Taking the perfect nuclear image: Quality control, acquisition, and processing techniques for cardiac SPECT, PET, and hybrid imaging

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Nuclear Cardiology for the past 40 years has distinguished itself in its ability to non-invasively assess regional myocardial blood flow and identify obstructive coronary disease. This has led to advances in managing the diagnosis, risk stratification, and prognostic assessment of cardiac patients. These advances have all been predicated on the collection of high quality nuclear image data. National and international professional societies have established guidelines for nuclear laboratories to maintain high quality nuclear cardiology services. In addition, laboratory accreditation has further advanced the goal of the establishing high quality standards for the provision of nuclear cardiology services. This article summarizes the principles of nuclear cardiology single photon emission computed tomography (SPECT) and positron emission tomography (PET) imaging and techniques for maintaining quality: from the calibration of imaging equipment to post processing techniques. It also will explore the quality considerations of newer technologies such as cadmium zinc telleride (CZT)-based SPECT systems and absolute blood flow measurement techniques using PET.

Key Words: Image artifacts • image processing • image reconstruction • PET imaging • SPECT

INTRODUCTION

Performance of high quality nuclear cardiac imaging is demanding. Equipment must be up to date and calibrated. Lab personnel need to be trained on pre-imaging quality-control steps, the imaging protocol, data acquisition and processing. In addition, these steps may need to be optimized for each patient, while avoiding short-cuts and improvisation. Finally, interpretation of the images must include quality assessment of instrumentation performance and adherence to protocol in order to differentiate artifact from disease.[1,2]

Perhaps the most significant, intrinsic limitation to nuclear cardiology is the small amount of radioactive tracer that may be injected. The combination of low count data and long acquisition times that are customary in nuclear cardiology are a direct source of poor resolution, motion artifacts, and noise texture when compared to other modalities. In addition, U.S. and international standards for acceptable radiation dosage continue to put downward pressure on what is considered acceptable tracer dosages.[3-5]

To put in perspective the challenge of nuclear imaging, consider that a routine nuclear cardiac perfusion study requires an acquisition time 200,000 times longer than conventional photography, while acquiring only a fraction of the counts per pixel! These long acquisition times make nuclear imaging particularly susceptible to patient motion. Motion artifacts can result from the external patient movement or by changes in the position of the patient's organs: such as diaphragm relaxation or cardiac motion diaphragm positioning. In a study of 48 patients, 17% of studies had significant motion,[6-8] appearing as everything from a small focal defect to a more significant ''hurricane'' artifact.[9] Motion correction programs are ubiquitous in nuclear cardiology, but often times fail to correct motion-related artifacts and can even introduce new artifacts.[10-12]

Photon attenuation and scatter is another major source of imaging artifacts and is often cited as the reason for low specificity when compared to coronary angiography.[13-15] Because of this, nuclear laboratories have explored the use of attenuation and scatter

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correction in cardiac SPECT to improve interpretive accuracy. Studies have reported significant improvements in normalcy and reduction in false-positive rates when attenuation correction is applied.[16-20] The benefit of attenuation and scatter correction may be more profound in targeted populations such as women and the obese.[21] It may also enable other applications such as stress only imaging.[22,23] Because of this, the American Society of Nuclear Cardiology and Society of Nuclear Medicine have issued a joint statement on attenuation correction recommending it when possible.[24] Despite these advantages and recommendations, attenuation and scatter correction for SPECT has not become widely adopted in the clinical setting.[25] In contrast to SPECT, nearly all commercially available PET imaging systems are equipped with attenuation correction apparatus, and attenuation and scatter correction are applied in nearly all cases. The routine application of attenuation correction in PET has been cited as a major reason for its higher specificity compared to SPECT.[26-29]

Detector blur and partial volume effects also can have an impact on the images, reducing sensitivity to defects and resulting in inaccurate measurements of quantities, such as LV volumes.[30,31] It has been demonstrated that partial volume artifacts can be reduced when a reconstruction zoom is employed[30] and when smaller pixel sizes are used.[31] In cardiac PET, partial volume effects can create hot spots in the papillary muscles and a fixed perfusion defect at the apex, presumably due to apical thinning along with dynamic motion.[32] Though the impact of PET partial volume effects are less significant for visual assessment, partial volume effects can introduce significant errors in absolute quantitative measurements, such as myocardial flow and flow reserve.[33,34]

High quality nuclear cardiology can be obtained by understanding the sources of artifact, implementing strategies that minimize their impact and judiciously correcting for those artifacts when necessary.

SPECT QUALITY CONTROL (QC), ARTIFACTS, AND CORRECTIONS

Camera Quality Control Artifacts

QC of the imaging system is essential for acquiring clinically useful image data. As one would never take a camera with a broken lens on vacation, one should never use a SPECT or PET camera that is not functioning properly. To be certain that a SPECT imaging system is working properly; a minimum of three measurements must be made[35]:

- *Uniformity:* This verifies that there are a proportional number of counts recorded at every location on the scanner.
- *Spatial linearity:* This verifies that photon events are recorded digitally in the correct location.
- *Center of rotation (COR):* This verifies that the camera rotates around the same point in space throughout the entire acquisition.

Older SPECT systems may also require energy peaking to confirm that the energy settings of the system are at the desired energy for the tracer that is being imaged.

Uniformity. Gamma camera sensitivity should be uniform across the entire face of the detector. To verify the uniform response to photon flux, a uniform sheet source of activity is placed on the detector face with the collimator on. A planar acquisition is then taken to a fixed count level and the uniformity of the image is measured (the extrinsic flood, see Figure 1). Alternatively, a flood can be acquired with the collimator removed (intrinsic flood) with a point source at a sufficient distance to create a uniform flooding of the detector system. The latter technique typically must be analyzed according to a proprietary analysis program to account for the geometry of the detector. Daily flood field extrinsic uniformity measurements should be performed to verify the system daily uniformity is $<7\%$.[35] Other limits may be required by the system manufacturer.

Artifacts caused by detector non-uniformity are unpredictable, because they depend on the severity of the discrepancy and where on the detector it is located. The interpreting physician or a designate should be charged with reviewing the uniformity data from each camera daily to confirm it meets the quality requirements. It is not sufficient to rely on a user's ability to see a uniformity error in the raw rotating planar data (Figure 2).

Linearity. Spatial linearity measurements use a bar phantom to verify that counts received by the detector are recorded in the correct place. Linearity phantoms are typically constructed out of a set of metal bars that attenuate the photons from either a point source or a sheet source. These metal bars appear as a series of lines on the detector surface. These images should be inspected to confirm that the bars are straight throughout the entire field of view. If the linearity phantom demonstrates nonlinearities, such as jagged lines or a wavy pattern, the system should not be used until service can correct the problem (Figure 3). Linearity should be verified at least weekly unless otherwise recommended by the manufacturer.[36]

Center of rotation. The COR QC measurement is performed to verify that the camera heads rotate

around a single point in space (Figure 4). Because most systems do not rotate around a single point, a COR correction must be applied to move the projection data to an isocenteric effective rotation. The COR check verifies both the mechanical integrity of the system and the accuracy of those corrections. The National Electrical Manufacturers Associations (NEMA) and the Intersocietal Accreditation Commission recommend that COR measurements be performed monthly.[35,36]

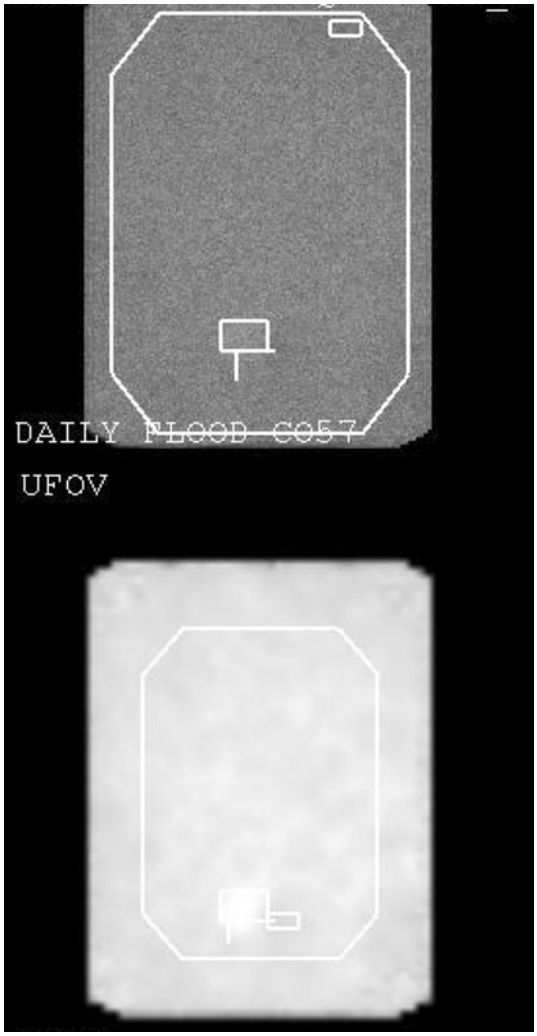


Figure 1. Extrinsic flood with a single tube out of compliance by 10%.

SPECT Acquisition-Related Artifacts

Motion. Motion artifacts can appear in any region of the myocardium, and are often visualized in the long axis views (Figure 5). Careful patient instruction about the importance of lying still, staff observation during the acquisition, and ongoing reinforcement of the instruction is the best strategy for overcoming motion artifacts. When significant motion is present in an image, repeat imaging may be required. Motion correction software should not be relied upon as a substitute for acquiring motion-free image data.

