The Value and Throughput of Rest Thallium-201/Stress Technetium -99m Sestamibi Dual-Isotope Myocardial SPECT

Çift İzotop Miyokardiyal SPECT İstirahat Talyum-201/Stres Teknesyum –99m Sestamibi Değeri ve İşlem Hacmi

Berna Okudan, MD, Thomas C. Smitherman, MD*

Department of Nuclear Medicine, Ankara Numune Research and Training Hospital, Ankara, *Turkiye*
Department of Nuclear Cardiology, University of Pittsburgh Medical School, *Pittsburgh, USA

Abstract

Myocardial perfusion scintigraphy is an established method in cardiology for the diagnosis and evaluation of coronary artery disease (CAD). Thallium-201 and Tc-99m sestamibi myocardial perfusion imaging has been widely accepted as non-invasive diagnostic procedure for detection of CAD, risk stratification and myocardial viability assessment. But, standard Tl-201 redistribution and same day or 2-day rest/stress Tc-99m sestamibi protocols are time-consuming. Hence, the dual isotope rest thallium-201/stress technetium-99m sestamibi gated single-photon emission tomography protocol has gained increasing popularity for these applications. Combining the use of thallium-201 with technetium-99m agents permits optimal image resolution and simultaneous assessment of viability. Dual-isotope imaging may be separate or simultaneous acquisition set-up. The more rapid completion of these studies is appreciated as an advantage by patients, technologists, interpreting and referring physicians, nurses and hospital management. Simultaneous imaging has the potential advantages of precise pixel registration and artifacts, if present, are identical in both thallium and sestamibi, and require only one set of imaging. Also, there are some disadvantages of spillover of activity from the Tc-99m to the Tl-201 window. Fortunately, despite this problem it can be overcome. Separate acquisition dual isotope also has some disadvantages. Difference in defect resolution in attenuation and scatter between T-201 and Tc-99m sestamibi potentially results in interpretation problems. But, studies about cost-effectiveness of dual isotope imaging showed that some selective elimination of the rest studies may decrease the cost of the nuclear procedures and should be considered in the current care health system. *(Anadolu Kardiyol Derg 2004; 4: 161-8)*
Key words: Dual isotope myocardial imaging-Tl-201-Tc-99m MIBI myocardial SPECT, Rest Tl-201/Stress Tc-99m MIBI

Özet

Miyokard perfüzyon sintigrafisi, koroner arter hastalığının (KAH) tanı ve değerlendirilmesinde, kardiyolojide, geniş kabul görmüş bir yöntemdir. Talyum-201 ve Tc-99m sestamibi miyokard perfüzyon görüntüleme, KAH'ın saptanması, risk belirlenmesi ve miyokard canlılığının saptanmasında, noninvazif bir tanı yöntemi olarak kullanılmaktadır. Ancak, standart Tl-201 redistribüsyon ve aynı gün veya 2 gün istirahat/stres sestamibi protokolu uzun ve zaman alıcıdır. Bu yüzden, dual izotop istirahat talyum-201/stres teknesyum-99m sestamibi "gated single-photon emission tomography" protokolü giderek artan bir popularite kazanmaktadır. Talyum-201 ve teknesyum 99-m'in birlikte kullanılması, optimal görüntüleme rezolüsyonu yanısıra, miyokard canlılığının aynı anda değerlendirilebilmesini sağlar. Dual-izotop görüntüleme, ayrı veya simultane akuzisyon protokolünde olabilir. Bu protokollerin daha hızlı olması, hasta, teknisyen, kardiyoloji nükleer tıp uzmanı, hemşire ve hastane yönetimi tarafından memnuniyetle karşılanmaktadır. Simultane görüntülemede, hem Tl-201 hem de sestamibi, tek bir akuzisyon işlemi ile görüntülenir ve hareket artefaktının ekarte edilmesini sağlar. Teknesyum-99m'un, Tl-201 enerji penceresi üzerindeki saçılım dezavantajı da, teknik olarak düzeltilebilmektedir. Bunun yanısıra, ayrı akuzisyon dual izotop protokolu da bazı dezavantajlara sahiptir. Talyum-201 and Tc-99m sestamibi arasındaki atenuasyon, saçılım ve defekt rezolüsyonu farkı, yorumlama problemlerine neden olablir. Dual izotop görüntüleme maliyet çalışmalarında, bazı seçilmiş hastalarda istirahat görüntülemenin elimine edilebilmesi, maliyeti azaltabilir. Bu özellik, sağlık sisteminde, maliyet azaltılması çalışmalarında göz önünde bulundurulmalıdır. *(Anadolu Kardiyol Derg 2004; 4: 161-8)*
Anahtar Kelimeler: Dual izotop miyokard görüntüleme, Tl-201-Tc-99m MIBI miyokardial SPECT, İstirahat Tl-201/Stres Tc-99m MIBI

Introduction

Myocardial perfusion scintigraphy is an established method in cardiology for the diagnosis and evaluation of coronary artery disease (CAD). Since its introduction, myocardial perfusion imaging has advanced significantly. Significant advances in the interpretation of test results were resulted from the development of objective, quantitative methods for analysis and display of myocardial perfusion images. This article provides an overview of technical and clinical aspects of Tl-201 myocardial SPECT, Tc-99m sestamibi

Address for correspondence: Berna Okudan, MD, P.K 104, Isparta/Türkiye
Cell-phone: 90 532 364 9024, Fax: 90 246 237 02 40, E-mail: brokudan@hotmail.com

imaging and rest Tl-201/sress Tc-99m sestamibi dual-isotope myocardial perfusion scintigraphy.

