EDITORIAL

Attenuation Correction, or the Emperor's New Clothes?

Thus far, experienced clinical interpreters of cardiac SPECT images have managed reasonably well without attenuation correction. Although SPECT myocardial perfusion imaging is used in millions of patients across the world, every interpreter of SPECT images is aware that the methodology has its flaws. Clearly, the most important shortcoming of SPECT myocardial perfusion imaging is the frequent occurrence of attenuation artifacts, potentially resulting in false-positive interpretations. The reported specificity of SPECT myocardial perfusion imaging in the literature consequently ranges widely, from as low as 40% to as high as 90% (*1*). Although referral bias has been recognized as one of several reasons for low specificity, attenuation artifacts are also likely culprits. Breast artifacts are somewhat less problematic on SPECT images than on planar images, but diaphragmatic attenuation of the inferior wall is a common and vexing problem on SPECT myocardial perfusion images.

Somewhat paradoxical perhaps, given these recognized drawbacks, is the well-established clinical usefulness of SPECT myocardial perfusion imaging. Experienced interpreters consistently achieve acceptable clinical sensitivities and specificities for the detection of coronary artery disease and are able to provide incremental prognostic information that goes well beyond that of the detection of angiographic coronary artery disease. Normal stress myocardial perfusion images are associated with a favorable prognosis, whereas markedly abnormal SPECT myocardial perfusion images predict poor outcome. Thus, SPECT myocardial perfusion imaging has become an important clinical patient management tool.

How can such good clinical results be reconciled with the notion that SPECT imaging is technically flawed? The answer to that question is that experienced interpreters have learned to "read around" artifacts (*2*). Several "tricks" are often used to identify artifacts. The interpreters may acquire additional right-side decubitus left lateral planar images (*3*), may perform prone imaging (*4*) or may review regional wall motion on electrocardiograph-gated images or on first-pass angiography. However, none of these aids provides unequivocal answers at all times with regard to the presence of artifacts. Substantial ambiguity remains. Moreover, patients with demonstrable attenuation artifacts also may have coronary artery disease. False-positive interpretations nevertheless are a considerable problem for less experienced interpreters and frequently trigger unnecessary cardiac catheterizations.

ATTENUATION-CORRECTION EXPERIENCE

In recent years several vendors and investigators have designed a variety of software packages and devices to correct for nonuniform attenuation on SPECT imaging. Some excellent and encouraging results have been reported by experienced investigators (*5*). However, many commercial and noncommercial methods appear to "work" in some patients, whereas in other patients they create more problems and new artifacts (*6–10*).

A disturbing example of this is reported in the article by Vidal et al. (*10*) in this issue of *The Journal of Nuclear Medicine*. The investigators tested a commercially available attenuation-correction method in patients with documented coronary artery disease. Attenuation correction substantially improved the specificity for detecting right coronary disease without affecting sensitivity. Thus, attenuation correction successfully decreased the number of false-positive defects in the inferior wall. However, the software package did not work so well for the anterior wall. In the anterior wall, attenuation correction resulted in unacceptably low sensitivity for detection of left anterior descending coronary artery disease, with preserved specificity. In other words, true-positive defects disappeared with attenuation correction, whereas the number of false-positive defects remained the same.

It is unclear how a system that works half of the time can be useful in clinical practice. Because attenuation correction is such a desirable goal, there seems to be a tendency among investigators to disregard disappointing results and develop a complex interpretation strategy that requires interpretation of both uncorrected and attenuation-corrected images. This approach is not very useful in clinical practice. It is also stated that new learning is necessary to interpret attenuation-corrected images. For example, on normal attenuation-corrected images substantial apical defects may be present and should be ignored (*10*). It seems that current results with attenuation correction very much resemble the "emperor's new clothes." The emperor in actuality is quite naked! Or, at best, half naked. Unfortunately, it is unclear which half of the emperor is naked.

HOW TO VALIDATE ATTENUATION CORRECTION

The design of software for correction of soft-tissue attenuation is a com-

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plex and iterative process (*11–15*). Initially the focus was simply on the creation of transmission attenuation maps. Subsequent clinical experience made clear that it is not sufficient to correct for nonuniform attenuation alone (*16*). Correction for the effect of scatter, varying spatial resolution, partial-volume effect and perhaps other, as yet unidentified, corrections for characteristics of the gamma camera acquisition systems must be incorporated. The experience with early versions of attenuation-correction methods has shown that one cannot hope to design an attenuation-correction method and expect that it will work immediately for patient imaging under all conditions. A substantial amount of trial and error obviously is needed before a flawless correction system is created that improves on the performance of the experienced human eye.

