Published in final edited form as:

PET Clin. 2020 October ; 15(4): 509–520. doi:10.1016/j.cpet.2020.06.007.

APPLICATIONS OF PET-MRI IN CARDIOVASCULAR DISORDERS

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Keywords

Cardiac Positron-Emission Tomography; Cardiac Magnetic Resonance Imaging; Cardiac PET/MRI; Ischemic Heart Disease; Myocardial Viability; Sarcoidosis; Cardiac Masses

INTRODUCTION

Over the last 15 to 20 years, there has been remarkable advance in cardiovascular magnetic resonance imaging (MRI) and Positron Emission Tomography (PET).¹ More recently, PET/MRI has been developed as an integrated imaging modality, using MRI data to provide attenuation correction for PET.² This technique utilizes the validated tools of MRI and PET to provide a complete morphological, functional, and physiological cardiac assessment, targeted at the specific cardiac condition by using specific MRI sequences and PET radiotracers.

This hybrid imaging approach has the potential to improve the diagnostic yield and assist in the management of a variety of cardiovascular disorders, such as ischemic heart disease, infiltrative diseases and inflammatory conditions. In this report, we review the individual strengths of cardiovascular PET and MRI, as well as the current applications, limitations, and future potential of hybrid PET/MRI.

TECHNICAL ASPECTS

Attenuation correction in PET/MRI

The loss of photons due to absorption in the body and/or hardware or scattering out of the detector field of view, also known as attenuation, is an important challenge in PET.

Attenuation correction is technically challenging in PET/MRI because MRI is based on proton density and relaxation of magnetization, which are not directly correlated with tissue density (Table 1).³

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disclosure statement

The authors have nothing to disclose.

One option for MRI-based attenuation correction is the atlas-based approach, where populational data is used to form a computational relationship between CT-derived attenuation and MRI pairs. In this method, a patient scanned with PET/MRI is matched to a set of MRI images within the atlas. Then, a pseudo-CT, generated from the atlas' MRI-CT pair, is used for attenuation data. This approach provides accurate attenuation correction for PET/MRI when there is similarity between a patient's MRI and atlas images. When the patient's anatomy varies substantially from the populational average, this method can lead to significant error.^{2,4}

Direct imaging methods, in contrast, use segmentation instead of an atlas-based approach. MRI voxels are segmented into categories, such as air, lung, soft tissue and fat. All voxels within the same category are assigned the same attenuation coefficient. Direct methods are faster than atlas-based approaches and they also account better for individual anatomical variability. However, assigning a constant attenuation coefficient to each 'segment' may cause errors in the estimation of radiotracer uptake. Nevertheless, this method has been shown to have adequate correlation with standardized uptake values (SUVs) obtained by PET/CT.^{2,5,6}

Respiratory and cardiac motion

The constant respiratory and cardiac motion is an important cause of image degradation in PET, causing dispersion of tracer activity and under- or over-estimation of hot/cold spots.⁷ Gating the images to periods of less motion in the cardiac cycle, as is done with CT, would dispose of valuable tracer counts, which can only be compensated by longer acquisition times or a higher dose of the radiotracer, none of which are desirable.^{8,9} Also, a breath hold is not possible because PET images are acquired over minutes, through many breathing cycles.^{8,10}

To circumvent this problem, direct anatomical data from MRI is used to track the respiratory and cardiac motion during the scan, creating 3D motion fields. The PET data is then reconstructed with the MRI-based motion fields, generating motion-corrected images with improved tracer quantification.^{8,10,11} In a study of 8 patients with suspected cardiac sarcoidosis who underwent ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) cardiac PET/MRI, motion-corrected images showed less blurring, better alignment of tracer activity and myocardial anatomy, and greater contrast-to-noise ratio as compared to no motion correction.⁸

Cardiac devices

Artifacts due to metallic cardiac implants constitute an important limitation in PET. In PET/MRI, nonmagnetic metallic cardiac devices lead to a signal void that falsely increases the object size. This leads to an underestimation of attenuation and tracer uptake. Furthermore, there are safety concerns about PET/MRI scanning in patients with cardiac devices, specifically device malfunction and heating. Since data on device compatibility is less available with 3 Tesla field strength as compared to 1.5 Tesla, many patients with cardiac devices are unsuitable for PET/MRI.¹²

