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Bridging Scales: Adapting RAPSODI for High-Precision Rat Brain MRI-Histology Co-Registration

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Introduction: Multimodal image co-registration between magnetic resonance imaging (MRI) and histology is a critical yet challenging task in neuroscience research. Understanding brain microstructure requires combining MRI, which provides non-invasive and versatile brain information at spatial resolutions ranging from 70 to 100 micrometers, with histology, which delivers subcellular detail at resolutions ranging from ~0.1 to 1.1 micrometers. Accurate co-registration of these complementary modalities is essential for investigating tissue changes across diverse neurological disorders. However, registering 2D histological sections to a 3D MRI volume is intrinsically difficult due to cross-modality contrast differences, resolution mismatch, and section defects such as tears, warping and missing pieces. Consequently, existing registration tools are often not directly compatible with our datasets, particularly when histological tissue is fragmented or incomplete.

Method and Materials: Our study uses a dataset of 22 adult rat brains from a moderate Traumatic Brain Injury (moTBI) model, scanned at 3- and 28-days post-injury using in-vivo and ex-vivo MRI, followed by histological sectioning and staining with Myelin and Nissl protocols. We implement and adapt RAPSODI (RAdiology Pathology Spatial Open-Source multi-Dimensional Integration) to our rat brain moTBI dataset. RAPSODI is an open-source image registration framework originally developed for prostate cancer patients, specifically to register presurgical MRI with histopathology images from radical prostatectomy specimens [1]. RAPSODI consists of three-stage pipelines. First, it generates a 3D reconstructed digital model of histology which serves as the representation of the tissue before sectioning. Second, the MRI slices and the corresponding histology slices are registered. Third, it uses optimized alignments to project the prostate and the cancer regions delineated in histological sections back onto MRI volume [1]. In our adaptation, we replace the prostate and cancer regions with our structural masks of brain anatomy and modify preprocessing pipelines to accommodate the format of our dataset. For the present analysis, we adapted the tool to a single rat brain of which the ex-vivo MRI data was acquired at 11.7 Tesla with T2-w sequence that has an isotropic spatial resolution of 70 micrometers. Histological sections were scanned at 0.1369 micrometers in-plane resolution and 60 micrometers through-plane resolution.

Results: As an initial implementation stage, we selected 30 slices of Nissl-stained coronal sections and corresponding ex-vivo MRI slices from a single rat brain. The histological scans were subsequently downsampled to 1.095 micrometers of in-plane resolution. Our co-registration optimization employed mean squared error with a reduced learning rate (0.005) of the gradient descent and stricter constraints on rotation, scaling, and shearing transformations. Then we co-registered the slices using the adapted RAPSODI framework to evaluate registration quality. The quality of the co-registration and alignment can be seen in the Figure1.

Conclusion: We present preliminary results for histology-MRI co-registration in rat brains. Future work will include a landmark-based evaluation and extend analysis beyond a single animal to the full cohort, reporting quantitative metrics alongside qualitative overlays.

[1] Rusu M, Shao W, Kunder CA, et al. Registration of presurgical MRI and histopathology images from radical prostatectomy via RAPSODI. Med Phys. 2020;47(9):4177-4188.

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