

MR-PET: Combining Function, Anatomy, and More

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It is widely accepted that coregistration of anatomical information improves the diagnostic value of functional imaging. At the moment, this is reflected in the success of hybrid scanners using PET and CT imaging. But the combination of PET and MR imaging may also offer advantages, such as higher soft tissue contrast in the MR anatomical images, real simultaneous acquisition, and minimum radiation exposure to the patient. Correlative imaging will open exciting new applications in oncology, neurology, and cardiology. For now, the compatibility of

PET detectors with magnetic fields still poses a technical challenge and space limitations inside the magnet must be resolved. There is no fully developed and mature clinical MR-PET system on the market yet, but the approach of using scintillation crystals inside the magnet combined with external photo sensors has been successfully implemented for small animal imaging. Semiconductor readout of scintillation crystals is in development and may offer the opportunity to develop a clinical MR-PET system.

Combining functional information from nuclear medical imaging with anatomical information from CT or MR images has become of great interest since PET tracers are becoming more and more specific. Image coregistration and fusion techniques have been developed and optimized for the interpretation of PET, CT, and MRI data. While the combination of PET and CT in one hardware device is already being used on a routine basis in oncology [1], the combination of PET with MR still exhibits several technical challenges.

This overview will explain the additional value of a combined MR-PET compared to advanced image coregistration methods for separately acquired images. Consequently, the following will show why research in this direction is indispensable. In principle, a combined MR-PET scanner with simultaneous measurements will provide functional and anatomical information at the same time in perfect spatial registration. Inaccuracies, which usually occur when separately acquired datasets with patient repositioning are combined, generally cannot emerge with hybrid system imaging.

In addition to precise anatomical information, MR may provide data from which PET attenuation correction factors can be estimated, thus transmission measurement with radioactive sources is not needed. Scaling methods will have to be developed to translate the MR signal intensity into attenuation factors of gamma rays with 511 keV.

Simultaneous MR-PET Measurements

A further advantage of performing PET in a high magnetic field is resolution enhancement due to reduced positron range. While this was the motivation for initial research of combined PET and MR [2], now the focus has shifted to simultaneous MR-PET measurements, since very high magnetic fields are needed to improve resolution for commonly used positron emitters such as F-18 or C-11.

Measurement times for a complete multislice image or 3D dataset in MRI are typically long compared to physiological timescales such as breathing or heartbeat. This is very similar to the PET measurement, which usually takes several minutes per bed position. In MRI, several techniques have been developed to overcome this problem. Some of them rely on the possibility of MR

to measure navigator signals very quickly. For example, the position of the intestine can be detected in real-time with MRI. This information can be used immediately in MRI to adjust the excited slice position in order to follow the moving anatomy. For the PET data, this information can be used retrospectively to rebin the detected events accordingly. Similar techniques are imaginable for cardiac applications.

Techniques, currently being developed for PET/CT, may be transferable to the situation in MR-PET. Optimized breathing protocols were developed for PET/CT systems, that limit alignment artifacts [3].

If the acquisition is already optimized, retrospective software processing has the potential to improve the situation. A variety of algorithms are available [4] and show acquisition inaccuracies in the order of only 2 mm in brain studies [5] and less than 10 mm in oncological studies of the thorax [6, 7].

One possibility to combine PET and MR in a single device would be similar to the axially shifted integration of PET and CT in the current PET/CT systems (Figure 1A), but this would not allow simultaneous acquisition. Only the full integration of a PET device inside the MR magnet (Figure 1B) would provide true simultaneous imaging. This would open the door to exciting new areas of application.

