Greatest opportunities for growth in nuclear cardiology

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The indispensable factor of sustaining any field of science or intellectual endeavor is the influx of new ideas and solutions to previously unsolved, but in principle solvable problems. Over the last four decades, myocardial perfusion imaging has been the dominant procedure in nuclear cardiology. A number of clinical trials have demonstrated the diagnostic and prognostic accuracy of gated myocardial perfusion studies with SPECT or PET, and its relevance for patient management.[1–3] However, it has become increasingly apparent that in the hands of the specialists, nuclear cardiology has grown progressively narrower (limited to myocardial perfusion imaging) rather than wider, extending to multitude of potential metabolic and molecular targets that can be explored for the diagnosis and treatment of various heart diseases.

The most fruitful areas of growth in nuclear imaging are those which have been neglected between the various established imaging disciplines. It is within these neglected boundaries where targeted radionuclide-based imaging offers the greatest opportunities for growth. An inherent advantage of nuclear imaging techniques is in the synergy that exists between the radionuclide tracers—that by their nature reflect biological and biochemical processes at the cellular level—and the underlying pathophysiological states being investigated. For example, the diagnosis of cardiac amyloidosis is challenging as the clinical manifestations of cardiac amyloidosis overlap with other heart diseases, and findings of electrocardiography and echocardiography are nonspecific. Early diagnosis of cardiac amyloidosis and the identification of the type of amyloid deposition have important clinical, therapeutic, and prognostic implications. ^{99m}Tc-pyrophosphate imaging provides the opportunity to diagnose cardiac amyloidosis, evaluate cardiac amyloid load quantitatively, differentiate light-chain amyloidosis from transthyretin-related cardiac amyloidosis, monitor disease progression, and assess response to treatment.

Targeting specific biological or chemical pathways to assess normal and abnormal cellular function in vivo is the basis of molecular imaging. For example, molecular imaging allows direct visualization and characterization of the sarcolemma and mitochondrial membrane integrity along with metabolic, neuronal, and enzymatic components of living cardiac cells. The ability to image the metabolic shift of energy production from fatty acids toward glucose in the setting of severe coronary artery disease and reduced blood flow has helped explain the pathophysiology of viable, hibernating myocardium, and critical patient management decisions regarding revascularization, left ventricular assist device placement, ablation therapy, transplantation, or continued medical therapy.[1] The important myocardial tissue component of the renin-angiotensin system is not directly accessible in clinical practice and the circulating neurohormonal levels are correlated poorly to their upregulation at the tissue level. Radionuclide imaging of myocardial renin-angiotensin-aldosterone system in a heart failure patient may offer a more direct, patient-specific, assessment of angiotensin-converting enzyme and angiotensin type-1 receptor activation that are linked to left ventricular remodeling. Targeting myocardial angiotensin-converting enzyme with radiolabeled Lisinopril, for example, may identify patients with increased myocardial angiotensin-converting enzyme activity, prospectively, and in the early stages of heart failure, before the transition to replacement fibrosis and left ventricular remodeling occurs.[4]

Progress in the areas of hybrid positron emission tomography-computed tomography (PET/CT) and

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positron emission tomography-magnetic resonance (PET/MR) imaging are equally important areas of growth in nuclear cardiology. Among patients with suspected cardiac mechanical device or prosthetic valve infection, recent publications advocate the use of ^{18}F-fluoro-2-deoxyglucose (FDG) with hybrid PET/CT imaging, particularly when anatomy-based imaging, such as echocardiography or CT, is uncertain or negative.[5] A potential advantage of FDG PET/CT is in its detection of inflammatory cells early in the infection process, at the site of the prosthetic valve infection before morphologic damages from the infectious process ensue. Similarly, the diagnosis of cardiac implantable electronic device infection, and accurate localization of the infection site, such as left ventricular assist device, defibrillator pocket, or pacemaker lead, remains clinically challenging.[6] Inconclusive diagnosis can lead to delayed antibiotic therapy, device extraction, or surgical intervention, which may have dire consequences on the patient. Such hybrid FDG PET/CT inflammatory imaging can also identify cardiac involvement of sarcoidosis and predict response to therapy that is paramount to improve the management of such patients and for risk stratification. The early diagnosis of cardiac sarcoidosis is imperative, as data suggest that high-dose steroid therapy should be administered to patients during the active inflammatory phase of the disease before the transition to replacement fibrosis and decline of left ventricular systolic function supervene.[1]

A significant majority of atherosclerotic plaque ruptures occur in arteries exhibiting none or only modest luminal narrowing. The pursuit for noninvasive molecular imaging probes that target plaque composition in parallel with recent advances in hybrid imaging has made it possible to identify early active inflammation and microcalcification process in atherosclerotic plaque, which is essential for understanding their vulnerability to rupture. FDG targets plaque macrophage glucose utilization and inflammation, while ^{18}F-sodium fluoride targets active molecular microcalcifications in atherosclerotic plaques. Emerging data suggest that vascular plaque uptake of these tracers is associated with cardiovascular events such as myocardial infarction and stroke. Hence, these imaging biomarkers may identify high-risk culprit plaque with active on-going inflammation and/or calcification far before structure calcification is seen on CT, and thereby serve as a tool to monitor the therapeutic effect of medications that block the inflammation and calcification process within a plaque.

Radiotracer-based molecular imaging is one of the most exciting, dynamic, and emerging areas of imaging in medicine. It provides a sensitive, noninvasive, quantitative tool for investigating preclinical and clinical abnormalities in myocardial perfusion,[7] function, metabolism, innervation, enzymatic, or receptor derangements and allows for monitoring disease progression and the effectiveness of medical therapy. The synthesis of molecular radiotracers in parallel with a series of technological advances in hybrid imaging has made it possible to investigate various preclinical and clinical cellular abnormalities in vivo, in various organs, with exceptional accuracy. These advances portend great opportunities for growth in nuclear cardiology.

Disclosure

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