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Deep Learning Approaches for Attenuation Correction in Myocardial Perfusion Imaging

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List of abbreviations

MPI = myocardial perfusion imaging

CAD = coronary artery disease

PET = positron emission tomography

SPECT = single photon emission computed tomography

RCA = right coronary artery

AC = attenuation correction

CT = computed tomography

DLAC = deep learning -based attenuation correction

CZT = cadmium-zinc-telluride

Myocardial perfusion imaging (MPI) has a well-established role in the diagnosis, risk stratification, and guiding management of chronic coronary artery disease (CAD). While the use of positron emission tomography (PET) and magnetic resonance perfusion imaging is increasing, single photon emission computed tomography (SPECT) continues to be the most widely utilized MPI technology.[1,2] Attenuation artifacts are a broadly acknowledged pitfall in nuclear MPI including SPECT and PET, typically causing reduction of measured tracer activity in the inferior wall of the left ventricular myocardium that is most often supplied by the right coronary artery (RCA), and can lead to false positive interpretation as an ischemic perfusion defect. Attenuation correction (AC) improves the diagnostic accuracy and especially the specificity of MPI in detection of obstructive CAD.[3,4] Therefore, AC is routinely applied in PET MPI and increasingly utilized with SPECT MPI, and can be easily achieved by a low-dose computed tomography (CT) scan when using integrated hybrid PET/CT and SPECT/CT systems. The importance of AC in reducing attenuation artifacts is further emphasized by the use of stress-only and stress-first MPI protocols which aim to avoid unnecessary rest MPI acquisitions.[5]

Based on a cross-sectional study conducted in 2013 it was estimated that almost 75% of nuclear MPI scans worldwide were performed without AC.[1] Since then, technological advances and increasing scientific evidence may have facilitated the use of AC for MPI, for example, by hybrid scanners becoming more common. Interestingly, new cardiac-dedicated SPECT devices may have advantages in reducing scan time or radiation exposure, but “easy” CT-based correction for attenuation is not possible for most cardiac-dedicated scanners due to lacking CT gantry.[6] This has been one of the motivators for developing deep learning -based AC methods (DLAC) which can be divided into two main categories: in indirect DLAC approaches attenuation maps (μ-maps) are generated from emission images and subsequently used in image reconstruction to get attenuation corrected perfusion images whereas in direct DLAC approaches attenuation corrected perfusion images are directly predicted from non-attenuation corrected perfusion images without the intermediate step of generating μ-maps.[7] Despite increasing interest in DLAC methods, only a few studies have investigated their diagnostic accuracy in detection of obstructive CAD. Hagio et al. tested their DLAC method in a multi-center cohort of more than 700 prospectively enrolled patients (flurpiridaz-301 trial) and found that DLAC SPECT as compared with non-attenuation corrected SPECT images improved the diagnostic accuracy for obstructive CAD defined by quantitative coronary angiography.[8] Per-patient specificity was significantly improved by 6.2%, with a small non-significant decrease (0.5%) in sensitivity. Shanbhag et al. evaluated another DLAC method in a selected group of 604 patients with same-day SPECT MPI and coronary CT angiography or a low likelihood of CAD, and found that DLAC significantly improved discrimination (area under the curve) for obstructive CAD as compared with non-attenuation corrected SPECT MPI, with DLAC demonstrating comparable performance to actual CT-based AC.[9]

In this issue of the Journal of Nuclear Cardiology, Sprauel et al. report their study assessing SPECT MPI with and without DLAC in comparison with [^{82}Rb]rubidium PET MPI.[10] The study cohort was derived from the RUBIS trial (Comparison of Rubidium PET and SPECT With CZT Crystals for Detection of Myocardial Ischemia in Overweighed Patients and Women) which originally recruited women and overweighed men – who are thought to have high risk for attenuation artifacts – to undergo both [^{99m}Tc]sestamibi MPI with a cardiac-dedicated cadmium-zinc-telluride (CZT) SPECT camera (D-SPECT; Spectrum Dynamics, Israel) and [^{82}Rb]rubidium PET MPI to enable head-to-head comparison of the two modalities.[11] In the current analysis, the investigators included 84 patients from the RUBIS trial based on the availability of image data. The SPECT perfusion images were reconstructed both without AC and with an indirect DLAC method commercialized by the scanner vendor, whereas rubidium PET images were reconstructed using CT-based AC. The authors identified a subgroup of 74 patients deemed to be at “very low CAD risk” based on the absence of significant coronary stenosis on angiography, stress electrocardiogram findings, anginal history, or cardiovascular adverse events during one-year follow-up, and assuming that these patients should have normal myocardial perfusion. They found that among these patients both DLAC SPECT and rubidium PET showed homogenous tracer uptake whereas non-attenuation corrected SPECT showed reduced stress activity in the RCA territory. The authors concluded that there is no more drop in the tracer activity in the RCA territory when using DLAC maps for SPECT reconstruction and the results by DLAC SPECT closely align with those obtained by rubidium PET.

Sprauel et al. should be recognized for their research work on a clinically important topic, with the main strength and novelty of their study lying in the comparison with rubidium PET MPI. However, some limitations should be kept in mind when interpreting the results. First, only 14 (17%) of the 84 included patients underwent invasive coronary angiography to confirm or exclude the diagnosis of obstructive CAD, and therefore, reliable conclusions cannot be made regarding the diagnostic accuracy of DLAC SPECT. To overcome this fact, the authors identified a “very low CAD risk” group of 74 patients who were assumed to be free from obstructive CAD and therefore having normal homogenous myocardial perfusion. Even if this assumption was true and these patients truly did not have obstructive CAD, conclusions could only be made regarding the specificity but not the sensitivity of DLAC SPECT. This aspect is further emphasized by their finding that the summed stress and summed difference scores were significantly lower for DLAC SPECT than for rubidium PET.[10] One potential explanation for this discrepancy could be that rubidium PET was performed with dipyridamole vasodilator stress whereas more than half of the SPECT scans were performed with physical exercise stress. However, future studies with routine use of coronary angiography preferably with pressure measurements are warranted to confirm that the potential improvement in specificity by DLAC is not at the cost of decreased sensitivity due to overcorrection of actual perfusion defects. Another remark can be made regarding the patient selection, and therefore, generalization of the results: the RUBIS trial aimed at inclusion of patients with intermediate pre-test probability of CAD, but only 12% of patients in the current analysis by Sprauel et al. were reported to have chest pain and a single patient had typical angina pectoris.[10,11] Accordingly, most patients were interpreted as non-ischemic by rubidium PET MPI while 23% were reported to have mild ischemia and only 5% had moderate-to-severe ischemia on PET.

The continuous evolution of medical imaging hardware necessitates the development of new software solutions, where artificial intelligence and machine learning hold great promise. However, these tools should be always carefully evaluated in clinically relevant settings before widespread adoption. If validated by further studies, DLAC is a compelling example of machine learning solutions that not only make things easier or faster but can really create something new and useful – such as synthetic attenuation maps – to potentially enhance diagnostic accuracy and improve patient outcomes.

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