MR-PET Application

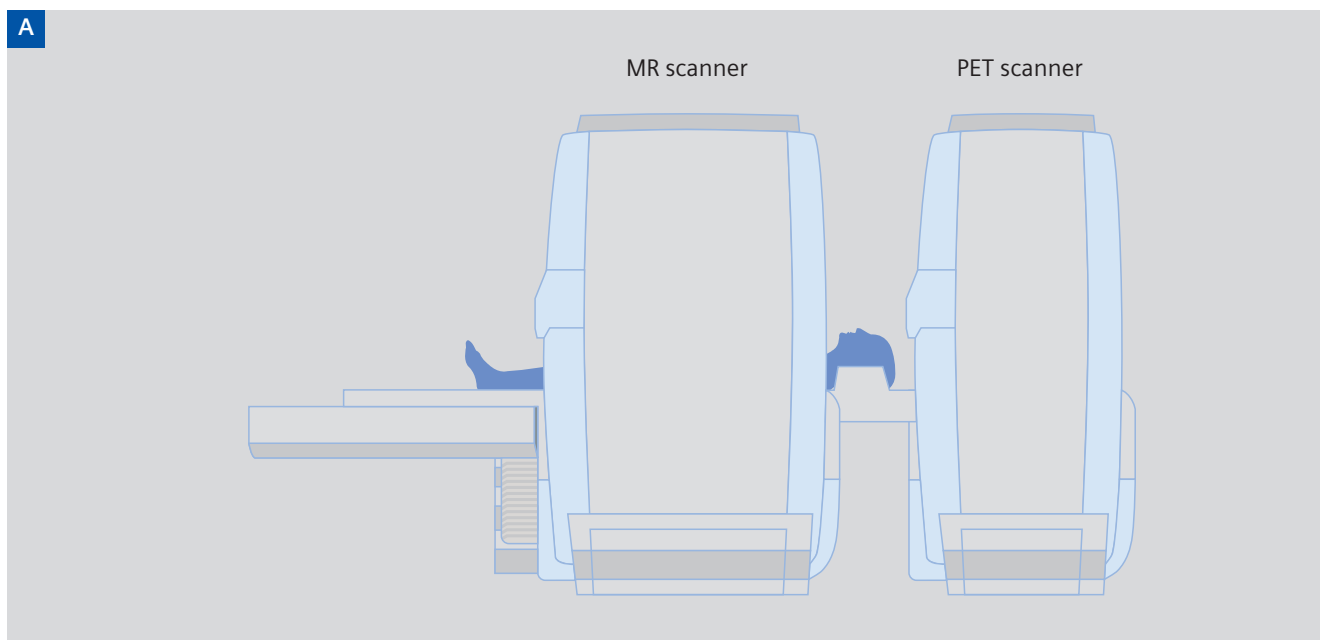
Various fields of practice would benefit from a combined MR-PET scanner; some of them are illustrated in the following. FDG-PET in Alzheimer's diagnosis is an established technique, but corrections for atrophy are currently based solely on estimates. With MR-PET, accurate correction would be possible using perfectly aligned MR data. Fusion of receptor displacement studies with PET and functional MRI (BOLD effect) can be beneficial when studying the interaction between receptor activation and regional perfusion. Even perfusion change effects in areas which are distant to the areas of receptor changes can be assessed. Using the same paradigm at the exact same time of PET and MR image acquisition may offer the unique opportunity to investigate the BOLD effect parallel to an O-15 water PET study. It would also offer the opportunity to study activation and deactivation effects in PET versus MRI. Another important clinical application area of MR-PET

in the neurological field is the simultaneous determination of functionally significant brain sections and delineation of tumor localization before surgery and radiotherapy. Also, MR perfusion data of stroke patients could be improved by functional PET information. Exact anatomical coregistration with the individual MRI dataset of a patient in an MR-PET scan would greatly improve the accuracy of localizing epileptic foci. Currently, this is done by coregistering the functional FDG-PET data and separately acquired MRI images (Figure 2).

In oncology, individualized treatment planning and therapy monitoring is of general interest. Specific functional information needs to be accompanied by anatomical reference. PET/CT imaging already delivers substantial results. The high soft tissue contrast of MRI and lower radiation exposure enables follow-up studies. Regional information from within the tumor is then needed, when testing effectiveness of drug

