PET/MRI: Technical Challenges and Recent Advances

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Abstract Integrated positron emission tomography (PET)/magnetic resonance imaging (MRI), which can provide complementary functional and anatomical information about a specific organ or body system at the molecular level, has become a powerful imaging modality to understand the molecular biology details, disease mechanisms, and pharmacokinetics in animals and humans. Although the first experiment on the PET/MRI was performed in the early 1990s, its clinical application was accomplished in recent years because there were various technical challenges in integrating PET and MRI in a single system with minimum mutual interference between PET and MRI. This paper presents the technical challenges and recent advances in combining PET and MRI along with several approaches for improving PET image quality of the PET/MRI hybrid imaging system.

Keywords Anatomical and functional information · MRI · PET · PET/MRI hybrid imaging system

Introduction

Positron emission tomography (PET) is one of the powerful imaging modalities that can provide functional information about a specific organ or body system at the molecular level. However, PET does not provide clear visualization of the anatomical structure because it has relatively poor spatial

resolution. PET/CT has been proposed to overcome this limitation, and this hybrid system provides more clinically useful information than either a PET or CT stand-alone system [1–3]. Recently, there has been great interest in the development of combined PET/magnetic resonance imaging (MRI) because MRI can not only offer anatomical information with excellent soft-tissue contrast, but it can also visualize the specific tissues and pathology using various imaging sequences compared to CT (Fig. 1) [4, 5]. Another advantage of MRI is the absence of ionizing radiation, thus allowing patients to undergo multiple scans without concerns about additional radiation exposure [6]. Moreover, simultaneous PET and MR image acquisition provides better spatial registration compared to the sequential acquisition of PET and CT by correcting a misalignment that may occur due to voluntary patient motion or involuntary motion of the organs caused by respiration, bowel movement, or filling of the urinary bladder during the scan [7–9].

There are several conceivable approaches to combining PET and MRI into a hybrid system (Fig. 2) [10]. The most straightforward approach is to place PET and MRI scanners in a tandem configuration with a minor modification of the PET. In tandem configuration, PET and MR images are sequentially acquired by moving a common patient bed between the two scanners, and it could lead to inaccurate registration of both images due to the voluntary and involuntary motions of the patient. Another approach is to insert a PET gantry inside the bore of a standard MRI scanner. This approach allows flexible operation of MRI, like a stand-alone device or PET/MRI hybrid device. In the insert configuration, the PET detector and dedicated electronics are compactly designed because of space constraint of an MR bore, and as a result, the transaxial field-of-view (FOV) of the PET insert would be reduced. The other approach is to fully integrate the PET and MRI scanners in a single gantry. This configuration has the most challenging technical issues associated with the mutual interference

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Fig. 1 Whole-body T1-weighted MR image with excellent soft tissue contrast (a), ^{18}F -Fluorodesoxyglucose (FDG) PET image (b), and MR/PET fused images (c) acquired using a hybrid PET/MRI (Source of material: <http://www.healthcare.siemens.com/magnetic-resonance-imaging/magnetom-world/publications/magnetom-flash>, Reprinted from MAGNETOM Flash (no. 46))

between the two imaging modalities including a major redesign of MRI, unlike the insert configuration. The similar feature between the insert and integration configurations is that

they allow shorter acquisition time and precise temporal and spatial registrations, resulting in simultaneous PET and MR image acquisition.

Fig. 2 Various PET-MRI hybrid system design methods: (a) tandem, (b) insert, (c) fully integrated configurations (Reprinted with permission from Vandenberghe et al. [10])

Technical Challenges in Combining PET and MRI

For combining PET and MRI into a hybrid system, a PET detector capable of operating in the strong magnetic field of MRI needs to be developed. Additionally, an RF shield should be carefully designed for maintaining homogeneity of MRI fields in the presence of a PET detector.

Conventional PET detectors are composed of a scintillation crystal coupled to a photomultiplier tube (PMT). Among the various scintillation materials, bismuth germanium oxide (BGO) and lutetium oxyorthosilicate (LSO) are the most widely used scintillation crystals for PET applications because BGO is a cost-effective scintillator with high effective atomic number (74) and high density (7.1 g/cm^3) and LSO has high density (7.4 g/cm^3), fast decay time ($\sim 40 \text{ ns}$) and high light output (25,000 photons/MeV). They are also suitable for PET/MRI applications because these crystals have magnetic susceptibility close to human tissue. On the other hand, gadolinium oxyorthosilicate (GSO) is not suitable for the PET/MRI because magnetic susceptibility of GSO is more than 1000 times greater than that of LSO or BGO due to gadolinium contained in GSO, and as a result, it leads to significant artifact and distortion in the MR image [11].

