Image-Guided Stereotactic Biopsy System for Small Animal Experiments

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Introduction: Advances in physiologic and molecular MRI-based techniques have greatly improved the capability to monitor in vivo the pathophysiologic behavior of pre-clinical small animal tumor models and their response to novel drug therapies. A critical part to confirming the accuracy of imaging techniques is the correlation of MRI measurements with tissue analysis parameters. The current standard requires careful whole-brain sectioning and slice-by-slice correlation with imaging, which is technically challenging, time consuming, and prone to user variability and error. Image-guided stereotactic biopsy offers a potentially feasible alternative to whole-brain histologic sectioning, by providing targeted imaging-tissue correlation that is less time consuming and more technically facile. Use of optical-based neuronavigational clinical systems in humans provide proof of concept for such correlations, but have coregistration errors (several millimeters) that are too large relative to small animal systems. Previous reports using expensive robotic systems in small animals offer promise of increased accuracy,[1,2] although expense and technical complexity may limit feasibility of widespread use. Furthermore, many such reports have described implementations that rely on MRI-incompatible hardware. In contrast, we present validation of a more economically viable mechanical-based image-guided stereotactic biopsy system that achieves sub-millimeter needle tip positioning accuracy and comprises hardware components that can be purchased for less than $15,000. For laboratories with ready access to an MRI-compatible stereotactic frame, implementation of the proposed methods would require only software development.

Methods: A Kopf Instruments 900M small animal MRI stereotactic instrument/holder and 1760-61-SB micro-manipulator with fine adjustment (David Kopf Instruments, Tujunga, CA, USA) were used to secure, register, and access stereotactic markers in imaging experiments. The holder and markers are shown in Fig. 1. Stereotactic markers were made from capillary tubes filled with vitamin E to serve as the targets and fiducials for initial experiments. The markers were secured to the small animal holder and 3D images were acquired with a 7T small-animal Bruker MRI (FLASH, TR=13.4 ms, TE=4.3 ms, α=40°, 256x256x128 matrix, FOV=8.0x8.0x4.0 cm). An example image is shown in Fig. 2, where the markers are visible. Target and fiducial coordinates were manually identified in acquired image volumes displayed through a custom multiplanar reconstruction interface developed in MATLAB (Mathworks, Inc., Natuck, MA, USA). A rigid body transformation was also implemented in MATLAB to convert coordinates from the image domain to coordinates in physical space.[3] The transformation used singular value decomposition (SVD) to minimize a centroid-based squared error objective, which is also known as the orthogonal Procrustes problem. The SVD-based solution was chosen for this application because it is particularly robust to noise. Stereotactic positioning accuracy was evaluated by quantifying the distance error between target coordinates measured in physical space and corresponding target coordinates that were transformed from the image domain.

Results: Three different stereotactic targets were identified in image data for each of two scans, and their coordinates were then transformed to physical space. Physical space coordinates for each of the three targets were also measured twice. Positioning errors for each target were evaluated for each combination of transformed and measured coordinates (12 total combinations). The positioning error values were distributed with a mean of 0.83 mm and a standard deviation of 0.26 mm.

Discussion: We present an economical mechanical-based MRI-guided small animal biopsy system that achieves sub-millimeter needle tip positioning accuracy. System performance was validated through multiple phantom experiments. Although similar results have been reported by others in previous studies, the methods used in those studies have not been validated or presented in detail to our knowledge[4]. Potential applications of this technique include: 1) validation of novel imaging techniques, such as cell-tracking; 2) guided tissue analysis of tumor subregions based on MRI parametric response to novel treatments; and 3) targeted access with other modalities that enable in vivo monitoring, such as confocal microscopy.

References:

[1] P Kazanzides, et al. "Development of an image-guided robot for small animal research". *Computer Aided Surgery*, Vol. 12(6), pp. 357–65, November 2007.
[2] A Ayadi, et al. "Fully Automated Image-Guided Needle Insertion: Application to small animal biopsies". *Proceedings of the 29th IEEE EMBS*, 2007.
[3] DW Eggert, et al. "Estimating 3-D rigid body transformations: a comparison of four major algorithms". *Mach. Vis. Appl.* Vol. 9, pp. 272-90, 1997.
[4] HE Rice, et al. "Superparamagnetic Iron Oxide Labeling and Transplantation of Adipose-Derived Stem Cells in Middle Cerebral Artery Occlusion-Injured Mice". *AJR*. Vol. 188, pp. 1101-1108, April 2007

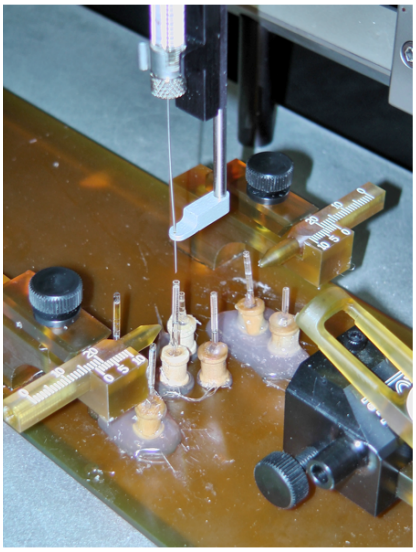

Figure 1. Small animal holder with stereotactic markers attached.

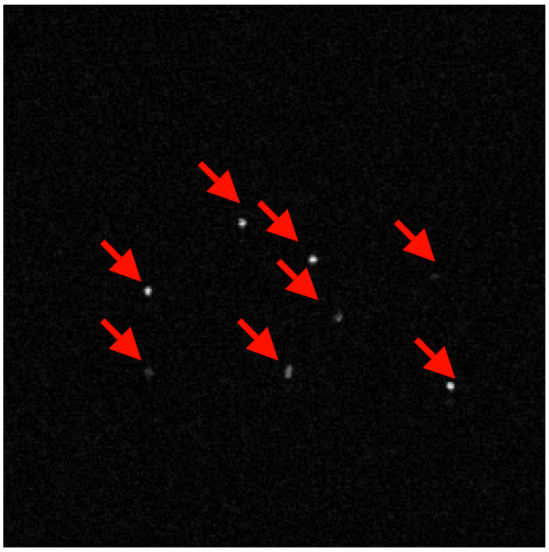

Figure 2. MRI data set showing eight stereotactic markers (fiducials and targets).