Intraoperative Registration of Pathology for Adjuvant Postoperative Radiotherapy

Project 4. Seminar Presentation

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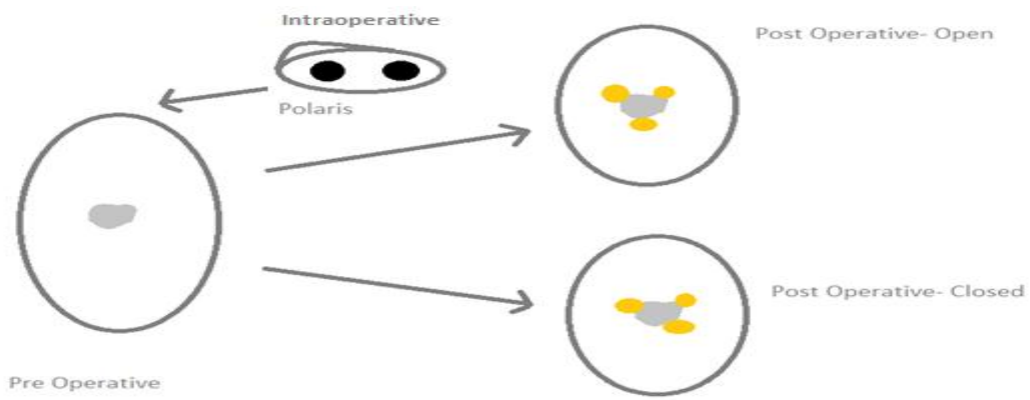
Project Overview

- Problem: Radiation oncologists over-estimate region for post-operative radiotherapy
- Need: A way to track and analyze tissue deformation after tumor excision
- Solution: Intra-operatively add marks around pathology to pre-operative CT; **register pre-operative CT to post-operative CT**



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Paper of Interest

B. B. Avants, C. L. Epstein, M. Grossman, and J. C. Gee,

“Symmetric Diffeomorphic Image Registration with Cross-Correlation: Evaluating Automated Labeling of Elderly and Neurodegerative Brain,”

Medical Image Analysis, Vol. 12, No. 1, pp.26-41, 2008.

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Definitions 1

- *Diffeomorphism* – 1) invertible function, 2) maps one manifold to another, 3) is smooth and has a smooth inverse
- *Manifold* – a topological space; resembles Euclidean space near each point
- *Cross-correlation* – measure of the similarity of two waveforms as a function of a time-lag that is applied to one of the waveforms
- *Euler-Lagrange equations* – for finding stationary solutions/optimizations
- *Geodesic* – shortest path between elements in a space

Definitions 2

- *Dice statistic* – overlap ratio; measures difference in size and location between two segmentations
- *Pearson correlation* – measure of linear correlation (dependence) between two variables
- *Gradient descent* – optimization algorithm to find min by taking steps proportional to negative gradient of function at current point
- *FTD* – frontotemporal dementia, a neurodegenerative disorder
- *Sulcus* – depression in the surface of the brain

Introduction

- Purpose: Propose a new deformable registration method; compare to other methods using brain MRI data
- Novel symmetric image normalization (SyN) method
- Goals: Maximize cross correlation within space of diffeomorphic maps, provide necessary Euler-Lagrange equations
- Compare SyN to elastic method and ITK (Insight ToolKit) implementation of Thirion's Demons method

