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Advances in multimodal neuroimaging: Hybrid MR–PET and MR–PET–EEG at 3 T and 9.4 T

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ABSTRACT

Multi-modal MR–PET–EEG data acquisition in simultaneous mode confers a number of advantages at 3 T and 9.4 T. The three modalities complement each other well; structural–functional imaging being the domain of MRI, molecular imaging with specific tracers is the strength of PET, and EEG provides a temporal dimension where the other two modalities are weak. The utility of hybrid MR–PET at 3 T in a clinical setting is presented and critically discussed. The potential problems and the putative gains to be accrued from hybrid imaging at 9.4 T, with examples from the human brain, are outlined. Steps on the road to 9.4 T multi-modal MR–PET–EEG are also illustrated. From an MR perspective, the potential for ultra-high resolution structural imaging is discussed and example images of the cerebellum with an isotropic resolution of 320 μm are presented, setting the stage for hybrid imaging at ultra-high field. Further, metabolic imaging is discussed and high-resolution images of the sodium distribution are presented. Examples of tumour imaging on a 3 T MR–PET system are presented and discussed. Finally, the perspectives for multi-modal imaging are discussed based on two on-going studies, the first comparing MR and PET methods for the measurement of perfusion and the second which looks at tumour delineation based on MRI contrasts but the knowledge of tumour extent is based on simultaneously acquired PET data.

1. Introduction

Tomographic imaging methodologies are essentially focused on the generation of tissue contrast in a given plane of interest. Contrast between different tissues arises from the differences in endogenous physical properties or through the introduction of exogenous "contrast agents". Often a single contrast, or multiple contrasts from the same imaging modality, simply do not suffice to enable a complete diagnostic decision to be reached or, in scientific studies, leave aspects of the question unanswered. As such, a desire to address the same problem in different imaging machines arises. Specifically, spatial co-localisation of the information from the different modalities might be desired or indeed, the introduction of a temporal dimension might be required.

Magnetic resonance imaging (MRI) is characterised by its excellent tissue contrast based on, for example, T_1 and T_2 relaxation times, proton density, and diffusion/flow properties. Due to this fact, it has been widely used for structural/diagnostic imaging in the clinic and also for functional brain imaging in neuroscientific research.

Positron emission tomography (PET) is a widely used and well-established tool for clinical tumour diagnostics and is the gold standard for metabolic imaging. In contrast to MRI, PET provides insights into physiological and pathophysiological processes, albeit at a comparatively low anatomical resolution. Consequently, as shown here in an example from brain tumour imaging (see below), PET can be seen as an outstanding complement to MRI with respect to its metabolic specificity and its ability to enable tumour differentiation and tumour extent mapping [1].

Recently, two major developments in the fields of MRI and PET have taken place. In the MRI domain, the field strength of scanners for human application has moved to the ultra-high field range of

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up to 9.4 T and even beyond. Ultra-high fields facilitate structural imaging with significantly higher spatial resolution, higher functional (BOLD) contrast [2], perhaps even at the level of columnar resolution, and enhanced image contrast [3]. Moreover, such ultra-high field MRI scanners open up the opportunity to perform non-proton MRI and spectroscopy with a reasonable, PET-like spatial resolution in the order of 3 mm isotropic [4–6].

Regarding the use of PET in the MRI environment, the use of photo multiplier tubes (PMTs), that are extremely sensitive to magnetic fields, has been abandoned in favour of avalanche photo diodes (APDs) that are field insensitive. The implementation of new detector technologies based on APDs has led to true hybrid MR–PET scanners, capable of simultaneous MRI and PET data acquisition and has thus negated the need to perform scans in two separate machines. These hybrid scanners have the advantage of measuring PET and MRI datasets that are intrinsically co-registered in time and space [7–9]. Furthermore, inclusion of a PET scanner inside an MRI system brings with it advantages for PET image reconstruction. Partial volume correction, attenuation and motion correction can be performed based on MRI images acquired simultaneously with the PET data. In particular, clinical applications and neuroscientific research will benefit from these recent developments in terms of opportunities for metabolic imaging, accurate receptor density mapping, and novel paradigms for brain function.

In the confines of this article, multimodal imaging is defined as the summation of information from different imaging modalities whereby it is noted that MRI could well be regarded as being inherently multimodal, given the plethora of contrast mechanisms that can be exploited to generate image contrast. The combination of MRI and PET will be discussed; the measurement of MRI and PET data in two separate scanners will not be addressed and attention will instead be focused on hybrid MR–PET scanners studying the human brain and that are capable of the acquisition of simultaneous datasets. Hybrid MR–PET data acquisition at 3 T and at 9.4 T in humans will be explored. Further, the additional introduction of a temporal dimension, in the form of electroencephalography (EEG), in hybrid mode, will also be presented and discussed. Multimodal imaging in the form of simultaneous MR–EEG, and the extension thereof to triple modality MR–PET–EEG will also be briefly presented; the rationale for triple modal imaging is presented in Fig. 1 in the form of "finger print" diagrams.

