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Coronary MR/PET of Micro-Calcification in Atherosclerosis

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Introduction

Positron Emission Tomography (PET) is an established non-invasive imaging technology that allows the activity of specific disease processes to be measured. PET imaging using the radiotracer ^{18}F-fludeoxyglucose (^{18}F-FDG)[1] has been used previously in the study of vascular inflammation in atherosclerotic plaque [1, 2]. FDG, a sugar analogue, is taken up more avidly by activated macrophages in the plaque compared to surrounding tissue. Consequently, increased ^{18}F-FDG PET signal is a biomarker for active disease. Recently, ^{18}F-sodium fluoride (^{18}F-NaF), a PET tracer used in bone imaging that preferentially binds to areas of micro-calcification, has emerged as a marker of vascular micro-calcification activity in both aortic stenosis and atherosclerosis [3-5]. Whilst coronary calcium scoring using Computed Tomography (CT) measures macro-calcification and is well-established as a prognostic marker of coronary artery disease, the earlier stage of active micro-calcification is potentially a valuable marker of disease activity and of use for identifying patients with increased atherosclerotic burden and increased risk who may benefit from more aggressive risk factor modification.

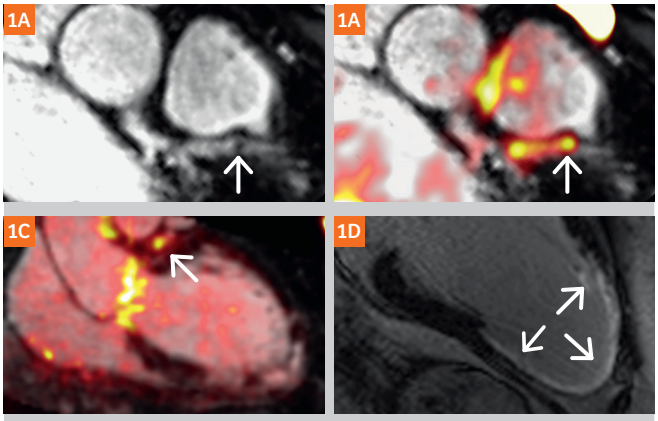

Figure 1: In a patient who had recently suffered a myocardial infarction, the culprit plaque is seen to cause aluminal stenosis in the left anterior descending artery seen on MR-angiography **(1A).** Elevated ^{18}F-NaF activity in the culprit plaque is identified by MR/PET and overlays the luminal stenosis seen on fused MR/PET-angiography **(1B),** and in a long axis view of the left ventricle **(1C).** Note uptake also in the wall of the aortic arch and the aortic valve. Extensive scarring is observed in late gadolinium enhanced MR in the territory of the lesion **(1D).**

Traditionally, cardiovascular PET imaging is performed using CT for anatomical and attenuation measurements. However, PET/CT imaging is limited by the additional radiation dose of CT, especially in chronic conditions such as atherosclerosis where serial imaging would be desirable. Moreover, vascular PET/CT imaging has predominantly focused on the aorta, carotid and peripheral arteries. Imaging of the coronary arteries, despite their great importance, is challenging owing to their small caliber and complex respiratory and cardiac motion. Although cardiac gating may be used in PET/CT to mitigate motion effects, data may invariably be lost. MR imaging on the other hand is well-suited for radiation-free imaging of cardiac motion required to correct PET data. The advent of hybrid systems combining PET cameras and Magnetic Resonance (MR) scanners is consequently of considerable interest for vascular imaging in atherosclerosis.

Coronary ^{18}F-NaF MR/PET imaging in a patient post myocardial infarction

A patient (male, 64 years old) with unstable coronary artery disease who was 6 months post myocardial infarction for which he did not undergo revascularization underwent MR/PET imaging on the Biograph mMR system. He was injected with 5 MBq/kg ^{18}F-NaF 30 minutes prior to PET imaging. PET data was acquired for 60 minutes. PET image reconstruction employed an iterative ordinary poisson ordered-subsets expectation-maximization algorithm with 21 subsets and 6 iterations incorporating point-spread-function resolution modeling [6], a 344 x 344 x 127 matrix and a 2 mm full-width-at-half-maximum Gaussian post-reconstruction filter. Attenuation correction included the body transmission coil and the 6-channel spine array mounted in the table, but omitted the 6-channel chest array used for cardiac imaging. Attenuation for the body was measured using a 6-7 minutes free-breathing golden-angle radial VIBE sequence2 to provide motion-averaged anatomical representation of the anatomy to match the PET data. Acquisition parameters

[1] The full prescribing information for the Fludeoxyglucose F18 injection can be found at page XX.

included 500 x 500 mm² coronal field-of-view, 72-88 slices covering the whole body with partial-Fourier Cartesian slice-encoding, 3 mm isotropic resolution, TR/TE 4.5/2.45 ms, in-phase TE, 9° flip angle, 1600 radial views. Images were segmented into background and soft tissue before being converted to μ-maps and incorporated into offline PET reconstruction software (e7-tools[2], Siemens Healthcare). Free-breathing MR-attenuation correction is used to eliminate artifacts that can appear in the PET images due to mismatch of PET emission and attenuation data. Additional MR data acquired simultaneously included anatomical axial HASTE, short- and long-axis TrueFISP cine imaging, 3D whole-heart contrast-enhanced coronary MR angiography [7] and short-axis late gadolinium enhanced imaging.

Increased ^{18}F-NaF uptake was identified in the culprit plaque in the left anterior descending coronary artery. The plaque could be seen on the MR angiography causing a proximal luminal stenosis that coincided with the hotspot on fused MR/PET images (Fig. 1). An extensive near-transmural myocardial infarction was observed on late gadolinium enhanced MR images, corresponding to the perfusion territory of this lesion.

The future of coronary MR/PET imaging

The preliminary work presented in this article has demonstrated the feasibility of coronary MR/PET imaging by successfully identifying active coronary disease in a patient post myocardial infarction. Additional technical development will improve the robustness and quantitative accuracy of attenuation correction methods for MR/PET.

Despite the superior coronary angiography and depiction of macro-coronary-calcification available with CT, combined MR/PET imaging is capable of excellent coronary angiography [8] and the potential for sensitive detection of macro-calcification [9] as well as having additional potential benefits. MR imaging provides a wealth of complementary information on plaque characteristics such as hemorrhage [9], vessel wall remodeling [10], and vessel wall permeability [11], as well as traditional cardiac MR measurements of morphology, function and scarring in a single scan. In addition, radiation-free MR imaging with its high spatial and temporal resolution has the potential to provide motion estimates that can be used to correct for the complex motion that affects coronary PET data, and will likely surpass cardiac gating that can be employed for PET/CT imaging.The continued development of ^{18}F-NaF as a tracer of atherosclerotic disease activity will be exciting. Studies are underway to examine whether coronary ^{18}F-NaF PET/CT provides prospective prediction of myocardial infarction in the PREFFIR trial (ClinicalTrial.gov NCT02278211). With increased interest in coronary MR/PET, the advent of new tracers targeting other aspects of the complex biology of atherosclerosis and thrombosis is an exciting possibility.Finally, the reduced radiation dose compared to PET/CT paves the way to investigate serial imaging of atherosclerotic disease activity in both clinical and research arenas.

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[2] WIP, the product is currently under development and is not for sale in the US and in other countries. Its future availability cannot be ensured.

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