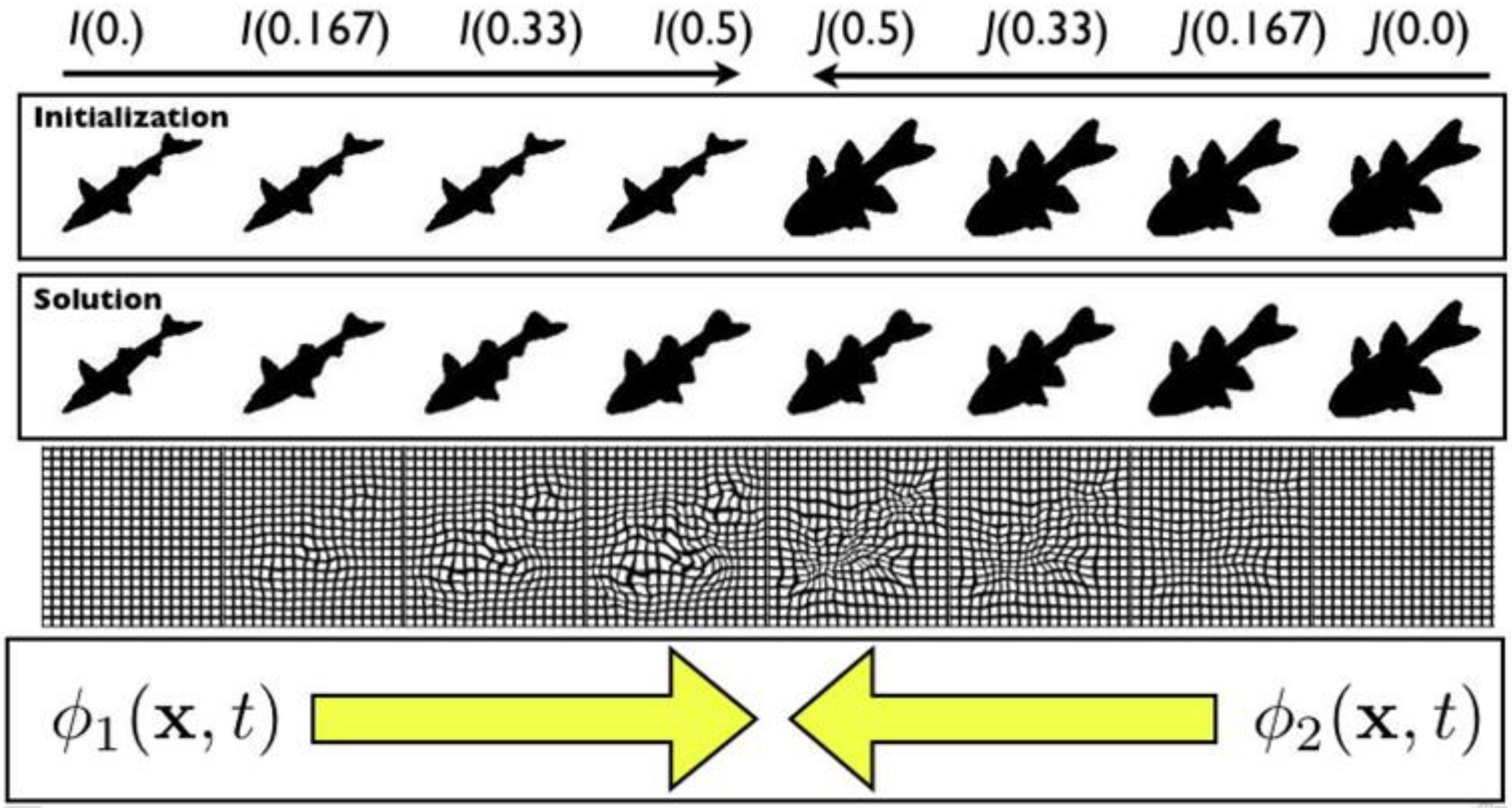
Registration Methods: Demons

- Uses an approximate elastic regularizer to solve an optical flow problem
- One image is “fixed” and the other “moves” by bringing its level sets into correspondence with the fixed image
- Agreement between Demons labeling and manual labeling of images has been shown[1]

Registration Methods: Symmetric Diffeomorphisms

- Constraints: Diff_0 with homeogenous BC's; symmetric; invertible
- Advantages they afford: genuine symmetry; same path; sub-pixel accurate invertible transformations in discrete domain
- Assumptions: **x** indicates identity position in image I and **z** indexes identity position of same anatomy in image J; diffeomorphism maps homologous anatomy

Registration Methods: Symmetric Diffeomorphisms



Source: Avants et al.

