In vivo-post mortem multimodal image registration in a rat glioma model

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Introduction: Histological staining techniques can identify the regulation of specific biomarkers in small animal models of glioma and provide indicators of cellular dysfunction. The correlation of *in vivo* imaging signal changes and molecular indicators of tissue damage in histological brain sections represents an important means of understanding the cellular mechanisms responsible for these changes under pathological conditions. This requires an accurate image registration that can compensate the distortions that occur in the brain during the extraction, fixation, and staining process. Here, we present the preliminary results obtained by applying an overall registration strategy for the fusion of *in vivo* PET and MRI data with *post mortem* brain images in a rat 9L-glioma model.

Methods: Experiments were conducted on male Wistar rats. Twelve days after intrastriatal injection of 9L rat glioma cells, we acquired T2-weighted MRI and 60 min dynamic PET using [18F]DPA-714 [1] for *in vivo* evaluation of peripheral benzodiazepine receptor (PBR) expression. Following *in vivo* imaging, animals were euthanized. The entire brains were cut into 20 μm-thick coronal sections and processed for H&E staining and PBR immunohistochemistry. A blockface photograph was also recorded prior to each section. The overall co-registration strategy relied on using the blockface photographs as an intermediate reference, onto which the *in vivo* MRI and PET images and the digitized histo- and immunohistochemical brain sections were registered separately and superimposed so as to obtain *in vivo-post mortem* registration [2;3].

Results: By way of feasibility study, the co-registration strategy was only performed on one rat's right hemisphere. As illustrated in Figure 1, after each registration task, both the external contours, the outer edges of the cortex and inner structures such as the corpus callosum, the hippocampus, the striatum and even the tumor were correctly superimposed whatever the modality.

Conclusions: We obtained promising registration results of T2-weighted MRI and [18F]DPA-714 PET with *post mortem* brain volumes. Once results from additional animals had been provided, our approach could be used to evaluate, quantify and compare tumor volume, pharmacokinetic and physiological parameters (e.g. ligand differential uptake areas within the tumor) measured from *in vivo* MRI and PET data with those derived from corresponding *post mortem* histo- and immunohistochemistry.

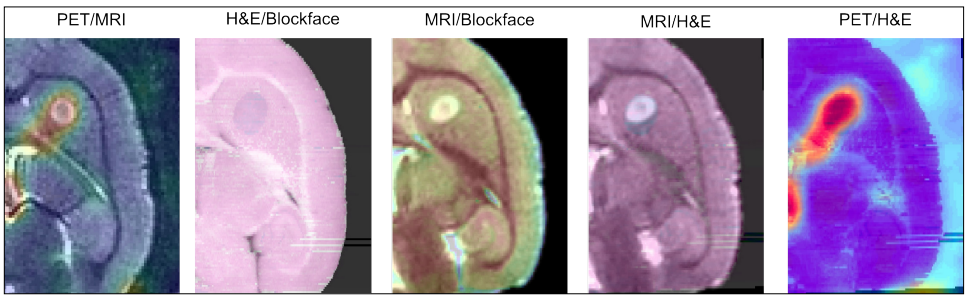

Fig1: Fusion of (A) PET (rainbow) and MRI (black and white), (B) Blockface (black and white) and H&E (pink) volumes, (C) MRI (black and white) and blockface volume (rainbow), (D) MRI (black and white) and H&E volume (pink) and (E) PET (rainbow) and H&E volume (black and white)

References:

1. Damont A et al; J label Compds Radiopharm. 51 (7): 286-292 (2008)
2. Dauguet J et al; J Neurosci Methods. 164 (1): 191–204 (2007)
3. Lebenberg J et al; Neuroimage. In press (2010)