. Various clinical settings, such as assessment of response to medical or resynchronization therapy in dilated or ischemic cardiomyopathy, prediction of outcome in chronic coronary artery disease with LV**

<sup>1</sup>Nuclear Medicine Unit  
Department of Clinical Physiopathology  
University of Florence, Florence, Italy  
<sup>2</sup>Division of Cardiology  
Misericordia e Dolce Hospital, Prato, Italy

**remodeling, evaluation of different treatment strategies in acute myocardial infarction, could take advantage from the unique combination of perfusion and functional data made possible by the use of gated SPECT. In conclusion, myocardial perfusion imaging with gated SPECT is a convincing reality in the field of cardiac imaging and has a still largely unexplored potential for a wider use in heart disease.**

**KEY WORDS:** Tomography, emission computed, single photon – Heart, radionuclide imaging – Myocardium.

Since its introduction, gated single-photon emission computed tomography (SPECT) has been a major breakthrough in the practice of nuclear cardiology.<sup>1, 2</sup> The possibility to simultaneously assess both myocardial perfusion and left ventricular (LV) wall motion has deeply modified the approach to myocardial perfusion imaging. Most importantly, several applications of the combination of perfusion and functional data have been proposed, opening the way to a more comprehensive and accurate evaluation of patients with suspected or known coronary artery disease. In this regard, gated SPECT could be presently considered the imaging technique nearest to the ideal concept of a diagnostic and prognostic “one-stop-shop” in the field of coronary artery disease. The aim

Address reprint requests to: R. Sciagrà, MD, Nuclear Medicine Unit, Department of Clinical Physiopathology, University of Florence, Viale Morgagni 85; 50134 Firenze, Italy. E-mail: r.sciagra@dfc.unifi.it

TABLE I.— Validation of gated SPECT LVEF and LV volume measurement against various reference methods.

Authors	Patients	Reference method	LVEF	End-diastolic vol.	End-systolic vol.
Williams <i>et al.</i> <sup>8</sup>	38	First pass	r=0.83		
Germano <i>et al.</i> <sup>9</sup>	65	First pass	r=0.91		
Kang <i>et al.</i> <sup>10</sup>	31	First pass	r=0.96		
Yang <i>et al.</i> <sup>11</sup>	21	ERNA	r=0.87		
Marinque <i>et al.</i> <sup>12</sup>	50	ERNA	r=0.82		
Vera <i>et al.</i> <sup>13</sup>	43	ERNA	r=0.80	r=0.86	r=0.89
Chua <i>et al.</i> <sup>14</sup>	62	ERNA	r=0.94	r=0.88	r=0.95
Nichols <i>et al.</i> <sup>15</sup>	66	Echocardiography	r=0.85		
Cwajg <i>et al.</i> <sup>16</sup>	109	Echocardiography	r=0.72	r=0.87	r=0.86
Nichols <i>et al.</i> <sup>17</sup>	33	Echocardiography	r=0.92	r=0.90	r=0.90
Vourvouri <i>et al.</i> <sup>18</sup>	32	Echocardiography	r=0.83	r=0.94	r=0.96
Williams <i>et al.</i> <sup>8</sup>	54	Ventriculography	r=0.93		
Nichols <i>et al.</i> <sup>15</sup>	58	Ventriculography	r=0.86	r=0.87	r=0.91
Yoshika <i>et al.</i> <sup>19</sup>	21	Ventriculography	r=0.87	r=0.73	r=0.83
Stollfuss <i>et al.</i> <sup>20</sup>	19	MRI	r=0.71		
Vaduganathan <i>et al.</i> <sup>21</sup>	25	MRI	r=0.93	r=0.81	r=0.92
Bax <i>et al.</i> <sup>22</sup>	22	MRI	r=0.90	r=0.84	r=0.87
Tadamura <i>et al.</i> <sup>23</sup>	20	MRI	r=0.94	r=0.92	r=0.97

ERNA: equilibrium radionuclide angiography; first-pass: first-pass ventriculography; MRI: magnetic resonance imaging; ventriculography: contrast ventriculography; vol.: volume.

of this review is to examine the state-of-the-art use of gated SPECT and to define its current value in the context of cardiac imaging.

### Technical issues

The basic principles of the electrocardiographic gating of SPECT are well known. The technical requirements for an acceptable study are nowadays fulfilled by most gamma camera systems. Similarly, the available processing algorithms allow a reliable calculation of functional parameters. However, the specific problems related to the electrocardiographic gating of tomographic studies should be kept in mind, since they may create unique artifacts. The presence of variability in the R-R interval may lead to major count loss in the later frames, which in turn may propagate in the reconstructed images in form of streaking artifacts, when the count-deficient frame is normalized to the reference frame. Filtering of low-counts, noisy projections may produce dark bands or apparent clumping of counts in the myocardial wall. Temporal blurring in the instance of major and persistent R-R interval variability may yield radial blurring of the reconstructed images, or affect the definition of the systolic frame and the consequent measurement of vol-

umes and ejection fraction (EF).<sup>3</sup> Nichols *et al.*<sup>4</sup> demonstrated a relationship between arrhythmia severity and changes in gated SPECT parameters: atrial fibrillation is clearly the most adverse condition and wall thickening assessment the most sensitive parameter, while EF appeared a quite robust measurement. In the case of atrial fibrillation, even summed perfusion images could be affected by gating artifacts.<sup>4,5</sup> Patients with severe arrhythmia pose a problem and may be considered unsuitable for gated SPECT imaging. In case of premature ventricular contractions, a rate of 1 every 6 beats has been proposed as the upper limit acceptable for gating.<sup>3</sup> More recently, ASNC proposed the limit of >20% of premature beats to classify a patient as not suitable for gated SPECT.<sup>2</sup>

The problem of count density is particularly relevant to Tl-201 gated SPECT, because the signal-to-noise ratio is clearly lower than in Tc-99m perfusion studies, and appropriate filtering must be used. On the other hand, filtering may interfere with the detection of ventricular boundaries and cause overestimation of EF. This is particularly important in case of small hearts, where it may be observed with the Tc-99m-labelled perfusion agents as well. However, the possibility to overcome these limitations by means of hardware zooming, filtering with high cut-off frequency and better system resolution has been demonstrated even

in pediatric patients.<sup>6</sup> Another possible source of defective edge detection is the presence of extensive and severe perfusion defects.<sup>7</sup>

### Validation of functional data derived from gated SPECT

As summarized in Table I,<sup>8-23</sup> a large number of clinical studies have convincingly proven the very good correlation between gated SPECT and other established techniques in the assessment of global LV function (LV volumes and LVEF) and in the evaluation of regional wall motion and thickening.<sup>8-17, 19-25</sup> Moreover, the reproducibility of gated SPECT measurements has been reported to be high. In a very recent study, Verberne *et al.*<sup>26</sup> demonstrated that in 22 patients who underwent 2 repeated gated SPECT acquisitions, the LVEF differed less than 1 EF unit: 0.9% (95% confidence interval – 1.15% to 1.33%). De Winter *et al.*<sup>27</sup> reported similar results in patients with LV dysfunction due to ischemic cardiomyopathy. Vallejo *et al.*<sup>28</sup> had observed slightly higher variations in repeated measurements, which appeared to be greater if the study was acquired after the injection of a low tracer dosage (555 MBq, 15 mCi). However, in the case of high-dose studies, the presence of perfusion defects did not affect the reproducibility of the LVEF measurement.<sup>28</sup> Differences exist when the processing algorithms currently available are compared: although this does not limit the overall clinical value of the various methods, it precludes the possibility to compare values that have not been obtained using the same procedure.<sup>29, 30</sup>

