# Validation of Vascular Lesion Characterizations by MRI-Postmortem Co-registration

M. Singh[1], A. Rajagopalan[2], D. Hwang[2], C. Zarow[3], A. Lee[3], W. Ellis[4], H. Chui[3]

[1]Radiology, University of Southern California, Los Angeles, California, United States, [2]Biomedical Engineering, University of Southern California, Los Angeles, California, United States, [3]Neurology, University of Southern California, Los Angeles, California, United States, [4]Neurology, University of California Davis, Sacramento, California, United States

## Introduction

Co-registering postmortem brain images to in-vivo MRIs of the same person when alive represents a powerful new approach of correlating histo-pathologic findings to MRI signatures of suspected regions. Focal hyperintensities in subcortical gray and white matter, specifically lacunes (irregular cavities containing strands of fibrillar connective tissue), are often used to diagnose vascular dementia. Since lacunes look similar to dilated perivascular spaces on MRIs, pathology is the current gold standard to differentiate between the two. The objective of this work was to validate the MRI characterization of vascular lesions, including lacunes and perivascular spaces, by co-registering microscopically identified lesions in postmortem brain samples to their location within 3D in-vivo MRIs of the same person.

## Method

To circumvent some of the problems of co-registering photographed slices of the post-mortem brain to clinical MRIs (for example, the time-gap between the last MRI and death which was average 2 years in this study, gross structural deformations in the brain at time of death and upon extraction from the cranial cavity, mismatches between slice thickness and orientation between the two modalities, portions of the brain falling free from the slices), we registered the hemispheres separately. Digital photographs of 5mm thick coronal hemispheric postmortem slices were first aligned with respect to each other through fiducial markers, stacked to form a volume, and then aligned coarsely to the corresponding MRI coronal hemispheric volume formed by stacking 1.5mm thick slices acquired by an SPGR T1-weighted sequence (GE 1.5T, TR/TE=24/5ms, 15deg flip angle, 1mm x 1mm in-plane resolution). After achieving coarse volume alignment, multiple postmortem slices were matched to their corresponding MRI volume by non-linear polynomial warping, relying on spatial correlation followed by mutual information maximization. Vascular lesions, however, were identified and marked on dual echo axial slices (TR/TE1/TE2=4500/14/85ms, 3mm thick slices) through their peculiar proton density and T2 characteristics. The marked locations were first mapped from axial to coronal sections by volume reslicing and then mapped onto the post-mortem slices by using the polynomial-transformation parameters found in the above warping step. Relatively large samples of the postmortem slices around these marks were then extracted and sent to a pathologist for stained microscopy. The pathologist sub-sliced the samples into 250 micron sections and marked regions where lacunes and/or periventricular spaces were identified histologically. The marked stained sections were manually re-registered to the original photographs of the post-mortem slices (even though a portion of some samples disintegrated during the sub-slicing, it was not difficult to align the samples back to their original location) to compare the type and location of vascular lesions identified by the pathologists to their in-vivo MRI characterization.

## Results

Two examples are shown below. Fig. 1(a): The location of a lacune (hyperintense proton density, hyperintense T2, isodense T1 with respect to background) is marked by a circle on the T2 image. Fig. 1(b): Top image shows a slice of the postmortem hemispheric image. Bottom image corresponds to co-registered MRI coronal volume with the marked location mapped from 1(a). The red mark in the post-mortem image shows the location of the lacune as derived from the MRI in 1(a). Fig. 1(c): The stained histological section re-registered to the original postmortem slice. Fig. 1(d): The stained section corresponding to the black circle shown in 1(c). This lesion was identified as a lacune by the pathologist, confirming the MRI identification, and its location was approximately 4mm below the centroid of the red mark obtained through MRI-postmortem co-registration. An example of a perivascular space is presented in Fig. 2, following the same order as in Fig. 1. The pathology concurred with the MRI identification and location (within 3 mm after co-registration). In a total of 6 subjects, the locations of lesions were correctly identified by co-registration to within 5mm in 1l/12 lesions, thereby validating our MRI characterization of vascular lesions. We conclude that MRI to pathology co-registration is viable, even when there is an average of 2 years gap between the last in-vivo MRI and postmortem.

Fig. 1

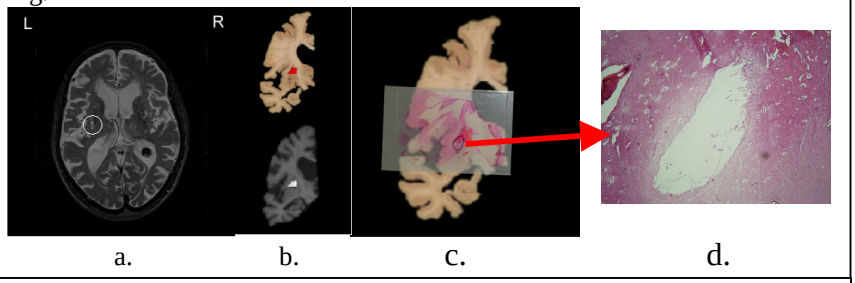


Fig. 2