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Cardiovascular PET/MR: Potential Role and Challenges

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Recently combined PET/MR hybrid systems have been introduced for human imaging. The technology is based on the premise that combining the relative strengths of the two approaches (Table) will result in improved patient management either through better performance of current clinical applications or perhaps the introduction of new applications. In depth summaries on the technical aspects of these systems have been reviewed elsewhere (1,2). However in these challenging medical economics times, legitimate questions arise as to whether there is a cardiovascular (CV) role for PET/MR and if so, what is pathway to clinical implementation? Described below are a few thoughts in support of such a role for CV PET/MR and on the challenges in performing it and moving it the clinic.

The Case for CV PET/MR

When visualized through the prism of CV hybrid imaging, the need for PET/MR reflects the following principles. The first is that merging of diverse but complimentary CV imaging parameters results in significant improvement in patient management when compared to the impact of the individual measurements. The most prominent example is PET/CT or SPECT/CT imaging of coronary anatomy (CT) and myocardial perfusion (PET or SPECT) in the management of patients of coronary artery disease. (3,4) Another clinical example is ¹⁸F-fluorodeoxyglucose imaging with PET to detect myocardial inflammation in areas of scar delineated by late contrast enhancement with MR to diagnose cardiac sarcoidosis. (5) Assuming the first principle to be correct, the second principle is that current imaging technologies do not perform these combined measurements optimally. There is increasing evidence supporting the first principle. For example in select patient populations, combining coronary anatomy with myocardial perfusion performed at rest and stress improves the detection of significant coronary artery disease, provides additional information regarding CV risk, and improves colocalization of culprit coronary artery lesions with inducible ischemia (3,4). Moreover, there is much anticipation that molecular imaging will identify unique biologic fingerprints of disease that will lead to new diagnostic and prognostic paradigms in the management of the cardiac patient. Given the superior sensitivity of

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Conflict of Interest

Dr. Robert J. Gropler reports having a Siemens Biograph mMR and Master Research Agreement with The Mallinckrodt Institute of Radiology.

Compliance with Ethics Guidelines

Human and Animal Rights and Informed Consent

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nuclear techniques it is likely that biologic signal detection will be performed with PET or SPECT based radiopharmaceuticals. However, the relatively poor spatial resolution of nuclear techniques requires accurate anatomic co-localization using imaging approaches with higher spatial resolution such as CT or MR. Thus, hybrid systems will be needed to fulfill this requirement. However it is also clear that, significant challenges remain in obtaining these multiple imaging parameters in a clinically efficient manner. Most notable is that with current hybrid systems many of these measurements (e.g., coronary angiography and myocardial perfusion), cannot be performed either simultaneously or even in parallel. Thus, to optimally select and obtain the various measurements that are performed sequentially requires semi-real time evaluation of the various image acquisitions which results in less efficient camera usage and laboratory work flow, increased physician-operator interaction, and likely longer patient stays in the laboratory. In addition, PET, SPECT and CT all use low dose ionizing radiation for signal detection. It should be noted that the sequential nature of the image acquisitions does not appear to have an unfavorable impact on diagnostic accuracy for current CV clinical applications, primarily because the required co-localization of imaging parameters (e.g., correlating an individual coronary artery stenosis with a specific myocardial perfusion abnormality) is fairly coarse and can be accomplished with image registration software. However, simultaneous acquisition will likely be needed for advanced molecular imaging techniques where optimal anatomic co-localization is needed (e.g., detecting inflamed coronary atheroma) as well as having the ability to simultaneously observe rapidly changing physiological and pathophysiological processes.

By dint of the preceding discussion there is an opportunity for PET/MR systems, particularly those with capability to perform simultaneous image acquisitions. Currently, there is one such system on the market with others under development. These systems will have the potential to perform quantitative measurements of multiple diverse but complimentary CV parameters in a timely manner with accurate image registration.