It has been shown that the lower limits of normalcy are slightly different, especially in the case of the LVEF, from those obtained using other imaging modalities. Recent studies have tried to identify the normal values in various groups of patients, demonstrating higher normal LVEF values in women than in men. Particularly, the lower limit of normal LVEF in men has been fixed at 41-43% and in women at 49-50%.<sup>31, 32</sup>

With regard to the assessment of regional function, the agreement between gated SPECT and echocardiography, which is the most used reference standard in clinical practice, has been reported to range from 91% to 56%.<sup>33, 34</sup> Of particular concern is the evaluation of regional function in patients with wide perfusion defects. In patients with prior infarction

and LV dysfunction, Leoncini *et al.*<sup>35</sup> could demonstrate a good agreement (68%) in the qualitative scoring of the regional wall motion between Tc-99m-sestamibi gated SPECT and echocardiography, with a  $k=0.54$ . No differences in the various coronary distribution territories were registered and the wall motion score index of the single coronary territories estimated using gated SPECT showed a good correlation with the corresponding value obtained using echocardiography (Spearman  $r=0.78$ ,  $p<0.0001$ ). These results were confirmed by Vourvouri *et al.*,<sup>18</sup> who, in a patient population with ischemic cardiomyopathy, demonstrated an overall 69% agreement ( $k=0.61$ ) between gated SPECT and echocardiography for the assessment of regional wall motion and a close correlation in the measurements of both LV volumes and LVEF. Bax *et al.*<sup>22</sup> performed a similar comparative study between gated SPECT and magnetic resonance imaging: together with the close correlation of LV volumes and LVEF, an excellent agreement in the assessment of regional wall motion was registered, with 83% exact agreement and  $k=0.77$ .

### Gated SPECT and diagnosis of coronary artery disease

It is well known that perfusion SPECT is highly sensitive but moderately specific for detecting coronary artery disease. One of the reasons that limit specificity is the presence of attenuation artifacts (breast tissue, diaphragm) that appear as perfusion defects and can be hardly differentiated from fixed defects caused by a previous myocardial infarction. By combining the evaluation of regional wall motion and thickening with the assessment of perfusion it is possible to distinguish an attenuation artifact, which will show some degree of preserved wall motion and thickening, from scarred tissue, which conversely will show absent or severely reduced wall motion and thickening.<sup>36</sup> Thus, the introduction of gated SPECT has increased the diagnostic accuracy of perfusion imaging by reducing the number of false positive or equivocal studies.

This was clearly established by Smanio *et al.*,<sup>37</sup> who showed that in 137 patients with low (<5%) pretest likelihood of coronary artery disease, the evaluation of gated images significantly increased the percentage of normally interpreted results (from 74% to 91%,  $p<0.001$ ), with a clear reduction in the cases classified

as probably normal or probably abnormal. More recently, Links *et al.*<sup>38</sup> demonstrated that gating and attenuation correction act synergistically in improving the diagnostic accuracy of perfusion SPECT. Furthermore, the use of gating increases the inter- and intraobserver reproducibility of the qualitative assessment of myocardial perfusion.<sup>39</sup> In a most recent study, the value of gated SPECT for discriminating infarct from artifact in perfusion imaging has been confirmed using tetrofosmin instead of sestamibi.<sup>40</sup> In theory, the demonstration of normal regional wall motion and thickening is very useful also to reinforce the operator's opinion in case of a normal stress study and could at least in selected cases make unnecessary the acquisition of a resting perfusion scan.<sup>41</sup> The gain in specificity caused by the use of gated SPECT is particularly important in women, and supports the consensus that gated myocardial perfusion SPECT is probably the modality of choice for the noninvasive evaluation of women with an intermediate pretest likelihood of coronary artery disease.<sup>42</sup>

Another diagnostic advantage of gated SPECT is based on the recognition in the poststress acquisition of regional wall motion and thickening abnormalities caused by the persistence of postischemic stunning.<sup>43</sup> This finding can be particularly useful to detect patients with multivessel coronary artery disease. In a study by Mazzanti *et al.*,<sup>44</sup> the detection of transient LV dilatation at 15 minutes after stress compared with postrest gated SPECT identified the patients with diffuse and severe coronary artery disease with high specificity (95%) and good sensitivity (71%). Sharir *et al.*<sup>45</sup> showed that considering either the presence of a severe perfusion defect or of a postexercise wall motion abnormality allowed the detection of any severely stenosed vessel with 82% sensitivity, compared with 49% sensitivity of a severe perfusion defect alone. Emmett *et al.*<sup>46</sup> observed that the presence of reversible regional wall motion abnormalities identified as severe the coronary artery stenoses with 53% sensitivity and 100% specificity and was able to stratify the patients according to the severity of angiographic stenoses with a high positive predictive value; furthermore, there was a good correlation between the presence of reversible regional wall motion abnormality and the coronary artery jeopardy score. Two studies by the same group pointed out that the combination of reversible perfusion defects and poststress regional wall motion abnormalities or poststress worsening of LV EF was significantly more sensitive in the

detection of multivessel coronary artery disease than reversible perfusion defects alone even using Tl-201 as the perfusion agent.<sup>47, 48</sup> Finally, Lima *et al.*<sup>49</sup> demonstrated that the number of abnormal territories by combined perfusion/function was a most powerful predictor of multivessel disease and significantly more abnormal territories in patients with three-vessel disease were detected by this approach than using perfusion alone (60% vs 46%,  $p < 0.05$ ). The evaluation of regional function has been shown to be useful in the interpretation of the septal perfusion abnormalities in patients with left bundle branch block.<sup>50</sup> Finally, the availability of functional data, particularly of those obtained from gated SPECT, has been shown to improve the diagnostic reliability of cardiac imaging in patients admitted to the emergency department because of chest pain.<sup>51</sup>

### Prognostic applications of gated SPECT

Gated SPECT offers important additional prognostic information over that given by perfusion data alone. The first and most obvious prognostic parameter is the resting LVEF, which importance cannot be overemphasized.<sup>52</sup> As recently demonstrated, this parameter has a predictive value for the development of heart failure in patients with a first non-complicated myocardial infarction.<sup>53</sup>

The widest experience about the prognostic value of the functional parameters derived from gated SPECT, however, is based on the poststress LVEF in the context of the dual isotope (rest Tl-201 – stress Tc-99m-sestamibi) protocols of the Cedars Sinai group. This parameter can be partly influenced by the presence of postischemic stunning and thus should be considered slightly different from a true resting LVEF. In a first report, Sharir *et al.*<sup>54</sup> proved the incremental prognostic value of the LV volumes and LVEF calculated using a poststress gated SPECT over the perfusion data of traditional perfusion SPECT. The incremental prognostic value was clearly apparent in the patients classified as intermediate risk on the basis of the perfusion pattern. In this group of patients, the functional parameters obtained using a poststress gated SPECT acquired 30 minutes after exercise differentiated the low risk patients (LVEF > 45% or end-systolic volume < 70 ml) from those at high risk of death (LVEF < 45% or end-systolic volume > 70 ml). In a later report, the same authors showed that perfusion data, in particu-