MYOCARDIAL PERFUSION IMAGING

PET perfusion

Historically, single photon-emission computed tomography (SPECT) has been the mainstay imaging for assessment of myocardial perfusion imaging (MPI). PET, however, has several advantages of SPECT, including improved spatial resolution, less radiation, better attenuation correction, and, more importantly, the potential for quantifying rest/stress regional blood flow with mathematical modeling of tracer uptake.^{13–15} Assessment of the myocardial blood flow (MBF) and coronary flow reserve are valuable tools for identifying endothelial dysfunction, microvascular disease, and improved risk stratification in patients with ischemic heart disease.^{6,14,16}

Radiotracers for perfusion

Tracers utilized in PET perfusion, summarized in Table 2, include ^{15}O -water, ^{82}Rb -RbCl and ^{13}N -NH₃. ^{15}O -water is a freely diffusible tracer; its accumulation and wash-out are independent of metabolic activity in the myocardium. As a result, it is the only tracer that has myocardial uptake in linear correlation with perfusion at all ranges of myocardial blood flow. Myocardial uptake of ^{13}N -NH₃ and ^{82}Rb -RbCl plateaus at hyperemic flows above 2–4 mL/g/min. ^{13}N -NH₃ is a non-diffusible tracer, retained in the myocardium as a function of blood flow and tissue metabolism. ^{82}Rb -RbCl is a potassium analog, taken up by myocardial cells by a Na/K ATP transporter. It has a very short half-life (75 seconds); however, it is more easily obtained than other tracers because it is generator-produced, obviating the need for an on-site cyclotron. ^{18}F -Flurpiridaz is only available as a tracer for research. It has the longest half-life of PET perfusion tracers (110 minutes), which potentially allows for performance of exercise perfusion studies, as well as transport of the agent between sites.^{13,14,17}

MRI perfusion

Stress MRI also has several advantages over SPECT, including no attenuation artifacts, significantly better spatial resolution, and no radiation. Stress MRI is typically done based on visual assessment, with gadolinium-based contrast agents (GBCA), with superior accuracy to SPECT.¹⁸ Importantly, semiquantitative and quantitative methods to assess MPI are also available and increasingly being used with stress MRI. One option is to apply a model of left ventricular (LV) segmentation and analyze each segment's time-intensity curve, i.e., the change in signal intensity over time after GBCE enhancement. The stress to rest ratio of the upslope or rate of increase in signal intensity can be used to calculate the myocardial perfusion reserve index.¹⁹ Although this method can correctly identify obstructive coronary artery disease with a sensitivity >90% and specificity of 70–80%, it also has been shown to underestimate coronary flow reserve when compared to ^{13}N -PET.^{20,21}

Exact quantification of MBF with MRI involves highly complex computations to deconvolute the time-intensity curve. The technique is limited by several challenges in the relationship between perfusion and change in signal intensity: (1) the extraction of GBCE is low and not exclusively dependent of blood flow; (2) the extraction of GBCE is non-linear

at higher flows; and (3) regional variation in magnetic or radiofrequency fields.^{6,19} Despite its limitations, this method provides accurate estimates of myocardial perfusion reserve, with similar sensitivity and specificity as compared to ¹³N-PET.²² In a recent study, there was a strong correlation between absolute flow values by PET and MRI in 29 individuals.²³

Hybrid PET/MRI for perfusion

Hybrid PET/MRI has the potential to combine the individual strengths of PET and MRI in the assessment of MPI, in particular the accuracy of quantitative MBF with PET, the high spatial resolution of MRI, and the use of cine MRI to assess for regional wall motion abnormalities. PET/MRI also adds the benefit of motion correction and lower exposure to ionizing radiation as compared to PET/CT. Finally, hybrid imaging will allow for cross-modality validation, such as comparing MRI-derived quantitative blood flow assessments with PET results, which has the potential to improve both imaging modalities.^{23–26} Despite these theoretical advantages, combined PET/MRI for perfusion imaging remains a research tool at this point.^{23,26} As with other potential applications of PET/MRI, expansion into clinical use is hindered by high costs, low availability, and more importantly, the current lack of data supporting an incremental value over each imaging modality independently.