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Registration Methods: Symmetric Diffeomorphisms

- Obtaining deformation grids:

$$\phi(\mathbf{x},1)=\phi(\mathbf{x},0)+\int_0^1 v(\phi(\mathbf{x},t),t)dt$$

$$D(\phi(\mathbf{x},0),\phi(\mathbf{x},1))=\int_0^1 \|v(\mathbf{x},t)\|_L dt$$

- Relationship between evolutions along diffeomorphism:

$$\begin{aligned} \phi_1(\mathbf{x},1)I&=J,\\ \phi_2^{-1}(\phi_1(\mathbf{x},t),1-t)I&=J,\\ \phi_2(\phi_2^{-1}(\phi_1(\mathbf{x},t),1-t),1-t)I&=\phi_2(\mathbf{z},(1-t)J,\\ \phi_1(\mathbf{x},t)I&=\phi_2(\mathbf{z},1-t)J, \end{aligned}$$

Registration Methods: Symmetric Diffeomorphisms

- From last slide, similarity term:

$$|\varphi_1(\boldsymbol{x}, t)I - \varphi_2(\mathbf{z}, 1-t)J|^2$$

- Optimization problem:

$$E_{sym}(I,J)=\inf_{\phi_1}\ \inf_{\phi_2}\ \int_{t=0}^{0.5}\left\{\left\|v_1(\mathbf{x},t)\right\|_L^2+\left\|v_2(\mathbf{x},t)\ \right\|_L^2\right\}dt+$$

$$\int_\Omega\left|I(\phi_1(0.5)) - J(\phi_2(0.5))\right|^2 d\Omega.$$

Subject to each $\phi_i \in \mathit{Diff}_0$ the solution of:

$$d\phi_i(\mathbf{x},t)/dt=v_i(\phi_i(\mathbf{x},t),t) \text{ with}$$

$$\phi_i(\mathbf{x},0)=\mathbf{Id} \text{ and } \phi_i^{-1}(\phi_i)=\mathbf{Id},\phi_i(\phi_i^{-1})=\mathbf{Id}.$$

Registration Methods: Cross Correlation w. SyN

- Going further – using symmetric diffeomorphism to find spatiotemporal mapping that maximizes cross correlation
- Elastic method: similarities and differences
- Cross correlation (CC): adaptive to intensity; simple inputs; robust to unpredictable illumination, reflectance
- CC term:

$$CC(\bar{I},\bar{J},\mathbf{x}) = \frac{<\bar{I},\bar{J}>^2}{<\bar{I}><\bar{J}>} = A^2/BC,$$

Registration Methods: Cross Correlation w. SyN

- Optimization problem:

$$E_{CC}(\bar{I},\bar{J}) = \inf_{\phi_1} \inf_{\phi_2} \int_{t=0}^{\frac{1}{2}} \left\{ \| v_1(\mathbf{x},t) \|_L^2 + \| v_2(\mathbf{x},t) \|_L^2 \right\} dt + \int_{\Omega} CC(\bar{I},\bar{J},\mathbf{x}) d\Omega.$$

Subject to each $\phi_i \in Diff_0$ the solution of:

$$d\phi_i(\mathbf{x},t)/dt = v_i(\phi_i(x,t),t) \text{ with}$$

$$\phi_i(\mathbf{x},0) = \mathbf{Id} \text{ and } \phi_i^{-1}(\phi_i) = \mathbf{Id}, \phi_i(\phi_i^{-1}) = \mathbf{Id}.$$

Registration Methods: Cross Correlation w. SyN

- Euler-Lagrange Equations:

$$\nabla_{\phi_1(\mathbf{x},0.5)} E_{CC}(\mathbf{x}), = 2Lv_1(\mathbf{x},0.5) + \frac{2A}{BC}(\bar{J}(\mathbf{x}) - \frac{A}{B}\bar{I}(\mathbf{x}))\ |D\phi_1\ |\nabla \bar{I}(\mathbf{x}),$$

$$\nabla_{\phi_2(\mathbf{x},0.5)} E_{CC}(\mathbf{x}), = 2Lv_2(\mathbf{x},0.5) + \frac{2A}{BC}(\bar{I}(\mathbf{x}) - \frac{A}{C}\bar{J}(\mathbf{x}))\ |D\phi_2\ |\nabla \bar{J}(\mathbf{x}).$$

