

## $^{82}\text{Rb}$ PET/CT: entering a new area of myocardial perfusion imaging?

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In this issue of the *European Journal of Nuclear Medicine and Molecular Imaging*, Flotats et al. [1] report a striking improvement in image quality of myocardial perfusion studies with the use of  $^{82}\text{Rb}$  PET/CT as compared to conventional  $^{99\text{m}}\text{Tc}$ -labelled SPECT/CT. When using PET/CT in concert with the positron-emitting myocardial perfusion tracer  $^{82}\text{Rb}$ , the improvement in image quality also manifested in a higher interpretative confidence and interreader agreement of  $^{82}\text{Rb}$  perfusion images than observed for  $^{99\text{m}}\text{Tc}$ -labelled SPECT/CT. In particular, the current study is unique in that  $^{82}\text{Rb}$  PET/CT and  $^{99\text{m}}\text{Tc}$ -labelled SPECT/CT were performed in the same patient with known or suspected coronary artery disease (CAD). Previous investigations commonly compared the sensitivity and specificity of cardiac PET versus SPECT perfusion imaging in the detection of flow-limiting epicardial lesions [2]. For example, Go et al. [3] showed sensitivity, specificity and accuracy of 95, 82 and 92 % for  $^{82}\text{Rb}$  PET and 79, 76 and 78 % for  $^{201}\text{Tl}$  SPECT for haemodynamically obstructive CAD lesions. Further, Stewart et al. [4] reported that overall sensitivity, specificity and accuracy of  $^{82}\text{Rb}$  PET for detection of coronary artery lesions  $\geq 50$  % diameter stenosis were 84, 88 and 85 %, respectively. In comparison to this, the performance of  $^{201}\text{Tl}$  SPECT revealed a sensitivity of 84 % but a low specificity of 53 % and a diagnostic accuracy of 79 %. The commonly higher sensitivity in the identification of flow-limiting epicardial lesions with  $^{82}\text{Rb}$  PET as compared with SPECT imaging, either with  $^{201}\text{Tl}$  or

$^{99\text{m}}\text{Tc}$ -labelled perfusion tracers, can be related to the higher spatial and contrast resolution of  $^{82}\text{Rb}$  PET, while the photon attenuation-free images of PET imaging may account for the relative increase in specificity [2].

The new investigation conducted by Flotats et al. [1] now adds further important information by addressing image quality of myocardial perfusion studies, and the resulting reader confidence, and interreader agreement when applying  $^{82}\text{Rb}$  PET/CT in direct comparison to  $^{99\text{m}}\text{Tc}$ -labelled SPECT/CT. As it was observed, image quality was estimated to be excellent or good in 63 % of PET, 33 % of attenuation-corrected (AC) SPECT and 22 % of non-AC SPECT images. Further, artefact-free images were more frequently observed with PET than with SPECT studies (PET 81 %, AC SPECT 22 % and non-AC SPECT 15 %). In this direction, significant liver or bowel uptake (or both) as well as attenuation artefacts can be assumed to have substantially affected the interpretation of the SPECT/CT images rendering the interpretative decision-making process more difficult or observer dependent for SPECT/CT than for PET/CT images. Not surprisingly, the reader certitude to grade stress-rest perfusion imaging into a normal or abnormal finding was highest for PET (85 %), followed by AC SPECT (30 %) and non-AC SPECT (7 %). This is also reflected by the interreader agreement which was superior for PET/CT than for those of SPECT/CT perfusion studies.

Several methodological aspects may account for the observations of Flotats et al. [1]. PET cameras identify paired photons (511 keV of energy each) produced by the positron annihilation effect. The paired 511 keV travel in the opposite direction at a  $180^\circ$  angle from each other [2]. This enables a precise localization of the positron decay applying the principle of coincidence detection and without collimation as used for SPECT [2, 5]. Without the use of collimators, PET cameras have a much higher sensitivity than do

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SPECT cameras, resulting in a higher spatial resolution in the range of 4–7 mm. Another aspect is the relatively higher extraction fraction of  $^{82}\text{Rb}$  at higher flows than those of  $^{99\text{m}}\text{Tc}$ -labelled perfusion tracers [6], which yields an increase in contrast resolution. Both the higher spatial and contrast resolution of  $^{82}\text{Rb}$  PET perfusion studies explain the reported higher sensitivity in the detection of CAD lesions as compared with  $^{201}\text{Tl}$  or  $^{99\text{m}}\text{Tc}$ -labelled perfusion tracers [2, 6]. Conversely, the robust attenuation correction of the PET emission data using the transmission source ( $^{68}\text{Ge}$  rotating rod source or CT) accounts for the reported increase in specificity of PET perfusion imaging when compared to conventional SPECT imaging [2, 7].

Another important aspect is that the gamma energy levels of PET radiotracers with 511 keV are considerably higher than those for  $^{99\text{m}}\text{Tc}$ -labelled perfusion tracers (140 keV) and  $^{201}\text{Tl}$  (70–90 keV) applied in cardiac SPECT imaging. This again renders PET imaging less prone to attenuation artefacts. Conceptually, although the two 511-keV photons produced by positron annihilations are less attenuated than a single 140-keV  $^{99\text{m}}\text{Tc}$  photon, there may be in fact more attenuation with PET than with SPECT imaging as two photons must be identified for coincidence detection. According to the principle of coincidence detection, however, the two photons travelling in opposite directions project along the same ray and they must pass through the same total amount of tissue independent of the localization where they were emitted [8]. The total measured attenuation in PET imaging therefore can be assumed to be similar anywhere along this projection line. This is in contrast to SPECT imaging, where there is no opposing photon in order to aid in localizing an annihilation event. Because of this, attenuation of photons in SPECT imaging can vary exponentially. PET emission data therefore can be precisely corrected for attenuation by simply multiplying each projection line with the appropriate AC factors determined from a transmission  $^{68}\text{Ge}$  line source or CT as compared to more complicated ones applied for SPECT [8]. The higher gamma energy levels of PET radiotracers with 511 keV and very solid and precise attenuation correction of PET emission data do not lead only to an increase in specificity but also to an increase in interpretative confidence of PET perfusion images as observed in the current study [1]. The technological advantages of PET over SPECT cameras, therefore, have led to a relatively higher sensitivity and specificity of myocardial perfusion PET or PET/CT scanners for detecting  $\geq 50$  or  $\geq 70$  % luminal epicardial narrowing around 92 and 90 %, respectively [2]. On the other hand, we need to bear in mind that reported PET or PET/CT perfusion studies were mostly performed in highly selected study populations, which may have biased, at least in part,

the relatively high sensitivity and specificity of PET perfusion studies in the detection of CAD lesions. The high spatial and contrast resolution in concert with photon attenuation-free images of PET, however, provide a higher image quality associated with a higher sensitivity and specificity of PET/CT perfusion imaging than for conventional SPECT or SPECT/CT. This again may explain the relative ease in the interpretation of PET/CT stress-rest perfusion images for the detection of flow-limiting epicardial lesions [1].

How current observations of Flotats et al. [1] with  $^{82}\text{Rb}$  PET/CT myocardial perfusion imaging compare with iterative image reconstruction or the implementation of new algorithms, so-called proprietary resolution recovery/noise reduction (RRNR) of SPECT/CT systems, or new ultrafast SPECT camera designs [8, 9], remain uncertain, which will certainly stimulate further comparative investigations and advancements in the field of scintigraphic myocardial perfusion imaging [10].

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