Post acquisition review of the rotating projection images for either vertical or horizontal skips in the rotation is used to identify the presence of patient motion. At the conclusion of the imaging study, the rotating projection data should be inspected for motion and when a large fraction of the frames demonstrate significant motion, the study should be repeated,[12,13,37] in particular if there is lateral motion.[38]

Interference from non-cardiac uptake. The two commercially available Tc-99m labeled myocardial perfusion radiotracers, sestamibi and tetrofosmin, are readily absorbed by the liver, bowel, stomach, and gall bladder. This non-cardiac uptake can often exceed the myocardial uptake, making image processing and interpretation difficult. Non-cardiac uptake can introduce two artifacts: the ramp filter artifact and scatter artifact (Figure 6).[13,39] The first of these artifacts, the ramp filter artifact, is a result of non-uniform attenuation reducing the brightness in some, but not all angles.[40] Because of these inconsistencies in the brightness of the liver in

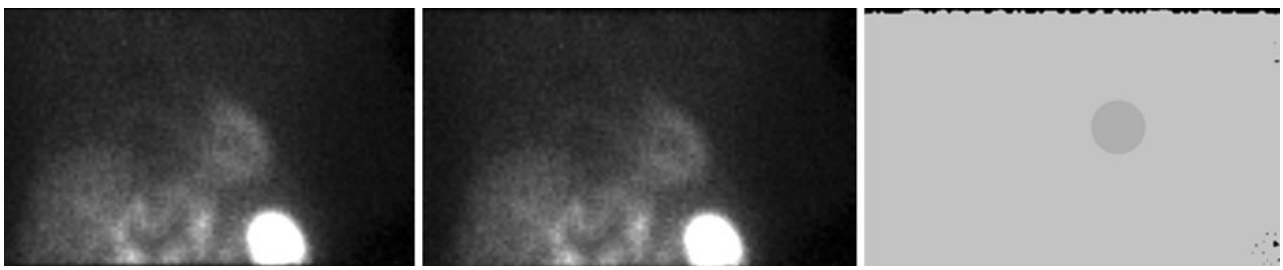


Figure 2. Displayed is an anterior projection from a SPECT study (*left*), the same study with a 10% loss of count in a circular ROI in the anterior wall of the heart (*center*), and the sensitivity mask identifying the circular ROI. A 10% loss of sensitivity is barely visible in the anterior wall of the center of the image of the patient, and yet it could have a significant impact on the interpretation of the study.

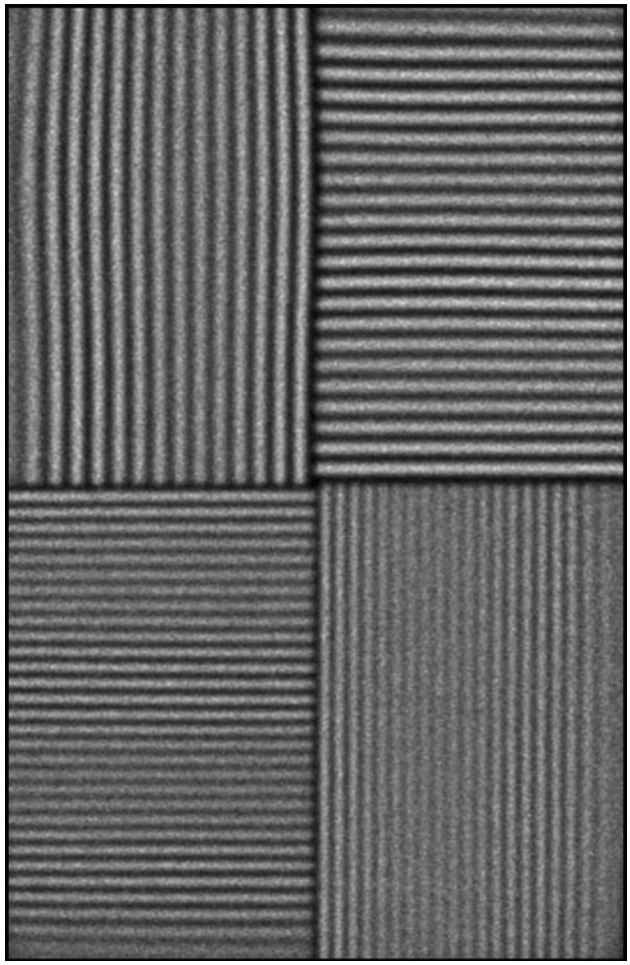


Figure 3. The *upper left corner* of this *bar phantom* demonstrates a wavy pattern indicating that the system is not properly tuned. The system should not be used until it has been serviced and the issue is resolved.

different projections, reconstructions will have dark patches extending well beyond the bright object, typically liver or bowel, into adjacent tissue.

True scatter artifacts are a result of photon scatter off of the electrons in the soft tissue causing the photon to be recorded at a distance from the point where it was created. These scatter photons have the effect of ''blurring'' of the primary image reducing resolution and blurring organs together. The scatter effect can render some portions of the image uninterpretable.

Supplemental exercise[41,42] has been shown to reduce the non-cardiac uptake of Tc-99m tracers. Some authors have suggested that drinking warm water or eating a fatty meal could result in reduced non-cardiac uptake, although there appears to be limited objective evidence to support these recommendations.[43]

ECG gating. The acquisition of ECG-gated myocardial perfusion images requires the measurement of an RR interval window to capture the maximal number of perfusion counts without compromising the functional assessment. This is ideally accomplished using an acquisition protocol that acquires the perfusion and functional data independently and simultaneously. However, for those systems that derive the perfusion data from the sum of the ECG-gated data, it is essential to select a RR window that captures the entire RR cycle. Generally, the more narrow the RR window, the more likely the RR interval will be truncated, leaving some of the ECG frames with low counts (Figure 7). In addition, frequent PVCs and arrhythmias can lead to a significant drop in functional measurements and can lead to changes in the perfusion assessment when the static data set is derived from the gated data.[44]

Software approaches to increasing signal to noise. Software approaches rely on incorporating the imaging system characteristics, such as attenuation, scatter, and depth-dependent collimator blur, etc. into an iterative reconstruction algorithm[45-48] to better

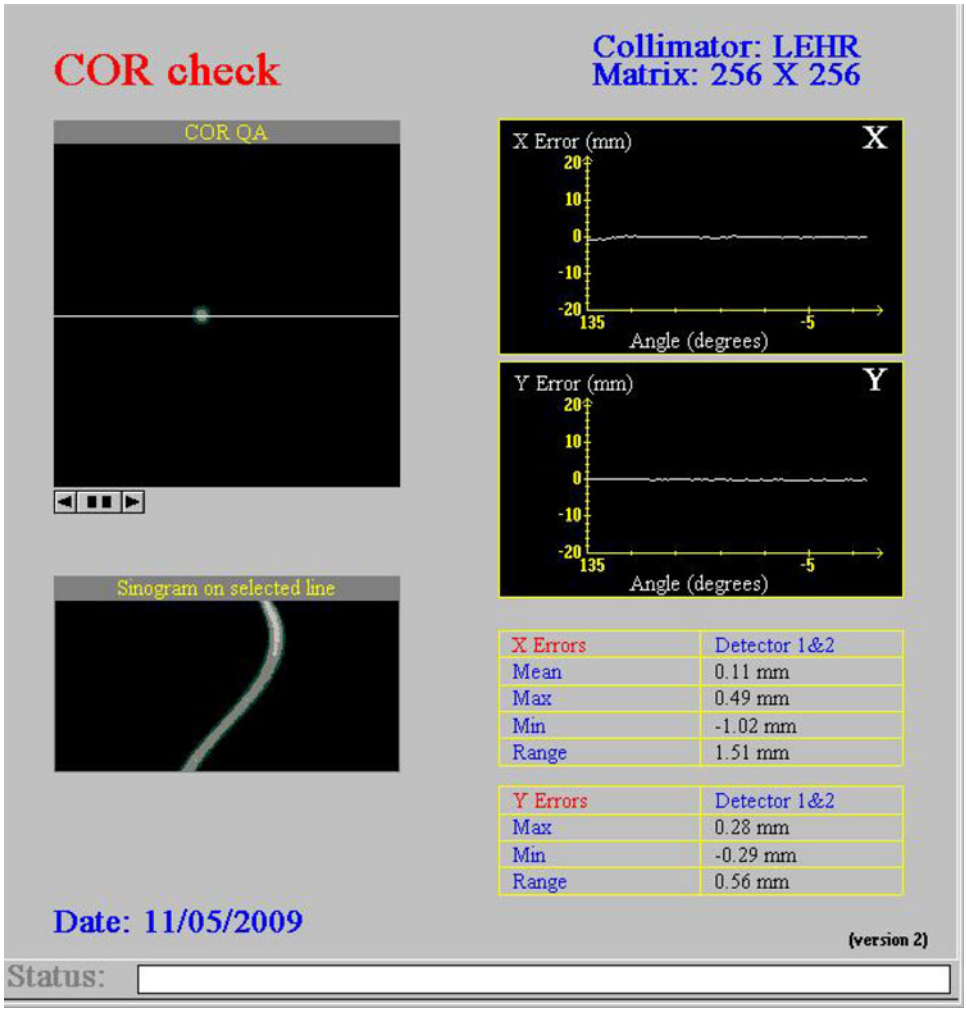


Figure 4. The COR is checked to verify the camera heads are appearing to rotate around a single point. This can be done with our or more point sources suspended in the field of view of the system.

concentrate the reconstructed counts spatially. This has the effect of reducing the blur in the image, effectively boosting the signal from the wall of the myocardium. It is important to note that these techniques do not increase counts, rather they improve the reconstructed resolution of the system (Figure 8). Because of this, improvements in signal to noise are most pronounced when performed in conjunction with attenuation and scatter correction.[48]

Hardware approaches to increasing signal to noise. Recent efforts to improve the noise characteristics have been made in imaging hardware and software. Several new imaging systems have been brought to market that utilize solid state scanning technologies.[49-51] These hardware-based approaches utilize focusing camera geometries to increase the camera sensitivity at the expense of field of view. Another advantage of these systems for cardiac SPECT is that they take advantage of newer detector materials and iterative reconstruction. These not only have increased system sensitivity but also allow for true dynamic imaging.

