Prompt-gamma compensation in Rb-82 myocardial perfusion 3D PET/CT: Effect on clinical practice

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PET imaging technology allows for absolute and relative myocardial blood flow analysis. In addition to the well-known positron emissions resulting in the production of annihilation radiation usually in the form of two 511 keV photons used for PET imaging, Rb-82 also emits 776 keV gamma rays with 13% abundance known as prompt gamma radiation.¹ The effect on the images of these gamma emissions is different from those of random events or scatter; they produce a background signal which is incorrectly detected as coincidence events with the annihilation 511 keV photons. These unwelcomed coincidences lead to artifacts in both the appearance of the Rb-82 myocardial uptake as well as in image quantification if not corrected. Note that this is a unique characteristic of the Rb-82 radionuclide, and does not occur with any of the other radionuclides used for cardiac imaging such as N-13, O-15, or F-18.

Most of the present PET scanners imaging in three dimensions are affected significantly more than the older PET scanners imaging in two-dimensional mode. The presence of lead septa in these older 2D PET scanners reduced the coincidence detection of many of these prompt gammas and 511 keV photons by stopping the prompt gamma rays coming from an off-angle to the 2D plane being imaged. Thus, the imaging artifacts due to prompt-gamma coincidences in 2D PET scanners were

considered negligible. As the number of 3D PET scanners imaging Rb-82 proliferated in cardiac imaging centers, this artifact became a potential source of misdiagnosis which must be corrected. In 3D PET imaging, the lack of lead septa presents a challenge due to the wide axial acceptance angle leading to many more coincidences of prompt gammas with annihilation photons. These incorrect recorded events produce photopenic artifacts often seen in the left ventricular myocardial anteroseptal wall leading to a reduction in specificity for detecting the absence of myocardial hypoperfusion.¹ A telltale sign of the presence of this prompt-gamma artifact was the unusual reduction in background activity around the left ventricle often obliterating the right ventricular myocardium.¹ The existence and effect of this prompt-gamma artifact in Rb-82 myocardial perfusion relative imaging as well as how industry has implemented prompt-gamma compensation (PGC) to correct for this artifact were previously reported by Esteves et al.¹

Like scatter, random and prompt gammas each represent a different mechanism for degrading imaging quality; thus, their correction algorithms are also different. Scatter and random corrections are well known, universally implemented, and not the focus of the present article. Briefly, this is how PGC works. It consists of six steps all happening in the sinogram space: First, (1) an emission sinogram, attenuation factor, and normalization factors are acquired from projection data obtained from the PET scanner and then converted to DICOM or similar. Then, (2) the contribution of scatter is estimated using attenuation factors in a scatter simulation on the normalized emission sinogram. (3) The data outside the body are fit to a linear combination of the prompt gamma and scatter. (4) The background radiation is removed from the normalized emission sinogram, creating a clean sinogram. (5) The clean sinogram is corrected for attenuation, and finally (6) the

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images are reconstructed. This method which is now patented by one of the manufacturers was initially described by Beattie et al.^{1–3}

In the current issue of the Journal of Nuclear Cardiology®, Armstrong et al.⁴ address for the first time the role that this same prompt-gamma coincidence artifact plays in absolute quantification measures, specifically myocardial blood flow (MBF) and myocardial flow reserve (MFR). As explained by Armstrong et al., PGC produces significant differences for absolute MBF measurements with the MBF increasing or decreasing depending on the patient's BMI and the vascular territory. MBF in male obese patients is decreased particularly in the left anterior descending (LAD) and left circumflex (LCx) vascular territories when PGC is applied. In non-obese patients, the impact of PGC on MBF measurements was to significantly increase in the RCA vascular territory values, but modest and unlikely to be clinically significant in the other territories. Increased BMI is a reflection of the amount of soft tissue, which will contribute to increased photon scatter. Armstrong et al. showed a general decrease in the PGC-corrected MBF as the patients' BMI increased. Right coronary artery (RCA) territory showed the greatest variability in absolute flow measurements, which is concordant to the findings by Esteves et al. when analyzing relative perfusion distributions. Note that the Esteves study was not focused on including BMI and gender on the analysis. An intriguing suggestion by Armstrong et al. is the need to consider the impact of PGC on the derivation of the Rb-82 extraction fraction calculation, and whether different kinetic models should be employed to derive MBF according to whether or not PGC is used. Regarding MFR measurements, Armstrong et al.⁴ report that the impact of PGC on MBF is consistent for a given patient, and as such, the percentage changes in rest and stress MBF are consistent; thus, MFR values are preserved.

The clinical impact of these findings is that these PGC corrections may affect the thresholds of normality for MBF; however, for MFR, the normal thresholds are expected to be minimally affected. Currently, these factors are not addressed in obese patients, but it is possible that further studies may be needed to develop a special correction applied for patients with BMI greater than 30. Clinical trials using 3D PET systems present results that are taken as reference values for clinical practice or even for future studies. These studies typically do not state if PGC was applied to acquisitions and processing of flow measurements.⁵ The information as to whether PGC was applied in the 3D PET scanners used as part of a Rb-82 clinical trial should be required of all publications.

Relative and absolute flow measurements ideally complement each other. Relative myocardial flow measurement will continue to be the mainstay for the assessment of CAD with imaging. Comparison with databases to assess deviations from normal will continue to be the most commonly used method that most clinicians are trained and familiar with. However, the medical literature, including updated guidelines, continues to provide evidence of the additional clinical information that absolute flow measurements provide in the clinical setting such as in triple-vessel coronary artery disease and the associated balanced ischemia, in microvascular disease,⁶ and in early coronary atherosclerosis.^{6–9} Absolute flow measurements with PET offer a non-invasive alternative to functional assessment of CAD, and also manifest earlier than the relative flow images, therefore implementing timely therapeutic measures.⁹

In the clinical setting, on a daily practice, several factors can impact our images and our quantitative results. Awareness of the prompt-gamma compensation algorithms in the equipment we use is of critical importance, particularly, if anteroseptal artifacts are commonly seen, if our practices include a large population of obese patients, or even more if MFR and MBF are being used clinically.

In most of today's state-of-the-art 3D PET scanners, prompt gamma compensation (PGC) is implemented by the manufacturer as part of the system used for cardiac imaging. Nevertheless, it is imperative that each site confirms that each of their 3D scanners performing Rb-82 myocardial perfusion imaging has implemented this compensation. This is true whether the images are analyzed by visual analysis, relative quantification, absolute quantification, or all of the above. Undoubtedly, the contributions by Esteves et al. and Armstrong et al. have made this issue clear.

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