MYOCARDIAL VIABILITY

Viability assessment seeks to differentiate infarcted myocardial tissue from ‘hibernating’ myocardium, a state of chronic hypoperfusion where the muscle is hypo- or a-kinetic, yet viable. Patients with viable myocardium have a greater improvement in systolic function following revascularization or medical therapy as compared to those without myocardial viability.²⁷ However, viability testing in the STICH trial did not significantly discriminate between patients who benefit vs. those who do not benefit from revascularization in ischemic cardiomyopathy.^{27,28}

Viability by PET

In PET, myocardial viability is examined with ¹⁸F-FDG. This glucose analogue is taken up by the cardiomyocytes through transmembrane glucose transporters, where it is then trapped intracellularly. To standardize glucose uptake in the test, patients typically receive insulin and oral glucose loading prior to the test.²⁹ The ¹⁸F-FDG tracer has a long half-life of approximately 110 minutes. If perfusion is impaired, the uptake of ¹⁸F-FDG indicates hibernating myocardium, whereas the absence of ¹⁸F-FDG uptake implies infarcted, non-viable tissue.^{30,31} A meta-analysis of 24 studies and over 750 patients found a sensitivity of 92% and a specificity of 63% of PET-viability for prediction of regional contractile function recovery after revascularization, though this data is limited by heterogeneous definitions of viability and regional wall motion recovery.³²

Viability by MRI

MRI utilizes GBCA and delayed enhancement imaging to determine myocardial viability. Unlike PET radiotracers, GBCA are not taken up by myocytes. When there is tissue necrosis or fibrosis, the distribution volume and retention of GBCA in tissue increases.^{31,33} The evaluation of viability by MRI is ultimately determined by the percentage of wall thickness

with LGE.³⁴ This is an important advantage of the MRI-based method, since the high spatial resolution of MRI with up to 1.5-mm in-plane resolution, allows for precise localization of LGE in the sub-endocardium, mid-myocardium, sub-epicardium, or transmurally.³⁴ In addition to being more available than PET for clinical use, MRI-based viability may be specifically preferred over PET in diabetic patients, since viability assessment with MRI is independent of glucose metabolism.

Hybrid PET-MRI for viability

PET/MRI has been shown to be feasible for assessment of viability, although it remains only investigational at this point. In a feasibility study, 20 patients with a history of myocardial infarction (MI) underwent PET/MRI; there was substantial agreement between PET and MRI-LGE images.³⁵ In a separate study, investigators found that nearly 20% of dysfunctional left ventricular segments imaged with PET/MRI within 1 week post-MI had discrepant viability findings between PET and MRI. These segments had worse functional recovery compared to segments viable by both PET and MRI.³⁶ Furthermore, PET/MRI imaging not only provides information on myocardial viability but also characterizes infarct-related remodeling with insight into the infarct tissue micro-environment, e.g. activation of metalloproteinases,³⁷ inflammatory and progenitor cell recruitment via chemokine receptor expression,³⁸ and stimulation of angiogenesis.³⁹

While it is conceivable that an improvement in the diagnostic assessment of myocardial viability with the hybrid PET/MRI approach may aid in the evaluation of challenging patients at high surgical risk and unclear benefit from revascularization, this remains to be proven in subsequent clinical studies.