PMTs are very sensitive to the magnetic field [12]. To employ PMT as a photosensor for PET/MRI, several research groups have proposed the method transferring scintillation light to the PMT using a long optical fiber (4–5 m), allowing placement of the PMT outside the fringe field [13–15].

However, long optical fiber causes a significant degradation of energy and timing resolution due to loss of scintillation light. In addition, a lot of extra space inside the MRI gantry is required because of huge number of optical fibers connected to the detectors of whole-body PET system. Avalanche photodiodes (APDs) have been proposed as an alternative to the PMT because these devices are compact and rugged as well as insensitive to the magnetic field [16, 17]. However, they have a small gain, large excess noise, and large performance fluctuation according to bias voltage and temperature. Recently, silicon photomultipliers (SiPMs) have been proposed as photosensors for PET/MRI because these devices have a high gain ($\sim 10^6$) similar to a standard PMT and excellent timing properties down to 100 ps [18], unlike the APDs as well as insensitivity to the magnetic field.

PET detector and electronics located inside the MRI should be shielded with conductive material to minimize the mutual interference between these PET components and MRI field generated by the RF coil. However, an eddy current can be induced around the conductive material by gradient field, and it can cause a heating problem in the PET detector and electronics. To reduce the eddy current while minimizing RF interference, several research groups have proposed various RF shielding methods for PET that use segmented thin copper with a thickness of a few tens of micrometers and cover the shielding material inside and outside of the PET gantry [19–21]. Recently, carbon fiber has been proposed as a new shielding material by several research groups and its usefulness has been successfully verified [22–25].

Recent Advances in Commercial Whole-body PET-MRI

There has been tremendous scientific and technological progress in the development of PET/MRI in recent years, in spite of the various technical challenges mentioned in the above section. Commercial whole-body PET/MRI systems have been launched by three major vendors (Philips Healthcare, Siemens Healthcare and GE Healthcare) (Fig. 3) and their characteristics are summarized in Table 1.

Among the three configurations for combining PET and MRI into a hybrid system, the tandem system is the first commercialized system because the technical challenges are much simpler than those in other configurations. Two commercial whole-body PET-MRI systems have been released by Philips Healthcare (Ingenuity TF PET/MRI) and GE Healthcare (Discovery PET/CT+MR combo). PET and MR images are sequentially acquired in both systems by moving a common patient bed between the PET and MRI scanners. Both systems offer time-of-flight (TOF) information that helps to improve signal to noise ratio (SNR) of PET image. The difference between the two systems depends on the location of both PET and MRI scanners. Ingenuity time-of-flight PET and MRI scanners are placed in the same room about 4.2 m apart, while GE's Discovery PET/CT and MRI are located in a separate room. Another difference is the attenuation correction method. Ingenuity TF system uses MRI data for attenuation correction of PET data, in contrast with GE trimodality system which uses CT data [10, 26–28].

The first fully integrated whole-body PET/MR was made commercially available by Siemens Healthcare in 2010

Fig. 3 Commercial whole-body PET/MRI launched by Philips Healthcare (a), Siemens Healthcare (b), and GE Healthcare (c, d) (Source of material: <http://www.healthcare.philips.com>, <http://www.healthcare.siemens.com>, <http://www3.gehealthcare.es>, <http://www3.gehealthcare.com>)

Table 1 Characteristics of commercial whole-body PET/MRI systems launched by three major vendors

Characteristic	Philips Healthcare	Siemens Healthcare	GE Healthcare	
Model	Ingenuity TF PET/MRI	Biograph mMR	Discovery PET/CT + MR	Signa PET/MRI
Acquisition mode	Sequential	Simultaneous	Sequential	Simultaneous
Sensitivity (cps/kBq)	7	13.2	7.5	21
Transverse resolution (mm)	4.9	4.4	4.0	3.9
Timing resolution (ns)	0.5	2.9	0.6	0.4
Attenuation correction achieved by:	MRI	MRI	CT	MRI

(Biograph mMR). The PET detector is installed between the gradient and body coils of 3-T MRI. Since PET detectors are located inside the MRI, an APD photosensor and dedicated front-end ASIC technology are applied to minimize mutual interference between PET and MRI. The radius of the RF coil is reduced to provide space for the PET detector. The Biograph mMR cannot provide TOF information because it has a timing resolution of 2.9 ns due to poor timing capability of an APD used as a PET photosensor, unlike Ingenuity TF and GE trimodality systems. Attenuation correction is achieved by using MRI data [10, 29].