lar the extent of perfusion defect reversibility, were the most powerful independent predictors of nonfatal myocardial infarction, whilst the poststress LVEF was an independent predictor of death.<sup>55</sup> The combination of perfusion and functional changes identifies 3 groups of patients at different risk of major cardiac events (death and myocardial infarction). Low risk patients are those without inducible ischemia and with poststress LVEF >30% or those with moderate inducible ischemia but with preserved LV function (LVEF >50%). Intermediate risk patients are those with severe ischemia and with poststress LVEF >30% or those with moderate ischemia and with mild-moderate LV dysfunction (poststress LVEF >30 and ≤50%). High-risk patients are those with poststress LVEF <30%. These observations were confirmed by other authors,<sup>56</sup> who demonstrated that a poststress LVEF <40% has a unfavorable prognostic meaning in the prediction of major cardiac events even in patients without scintigraphic findings of ischemia. Hashimoto *et al.*<sup>57</sup> showed the incremental prognostic value of combined perfusion/function in patients candidate to major non-cardiac surgery. Spinelli *et al.*<sup>58</sup> demonstrated the incremental prognostic value of the assessment of regional ventricular function by gated SPECT in patients with acute myocardial infarction. Travin *et al.*<sup>59</sup> established the incremental prognostic value of regional wall motion abnormalities and LVEF in patients studied for suspect coronary artery disease and who were not submitted to early revascularization procedures. Most recently, Thomas *et al.*<sup>60</sup> demonstrated the prognostic value of functional parameters, including transient ischemic dilatation and LVEF in a large population of patients studied in an outpatient setting. In this study, both the increasing ischemic burden and the lower LVEF were related to a worse prognosis and to a higher rate of angiographic studies and revascularization procedures.

### Gated SPECT and myocardial viability

The recognition of viable myocardium in patients with LV dysfunction of ischemic origin has become a major task of diagnostic imaging in cardiology. From the very beginning of gated SPECT, various studies examined whether the gating of perfusion images might be helpful for improving the accuracy of myocardial perfusion scintigraphy in the prediction of reversible regional dysfunction. The most straightfor-

ward approach was to include in the definition of viable myocardium all segments with preserved thickening, independently of their perfusion pattern. Using this approach, Levine *et al.*<sup>61</sup> and Duncan *et al.*<sup>62</sup> were able to predict the functional recovery after revascularization with a sensitivity and accuracy higher than using resting Tc-99m-sestamibi perfusion data alone and comparable to those achieved with Tl-201 redistribution imaging. On the other hand, Stollfuss *et al.*<sup>20</sup> did not find any significant improvement in sensitivity and specificity using the regional thickening than using perfusion data alone. More recently, Mabuchi *et al.*<sup>63</sup> reported very good results using the resting wall thickening data derived from the QGS program for predicting the presence of reversible dysfunction. However, Kang *et al.*<sup>64</sup> were unable to demonstrate a significant predictive value of preserved thickening in a large group of patients submitted to resting Tl-201 and dipyridamole sestamibi gated SPECT. Although in this study the influence of postischemic stunning on regional wall thickening should be considered, it must be reminded that the absence of systolic thickening does not exclude the presence of myocardial viability and, conversely, preserved thickening in the instance of subendocardial infarction does not imply a further improvement in regional function after revascularization.

Another approach was suggested by the observation that the activity thresholds for Tl-201 or Tc-99m-sestamibi that best separate the segments with from those without reversible dysfunction are different according to the severity of baseline echocardiographic asynergy, being higher in the hypokinetic than in the a-dyskinetic segments.<sup>65</sup> Gated SPECT is very well suited to recognize the dysfunctional myocardial segments, to classify them on the basis of the severity of baseline asynergy and to directly estimate the tracer activity within the dysfunctional segment. This simplifies the use of appropriate activity thresholds according to the degree of regional asynergy without the inherent difficulty of overlapping images obtained by different modalities. Leoncini *et al.*<sup>66</sup> demonstrated that the use of a ≥50% activity threshold for the a-dyskinetic segments and >68% for the hypokinetic segments, as identified on the basis of gated SPECT wall motion analysis, allowed a significant increase in specificity (from 54% to 73%,  $p < 0.0001$ ) and accuracy (from 64% to 74%,  $p < 0.02$ ) of nitrate-enhanced Tc-99m sestamibi perfusion imaging, without a significant decrease in sensitivity (from 83% to 76%).

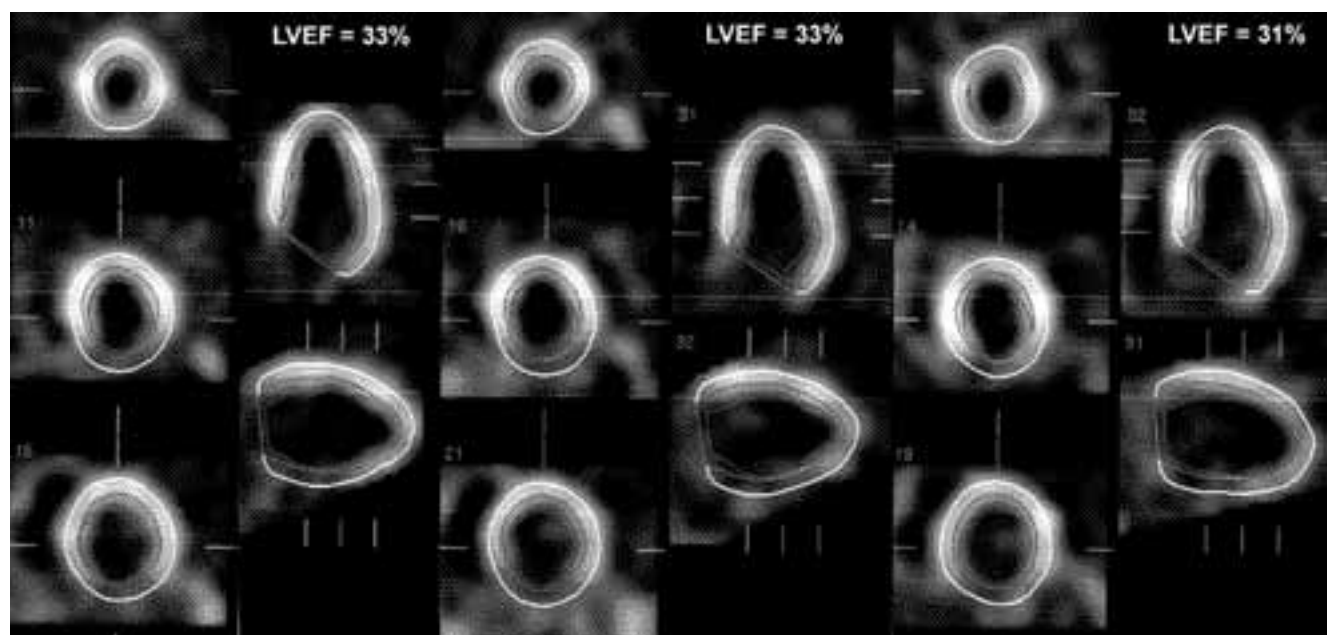


Figure 1.—Gated SPECT studies of a patient with coronary artery disease and LV dysfunction. From left to right: short axis slices, midventricular horizontal (top) and vertical (bottom) long axis slices of the prevascularization nitrate-enhanced baseline study (columns 1 and 2); corresponding slices of the low-dose dobutamine study (columns 3 and 4) and of the postrevascularization follow-up study (columns 5 and 6). The absence of changes in regional wall motion and LVEF during inotropic stimulation predicts the lack of improvement after revascularization.