One such system utilizes nine independent scanning detectors to concentrate the imaging on a small field of view, centered on the heart (D-SPECT, Spectrum Dynamics, Haifa, Israel). These systems do not have the same QC steps as a conventional Anger SPECT system. Daily QC consists of three QC steps: (1) global homogeneity, (2) regional homogeneity, and (3) field of view.[51]

Another approach that does not require any rotation is the uses of multi-pinhole SPECT, allowing for true dynamic tomographic imaging.[52] QC of these systems requires the use of a square flood source. The software performs a pass/fail test for: pulse height analysis, energy peaking, uniformity, and faulty pixels.[53]

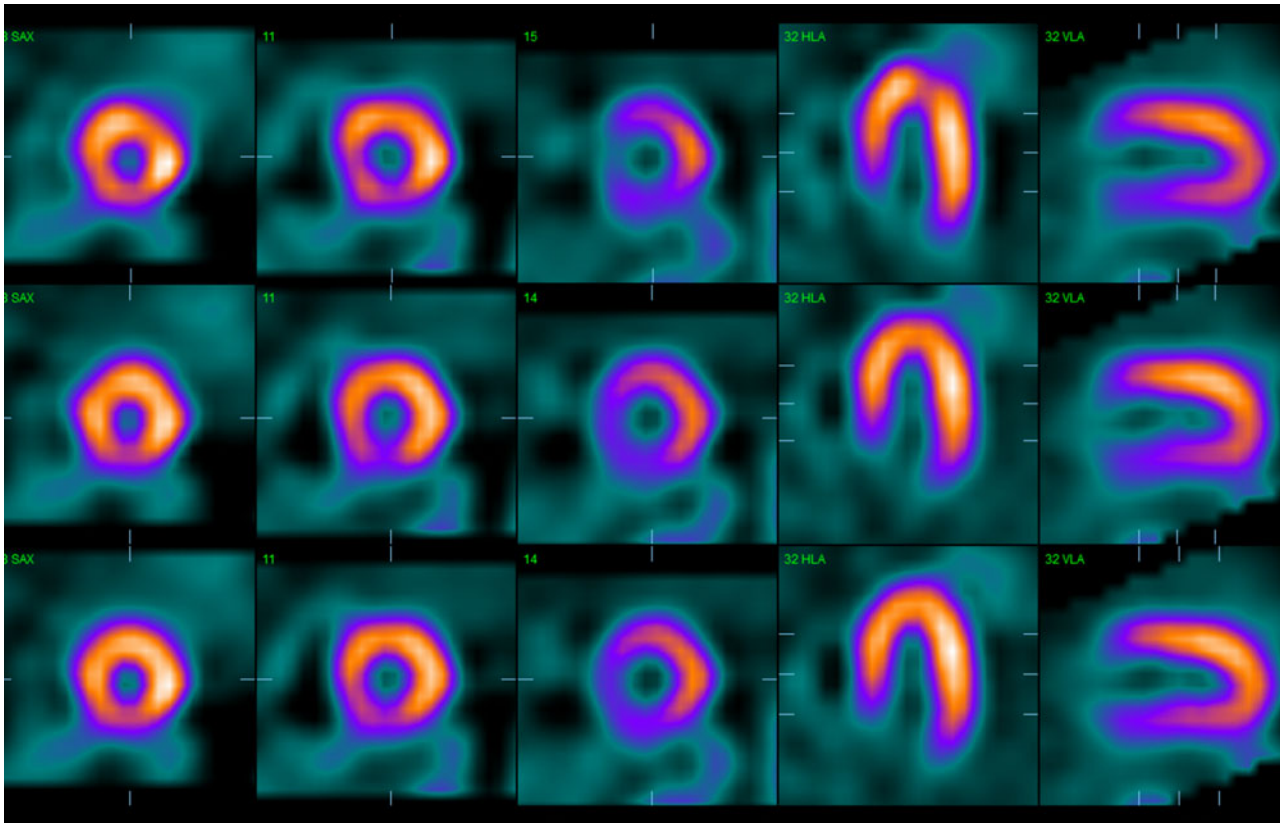


Figure 5. Effect of motion on a stress sestamibi study: *top row* 1 pixel of lateral shift in 25% of the frames, *middle row* 1 pixel of shift vertically in 25% of the frames, *bottom row* motion free.

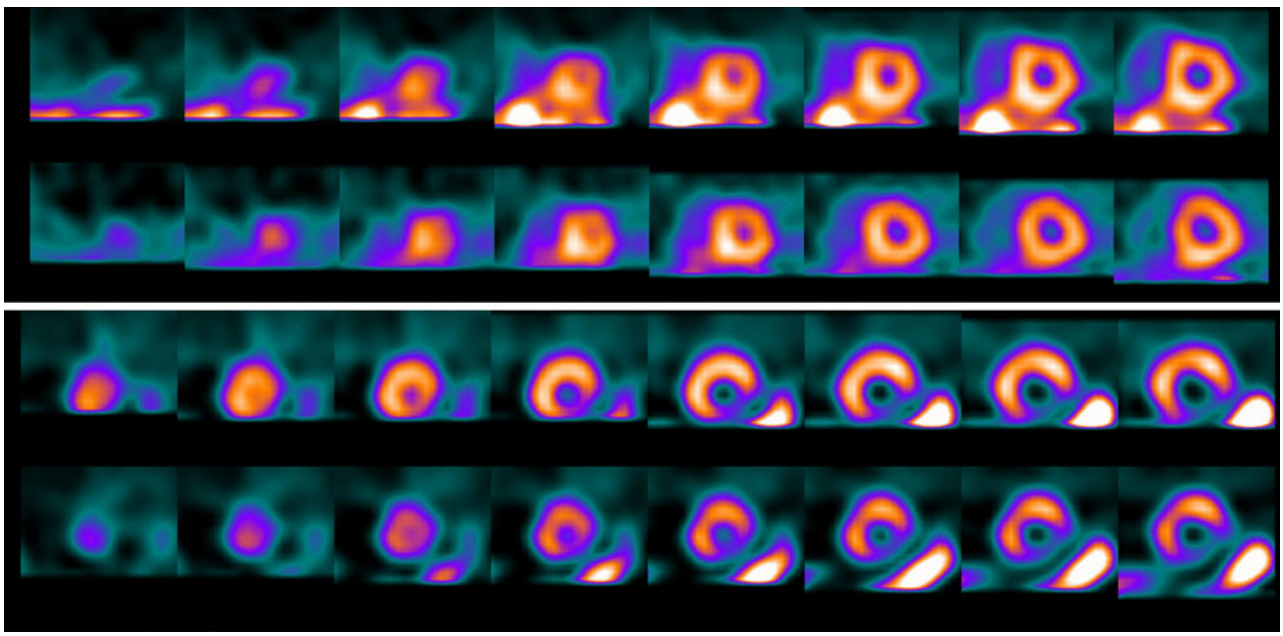


Figure 6. Non-cardiac uptake and render cardiac SPECT study non-diagnostic. The *top image* is an example of cardiac study that has excess liver uptake that spills over into the inferior wall of the myocardium. The lower study is a ''ramp-filter artifact'' that is caused by the inconsistent views of the bowel activity, creating a drop in counts in the surrounding regions.

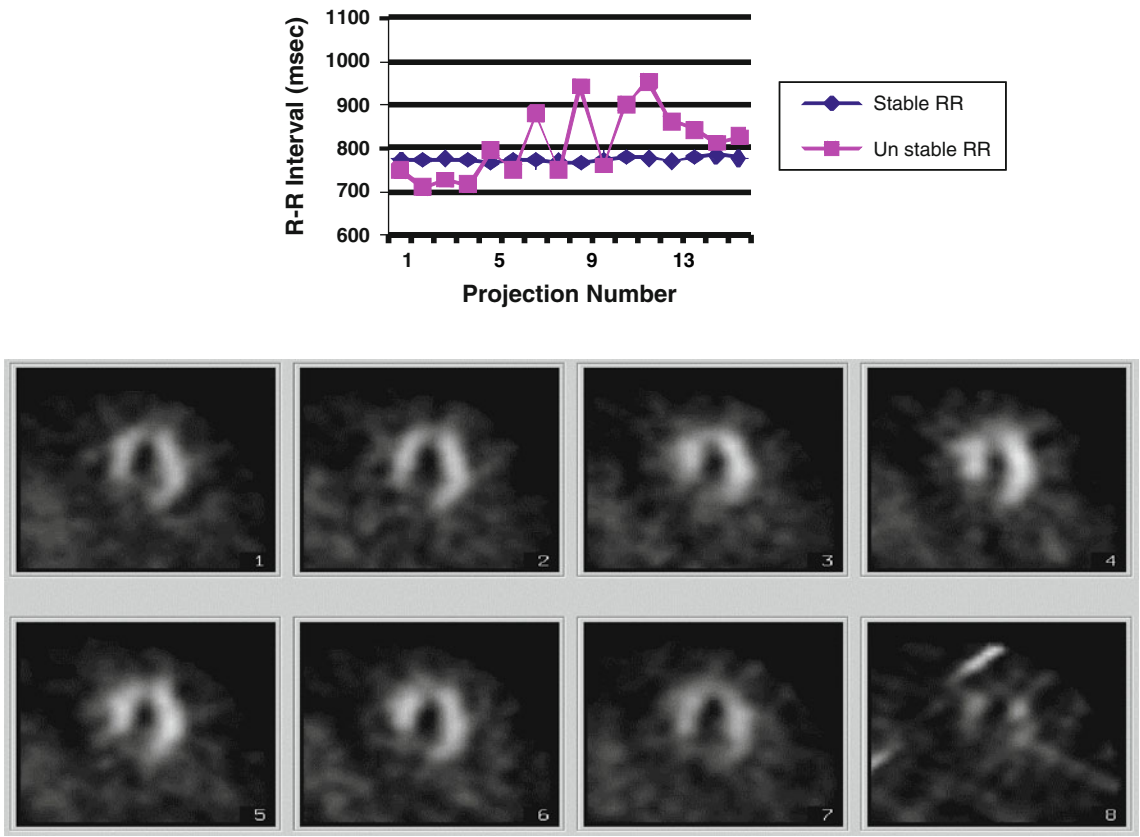


Figure 7. A poor ECG gate or heart rate variability can introduce a streaking artifact in the images. When these artifacts are severe enough, if can also impact the perfusion data. For those systems that do not allow for a separate non-gate buffer image, ECG gating may not be possible.

One of the major limitations of these systems is that motion correction programs are typically not available. Motion artifacts on these systems will have a less predictable result, not only introducing perfusion artifacts but also distorting the shape of the myocardium (see Figure 9). Acquisition times should be kept low to avoid patient motion and the technologist should routinely inspect the post acquisition data for evidence of patient motion and re-scan the patient when excessive motion is observed.

