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CASE REPORT

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Fluorodeoxyglucose PET/MRI in oncology: potential benefit when malignancy co-exists with inflammation

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Abstract

Despite increasing numbers of PET/MRI units worldwide, experience with this technology is currently limited. To date, studies comparing PET/CT and PET/MRI in oncology have largely shown equivalent diagnostic performance. There is therefore a need to identify sub-groups of patients for whom the diagnostic of PET/MRI may exceed that of PET/CT. Although confirmatory research is required, PET/MRI offers the promise of improved imaging evaluation for patients on immunotherapy where the assessment of malignancy may be complicated by the presence of treatment-related inflammation.

Keywords: *PET/MRI, immune related adverse events, treatment related inflammation, benefits of PET/MRI, immunotherapy*

Introduction

Hybrid PET/MRI is a relatively new modality in the medical field which combines PET and MRI within a single imaging device. Integration of PET with MRI rather than CT has several potential advantages including a) an ability to perform in a single procedure, examinations that would otherwise have to be performed on separate devices, b) reduced radiation exposure for patients through the use of MRI rather than CT to correct PET images for the attenuation of emitted radiation by overlying tissue, c) more accurate anatomical localisation of areas of radiotracer uptake on account of simultaneous rather an sequential acquisition of MRI and PET , and d) compensation for the reduced conspicuity of abnormal radiotracer uptake in organs with background physiological tracer uptake such as the liver and bone marrow. However, the extent to which these technical benefits lead to improvements in clinical outcomes remains unclear. To date, studies comparing PET/CT and PET/MRI in oncology have largely shown equivalent diagnostic performance [1,2]. There is therefore a need to identify sub-groups of patients for whom the diagnostic of PET/MRI may exceed that of PET/CT. Patients undergoing immunotherapy during which malignancy may co-exist with inflammation may represent one such sub-group.

Case

The recent introduction of immune targeted therapy has brought a transformational change in the oncological field of medicine. However, this innovation in cancer care has also created specific difficulties in the assessment of treatment response due to the potential for inflammatory complications that are associated with immunotherapy [3]. Even advanced imaging methods for the assessment of treatmen t response such as FDG-PET/CT are frequently unable to distinguish inflammatory complications from tumour progression due to the fact that malignant tissues and inflammatory cells both exhibit increased radiotracer uptake [4,5]. Failure to distinguish an adverse inflammatory event from true disease progression can potentially lead to inappropriate patient management.

Table 1 outlines some of the more common inflammatory events associated with immune check point inhibitor therapy along with corresponding benefits that can potentially be realised by using PET/MRI in place of PET/CT for the evaluation of patients during therapy with these agents. On occasions, these benefits can be further enhanced by improved tissue contrast afforded by MRI within tumour tissue itself, for example the high signal on T1 images seen in some cases of melanoma [6].

Immune-related event	Potential benefit of MRI over CT
Hypophysitis	Superior delineation of pituitary morphology and contrast enhancement
Thyroiditis	Assessment of contrast enhancement not complicated by tissue iodine content
Lymph Nodes	Superior assessment of node morphology and fat content.
Colitis	Superior delineation of bowel wall thickening and contrast enhancement

Table 1. *Frequently encountered immune related events corresponding to their potential benefit of MRI over CT.*

The above benefits are illustrated in Figures 1 and 2 which display PET/MRI findings of thyroiditis and bowel inflammation in a patient with advanced melanoma undergoing immune checkpoint inhibitor therapy with Ipilimumab and Nivolumab. The patient, presenting with severe vomiting and diarrhoea, underwent a PET scan primarily to assess for melanoma deposits within the bowel. However, there was significant FDG uptake throughout the small bowel and colon, with contrast enhancement on MRI. This enhancement, comparable to vascular structures was consistent with the diagnosis of colitis. However, the widespread FDG uptake throughout the bowel rendered identification of possible melanoma serosal deposits difficult. Nonetheless, the pre-contrast T1 MRI images revealed two small foci of high T1 signal in the small bowel and ascending colon, compatible with melanin deposits within serosal metastases. These foci were seen to be non-FDG avid, in keeping with metabolic response to treatment

