Artificial intelligence-based quantification of cardiac ^{18}F -sodium fluoride uptake

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Aside from playing an important role in imaging bone malignancies ^{18}F -sodium fluoride is increasingly being employed for the assessment of disease activity in the cardiovascular system. In atherosclerosis it has been demonstrated on multiple cohorts that ^{18}F -NaF uptake across multiple vascular beds is positively correlated with the extent of atherosclerosis, cardiovascular risk scores, and adverse coronary plaque morphology.^{1–3} More recently it was demonstrated that ^{18}F -NaF coronary uptake predicts future progression of coronary artery disease and predicts future myocardial infarction in patients with established atherosclerotic disease over and above risk scores and measures of disease burden derived from computed tomography.^{4–6} While high ^{18}F -NaF uptake (coronary microcalcification activity >1.56) was associated with a >7-fold risk of myocardial infarction, patients with no coronary ^{18}F -NaF activity had an excellent prognosis with no myocardial infarctions observed in this group despite their advanced coronary plaque burden.⁶ ^{18}F -NaF might therefore provide an important risk stratification tool in the population of patients with advanced, established atherosclerosis in who prognosis prediction is currently challenging.

While ^{18}F -NaF PET/CT cardiac imaging has real clinical potential for refining risk stratification in coronary artery disease this promising imaging modality

remains very complex. To date two distinct methods for uptake quantification have been proposed. The coronary-specific method which focuses exclusively on coronary uptake and the global method which aims to determine the total ^{18}F -NaF activity within the entire cardiac silhouette.⁷ The coronary-specific approach has recently been refined with a decided method for quantifying whole vessel ^{18}F -NaF uptake - the coronary microcalcification activity, motion correction techniques, and methods for offsetting differences in tracer injection to image acquisition delays.^{8–12} The global, whole-heart approach is simpler and might be easier to adopt in to clinical practice; however, its clinical implications, especially its potential to predict adverse events remains to be shown. Additionally, despite the simplicity of the acquisition, the whole-heart method is labor intensive at the stage of image analysis as it requires up to 30 min of manual segmentation.

In their study Piri et al. have evaluated the accuracy of an automated artificial intelligence-based segmentation of the heart for ^{18}F -NaF PET/CT.¹³ In their study the convolutional neuronal network (CNN)-based cardiac measures were about 0–4 percent higher than those obtained by expert readers, but did not require any human intervention. The CNN-based segmentation was executed much faster than manual segmentation (1 vs. 30 min) and had an inborn 100 percent repeatability compared to a 0–0.5 percent intra-operator deviation and 0–1 percent inter-operator deviation on repeated manual segmentation. Importantly the novel approach was developed using images obtained on a scanner different from the ones used in the current study, suggesting that CNN-based algorithms can be used reliably disregarding the clinical setting and the PET/CT scanner used. While the aforementioned generalizability is encouraging, it should be noted that the CNN was trained on a set of 25 scans from an external database which was further divided into a training set of 17 scans and a validation

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set of 8 scans. Given the size of the derivation cohort the results of the study should be interpreted with caution.

Over the past decade artificial intelligence has become an increasingly important tool, with rapidly expanding implications for nuclear cardiology. To date it was shown to enhance image processing and segmentation, assist with image reporting, and improve disease diagnosis or risk prediction.¹⁴ Accurate myocardial segmentation is a key component to ensuring the precision of subsequent image quantification and interpretation in SPECT and PET. While most SPECT and PET interpretation software can already perform this process automatically, we lack such dedicated tools for ^{18}F -NaF cardiovascular PET/CT. Given the complexity and level of expertise and/or time commitment required for analysis of ^{18}F -NaF cardiovascular PET/CT artificial intelligence approaches provide hope that this promising imaging modality could be disseminated beyond experienced academic centers.

The study by Piri et al is the first to test a fully automatic region of interest segmentation for cardiac ^{18}F -NaF PET/CT. Since for the global ^{18}F -NaF uptake assessment method, the entire heart is the region of interest the CNN was segmenting the whole heart. Similar approaches have been recently employed for other advanced cardiac imaging applications - for instance for pericardial adipose tissue segmentation.¹⁵ Because higher than bloodpool ^{18}F -NaF activity within the heart silhouette can originate not only from atherosclerotic plaque, but also cardiac valves, infarcted myocardium and pericardial calcifications, fully automated whole-heart ^{18}F -NaF uptake quantification can potentially lead to misleading results. Future studies should therefore test (and potentially optimize) the proposed approach in patients with non-coronary ^{18}F -NaF heart uptake and develop methods to avoid this signal contaminating ^{18}F -NaF originating from regions of atheroma.

Aside from facilitating image analysis artificial intelligence methods can be used for enhanced risk stratification. Classical machine-learning algorithms assess existing observations to determine which features are predictive of outcomes and then use this information to predict the outcomes of future observations. Such algorithms use pre-coded data (such as result of image quantification or clinical features) but are not explicitly programmed with a priori assumptions about the importance of the different features. These algorithms are well suited to integrate the vast amount of clinical and multimodality imaging information from nuclear cardiology studies in order to improve disease diagnosis or risk prediction.¹⁶ In the context of ^{18}F -NaF cardiovascular PET/CT it was demonstrated that inclusion of coronary CT angiography and ^{18}F -NaF PET in a

machine-learning model provides an opportunity for superior prediction of future myocardial infarction compared to any of these imaging modalities in isolation.¹⁷

Since ^{18}F -NaF uptake provides an assessment of disease activity across multiple cardiovascular conditions including aortic valve stenosis, bioprosthetic valve degeneration, and aortic disease in the future further efforts should be made to employ artificial intelligence approaches for streamlining ^{18}F -NaF PET/CT image analysis in all these disease states.¹⁸⁻²⁰ Indeed, such artificial intelligence methods for automated image analysis might help accelerate the clinical adoption of this promising molecular imaging technique.

Disclosures

The authors declare that they have no conflict of interest.

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