Post Acquisition Corrections

SPECT image motion correction algorithms. The most common correction applied in SPECT is motion correction. These algorithms take advantage of the correlation between the angles and the time the projection is acquired. Though it is possible to manually shift the individual frames of the projection data, most motion correction algorithms employ an automatic motion correction algorithm. One such algorithm utilizes a pattern matching and segmentation algorithm to identify the motion of the myocardium.[54] Another algorithm uses a projection, reconstruction, reprojection algorithm for iteratively developing the patient motion model.[55]

Automatic motion correction algorithms can produce erroneous results because of non-cardiac uptake, coronary disease patterns, and complicated patient motion. The result is incorrectly motion corrected datasets that can introduce more artifacts than the original dataset. A study of motion correction algorithms demonstrated the automatic motion correction algorithms can introduce as many artifacts as they correct,[11] and therefore automatic correction routines should be carefully inspected to confirm the motion correction is applied correctly.

Attenuation & scatter correction (SPECT). One of the most significant sources on diagnostic uncertainty in cardiac SPECT is soft tissue attenuation and photon scatter. One solution that has been utilized is to use gender-specific normal files to account for these gross variations in uniformity, such as breast and diaphragm attenuation.[56-60] However, patient to patient variability of the attenuation pattern, due to patient size, breast size, abdominal fat, elevation of the diaphragm, etc. limit the usefulness of these ''one-size-fits-all'' approaches to compensating for attenuation.

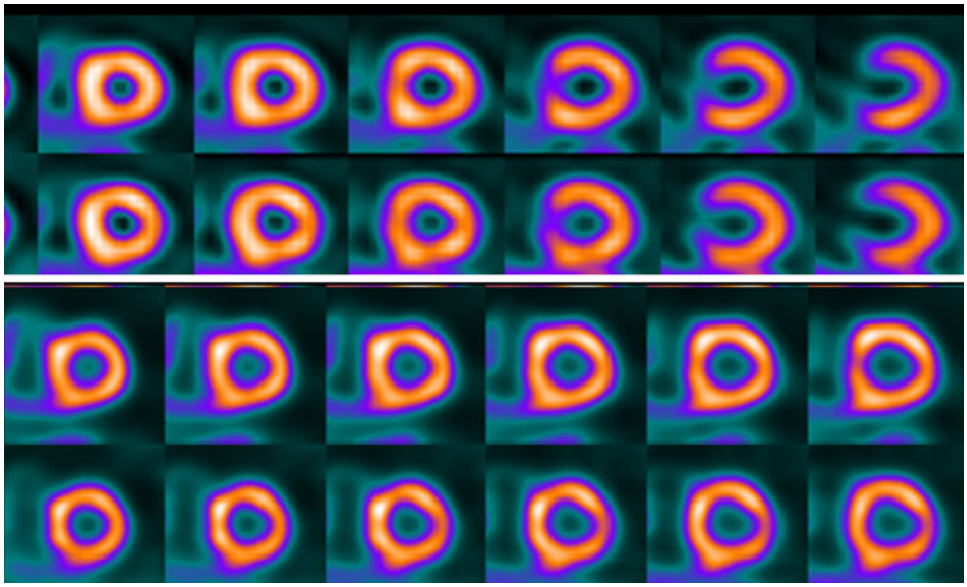


Figure 8. Reconstruction-based resolution recovery can produce an improvement in the resolution and signal to noise in structures diminished by the partial volume effect.

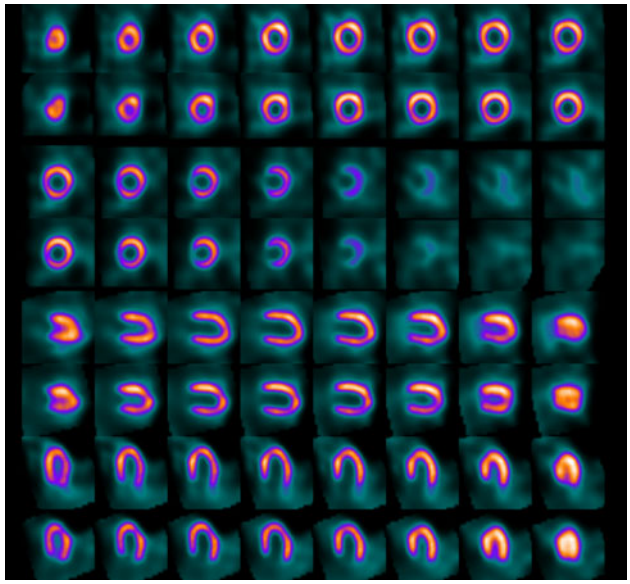


Figure 9. Rest/stress perfusion study acquired using a DSPECT system on a patient that moved during the study, distorting the shape of the myocardium.

Tung et al[61] proposed a method for using a system of line sources to obtain a patient-specific attenuation map for compensating for attenuation. This map is applied to an iterative reconstruction algorithm to compensate for photon losses due to attenuation. This approach has the advantage of obtaining a patient-specific attenuation map without significantly increasing radiation dosage and could be acquired simultaneously to the emission data. The one limitation of this approach was the transmission data could be of poor quality; however, iterative reconstruction of the line source data could significantly improve the quality of the reconstructed transmissions maps.[62]

Another approach is to acquire transmission data using a x-ray-based computed tomography.[63] SPECT-CT systems can employ a conventional multi-slice CT system, capable of acquiring high resolution, diagnostic quality data and/or low dose, attenuation correction-specific x-ray tubes. Though CT-based transmission maps can be of high quality, they can be misregistered

with the emission data and have the same challenges with patient breath holding observed with PET/CT imaging.

Photon scatter in SPECT can also impact the final image by reducing image contrast and creating spillover from non-cardiac structures into the myocardium. The most common approach to removing photon scatter is to acquire a second or third image window near the primary photo-peak energy window. This scatter image can then be used to subtract the scatter component from the primary image.[64] These adjacent energy window techniques can improve overall image contrast; however, they are not accurate enough to improve edge detection. More sophisticated multi-energy approaches[65,66] and model-based approaches[67] can also be used to improve the scatter correction model and edge detection.

PET AND PET/CT QC, ARTIFACTS, AND CORRECTIONS

QC of PET and PET/CT Systems

In contrast to SPECT, PET relies on the recording of two photon events in a ring of detectors to create a single true event. This places new requirements on the QC procedures for these systems. When a detector is calibrated incorrectly, it affects performance *in combination* with every other detector in the camera. Therefore, the impact of one poorly performing detector can extend well beyond the location of that detector, making it imperative that systems are checked daily and routine maintenance is performed regularly to insure optimal system performance.

There are four major QC steps that are necessary to maintain a PET system[36]:

(1) Daily Blank Scan: Used for testing the uniformity of the system and for normalizing attenuation maps from line source, ''dedicated PET,'' systems.

(2) Normalization: This is used to correct to the inherent differences in sensitivities of the slices, in particular, the edges of the field of view are less sensitive than at the center (Figure 10). Artifacts from a poor normalization can be recognized as linear streaks horizontally in the images (Figure 11). The normalization scan can be performed either by the user or the camera vendor. Any time the normalization scan is updated, the user should closely inspect the normalization scan and the blank scan should also be updated using the new normalization.

(3) Bucket setup or tube balancing: The sensitivity of each tube can be influenced by temperature, the time the system has been on and if there has either been a power surge or sudden power loss. The daily blank scan must be inspected each day to identify if the tubes need re-balancing and a bucket setup should be run by service regularly. A bucket problem can be identified as a dark ''block'' in the rotating sinogram data (Figure 12).

(4) Line source activity (dedicated PET only): For systems employing line source attenuation, it is important that line sources have adequate activity. If the source strength drops below a threshold, the system will not be able to reconstruct the transmission map. Users should regularly inspect the quality of their transmission data and replace rods according to their manufacturers' recommendations.

The blank scan is the equivalent of the uniformity scan for SPECT and also the attenuation reference scan if attenuation correction is used. This scan is typically performed overnight using a line sources or a cylindrical flood to expose the entire system. The daily blank scan should be inspected daily both visually and quantitatively prior to any clinical scanning. If a detector fails this QC step, the scanner should not be used until the system is either recalibrated by the user or serviced.

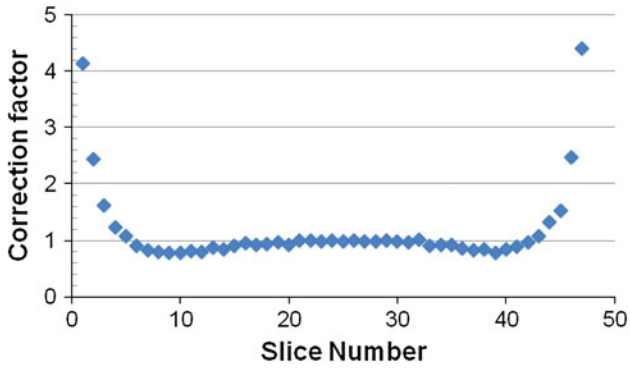


Figure 10. The normalization for a PET scan accounts for the variability in system sensitivity between transverse slices.

