What is the optimal activity ratio for same-day myocardial perfusion SPECT?

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Myocardial perfusion SPECT with the Tc-99m tracers sestamibi (MIBI) and tetrofosmin has been performed clinically for decades and forms the backbone of nuclear cardiac imaging for patients with coronary artery disease (CAD). The favorable physical characteristics of Tc-99m, compared with Tl-201, leads to improved image quality and reduced patient radiation exposure.

For Tc-99m tracers, practice is split among same-day and two-day imaging protocols and there are advantages and disadvantages for both approaches. Same-day imaging protocols provide the convenience of a single visit to the center, which is particularly advantageous for patients traveling substantial distance. However, the lack of significant tracer redistribution for both MIBI and tetrofosmin mandates the need for a second injection of tracer to show differences of perfusion during resting and stress conditions. As the second imaging session is typically performed 3 to 4 hours after the first imaging session, the inevitable presence of residual tracer within the myocardium due to the 6-hour Tc-99m half-life requires the activity in the second injection to be greater to reduce the appearances of the residual activity distribution from the first injection—a phenomenon that has been referred to as “shine-through” or “ghosting”.

HISTORY AND PRACTICE

The first use of MIBI in the late 1980s¹ predates the introduction of tetrofosmin² and hence it is these preliminary studies using MIBI that set the precedent for the same-day regime of activity ratios. Over the following decade, several studies were published that evaluated the use of both MIBI and tetrofosmin in same-day imaging. A summary of a selection of these studies is given in Table 1. As can be seen from the data in the table, the earlier studies with MIBI focused on a rest-stress protocol opposed to a stress-rest protocol, with the former being shown to provide the superior ability to identify areas of ischemia.^{3,4} The increased focus on reducing radiation dose to patients advocates the use of stress-first, stress-only protocols where the follow-on resting acquisition, which carries a greater radiation burden, can be canceled if not required.⁵ Hence modern practice is likely to perform the stress imaging first, which will facilitate the use of stress-first, stress-only imaging. This requires perfusion in the follow-on resting image to fully mask any regional tracer reduction in the stress images to differentiate reversible ischemia from non-reversible infarct.

While early studies have evaluated the order in which to perform rest and stress imaging for same-day protocols, very little work was published looking at the optimal ratio of the activity for the two injections. In the preliminary work on MIBI by Taillefer et al¹ the authors referred to unpublished data evaluating some patients with known CAD using stress-first imaging and a ratio of approximately 1:2. They stated that defects in the MIBI images did not appear completely reversible while the comparison Tl-201 images did show complete reversibility. In their published data, images were acquired in planar format, rather than SPECT, and hence it is reasonable to assume this unpublished work is also planar.

The lack of early work systematically evaluating various activity ratios for same-day imaging resulted in the 1:3 ratio becoming the de facto choice and was

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Figure 1. Simplified illustration showing the effect of an anterior-inferior count gradient resulting from attenuation. The top images represent polar plots from the follow-on “rest” image with a defect placed in the anterior wall (*left*) and inferior wall (*right*) on the initial “stress” image. The profiles below represent the anterior-inferior counts along the dashed line and were replicate the intensity of a stress:rest ratio of 1:2 and the shaded area indicates the region that is not defect along the profiles. Despite the true defect contrast being the same in both positions, the measured average counts along the profile in the inferior defect are 25% lower than those measured in the anterior defect. Paradoxically, the measured average counts along the profile in the remaining ventricle are 6% greater in the case with the inferior perfusion defect. This causes differences in measured defect contrast due to the count gradient. Note for simplicity axis values are not shown on the profiles.

incorporated into early European and North American guidelines^{14,15} and has continued to propagate to more current guidelines.¹⁶ In 2015 a working group on behalf of the IAEA published results from a worldwide survey of nuclear cardiology protocols.¹⁷ This work presented several recommendations for best practice in radiation dose reduction for nuclear cardiology. One recommendation, based on guidelines, was to ensure that the activity of the second injection was not less than three times that of the first in order to avoid shine-through artifacts. Interestingly, the survey results stated that only 15% of the 55 North American laboratories that supplied data followed this recommendation. This suggests that the majority of laboratories administered less than three times the activity for the second image for same-day procedures.

Early studies assessing same-day protocols on patients made comparison with Tl-201 imaging. More recently, the availability of cardiac phantoms provides a ground-truth activity distribution with the same Tc-99m tracers allowing known perfusion defects within the left

ventricle. A small number of studies have investigated the effect of shine-through using cardiac phantoms.

DePuey et al¹² placed a defect in the anterior wall of a cardiac phantom and simulated both rest-stress and stress-rest protocols with a range of activity ratios. The authors measured defect contrast using counts per pixel in the area of the defect. In their stress-rest protocol with activity ratios of 1:1 to 1:8, the shine-through of the defect from the first scan into the second resting scan showed only small reduction as the activity ratio was increased above 1:2.5.

