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Received Jun 7, 2021; accepted Jun 7, 2021
doi:10.1007/s12350-021-02700-z

See related article, https://doi.org/10.1007/s12350-021-02649-z.

Atherosclerotic cardiovascular disease is the most common cause of death worldwide. In this disease, the atherosclerotic plaques can either be densely calcified and stable or active, progressing over time with an increased risk of rupturing. Atherosclerosis starts initially as fatty streaks, progresses to fibrous plaques with inflammatory cells, and eventually develops advanced lesions such as a thin-capped fibroatheroma (i.e., vulnerable plaque) containing a lipid-rich necrotic core with areas of macrophages and microcalcifications. The two features of atherosclerotic plaque progression are active inflammation and microcalcifications.

Positron emission tomography (PET) imaging using 18F-fluorodeoxyglucose detects active inflammation. However, the evaluation of plaque inflammation can be limited by inability (e.g., descending aorta and the liver) or incomplete (e.g., coronary arteries and the myocardium) suppression of normal physiological glucose metabolism of the adjacent organ. In terms of macroscopic atherosclerotic plaque calcifications, it can be detected by computed tomography (CT), but the spatial resolution of CT cannot detect all the microcalcifications within a vulnerable plaque that are at risk of rupture, hemorrhage, and thrombosis formation. 18F-sodium fluoride (18F-NaF) PET imaging is a measure of ossification as the tracer binds to hydroxyapatite, a crystalline structure that is present in bones and atherosclerotic plaques.[1,2] It binds to the microcalcifications within atherosclerotic plaques that are too small to be detected by CT,[3] and its uptake is indicative of active vascular calcification.[1] For example, Dweck et al. showed that 41% of patients with coronary Agatston scores >1000 had no significant 18F-NaF uptake (i.e., calcified and stable dormant disease).[4] Vice versa, other patients also had areas of increased tracer uptake in regions remote from established calcium deposits (i.e., active and high-risk plaques). Therefore, 18F-NaF PET imaging may permit quantification of early-stage atherosclerosis and disease activity.

In the current issue of the Journal, Piri and colleagues compared aortic segmentation of 18F-NaF PET images using artificial intelligence (AI)-based convolutional neural networks (CNN)-automated segmentation against current standard manual segmentation.[5] Compared to the traditional manual segmentation which can take 1-2 hours to perform, CNN-based segmentation can be performed within a minute without any human intervention. When comparing the results, there were small but significant differences between CNN-based and manually derived measurements. Specifically, total arterial wall volume, maximum standardized uptake values (SUVs), and total SUV were on average 15% lower with the CNN-based technique, whereas mean SUV was not significantly different between the 2 techniques. The higher manual measurements were presumably secondary to ''errors'' from including 18F-NaF uptake from the adjacent vertebral bodies when manually contouring.

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J Nucl Cardiol
1071-3581/$34.00

Published online: 21 July 2021

One of the strengths of the present study was demonstrating the ability of AI to automate clinical processes such as image and data analyses to improve time efficiency and measurement reproducibility. Secondly, the novel use of 18F-NaF PET imaging adds to the current literature on using it as a marker of atherosclerotic disease activity. However, there are a few technical and clinical questions that remain unanswered. For example, the AI software was trained using only a small dataset of 339 manually annotated non-contrast CT images. The ability of the software to automatically segment ''unusual'' anatomy such as an extremely tortuous aorta is unknown. Secondly, the software defined the aortic wall as only 5 mm thick. Therefore, the performance of the software in an aorta with complex atheroma, aneurysms, or occlusions are untested and unknown. Finally, although it is indisputable that AI can significantly reduce the time required for manual segmentation, reduce measurement variability, and therefore improve workflow, more repeatable measurements do not automatically equate to more accurate measurements. In the absence of a true ''gold standard,'' it is impossible to determine if CNN-based aortic segmentation is more accurate than manual segmentation. This important concept is not only relevant for this article but is also applicable for the use of AI in medical imaging in general: the lack of a gold standard does not allow one to state that AI is more accurate, only that the reproducibility is higher and accompanied by significant time saving on data analysis.

On the topic of measurement accuracy, one must also address the question of clinical applicability. More repeatable measurements do not always result in a change in clinical practice or patient outcome. A good example is the evolution of left ventricular (LV) volumes and ejection fraction (EF) quantification from Simpson's biplane to 3-dimensional echocardiography. A more accurate 3-dimensional LV volume and EF measurement that closely approximates the gold-standard cardiac magnetic resonance imaging has not translated into widespread clinical uptake of 3-dimensional echocardiography. More importantly, most studies to date on 18F-NaF PET imaging and high-risk vulnerable plaques have mainly focused on the coronary and carotid arteries, not on the aorta.[6] Therefore, it is unknown if 18F-NaF uptake in the aorta has similar prognostic value as uptake in the coronary arteries.

Our current clinical strategy of focusing on risk scoring systems, assessing vascular stenosis severity, and evaluating various plaque morphologies as indirect measures of plaque vulnerability have been disappointing. In contrast, 18F-NaF PET imaging may provide a different strategy that directly evaluates atherosclerotic disease activity. Therefore, Piri and colleagues should be congratulated for the novelty of their work as theirs was the first study to utilize and show that AI can potentially improve clinical workflow and patient throughput. Future studies should focus on applying AI image quantification in other vascular beds such as the coronary arteries, determine the diagnostic accuracies of these techniques, and ideally demonstrate an incremental prognostic value compared to current clinical standard.

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