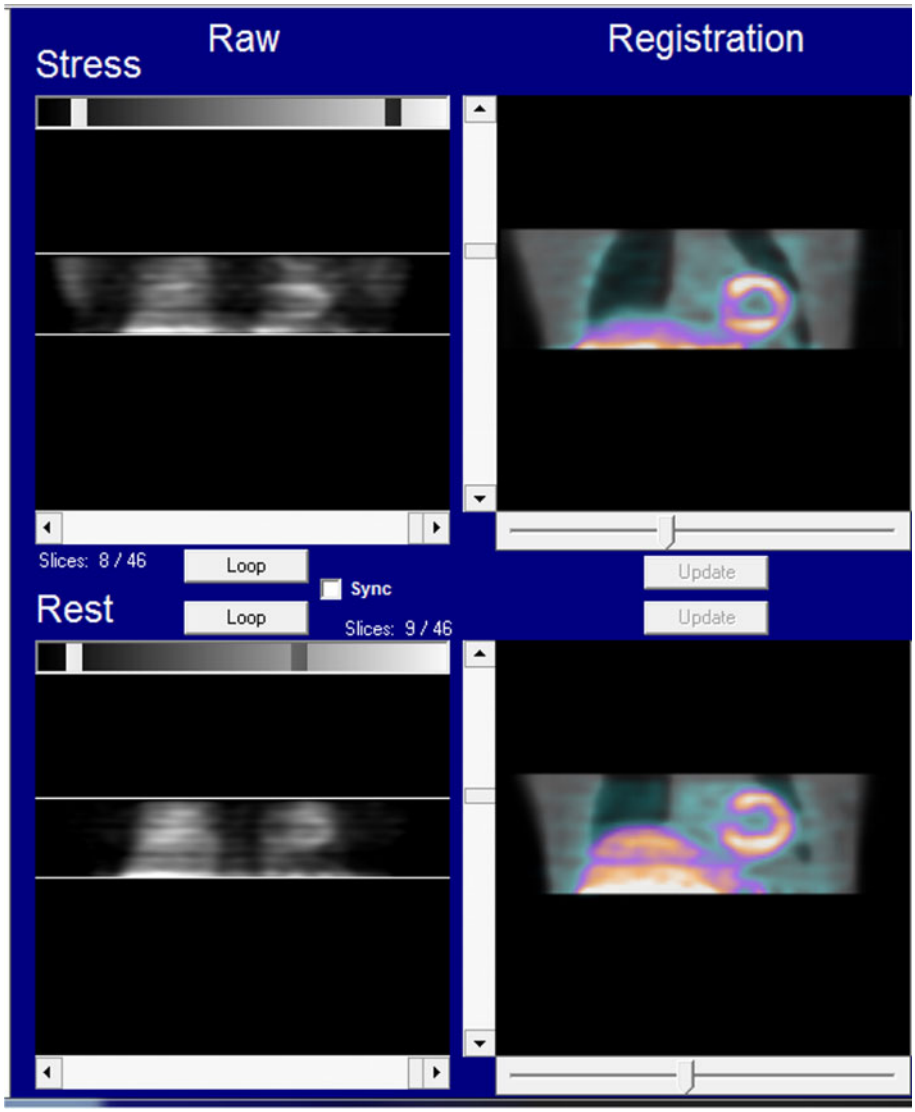


Figure 11. Poor normalization in PET will result in a streaking through the images. Correction of this can only be accomplished by reacquiring the normalization file.

Hybrid imaging systems that use CT for attenuation correction have additional QC requirements. Systems must be checked for high and low contrast resolution, uniformity, noise, CT number accuracy, and slice thickness.[36] These measurements are typically performed automatically by the system, but the results of these tests should be checked daily to insure that they meet manufacturer's recommendations.

PET and PET/CT Acquisition-Related Artifacts and Corrections

Misregistration. One of the most significant sources of artifact in cardiac PET is misregistration of the transmission and emission datasets in space. This artifact is a result of the sequential acquisition of the emission and transmission datasets. Specifically, when a patient moves between these two scans, the attenuation correction cannot be properly applied without correcting for the patient movement (Figure 13).

In a study of 1,177 patients, Loghin et al[68] reported that 21% of all resting cardiac PET studies had detectable misregistration artifacts, and in a separate study it was observed as little as 1 cm can introduce a 10% drop in lateral wall counts.[69] Gould et al[70] examined the effect on misregistration on image interpretation and demonstrated as many as 40% of all PET/CT studies would have a change in diagnosis after misregistration correction was applied. Imaging guidelines recommended that all cardiac PET studies be routinely

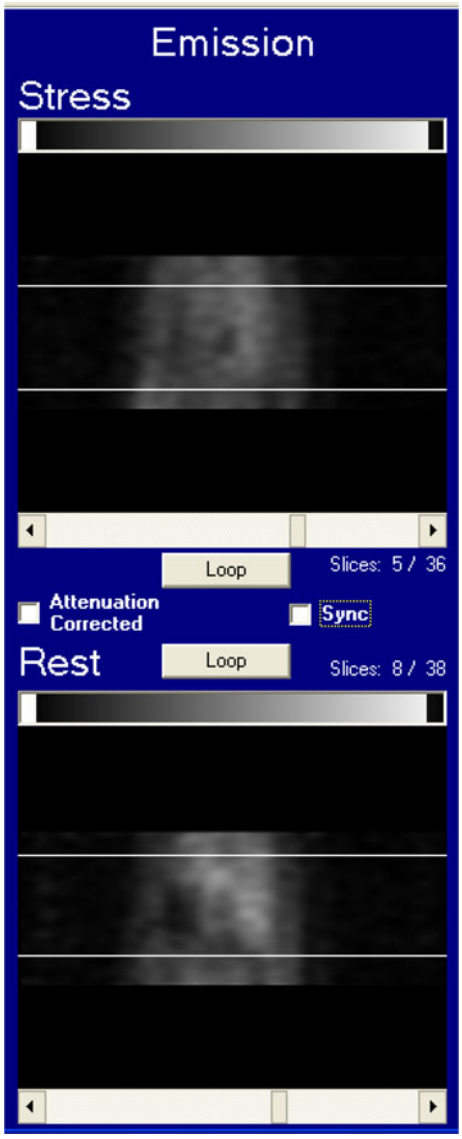


Figure 12. Tube failure will result in a *dark block* in the rotating images.

examined for misregistration and corrected whenever possible.[2]

By far the most common technique for misregistration correction is a rigid shift of the transmission and emission datasets.[71] The user can interactively visualize an overlay of the transmission and emission data and move one of the datasets relative to the other until a satisfactory positioning is obtained. These offsets can then be used to re-reconstruct the tomographic data.

Intrascan motion. Another potential source of interpretive uncertainty is intrascan motion from respiration, coughing, talking, or patient motion.[72] This motion is different than misregistration because all of the motion is confined to the emission dataset. Unlike SPECT imaging, intrascan motion cannot be seen by reviewing the rotating projection, or sinogram data. To detect intrascan motion, the clinician must carefully inspect the reconstructed data for losses in image fidelity. For those patients with a single movement the intrascan motion artifact will appear as two matching image defects, 180° apart (Figure 14). This can be complicated if a patient moves more than once, as the resulting image can appear more uniformly blurred.

At this time, there are no commercially available intrascan motion correction algorithms; however, there are several investigators exploring approaches that incorporate dynamic list-mode data.[73] Because of this, care should be taken to insure patients are still and awake throughout the study.

3D scatter and prompt gamma correction. Interest in lower patient dosages and higher count density has increased interest in imaging without septa (3D only mode). This has the potential of increasing the sensitivity of the system by a factor of 2-5 times.[74] One of the challenges of 3D imaging is the increased photon scatter component requires accurate scatter compensation. The most common approach utilizes a model-based approach to estimate the scatter component.[75-77] These methods perform well for N-13 and F-18 studies, however, they must be modified to account for the additional, 776 keV prompt gamma in 13% of Rb-82 decay events.[78]. When these photons are not accounted for, the over-correction for scatter can reduce specificity from 90% to 22%.[78]

PET/CT-specific artifacts. Cardiac PET studies can be corrected for attenuation either using line source or a CT-based transmission study using a relatively short acquisition time, <2 minutes.[79,80] Despite the fact CT studies have generally more counts than line source attenuation maps; CT-specific artifacts can make PET/CT more challenging than line source attenuation correction.[70] The two major sources of potential artifacts in PET/CT are: improper patient breath holds during the CT and metallic implants.

There are three common techniques for the breath hold for CT attenuation correction:

(1) Cine CT/free breathing: The CT scanner performs multiple CT scans over the same point to obtain an average diaphragm position. Tube current is also reduced to minimize radiation. This creates an averaging effect similar to dedicated PET.[81]
(2) End-expiration breath hold: The patient is instructed to hold their breath after breathing out to achieve a best positioning of the diaphragm. This differs from end-inspiration breathholding, which distort the shape of the lungs and lowers the diaphragm.[82,83]

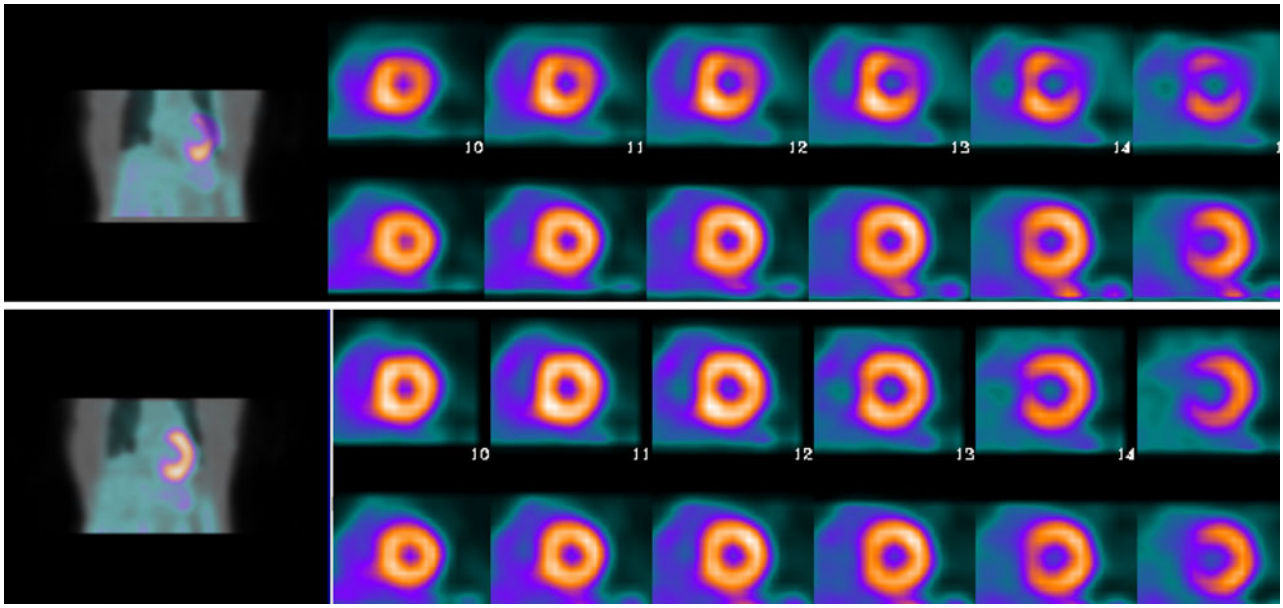
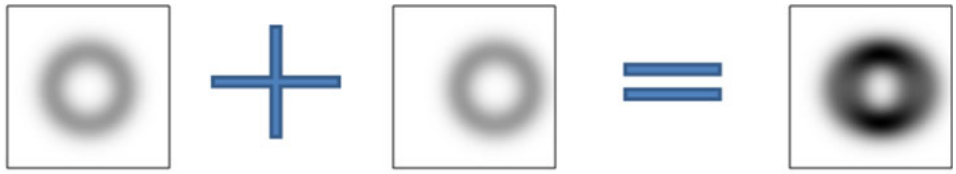


Figure 13. The *top rows* demonstrate a study with 1 cm of misregistration between the emission and transmission datasets. The *bottom row* demonstrates the reconstruction with the proper registration.