INFLAMMATION

Following an acute myocardial infarction (MI), there is a pro-inflammatory response in the myocardial tissue, which is subsequently exacerbated by reperfusion injury and may contribute up to 50% of the final MI expansion.⁴⁰ The degree of inflammation within a few days of an acute MI has been linked to adverse LV remodeling and worse systolic function over time.^{41,42}

¹⁸F-FDG-PET/MRI has the potential to quantify the inflammatory response post-MI with the PET-portion, matched with the high spatial resolution of MRI-morphology and functional data. The uptake of ¹⁸F-FDG predominantly by inflammatory cells, such as monocytes and macrophages, depends on adequate suppression of myocyte glucose uptake. This is accomplished by shifting myocardial metabolism from glucose to free fatty acids with a high fat, no-carbohydrate diet followed by a fast of 4–12 hours and unfractionated heparin given 15 minutes prior to the study.⁴³ The intensity of ¹⁸F-FDG uptake in the myocardium within the first 5 days following acute MI has been correlated with adverse LV functional outcomes assessed by MRI at 6 months, independently of infarct size.⁴⁴

Animal models have shown feasibility of PET/MRI to assess monocyte response and inflammation after an acute MI.⁴⁵ Although the technique has been utilized in individual patients, there are no reported prospective studies or case series relating inflammation as

assessed by PET/MRI to post-MI outcomes.³¹ Future research is needed to uncover the relationship between PET/MRI results and scar formation vs. functional recovery.

IMAGING OF ATHEROSCLEROTIC PLAQUE

MRI in atherosclerosis imaging

PET/MRI has the potential to be used for anatomical and functional study of atherosclerotic plaque. With regards to anatomy, MRI angiography can adequately define the course of large epicardial vessels, being well suited to assess coronary artery anomalies and the course of surgical coronary bypass grafts.⁴⁶ MRI has also been studied to evaluate coronary stenosis. In a study of 12 individuals with known coronary plaques CT angiography, MRI with black blood sequence, designed to null signals (black) from blood, accurately identified plaques in the proximal and middle segments of coronary arteries.⁴⁷ Intracoronary thrombus in acute MI can also be identified with MRI, taking advantage of short T1 values of methemoglobin found in acute thrombus and plaque hemorrhage.⁴⁸

PET in atherosclerosis imaging

PET, on the other hand, can offer molecular imaging to delineate biological processes in plaque. As previously described, ¹⁸F-FDG can determine the inflammatory response, particularly after an acute MI. In stable plaque, however, a study with 8 patients found no correlation between ¹⁸F-FDG uptake and CD68+ macrophages in patients with plaque in the superficial femoral artery.⁴⁹

Another tracer with applicability in plaque imaging is ¹⁸F-sodium fluoride (NaF). ¹⁸F-NaF is used most commonly in bone imaging. Most of the tracer is retained by bone after a single pass and added to the bone forming matrix.⁵⁰ In fact, ¹⁸F-NaF uptake identifies active tissue calcification in aortic stenosis, thereby predicting disease progression.⁵¹ In coronary imaging, ¹⁸F-NaF can detect subclinical calcification and its uptake accurately identifies the culprit plaque in >90% of patients with MI, more so than ¹⁸F-FDG.⁵² In carotid plaque, it is associated with active calcification, macrophage infiltration, and apoptosis.⁵² In patients with stable angina, ¹⁸F-NaF uptake correlates with high-risk features on intravascular ultrasound.⁵²

PET/MRI in atherosclerosis imaging

In the first report of coronary artery hybrid PET/MRI, Robson and colleagues successfully imaged 23 patients with risk factors or diagnosed coronary artery disease using either ¹⁸F-NaF or ¹⁸F-FDG. The authors demonstrated feasibility and also how to improve the technique based on their experience, by using a novel free-breathing attenuation correction approach and increasing the number of reconstruction iterations.⁵³ One challenge of atherosclerotic plaque burden imaging is the rather low radiotracer uptake in addition to signal hampering by cardiac and respiratory motion. Gating MRI for motion correction potentially can overcome some of these limitations by improving the contrast and spatial resolution of vulnerable plaque composition.³⁹

It remains to be proven whether hybrid PET/MRI can effectively combine anatomical with physiological data to identify high-risk plaques beyond the risk prediction granted by total atherosclerotic burden (e.g., CT angiography). Similarly, the technology might be studied to predict recurrence of events after an acute coronary syndrome, and potentially guide prevention strategies.

