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Commentary to Quantitative PET/MRI Evaluation and Application in Neurology

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With the high spatial resolution of magnetic resonance imaging (MRI) particularly for the soft tissue such as in brain and non-ion radiation involved, the integrative positron emission tomography (PET)/MRI system is expected to provide almost equivalent image quality compared with PET alone or PET/CT system, and simultaneous MRI information that is not conventionally available [1]. PET-MRI opens new horizons in multi-parametric neuroimaging for clinical research that allows simultaneous imaging of multiple parametric changes such as blood flow and metabolism at the same time. While MRI could provide superior structural information, applying MRI anatomical priors to reduce the PET partial volume effect could be achieved to improve spatial resolution of PET images for clinical and research usages. The PET/MRI scanner might help address these issues with advantages of reduced scan time and simultaneous nature of data acquisition. For the past few years, multiple applications of the integrated PET/MRI imaging including inflammation, functional metabolism and microstructure mapping have been reported [1,2]. Further applications in brain tumors and cancer response monitoring have reported complementary and valid information that this relatively new modality could achieve based on newly developed techniques. Newer and better MRI-based attenuation correction (AC) such as zero TE (ZTE) for more bone-related tissue signal detection and faster reconstruction compared to UTE/Dixon has been reported [3-6]. Advanced MRI-based motion correction for PET image reconstruction, newer PET time of flight reconstruction and incorporation with compressed sensing techniques have offered attractive superior temporal and spatial resolutions for disease diagnosis and prevention [7-9]. We briefly review the applications of PET/MRI in neurology with two examples in Alzheimer's disease and brain tumor cases in this commentary.

Numerous imaging studies in Alzheimer's disease (AD) have been performed to study characteristic brain alterations including brain atrophy with earlier involvement of medial temporal lobe [10], brain hypo- perfusion in the posterior cingulate and parietal regions [11], reduced functional and structural connectivity in the default mode network (DMN) based on MRI findings [12] and hypo-metabolism based on PET imaging findings [13]. A regional coupling between metabolism of glucose (via PET kinetic analysis) and cerebral blood flow (CBF) had been reported with reductions post-caffeine compared to pre-caffeine conditions in controls [14], and in demented patients [15] based on separate scans. An evaluation of the real-time coupling of these two key imaging parameters with simultaneous acquisitions had not been performed before. For example, FDG metabolism had been found to increase twice as the energy brain activation needs (i.e., larger change in metabolism than change in CBF), and at a later time the unmetabolited fraction of the tracer was cleared off so that the tissue concentration of the tracer could reflect the metabolic rate [16,17]. Neurovascular coupling between neurochemistry (e.g., dopamine receptor occupancy) and hemodynamic change (e.g., cerebral blood volume) using simultaneous PET/fMRI acquisitions had been reported recently with similar temporal profile and dose response in non-human primates [18]. Translational studies of neurovascular and neuro-metabolic coupling effects in human beings and patients remain challenging due to inter-subject variability and lack of control template. Despite these challenges, the integrated PET/MRI scanner gained popularity due to some advantages including intrinsic between-modality image registration, better interpretation of underlying co-existing pathophysiological events, and most importantly, less patient discomfort [19].

The article by Zhou [2] had evaluated the most up-to-date PET/MRI scanner performance with multiple functional and structural metrics together with application demonstrations. Voxel-wise analyses in the template space also showed the majority of brain voxels (>95%) with significant correlations (r>0.54, P<0.05) between PET/MRI with Dixon MR-based AC method and PET/CT based on SUVR (standard uptake value ratio, a quantitative metric of normalized PET tracer dosage uptake) choosing cerebellum as the reference region (Figure 1A). A tight coupling between PET/MRI PET image and PET/CT PET image with a slope of fitting close to 1 in the middle temporal gyrus (MTG) was demonstrated in (Figure 1B). Furthermore, the global mean difference based on SUVR between PET/MRI and PET/CT was small using Dixon MR-based AC and PET/CT (difference=4%), And our findings agree with currently accepted notion that the MRI-based AC could achieve comparable imaging quality to standard-CT AC, with ≤ 5% differences between the PET/MRI and PET/CT PET images. The integrated PET/MRI images showed comparable image quality to stand-alone imaging modality (both MRI and PET) with the gains of simultaneous multi-parametric acquisitions, reduced scan time and potential patient discomfort. Furthermore, tight correlation between blood flow and

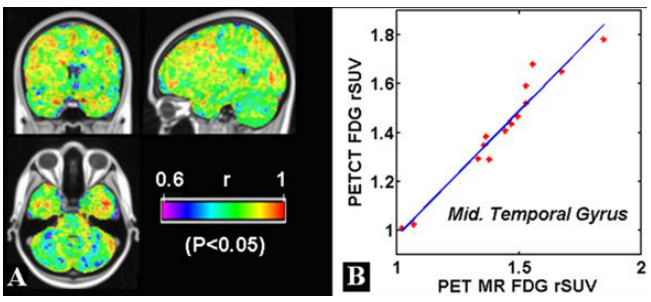

Figure 1: A: Voxel-wise Dixon-based PET/MRI correlation with PET/CT also showed highly consistent pattern between two PET images (r>0.6, P<0.05). An example of the SUVR values in the middle temporal gyrus (MTG) from PET/MRI and PET/CT was shown in B, with a tight coupling between two PET images (slope of fitting=1) [2].