Myocardial perfusion scintigraphy with Thallium-201

Numerous clinical studies have validated the use of myocardial perfusion imaging with Tl-201 for detection and evaluation of coronary artery disease (CAD). In addition, Tl-201 scintigraphy plays a valuable role in the risk stratification of patients with suspected or known CAD to determine prognosis.

Thallium is a metallic element in group IIIA of the periodic table, with biologic properties similar but not identical to those of potassium. Thallium 201 is a cyclotron product and decays by electron capture to mercury 201; emitting mercury x-rays of 69 to 83 keV (94.4 percent abundant) and thallium gamma rays of 167 keV (10 percent abundant) and 135 keV (3 percent abundant). To improve the sensitivity of Tl-201 imaging, a 20 percent of energy window centered on the 70-71 keV peak is used to reduce the scatter associated with lower energy photons [1-3]. A second 20 percent of energy window centered on 167 keV is also used on cameras that can acquire images simultaneously at different energies. The physical half-life of Tl-201 is 73 h. For Tl-201, the usual intravenously administered activity for clinical imaging in adults is approximately 2.0 to 3.0 mCi (74 to 111 MBq). Estimated total body radiation exposure dose for Tl-201 is 0.72 rad/ 3mCi (1, 2). Firstly, transport of thallium across the cellular membrane presumed to be the sodium-potassium ATP'ase pump and this theory has been confirmed (3).

Since its introduction into clinical use in 1970's, Tl-201 myocardial perfusion imaging has been widely accepted as non-invasive diagnostic procedure for detection of CAD, risk stratification and myocardial viability assessment (4-6). Conventionally, Tl-201 imaging is performed in conjunction with physical exercise or pharmacological stress and redistribution. Following injection at peak stress, Tl-201 is taken up by myocardium in proportion to regional blood flow. After the rapid initial uptake of Tl-201 by the normal myocardium, there begins a slower washout process of thallium from the myocardial intracellular compartment back into the vascular compartment. At the same time, there is a representation of additional blood-borne thallium to the myocardial cells for reextraction provided by the large pool of the injected radioisotope that was initially hold by other organs of the body.

This aforementioned simultaneous process of thallium washout and re-extraction across the cell membrane provide a mean for a dynamic equilibrium between intracellular and extracellular thallium, which defines the phenomenon known as "redistribution". Unlike the re-extraction of Tl-201 by the myocardium from the circulating blood pool, the washout component of redistribution is strongly dependent on coronary perfusion, with ischemic areas demonstrating much slower washout then normal regions. Also, heart rates and gender are another factors affecting on thallium washout (3, 7).

Protocols

A number of modifications in Tl-201 imaging protocol have been suggested to overcome the Tl-201 imaging shortcomings. These protocols are mainly Thallium stress-delayed, Thallium rest-redistribution and Thallium reinjection imaging protocols. Redistribution images are obtained at 3 to 4 hours after the initial study. Repeat imaging at 24 hours after rest injection and also reinjection may further enhance the detection of redistribution in severe defects (8, 9).

Patients should remain NPO (non peroral) for 4 to 6 hours before the exercise test. This allows to decrease splanchnic blood flow and; therefore, diminish thallium uptake in the bowel and liver. Calcium channel blockers and b blockers should be discontinued, if possible, for a sufficient length of time before the examination to avoid any interference with obtaining an adequate stress by limiting heart rate response. Long-acting nitrates should also be withheld on the day of testing. The relatively low energy of the decay photons and the long half-life of Tl-201 limit the use of Tl-201 to assess functional myocardial parameters such as ejection fraction, wall motion, and wall thickness. Various modifications, such as increasing acquisition times or maximizing the administered dose have been used to improve Tl-201 myocardial perfusion images. Though some investigators have used these modifications to acquire clinically useful gated SPECT images using Tl-201, it has not been adopted widely because of long acquisition times and the continued perception of poor image quality (10-12).

