Future of nuclear cardiology is bright: Promise of cardiac PET/CT and artificial intelligence

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The effective use of medical and invasive coronary artery disease (CAD) therapies requires reliable and objective noninvasive imaging methods for assessment of disease and potential for treatment. Noninvasive CAD evaluation includes various imaging techniques that assess the anatomic burden of atherosclerosis and quantify the extent and severity of myocardial ischemia. Myocardial perfusion imaging (MPI) is currently the most widely used approach to assess ischemia in patients. MPI is most commonly performed with SPECT in the USA. However, traditional relative perfusion assessment by SPECT MPI is relatively insensitive to diffuse atherosclerosis and microvascular disease. In contrast, PET quantification of myocardial blood flow (in mL/min/g of myocardium) and flow reserve provides absolute measurements which can characterize these conditions. The flow measures provide robust diagnosis of obstructive and nonobstructive CAD^{1–3} and significantly improve risk stratification.⁴ The ability to quantify myocardial blood flow with PET allows a level of risk assessment well beyond that achieved with only relative analysis of regional perfusion defects. Beyond risk stratification, quantitative flow analysis may enable selecting patients who may benefit from revascularization—a potentially powerful clinical tool—especially in light of the limitations of visually determined ischemia measures from SPECT as reported by the ISCHEMIA trial.⁵

Beyond perfusion, flow, and functional information, current cardiac PET/CT scans always include ungated, low-dose CT scans for attenuation correction. These auxiliary CT images are often underutilized clinically, but they contain important information and could be

efficiently repurposed to estimate the complementary anatomical aspects of atherosclerosis. Quantification of coronary artery calcium (CAC) by CT provides an accurate measure of atherosclerotic burden. Additionally, the CAC measure provides unique, actionable clinical information to guide the intensity of preventative therapy—complementing the information provided by perfusion and flow quantification. Complementary diagnostic role of CT and PET has been demonstrated with the combined quantitative PET+CAC score, which increased the diagnostic performance of PET^{6,7} as evaluated in comparison with invasive angiography.

In part due to these multifaceted benefits, PET has been the fastest growing cardiovascular imaging modality over the last decade in the USA (146% Medicare growth 2010–2019).⁸ However, there are currently no techniques to effectively combine flow measurements with perfusion data and other imaging markers, including CAC obtained during cardiac PET/CT scan, and realize the full potential of this powerful modality. While PET/CT MPI affords comprehensive quantitative opportunities, the clinical PET/CT image analysis remains complex and can be technically more demanding than SPECT MPI. This technical complexity is currently a major bottleneck for rapid clinical expansion of cardiac PET/CT.

New artificial intelligence (AI) tools have the potential to dramatically enhance the utility of cardiac PET/CT in the near future. Incorporation of AI techniques to standardize and automate processing of cardiac PET/CT can improve diagnosis, risk prediction, and ultimately patient care. The wealth of imaging variables, which can be automatically extracted from PET/CT scans, offers new opportunities—but it will require efficient methods for integrating the diverse data. AI applied to SPECT and CT has already demonstrated improved prediction of disease and outcomes by combining imaging and clinical parameters^{9–22} and prediction of angiographic CAD.^{23,24} AI surpassed the clinical interpretation of SPECT MPI for

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revascularization^{9,17} and major adverse cardiac events prediction.^{12,16} AI methods can explain to the physician the specific importance of contributing features.^{16,25} AI-generated image attention maps can point to disease regions driving the CAD diagnosis.²⁶ While routine quantification of CAC scores from associated CT scans associated with PET/CT may be burdensome in the clinical practice, it is possible to obtain quantitative CAC estimates from CTAC in a fully automated fashion with deep learning networks. Deep learning was applied for quantification of calcium in ungated CT scans from the National Lung Screening Trial.²⁷ CAC scores derived automatically from CTAC were shown to correlate well with CAC scores from separate gated CT.²⁸ Beyond calcium, deep learning was applied for fully automated segmentation of epicardial adipose tissue from cardiac CT^{29,30}—a novel CT parameter, which added independent prognostic information to coronary CAC scores.¹³ The new AI techniques to extract and integrate quantitative information can be efficiently translated to PET/CT imaging. Due to the intrinsically rich information available in flow, perfusion, and CT images, cardiac PET/CT enhanced with AI methods has a true potential to become a frontline modality for a wide range of cardiovascular applications.

Disclosures

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