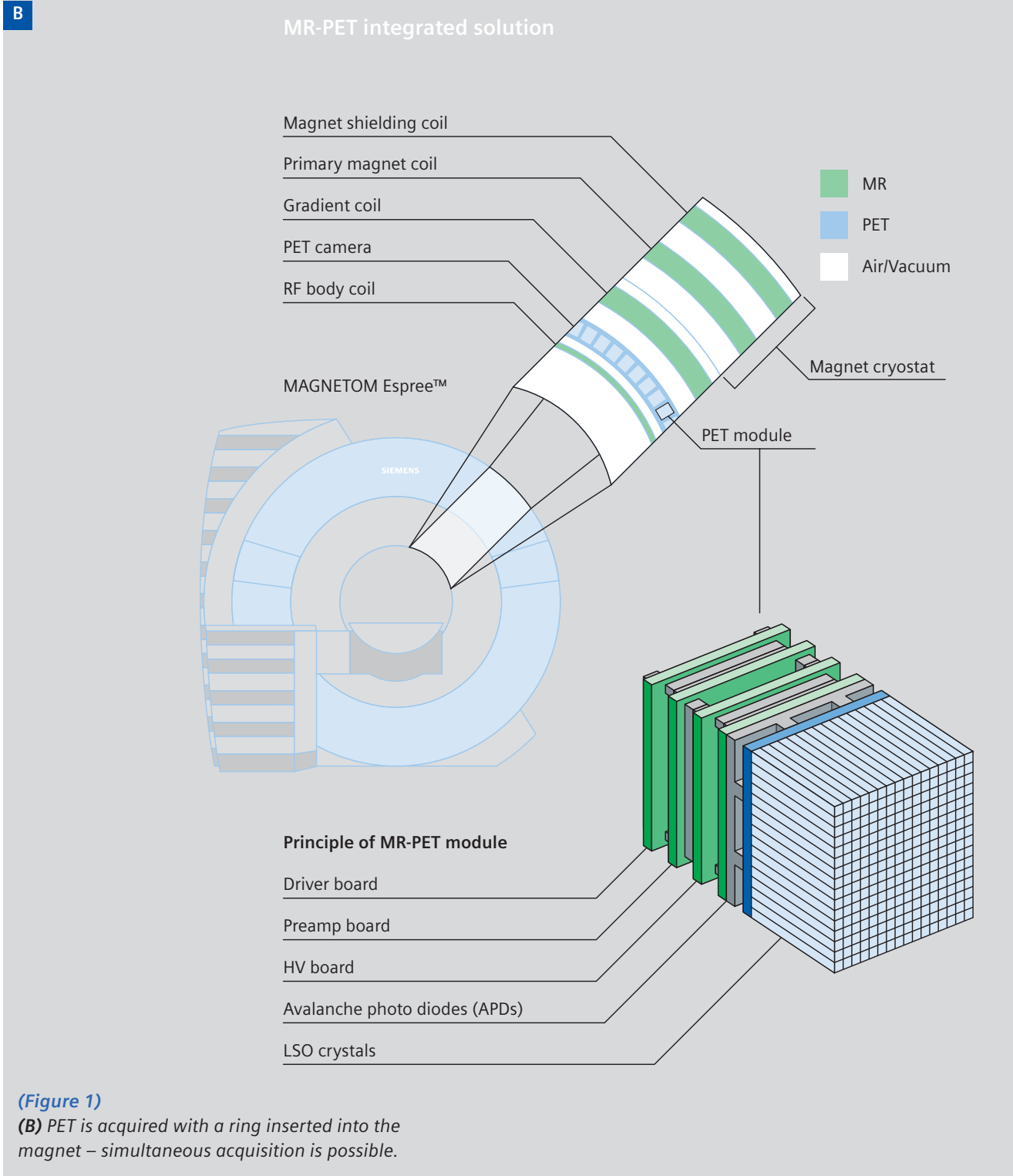
delivery within a tumor [8]. In this case, perfect spatial resolution is required. Not only functional-anatomical correlation can be determined with MR-PET, but also correlation of different functional information. For example, diffusion parameters can be measured simultaneously with the receptor status determined by PET tracers. Longitudinal studies will be possible during the course of pharmacological treatment, providing information for individualized therapy.

Cardiac applications would certainly profit from an MR-PET approach as well. Although the benefits of the "one-stop shop" with MRI are widely known and accepted, there are limitations. The assessment of myocardial blood flow (MBF) with MRI is still limited to visual analysis with dynamic imaging after injection of contrast media. Even when analyzed semiquantitatively, an underestimation of flow can be observed [9] in MRI studies. In contrast, using flow tracers such as N-13 ammonia or O-15 water, PET is able to delineate the absolute MBF reproducibly over a wide range of



(Figure 1)
Possible geometry of a combined MR-PET scanner.