2. Hybrid MR–PET scanner construction

The prototype 3 T MR–PET scanner used to obtain the results described herein comprises a commercially-available 3 T Siemens Tim Trio MR system and a custom-built BrainPET insert designed especially for brain imaging (Siemens Healthcare, Erlangen, Germany). The 9.4 T hybrid is also a Siemens prototype system based around a magnet with a warm-bore diameter of 90 cm and a PET insert that is nearly identical to that of the 3 T scanner. The BrainPET insert (Fig. 2) is a compact cylinder (length of 72 cm and an outer diameter of 60 cm) consisting of 32 copper-shielded detector cassettes each with six detector modules. The diameter of the PET field-of-view is 31.4 cm and 19.2 cm in the axial direction. The front end of the detector module is a 12×12 matrix of individual lutetium oxyorthosilicate (LSO) crystals coupled to a 3×3 array of APDs thus rendering the detector insensitive to the magnetic field of the MR system. The small volume of the LSO crystals measuring $2.5 \times 2.5 \times 20\ mm^3$ leads to a central PET image resolution of about 3 mm [10]; this is one of the best spatial resolutions for

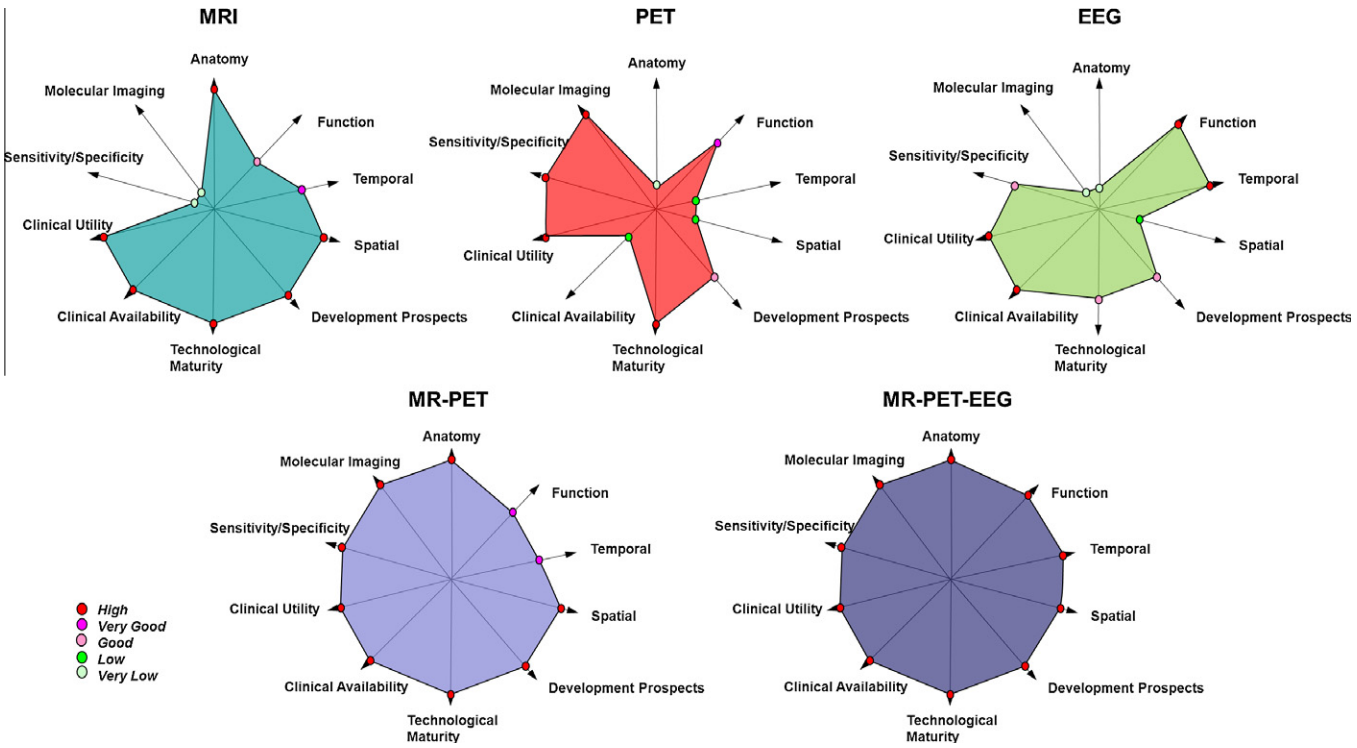

Fig. 1. Fingerprint diagrams giving an overview of the strengths of MRI, PET and hybrid MR–PET, and hybrid MR–PET–EEG. Starting at the origin, the further one traverses along a given axis, the better that particular attribute is fulfilled. MRI can provide exquisite spatial resolution and the technology is widely available. However, MRI is not strong in the area of molecular imaging and its specificity is also somewhat limited. PET on the other hand, has poorer spatial and temporal resolution than MRI but it is extremely specific – an attribute conferred upon it by the choice of radiolabelled tracer – and is also very sensitive. Both MRI and PET have a poor temporal resolution regarding mapping of brain function, for example. In a hybrid scanner capable of simultaneous measurement of all three dataset, all the chosen attributes are fulfilled in entirety.