SARCOIDOSIS

Sarcoidosis is a multi-system inflammatory condition, of unknown etiology, characterized by the presence of noncaseating granulomas. The diagnosis of cardiac sarcoidosis is particularly challenging due to the wide spectrum of clinical manifestations and lack of a 'gold-standard' testing strategy. The low yield and invasive nature of endomyocardial biopsy underscore the importance of imaging for the diagnosis of cardiac sarcoid.^{54,55} The disease is patchy, multifocal, and progresses from edema and inflammation to fibrosis and scarring.⁵⁵

MRI in sarcoidosis

Cardiac MRI can evaluate for cardiac sarcoidosis in all these stages. Scar can be identified by ventricular wall thinning and, more importantly, LGE. As previously described, the spatial resolution of MRI allows for precise localization of LGE. Classically, cardiac sarcoidosis follows a non-coronary distribution, with subepicardial and mid-myocardium LGE involving the basal septal and inferolateral walls, although various patterns can be seen.⁵⁶ The extent of LGE is a strong, independent predictor of major adverse cardiac events in sarcoidosis.⁵⁷ Edema and acute inflammatory changes can be identified with T2 mapping, an important sequence in complement to LGE.⁵⁸ Finally, cine MRI can accurately assess the extent of right and left ventricular systolic dysfunction, also important prognostic markers in cardiac sarcoidosis.⁵⁵

PET in sarcoidosis

Similarly, PET is also a valuable tool in the diagnosis and staging (inflammation vs. fibrosis) of cardiac sarcoidosis. This is done with perfusion ($^{13}\text{N-NH}_3$ or $^{82}\text{Rb-RbCl}$) and metabolic ($^{18}\text{F-FDG}$) imaging. In the presence of active inflammation, macrophages have an increased metabolic rate and glucose uptake. As previously discussed, a special care with dietary suppression of myocardial glucose uptake is needed for optimal image quality. The presence of increased $^{18}\text{F-FDG}$ uptake in the presence of normal (early disease) or reduced perfusion (progressive disease) indicates active inflammation. In contrast, a severe perfusion defect with minimal or no $^{18}\text{F-FDG}$ uptake implies fibrosis and scarring.⁵⁶ Repeated $^{18}\text{F-FDG}$ PET studies have a role in the serial examination of patients with cardiac sarcoidosis, guiding immunosuppressive therapy and monitoring the response to treatment.^{56,59}

Hybrid PET/MRI in sarcoidosis

Comparing the efficacy of $^{18}\text{F-FDG}$ PET and MRI in the diagnosis of sarcoidosis is limited by the lack of a gold standard diagnostic tool. In a study with 21 patients suspected of having cardiac sarcoid, including 8 confirmed by the Japanese Ministry of Health (JMH) criteria, $^{18}\text{F-FDG}$ PET had a higher sensitivity as compared to MRI (88 vs .75%), albeit with

lower specificity (39% vs. 77%).⁶⁰ However, the often-quoted JMH criteria for cardiac sarcoidosis may perform inferiorly to the diagnostic yield of MRI and ¹⁸F-FDG PET.⁵⁶

Rather than choosing one modality over the other, however, sarcoidosis is a condition in which PET and MRI are truly complementary to each other (Figure 1). Hybrid PET/MRI may evolve to play a larger role in the diagnosis and assessment of the immunosuppressive treatment response of cardiac sarcoidosis. A pioneer study by Wicks and colleagues showed improved sensitivity of combined PET/MRI (94%) as compared to PET (85%) or MRI (82%) alone in 51 patients with suspected cardiac sarcoid. There was also poor agreement between modalities in the location of cardiac abnormalities, suggesting that they offer complementary information about the disease process.⁶¹

AMYLOIDOSIS

Cardiac amyloidosis is an infiltrative cardiomyopathy caused by the deposit of amyloid, an abnormally folded protein, in the myocardium. The source of amyloid when there is cardiac involvement is either transthyretin (TTR), in TTR-amyloidosis, or monoclonal immunoglobulin light chains in amyloid light-chain (AL) amyloid.