- Algorithm 1: Allows rapid computation of E.L. equations

1. Deform *I* by $\varphi_1(0.5)$ and *J* by $\varphi_2(0.5)$.
2. Calculate $\bar{I}$ and $\bar{J}$ from the result of step (1).
3. Calculate and store images representing *A*, *B* and *C*.

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Registration Methods: Cross Correlation w. SyN

- LPF method used to check that spatiotemporal maps satisfy ODE and invertibility constraints
- Algorithm 2:

1. **while** $||\psi^{-1}(\varphi(\mathbf{x})) - \mathbf{x}||_\infty > \varepsilon^2 r$ **do**
2. Compute $\boldsymbol{v}^{-1}(\mathbf{x}) = \psi^{-1}(\varphi(\mathbf{x})) - \mathbf{x}$.
3. Find scalar γ such that $||\boldsymbol{v}^{-1}||_\infty = 0.5r$.
4. Integrate ψ^{-1} s.t. $\psi^{-1}(\tilde{\mathbf{y}}, t)+ = \gamma\, \boldsymbol{v}^{-1}(\psi^{-1}(\tilde{\mathbf{y}}, t))$.
5. **end while**

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Registration Methods: Cross Correlation w. SyN

- Algorithm 3: Overview of SyN method with CC

1. Initialize $\varphi_1 = \mathbf{Id} = \varphi_1{}^{-1}$ and $\varphi_2 = \mathbf{Id} = \varphi_2{}^{-1}$.
2. Repeat the following steps until convergence:
3. Compute the CC as described in Algorithm 1.
4. Compute each $\boldsymbol{v}_i$ by smoothing the result of step (3) in this table.
5. Update each φ_i by $\boldsymbol{v}_i$ through the ODE described by $\phi(\mathbf{x},t+\Delta t) \leftarrow \phi(\mathbf{x},t)+\Delta t\ v(\phi(\mathbf{x},t),t)$.
6. Use Algorithm 2 to get the inverses of the φ_i.
7. Generate the time 1 solutions from $\phi_1(1)=\phi_2^{-1}(\phi_1(\mathbf{x},0.5),0.5)$ and $\phi_1^{-1}(1)=\phi_2(1)=\phi_1^{-1}(\phi_2(\mathbf{x},0.5),0.5)$