GE Healthcare also developed fully integrated PET/MRI (Signa PET/MRI) in 2013. The SiPM and lutetium based scintillator are used to construct the PET detector and the detectors are inserted into the RF coil. Signa PET/MRI provides superior timing performance (390 ps) than commercial PET/MRIs offered by other vendors and this system uses the MR-based attenuation correction method, similar to Ingenuity TF PET/MRI and Biograph mMR [28, 30, 31].

New Trends in MR-compatible PET Design

Although many efforts in developing the PET/MRI hybrid system have been made by various research groups, this paper

discusses three unique design concepts, which are different from the PET/MRI design commercially offered by three major vendors. First of all, a PET insert capable of operating inside a 3-T clinical MRI has recently been developed by using digital silicon photomultipliers (dSiPMs) [32]. The dSiPM does not require additional electronics to digitize the output signal from a sensor and has lower power consumption compared to analog SiPM requiring additional electronics for digitization. While the current PET insert has been developed for preclinical PET application, the architecture of the PET detector and electronics can be applied to clinical whole-body PET without significant modification. The detector modules are cooled using a combined water and air chilling system and are shielded with housing of 0.8 mm thick carbon fiber composite to minimize eddy currents induced on the housing (Fig. 4). Although the developed prototype PET insert has very attractive features, it has various unresolved issues such as signal-to-noise ratio (SNR) degradation between 2–15 %, ghosting artifact generated in echo planar imaging sequences, and relative degradation of the energy resolution ($\leq 10\%$) and timing resolution ($\leq 15\%$) [33].

An insertable PET/MRI system, which employs the charge transmission method that transfer charge signal from photosensor to electronics using a long cable, has been developed for human brain imaging in our laboratory [34–36]. Only

Fig. 4 MR-compatible PET detector module equipped with digital SiPM (Reprinted with permission from Wehner et al. [32])

PET detectors consisting of LYSO crystals and SiPM arrays are inserted inside the MR bore, and additional electronics are located outside the 3-T clinical MRI bore to minimize the mutual interference between PET and MRI (Fig. 5). The PET gantry is shielded with a gold-plated conductive fabric tape, which provides sufficient shielding effectiveness as well as flexible shielding geometry. Excellent cross-compatibility between PET and MRI has been acquired by applying the charge transmission method and the new shielding method. However, the current brain PET insert has a limitation such as complexity associated with handling large numbers of charge signal transmission cables.

A PET insert is generally located outside the RF transmit/receive coil in order to transmit and receive the RF signals without interference caused by PET (Fig. 6). Recently, the RF-transmissive PET insert positioned inside the RF body coil has been developed [37–40]. The major advantages of this system are that the PET can be inserted into the conventional MR system and the built-in MR body coil can be used as a receiver coil as well as an RF transmit coil. For this purpose, the PET insert is electrically floated relative to the MRI RF ground by using the electro-optical coupling method and lead-acid-gel battery for supplying power to the PET. However, this design causes significant attenuation of RF signal intensity due to positioning of the PET insert inside the body coil which needs to be improved.

MRI Based Attenuation Correction

For quantitative PET imaging, the reconstructed data need to be corrected for attenuation. Direct measurement of linear attenuation coefficients at 511 keV is not possible using MRI data acquired by the integrated PET/MRI. The available methods for MR-based attenuation correction (AC) can be grouped into three categories including segmentation-based methods, template or atlas registration-based methods, and joint estimation-based methods.

At present, the segmentation-based methods are the most widely used approach. PET images are co-registered to MR images and then MR images are segmented into different

tissue or attenuation areas (i.e., bone, fat, lung, and air) [41, 42]. The regions are then labeled on the basis of their anatomical location and pre-defined attenuation coefficients are assigned to these regions. The main sources of error and inaccuracy of this approach are those involved in the segmentation procedure, the misclassification of regions and the inability to account for attenuation coefficients that vary from subject to subject. The challenging task in these methods is to distinguish bone tissue from air-filled cavities since both imaging objects appear to have the same intensity range on MRI. Ultrashort echo time (UTE) sequence has been used successfully to visualize cortical bone and the attenuation correction in the head and neck region needed to distinguish air and bone can be performed with UTE [43]. Furthermore, the Dixon sequence was used to distinguish water and fat for the segmentation of attenuation-relevant regions in the brain and whole body. With use of these methods, it was reported that a high correlation can be achieved with the reference PET data using CT-based attenuation correction [41].