A crucial question is how to validate each new rendition of an attenuation-correction software package. It is impossible for several reasons to conduct extensive clinical trials every time a new software version is ready to be tested. First, this would be prohibitively expensive. Second, this would be time consuming. Third, coronary angiography is a flawed gold standard and results may still be equivocal. Fourth, the sensitivity and specificity of conventional image interpretation by experienced interpreters (who consider the possibility of artifacts) are already quite good and may be difficult to improve on. Finally, attenuation artifacts can be a serious problem in some, but not all, patients. Thus, patient selection may introduce an unintentional bias and skew results. For instance, demonstrating that regional radiotracer uptake in healthy subjects is more homogeneous with attenuation correction than without does not necessarily imply that the method will appropriately correct in patients with marked attenuation artifacts (*9*).

Attenuation correction aims to correct a physics problem. Most currently available attenuation-correction packages presumably have gone through some testing on phantoms. If so, why then so many disappointments and partially successful clinical results? Attenuation in the human body is nonuniform, and the degree of attenuation and the magnitude of problems it creates in SPECT imaging vary considerably from individual to individual. Unfortunately, one cannot simply predict the occurrence of attenuation artifacts on the basis of the patient's body habitus. Phantom studies that do not simulate the entire physiological range of attenuation μ-values, patient sizes, scatter and resolution variation with depth are inadequate for preclinical testing. Clinical interpreters will argue that phantom simulation is never close enough to "real" patient imaging to replace clinical testing in patients. This is certainly true, for example, in phantom simulation of myocardial perfusion defects. Fillable defect inserts in a cardiac phantom poorly imitate human myocardial infarction or stress-induced hypoperfusion. Phantom images of such defects never truly approximate real myocardial perfusion defects. However, for the evaluation of the effects of nonuniform attenuation, which is a physics problem, it is entirely appropriate to use phantom simulation. Varying degrees of photon attenuation, scatter and resolution changes can be studied in a series of physics experiments.

A PROPOSAL FOR PRECLINICAL TESTING AND VALIDATION

I propose that substantial expense and frustration can be avoided when new attenuation-correction packages are not evaluated in the first instance in clinical trials, but rather in a standardized series of physics experiments using phantom configurations that recreate commonly seen SPECT artifacts in humans. The phantom should resemble as closely as possible the human chest, including the spine, fillable lungs, fillable liver, fillable gut, diaphragm with variable positioning, fillable heart with fillable defects and fillable breasts of varying sizes. By filling the fillable "organs" with a number nonradioactive liquids with varying μ values (*17*) or with varying concentrations of radioactivity (liver, gut and lungs) the wide spectrum of human SPECT images may be mimicked closely. In addition, a standardized set of different scattering material should be used for image acquisitions. Finally, imaging should be acquired using standardized circular and noncircular orbits to address the issue of varying spatial resolution. A most important aspect of this set of experiments is that all variables can be known, are measurable and thus represent the true benchmark for correction. Such a standardized phantom experiment also will allow for testing of several as yet incompletely explored imaging variables, e.g., required minimal strength of transmission source, optimal range of transmission-emission count densities ratios, effect of attenuating organs with emanating photons (*18*) and other tests.

Quantitative Analysis

It is not sufficient to inspect images visually and conclude that the distribution of radiotracer appears more homogeneous after correction. Differences may be subtle and are dependent on image normalization and image display. A mandatory aspect of the evaluation of attenuation packages should be quantitative analysis (*15,17,18*). Homogeneity (or lack thereof) of count distribution can expressed as mean percent variability. Quantification is objective, more reliable and more sensitive than the human eye to measure subtle differences produced by a new version of attenuation correction under testing.

Standardized Validation

I propose that it is the prerogative of the professional societies to define the testing standard for SPECT attenuation-correction systems. This, then, should become the standard for industrial preclinical testing of attenuation-correction packages. Thus, it will be easier for the nuclear medicine community to compare the performance of various attenuation-correction products.

Experimental Validation

Not all confounding variables, such as the effects of scatter, collimator-detector blurring, cardiac and respira-

tory motion and changing extracardiac background can be fully addressed in static phantom studies or computer simulations. This may require additional in vivo testing in experimental animal models, in which potential confounding variables can be isolated and controlled to a certain extent. Ultimately, validation can be derived from postmortem tissue analysis.

CONCLUSION

There is no disagreement that the development of an accurate methodology for attenuation correction is important for the continued advancement of SPECT myocardial perfusion imaging. In addition to achieving the main objective, i.e., abolishing false-positive defects, corrected images would allow for better quantification of perfusion abnormalities and for achieving the ultimate goal of absolute quantification of myocardial blood flow.

There is considerable uncertainty, confusion and skepticism about the true reliability and value of currently available attenuation-correction packages. Although commonly referred to as "attenuation correction," these packages also contain novel image acquisition and image reconstruction algorithms in addition to attenuation correction, scatter correction and image resolution compensation. Each of these variables needs to be better understood and tested before clinical implementation.

Newly developed methods for attenuation correction should be validated using generally accepted standardized testing protocols before launching clinical trials in patients. Hopefully, the emperor then will be dressed more appropriately.

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