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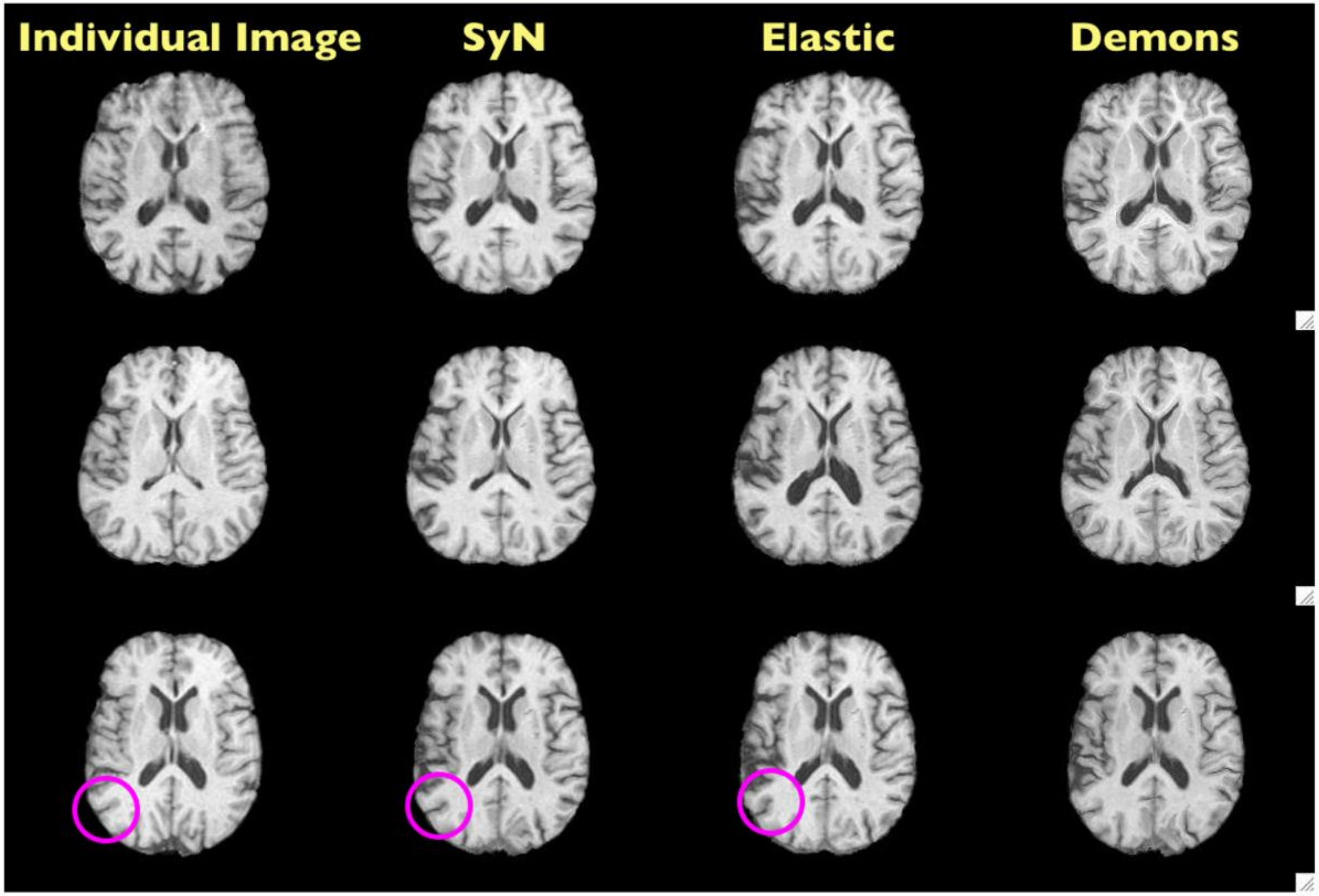
Implementation in ITK and Testing

- Same ITK code base used by Demons; different similarity metric and transformation model
- Test cross correlation effectiveness by evaluating Demons vs Elastic
- Test SyN's transformation model effectiveness by evaluating difference between

Data and Experiments

- 20 T1 MRI images, 10 elderly brains and 10 with FTD
- Template brain with labels of cortex, hippocampus, amygdala, cerebellum
- 60 deformable registrations: 1 per image per method
- Evaluation: Dice overlap ratios between automatic and manual (gold standard) structural segmentations
- Ratio of running times: Demons 1, elastic CC 4.2, SyN 5.5

Results and Discussion



Source: Avants et al.

