EDITORIAL

PET-derived bone information from 18F-sodium fluoride: A perfect match for whole-body PET/MR attenuation correction?

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Following its introduction in 2011, the integrated positron emission tomography (PET)/MR (magnetic resonance imaging) systems received significant interest especially within the neurological societies because of the ideal combination of the superior soft-tissue contrast provided by MR and the functional information obtained from PET.[1,2] Although the main application of hybrid PET/MR imaging to oncology and neurology studies,[3] this hybrid modality is of keen interest to cardiology where its potential applications are considered strong for studies of cardiac inflammation, ischemic heart disease and ischemic cardiomyopathies as discussed in the joint position statement between the European Society of Cardiovascular Radiology (ESCR) and European Association of Nuclear Medicine (EANM).[4]

Although PET/MR systems and their applications are becoming more widespread, the quantitative accuracy of these systems are still in question because of the difficulties related to PET attenuation correction (AC) maps [5,6] derived from MR images. Unlike the use of photon transmission-based AC maps obtained for standalone PET and PET/CT systems (rotating rods or CT, respectively), the attenuation maps for PET/MR are obtained from dedicated MR imaging acquisitions—with current products based on the DIXON sequence.[2,7] While the DIXON sequence permits segmentation of the body into fat and soft-tissue types (which can be expanded into four tissue classifications of water, fat, lung and air), it does not allow for detection of the dense bones which account for the most attenuating parts in the body.[2,8]

Initial PET/MR studies evaluated the ''missing-bone'' effects, which were found to pose significant problems for neurological studies [9,10] and for lesions in the proximity of skeletal bones in whole-body applications.[11,12] In cardiac PET/MR studies, the missing-bone effects have been shown to have little or no effect on the qualitative and quantitative assessments [13,14]; however, it is not certain that disregarding bone structures in the AC maps can be ignored for other cardiovascular applications. The evaluation of atherosclerosis in the carotid arteries is one such application, where the vessels are in close proximity to bony structures. While the DIXON AC maps have been proved acceptable for oncological studies in the neck region,[15] the ''missing-bone effect'' might introduce significant reductions in the commonly used target-to-background ratios used for the assessment of atherosclerosis.[16]

To compensate for the missing bones in the DIXON AC maps, the utilization of template-based methods using bone-inserts obtained from a standard CT scans have been proposed,[17] while the use of dedicated MR sequences (ultra-short time echo [UTE] or zero-time echo [ZTE]) have been shown capable of segmenting the bones in the head/neck region.[10]

Another potential solution to identify the cortical bones is by performing ^{18}F-sodium fluoride (^{18}F-NaF) PET scans.[18] Since 2012, this tracer has gained significant interest in the assessment of cardiovascular diseases because of its uptake in areas with active microcalcification.[16,19–21] This tracer is also used for bone cancer imaging.[22,23] The combined growth in interest for cardiovascular plaque imaging and the potential use of bone identification for hybrid PET/MR scans might be an ideal match in the search of a reliable method to introduce the bone in the standard DIXON AC maps.[8] In

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the current issue of the *Journal of Nuclear Cardiology*, Karakatsanis et al. [24] investigate the feasibility of utilizing dynamic ^{18}F-NaF PET scans to identify the bone structures and combine this information with the standard four tissue classifications on the standard DIXON AC maps.

In their study, Karakatsanis et al. evaluated three different applications of kinetic modeling of the bone uptake during dynamic acquisitions, using either ^{18}F-NaF injections as stand-alone applications or combined with ^{18}F-FDG in a dual-tracer imaging protocol. The technique proposed to identify the skeletal bones were tested in two cohorts, one with and one without prior indication of atherosclerosis to establish the stability of the technique in patients with known tracer uptake outside the skeleton. In the analyses, the authors compared the uptake observed in the lesions observed at the vertebral bones and in the carotid bifurcations for reconstructions with and without the PET-derived bone information in the attenuation corrections. As expected, the missing bone effect resulted in target-to-background decrease of up to 18%. This decrease was caused by the underestimation of the linear attenuation coefficients of the standard DIXON-assigned values (0.1 cm^{-1}) in comparison to the linear attenuation coefficient of 0.12 cm^{-1} assigned to the bones in the MR-based AC maps.[25]

While this novel technique holds promise to improve cardiovascular PET/MR studies, it has some potential shortcomings which might affect its utilization in the clinical routine. The uptake patterns for certain applications such as aortic stenosis and valves might introduce false-positive skeletal bones in the images which will challenge the accuracy of the bone-inserts in the AC maps. Another potential problem with the PET-derived bone-mappings is the technical challenge associated with dual-tracer injections, and potential cross-contamination of uptake patterns for both tracers. Finally, the use of ^{18}F-NaF as an AC technique is associated with a considerable radiation dose (0.024 mSv/MBq[26]—approximately 4.3 mSv for injections of 180 MBq as proposed by Karakatsanis[24]), in comparison to the low-dose CTAC maps which can be as low as 0.4 mSv.[27]

Do the current findings presented by Karakatsanis et al. mean that AC for whole-body PET/MR applications has been resolved by ^{18}F-NaF approach? Not necessarily, as the DIXON AC maps still rely on assumed attenuation coefficients in segmented classes of tissues, in comparison to the true linear AC values obtained for CT images. Nevertheless, the proposed technique offers an interesting and novel approach that might reduce the bias observed in absolute quantification of whole-body PET/MR scans when compared to PET/CT systems.

Disclosure

Martin Lyngby Lassen and Piotr J. Slomka declare that they have no conflict of interest relevant to this manuscript.

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