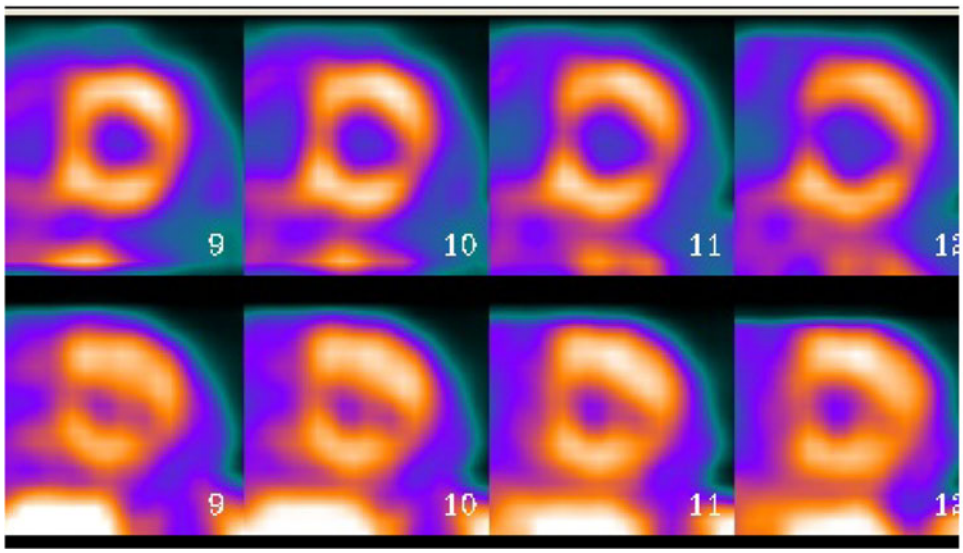


Figure 14. Intrascan motion is an un-correctable artifact cause by a patient moving during the emission phase of cardiac PET image. The *top image* is an example of the addition of two short axis studies that have been shifted by 15 mm relative to each other, producing two artifacts, 180° from each other. *Below* is a patient example of lateral intrascan motion.

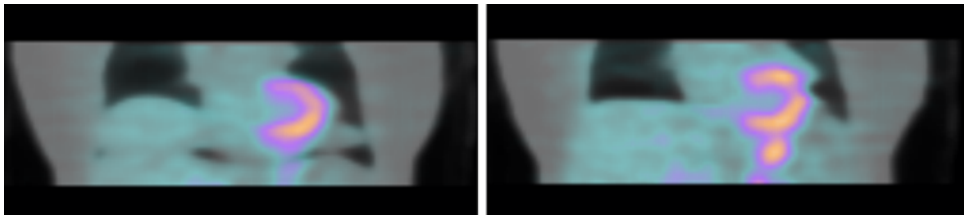


Figure 15. Two examples of breathing artifacts during a free breathing protocol. The *left image* is an example of the patient taking a deep breath during the middle of the scan resulting in the liver being imaged in two different places. On the *right* is an example of a smaller breath, leading to a choppy boundary between the mediastinum and the lung.

(3) Shallow-free breathing: The patient is allowed to breathe throughout the CT scan; however, they are instructed to take small breaths.[84]

In principle, all of these techniques can obtain good quality transmission scans; however, some scanners may be incapable of performing the desired CT scan.

Cine CT/free breathing: This technique is very straight forward to apply for compatible scanners because it requires little effort on the part of the patient to acquire this type of CT map. The drawback is that leaving the patient in the scanner for up to 1 minute could potentially deliver an unacceptably high radiation dosage, unless a very low tube current is possible (<8 mAs). It may also be necessary to employ a CT reconstruction algorithm that is specific to the Cine CT/free breath protocol. Users should consult with their PET/CT vendor to confirm that their scanners can deliver correct x-ray tube settings and reconstruction to perform this protocol.

End-expiration breath hold: This technique relies on training the patient prior to the study on how to hold their breath during the end-expiration pause of the breath cycle. During normal breathing, the diaphragm spends most of its time in a light expiration phase, with short cycles between inspiration and expiration movement. This protocol attempts to extend the time of the expiration pause to allow for the CT scan. For most multi-slice systems (≥16 slices) the duration of the breath hold is <10 seconds. However, breath holds for 2 and 4 slice systems can exceed 20 seconds, making them prohibitively long for many cardiac patients.

It is essential in performing the end-expiration breath hold that the patient practice the breath hold with the technologist or nurse prior to being placed in the PET/CT scanner.

Shallow-free breath: The shallow-free breath protocol can be employed on most systems. The protocol encourages the patient to maintain a light breathing respiratory cycle to minimize diaphragm motion. This technique can produce good quality transmission maps; however, if the patient cannot maintain shallow breathing or if they take a breath at the wrong time, the resulting transmission map can be un-usable (Figure 15). If the shallow-free breath protocol is used, the technologist must review the transmission study immediately after the CT scan and repeat the CT scan if necessary.

Metal artifacts. Patients with implanted metal devices, surgical clips, wires, etc. can be challenging to image with PET/CT because of the high efficiency of metals to absorb x-rays. Metal objects influence the attenuation of x-rays between 10 keV and 100 keV because of high attenuation of metal due to the photoelectric effect. However at the energies of positron annihilations (511 keV), the attenuation due to the photoelectric effect is small in relation to the more dominant Compton scatter effects. The presence of these metal objects near the heart can introduce artifacts in upwards of 50% of patients.[85] However, the presence of metallic objects in the field of view of the heart should not be considered necessarily a contraindication to cardiac PET/CT imaging, when appropriate corrections are applied.[80,85]

Several approaches have been proposed for removing the influence of metallic objects from the CT attenuation maps.[80,86] One approach to correcting for this is a simple replacement or segmentation of the transmission maps of water attenuation values in regions with known metallic artifacts is sufficient to correct CT attenuation maps that are influenced by metal.[86] Another algorithm utilizes a thresholding and reprojection reconstruction technique which offers a more quantitative approach to remove the influence of metallic objects.[80]

QC of absolute blood flow measurements. Absolute blood flow measurements using myocardial perfusion PET are rapidly gaining acceptance because of their ability to assess normality and identify disease in challenging patients.[87-89] These techniques rely on a dynamic acquisition of the tracer kinetics and a model for tracer transport from the blood into the cell. A simplistic, yet complete way of modeling the transport of radiotracer from the blood pool into the myocardium is by using a two-compartment model.[90] The

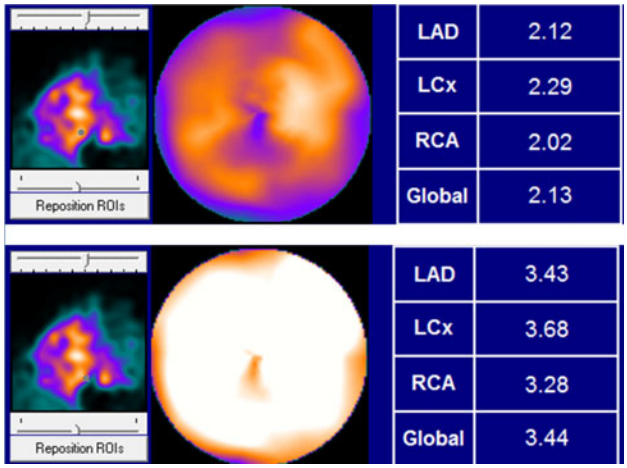


Figure 16. Incorrect positioning of the blood pool ROI can lead to significant changes in the calculated absolute perfusion (units are in mL/mg/minute).

model is characterized by three parameters describing the movement of tracer between the various compartments: (1) K1 represents the initial tracer uptake, (2) k2 represents the tracer washout from the myocardium, and (3) k3 reflects the retention of the tracer in the myocardium (see Figure 14). This model can be simplified to a single compartment model encompassing the blood and the myocardial partition.[91,92]

To calculate the absolute blood flow, it is necessary to obtain a dynamic series of measurements of the blood pool concentration and the myocardial uptake. This can be obtained as either a dynamic framed data set or a list-mode study. Unlike perfusion PET, these dynamic acquisitions must be started before the infusion of the PET tracer. Ideally, the first dynamic frame is free of any counts from the radiotracer. Beginning the acquisition late can lead to an underestimation of the blood pool concentration and thereby an overestimation of the myocardial blood flow. To avoid these quantitation errors, the dynamic data must be inspected for:

(1) Minimal counts in the first frame.
(2) Early blood pool stage clearly visualized.
(3) Sufficient counts in the frames containing the uptake information.
(4) Adequate blood pool clearance in the later stages of the dynamic study.

Reconstruction of the dynamic studies requires utilizing a reconstruction algorithm that maintains the absolute concentration (or at the very least the relative relationship between reconstructed counts and activity).

Accurate measurement of the myocardial uptake can be challenging due to the effect of spillover from the blood pool into the myocardium and blurring. Because of this, a partial volume correction must be applied to obtain an accurate estimate of the myocardial uptake.[92,93] These partial volume corrections are very sensitive to the filtering of the image and therefore adjustments to the image filtering must always be done in accordance with the quantitation software used.

In addition to the accurate location of the myocardial boundary, it is essential that the blood pool ROI is appropriately centered over the target structure (either the left atrium or left ventricle). Inaccurate positioning of the blood pool ROI can cause quantitative inaccuracies in the flow calculation and potentially mask true disease (Figure 16).

SUMMARY

Avoidance of imaging artifacts, whenever possible and correcting for artifacts when necessary is essential for maintaining the diagnostic accuracy of an imaging test. The best strategy for avoiding artifacts is:

(1) Establish a quality maintenance program for the instrumentation.
(2) Create written imaging protocol, train all relevant personnel on the application of the protocol and provide feedback as to the adherence to the protocol.
(3) Acquire data with the intention of *not* using post acquisition correction algorithms
(4) Staying with the patient to insure patient compliance with the imaging protocol
(5) Apply post acquisition corrections sparingly.
(6) Obtaining and maintaining laboratory accreditation to insure the quality improvement program in place meets national guidelines.