The template or atlas registration-based methods employ a stored template or atlas [44–47]. After a PET/MRI examination, MR images of the corresponding patient are transformed to match the template or atlas. The transformation information between individual patients and their templates or atlases can be subsequently used to generate a patient-specific attenuation map from the template or atlas attenuation map (Fig. 7) [48]. The potential advantage of this technique is that the template can incorporate much more structural details compared to the segmented and labeled technique. Whilst the method may be effective for the brain, accounting for all the anatomical variation in the body will be very difficult. The applicability will also remain limited to a population without anatomical abnormalities.

The joint estimation-based methods use PET emission data and MR anatomic information to create attenuation maps [49]. These methods are based on algorithms of maximum likelihood reconstruction of attenuation and activity (MLAA) developed prior to the advent of integrated PET/MRI systems. PET activity distribution and attenuation are estimated jointly from the PET emission data themselves. By exploiting the consistency conditions that must be satisfied by the non-

Fig. 5 Insertable PET/MRI system employing analog SiPM and charge transmission method (Reprinted with permission from Jung et al. [36])

Fig. 6 RF-transmissive PET detector insert applying the electro-optical coupling method (Image courtesy of Dr. Crag S. Levin, Stanford University)

attenuated data one can derive the attenuation sinogram directly from the emission data. Since the emission data are not sufficient for deriving the attenuation correction factor, the TOF information or MR anatomical prior knowledge or both are employed to improve the accuracy of estimation [50, 51]. The available emission data can also be used as an input for solving the problem of truncated data occurred by a small FOV in MRI. To determine the truncated part of the attenuation map, a modified MLAA algorithm can be applied. In general the joint estimation based methods have the following important limitations: they are only applicable to a PET image that provides reasonable anatomic detail such as the FDG study, they cannot generate attenuation maps of objects outside the patient that do not generate emission data and their accuracy is affected by scatter events.

There are a few common challenges in the development of an attenuation correction method based on MR images. Hardware components such as the PET/MRI patient table and the RF coils are not visible in the MRI-based attenuation images (Fig. 8) [52, 53]. Predefined attenuation maps for the patient table and RF coils have to be added to the patient attenuation map before the PET reconstruction.

The FOV in MRI (45–50 cm) is smaller than the FOV in PET, and this cause truncation errors in patients. In order to solve truncation errors, the outer contour of the patient can be estimated from PET emission images, and missing information in the attenuation image can be filled in using the patient's outer contour [52, 53]. The other approach is to extend the FOV in MRI from the conventional 50 cm to, for example, 60 cm.

New improved MR-based AC methods are still under development and are part of future research. Further improvements in the MR-based AC are essential to provide accurate quantification of regional PET trace uptake, which is important for accurate diagnosis and treatment monitoring.

Motion Correction

Motion artifacts can significantly degrade the effective resolution of PET systems. Motion makes it difficult to detect small lesions, accurately quantify tracer uptake in therapy monitoring studies and precisely define the tumor volume for radiotherapy and surgical planning. Furthermore, the mismatch between the attenuation and emission data when the two are acquired sequentially leads to inaccurate quantification and image artifacts [54]. With respect to voluntary motion, patient motion can occur because of long scan time but it

Fig. 7 Steps in a template-based attenuation correction approach for brain PET/MRI: the MR template is transformed to match the individual MR image. The obtained transformation matrix is applied to warp the attenuation map template to generate an individualized

attenuation map, to which the coil attenuation map is added to generate a complete patient-specific attenuation map (Reprinted with permission from Wagenknecht et al. [48])

Fig. 8 In PET/MR, coils and other MR devices that should not appear in the MR images must be generated as template images in PET transmission scans and should be added to the attenuation map. Examples of a spine, a head coil and a patient table (a) as well as one transaxial slice of the corresponding templates generated from PET transmission scans are shown (b) (Reprinted with permission from Wagenknecht et al. [48])

can be reduced through patient cooperation, the use of positioning aids, and by reducing the scan time. With respect to involuntary motion, breathing and cardiac motion are the most important source of motion in whole-body PET/MRI studies. Involuntary motion artifact can be improved by using external devices such as belts, triggering, and optical cameras [55] and MR data.