An alternative and probably more promising approach is based on the capability of gated SPECT to detect the regional wall motion and systolic thickening changes induced by inotropic stimulation and hence to assess the contractile reserve, which is another well established marker of myocardial viability, as clearly demonstrated by echocardiographic studies.<sup>35, 67-69</sup> In the comparison with FDG PET, the use of contractile reserve assessed by gated SPECT significantly increased the specificity over perfusion data alone (100% vs 52%,  $p < 0.05$ ).<sup>70</sup> However, sensitivity for FDG PET viable myocardium appeared to be lower than that registered using tracer uptake threshold criteria.<sup>71</sup> The gated SPECT evaluation of the contractile reserve predicted the postrevascularization functional recovery with higher specificity (88% vs 55%) but lower sensitivity (64% vs 85%) than tracer activity.<sup>72</sup> However, it was found that the higher specificity of contractile reserve is particularly remarkable in the baseline hypokinetic and the higher sensitivity of perfusion tracer activity is more apparent in the baseline a-dyskinetic ones. Thus, a combined approach that defines viable the hypokinetic seg-

ments according to their contractile reserve assessed using gated SPECT under dobutamine infusion and the a-dyskinetic segments according to their tracer activity allows to predict the presence of reversible regional dysfunction with significantly higher specificity (83%) and accuracy (81%) than using perfusion imaging alone, and significantly higher sensitivity (78%) than using contractile reserve alone.<sup>72</sup> The advantage of combining perfusion threshold, inotropic and/or ischemic response to low dose dobutamine for the prediction of postrevascularization recovery was confirmed by Zafir *et al.*<sup>73</sup> In a different setting of patients studied after acute myocardial infarction, Simoes *et al.* demonstrated the feasibility of low dose dobutamine gated SPECT even using Tl-201 as the perfusion tracer and confirmed the increase in specificity obtained by adding the contractile reserve data to the assessment of tracer uptake.<sup>74</sup> Similar results have been recently reported by Heiba *et al.* using low dose dobutamine in conjunction with the Tl-201 study of the dual isotope imaging protocol.<sup>75</sup>

An additional advantage of performing the simultaneous assessment of perfusion and functional

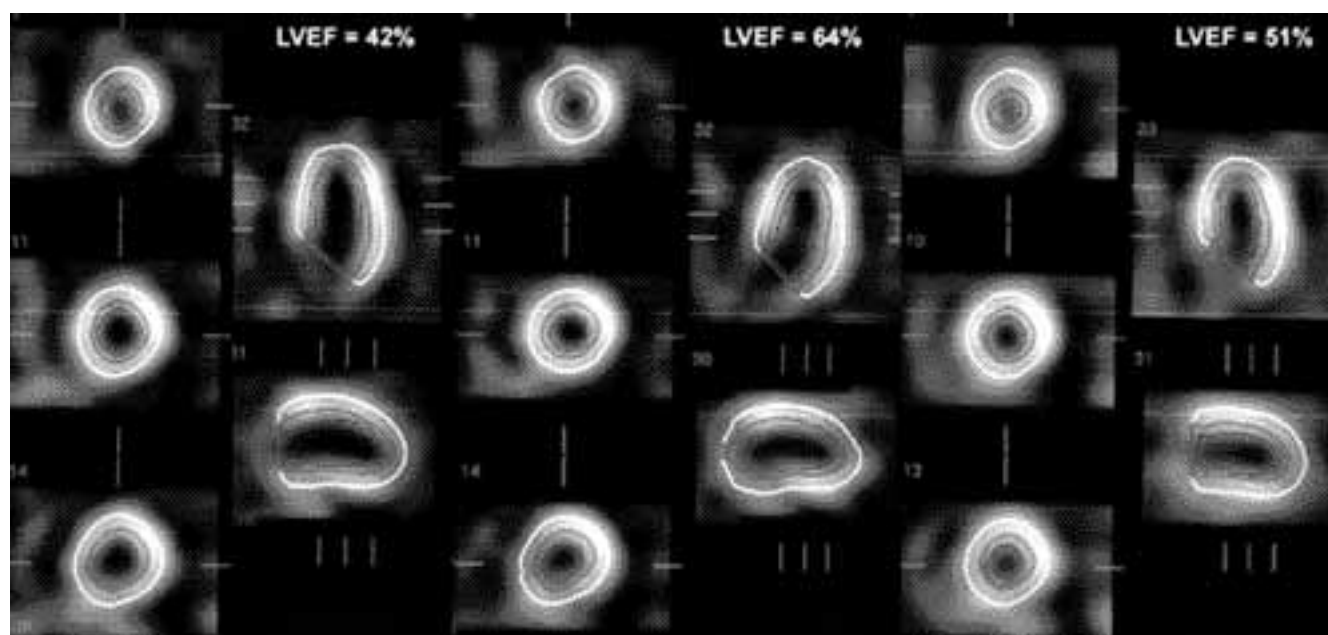


Figure 2.—Gated SPECT studies of a patient with coronary artery disease and LV dysfunction. Same image disposition as in Figure 1. The significant improvement in regional wall motion and the increase in LVEF during inotropic stimulation are predictive of postrevascularization recovery.

changes induced by an inotropic stimulation is the possibility to differentiate between the various physiopathologic conditions that lead to LV dysfunction. In the experimental setting, Chin *et al.*<sup>76</sup> demonstrated the value of this combined approach to differentiate between viable non-functioning myocardium and nontransmural scarring in a model of canine stunning and subendocardial infarction. In a human study, Sciagrà *et al.* used the combined perfusion/function assessment to differentiate between chronic stunning and true hibernation.<sup>77</sup>

Although the regional functional recovery is the established reference standard to define the presence of viable hibernating myocardium, in clinical terms the main purpose of viability imaging is to predict the presence and the amount of recovery in global LV function after successful revascularization.<sup>78</sup> It has been proven that the LVEF increase after revascularization is related to the extent of viable myocardium.<sup>79, 80</sup> However, a direct estimate of the future LVEF changes would be desirable. The reproducibility of gated SPECT functional data is very interesting for this aim. Leoncini *et al.*<sup>81</sup> observed a good correlation between the LVEF values measured during dobutamine infusion and those registered after revascu-

larization ( $r=0.84$ ,  $p<0.00001$ ). Furthermore, a LVEF increase  $\geq 5$  EF units during dobutamine predicted an increase  $\geq 5$  EF units after revascularization with 77% accuracy, 73% positive and 81% negative predictive value. Figure 1 and Figure 2 show typical examples of low-dose dobutamine gated SPECT studies in the setting of ischemic cardiomyopathy.

### Perfusion gated SPECT beyond perfusion

As described in the previous sections, the additional value of gating perfusion SPECT is certainly high. However, in the last few years, there is a growing number of reports describing settings in which the main purpose of the execution of gated SPECT is not the assessment of myocardial perfusion but the evaluation of ventricular function. The feasibility of gated SPECT and the good reproducibility of its functional measurements are the prerequisites for the novel applications of this technique. The clinical settings in which gated SPECT has been proposed to estimate functional changes are mainly those related to the presence of LV dysfunction.