Nkoulou et al¹¹ performed phantom and clinical evaluation of stress-rest imaging using a 1:1 activity ratio and compared to a 1:3 ratio with the latter achieved using a top-up injection. The authors performed a subtraction of the residual stress activity on the 1:1 rest images and compared summed scores obtained from the 1:3 images. They observed very little difference in the comparison for the 1:1 rest images once the residual activity subtraction had been performed and concluded that the subtraction technique could provide a means of avoiding any increase in activity for the second injection.

Work by van Dijk et al¹³ evaluated various activity ratios in a stress-rest same-day protocol for both clinical and phantom data. The authors’ phantom work firstly acquired “stress” SPECT images of cardiac phantom with 100% defect and 50% defect at fixed locations within the cardiac insert followed by “rest” acquisitions with no defects performed over varying scan times to simulate activity ratios of 1:1 to 1:4. They performed quantitative analysis using the 1:4 images as the reference. They concluded that a 1:2 activity ratio was adequate for a 3-hour delay between the two imaging sessions.

These phantom studies placed the defect in fixed locations on single gamma camera systems, hence it is possible that differences due to equipment and defect position may occur. In this issue, Zoccarato et al¹⁸ build on these phantom studies with images acquired on two cameras and with the defect placed the anterior, lateral, inferior and septal walls to simulate an ischemic stress image. Like other recent studies the authors simulate a stress-rest protocol where sufficient activity in the rest injection is required to remove the residual appearance of the perfusion defect from the first stress image.

They evaluate activity ratios of 1:1 to 1:3 and their analysis technique compares the count density in the defect compared with the remaining cardiac insert for the various images. The authors define the image contrast of the perfusion effect, IC_{PD} , as

Table 1. Summary of a selection of studies that have evaluated various activity protocols for same-day myocardial perfusion imaging

References	Tracer	Image order	First injection	Second injection	Ratio
Taillefer ¹	MIBI	Rest-stress	259–370 MBq (7–10 mCi)	925–1110 MBq (25–30 mCi)	Approx. 1:3.5 to 1:4
Taillefer ⁴	MIBI	Rest-stress and Stress-rest	259 MBq (7 mCi)	925 MBq (25 mCi)	1:3.5
Borges-Neto ⁶	MIBI	Rest-stress	370 MBq (10 mCi)	1110 MBq (30 mCi)	1:3
Heo ³	MIBI	Rest-stress and Stress-rest	185–296 MBq (5–8 mCi)	925 MBq (15–25 mCi)	1:3
Jain ²	TF	Stress-rest	222–296 MBq (6–8 mCi)	814–888 MBq (22–24 mCi)	Approx. 1:3 to 1:3.6
Van Train ⁷	MIBI	Rest-stress	4 MBq/kg (0.11 mCi/kg)	11.5 MBq/kg (0.31 mCi/kg)	1:3
Braa ⁸	TF	Stress-rest	296–370 MBq (8–10 mCi)	888–1110 MBq (24–30 mCi)	1:3
Yong ⁹	TF	Stress-rest and Rest-stress	250 MBq (6.8 mCi)	750 MBq (20.3 mCi)	1:3
He ¹⁰	MIBI	Stress-rest	370 MBq (10 mCi)	1110 MBq (30 mCi)	1:3
Nkoulou ¹¹	TF	Stress-rest	320 MBq (8.6 mCi)	320/960 MBq (8.6/25.9 mCi)	1:1 / 1:3
DePuey ¹²	MIBI	Stress-rest	192 MBq (5.2 mCi)	1328 MBq (35.9 mCi)	Approx. 1:7
van Dijk ¹³	TF	Stress-rest	200 MBq (5.4 mCi)	Variable (simulated)	1:1 to 1:4

TF tetrofosmin, MIBI sestamibi

$$IC_{PD} = \frac{C_{LV} - C_{PD}}{C_{LV} + C_{PD}}$$

where C_{LV} and C_{PD} are the average counts per pixel in the entire left ventricle (other than the perfusion defect) and the perfusion defect respectively. As with some previous studies the authors did not perform attenuation correction and so the measured count density in the cardiac insert is not uniform irrespective of whether a defect is present. The difference in the measured average counts in these areas will differ due to attenuation, as is shown in Figure 1. Hence an additional set of images are required to normalize the effect of attenuation.

By employing systematic analysis techniques and ground-truth phantom data these authors, like the previous studies of van Dijk et al and Nkoulou et al, demonstrate that the typical practice of using a 1:3

activity ratio for same-day myocardial perfusion SPECT may not be necessary and ratios of 1:2 may give acceptably low shine-through. It would be prudent for centers to perform similar evaluation before changing practice to ensure that the proposals would be applicable for the particular local protocol and equipment. It is also not clear whether these lower activity ratios could be applied to rest-stress same-day imaging. However, one could make the argument that stress-rest would be more desirable from a dose reduction perspective as the rest scan could be canceled if the stress appears normal. While the old phrase “if it isn’t broke don’t fix it” perhaps reflects the lack of change in recommendations passed through various iterations of imaging guidelines these studies all emphasize the need to reflect and re-evaluate practice as equipment and analysis techniques progress.

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