In vivo MRI-based 3-D Printed Molds and Individualized Tissue Sectioning Apparatuses Improve MRI-Histopathologic Co-Registration in Brain Cancer Patients

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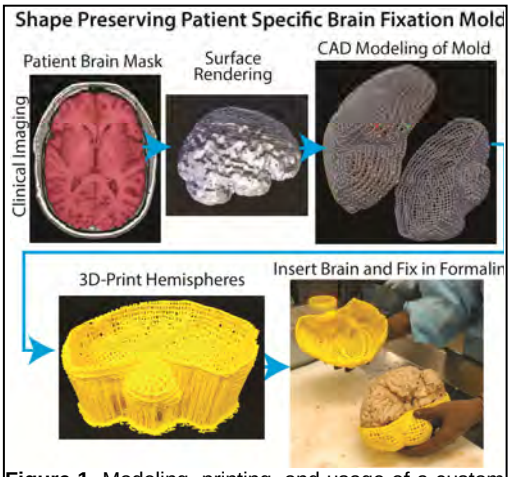

Figure 1. Modeling, printing, and usage of a custom 3D-printed mold for shape preservation of the brain during fixation.

Target Audience: Scientists and clinicians interested in correlating histology to MRI in the brain.

Purpose A recent report presents a novel method using 3D printing to generate custom slicing boxes for brain sectioning based off of MRI[1]. This study uses ex-vivo scanning to generate to design and 3D print the individualized cutting box. The results from this study are quite promising for precisely co-registering ex-vivo imaging and brain slices.

Methods co-registering histology and in-vivo imaging have been used to validate imaging biomarkers of brian tumor invasion[2]. Tissue preparation and sectioning orientation are critical for this type of study. Without aid of a brain slicing apparatus, it is difficult to orient tissue. Systematic error can occur from inaccurate leveling and unstable manual slicing.

Tissue distortion during formalin fixation is a significant issue when trying to correlate clinical imaging to histology[3,4]. Following removal, brains are commonly placed in containers containing formalin without encasement to prevent the brain from flattening. This distortion makes co-registration to clinical in-vivo imaging difficult.

This study accomplishes three things. First, we introduce a technique for creating patient specific fixation molds for preventing brain distortion during fixation. Second, we generate individualized tissue sectioning apparatus' (ITSAs) based on axial imaging gathered in-vivo clinically. We then quantitatively compare tissue slices to MRI slices to determine the average discrepancy.

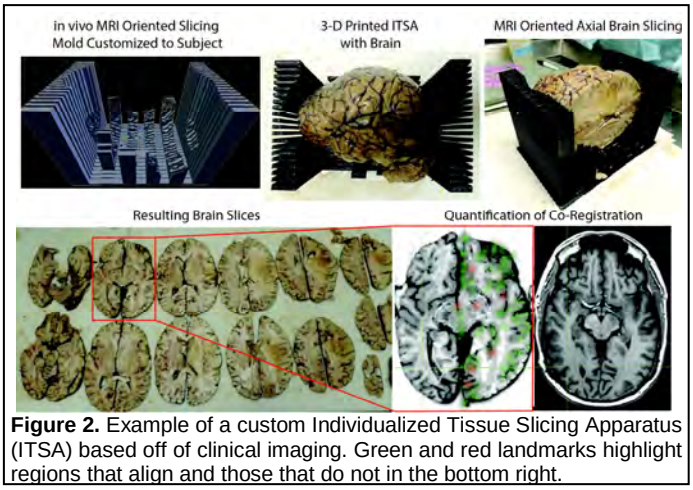

Figure 2. Example of a custom Individualized Tissue Slicing Apparatus (ITSA) based off of clinical imaging. Green and red landmarks highlight regions that align and those that do not in the bottom right.

Methods Three high-grade glioma patients undergoing brain only autopsies were included in this analysis. A clinically acquired MRI was used to render 3D computer assisted drafting (CAD) models. To generate a fixation cage for preventing tissue distortion, a high-resolution 3D-T1-weighted MRI scan was used to generate a solidified mesh with approximately 500 holes to allow formalin exposure (Figure 1). The left and right hemispheric meshes were then 3D printed in plastic using a MakerBot Replicator2X. The brains were fixed in formalin for approximately 14 days within the plastic meshes.

To generate a slicing mold each patient, the shell from the 3D-T1-weighted scan was combined with the slice profile of 6.5mm thicker-cut images. A slicing mold was then designed and 3D-printed with slots oriented vertically with the brain lying on its side within the mold.

To assess co-registration, photographs were taken of each slice and converted to 192*256*1 volumes similar to the patient's MRI. The histology was then manually rotated, translated, and scaled to match surface features as closely as possible to the patient's final clinical MRI. To quantify co-registration, landmarks (i.e. apex of a gyrus or sulcus) were defined and a distance between the corresponding landmarks was calculated (Figure 2).

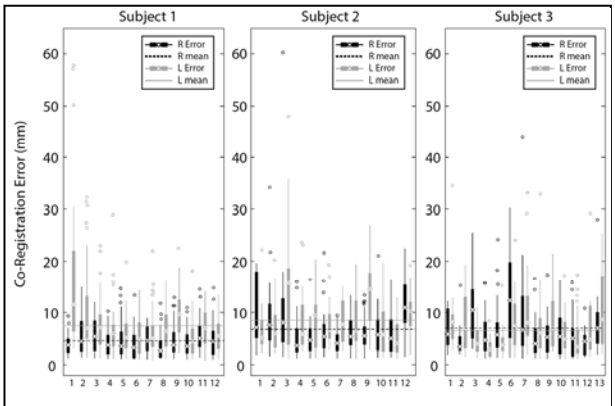

Figure 3. Co-registration error plotted against slice for each patient. The error in the x,y plane was 6.26mm for the Subject 1, 8.12mm for Subject 2, and 8.16mm for Subject 3.

Results Whole brain average co-registration error in the x,y plane was 6.26mm for the Subject 1, 8.12mm for Subject 2, and 8.16mm for Subject 3 (Figure 3). Differences were greatest at the edges of the brain, furthest from the middle of the ITSA. There was also greater error in the left hemisphere than the right due to greater freedom for the knife to move in the slots at the top.

Discussion We present a novel method for preserving the shape of a brain during fixation and for slicing it in the same orientation as the patient's last clinical scan. We find that landmarks align well after slicing.

References 1. Absinta M et al. J Neuropathol Exp Neurol; 2014. 2. LaViolette, P.S., *et al. Neuro-Oncology.* 2014.3. Schmierer K, et al. Magn Reson Med 2008. 4. Weisbecker V. Brain Struct Funct 2012.

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