(A) The two devices are aligned with an axial shift – sequential imaging.

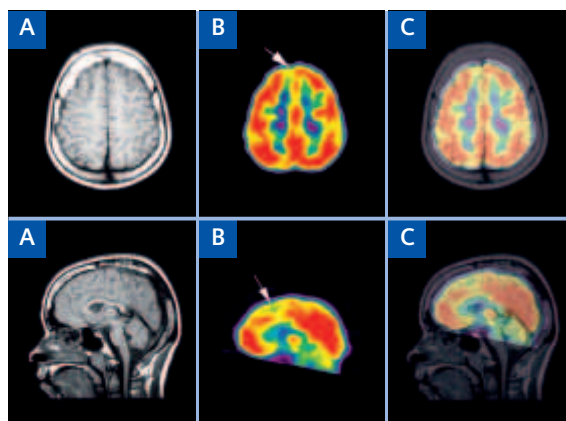


physiological values. Very similarly, late enhancement MRI techniques delineate infarct tissue with an unprecedented spatial resolution [10]. The extent of viable, but compromised tissue area is of special clinical interest (hibernating myocardium). In contrast, FDG-PET suffers from reduced resolution, but provides a high degree of specificity to delineate living cells using metabolic tracers in the myocardium, which would benefit from revascularization procedures. Thus, an obvious strategy would combine the high-resolution images from MRI depicting wall thickness and wall motion, scar tissue, coronary anatomy, and plaque burden, and supplement them with very specific, quantitative information about tissue viability and blood flow.

The Technical Challenge

The main problem in combining PET and MRI arises from the fact that photomultiplier tubes cannot be operated in a magnetic field without degradation of performance. In addition, there is only very limited space when considering PET detector placement in the magnet. Therefore, it is not possible to use the standard PET detector, comprising crystal arrays and photomultiplier tubes, in a combined MR-PET imaging system. Simon Cherry's group started developing MR-compatible PET detectors at UCLA [11]. The detector principle is based on the use of long optical fibers, which guide the light from scintillation crystals positioned within the magnetic field to position-sensitive photomultiplier tubes outside, where the fringe field drops below 10 mT. The length of the light guide is 3–4 meters. Based on this technology, the first simultaneous PET and MR imaging of phantoms at 1.5 T was performed with a single-layer LSO ring of 54 mm diameter [12]. Artifact-free simultaneous PET and MRI could be demonstrated with this prototype system and various MR scanning protocols [13]. The feasibility of simultaneous PET and MR imaging as well as MR spectroscopy for small animals has been shown using a similar prototype [14].

The PET device performed poorly [14], the main reasons for this being the limited axial extent, low sensitivity, and the long light guides. For larger axial coverage of the PET insert, it may be advantageous to use a different detector concept. Avalanche photodiodes (APDs) have been used in prototype small animal PET systems [15, 16] to read out the scintillation light from bismuth germanate (BGO) or Cerium doped lutetium oxyortho



(Figure 2)

Example of a FDG-PET brain study for the localization of epileptic foci. Separately acquired PET and MRI image sets are coregistered for anatomical identification of hypometabolic foci (arrow). Transversal and sagittal slices of MRI, PET, and fused images are shown.

(Courtesy of Dr. A. Drzezza, Department of Nuclear Medicine, TU München)

silicate (LSO) crystals. The main advantage is that APDs operate in high magnetic fields without performance degradation [17]. In addition, these semiconductor detectors are very compact, thus offering the opportunity to build very compact modules with potentially minimum interference with MR imaging [18]. Figure 3 shows a photomultiplier tube as it is typically used in a PET scanner and an APD matrix used for reading out scintillation crystals. Compared to the solution described previously, this would involve the introduction of electronic circuits in the magnetic field. Siemens recently showed the first results of this approach using an insert with sectors of LSO-APD detectors.

Conclusion

MR-PET will be a very valuable clinical tool with the advantage of minimum radiation exposure in comparison with PET/CT. Many innovative examination methods are envisioned in oncology, neurology, and cardiology. The development of a PET insert seems feasible, offering the opportunity for true simultaneous PET and MR imaging. ▶



(Figure 3)

Photograph of a photomultiplier tube as it is used in PET scanners and an APD array suitable for operation in the magnetic field.



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