Challenges of PET/MR

As with all new imaging technologies significant challenges must be overcome and PET/MR is not unique in this regard. From a technical perspective, the first order of business is to develop an accurate MR method to perform photon attenuation correction. Numerous methods have been proposed but it appears the 2-point Dixon method appears to be the most promising. (6) To take advantage of the fully quantitative capability of PET/MR, motion correction algorithms need to be developed that account for the differences in PET versus MR data acquisitions (volumetric versus serial, respectively) and permit simultaneous PET and MR ECG- and respiratory motion correction. This requirement is most relevant where fine alignment is necessary and/or simultaneous acquisitions are required, such as assessing myocardial infarct border-zone metabolic activity or implementing molecular image applications. Such advancements are not needed for parallel PET/MR acquisitions such as performing combined MR coronary angiography with PET myocardial perfusion imaging. MR coronary artery angiography remains challenging by motion artifacts, relatively low signal, and limited spatial resolution. Recent technical advances in fast imaging (e.g., 3.0T, parallel imaging and compressed sensing) have dramatically improved the imaging quality for better reliability. However, whole-heart coverage (to mimic CT angiography) still requires relatively long acquisition times (~ 15 min), so further refinements are needed. (7,8) Beyond development of new acquisition protocols, other challenges must be overcome. Currently, N-13 ammonia is the only PET perfusion radiopharmaceutical that can be used clinically since the Rubidium-82 infusion system is not MR compatible. Others include the efficient management of very large data sets, shortening image processing times and

developing appropriate image display workstations. Moreover, new training programs will be needed for both physicians and technologists.

Clearly PET/MR offers tremendous opportunities from a CV research perspective with readily available applications. In contrast, identifying the CV clinical applications of PET/MR and how to gain their acceptance is less clear. Development of clinical uses for PET/MR can be viewed as occurring in two phases. The first is to use it to measure current imaging parameters in a way that provides a distinct advantage over current imaging methods (e.g., coronary angiography, perfusion and function) whereas the second phase represents future applications such as CV molecular imaging. Indeed based on the preceding discussion, one could argue that PET/MR is ideally suited for advanced molecular imaging techniques. Viewed in this way several steps will need to occur for this technology to be successful. In addition to overcoming the challenges listed above, PET/MR systems must be fully cardiac capable and not represent a compromise in performance when compared with either standalones or other hybrid technologies. Initial promising clinical applications that take advantage of the unique aspects of PET/MR need to be identified and the imaging schemes developed. One logical example is to perform parallel imaging of stress PET myocardial perfusion imaging with MR coronary angiography and late enhancement imaging (Figure). With such a protocol one could detect the presence or absence of coronary artery stenosis that could be linked to the presence of regional or global abnormalities in stress myocardial blood flow (in mL/g/min) and regional ischemia or infarction based on the comparison of relative flow differences at stress with the absence or presence of late enhancement, respectively. If shown to be accurate, such a protocol would have very wide application while offering efficient scanner usage. Other more boutique-like applications might be the detection of cardiac sarcoidosis or more comprehensive evaluation of viable myocardium to better predict recovery of function after coronary revascularization. Next the salutary effects of these approaches relative to current standard methods would need to be demonstrated. However if successful, these initial applications should help maintain interest in the technology by both industry and the medical community so that advances continue in both hardware and imaging algorithms until molecular imaging probes are ready for CV clinical use.

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Figure 1.

Proposed PET/MR scheme that combines coronary angiography with measurements of myocardial perfusion and function. AC- Attenuation correction; N-13 NH₃ (ammonia); MPI –Myocardial perfusion imaging; DCE - Delayed contrast enhancement; qMBF – quantitative myocardial blood flow (mL/g/min); rMBF- relative myocardial blood flow; LVF – Left ventricular function,

Table 1

Relative Strengths and Weaknesses of PET and MR

	PET	MR
Sensitivity	10^{-11} – 10^{-12} mol/L	10^{-3} – 10^{-5} mol/L
Spatial Resolution	1–2 mm	50–250 μ m
Temporal Resolution	Modest	High
Characterization of Anatomy & Function	Yes but limited	Comprehensive
Coronary Angiography	No	Yes
Tissue Characterization	Limited to PET Probes Used	Diverse
Whole-heart Coverage	Yes	Yes but not for all applications
Need for Intravenous Contrast	No	Yes
Ionizing Radiation Exposure	Yes	No