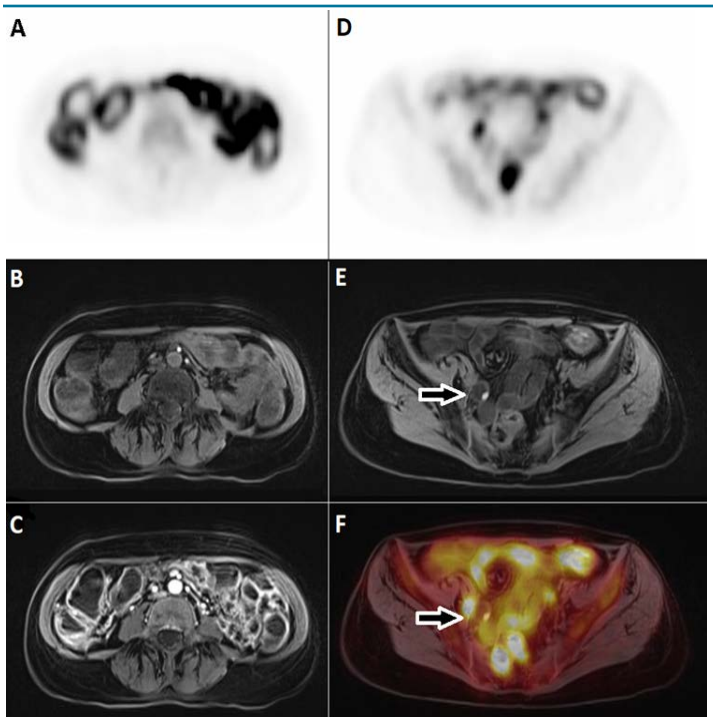

Figure 1. *PET images at two levels in the abdomen and pelvis, along with simultaneously acquired pre- and post- TR1 MRI. A, B and C demonstrates the widespread FDG uptake on PET sequence and corresponding contrast enhancement, consistent with colitis, potentially masking serosal deposits. D and E demonstrates another level in the abdomen with persistent FDG uptake in the bowel, but a focus of high-intensity T1 signal (arrow) visible on pre-contrast MRI consistent with serosal disease. The fused image F, of the same slice shows a non FDG avid focus, compatible with treated disease.*

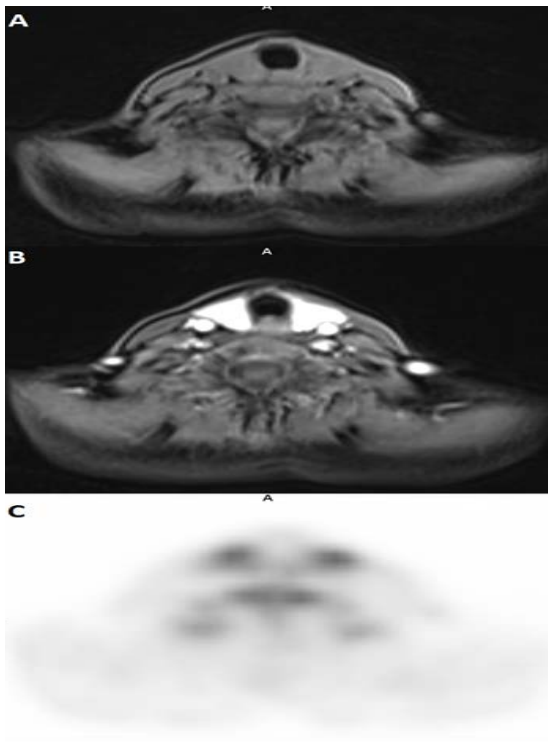

Figure 2. *Images of the thyroid on pre-contrast T1 MRI (A), post contrast T1 MRI (B) and PET (C) demonstrating the intense contrast enhancement, comparable to vascular structures corresponding to diffuse FDG uptake throughout the thyroid gland consistent with thyroiditis.*

(Figure 1). Diffuse FDG uptake within the thyroid was also seen associated with intense contrast enhancement, confirming thyroiditis as a synchronous second immune related adverse event in the same patient (Figure 2).

As highlighted in table 1, one of the many adverse inflammatory events includes checkpoint inhibitor–induced colitis, an event which has been recognised more commonly to date, that varies in severity from mild diarrhoea and abdominal pain (grade 1-2) to severe colitis (grade 3), intestinal perforation (grade 4), and even death (grade 5) [7-9]. A recent study by Seith et al explored the use of PET/MRI in assessing response to PD-1 therapy in melanoma patients; although, it's potential utility in the identification of inflammatory complications from treatment was not discussed [10]. MRI assessment of bowel inflammation has been previously shown to be superior to CT [11]. This superiority would translate into an advantage when simultaneous PET imaging is performed with MRI over CT. Additionally; a recent study highlights the usefulness of PET/MRI in detecting colitis, reaffirming the effectiveness of utilising PET/MRI in the identification of immunotherapy related colitis [12]. The high T1 signal associated with melanin with melanoma metastases on contrast MRI aided the identification of tumour deposits, further emphasizing on the efficacy of this modality. In the absence of MRI, this study would have been inconclusive due to the limitations of the CT component.

Concuslion

Despite increasing numbers of PET/MRI units worldwide, experience with this technology is currently limited. In the absence of clear evidence of improved diagnostic performance over PET/CT in routine oncological applications, there is a need to identify clinical scenarios for which the benefits of PET/MRI can be maximally exploited. Although confirmatory research is required, PET/MRI offers the promise of improved imaging evaluation for patients on immunotherapy where the assessment of malignancy may be complicated by the presence of treatment-related inflammation.

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