In gating, list-mode data are filtered on the basis of the respiratory state or cardiac phase such that only counts from a single respiratory or cardiac state are used for image reconstruction. This is accomplished by using an external device to obtain the respiratory or cardiac signal, which is used as a surrogate for internal organ motion. Although external devices can correct for motion using PET data alone, there are disadvantages since additional devices are needed for respiratory or

cardiac gating, thus increasing the technical complexity and limiting the clinical usefulness.

In the simple approach using MR data, the respiration model can be constructed from a series of 2D images repeatedly acquired over several respiratory cycles from end-expiration to end-inspiration using MR images (Fig. 9) [56]. The sagittally oriented images acquired using a 2D MR multislice gradient-echo sequence are used to generate a series of 3D volumes corresponding to different points during the respiratory cycle. In simultaneous PET/MRI data, PET motion correction can be performed using a motion model from respiratory-gated MR volumes. More advanced MR techniques including tagged MRI, phase contrast MRI, and pulsed-field-gradient methods can also be used to estimate the nonlinear motion of internal organs.

Fig. 9 Self-gated MR image (black: lung compartment) overlaid with original attenuation map at end-expiration (a) and the warped attenuation map at end-inspiration (b) (Reprinted with permission from Grimm et al. [56])

In post image processing using MR data, MR gating signals caused by MR gating images can be applied to warp the reconstructed PET images corresponding to each of the gates [57, 58]. This simple approach with the use of software only was performed in some of the early studies in which PET-derived motion images were applied to each of the gated frames but recent studies on the integrated PET/MRI scanner were performed using MR-derived motion images.

Additional PET Image Processing Using MR Images

PET/MRI also offers potential benefits that help in the improvement of PET images. High resolution anatomical information from MRI can be used to enhance PET image quality, which is especially important for the brain image [59]. Partial volume effect in PET images can be corrected using high resolution MR images and PET reconstruction can be modified and improved with prior information derived from MRI [60, 61]. Additionally, MRI provides higher soft-tissue contrast in comparison with CT, making it easier to define the regions of interest in PET images that do not provide anatomic details such as neuro-receptors or ligands for PET/MRI.

Conclusions

PET/MRI is a new hybrid imaging modality that can provide complementary functional and anatomical information about a specific organ or body system at the molecular level. Although, the tandem PET/MRI system was developed first because it can be easily designed, a fully integrated PET/MRI system has been developed recently and it is increasingly being used by clinicians and researchers. Although validation of the clinical usefulness and investigation of the various methods that helps to improve PET image quality using MR data are still ongoing, if these ongoing processes are completed, we prospect that PET/MRI will become a powerful imaging instrumentation that can be used as an alternative to PET/CT.

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Conflict of Interest Jin Ho Jung, Yong Choi and Ki Chun Im declare that they have no conflict of interest.

