Tracking Brain Ventricle Expansion in Alzheimer Disease Using Combined Intensity and Shape-based Segmentation

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Introduction

Interventricular foramen Opening through which fluid drains from lateral to third ventricle

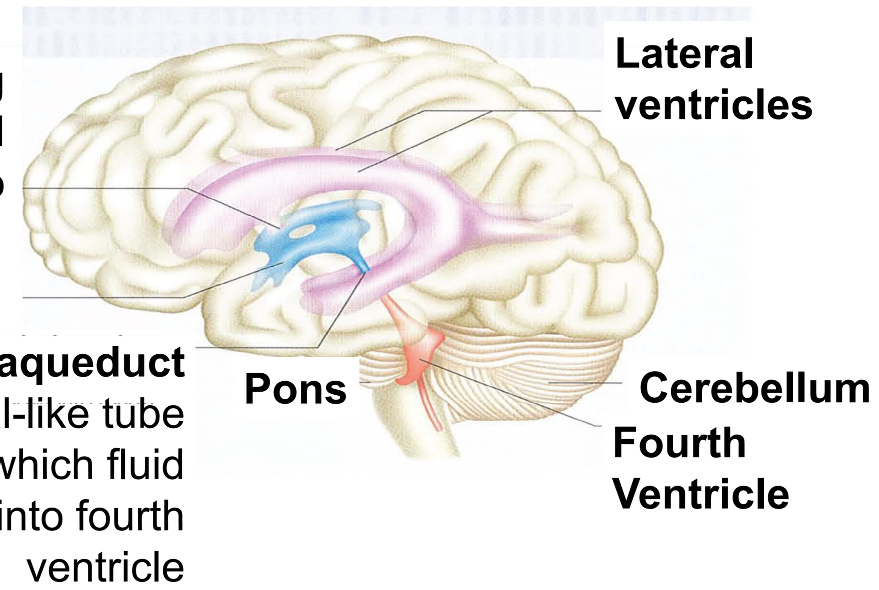


Figure 1: Illustration of Ventricles in the Brain [1]

- Brain ventricles (Figure 1, [1]) are fluid-filled cavities in the brain that increase in size at different rates in people aging normally, those with mild cognitive impairment (MCI) or those with Alzheimer disease [2].
- Such pathological changes can be measured from repeated high resolution magnetic resonance imaging (MRI) of the brain.
- Our overall goal is to develop and implement advanced algorithms that adapt and combine several segmentation approaches to increase the accuracy and precision of brain ventricle volume measurements.
- The goal of the present study was to fully automate segmentation of the lateral ventricles.

Limitations of Existing Methods

- Current automated ventricle segmentation methods do not consistently identify the temporal horns in all subjects.
- Automated segmentation algorithms have previously used deformable registration to map ventricle volumes between an atlas and a subject, but such indirect segmentation can lead to inaccuracies [3].
- Segmentation methods performed directly on images require user interaction to make corrections, decreasing speed and leading to bias.

Algorithm: General

- Seed points are identified by automatically mapping predefined points from within the ventricles of a brain atlas to the ventricles in individual subjects.
- This mapping utilizes a deformation field obtained from a deformable registration that warps the brain of the subjects into the brain atlas.
- Using the mapped seeds points, intensity-based fuzzy connectedness segmentation [4] is used to generate an initial segmentation, followed by a refinement of the segmentation using shape-based expectation-maximization (EM) [5].

Algorithm: Details

Select Ventricle in Atlas
↓
Deform Subject into Atlas
↓
Map Seeds from Atlas to Subject
↓
Confidence Connected Segmentation
↓
Fuzzy Connected Segmentation
↓
Expectation Maximization Segmentation
↓
Merge Segmentations
↓
Crop Segmentations
↓
Refine Horns
↓
Partial Volume Corrections

•A single series of brain image slices is chosen as an ***atlas*** or template and predefined ***seeds are selected.***

• ***Seed points are automatically mapped*** from the main body and posterior and temporal horns of ventricles of the atlas to ventricles in each subject. This mapping utilizes a deformation field that has been obtained from a multi-scaled ***diffeomorphic deformable registration*** [6-8] that warps the brain of the subject into the atlas.

•A ***confidence connected segmentation*** [9] includes voxels neighbouring the mapped seeds whose intensities are close to the mean of seed intensities.

• The mean and standard deviation of all voxels contained in the confidence connected segmentation are used to initialize a ***fuzzy connectedness algorithm*** [4] based on membership probabilities for every pair of voxels.

• ***Expectation Maximization (EM) segmentation*** [5] based on probability maps and atlas registrations, is used to capture horn details. ***The horn segmentation is refined*** by including isolated horn pieces.

• Segmentations are currently cropped manually in Slicer [10]. ***Automated cropping*** is being developed to remove the third ventricle.

• **Future Refinement**: Wrap a ***mesh*** around the segmented ventricles. Level sets and mixture models will be used to correct ***partial volume*** errors.