Myocardial perfusion scintigraphy with Technetium-99m sestamibi

New myocardial perfusion agents labeled with Tc-99m have been developed to circumvent the radiophysical limitations of Tl-201 (13, 14). Myocardial perfusion agents labeled with Tc-99m isonitriles, particularly Tc-99m sestamibi has some advantages over Tl-201, including on-site availability and higher-quality images. Tc-99m methoxyisobutyl isonitrile (Tc-

99m sestamibi) is a member of Tc-99m isonitrile group that exhibited the best biological properties for clinical application (15). In comparison with other compounds in this group, Tc-99m sestamibi is positively charged particle and predominantly is bound to mitochondria. Its transport across the cell membrane is not dependent on ATP due to its high lipophilicity. The initial myocardial uptake is directly related to myocardial blood flow but with a "decrease" in uptake occurring at high flow rates (16). After IV injection, initial concentration of sestamibi is the highest in the heart and liver. Tc-99m labeled methoxyisobutyl isonitrile (Technetium-99m sestamibi) initially distributes in the myocardium proportional to flow, similar to thallium-201 (16, 17). This trace reportedly does not demonstrate significant delayed redistribution during low flow and shows minimal delayed redistribution after initial IV administration but the lack of substantial redistribution necessitates separate injections of the tracer during stress and at rest (16). But after transient ischemia, delayed redistribution clearly occurs (18, 19). Therefore, to assess stress defect reversibility with Tc-99m sestamibi, a two-injection protocol is required.

Protocols

Diagnostic evaluation using post-stress and subsequent delayed resting imaging requires two separate injections, one at peak stress and a later one at rest. Ideally stress and rest imaging with Tc-99m agents should be performed on two separate days (2-day imaging protocol). In this protocol, stress and rest injections, each with 15-30 mCi, may be performed on two separate days. However, because of logistical reasons, both stress and rest studies are often performed on the same day (1-day imaging protocol). One protocol employs a resting injection of 8-10 mCi, followed by an injection of 25-30- mCi of Tc-99m-sestamibi at peak exercise. There was exact concordance in the detection of reversible and fixed defects with these two same-day, split-dose protocols. A delay of 2 to 3 hours is required between the two injections to allow time for the adequate clearance of the firstly injected radiotracer from the hepatobiliary and gastrointestinal system. For the sestamibi, the minimum delay time of 60 to 90 minutes for rest, 15 to 20 minutes for exercise, 45 to 60 minutes for pharmacological stress following radiopharmaceutical injection are optimal (8, 9). A two-day protocol is optimal from the standpoint of defect contrast because it avoids contamination from one image acquisition to the next and it also provides optimal defect contrast with minimal background activity. An unequivocally normal stress Tc-99m sestamibi study on Day 1 may eliminate the need to perform the rest study on the second day. This circumstance can decrease effectively diagnostic costs.

Dual-isotope imaging

Stress radionuclide myocardial imaging was used as modality to evaluate patients with known or suspected coronary artery disease. The dual isotope rest thallium-201/stress technetium-99m sestamibi gated single-photon emission tomography protocol has gained increasing popularity for these applications.

By combining the use of thallium-201, the optimal radioisotope for assessment of viability, with technetium-99m labeled agents, maximization of clinical information can be achieved. These radionuclide agents permit optimal image resolution and simultaneous assessment of viability information (20). Dual-isotope imaging may be separate or simultaneous acquisition set-up.

Rest Thallium-201/ stress Technetium-99m sestamibi dual-isotope imaging

Protocol

In dual-isotope imaging, 1-day, rest imaging using Tl-201 (2.5 to 3.5 mCi) [92.5 to 129,5 MBq] is first obtained within 10 minutes after injection of isotope, followed shortly by a stress study with Tc-99m sestamibi (25 mCi)(925 MBq). Tc-99m sestamibi SPECT is begun 15-30 minutes after isotope injection (21).

Potential advantages and disadvantages of separate acquisition rest Tl-201/stress sestamibi dual-Isotope

As early of 1994, separate acquisition rest Tl-201 and stress sestamibi dual-isotope SPECT is used (21). This approach is highly efficient. In comparison to rest/stress sestamibi same-day protocols, separate acquisition dual-isotope eliminates the 1-hour waiting period between rest-sestamibi injection and SPECT. It eliminates the delay between SPECT acquisitions required by stress redistribution Tl-201 and suggested for same day rest/stress sestamibi studies. Therefore, an entire (rest and stress) study can be completed in approximately 2 hours (22). However, Weinman et al. demonstrated that the average duration of procedure was 194 ± 39 min (23). Also, patients can be brought back for late imaging the next day, or a rest-redistribution study can be completed before the sestamibi injection and provides the detection of an additional 8 percent to 15 percent of reversible segments, which would go undetected by