In patients with recent-onset idiopathic dilated cardiomyopathy, Kasama *et al.*<sup>82</sup> could demonstrate that the LVEF changes induced by low dose dobutamine and evaluated using gated SPECT were predictive of the response to medical treatment, whilst the perfusion pattern was useless in this regard. Fukuchi *et al.*<sup>83</sup> examined using gated SPECT patients with established idiopathic dilated cardiomyopathy and demonstrated that the size of the perfusion defects and the sphericity index derived from gated SPECT volumes were both predictive of the response to  $\beta$ -blocker therapy. In patients with severe heart failure due to idiopathic dilated or ischemic cardiomyopathy submitted to cardiac resynchronization therapy with biventricular pacing, Sciagrà *et al.*<sup>84</sup> examined the changes in LV volumes and EF using repeated gated SPECT studies and observed that a significant objective improvement in functional parameters was detected only in the patients without perfusion defects. In a similar setting, Tsurugaya *et al.*<sup>85</sup> could classify the patients in responders and nonresponders to biventricular pacing on the basis of the improvement in LV synchrony assessed by repeated gated SPECT studies performed before and shortly after the onset of cardiac resynchronization therapy. In patients with severe LV dysfunction due to prior infarction, Fujii *et al.*<sup>86</sup> studied by gated SPECT the functional changes produced by endoventricular circular patch plasty performed in addition to coronary artery bypass grafting. They could demonstrate both short- and long-term reverse remodeling, with significant reduction in LV volumes and increase in LVEF. Most recently, Schäfers *et al.*<sup>87</sup> used gated SPECT to examine the evolution of myocardial remodeling in dilated cardiomyopathy after partial left ventriculectomy and mitral valve repair: the authors could identify a significant decrease in both end-diastolic and end-systolic volumes and an increase in LV ejection fraction early after the intervention, with further, albeit not statistically significant, improvement at late follow-up approximately 1 year later.

The evaluation of functional data can be an indication for performing gated SPECT in patients with preserved LV function as well. Zellweger *et al.*<sup>88</sup> studied patients treated with percutaneous coronary interventions and detected the presence of reverse remodeling with a significant decrease in both LV volumes in the patients without prior infarction and a significant decrease in endsystolic volume only in those with previous infarction. Another field of application of gated SPECT functional data is the characteriza-

tion of regional wall motion abnormalities. For instance, Giubbini *et al.*<sup>89</sup> recently demonstrated that the combination of functional and perfusion data obtained from gated SPECT is the optimal approach to interpret the meaning of septal wall motion abnormalities in patients submitted to coronary artery bypass grafting. It is well known that gating offers major advantages for evaluating the meaning of septal perfusion defects in patients with left bundle branch block<sup>47</sup> and a recent study suggests that it could be a most important tool to clarify the many unresolved issues of this electrocardiographic pattern.<sup>90</sup> Finally, the execution of repeated gated SPECT studies appears a valuable method to assess the effectiveness of primary percutaneous coronary interventions in the setting of acute myocardial infarction, offering the possibility to directly correlate the extent of myocardial salvage with the degree of functional recovery.<sup>91, 92</sup>

Although these functional indications to gated SPECT are still investigational, they open the way to a more widespread use of perfusion imaging. There are no doubts that the execution of gated SPECT in patients in whom perfusion data are redundant will be limited to particular cases. Nevertheless, as shown by several examples, the availability of both perfusion and functional data is significantly advantageous in various circumstances, and not necessarily the most important is the perfusion pattern. Moreover, because of the overwhelming prevalence of coronary artery disease as etiology of LV dysfunction, the execution of gated SPECT in patients presenting with heart failure symptoms is fully justified both from the point of view of establishing the diagnosis and of assessing the functional status. Therefore, it is predictable that we will assist to a growing use of perfusion gated SPECT and to the expansion of its indications, at least until other imaging modalities will not be capable to achieve the same degree of feasibility and reliability in the assessment of perfusion and function.

## References

1. Mansoor MR, Heller GV. Gated SPECT imaging. *Semin Nucl Med* 1999;29:271-8.
2. ASNC Executive Council. American Society of Nuclear Cardiology position statement on electrocardiographic gating of myocardial perfusion SPECT scintigrams. *J Nucl Cardiol* 1999;6:470-1.
3. Cullom SJ, Case JA, Bateman TM. Electrocardiographically gated myocardial perfusion SPECT: technical principles and quality control considerations. *J Nucl Cardiol* 1998;5:418-25.
4. Nichols K, Dorbala S, DePuey EG, Yao SS, Sharma A, Rozanski A. Influence of arrhythmias on gated SPECT myocardial perfusion and