Software Validation

- A polycarbonate ventricle phantom in a brain mold of agar solution was created to validate accuracy of the software [11].
- T_1-weighted MR images from the Alzheimer Disease Neuroimaging Initiative (ADNI) were used to test and validate software including Normal Elderly Controls (NEC), subjects with Mild Cognitive Impairment (MCI), and subjects with Alzheimer Disease (AD) at baseline and at 24 months.

	NEC	MCI	AD
Population	25	19	24
Age ± (SD) (Baseline)	76.6 (4)	75.4 (7)	77.3 (6)
Sex (M)	14	15	12

Results

- The phantom was segmented using fuzzy connectedness to within 0.8% of its true volume [11]. Figure 2 shows an MRI image of the phantom and a visualization of the ventricle segmentation.

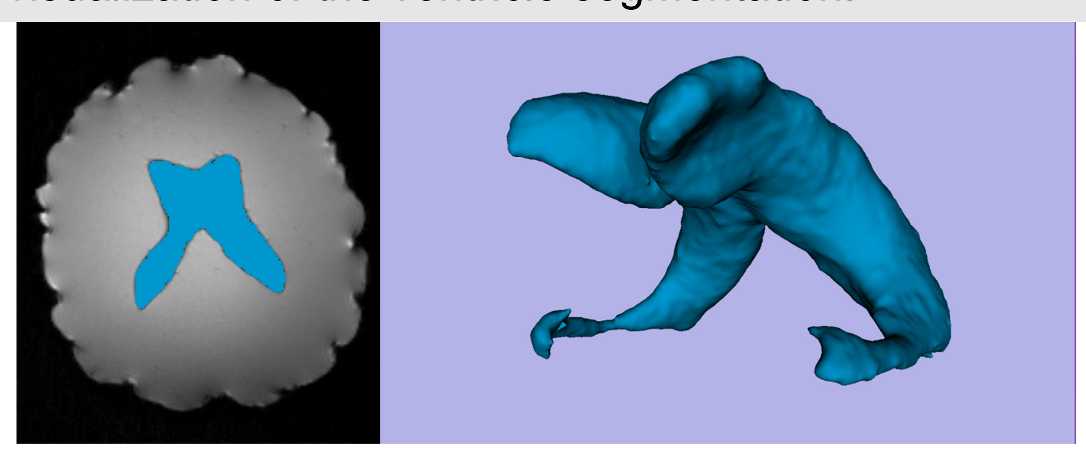


Figure 2: Brain Ventricle Phantom

- A diffeomorphic deformable registration was implemented to automatically place seed points.
- Accuracy was qualitatively assessed. (compare Figures 3(a) and (b)).

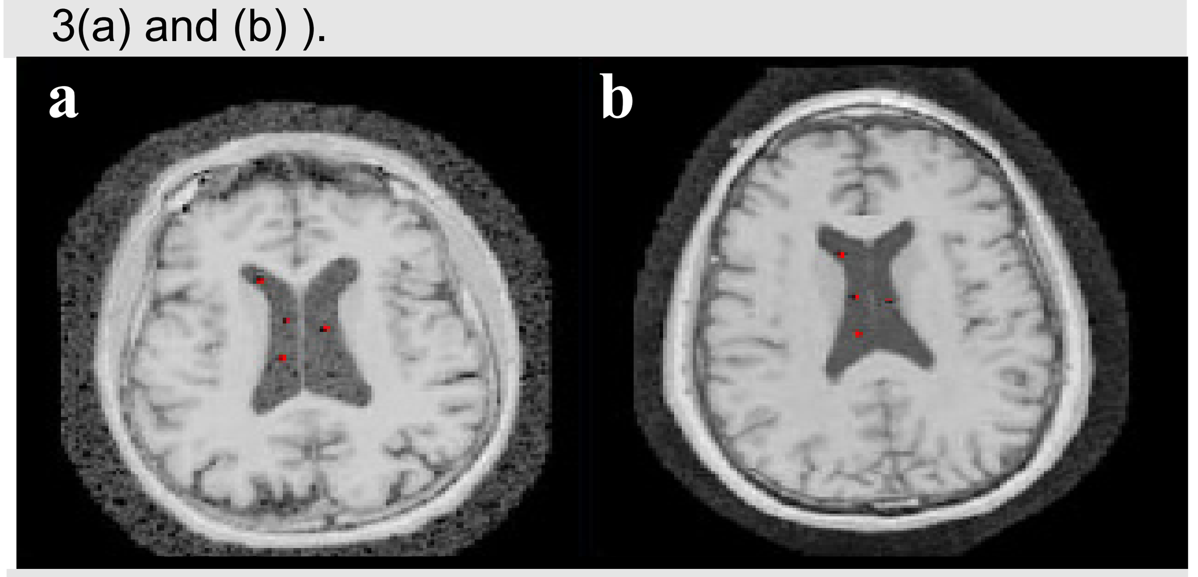
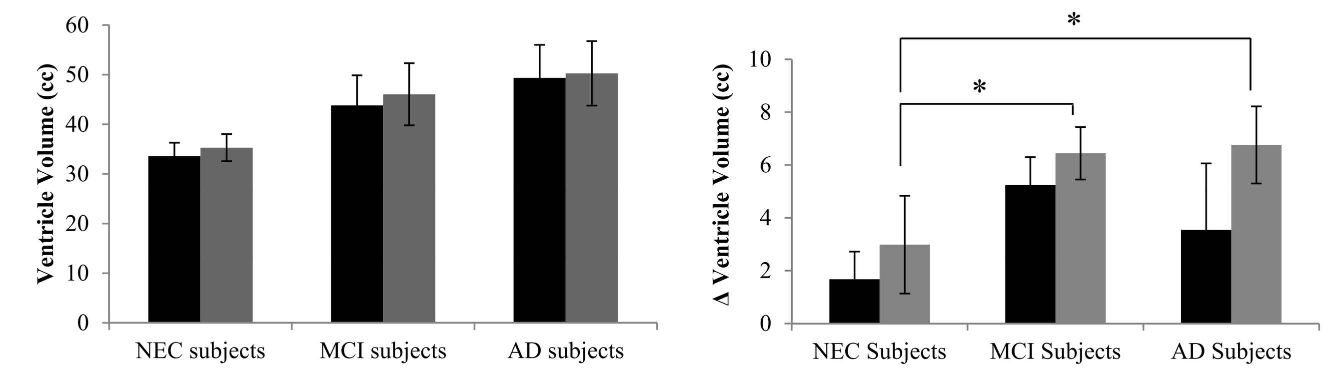