rest scintigraphy alone (24). But, in the separate acquisition dual-isotope SPECT procedure is described to minimize contrast reduction. Due to the low abundance of high-energy Tl-201 photons, which scatter into the Tc-99m window, the contribution of Tl-201 scatter on the Tc-99m sestamibi images at these doses employed is only 2.9 percent (25). Loutfi et al. reported that for detecting myocardial ischemia or viability, the dual-tracer Tl-MIBI acquisition technique appears superior to the single tracer Tc-99m sestamibi protocol (26). They also indicated that excessive liver uptake on the Tc-99m sestamibi was resolved by using liver shielding-electronic masking of liver uptake and scaling images to the highest count within the myocardium. Fukuoka et al. demonstrated that exercise Tl-201/rest Tc-99m tetrofosmin dual-isotope SPECT with scatter correction could identify coronary artery disease with excellent diagnostic accuracy. Myocardial uptake of rest Tc-99m tetrofosmin image in dual-isotope SPECT is comparable with that of reinjection Tl-201 imaging for assessing myocardial viability. Moreover, additional gated SPECT provides useful information about left ventricle function similar to that of left ventriculography (LVG) when therapeutic strategies are being considered for patients with ischemic heart disease. This sequential protocol for evaluating myocardial ischemia and function can be completed approximately in 2 hours (27). Groutars et al. suggested that Tl-201 cross-talk in the Tc-99m window may be low and functionally and clinically unimportant (28). Hachamovitch et al. studied exercise dual isotope SPECT for risk stratification in patients with normal resting ECGs. Stress SPECT yields incremental prognostic value and enhanced risk stratification in patients with normal resting ECGs in a cost-effective manner (29). Paeng et al. studied an advantage of dual isotope SPECT. Paeng et al. examined that to optimize the use of thallium-201 rest-redistribution study in Tl-201/technetium 99m sestamibi dual-isotope SPECT, the predictability of Tl-201 rest-redistribution for viable myocardium. They suggested that dysfunctional myocardium with persistent perfusion decrease should be assessed by Tl-201 redistribution SPECT and it is possible to discriminate hibernating and stunned myocardium (30). The other advantages of dual isotope myocardial SPECT is that elimination of the rest study in patients with normal stress images. This application rarely alters interpretation. Rest studies are the most useful in images with abnormal or equivocal stress images. Such selective elimination of the rest studies may decrease the cost of the nuclear procedures and should be considered in the current managed care health system (31).

Simultaneous dual-isotope myocardial imaging protocols

Simultaneous dual-isotope imaging allows that rest Tl-201/stress Tc-99m sestamibi imaging can be performed together. In the simultaneous dual-isotope study thallium 201 SPECT imaging is not performed immediately following Tl-201 injection at rest; and, Tc-99m sestamibi was injected to the patient at the peak of stress. Approximately 15 minutes later, dual-isotope myocardial perfusion SPECT is performed. The entire procedure is completed in less than 1 hour, with a requirement of one SPECT acquisition of approximately 20 minutes duration. Generally, simultaneous acquisition would have many advantages in comparison with the conventional stress and rest protocols it halves camera utilization time (25, 32, 33).

Potential advantages and disadvantages of simultaneous acquisition rest Tl-201/stress sestamibi dual-isotope

This protocol could improve patient throughput and scheduling since only one SPECT acquisition is employed. It would reduce the frequency of unrecognized artifacts associated with separate stress and rest image acquisitions (22). Unlu et al. found a good correlation and no significant difference between separate and simultaneous acquisition methods (34). However, Kiat et al. (25) and Kwok et al. (33) did a feasibility study of simultaneous dual-isotope rest/stress myocardial perfusion scintigraphy. They concluded that the current scintillation camera computer system did not provide the ability to eliminate "cross-talk" and without this adjustment they did not recommend a simultaneous dual-isotope method (25, 33). Nevertheless, because of higher energy of the Tc-99m photons and the higher dose of Tc-99m sestamibi used, compared with that of Tl-201, Tc-99m sestamibi cross-talk into dual-rest Tl-201 images has the potential to obscure Tl-201 defects without correction. Kiat et al. reported that Tc-99m cross-talk into Tl-201 window contributed 27 percent of the dual Tl-201 counts (25). However, Lowe et al. reported a 10 percent reduction in defect contrast in dual Tl-201 as a result of Tc-99m cross-talk and suggested that these changes were minimal (35). But, Yang et al. pointed out that by using the three window techniques; "cross-talk" interference could be significantly reduced (36). Also, Nakamura et al. indicated that simultaneous dual-isotope

imaging with Moore's correction method is feasible, with acceptable accuracy for detection of coronary artery disease and a small amount of cross-talk into each window (37). Besides, Knesaurek et al. reported that a cross-talk correction method based on the assumption that the transformations, which modify the primary energy window images into the scatter images as viewed in the other energy windows. Knesaurek et al. also developed a novel transformation method for the correction of cross-talk in simultaneous dual-isotope SPECT imaging and concluded that the transformation three-window, dual radionuclide correction method with restoration improves the quality of simultaneous rest Tl-201/stress Tc-99m sestamibi SPECT imaging (38). This method demonstrated that the sensitivities and specifities for CAD detection are similar to those in published studies with Tl-201 or Tc-99m sestamibi alone. This method have several advantages compared with standard Tl-201 or Tc-99m sestamibi protocol and is one of the current procedures of choice for performing same-day stress myocardial perfusion and myocardial viability SPECT studies (39). Moreover, Hannequin et al. reported the first clinical results obtained with the spectral deconvolution technique photon energy recovery (PER) for cross-talk stress technetium-99m sestamibi myocardial perfusion SPECT. Photon energy recovery (PER) is quantitatively efficient to correct for cross-talk in patients investigated with simultaneous rest Tl-201/stress Tc-99m sestamibi myocardial SPECT (40).