Technologists and clinicians should not feel that there is a necessary trade-off between quality and laboratory

efficiency. Poor quality images take significantly more time to process, interpret, and report than high quality images. If the shortest distance between two points is a straight line, the longest distance is the short cut.

References

1. Thomas A, Holly TA, Abbot BG, Mallah MA, Calnon DA, Cohen MC, et al. Single photon emission computed tomograph. J Nucl Cardiol 2010;17:941-73.
2. Dilsizian V et al. ASNC imaging guidelines for nuclear cardiology procedures: PET myocardial perfusion and metabolism clinical imaging. J Nucl Cardiol 2009;16(4):651. http://www.asnc.org/imageuploads/ImagingGuidelinesPETJuly2009.pdf.
3. International Atomic Energy Agency. Radiological Protection for Medical Exposition to Ionizing Radiation. IAEA Safety Standard; 2002: RS-G-15.
4. Cerqueira MD, Allman KC, Ficaro EP, Hansen CL, Nichols KJ, Thompson RC. American Society for Nuclear Cardiology Information Statement: Recommendations for reducing radiation exposure in myocardial perfusion imaging. J Nucl Cardiol 2010;17:709-18.
5. SNM position statement on dose optimization for nuclear medicine and molecular imaging procedures, June 2012. http://interactive.snm.org/docs/SNM_Position_Statement_on_Dose_Optimization_FINAL_June_2012.pdf. Accessed 11 June 2012.
6. Friedman J, Berman DS, Van Train K, et al. Patient motion in thallium-201 myocardial SPECT imaging: An easily identified frequent source of artifactual defect. Clin Nucl Med 1988;13:321-4.
7. DePuey EG, Garcia EV. Optimal specificity of thallium-201 SPECT through recognition of imaging artifacts. J Nucl Med 1989;30:441-9.
8. Friedman J, Van Train K, Maddahi J, et al. ''Upward creep'' of the heart: A frequent source of false-positive reversible defects during thallium-201 stress-redistribution SPECT. J Nucl Med 1989;30:1718-22.
9. Sorrell V, Figueroa B, Hansen CL. The ''hurricane sign'': Evidence of patient motion artifact on cardiac single-photon emission computed tomographic imaging. J Nucl Cardiol 1996;3:86-8.
10. Wheat JM, et al. Incidence and characterization of patient motion in myocardial perfusion SPECT: Part 1. J Nucl Med Technol 2004;32(2):60-5.
11. Botvinick EH, Zhu YY, O'Connell WJ, Dae MW. A quantitative assessment of patient motion and its effect on myocardial perfusion SPECT images. J Nucl Med 1993;34:303-10.
12. Massardo T, Jaimovich R, Faure R, Muñoz M, Alay R, Gatica H. Motion correction and myocardial perfusion SPECT using manufacturer provided software. Does it affect image interpretation? Eur J Nucl Med Mol Imaging 2010;37(4):758-64.
13. DePuey EG. How to detect and avoid myocardial perfusion SPECT artifacts. J Nucl Med 1994;35:699-702.
14. 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.
15. Picano E, Bedetti G, Varga A, Cseh E. The comparable diagnostic accuracies of dobutamine-stress and dipyridamole-stress echocardiographies: A meta-analysis. Coron Artery Dis 2000;11:151-9.
16. Duvernoy CS, Ficaro EP, Karabajakian MZ, Rose PA, Corbett JR. Improved detection of left main coronary artery disease with attenuation-corrected SPECT. J Nucl Cardiol 2000;7:639-48.
17. Hendel RC, Berman DS, Cullom SJ, Follansbee W, Heller GV, Kiat H, et al. Multicenter clinical trial to evaluate the efficacy of correction for photon attenuation and scatter in SPECT myocardial perfusion imaging. Circulation 1999;99:2742-9.
18. Ficaro EA, Fessler JA, Shreve PD, Kritzman JN, Rose PA, Corbett JR. Simultaneous transmission/emission myocardial perfusion tomography: Diagnostic accuracy of attenuation corrected Tc-99m sestamibi single-photon emission computed tomography. Circulation 1996;93:463-73.
19. Cullom SJ, Case JA, Bateman TM. Attenuation correction of cardiac SPECT: Clinical and developmental challenges. J Nucl Med 2000;41:860-2.
20. Corbett JR, Ficaro EP. Clinical review of attenuation-corrected cardiac SPECT. J Nucl Cardiol 1999;6:54-68.
21. Thompson RC, Heller GV, Johnson LL, Case JA, Cullom SJ, Garcia EV, et al. Value of attenuation correction on ECG-gated SPECT myocardial perfusion imaging related to body mass index. J Nucl Cardiol 2005;12:195-202.
22. Bateman TM, Heller GV, McGhie AI, Courter SA, Kennedy KF, Katten D, et al. Application of simultaneous Gd-153 line source attenuation correction to half-time stress only SPECT acquisitions: A multicenter clinical evaluation. J Am Coll Cardiol 2008;51(Suppl A):A171.
23. Heller GV, Bateman TM, Johnson LL, Cullom SJ, Case JA, Galt JR, et al. Clinical value of attenuation correction in stress-only Tc-99m sestamibi SPECT imaging. J Nucl Cardiol 2004;11:273-81.
24. Hendel RC, Corbett JR, Cullom SJ, DePuey EG, Garcia EV, Bateman TM. The value and practice of attenuation correction for myocardial perfusion SPECT imaging: A joint position statement from the American Society of Nuclear Cardiology and the Society of Nuclear Medicine. J Nucl Cardiol 2002;9:135-43.
25. Hendel RC. Attenuation correction: Eternal dilemma or real improvement? Q J Nucl Med Mol Imaging 2005;49:30-42.
26. Bateman TM, Heller GV, McGhie AI, et al. Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: Comparison with ECG-gated Tc-99m sestamibi SPECT. J Nucl Cardiol 2006;13:24-33.
27. Sampson UK, Limaye A, Dorbala S, et al. Diagnostic accuracy of rubidium-82 myocardial perfusion imaging with hybrid positron emission tomography/computed tomography (PET-CT) in the detection of coronary artery disease. J Am Coll Cardiol 2007;49:1052-8.
28. Hachamovitch R, Jonson JR, Hlatky MA, Cantagallo L, Johnson BH, Coughlan M, et al. The study of myocardial perfusion and coronary anatomy imaging roles in CAD (SPARC): Design, rationale, and baseline patient characteristics of a prospective, multicenter observational registry comparing PET, SPECT, and CTA for resource utilization and clinical outcome. J Nucl Cardiol 2009;16:935-48.
29. McArdel BA, Dowsley TF, deKemp RA, Wellis GA, Beanlands RS. Does Rubidium-82 PET have superior accuracy to SPECT perfusion imaging for the diagnosis of obstructive coronary disease? A systematic review and meta-analysis. J Am Coll Cardiol 2012;60:1828-37.
30. Schwartz R, Mixon L, Germano G, Chaudry I, Armstrong K, Mackin M. Gated SPECT reconstruction with zoom and depth dependent filter improves accuracy of volume and LVEF in small hearts. J Nucl Cardiol 1999;6:S17 (abstract).
31. Ezuddin S, Sfakianakis G, Pay I, Sanchez P. Comparative study to determine the effect of different zoom factors on the calculation of LVEF from gated myocardial perfusion SPECT with TL-201 and Tc-99m sestamibi in patients with small hearts. J Nucl Med 1999;40:169P (abstract).
32. Johnson KM, Johnson HE, Dowe DA. Left ventricular apical thinning as normal anatomy. J Comput Assist Tomogr 2009;33:334-7.
33. Haber SF, Derenzo SE, Uber D. Application of mathematical removal of positron blurring in positron emission tomography. IEEE Trans Nucl Sci 1990;37:1293-9.