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References

1. Bar-Shalom R, Yefremov N, Guralnik L, Gaitini D, Frenkel A, Kuten A, et al. Clinical performance of PET/CT in evaluation of cancer: additional value for diagnostic imaging and patient management. *J Nucl Med*. 2003;44:1200–9.
2. Antoch G, Saoudi N, Kuehl H, Dahmen G, Mueller SP, Beyer T, et al. Accuracy of whole-body dual-modality fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (FDG-PET/CT) for tumor staging in solid tumors: comparison with CT and PET. *J Clin Oncol*. 2004;22:4357–68.
3. Scarfone C, Lavelly WC, Cmelak AJ, Delbeke D, Martin WH, Billheimer D, et al. Prospective feasibility trial of radiotherapy target definition for head and neck cancer using 3-dimensional PET and CT imaging. *J Nucl Med*. 2004;45: 543–52.
4. Zaidi H, Mawlawi O. Simultaneous PET/MR will replace PET/CT as the molecular multimodality imaging platform of choice. *Med Phys*. 2007;34:1525–8.
5. Heesakkers RA, Hövels AM, Jager GJ, van den Bosch HC, Witjes JA, Raat HP, et al. MRI with a lymph-node-specific contrast agent as an alternative to CT scan and lymph-node dissection in patients with prostate cancer: a prospective multicohort study. *Lancet Oncol*. 2008;9:850–6.
6. Brix G, Lechel U, Glatting G, Ziegler SI, Münzing W, Müller SP. Radiation exposure of patients undergoing whole-body dual-modality ¹⁸F-FDG PET/CT examinations. *J Nucl Med*. 2005;46:608–13.
7. Shan ZY, Mateja SJ, Reddick WE, Glass JO, Shulkin BL. Retrospective evaluation of PET-MRI registration algorithms. *J Digit Imaging*. 2011;24:485–93.
8. Chun SY, Reese TG, Ouyang J, Guerin B, Catana C, Zhu X, et al. MRI-based nonrigid motion correction in simultaneous PET/MRI. *J Nucl Med*. 2012;53:1284–91.
9. Brendle CB, Schmidt H, Fleischer S, Braeuning UH, Pfannenberger CA, Schwenzer NF. Simultaneously acquired MR/PET images compared with sequential MR/PET and PET/CT: alignment quality. *Radiology*. 2013;268:190–9.
10. Vandenberghe S, Marsden PK. PET-MRI: a review of challenges and solutions in the development of integrated multimodality imaging. *Phys Med Biol*. 2015;60:R115–54.
11. Yamamoto S, Kuroda K, Senda M. Scintillator selection for MR-compatible gamma detectors. *IEEE Trans Nucl Sci*. 2003;50:1683–5.
12. Pichler B, Wehrli HF, Kolb A, Judenhofer MS. PET/MRI: the next generation of multi-modality imaging? *Semin Nucl Med*. 2008;38: 199–208.
13. Slaters RB, Farahani K, Shao Y, Taylor J, Summers PE, Williams S, et al. A study of artifacts in simultaneous PET and MR imaging using a prototype MR compatible PET scanner. *Phys Med Biol*. 1999;44:2015–27.
14. Raylman RR, Majewski S, Lemieux S, Velana SS, Krossb B, Popov V, et al. Initial tests of a prototype MRI-compatible PET imager. *Nucl Inst Meth A*. 2006;569:306–9.
15. Mackewn JE, Halsted P, Charles-Edwards G, Page R, Totman JJ, Sunassee K, et al. Performance evaluation of an MRI-compatible pre-clinical PET system using long optical fibers. *IEEE Trans Nucl Sci*. 2010;57:1052–62.
16. Wu Y, Catana C, Farrell R, Dokhale PA, Shah KS, Qi J, et al. PET performance evaluation of an MR-compatible PET insert. *IEEE Trans Nucl Sci*. 2009;56:574–80.
17. Maramraju SH, Smith SD, Junnarkar SS, Schulz D, Stoll S, Ravindranath B, et al. Small animal simultaneous PET/MRI: initial