- function quantification. *J Nucl Med* 1999;40:924-34.
5. Nichols K, Yao SS, Kamran M, Faber TL, Cooke CD, DePuey EG. Clinical impact of arrhythmias on gated SPECT cardiac myocardial perfusion and function assessment. *J Nucl Cardiol* 2001;8:19-30.
  6. Nakajima K, Taki J, Higuchi T, Kawano M, Taniguchi M, Maruhashi K *et al*. Gated SPET quantification of small hearts: mathematical simulation and clinical application. *Eur J Nucl Med* 2000;27:1372-9.
  7. Achtert AD, King MA, Dahlberg ST, Pretorius PH, LaCroix KJ, Tsui BM. An investigation of the estimation of ejection fractions and cardiac volumes by a quantitative gated SPECT software package in simulated gated SPECT images. *J Nucl Cardiol* 1998;5:144-52.
  8. Williams KA, Taillon LA. Left ventricular function in patients with coronary artery disease assessed by gated tomographic myocardial perfusion images. Comparison with assessment by contrast ventriculography and first-pass radionuclide angiography. *J Am Coll Cardiol* 1996;27:173-81.
  9. Germano G, Erel J, Lewin H, Kavanagh PB, Berman DS. Automatic quantification of regional myocardial wall motion and thickening from gated technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography. *J Am Coll Cardiol* 1997;30:1360-7.
  10. Kang X, Berman DS, Van Train KF, Amanullah AM, Areeda J, Friedman JD *et al*. Clinical validation of automatic quantitative defect size in rest technetium-99m-sestamibi myocardial perfusion SPECT. *J Nucl Med* 1997;38:1441-6.
  11. Yang KTA, Chen HD. Evaluation of global and regional left ventricular function using technetium-99m sestamibi ECG-gated single-photon emission tomography. *Eur J Nucl Med* 1998;25:515-21.
  12. Manrique A, Faraggi M, Vera P, Vilain D, Lebtahi R, Cribier A *et al*. 201-Tl and 99m-Tc-MIBI gated SPECT in patients with large perfusion defects and left ventricular dysfunction: comparison with equilibrium radionuclide angiography. *J Nucl Med* 1999;40:805-9.
  13. Vera P, Koning R, Cribier A, Manrique A. Comparison of three-dimensional gated SPECT methods with thallium in patients with large myocardial infarction. *J Nucl Cardiol* 2000;7:312-9.
  14. Chua T, Yin LC, Thiag TH, Choo TB, Ping DZ, Leng LY. Accuracy of the automated assessment of left ventricular function with gated perfusion SPECT in the presence of perfusion defects and left ventricular dysfunction: correlation with equilibrium radionuclide ventriculography and echocardiography. *J Nucl Cardiol* 2000;7:301-11.
  15. Nichols K, Amis J, dePuey G, Mieres J, Malhotra S, Rozanski A. Relationship of gated SPECT ventricular function parameters to angiographic measurements. *J Nucl Cardiol* 1998;5:295-303.
  16. Cwajg E, Cwajg J, He ZX, Hwang WS, Keng F, Nagueh SF *et al*. Gated myocardial perfusion tomography for the assessment of left ventricular function and volumes: comparison with echocardiography. *J Nucl Med* 1999;40:1857-65.
  17. Nichols K, Lefkowitz D, Faber T, Folks R, Cooke D, Garcia EV *et al*. Echocardiographic validation of gated SPECT ventricular function measurements. *J Nucl Med* 2000;41:1308-14.
  18. Vourvouri EC, Poldermans D, Bax JJ, Sianos G, Sozzi FB, Schinkel AF *et al*. Evaluation of left ventricular function and volumes in patients with ischaemic cardiomyopathy: gated single-photon emission computed tomography versus two-dimensional echocardiography. *Eur J Nucl Med* 2001;28:1610-5.
  19. Yoshika J, Hasegawa S, Yamaguchi H, Tokita N, Paul AK, Xiuli M *et al*. Left ventricular volumes and ejection fraction calculated from quantitative electrocardiogram-gated 99m Tc-tetrofosmin myocardial SPECT. *J Nucl Med* 1999;40:1693-8.
  20. Stollfuss JC, Haas F, Matsunari I, Neverve J, Nekolla S, Schneider-Eicke J *et al*. Regional myocardial wall thickening and global ejection fraction in patients with low angiographic left ventricular ejection fraction assessed by visual and quantitative resting ECG-gated 99m Tetrofosmin single-photon emission tomography and magnetic resonance imaging. *Eur J Nucl Med* 1998;25:522-30.
  21. Vaduganathan P, He ZX, Vick W, Mahmarian JJ, Verani MS. Evaluation of left ventricular wall motion, volumes and ejection fraction by gated myocardial tomography with technetium 99m-labeled tetrofosmin: a comparison with cine magnetic resonance imaging. *J Nucl Cardiol* 1999;6:3-10.
  22. Bax JJ, Lamb H, Dibbets P, Pelikan H, Boersma E, Viergever EP *et al*. Comparison of gated single-photon emission computed tomography with magnetic resonance imaging for evaluation of left ventricular function in ischemic cardiomyopathy. *Am J Cardiol* 2000;86:1299-305.
  23. Tadamura E, Kudoh T, Motooka M, Inubushi M, Shirakawa S, Hattori N *et al*. Assessment of regional and global left ventricular function by reinjection Tl-201 and rest Tc-99m sestamibi ECG-gated SPECT. Comparison with three-dimensional magnetic resonance imaging. *J Am Coll Cardiol* 1999;33:991-7.
  24. Germano G, Kiat H, Kavanagh PB, Moriel M, Mazzanti M, Su HT *et al*. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. *J Nucl Med* 1995;36:2138-47.
  25. Gunning MG, Anagnostopoulos C, Davies G, Format SM, Ell PJ, Underwood SR. Gated technetium-99m-tetrofosmin SPECT and cine MRI to assess left ventricular contraction. *J Nucl Med* 1997;38:438-42.
  26. Verberne HJ, Dijkgraaf MG, Somsen GA, van Eck-Smit BL. Stress-related variations in left ventricular function as assessed with gated myocardial perfusion SPECT. *J Nucl Cardiol* 2003;10:456-63.
  27. De Winter O, De Bondt P, Van De Wiele C, De Backer G, Dierckx RA, De Sutter J. Day-to-day variability of global left ventricular functional and perfusional measurements by quantitative gated SPECT using Tc-99m tetrofosmin in patients with heart failure due to coronary artery disease. *J Nucl Cardiol* 2004;11:47-52.
  28. Vallejo E, Chaya H, Plancarte G, Victoria D, Bialostozky D. Variability of serial same-day left ventricular ejection fraction using quantitative gated SPECT. *J Nucl Cardiol* 2002;9:377-84.
  29. Nakajima K, Higuchi T, Taki J, Kawano M, Tonami N. Accuracy of ventricular volume and ejection fraction measured by gated myocardial SPECT: comparison of 4 software programs. *J Nucl Med* 2001;42:1571-8.
  30. Nichols K, Santana CA, Folks R, Krawczynska E, Cooke CD, Faber TL *et al*. Comparison between ECTb and QGS for assessment of left ventricular function from gated myocardial perfusion SPECT. *J Nucl Cardiol* 2002;9:285-93.
  31. Rozanski A, Nichols K, Yao SS, Malholtra S, Cohen R, DePuey EG. Development and application of normal limits for left ventricular ejection fraction and volume measurements from 99mTc-sestamibi myocardial perfusion gated SPECT. *J Nucl Med* 2000;41:1445-50.
  32. Ababneh AA, Sciacca RR, Kim B, Bergmann SR. Normal limits for left ventricular ejection fraction and volumes estimated with gated myocardial perfusion imaging in patients with normal exercise test results: influence of tracer, gender, and acquisition camera. *J Nucl Cardiol* 2000;7:661-8.
  33. Chua T, Kiat H, Germano G, Maurer G, van Train K, Friedman J *et al*. Gated technetium-99m sestamibi for simultaneous assessment of stress myocardial perfusion, postexercise regional ventricular function and myocardial viability. Correlation with echocardiography and rest thallium-201 scintigraphy. *J Am Coll Cardiol* 1994;23:1107-14.
  34. Nichols K, DePuey EG, Krasnow N, Lefkowitz D, Rozanski A. Reliability of enhanced gated SPECT in assessing wall motion of severely hypoperfused myocardium: echocardiographic validation. *J Nucl Cardiol* 1998;5:387-94.
  35. Leoncini M, Marcucci G, Sciagrà R, Frascarelli F, Traini AM, Mondanelli D *et al*. Nitrate-enhanced gated Tc-99m Sestamibi SPECT for evaluating regional wall motion at baseline and during low dose dobutamine infusion in patients with chronic coronary artery disease and left ventricular dysfunction. Comparison with two-dimensional echocardiography. *J Nucl Cardiol* 2000;7:426-31.
  36. DePuey EG, Rozanski A. Using gated technetium-99m-sestamibi SPECT to characterize fixed myocardial defects as infarct or artifact. *J Nucl Med* 1995;36:952-5.
  37. Smanio PE, Watson DD, Segalla DL, Vinson EL, Smith WH, Beller