In patients with suspected amyloidosis, cardiac MRI can identify a phenotype of restrictive cardiomyopathy (biatrial enlargement, increased wall thickness) and evaluate LV function with cine imaging. LGE in a non-coronary distribution can be absent, subendocardial, or transmural according to an increasing burden of amyloid.⁶² A meta-analysis including 257 patients reported a sensitivity and specificity of 85% and 92%, respectively, of MRI in the diagnosis of amyloidosis. Importantly, however, MRI is unable to differentiate amyloid types.⁶³

There is ongoing research with PET in the field of cardiac amyloidosis. Thus far, ¹¹C-Pittsburgh B and ¹⁸F-florbetapir have demonstrated some success in early studies in differentiating patients with vs. without cardiac amyloid.^{64,65} It should be noted that PET and MRI cannot yet reliably differentiate TTR vs. AL amyloid. SPECT with technetium-99m remains the most validated imaging tool for such assessment.

In a pioneer study of hybrid PET/MRI for the evaluation of cardiac amyloid, investigators compared 4 TTR-amyloid, 3 AL-amyloid, and 7 control individuals with ¹⁸F-sodium fluoride PET/MRI. Results showed low uptake of ¹⁸F-sodium fluoride in controls and those with AL amyloid, as compared to an increased uptake in patients with TTR amyloid, which correlated with regions of LGE on MRI. Although these results are encouraging, further studies are warranted to validate these findings in a larger sample size and compare PET/MRI to other imaging alternatives in cardiac amyloidosis.⁶⁶

MYOCARDITIS

MRI is recommended by guidelines in the diagnostic and prognostic evaluation of patients with suspected myocarditis.^{67,68} Myocardial inflammation, capillary leak, edema, myocyte injury, and ultimately scar can be identified with special sequences in MRI. Tissue edema prolongs both T1 and T2 relaxation times and is best assessed by T2-weighted images. T1-

weighted spin echo images and early GBCA enhancement can identify capillary leak. LGE identifies myocyte necrosis and fibrosis. These sequences are part of the revised Lake Louise criteria for the diagnosis of myocarditis.⁶⁹ Classically, myocarditis causes patchy disease in the subepicardium of basal and mid infero-lateral walls, although it can present heterogeneously, much like sarcoidosis.⁶⁹

Assessment and differentiation between acute and chronic inflammation by ¹⁸F-FDG PET, as previously described, can also be utilized to evaluate for myocarditis (Figure 2). A study of hybrid PET/MRI in 65 patients with suspected myocarditis showed good agreement between PET and T2-weighted imaging ($\kappa = 0.75$). PET had near-perfect specificity; however, because PET focuses exclusively on macrophage uptake of ¹⁸F-FDG, without properly evaluating capillary leak and edema, it has a low sensitivity (74%) when compared to MRI.⁷⁰ ¹⁸F-FDG-PET/MRI is well suited to differentiate between acute and chronic myocarditis and possibly guide treatment options, however, at this time, it is still unknown if PET/MRI can enhance the endomyocardial biopsy in cases of suspected myocarditis and add potential value in clinical decision making any better than either imaging modality alone.

CARDIAC MASSES

Cardiac MRI is perhaps the best imaging modality to characterize cardiac masses due to its many attributes in structural and functional assessment; tissue characterization (T1- and T2-weighted imaging); and evaluation of perfusion (tumor vascularity).⁷¹ In a study of 55 individuals with cardiac masses, cardiac MRI differentiated malignant vs. benign lesions with an area under the curve (receiver-operating characteristics) of nearly 0.9.⁷² Due to the increased metabolic activity of malignant tumors, ¹⁸F-FDG PET also has the potential to differentiate malignant vs. benign cardiac masses, with an accuracy reported as high as 95% in one study.⁷³

In an elegant study, Nensa and colleagues evaluated the diagnostic yield of hybrid PET/MRI as compared to each individual modality in 20 patients with various benign and malignant masses. Using all available features in MRI and a maximum SUV cutoff of 5.2 in ¹⁸F-FDG PET, both modalities had 100% sensitivity and 92% specificity for the diagnosis of malignant cases. By combining both modalities, specificity improved to 100%.⁷⁴ A separate study also reported the utility of hybrid PET/MRI in the evaluation of 6 patients with cardiac masses.⁷⁵ Finally, ¹⁸F-FDG-PET/MRI adds further clinical value in the planning stage of surgical resection, particularly in patients with complex infiltration of cardiac structures as well as during the follow-up period to assess for potential recurrence after surgical intervention.⁷⁶

