FreeSurfer Parcellation of Brains Containing Large Infarcts

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Introduction: Volumetric analyses of brain regions play a key role in investigating the progression of neurological disorders such as Alzheimer disease or vascular dementia in elderly subjects [1]. FreeSurfer [2] is a robust validated software package for cortical and sub-cortical segmentation of structural MRI. However, FreeSurfer classification is highly dependent on the integrity of neighborhood voxels and their structure [3] and frequently fails in the presence of lesions or cerebral infarcts often present in elderly subjects. Not only structures within, or in the vicinity of, an infarct are affected, but distal regions may also be misclassified. A previous study circumvented this problem by "filling" in the infarct with tissue from the contralateral homologous region [4]. However the previous approach requires labor-intensive tracings of sulci. The objective of this work was to develop and validate a similar filling technique but with no manual intervention, so that it could be used to analyze large-scale volumetric studies requiring FreeSurfer parcellation of cortical/subcortical regions.

Method: As subjects undergoing an MRI scan are typically not positioned exactly symmetrical with respect to the midline of the brain, identification of homologous regions in the contralateral hemisphere requires an accurate realignment and spatial normalization of the brain. Spatial normalization of T1-weighted images being subjected to FreeSurfer analysis was accomplished by SPM affine and non-linear transformations [5] that map the coordinates of the subject's brain to the MNI template. The infarct boundaries were outlined manually to create a mask. It was then filled-in with the mean intensity of the T1 brain volume excluding the infarct and ventricles, as without such uniform filling, normalization often failed. Following normalization, the left and right hemispheres of the brain were interchanged (in MNI space) and normalized a second time. This step is equivalent to co-registering the contralateral hemisphere to the infarct-containing hemisphere and reduces the inter-hemispherical differences from morphological distortions likely to be caused by the infarct. The volume was then mapped back to the subject space using the inverse deformation field. Finally, voxels corresponding to the infarct were inserted into the original subject data from this inverse mapped image. To validate our technique, cerebral infarcts from 7 stroke patients were inserted one at-a-time in T1 images of 7 normal elderly subjects in whom the ground truth of FreeSurfer analysis was known. After contralateral filling as above, FreeSurfer outputs from all studies were evaluated quantitatively by comparing ratios of the cortical and subcortical volumes to their ground truth respectively, before and after filling the stroke.

Results and Discussion: An example of FreeSurfer brain parcellation in a stroke patient containing a relatively large infarct is shown in Figure 1. Significant changes were seen before and after filling-in the infarcted region. However, the ground truth is unknown in this case. Results of a validation simulation study where the ground truth is known are presented in Figure 2. An example of a simulated stroke/infarct region is shown in (a). Fig.2 (b) displays the ground truth parcellation, while (c) the result after inserting this infarct. The yellow circles indicate regions outside the infarcted region that show high deviation from the ground truth. The similarity of the parcellation between the ground truth and the result after filling, shown in (d) is remarkable. Fig. 3(a) shows the ratios for one simulation study using five brain volumes. The plot clearly exhibits a smaller error bar for the filled case. Histograms generated from averaged ratios of all combined simulation studies (7x7) for the filled and unfilled cases are fit to a Gaussian distribution and shown in Fig. 3 (b). The filled volumes have a mean closer to 1.0 and 35 % smaller standard deviation, reflecting the closeness of the reconstruction to the ground truth.

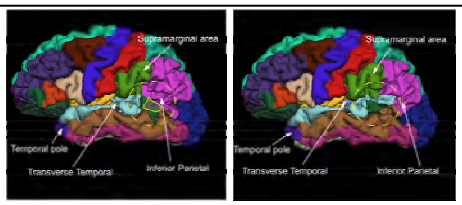

Figure 1: FreeSurfer parcellation before (left) and after (right) filling the infarct in a patient. The dotted circles indicate significant changes

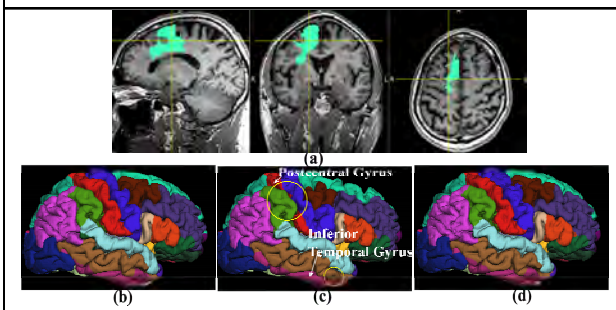

Figure 2: FreeSurfer parcellation result for validation study. (a) T1 slices showing simulated infarct; b) Ground truth FreeSurfer parcellation; c) FreeSurfer parcellation before filling simulated stroke; d) FreeSurfer parcellation after filling. Circles highlight regions where significant distortions have been corrected after filling.

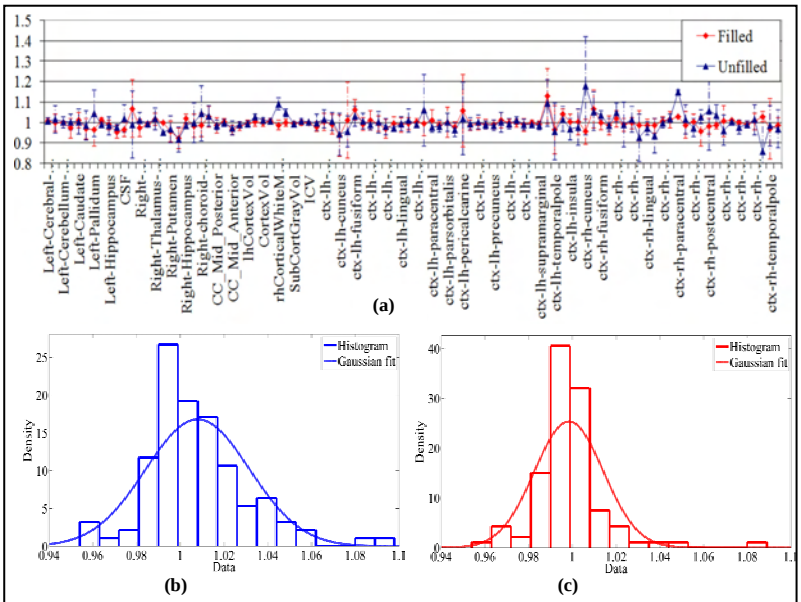

Figure 3: (a) Ratios of cortical/subcortical volumes with respect to the ground truth before and after filling an infarcted region inserted in the T1 images of 5 subjects. Improvement in recovering most regions is seen (ratios closer to 1.0) after filling. Histograms and Gaussian distribution fits computed from ratios of ground truth to unfilled volumes, averaged over all 7x7 simulations are shown in (b) before filling and (c) after filling, showing a mean closer to 1.0 and 35% reduction in the standard deviation after filling.

Out of 16 stroke brain volumes investigated in this study, FreeSurfer failed to complete processing on half of them before our technique was applied. All 16 volumes were processed successfully after filling. The results above suggest that our filling approach is a promising technique to conduct accurate volumetric analyses of brain structure even in the presence of cerebral infarcts, requires no manual interaction after outlining the infarcted region, and is thus suited to automate processing of large-scale clinical studies.

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