

# Automatic Computation of Normalized Brain Volume on 3D T1-Weighted MRI Scans Without Registration to Standard Space

Elizabeth Wicks<sup>1</sup>, Jason P.C. Chiu<sup>1</sup>, Lisa Y.W. Tang<sup>1,2</sup>, Kevin Lam<sup>1</sup>, Andrew Riddehough<sup>1</sup>, David K.B. Li<sup>1,2</sup>, Anthony Traboulsee<sup>1</sup>, and Roger Tam<sup>1,2</sup>

<sup>1</sup>MS/MRI Research Group, Division of Neurology, University of British Columbia, Vancouver, BC, Canada, <sup>2</sup>Dept. of Radiology, University of British Columbia, BC, Canada

## Purpose

Brain volume has been shown to be an important surrogate biomarker of neurodegeneration, such as in multiple sclerosis<sup>1</sup>. However, normalization is required to account for the variation in individual skull size and scanner voxel drift. A popular method for normalization is to perform affine registration of the skull region to a standard template, such as in FSL SIENAX<sup>2</sup>, yet this process is a source of measurement noise. Alternatively, the intradural volume can be computed directly and used as a normalization factor, resulting in a brain volume fraction (BVF). Intradural volume computation is challenging on 3D T1-weighted MRI scans due to the poor contrast between the cerebrospinal fluid (CSF) and the skull. To overcome these challenges, we have developed a new method of obtaining the intradural volume on T1w images that does not require registration, but instead analyzes local intensity profiles to robustly identify the CSF-dura boundary. We validated our method against an established method<sup>3</sup> of BVF computation that uses T2w/PDw scans, which have strong CSF signal.

## Method

To determine the BVF, the intradural volume (ID) was first computed by detecting the boundary of the dura. Next, the brain was segmented into white matter (WM), grey matter (GM) and cerebrospinal fluid (CSF). The BVF was then calculated as  $BVF = (\text{parenchymal volume}) / ID = (GM + WM) / ID$ .

The images were resampled to isotropic resolution and corrected for signal inhomogeneity<sup>4</sup>. Surface voxels of brain were extracted using a hybrid of two brain extraction algorithms: ROBEX<sup>5</sup> and BET<sup>6</sup>. Then, a normal vector was computed on each surface voxel, along which the dura is sought.

The three largest decreases in the intensity profile along each search vector were found in a bounded bidirectional search. The closest point of the three to the starting point of the search was determined to be the "point of decrease". The "point of increase" was detected similarly. Of these two points, the one furthest away from the starting point was determined to be a point on the dura.

As the dura is between the CSF and skull, and is brighter than both of them, at least one of the two points described above would capture either the CSF-dura or dura-skull boundaries. Taking the furthest point from the surface avoids the error of capturing the GM-CSF boundary. Sampling the three largest decreases/increases avoids capturing points on the bone marrow or fat, which are also bright.

To account for regional variations, the brain was automatically divided into three sections along the superior-inferior axis, landmarked by the middle of the eyeballs, and halfway between the eyeballs and the top of skull. For the top section of the brain, two searches were conducted at each surface point: one along the surface normal and another along the upward direction. Each search ranged from 1mm inward to 10mm outward. For the middle section, the search was conducted from 5mm inward to 10mm outward along the normal. For the inferior-most section of the brain, as the dura is not detectable, the search was not performed and the dura was assumed to be 1mm outward from the brain surface.

After obtaining the ID from the surface of dura (Figure 1), segmentation of CSF, GM, and WM was performed using an MRF-based EM algorithm<sup>7</sup>.

## Results

Validation was performed on a dataset from a completed multiple sclerosis clinical trial with 131 patients scanned at 58 sites. Every patient was scanned at two time points, each of which has T1w and T2w/PDw scans. The T1w scans were acquired with resolution 256x256x60, voxel size = 0.937mm to 1mm along each axis, TE = 1.403-6.889ms, TR = 1.1-15ms, and flip angle = 8-25 degrees. The T2w/PDw scans were acquired with resolution 256x256x60, voxel size = 0.937mm x 0.937mm x 3mm, TE = 8-24.399ms, TR = 2-4.32s, and flip angle = 90-180 degrees. The average BVF of the patients was 0.7336 +/- 0.0320 when calculated using the new method on T1w images, and 0.7611 +/- 0.0598 when calculated with the established method on T2w/PDw images. The Pearson correlation between these two sets of results was 0.845. SIENAX was run on the same T1w images and the correlation between the results of SIENAX and those of the T2w/PDw method was 0.789, which is significantly lower than our method (Williams' test, p = 0.0281).

## Discussion

We have demonstrated that the surface of the dura can be reliably detected and used to improve the accuracy of BVF computation over a standard template approach. This can avoid known errors due to affine registration with template images. The method is fully automated and computationally efficient, which significantly speeds up processing of large datasets, in comparison to methods that require manual correction<sup>8</sup>.

## Conclusion

We have developed a fully automated method of computing BVF using dural surface on T1w images without registration to standard space. This method correlated strongly to an established method on T2w/PDw scans.

## References

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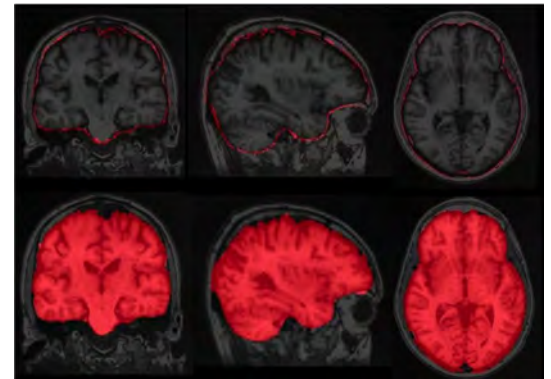


Figure 1: (Top) Points on dura detected, (Bottom) Interior of dura surface is filled in to compute intradural volume.