POSTMORTEM MRI TO GUIDE PATHOLOGICAL LOCALIZATION: INDIVIDUALIZED, 3D-PRINTED CUTTING BOXES FOR FIXED BRAINS

MARTINA ABSINTA[1,2], GOVIND NAIR[1], THOMAS TALBOT[3], MASSIMO FILIPPI[2], ABHIK RAY-CHAUDHURY[4], CARLOS A. PARDO[5], and DANIEL S. REICH[1]

[1]Translational Neuroradiology Unit, National Institute of Neurological Disorders and Stroke (NINDS), NIH, BETHESDA, MARYLAND, United States, [2]Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, MILAN, MILAN, Italy, [3]The Laboratory of Cellular and Synaptic Neurophysiology, NICHD, NIH, BETHESDA, MARYLAND, United States, [4]Surgical Neurology Branch, NINDS, NIH, BETHESDA, MARYLAND, United States, [5]Department of Neurology, Johns Hopkins School of Medicine, BALTIMORE, MARYLAND, United States

Target audience. Researchers and physicians interested in ex vivo MRI and technical improvements in MRI-pathological correlations.

Purpose. Interfacing MRI and pathology is especially important to understand the pathological basis of MRI signal changes *in vivo*; however, the match between the standard pathological cut (thick, non-parallel, hand-cut coronal brain slabs) and the postmortem MRI is time-consuming and often not sufficiently accurate. The aim of this project is to develop technology to integrate postmortem, high-resolution MRI into the planning and execution of the pathological analysis through precise localization of the target and coordinates of cut.

Methods. We built a customized cutting box for a formalin-fixed whole-brain (59-year-old man patient affected by multiple sclerosis [MS]). On postmortem MRI, we defined a frontal cortical lesion as the target of our study. Whole-brain 7T T1-MPRAGE data were acquired coronally (parallel to the mammillary bodies) with 0.6-mm isotropic voxels and imported into MIPAV and 3D-design software packages (Osirix www.osirix-viewer.com/; Netfabb Basic http://www.netfabb.com/; MeshLab http://meshlab.sourceforge.net/). The surface of the brain was rendered, and a mold was created to conform to the inferior (skull base) surface (Fig. 1A). Parallel, coronally oriented 1.2-mm wide gaps to accommodate a brain-cutting knife, were placed every 4.8 mm, yielding 24 6-mm slabs. The box was printed using a 3D-printer (Stratasys Dimension Elite) in 101 hours 21 minutes (material cost ~$400) (Fig. 1A). After the brain was placed in the box, the slabs were cut consecutively from the center (Fig. 1B) toward the occipital lobe and subsequently toward the frontal lobe. Each slab was removed and labeled immediately after it was cut. Match between the slabs' gross anatomy and the coronal T1-MPRAGE data was determined visually according to cortical profiles. 2D-coregistration between photos of slab surfaces and correspondent slices on MRI was performed in MIPAV. For comparison, the cutting performance was tested in a second fixed whole-brain (55-year-old female affected by MS) that underwent standard pathological sectioning, starting from a plane passing through the mammillary bodies.

Results. The fixed brain fit perfectly within the cutting box (Fig. 1B). After cutting, the gross anatomy of the anterior and posterior surfaces of slab #13 (slab of interest) matched with the corresponding MRI slices. Optimal registration was achieved using an affine followed by a landmark thin-plate registration (Fig. 2). Due to slight shifting of the brain within the cutting box as slices were removed, the match was less accurate for #2, 9, 10, 15, 18 and 20 cutting lines (25% of total; Fig. 3A). By contrast, the cutting performance with the standard approach is extremely poor; 13 of 15 ~1cm-thick slabs (86%) were not parallel each other and to the plane passing through the mammillary bodies (Fig. 3B).

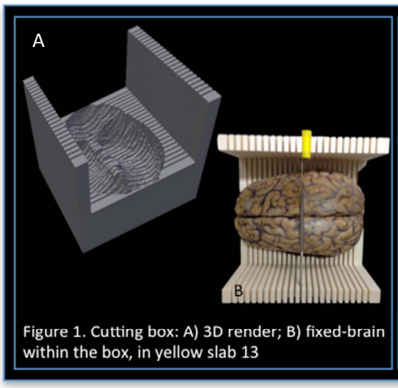

Figure 1. Cutting box: A) 3D render; B) fixed-brain within the box, in yellow slab 13

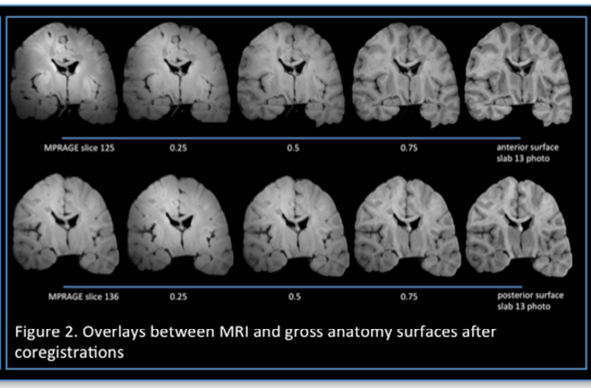

Figure 2. Overlays between MRI and gross anatomy surfaces after coregistrations

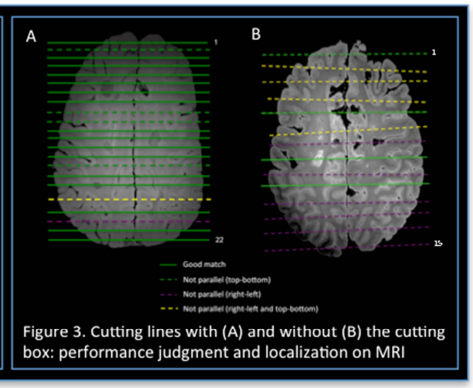

Figure 3. Cutting lines with (A) and without (B) the cutting box: performance judgment and localization on MRI

Discussion. The cutting performance is superior using the cutting box. The MRI target (cortical lesion) was correctly localized after the pathological cut in the expected slab. Optimal coregistration between MRI and pathology was easily achieved, and matching the pathological sections and MRI scans was not time-consuming (~1 hour *vs.* ~10-15 hours required after standard sectioning). Finally, a slab thickness <1 cm can be reliably obtained only with the cutting box.

Conclusion. The use of an individually rendered, 3D-printed cutting box for fixed brains can improve the speed, quality, and accuracy of pathological localization of small lesions identified on MRI, such as commonly occur in MS.