Tc-99m Sestamibi gated acquisition

The other advantages of dual isotope imaging with Tl-201/Tc-99m sestamibi SPECT are availability and suitability for gated acquisition and combined perfusion with functional assessment (motion, thickening, left ventricular ejection fraction (LVEF) using one injection and one imaging sequence) (10, 41-46). However, some studies reported that LVEF can be assessed by Tl-201 ECG-gated SPECT (10, 11, 44). The results showed that Tl-201 could provide clinically satisfactory LV functional information, whereas Tc-99m MIBI is more accurate and reliable for the assessment of LV function in a shorter acquisition time. Eelctrocardiogram-gated SPECT with Tl-201 shows the poorer myocardial count rate and image quality in comparison with Tc-99m myocardial perfusion tracers (10, 11). Therefore, a long acquisition time was used in studies. Thus, ECG-gated Tl-201 SPECT may not be feasible in busy laboratories. Patients discomfort and motion due to the long acquisition time may also cause problems (47). But, Wadhwa et al. concluded that application of energy window optimization (EWO) to Tl-201 imaging allows good-quality gated SPECT myocardial perfusion images to be acquired without the need to increase the acquisition time or the dose of Tl-201 as modifiers to improve image quality (48). Mazzanti et al. reported that Tl-201/stress Tc-99m sestamibi dual isotope myocardial perfusion SPECT is also useful for the identification of patients with severe and extensive coronary artery disease. The automatic measurement of transient ischemic dilatation in dual-isotope myocardial perfusion SPECT is clinically useful marker for CAD (49). Germano et al. developed an automatic quantitative algorithm for the measurement of regional wall motion and wall thickening from three-dimensional gated Tc-99m sestamibi myocardial perfusion SPECT images (50).

Is technetium-99m sestamibi adequate for detection of myocardial viability?

Irreversible defects identified by rest/stress Tc-99m sestamibi imaging might erroneously be identified as reversible by rest Tl-201 / stress Tc-99m sestamibi dual-isotope imaging. As two radioisotopes emitting photons with different energies are used in the dual-isotope approach, differences in defect resolution may occur (21). Also, there are differences in attenuation and scatter between Tl-201 and Tc-99m sestamibi, potentially resulting in the appearance of reverse redistribution of defects that are mildly reversible. Another consideration for dual-isotope imaging is the remarkable variation of tracer distribution concentration to the extracardiac organs. For the Tl-201 liver activity is minimal in stress images but greater in resting studies, the amount of the liver activity varies depending on the injection to imaging interval. Bowel tracer concentration may be considerable and may be two or three times greater than that in the myocardium. If Tc-99m sestamibi bowel activity scatters into the Tl-201 photo peak, an inferior Tc-99m sestamibi stress defect might appear reversible in the Tl-201 rest study (37). Although Tl-201 scintigraphy has been valuable for the assessment of myocardial perfusion and viability this radiotracer has significant limitations related to the physical properties; therefore, Tc-99m-labelled agents are being used increasingly in evaluation of viability. On the other hand, from the viability point of view, the role of Tc-99m based myocardial perfusion agents is deferred, and the value of Tc-99m sestamibi remained controversial and some studies sho-

wed that Tc-99m agents, particularly Tc-99m sestamibi, significantly underestimated the extent of hypoperfused myocardium, whereas other studies suggest that Tc-99m is valuable and comparable to Tl-201 for viability assessment. Earlier studies suggested that Tc-99m sestamibi was not a good viability agent (51). Because in most previous publications, myocardial viability has been defined on the basis of an improvement in wall motion after coronary artery bypass surgery (CABG).

However, nowadays, later studies indicate that Tc-99m sestamibi may also be a good viability marker (52-54). Kauffman et al. reported similar Tc-99m sestamibi and delayed Tl-201 activities in defects (53). Dilsizian et al. also compared results of stress-redistribution-reinjection Tl-201 SPECT with Tc-99m sestamibi SPECT and found 93 percent concordance rate when the regional activities of the two tracers quantified (55). Maes et al reported that sestamibi uptake was significantly higher in areas considered viable by 18F-fluorodeoxyglucose and in regions with improved regional contraction after CABG (54). Also, Dakik et al. demonstrated a close relationship between Tc-99m sestamibi activity and the extent of histologically documented myocardial viability in patients referred for CABG and their results lend support to the use of Tc-99m sestamibi as a viability marker (56). Kiser et al. in their series, the ability of Tl-201, sestamibi and teboroxime to establish the existence of viable myocardium was compared with that of F-18 FDG concluded that there was no significant difference in the prediction of viable myocardium between Tl-201, sestamibi and teboroxime (57). In addition, Takehana et al. concluded that resting perfusion imaging with Tc-99m sestamibi accurately determined viability of the infarct zone despite reperfusion through a residual stenosis. Tc-99m sestamibi imaging was proved to be useful in the clinical setting for the prediction of the amount of salvaged myocardium (58). Finally, the present data reported in the studies yield further evidence that sestamibi may be a valid viability agent when administered at an appropriate time.