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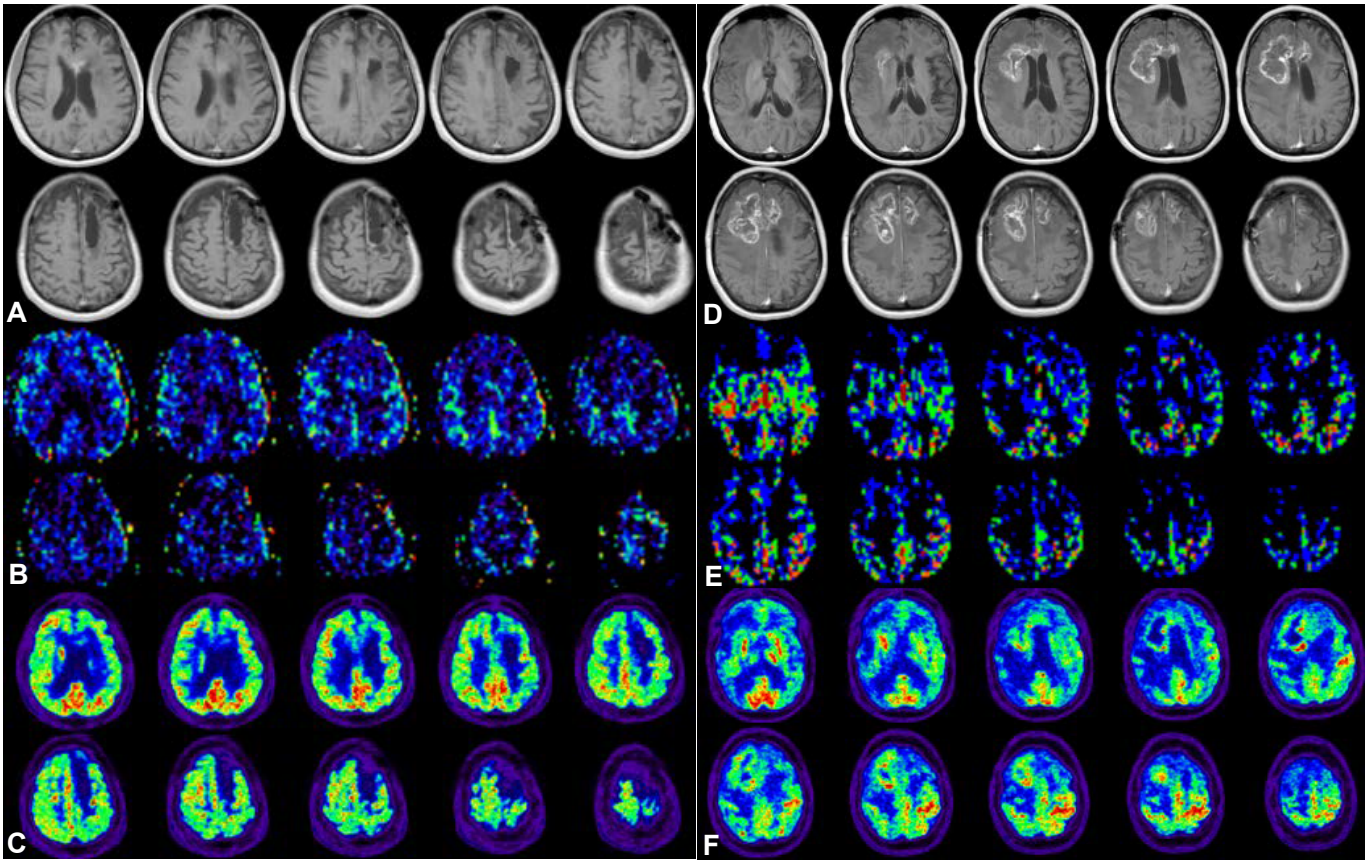

Figure 2: T1-weighted image (A, D), relative cerebral blood flow obtained form pulsed ASL (B, E) and metabolic PET-FDG uptake (C, F) in a probably benign brain tumor case (A-C) and a glioblastoma multiforme case (D-F) using integrated PET/MRI scanner. Compared to benign tumor patient, the glioblastoma patient showed abnormal hyperintensity on T1, increased relative cerebral blood flow and increased or abnormal FDG uptake pattern in the affected area [1].

metabolism was found in several brain gray matter regions including the temporal lobe in patients [1,2].

Tumor growth typically requires new blood vessel formation, causing changes in neurovascular and neurometabolic measures such as blood brain barrier (BBB) permeability, blood flow and metabolism [20]. Typical microstructure alteration of tumor characteristics include changes of diffusion of cell density of tumors and extracellular space narrowing and restricted diffusion properties compared to surrounding tissue types. For instance, using multiple imaging metrics obtained from the integrated PET/MRI scanner, we could differentiate images of MRI T1, CBF and PET- FDG uptake of a possible benign tumor case and a glioblastoma multiforme case. (Figure 2) demonstrated representative images of MRI T1, CBF and PET-FDG uptake of a possible benign tumor case (A-C) and a glioblastoma multiforme case (D-F) [1]. Compared to benign tumor patient, the glioblastoma patient showed abnormal hyperintensity on T1, hyperperfusion and increased FDG uptake in the affected area. Our study described the convenience and feasibility of using simultaneous MRI and PET modality to characterize structural, functional, and molecular signatures of brain tumor. We had demonstrated the abnormal increased metabolic PET and MRI hyperintensity and higher blood flow of glioblastoma compared to a benign tumor case. Further study with more subjects and an automatic multi-imaging feature classification to obtain an objective integrated score to predict disease survival rate and recurrence is warranted in the future [20] for the relatively new integrated PET/MRI scanner.

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