

The Road to Quantitation of Regional Myocardial Uptake of Tracer

Myocardial perfusion SPECT has been established as a noninvasive method for evaluation of coronary artery disease. For semiquantitative analysis, myocardial activity is conventionally measured relative to the region of most intense uptake. On the other hand, the absolute measurement of megabecquerels of tracer per gram of tissue has been an elusive goal. For this purpose, several factors—including limited spatial resolution, cardiac motion, Compton scatter, and photon attenuation—may preclude a linear relationship between the observed counts and the true tracer distribution (1–3).

When a photon undergoes Compton scattering through interaction with an electron, it changes direction and loses energy. Scatter compensation requires estimation of the number of scattered photons in each pixel of the image. One widely used method for scatter compensation is the energy window-based method with use of either a second energy window at lower energy than the photopeak window (4) or a triple-energy window at the lower and the higher energy windows (5). A fraction of this window is subtracted from the photopeak window. Other methods for scatter compensation include the deconvolution technique and the reconstruction-based technique (3).

Attenuation creates significant artifacts on SPECT images and, thus, obviates tracer distribution. ^{99m}Tc -labeled perfusion tracers provide less attenuation artifacts than ^{201}Tl because of

emission of higher energy photons, but ^{99m}Tc -labeled tracers still create a large amount of artifacts. The most common effects are artifacts associated with breast attenuation in women and diaphragmatic attenuation in men. Although clinicians are aware of these artifacts, in general, such artifacts may create artifactual perfusion abnormalities or even mask the severity of perfusion abnormalities. Thus, reliable attenuation compensation methods are required for SPECT perfusion imaging.

The easiest and most common methods for attenuation correction are the prereconstruction method of Sorenson (6) and the postreconstruction method of Chang (7). Both methods assume that the attenuation is homogeneous within the body. These corrections are quite effective in liver or brain SPECT; however, this assumption is incorrect in the thorax, where quite different attenuation sources exist, such as in the lung (air), mediastinum, and bone.

Transmission scanning is required to create an accurate attenuation map in areas with nonhomogeneous attenuation. Over several years, a variety of SPECT equipment has been designed for transmission imaging with SPECT scanners using a single line source, flood source, or scanning line sources (8–12). A canine study by Li et al. (13) showed that the distribution on the SPECT images correlated with well counter values with nonuniform attenuation correction, whereas the attenuation effects may be overestimated with uniform attenuation correction. Several studies have shown the advantages of SPECT perfusion after attenuation correction for better diagnosis of coronary artery disease by minimizing the false-positive rate. Multicenter clinical trials showed significant improvement in the diagnostic accuracy

for detecting coronary artery disease with attenuation and scatter correction (14). The major limitations of attenuation correction using radioactive tracers are preparation of radionuclides for transmission imaging and image noise after attenuation correction with transmission images. Several trials have been performed to reduce image noise using a variety of reconstruction algorithms (3).

Another idea is transmission images using x-ray imaging for attenuation correction (15,16). The x-ray images produce a much higher photon flux and higher quality images than do the radionuclide sources. A recently introduced commercial CT–SPECT system has focused on combined imaging, which has several advantages. CT images and SPECT images are obtained sequentially (although not simultaneously) by moving the patient table without need of major patient registration. Such combined study represents a fusion of anatomic information with functional or biochemical information (or both) in a manner that answers specific diagnostic and therapeutic questions (17). This image fusion may minimize the limitation of poor spatial resolution of SPECT images. In addition, CT attenuation maps can be used for attenuation correction for SPECT quantitation. Furthermore, precise anatomic information may be used for partial-volume correction.

In this issue of *The Journal of Nuclear Medicine*, Da Silva et al. (18) applied the CT–SPECT imaging system for absolute quantitation of regional myocardial uptake of perfusion tracer with SPECT. They used CT images for attenuation correction. In addition, they have attempted to correct partial-volume errors on a pixel-by-pixel basis using mathematic modeling by calculating the geometric extent of

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the myocardium. The authors concluded that the pixel intensities after these corrections and calibration correlated well with the ex vivo activity concentration in megabecquerels per gram of excised porcine myocardium. To our knowledge, this is the first report of absolute quantitation of regional myocardial uptake of the perfusion tracer after corrections of photon attenuation, scatter, and partial-volume effect using CT images.

On the other hand, additional factors must be considered for quantitation of the tracer uptake. Cardiac motion and wall thickening seem to be important factors for quantitation of the tracer in vivo. Although gated acquisition is available for both SPECT and CT imaging in most recent instruments, this system cannot provide gated CT images for superimposition. Da Silva et al. (18) did not use gated SPECT images in this study. The excised myocardium may mimic myocardium at end-diastolic phase and, thus, the correlation of the concentrations on the in vivo images and ex vivo concentration may potentially cause errors. In addition, the authors did not use different energy windows for scatter correction, although they insisted that this study included correction of Compton scatter.

We consider another important issue for quantitation of myocardial tracer distribution: absolute quantification of regional myocardial blood flow in milliliters per gram per minute, which is well calculated with PET and ^{13}N -ammonia or ^{15}O -water. Once the actual concentration of the perfusion tracer is estimated, absolute myocardial blood flow can be estimated using the optimum tracer kinetic model and the input function of the perfusion tracer. For this purpose, $^{99\text{m}}\text{Tc}$ -labeled perfusion tracers may not be suitable agents. Because they show significant roll-off in the extraction fraction in the myocardium in the high flow range, the flow estimated by these tracers may be underestimated in the normal myocardium (19). This underestimation might be corrected using the permeability surface product values of the Renkin and Crone model (20). However, such

correction may create a large error in the high flow range, particularly with use of perfusion tracers with the low extraction fraction.

Another important issue may be how much quantitation of perfusion tracer is required in the clinical setting in the next decades. In the present clinical setting, qualitative perfusion SPECT imaging has provided valuable information for the diagnosis and management of patients with coronary artery disease. Attenuation and scatter compensations will improve the diagnostic accuracy of perfusion SPECT imaging. In most circumstances, quantitative assessment of perfusion is not necessary. On the other hand, quantitative perfusion imaging should play an important role in the study of diffuse myocardial diseases, such as microvessel disease, triple-vessel disease, or cardiomyopathy. Furthermore, such quantitation seems to be valuable for precise assessment of treatment effects. Recent reports have shown the change of coronary flow reserve estimated by PET and ^{13}N -ammonia in the treatment of hyperlipidemia (21,22). We believe similar study may possible using quantitative SPECT with a suitable perfusion tracer and an appropriate tracer kinetic model.

We consider that the report of Da Silva et al. (18) is not the final goal but is a good start for quantitative analysis of perfusion SPECT. This progress will further enhance quantitative analysis of SPECT imaging.

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