- experiences in a 9.4 T microMRI. *Phys Med Biol.* 2011;56:2459–80.
18. Schaart DR, Seifert S, Vinke R, Dam HT, Dendooven P, Löhner H, et al. LaBr(3):Ce and SiPMs for time-of-flight PET: achieving 100 ps coincidence resolving time. *Phys Med Biol.* 2010;55:N179–89.
 19. Pichler BJ, Judenhofer MS, Catana C, Walton JH, Kneilling M, Nutt RE, et al. Performance test of an LSO-APD detector in a 7-T MRI scanner for simultaneous PET/MRI. *J Nucl Med.* 2006;47:639–47.
 20. Peng BJ, Walton JH, Cherry SR, Willig-Onwuachi J. Studies of the interactions of an MRI system with the shielding in a combined PET/MRI scanner. *Phys Med Biol.* 2010;55:265–80.
 21. Maramraju SH, Smith SD, Rescia S, Stoll S, Budassi M, Vaska P, et al. Electromagnetic interactions in a shielded PET/MRI system for simultaneous PET/MR imaging in 9.4 T: evaluation and results. *IEEE Trans Nucl Sci.* 2012;59:1892–9.
 22. Chung DDL. Electromagnetic interference shielding effectiveness of carbon materials. *Carbon N Y.* 2001;39:279–85.
 23. Duppenbecker PM, Wehner J, Renz W, Lodomez S, Truhn D, Marsden PK, et al. Gradient transparent RF housing for simultaneous PET/MRI using carbon fiber composites. *IEEE Nuclear Science Symp. and Medical Imaging Conf.* 2012;M18-2.
 24. Wehner J, Weissler B, Dueppenbecker P, Gebhardt P, Schug D, Ruetten W, et al. PET/MRI insert using digital SiPMs: investigation of MR-compatibility. *Nucl Instr and Meth A.* 2014;734:116–21.
 25. Peng BJ, Wu Y, Cherry SR, Walton JH. New shielding configurations for a simultaneous PET/MRI scanner at 7T. *J Magn Reson.* 2014;239:50–6.
 26. Zaidi H, Ojha N, Morich M, Griesmer J, Hu Z, Maniawski P, et al. Design and performance evaluation of a whole-body Ingenuity TF PET-MRI system. *Phys Med Biol.* 2011;56:3091–106.
 27. Kuhn FP, Hüllner M, Mader CE, Kastrinidis N, Huber GF, von Schulthess GK, et al. Contrast-enhanced PET/MR imaging versus contrast-enhanced PET/CT in head and neck cancer: how much MR information is needed? *J Nucl Med.* 2014;55:551–8.
 28. Hu Z, Yang W, Liu H, Wang K, Bao C, Song T, et al. From PET/CT to PET/MRI: advances in instrumentation and clinical applications. *Mol Pharm.* 2014;11:3798–809.
 29. Delso G, Fürst S, Jakoby B, Ladebeck R, Ganter C, Nekolla SG, et al. Performance measurements of the Siemens mMR integrated whole-body PET/MR scanner. *J Nucl Med.* 2011;52:1914–22.
 30. Levin C, Glover G, Deller T, McDaniel D, Peterson W, Maramraju SH. Prototype time-of-flight PET ring integrated with a 3T MRI system for simultaneous whole-body PET/MR imaging. *J Nucl Med.* 2013;54:148.
 31. Jagaru A, Minamimoto R, Levin C, Barkhodari A, Jamali M, Holley D, et al. The potential of TOF PET-MRI for reducing artifacts in PET images. *EJNMMI Physics.* 2015;2:A77.
 32. Wehner J, Weissler B, Dueppenbecker PM, Gebhardt P, Schug D, Ruetten W, et al. PET/MRI insert using digital SiPMs: investigation of MR-compatibility. *Nucl Instr and Meth A.* 2014;734:116–21.
 33. Wehner J, Weissler B, Dueppenbecker PM, Gebhardt P, Goldschmidt B, Schug D, et al. MR-compatibility assessment of the first preclinical PET-MRI insert equipped with digital silicon photomultipliers. *Phys Med Biol.* 2015;60:2231–55.
 34. Kang J, Choi Y, Hong KJ, Jung JH, Hu W, Huh YS, et al. A feasibility study of photosensor charge signal transmission to pre-amplifier using long cable for development of hybrid PET-MRI. *Med Phys.* 2010;37:5655–64.
 35. Hong KJ, Choi Y, Jung JH, Kang J, Hu W, Lim HK, et al. A prototype MR insertable brain PET using tileable GAPD arrays. *Med Phys.* 2013;40:042503.
 36. Jung JH, Choi Y, Jung J, Kim S, Lim HK, Im KC, et al. Development of PET/MRI with insertable PET for simultaneous PET and MR imaging of human brain. *Med Phys.* 2015;42:2354–63.
 37. Bieniosek MF, Olcott PD, Levin CS. Readout strategy of an electro-optical coupled PET detector for time-of-flight PET/MRI. *Phys Med Biol.* 2013;58:7227–38.
 38. Olcott PD, Glover G, Levin CS. Cross-strip multiplexed electro-optical coupled scintillation detector for integrated PET/MRI. *IEEE Trans Nucl Sci.* 2013;6:3198–204.
 39. Lee BJ, Grant AM, Chang C-M, Glover GH, Levin CS. RF-transmissive PET detector insert for simultaneous PET/MRI. *IEEE Nuclear Science Symp. and Medical Imaging Conf.* 2014;M08-1.
 40. Lee BJ, Grant AM, Chang C-M, Watkins R, Levin CS. MR performance evaluation of an RF-penetrable PET insert with integrated RF receive coil for simultaneous PET/MRI. *J Nucl Med.* 2015;56:1854.
 41. Martinez-Moller A, Souvatzoglou M, Delso G, Bundschuh RA, Chelidhote C, Ziegler SI, et al. Tissue classification as a potential approach for attenuation correction in whole-body PET/MRI: Evaluation with PET/CT data. *J Nucl Med.* 2003;50:520–6.
 42. Schulz V, Torres-Espallardo I, Renisch S, Hu Z, Ojha N, Bornert P, et al. Automatic, three-segment, MR-based attenuation correction for whole-body PET/MR data. *Eur J Nucl Med Mol Imaging.* 2011;38:138–52.
 43. Grodzki DM, Jakob PM, Heismann B. Ultrashort echo time imaging using pointwise encoding time reduction with radial acquisition (PETRA). *Magn Reson Med.* 2012;67:510–8.
 44. Montandon ML, Zaidi H. Atlas-guided non-uniform attenuation correction in cerebral 3D PET imaging. *Neuroimage.* 2005;25:278–86.
 45. Hofmann M, Steinke F, Scheel V, Charpiat G, Farquhar J, Aschoff P, et al. MRI-based attenuation correction for PET/MRI: a novel approach combining pattern recognition and atlas registration. *J Nucl Med.* 2008;49:1875–83.
 46. Hofmann M, Bezrukov I, Mantlik F, Aschoff P, Steinke F, Beyer T, et al. MRI-based attenuation correction for whole-body PET/MRI: quantitative evaluation of segmentation and atlas-based methods. *J Nucl Med.* 2011;52:1392–9.
 47. Nuyts J, Dupont P, Stroobants S, Banninck R, Mortelmans L, Suetens P. Simultaneous maximum a posteriori reconstruction of attenuation and activity distributions from emission sonograms. *IEEE Trans Med Imaging.* 1999;18:393–403.
 48. Wagenknecht G, Kaiser HJ, Mottaghy FM, Herzog H. MRI for attenuation correction in PET: methods and challenges. *Magn Reson Mater Phys.* 2013;26:99–113.
 49. Defrise M, Rezaei A, Nuyts J. Time-of-flight PET data determine the attenuation sinogram up to a constant. *Phys Med Biol.* 2012;57:885–99.
 50. Mehranian A, Zaidi H. Clinical assessment of emission- and segmentation-based MR-guided attenuation correction in whole-body time-of-flight PET/MR imaging. *J Nucl Med.* 2015;56:877–83.
 51. Paulus D, Braun H, Aklan B, Quick HH. Simultaneous PET/MR imaging: MR-based attenuation correction of local radiofrequency surface coils. *Med Phys.* 2012;39:4306–15.
 52. Delso G, Martinez-Moller A, Bundschuh RA, Nekolla SG, Ziegler SI. The effect of limited MR field of view in MR/PET attenuation correction. *Med Phys.* 2010;37:2804–12.
 53. Nuyts J, Bal G, Kehren F, Fenchel M, Michel C, Watson C. Completion of a truncated attenuation image from the attenuated PET emission data. *IEEE Trans Med Imaging.* 2013;32:237–46.