Figure 3: Warping and Seed Mapping. (a) Original Atlas with 4 seeds, (b) Original Subject with 4 mapped seeds

- The fuzzy connectedness segmentation is shown in Figure 4 below for a subject with AD at baseline (left) and 24 months (right) showing an increase of 2 cc.

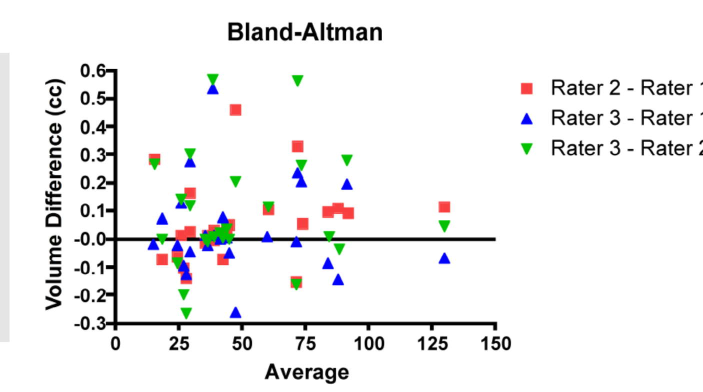
Figure 4: Ventricle segmentation of a subject with Alzheimer disease at baseline (left) and at 24 months (right).

Results



- Left panel: average baseline volume (cm^3) comparison of Fuzzy segmentation (left) vs combining Fuzzy and EM segmentation (right) (25 NEC, 19 MCI, 24 AD).
- Right panel: difference in volume (cm^3) between Baseline and 24 months for Fuzzy (left) and combined Fuzzy and EM (right).
- Significant volume increase was detected over 24 months in MCI (* $p < 0.001$) and AD subjects (* $p < 0.001$), with a significant difference between MCI/NEC, and AD/NEC.

- Inter rater reliability compared in AD baseline images (3 raters). Intra Class correlation was 1.0.



Conclusions

- Deformable registration was successfully used to map seed points.
- A novel texture based fuzzy connectedness algorithm was implemented that uses mapped seeds and works well on capturing the ventricle body.
- A shape based refinement was implemented using expectation-maximization that works well on capturing horn details.
- Future enhancements include automated cropping and partial volume correction using a mesh and mixture models.

References

[1] Illustration of ventricles from "The Human Body book" by Steve Parker, London: Dorling Kindersley, 2007.
[2] S. M. Nestor, et al., Brain **131**: 2443-2454, 2008.
[3] V. S. Fonov, et al., e-poster 4255 at Joint Annual Meeting ISMRM – ESMRMB 2010.
[4] P. K. Saha, et al., Computer Vision and Image Understanding, **83**(3): 275-295, 2001.
[5] K. Pohl, et al., IEEE Transactions on Medical Imaging, 26 (9):1201-1212, 2007.
[6] T. Vercauteren, et al., The Insight Journal 2007 MICCAI Open Science Workshop.
[7] T. Vercauteren, et al., In Proceedings of the 10th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'07), volume 4792 of Lecture Notes in Computer Science, pages 319-326, Brisbane, Australia, October 2007, Springer-Verlag.
[8] J-P. Thirion, Medical Image Analysis, 2(3):243-260, 1998.
[9] L. Ibanez, et al. The ITK Software Guide, Kitware Inc., 2005.
[10] Slicer is an open-source program at http://www.slicer.org
[11] A.F. Khan, et al., Journal of Magnetic Resonance Imaging, 2012 Mar. 7. doi: 10.1002/jmri.23612.

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