34. Wassenaar R, deKemp RA. Characterization of PET partial volume corrections for variable myocardial wall thicknesses. IEEE Trans Nucl Sci 2006;53:175-80.
35. National Electronics Manufacturers Association. Performance Measurements of Gamma Cameras, NEMA NU 1-2007, Dec 2007.
36. The IAC Standards and Guidelines for Nuclear/PET Accreditation. Intersocietal Accreditation Commission, 2012. http://intersocietal.org/nuclear/standards/IACNuclearPETStandards2012.pdf. Accessed 15 August 2012.
37. Cooper JA, Neumann PH, McCandless BK. Effect of patient motion on tomographic myocardial perfusion imaging. J Nucl Med 1992;33:1566-71.
38. O'Connor MK, Kanal KM, Gebhard MW, Rossman PJ. Comparison of four motion correction techniques in SPECT imaging of the heart: A cardiac phantom study. J Nucl Med 1998;39:2027-34.
39. Van Dongen A, van Rijk PP. Minimizing liver, bowel and gastric activity in myocardial perfusion SPECT. J Nucl Med 2000;41:1315-7.
40. King MA, Tsui BMW, Pan T-S. Attenuation compensation for cardiac single-photon emission computed tomographic imaging; Part 1. Impact of attenuation and methods of estimating attenuation maps. J Nucl Cardiol 1995;2:513-24.
41. Vitola JV, Brambatti JC, Caligaris F, et al. Exercise supplementation to dipyridamole prevents hypotension, improves electrocardiogram sensitivity, and increases heart-to-liver activity ratio on Tc-99m sestamibi imaging. J Nucl Cardiol 2001;8:652-9.
42. Henzlova MJ, Cerqueria MD, Mahmarian JJ, Yao S-S. Stress protocols and tracers. J Nucl Cardiol 2006;13:e80-90.
43. Taillefer R, editor. Nuclear Cardiology. New York: McGraw Hill; 2004.
44. Sciagra R, Sotgia B, Boni N, Pupi A. Assessment of the influence of atrial fibrillation on gated SPECT perfusion data by comparison with simultaneously acquired nongated SPECT data. J Nucl Med 2008;49:1283-7.
45. Kadrmas DJ, Frey EC, Karimi SS, Tsui BM. Fast implementations of reconstruction-based scatter compensation in fully 3D SPECT image reconstruction. Phys Med Biol 1998;43:857-73.
46. Borges-Neto S, Pagnanelli RA, Shaw LK, et al. Clinical results of a novel wide beam reconstruction method for shortening scan time of Tc-99m cardiac SPECT perfusion studies. J Nucl Cardiol 2007;14:555-65.
47. Druz RS, Phillips LM, Chugkowski M, Boutis L, Rutkin B, Katz S. Wide-beam reconstruction half-time SPECT improves diagnostic certainty and preserves normalcy and accuracy: A quantitative perfusion analysis. J Nucl Cardiol 2011;18:52-61.
48. Venero CV, Heller GV, Bateman TM, et al. A multicenter evaluation of a new post-processing method with depth-dependent collimator resolution applied to full-time and half-time acquisitions without and with simultaneously acquired attenuation correction. J Nucl Cardiol 2009;16:714-25.
49. Gambhir SS, Berman DS, Ziffer J, et al. A novel high-sensitivity rapid-acquisition single-photon cardiac imaging camera. J Nucl Med 2009;50:635-43.
50. Hawman PC, Haines EJ. The cardiofocal collimator: A variable-focus collimator for cardiac SPECT. Phys Med Biol 1994;39:439-50.
51. D-SPECT User Manual, Sept. 2011, version MAN0003 Rev. G.1.
52. Esteves FP, Raggi P, Folks Rd, Zeidar Z, Askew WA, Rispler S, et al. Novel solid-state-detector dedicated cardiac camera for fast myocardial perfusion imaging: Multicenter comparison with standard dual detector cameras. J Nucl Cardiol 2009;16:927-34.
53. Garcia EV. Cardiac dedicated ultrafast SPECT cameras: New designs and clinical implications. J Nucl Med 2011;52:210-7.
54. Matsumoto N, Berman DS, Kavanagh PB, Gerlach J, Hayes SW, Lewin HC, et al. Quantitative assessment of motion artifacts and validation of a new motion-correction program for myocardial perfusion SPECT. J Nucl Med 2001;42:687-94.
55. Bai C, Maddahi J, Kindem J, Conwell R, Gurley M, Old R. Development and evaluation of a new fully automatic motion detection and correction technique in cardiac SPECT imaging. J Nucl Cardiol 2009;16:580-9.
56. 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.
57. Eisner RL, Tamas MJ, Cloninger K, Shonkoff D, Oates JA, Gober AM, et al. Normal SPECT thallium-201 bull's-eye display: Gender differences. J Nucl Med 1988;29:1901-9.
58. Germano G, Kavanagh PB, Waechter P, Areeda J, Van Kriekinge S, Sharir T, et al. A new algorithm for the quantification of myocardial perfusion SPECT. I: Technical principles and reproducibility. J Nucl Med 2000;41:712-9.
59. Ficaro EP, Lee BC, Kritzman JN, Corbett JR. Corridor4DM: The Michigan method for quantitative nuclear cardiology. J Nucl Cardiol 2007;4:455-65.
60. Grossman GB, Garcia EV, Bateman TM, et al. Quantitative Tc-99m sestamibi attenuation-corrected SPECT: Development and multicenter trial validation of myocardial perfusion stress gender-independent normal database in an obese population. J Nucl Cardiol 2004;11:263-72.
61. Tung C-H, Gullberg GT, Zeng GL, Christian PE, Datz FL, Morgan HT. Nonuniform attenuation correction using simultaneous transmission and emission converging tomography. IEEE Trans Nucl Sci 1992;39:1134-43.
62. Case JA, Hsu BL, Bateman TM, Cullom SJ. A Bayesian iterative transmission gradient reconstruction algorithm for cardiac SPECT attenuation correction. J Nucl Cardiol 2007;14:324-33.
63. Bocher M, Balan A, Krausz Y, Shrem Y, Lonn A, Wilk M, et al. Gamma camera mounted anatomical x-ray tomography: Technology, system characteristics and first images. Eur J Nucl Med 2000;27:619-27.
64. Ogawa K. Simulation study of triple-energy-window scatter correction in combined Tl-201, Tc-99m SPECT. Ann Nucl Med 1994;8(4):277-81.
65. Hsu B, Cullom SJ, Bateman TM, Case JA. Energy-based correction of I-123 high-energy contaminants degrading gamma camera uniformity. J Nucl Med 2006;47:193P.
66. Gagnon D, Todd-Pokropek A, Arsenault A, Dupras G. Introduction to holospectral imaging in nuclear medicine for scatter subtraction. IEEE Trans Med Imaging 1989;8:245-50.
67. Frey EC, Tsui BMW. A new method for modeling the spatially variant, object dependent scatter response function in SPECT. IEEE Nucl Sci Symp Med Imaging Conf Rec 1996;2:1082-6.
68. Loghin C, Sdringola S, Gould KL. Common artifacts in PET myocardial perfusion images due to attenuation-emission misregistration: Clinical significance, causes, and solutions. J Nucl Med 2004;45:1029-39.
69. Case JA, Heller GV, Cullom SJ, Hsu BL, Noble GL, Masse M, et al. Sensitivity of myocardial perfusion PET/CT imaging scan appearance on accurate transmission/emission registration. J Nucl Cardiol 2005;12:S117.
70. Gould L, Pan T-S, Laghin C, Johnson NP, Guha A, Sdringola S. Frequent diagnostic errors in cardiac PET/CT due to misregistration of CT attenuation and emission PET images: A definite analysis of causes, consequences and corrections. J Nucl Med 2007;48:1112-21.
71. Martinez-Moller A, Souvatzoglou M, Navab N, Schwaiger M, Nekolla SG. Artifacts from misaligned CT in cardiac perfusion

PET/CT studies: Frequency, effects, and potential solutions. J Nucl Med 2007;48:188-93.
72. Livieratos L, Rajappan K, Stegger L, Schafers K, Bailey DL, Camici PG. Respiratory gating of cardiac PET data in list-mode acquisition. Eur J Nucl Med Mol Imaging 2006;33:584-8.
73. Woo J, Cheng V, Dey D, Lazewatzky J, Ramesh A, Hayes S, et al. Automatic 3D registration of dynamic stress and rest (82)Rb and flurpiridaz F 18 myocardial perfusion PET data for patient motion detection and correction. Med Phys 2011;38: 6313-26.
74. Townsend DW. From 3D positron emission tomography to positron emission tomography/computed tomography: What did we learn? Mol Imaging Biol 2004;6:275-90.
75. Ollinger JM. Model-based scatter correction for fully 3D PET. Phys Med Biol 1996;41:153-76.
76. Werling A. Model-based scatter correction for positron emission tomography (in German). Med Phys 2002;29:105.
77. Watson C, Newport D, Casey M, DeKemp R, Beanlands R, Schmand M. Evaluation of simulation-based scatter correction for 3-D PET cardiac imaging. IEEE Nucl Sci Symp Conf Rec 1997;44:90-7.
78. Esteves FP, Nye JA, Khan A, Folks RD, Raghuveer KH, Garcia EV, et al. Prompt-gamma compensation in Rb-82 myocardial perfusion 3D PET/CT. J Nucl Cardiol 2010;17:247-53.
79. Kinahan PE, Townsend DW, Beyer T, Sashin D. Attenuation correction for a combined 3D PET/CT scanner. Med Phys 1998;25:2046-53.
80. Hsu BL, Case JA, Moser KW, Bateman TM, Cullom SJ. Reconstruction of rapidly acquired Germanium-68 transmission scans for cardiac PET attenuation correction. J Nucl Cardiol 2007;14:706-14.
81. Alessio AM, Kohlmyer S, Branch K, Chen G, Caldwell J, Kinahan P. Cine CT for attenuation correction in cardiac PET/CT. J Nucl Med 2007;48:794-801.
82. de Juan R, Seifert B, Berthold T, von Schulthess GK, Goerres GW. Clinical evaluation of a breathing protocol for PET/CT. Eur Radiol 2004;14:1118-23.
83. Beyer T, Antoch G, Blodgett T, Freudenberg LF, Akhurst T, Mueller S. Dual-modality PET/CT imaging: The effect of respiratory motion on combined image quality in clinical oncology. Eur J Nucl Med Mol Imaging 2003;30:588-96.
84. Goerres GW, Kamel E, Heidelberg TN, Schwitter MR, Burger C, von Schulthess GK. PET-CT image co-registration in the thorax: Influence of respiration. Eur J Nucl Med Mol Imaging 2002;29:351-60.
85. DiFilippo FP, Brunken RC. Do pacemaker leads and ICDs cause metal-related artifact in cardiac PET/CT. J Nucl Med 2005; 46:436-43.
86. Abdoli M, Dierckx RAJO, Zaidi H. Metal artifact reduction strategies for improved attenuation correction in hybrid PET/CT imaging. Med Phys 2012;39:3343-61.
87. Di Carli M, Czernin J, Hoh CK, Gerbaudo VH, Brunken RC, Huang SC, et al. Relation among stenosis severity, myocardial blood flow, and flow reserve in patients with coronary artery disease. Circulation 1995;91:1944-51.
88. Ziadi MC, deKemp RA, Williams K, Guo A, Renaud JM, Chow BJW, et al. Does quantification of myocardial flow reserve using rubidium-82 positron emission tomography facilitate detection of multivessel coronary artery disease? J Nucl Cardiol 2012;19:670-80.
89. Rader VJ, Courter SA, Case JA, Kennedy KF, Bateman TM. Prevalence and correlates of impaired myocardial blood flow reserve in patients with normal myocardial perfusion rubidium-82 positron emission tomography. Circulation 2010;122:A14503.
90. Hutchins GD, Schwaiger M, Rosenspire KC, Krivokapich J, Shelbert H, Kuhl DE. Noninvasive quantification of regional blood flow in the human heart using N-13 ammonia and dynamic positron emission tomographic imaging. J Am Col Cardiol 1990;5:1032-42.
91. Yoshida K, Mullani N, Gould KL. Coronary flow and flow reserve by PET simplified for clinical applications using rubidium-82 or nitrogen-13-ammonia. J Nucl Med 1996;37:1701-12.
92. Lortie M, Beanlands RS, Yoshinaga K, Klein R, DaSalvia JN, deKemp RA. Quantification of myocardial blood flow with ^{82}Rb dynamic PET imaging. Eur J Nucl Med Mol Imaging 2007;34: 1765-74.
93. Hutchins GD, Caraher JM, Raylman RR. A region of interest strategy for minimizing resolution distortions in quantitative myocardial PET studies. J Nucl Med 1992;33:1243-50.