CONCLUSION

Integrated cardiac PET/MRI is a powerful imaging modality that combines the strengths of MRI in morphology, function and tissue characterization, with the physiological data from PET (Table 3). Combined PET/MRI has the potential to assist in the diagnosis and management of many cardiovascular conditions, such as ischemic heart disease, infiltrative cardiomyopathies, inflammatory disorders, and cardiac tumors. Current barriers to the

growth of PET/MRI include cost, availability, challenges with attenuation correction, and limited data demonstrating improved diagnostic efficacy or clinical outcomes over competing methods. Nevertheless, PET/MRI is emerging as an advancement to PET/CT, with less radiation and improved imaging quality in selected indications. The superior molecular and multi-parametric imaging potential of PET/MRI are emerging and likely will change the future field of cardiovascular imaging.

Acknowledgments:

Dr. Leucker is supported by an American Heart Association Career Development Award (19CDA34760040) and a pilot project award from the NIH National Institute on Aging, Johns Hopkins Older Americans Independence Center (P30AG021334).

Dr. Cardoso is the Pollin Cardiovascular Prevention Fellow at Johns Hopkins Hospital, supported by the Ciccarone Center for the Prevention of Cardiovascular Disease.

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Key Points

1. Integrated cardiac hybrid positron emission tomography (PET)/magnetic resonance imaging (MRI) is an emerging imaging modality that combines anatomical and functional data from MRI and physiologic data from PET.
2. This hybrid approach has the potential to improve diagnostic and prognostic imaging for a number of cardiovascular applications, such as ischemic heart disease, inflammatory disorders, infiltrative disease, and cardiac masses.
3. Limitations to the expansion of PET/MRI use include cost, availability, and technical challenges in attenuation correction with MRI instead of computed tomography (CT).
4. Though there is enormous potential, thus far research in cardiac PET/MRI has been limited mostly to feasibility data. Next, studies should assess comparative effectiveness in relation to alternative imaging modalities.

Synopsis

Cardiac PET/MRI is an integrated imaging approach that requires less radiation as compared to PET/CT and combines the high spatial resolution and morphological data from MRI with the physiological information from PET. This hybrid approach has the potential to improve the diagnostic and prognostic evaluation of several cardiovascular conditions, such as ischemic heart disease, infiltrative diseases such as sarcoidosis, acute and chronic myocarditis, and cardiac masses. Herein, we discuss the strengths of PET and MRI in several cardiovascular conditions in which PET/MRI may be used; the challenges and potential of PET/MRI; and the current data on the application of this powerful hybrid imaging modality.

Figure 1:

A case of a 32-year-old man who presented with acute chest pain, general malaise, recurring fevers, and palpitations. Further work-up revealed an ECG demonstrating an incomplete right bundle branch block, persistent precordial S-waves, and a flattened T-wave in lead III. In the initial Positron emission tomography/magnetic resonance imaging (PET/MRI) scan, a bihilar lymphadenopathy (**Panel A, stars**) and patchy late-gadolinium enhancement (LGE) in lateral left-ventricular wall was found (**Panel A, arrows**), which was in excellent agreement with the increased ^{18}F -fluorodeoxyglucose (FDG) uptake found in PET images (**Panel B, arrows**). Based on the imaging findings, sarcoidosis with cardiac involvement was diagnosed and treatment with a corticosteroid pulse therapy and sequential dose tapering was initiated.

While LGE in the lateral left-ventricular wall remained constant in follow-up scans, FDG uptake was slightly reduced after 4 weeks (**Panel C**) and significantly reduced after 4

months (**Panel D**). The decreasing FDG uptake correlated with the improvement of clinical symptoms.

PET/MRI is an emerging imaging modality in the diagnosis, monitoring of disease activity and assessment of the immunosuppressive treatment response of cardiac sarcoidosis.