54. Ouyang J, Li Q, Fakhri GE. Magnetic resonance-based motion correction for positron emission tomography imaging. *Semin Nucl Med.* 2013;43:60–7.
55. Rahmim A, Rousset O, Zaidi H. Strategies for motion tracking and correction in PET. *PET Clin.* 2007;2:251–66.
56. Grimm R, Furst S, Souvatzoglou M, Forman C, Hutter JM, Dregely I, et al. Self-gated MRI motion modeling for respiratory motion compensation in integrated PET/MRI. *Med Image Anal.* 2015;19: 110–20.
57. Dikaivos N, Izquierdo-Garcia D, Graves MJ, Mani V, Fayad ZA, Fryer TD. MRI-based motion correction of thoracic PET: initial comparison of acquisition protocols and correction strategies suitable for simultaneous PET/MRI systems. *Eur Radiol.* 2012;22: 439–46.
58. Bai B, Li Q, Leahy RM. Magnetic resonance-guided positron emission tomography image reconstruction. *Semin Nucl Med.* 2013;43: 30–44.
59. Muller-Gartner HW, Links JM, Prince JL, Bryan RN, McVeigh E, Leal JP, et al. Measurement of radiotracer concentration in brain gray matter using positron emission tomography: MRI-based correction for partial volume effects. *J Cereb Blood Flow Metab.* 1992;12:571–83.
60. Rousset OG, Ma Y, Evans AC. Correction for partial volume effects in PET: principle and validation. *J Nucl Med.* 1998;39:904–11.
61. Wurslin C, Schmidt H, Martirosian P, Brendle C, Boss A, Schwenzer NF, et al. Respiratory motion correction in oncologic PET using T1-weighted MR imaging on a simultaneous whole-body PET/MR system. *J Nucl Med.* 2013;54:464–71.