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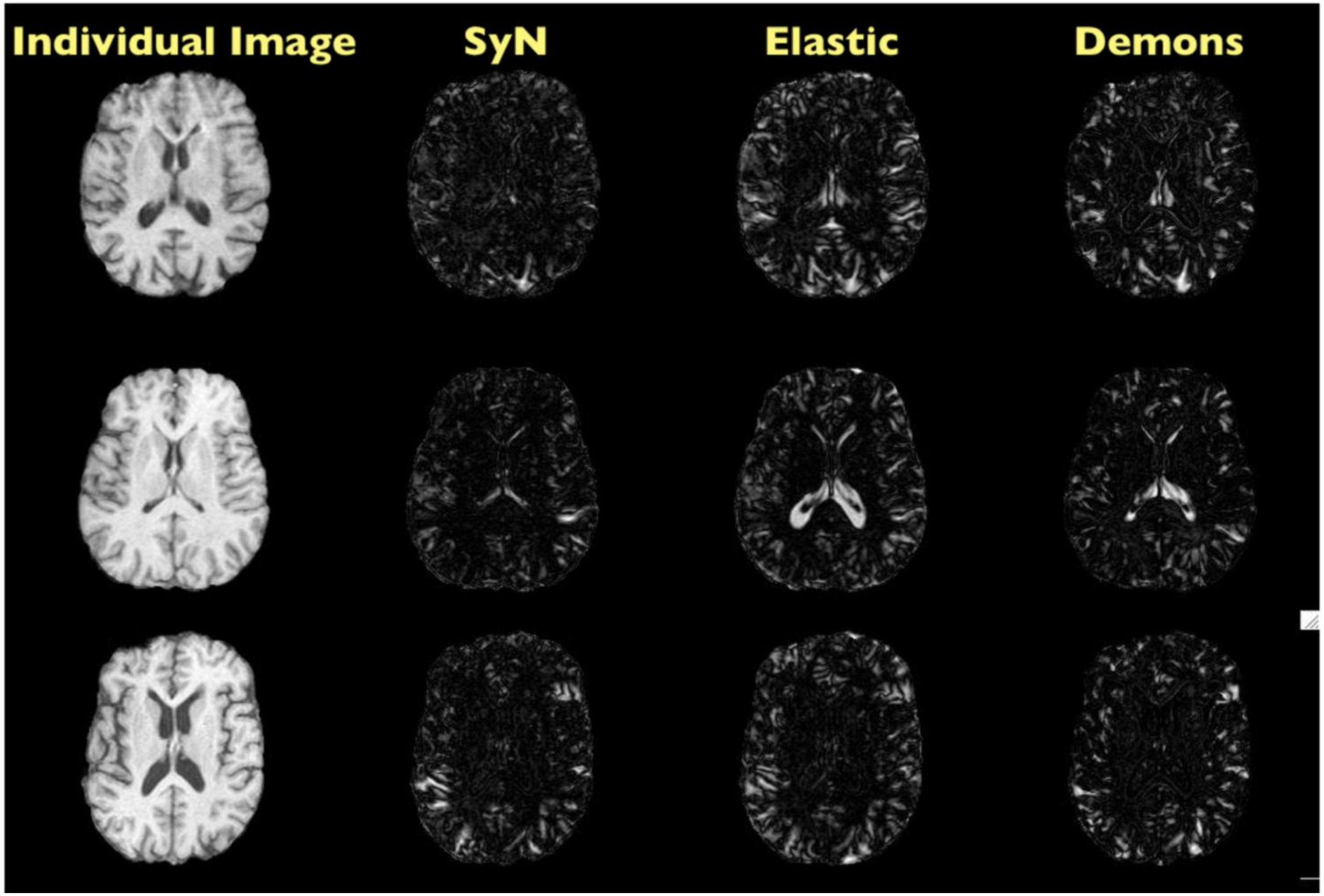
Results and Discussion



Source: Avants et al.