Conclusions

Standard Tl-201 redistribution and same day or 2-day rest/stress Tc-99m sestamibi protocols are time-consuming. However, coordination of stress testing and imaging is more flexible. The separate or simultaneous acquisition dual-isotope protocol is shorter than standard Tl-201 or Tc-99m sestamibi protocols. Thus the more rapid completion of studies is appreciated as an advantage by patients, technologists, interpreting and referring physicians, nurses and hospital management. Simultaneous imaging has the potential advantages of precise pixel registration and artifacts, if present, which are identical in both thallium and sestamibi, and requires only one set of imaging. But, there are some disadvantages of spillover of activity from the Tc-99m to the Tl-201 window. Separate dual isotope acquisition also have some disadvantages. Difference in defect resolution in attenuation and scatter between T-201 and Tc-99m sestamibi potentially results in interpretation problems. Also, studies about cost-effectivity of dual isotope imaging showed that in patients with normal stress images elimination of the rest study rarely alters interpretation. Rest studies are most useful in images with abnormal or equivocal stress images. Such selective elimination of the rest studies may decrease the cost of the nuclear procedures and should be considered in the current managed care health system.

References

1. Atkins HL, Budinger TF, Lebowitz E, et al. Thallium-201 for medical use: Part 3: Human distribution and physical imaging properties. J Nucl Med 1977; 18: 133-40.
2. Krahwinkel W, Herzog H, Feinendegen LE. Pharmacokinetics of thallium-201 in normal individuals after routine myocardial scintigraphy. J Nucl Med 1988; 29:1582-86.
3. Gerson MC. Cardiac Nuclear Medicine, 3rd ed. McGraw Hill, USA: 1997, pp 9.
4. Garcia EV, Van Train K, Maddahi J. Quantification of rotational thallium-201 myocardial tomography. J Nucl Med 1985; 26: 17-26.
5. Mahmarian JJ, Verani MS. Exercise thallium-201 perfusion scintigraphy in the assessment of coronary artery disease. Am J Cardiol. 1991; 67: 2D-11D.
6. Lemlek J, Heo J, Iskandrian AS. The clinical relevance of myocardial viability in patient management. Am Heart J 1992; 124: 1327-31.
7. Pohost GM, Zir LM, Moore RH, McKusick KA, Guiney TE, Beller GA. Differentiation of transiently ischemic from infarcted myocardium by serial imaging after a single dose of thallium-201. Circulation 1977; 55: 294-302.
8. Mettler AF, Guiberteau MJ. Essentials of nuclear medicine imaging. (3th edition) 1991; Philadelphia; WB Saunders Company: 95-131.
9. Imaging Guidelines for Nuclear Cardiology (Part 1,2). J Nuc Cardiol 2001, 8(Suppl): G5-G58.