- GA. Value of gating of technetium-99m sestamibi single-photon emission computed tomographic imaging. *J Am Coll Cardiol* 1997;30:1687-92.
38. Links JM, DePuey EG, Taillefer R, Becker LC. Attenuation correction and gating synergistically improve the diagnostic accuracy of myocardial perfusion SPECT. *J Nucl Cardiol* 2002;9:183-7.
  39. Danias PG, Ahlberg AW, Travin MI, Mahr NC, Abreu JE, Marini D *et al*. Visual assessment of left ventricular perfusion and function with electrocardiography-gated SPECT has high intraobserver and interobserver reproducibility among experienced nuclear cardiologists and cardiology trainees. *J Nucl Cardiol* 2002;9:263-70.
  40. Fleischmann S, Koepfli P, Namdar M, Wyss CA, Jenni R, Kaufmann PA. Gated 99mTc-Tetrofosmin SPECT for discriminating infarct from artifact in fixed myocardial perfusion defects. *J Nucl Med* 2004;45:754-75.
  41. Santana CA, Garcia EV, Vansant JP, Krawczynska EG, Folks RD, Cooke CD *et al*. Gated stress-only 99mTc myocardial perfusion SPECT imaging accurately assesses coronary artery disease. *Nucl Med Commun* 2003;24:241-9.
  42. Mieres JH, Shaw LJ, Hendel RC, Miller DD, Bonow RO, Berman DS *et al*. American Society of Nuclear Cardiology Task Force on Women and Heart Disease Writing Group on Perfusion Imaging in Women. A report of the American Society of Nuclear Cardiology Task Force on Women and Heart Disease (Writing Group on Perfusion Imaging in Women). *J Nucl Cardiol* 2003;10:95-101.
  43. Johnson LL, Verdesca SA, Aude WY, Xavier RC, Nott LT, Campanella MW *et al*. Postischemic stunning can affect left ventricular ejection fraction and regional wall motion on post-stress gated sestamibi tomograms. *J Am Coll Cardiol* 1997;30:1641-8.
  44. Mazzanti M, Germano G, Kiat H, Kavanagh PB, Alexanderson E, Friedman JD *et al*. Identification of severe and extensive coronary artery disease by automatic measurement of transient ischemic dilatation of the left ventricle in dual-isotope myocardial perfusion SPECT. *J Am Coll Cardiol* 1996;27:1612-20.
  45. Sharir T, Bacher-Stier C, Dhar S, Lewin HC, Miranda R, Friedman JD *et al*. Identification of severe and extensive coronary artery disease by postexercise regional wall motion abnormalities in Tc-99m sestamibi gated single-photon emission computed tomography. *Am J Cardiol* 2000;86:1171-5.
  46. Emmett L, Iwanochko RM, Freeman MR, Barolet A, Lee DS, Husain M. Reversible regional wall motion abnormalities on exercise technetium-99m-gated cardiac single photon emission computed tomography predict high-grade angiographic stenoses. *J Am Coll Cardiol* 2002;39:991-8.
  47. Yamagishi H, Shirai N, Yoshiyama M, Teragaki M, Akioka K, Takeuchi K *et al*. Incremental value of left ventricular ejection fraction for detection of multivessel coronary artery disease in exercise (201)Tl gated myocardial perfusion imaging. *J Nucl Med* 2002;43:131-9.
  48. Shirai N, Yamagishi H, Yoshiyama M, Teragaki M, Akioka K, Takeuchi K *et al*. Incremental value of assessment of regional wall motion for detection of multivessel coronary artery disease in exercise (201)Tl gated myocardial perfusion imaging. *J Nucl Med* 2002;43:443-50.
  49. Lima RS, Watson DD, Goode AR, Siadaty MS, Ragosta M, Beller GA *et al*. Incremental value of combined perfusion and function over perfusion alone by gated SPECT myocardial perfusion imaging for detection of severe three-vessel coronary artery disease. *J Am Coll Cardiol* 2003;42:64-70.
  50. Sugihara H, Tamaki N, Nozawa M, Ohmura T, Inamoto Y, Taniguchi Y *et al*. Septal perfusion and wall thickening in patients with left bundle branch block assessed by technetium-99m-sestamibi gated tomography. *J Nucl Med* 1997;38:545-7.
  51. Kaul S, Senior R, Firschke C, Wang XQ, Lindner J, Villanueva FS *et al*. Incremental value of cardiac imaging in patients presenting to the emergency department with chest pain and without ST-segment elevation: a multicenter study. *Am Heart J* 2004;148:129-36.
  52. The Multicenter Postinfarction Research Group: risk stratification and survival after myocardial infarction. *N Engl J Med* 1983;310:331-6.
  53. Candell-Riera J, Llevadot J, Santana C, Castell J, Aguade S, Armadans L *et al*. Prognostic assessment of uncomplicated first myocardial infarction by exercise echocardiography and Tc-99m tetrofosmin gated SPECT. *J Nucl Cardiol* 2001;8:122-8.
  54. Sharir T, Germano G, Kavanagh PB, Lai S, Cohen I, Lewin HC *et al*. Incremental prognostic value of post-stress left ventricular ejection fraction and volume by gated myocardial perfusion single photon emission computed tomography. *Circulation* 1999;100:1035-42.
  55. Sharir T, Germano G, Kang X, Lewin HC, Miranda R, Cohen I *et al*. Prediction of myocardial infarction versus cardiac death by gated myocardial perfusion SPECT: risk stratification by the amount of stress-induced ischemia and the poststress ejection fraction. *J Nucl Med* 2001;42:831-7.
  56. Kroll D, Farah W, McKendall GR, Reinert SE, Johnson LL. Prognostic value of stress-gated Tc-99m sestamibi SPECT after acute myocardial infarction. *Am J Cardiol* 2001;87:381-6.
  57. Hashimoto J, Suzuki T, Nakahara T, Kosuda S, Kubo A. Preoperative risk stratification using stress myocardial perfusion scintigraphy with electrocardiographic gating. *J Nucl Med* 2003;44:385-90.
  58. Spinelli L, Petretta M, Acampa W, He W, Petretta A, Bonaduce D *et al*. Prognostic value of combined assessment of regional left ventricular function and myocardial perfusion by dobutamine and rest gated SPECT in patients with uncomplicated acute myocardial infarction. *J Nucl Med* 2003;44:1023-9.
  59. Travin MI, Heller GV, Johnson LL, Katten D, Ahlberg AW, Isasi CR *et al*. The prognostic value of ECG-gated SPECT imaging in patients undergoing stress Tc-99m sestamibi myocardial perfusion imaging. *J Nucl Cardiol* 2004;11:253-62.
  60. Thomas GS, Miyamoto MI, Morello AP 3rd, Majmundar H, Thomas JJ, Sampson CH *et al*. Technetium 99m sestamibi myocardial perfusion imaging predicts clinical outcome in the community outpatient setting. The Nuclear Utility in the Community (NUC) study. *J Am Coll Cardiol* 2004;43:213-23.
  61. Levine MG, McGill CC, Ahlberg AW, White MP, Giri S, Shareef B *et al*. Functional assessment with electrocardiographic gated single-photon emission computed tomography improves the ability of technetium-99m sestamibi myocardial perfusion imaging to predict myocardial viability in patients undergoing revascularization. *Am J Cardiol* 1999;83:1-5.
  62. Duncan BH, Ahlberg AW, Levine MG, McGill CC, Mann A, White MP *et al*. Comparison of electrocardiographic-gated technetium-99m sestamibi single-photon emission computed tomographic imaging and rest-redistribution thallium-201 in the prediction of myocardial viability. *Am J Cardiol* 2000;85:680-4.
  63. Mabuchi M, Kubo N, Morita K, Makino Y, Matsui Y, Murashita T *et al*. Prediction of functional recovery after coronary bypass surgery using quantitative gated myocardial perfusion SPECT. *Nucl Med Commun* 2003;24:625-31.
  64. Kang WJ, Lee DS, Paeng JC, Kim KB, Chung JK, Lee MC. Prognostic value of rest (201)Tl-dipyridamole stress (99m)Tc-sestamibi gated SPECT for predicting patient-based clinical outcomes after bypass surgery in patients with ischemic left ventricular dysfunction. *J Nucl Med* 2003;44:1735-40.
  65. Cuocolo A, Acampa W, Nicolai E, Pace L, Petretta M, Salvatore M. Quantitative thallium-201 and technetium-99m sestamibi tomography at rest in detection of myocardial viability in patients with chronic ischemic left ventricular dysfunction. *J Nucl Cardiol* 2000;7:8-15.
  66. Leoncini M, Marcucci, Scigrà R, Frascarelli F, Bellandi F, Gallopin M *et al*. Usefulness of distinct activity thresholds according to baseline regional asynergy for predicting functional recovery in patients with chronic coronary artery disease and left ventricular dysfunction. A study with nitrate-enhanced Sestamibi gated SPECT. *J Nucl Cardiol* 2001;8:555-60.
  67. Qureshi U, Nagueh SF, Afridi I, Vaduganathan P, Blaustein A, Verani MS *et al*. Dobutamine echocardiography and quantitative rest-redistribution 201Tl tomography in myocardial hibernation.

