Low-dose 3D ^{82}Rb PET

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3D PET TECHNOLOGY

3D PET systems were introduced for oncological imaging almost a decade ago and are now universally used. The principal advantage of the 3D PET acquisition (accepting photons from all angles) over the 2D PET with parallel septa is much higher sensitivity (4–6 times) for photon detection, albeit at the cost of increased scatter fraction and more complex image reconstruction.¹ 3D ^{82}Rb PET acquisition has presented image quality problems due to increased random events when previous generation 2D–3D BGO scanners were used.² Furthermore, until recently, the interference of prompt gamma emission during ^{82}Rb decay with scatter correction on 3D systems was not fully recognized.³ Most literature in cardiac PET imaging describes studies performed in 2D mode.⁴ However, currently the users of new PET/CT equipment are unable to acquire images in 2D since almost all new scanners operate in 3D mode only and come without septa. Therefore, the optimal use of such 3D PET/CT for cardiac imaging and in particular for ^{82}Rb imaging is of great interest to the nuclear cardiology community.

IMPORTANCE OF LOW-DOSE PET

The increased sensitivity of the new 3D PET/CT systems can be utilized to reduce radiation exposure to the patient during the myocardial perfusion imaging scan. Although the true effect of radiation exposures lower than 100 mSv on cancer risk is unknown as the risk estimates are extrapolated linearly from higher doses,^{5,6} radiation exposure and discussion of cardiac imaging's contribution to hypothetical (but possible) cancer have been recently highlighted. Therefore, from

the patient's perspective, radiation exposure "as low as reasonably achievable" is very desirable.

ARTICLE

The accuracy of low-dose 3D PET/CT for detecting coronary artery disease (CAD) was assessed in an article by Kaster et al in this issue of the Journal of Nuclear Cardiology.⁷ The authors evaluated a total of 70 patients with coronary angiography correlation and 77 patients with low likelihood (LLk) of CAD to assess the diagnostic accuracy of low-dose 3D ^{82}Rb -PET (weight-dependent 10 MBq/kg, translating from the SI units for the US audience, approximately 0.12 mCi/lb). Automatic relative quantification (with automatically derived summed stress scores) and quantification of transient ischemic dilation (TID) were used, without absolute flow measurements and without visual reading by the physicians. They report that by automated analysis they achieved perfect sensitivity (100%) and 48% specificity for the detection of obstructive stenosis in the angiographic group. The specificity improved to 78% without sensitivity loss in a subgroup ($n = 45$) excluding patients with acute myocardial infarction and low ejection fraction. It should be noted that to achieve 100% sensitivity, the authors modify perfusion abnormality thresholds depending on the TID variable. The sensitivity was 95% by perfusion analysis alone. The receiver operator characteristics areas under-curve (ROC-AUC) ranged from 0.92 to 0.97. As expected with relative perfusion defect assessment, per-vessel results showed lower performance, but were still reasonable (59%–69% sensitivity and 87%–89% specificity). These are very encouraging results, in particular taking into account the fact that this level of accuracy was achieved without the subjective visual reading, and therefore could be easily reproduced in any laboratory. In addition, these results have been obtained with low-dose ^{82}Rb imaging.

RADIATION DOSE

For ^{82}Rb imaging, the typical injected dose for the 2D PET system with septa has been recommended to be 40–60 mCi.⁴ The estimated patient radiation doses have recently been revised down to 3.7 mSv for ^{82}Rb PET scans with 80 mCi total injected dose (stress + rest) by more precise patient-specific calculations.⁸ The protocol of Kaster et al involved weight-based dosing, but the

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average injected dose in their study was 25.8 mCi, with average patient weight of 210 ± 51 lbs (de Kemp R., unpublished data). Thus, the overall average patient radiation dose would be in the order of 2.4 mSv and just 1.2 mSv for the stress component. Of note, the two CT attenuation correction scans for stress and rest add another 0.8 mSv. Therefore, the entire PET/CT ^{82}Rb stress–rest scan could result, on the average, in a 3.6 mSv patient dose, with significantly lower dose in thinner patients. This comprehensive exam could also provide absolute flow data (not used in Kaster et al study, but collected nonetheless as a part of the imaging protocol) as well as CT maps, which could be used for calcium scoring.⁹ Incidentally, another benefit from using the lower injected dose could be more reliable absolute flow data, as the initial ^{82}Rb count rate during 3D PET acquisition may present challenges in accurate measurement of the left ventricular input function for the kinetic analysis.

QUANTITATIVE SOFTWARE

The study by Kaster et al is, to our knowledge, the third report of fully automated quantitative analysis applied to ^{82}Rb PET/CT. Previously, automatic analysis has been performed with other quantitative method for 2-D PET/CT.¹⁰ In addition, our group has recently demonstrated fully automated analysis (QPET) applied to 3D PET/CT ^{82}Rb analysis on a different scanner, achieving similar results to Kaster et al (sensitivity 93%, specificity 77%) without incorporation of TID into the quantification.¹¹ Although these software tools may differ in performance when directly compared,¹² the three reported to date ^{82}Rb PET studies show similar accuracy for automated analysis. From our SPECT experience in a recent large study ($n = 995$ cases), the accuracy of the automated analysis is equal to that of visual 17-segment scoring by expert observers,¹³ and is more reproducible.¹⁴ Such large comparative studies have not been conducted for PET, but the study by Kaster et al, together with previous studies by Nakazato et al¹¹ and Santana et al¹⁰ indicate that automated quantification of ^{82}Rb PET is also well suited for the task of detecting obstructive CAD. It is encouraging to see computer analysis used as a standard for perfusion reporting because it removes the experience of the laboratory as a confounding factor.

LIMITATIONS

The study by Kaster et al has nevertheless some limitations, which will need to be addressed in future studies. As noted by the authors, the population size for angiographic correlation was small. Furthermore, the excellent results reported were based on an approach that

did not separate the findings into a training and validation set, apart from the patients with a LLk of disease used for the normal database creation. Thus, deriving the optimal threshold (such as 1.5 standard deviations) and using the optimal TID rules to maximize performance was done on the same data, which were used in the final analysis. Even though the authors were limited by the small number of patients, a tenfold cross-validation could have been performed that might have made their findings more robust. It remains to be seen what overall accuracy can be achieved if the criteria developed in their study were applied in a separate prospective group. When comparing the results to previous studies, one should keep in mind that Kaster et al have used visual angiography results and excluded lesions in distal branches, subsequent diagonal/marginal branches, posterior descending artery, and postero-lateral segments. Although these lesions may have a small effect on perfusion, the sensitivity achieved by considering patients with disease in smaller vessels as not having CAD results in a higher sensitivity of testing than if these lesions were included. Almost all prior publications have considered such lesions as meeting criteria for CAD.

CONCLUSION

In the article by Kaster et al, encouraging results have been shown for low-dose ^{82}Rb PET analyzed with automated software for the detection of obstructive CAD. Combined with prior similar reports, these results indicate that the nuclear cardiology community may be evolving to the point where truly low-dose imaging becomes routine. Furthermore, automated analysis, not reliant on the observer's expertise, could be used to provide an objective interpretation of such studies.

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