10. Germano G, Erel J, Kiat H, Kavanagh PB, Berman DS. Quantitative LVEF and qualitative regional function from gated thallium-201 perfusion SPECT. J Nucl Med 1997; 38: 749-54.
11. Maunoury C, Chen CC, Chua KB, Thompson CJ. Quantification of left ventricular function with thallium-201 and technetium-99m-sestamibi myocardial gated SPECT. J Nucl Med 1997; 38: 958-61.
12. Mochizuki T, Murase K, Fujiwara Y, et al. ECG-gated thallium-201 myocardial SPECT in patients with old myocardial infarction compared with ECG-gated blood pool SPECT. Ann Nucl Med 199 1;5: 47-51.
13. Berman DS, Kiat H, Van Train K, Garcia E, Friedman J, Maddahi J. Technetium 99m sestamibi in the assessment of chronic coronary artery disease. Semin Nucl Med 1991; 21:190-212.
14. Beller GA, Watson DD. Physiological basis of myocardial perfusion imaging with the technetium 99m agents. Semin Nucl Med 1991; 21: 173-81.
15. Mousa SA, Williams SJ, Sands H. Characterization of in vivo chemistry of cations in the heart. J Nucl Med 1987; 28:1351-7.
16. Okada RD, Glover D, Gaffney T, Williams S. Myocardial kinetics of technetium-99m-hexakis-2-methoxy-2-methylpropyl-isonitrile. Circulation 1988; 77: 491-8.
17. Canby RC, Silber S, Pohost GM. Relations of the myocardial imaging agents 99mTc-MIBI and 201Tl to myocardial blood flow in a canine model of myocardial ischemic insult. Circulation 1990; 81: 289-96.
18. Sinusas AJ, Shi Q, Vitols PJ, et al. Impact of regional ventricular function, geometry, and dobutamine stress on quantitative 99mTc-sestamibi defect size. Circulation 1993; 88: 2224-34.
19. Li QS, Solot G, Frank TL, Wagner HN Jr, Becker LC. Myocardial redistribution of technetium-99m-methoxyisobutyl isonitrile (SESTAMIBI). J Nucl Med 1990; 31: 1069-76.
20. Hachamovitch R. Clinical application of rest thallium-201/Stress technetium-99m sestamibi dual isotope myocardial perfusion single-photon emission computed tomography. Cardiol Rev 1999; 7: 83-91.
21. Berman DS, Kiat H, Friedman JD, et al. Separate acquisition rest thallium-201/stress technetium-99m sestamibi dual-isotope myocardial perfusion single-photon emission computed tomography: a clinical validation study. J Am Coll Cardiol 1993; 22: 1455-64.
22. Berman DS, Kiat HS, Van Train KF, Germano G, Maddahi J, Friedman JD. Myocardial perfusion imaging with technetium-99m-sestamibi: comparative analysis of available imaging protocols. J Nucl Med 1994;35: 681-8.
23. Weinmann P, Foult JM, Le Guludec D, et al. Dual-isotope myocardial imaging: feasibility, advantages and limitations. Preliminary report on 231 consecutive patients. Eur J Nucl Med 1994; 21:212-5.
24. Dilsizian V, Bonow RO. Current diagnostic techniques of assessing myocardial viability in patients with hibernating and stunned myocardium. Circulation 1993; 87: 1-20.
25. Kiat H, Germano G, Friedman J, et al. Comparative feasibility of separate or simultaneous rest thallium-201/stress technetium-99m-sestamibi dual-isotope myocardial perfusion SPECT. J Nucl Med 1994; 35: 542-8.
26. Loutfi I, Singh A. Comparison of single-tracer (technetium-99m-sestamibi) and dual-tracer (thallium-201 chloride and technetium-99m-sestamibi) protocols for identification of myocardial ischemia. Invest Radiol 1995; 30: 367-71.
27. Fukuoka S, Maeno M, Nakagawa S, Fukunaga T, Yamada H, Eto T. Feasibility of myocardial dual-isotope perfusion imaging combined with gated single photon emission tomography for assessing coronary artery disease. Nucl Med Commun 2002; 23:19-29.
28. Groutars RG, Verzijlbergen JF, Muller AJ, et al. Prognostic value and quality of life in patients with normal rest thallium-201/stress technetium 99m-tetrofosmin dual-isotope myocardial SPECT. J Nucl Cardiol 2000; 7: 333-41.
29. Hachamovitch R, Berman DS, Kiat H, Cohen I, Friedman JD, Shaw LJ. Value of stress myocardial perfusion single photon emission computed tomography in patients with normal resting electrocardiograms: an evaluation of incremental prognostic value and cost-effectiveness. Circulation 2002; 19: 823-9.
30. Paeng JC, Lee DS, Cheon GJ, Kim KB, Yeo JS, Chung JK, Lee MC. Consideration of perfusion reserve in viability assessment by myocardial Tl-201 rest-redistribution SPECT: a quantitative study with dual-isotope SPECT. J Nucl Cardiol 2002; 9:68-74.
31. Milan E, Giubbini R, Gioia G, Terzi A, Iskandrian AE. A cost-effective sestamibi protocol in the managed health care era. J Nucl Cardiol 1997; 4: 509-14.
32. Berman DS, Kiat H, Maddahi J. The new 99mTc myocardial perfusion imaging agents: 99mTc-sestamibi and 99mTc-teboroxime. Circulation 1991; 84 (Suppl): I7-21.
33. Kwok CG, Wu S, Tsang HP, Strauss HW. Feasibility of simultaneous dual-isotope myocardial perfusion acquisition using a lower dose of sestamibi. Eur J Nucl Med 1997; 24: 281-5.
34. Unlu M, Gunaydin S, Ilgin N, Inanir S, Gokcora N, Gokgoz L. Dual isotope myocardial perfusion SPECT in the detection of coronary artery disease: comparison of separate and simultaneous acquisition protocols. J Nucl Biol Med 1993; 37: 233-7.
35. Lowe VJ, Greer KL, Hanson MW, Jaszczak RJ, Coleman RE. Cardiac phantom evaluation of simultaneously acquired dual-isotope rest thallium-201/stress technetium-99m SPECT images. J Nucl Med 1993; 34: 1998-2006.