- Relation of contractile reserve to 201Tl uptake and comparative prediction of recovery of function. *Circulation* 1997;95:626-35.
68. Everaert H, Vanhove C, Franken PR. Effects of low-dose dobutamine on left ventricular function in normal subjects as assessed by gated single-photon emission tomography myocardial perfusion studies. *Eur J Nucl Med* 1999;26:1298-303.
  69. Everaert H, Vanhove C, Franken PR. Low-dose dobutamine gated single-photon emission tomography: comparison with stress echocardiography. *Eur J Nucl Med* 2000;27:413-8.
  70. Yoshinaga K, Morita K, Yamada S, Komuro K, Katoh C, Ito Y *et al.* Low-dose dobutamine electrocardiograph-gated myocardial SPECT for identifying viable myocardium: comparison with dobutamine stress echocardiography and PET. *J Nucl Med* 2001;42:838-44.
  71. Yamagishi H, Akioka K, Hirata K, Sakanoue Y, Toda I, Yoshiyama M *et al.* Dobutamine stress electrocardiography-gated Tc-99m tetrofosmin SPECT for detection of viable but dysfunctional myocardium. *J Nucl Cardiol* 2001;8:58-67.
  72. Leoncini M, Marcucci G, Sciagrà R, Frascarelli F, Simonetti I, Bini L *et al.* Prediction of functional recovery in patients with chronic coronary artery disease and left ventricular dysfunction combining the evaluation of myocardial perfusion and contractile reserve using nitrate-enhanced technetium-99m Sestamibi gated single-photon emission computed tomography and dobutamine stress. *Am J Cardiol* 2001;87:1346-50.
  73. Zafir N, Arditi A, Ben-Gal T, Solodky A, Hassid Y, Sulkes J *et al.* Additive value of low-dose dobutamine to technetium-99m sestamibi-gated single-photon emission computed tomography for prediction of wall motion improvement in patients undergoing coronary artery bypass graft. *Clin Cardiol* 2003;26:530-5.
  74. Simoes MV, de Almeida-Filho OC, Pintya AO, de Figueiredo AB, Antloga CM, Salis FV *et al.* Prediction of left ventricular wall motion recovery after acute myocardial infarction by Tl-201 gated SPECT: incremental value of integrated contractile reserve assessment. *J Nucl Cardiol* 2002;9:294-303.
  75. Heiba SI, Abdel-Dayem HM, Gould R, Bernaski E, Morlote M, El-Zeftawy H *et al.* Value of low-dose dobutamine addition to routine dual isotope gated SPECT myocardial imaging in patients with healed myocardial infarction or abnormal wall thickening by echocardiogram. *Am J Cardiol* 2004;93:300-6.
  76. Chin BB, Esposito G, Kraitchman DL. Myocardial contractile reserve and perfusion defect severity with rest and stress dobutamine (99m)Tc-sestamibi SPECT in canine stunning and subendocardial infarction. *J Nucl Med* 2002;43:540-50.
  77. Sciagrà R, Leoncini M, Mennuti A, Dabizzi RP, Pupi A. Classification of ischemic dysfunctional myocardium combining perfusion quantification and contractile reserve evaluation using nitrate-enhanced gated single photon emission computed tomography with dobutamine test. *Q J Nucl Med* 2004;48:4-11.
  78. Marwick TH. The viable myocardium: epidemiology, detection, and clinical implications. *Lancet* 1998;351:815-9.
  79. Bax JJ, Poldermans D, Elhendy A, Cornel JH, Boersma E, Rambaldi R *et al.* Improvement in left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine echocardiography. *J Am Coll Cardiol* 1999;34:163-9.
  80. Sciagrà R, Leoncini M, Cannizzaro G, Marcucci G, Pupi A, Bisi G. Predicting revascularization outcome in patients with coronary artery disease and left ventricular dysfunction (data from the SEMINATOR study). *Am J Cardiol* 2002;89:1369-73.
  81. Leoncini M, Sciagrà R, Maioli M, Bellandi F, Marcucci G, Sestini S *et al.* Usefulness of dobutamine Tc-99m sestamibi-gated single-photon emission computed tomography for prediction of left ventricular ejection fraction outcome after coronary revascularization for ischemic cardiomyopathy. *Am J Cardiol* 2002;89:817-21.
  82. Kasama S, Toyama T, Kumakura H, Takayama Y, Ichikawa S, Suzuki T *et al.* Myocardial contractile reserve determined by dobutamine stress Tc-99m tetrofosmin quantitative gated SPECT predicts late spontaneous improvement in cardiac function in patients with recent-onset dilated cardiomyopathy. *J Nucl Cardiol* 2003;10:607-14.
  83. Fukuchi K, Yasumura Y, Kiso K, Hayashida K, Miyatake K, Ishida Y. Gated myocardial SPECT to predict response to beta-blocker therapy in patients with idiopathic dilated cardiomyopathy. *J Nucl Med* 2004;45:527-31.
  84. Sciagrà R, Giaccardi M, Porciani MC, Colella A, Michelucci A, Pieragnoli P *et al.* Myocardial perfusion imaging using gated SPECT in heart failure patients undergoing cardiac resynchronization therapy. *J Nucl Med* 2004;45:164-8.
  85. Tsurugaya H, Tada H, Toyama T, Naito S, Adachi H, Seki RT *et al.* Usefulness of quantitative gated single-photon emission computed tomography to evaluate ventricular synchrony in patients receiving biventricular pacing. *Am J Cardiol* 2004;94:127-30.
  86. Fujii H, Ohashi H, Tsutsumi Y, Kawai T, Iino K, Onaka M. Radionuclide study of mid-term left ventricular function after endoventricular circular patch plasty. *Eur J Cardiothorac Surg* 2004;26:125-8.
  87. Schäfers M, Stypmann JW, Wilhelm MJ, Stegger L, Kies P, Hermann S *et al.* Functional changes after partial left ventriculectomy and mitral valve repair assessed by gated perfusion SPECT. *J Nucl Med* 2004;45:1605-10.
  88. Zellweger MJ, Tabacek G, Zutter AW, Weinbacher M, Cron TA, Muller-Brand J *et al.* Evidence for left ventricular remodeling after percutaneous coronary intervention: effect of percutaneous coronary intervention on left ventricular ejection fraction and volumes. *Int J Cardiol* 2004;96:197-201.
  89. Giubbini R, Rossini P, Bertagna F, Bosio G, Paghera B, Pizzocaro C *et al.* Value of gated SPECT in the analysis of regional wall motion of the interventricular septum after coronary artery bypass grafting. *Eur J Nucl Med Mol Imaging* 2004;31:1371-7.
  90. Kasai T, Depuey EG, Shah AA. Decreased septal wall thickening in patients with left bundle branch block. *J Nucl Cardiol* 2004;11:32-7.
  91. Leoncini M, Bellandi F, Sciagrà R, Maioli M, Toso A, Coppola A *et al.* Gated SPECT evaluation of the relationship between admission troponin I, myocardial salvage, and functional recovery in acute myocardial infarction treated by abciximab and early primary angioplasty. *J Nucl Med* 2004;45:739-44.
  92. Leoncini M, Bellandi F, Sciagrà R, Maioli M, Toso A, Sestini S *et al.* Use of (99m)Tc-sestamibi gated SPECT to assess the influence of anterograde flow before primary coronary angioplasty on tissue salvage and functional recovery in acute myocardial infarction. *Eur J Nucl Med Mol Imaging* 2004;31:1378-85.