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Figure 2.

A case of a 21-year-old man who presented with chest pain, generalized lymphadenopathy and splenomegaly. Further work-up revealed, diffuse repolarization abnormalities on ECG, elevated troponin T, impaired left ventricular systolic function and no evidence of coronary artery disease on angiography. Polymerase chain reaction showed Epstein Barr Virus DNA in the peripheral blood.

Acute myocarditis was confirmed on cardiac magnetic resonance imaging (MRI) in the presence of focal intramyocardial nodules (**A**, white arrows) as well as diffuse subepicardial enhancement (blue arrow) of the lateral wall with an inversion-recovery sequence acquired 10 minutes after injection of gadolinium chelate (0.2 mmol/L of Magnevist; Bayer Healthcare, Germany). However, on T2-weighted images only a weak focal intramyocardial as well as diffuse subepicardial signal of the lateral wall compatible with local edema could be identified (**B**, white arrows). One hour after injection of 18F-fluorodeoxyglucose (FDG; 4 Mega-Becquerels/kg), the Positron emission tomography (PET) scan revealed an intense radiotracer in the lateral wall only, suggestive of active inflammation in this territory (**C**, white arrows). Fused PET/MR images of the heart (**D**, white arrows) confirmed the colocalization of FDG uptake within the areas of late gadolinium enhancement on MRI. PET/MRI in detection of acute myocarditis offers the combination of high spatial resolution of MRI for the identification of lesions and the high sensitivity of FDG for the detection of acute inflammatory processes.

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Table 1.

Technical aspects of PET/MRI

Attenuation correction	<ul style="list-style-type: none"> • Atlas-based approach <ul style="list-style-type: none"> – A patient's MRI is matched to a set of MRI images within the atlas – A "pseudo-CT" is created from the chosen MRI-CT pair in the atlas – "Pseudo-CT" is used for attenuation correction • Direct methods <ul style="list-style-type: none"> – Segments MRI images into categories, such as air, lung, fat, etc – Voxels within the same category are given the same attenuation coefficient
Respiratory and cardiac motion	<ul style="list-style-type: none"> • Takes advantage of spatial and temporal resolution of MRI • MRI is used to create 3D motion fields • 3D motion fields provide motion correction for PET imaging
Cardiac devices	<ul style="list-style-type: none"> • Signal void in MRI leads to underestimation of attenuation and tracer uptake • Limited device data on safety of MRI scanning with 3 Tesla field strength

Table 2.

Commonly used radiotracers in PET perfusion.

Tracer	Molecule	Half-life	Produced
^{82}Rb	RbCl	76 seconds	Cyclotron
^{13}N	NH_3	10 minutes	Cyclotron
^{15}O	H_2O	122 seconds	Generator
^{18}F	Flurpiridaz	110 minutes	Cyclotron

Table 3.

Summary of advantages and limitations of PET, MRI, and hybrid PET/MRI

PET	Advantages	<ul style="list-style-type: none"> • Less radiation compared to SPECT • Quantitative assessment of rest/stress regional blood flow by computing perfusion tracer uptake • Molecular imaging with specific PET tracers for each condition
	Disadvantages	<ul style="list-style-type: none"> • Poor spatial resolution • Attenuation correction with CT adds radiation
MRI	Advantages	<ul style="list-style-type: none"> • Excellent spatial and temporal resolution • Use of cine MRI for gold-standard evaluation of ventricular function and regional wall motion abnormalities • No radiation • Gadolinium based contrast agents allow for perfusion and delayed enhancement imaging
	Disadvantages	<ul style="list-style-type: none"> • Limited quantification of myocardial blood flow
PET/MR 1	Advantages	<ul style="list-style-type: none"> • High spatial resolution of MRI • Quantitative myocardial blood flow assessment with PET • Molecular imaging can target different diseases with specific PET tracers • Lower radiation compared to PET/CT
	Disadvantages	<ul style="list-style-type: none"> • Limited availability • Increased cost • Few studies showing incremental benefit over non-hybrid imaging modalities • Technical challenges with the use of MRI data for attenuation correction