36. Yang DC, Ragasa E, Gould L, et al. Radionuclide simultaneous dual-isotope stress myocardial perfusion study using the "three window technique". Clin Nucl Med 1993; 18: 852-7.
37. Nakamura M, Takeda K, Ichihara T. et al. Feasibility of simultaneous stress 99mTc-sestamibi/rest 201Tl dual-isotope myocardial perfusion SPECT in the detection of coronary artery disease. J Nucl Med 1999; 40: 895-903.
38. Knesaurek K, Machac J. Enhanced cross-talk correction technique for simultaneous dual-isotope imaging: a TL-201/Tc-99m myocardial perfusion SPECT dog study. Med Phys 1997; 24:1914-23.
39. Knesaurek K, Machac J. A transformation cross-talk technique for simultaneous dual radionuclide imaging: a myocardial perfusion 201Tl/99mTc sestamibi dog SPECT study. Br J Radiol 1999; 72: 872-81.
40. Hannequin P, Weinmann P, Mas J, Vinot S. Preliminary clinical results of photon energy recovery in simultaneous rest Tl-201/stress Tc-99m sestamibi myocardial SPECT. J Nucl Cardiol 2001; 8: 144-51.
41. Mannting F, Morgan-Mannting MG. Gated SPECT with technetium-99m-sestamibi for assessment of myocardial perfusion abnormalities. J Nucl Med 1993; 34: 601-8.
42. Tischler MD, Niggel JB, Battle RW, Fairbank JT, Brown KA. Validation of global and segmental left ventricular contractile function using gated planar technetium-99m sestamibi myocardial perfusion imaging. J Am Coll Cardiol 1994; 23:141-5.
43. DePuey EG, Nichols K, Dobrinsky C. Left ventricular ejection fraction assessed from gated technetium-99m-sestamibi SPECT. J Nucl Med 1993; 34: 1871-6.
44. Taillefer R, DePuey EG, Udelson JE, Beller GA, Latour Y, Reeves F. Comparative diagnostic accuracy of Tl-201 and Tc-99m sestamibi SPECT imaging (perfusion and ECG-gated SPECT) in detecting coronary artery disease in women. J Am Coll Cardiol 1997; 29:69-77.
45. Germano G, Berman DS. On the accuracy and reproducibility of quantitative gated myocardial perfusion SPECT. J Nucl Med 1999; 40: 810-3.
46. Germano G, Berman DS. Quantitative gated SPECT. J Nucl Med 2001; 4: 528-9.
47. Tadamura E, Kudoh T, Motooka M, et al. Assessment of regional and global left ventricular function by reinjection T1-201 and rest Tc-99m sestamibi ECG-gated SPECT: comparison with three-dimensional magnetic resonance imaging. J Am Coll Cardiol 1999; 33: 991-7.
48. Wadhwa SS, Mansberg R, Wilkinson D, Abbati D. Gated TI-201 myocardial perfusion SPECT: application of energy window optimization. Clin Nucl Med 1999; 24: 479-82.
49. Mazzanti M, Germano G, Kiat H. et al. Identification of severe and extensive coronary artery disease by automatic measurement of transient ischemic dilation of the left ventricle in dual-isotope myocardial perfusion SPECT. J Am Coll Cardiol 1996; 27:1612-20.
50. Germano G, Erel J, Lewin H, Kavanagh PB, Berman DS. Automatic quantitation 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.
51. Marzullo P, Sambuceti G, Parodi O. The role of sestamibi scintigraphy in the radioisotopic assessment of myocardial viability. J Nucl Med 1992; 33:1925-30.
52. Cuocolo A, Pace L, Ricciardelli B, Chiariello M, Trimarco B, Salvatore M. Identification of viable myocardium in patients with chronic coronary artery disease: comparison of thallium-201 scintigraphy with reinjection and technetium-99m-methoxyisobutyl isonitrile. J Nucl Med 1992; 33: 505-11.
53. Kauffman GJ, Boyne TS, Watson DD, Smith WH, Beller GA. Comparison of rest thallium-201 imaging and rest technetium-99m sestamibi imaging for assessment of myocardial viability in patients with coronary artery disease and severe left ventricular dysfunction. J Am Coll Cardiol 1996; 27: 1592-7.
54. Maes AF, Borgers M, Flameng W, et al. Assessment of myocardial viability in chronic coronary artery disease using technetium-99m sestamibi SPECT. Correlation with histologic and positron emission tomographic studies and functional follow-up. J Am Coll Cardiol 1997; 29:62-8.
55. Dilsizian V, Arrighi JA, Diodati JG, et al. Myocardial viability in patients with chronic coronary artery disease. Comparison of 99mTc-sestamibi with thallium reinjection and [18F]fluorodeoxyglucose. Circulation 1994; 89: 578-87.
56. Dakik HA, Howell JF, Lawrie GM, et al. Assessment of myocardial viability with 99mTc-sestamibi tomography before coronary bypass graft surgery: correlation with histopathology and postoperative improvement in cardiac function. Circulation 1997; 96:2892-8.
57. Kiser JW, Drane WE, Mastin ST, Nicole MW. Prediction of myocardial viability: Tl-201 versus sestamibi versus teboroxime compared with FDG uptake. Clin Nucl Med 1998; 23: 432-6.
58. Takehana K, Ruiz M, Petruzella FD, Watson DD, Beller GA, Glover DK. Tc-99m sestamibi defect magnitude predicts the amount of viable myocardium after coronary reperfusion despite the presence of severe residual stenosis. J Nucl Cardiol 2001; 8: 40-8.