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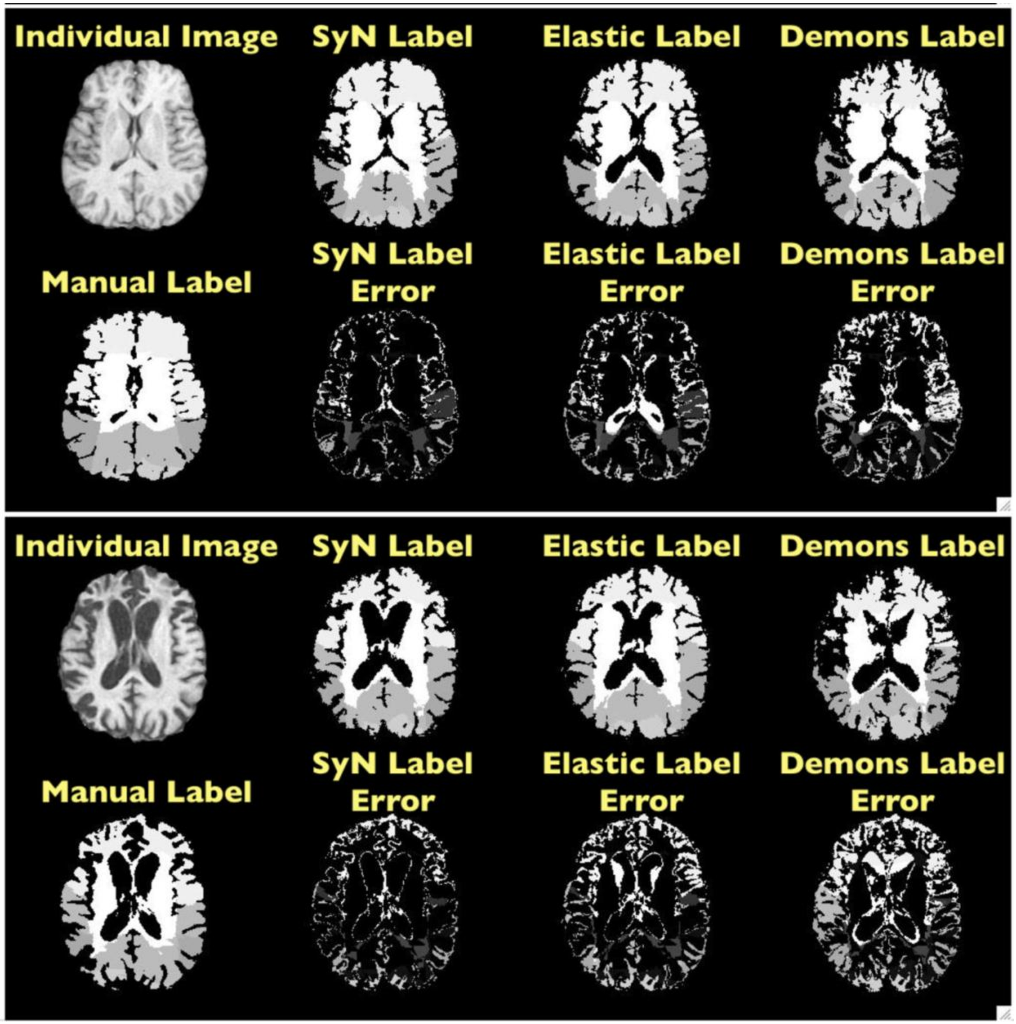
Results and Discussion



Source: Avants et al.

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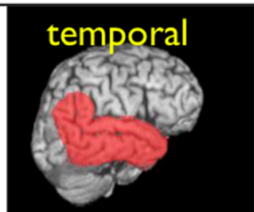
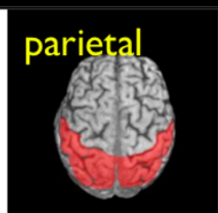
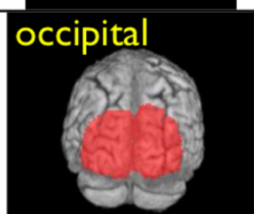
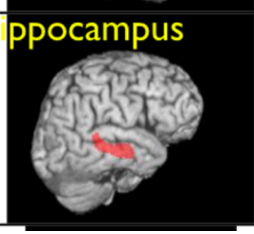
Results and Discussion

Structure	Demons	Elastic XCor > Demons	SyN XCor > Elastic
	Mean+-Sigma: 0.76 +- 0.021	0.81 +- 0.02	0.84 +- 0.019
	Min - Max : [0.69-0.79]	[0.76-0.84]	[0.79-0.87]
	Significance:	p< 0.0001	p< 0.0001
	0.69 +- 0.034	0.74 +- 0.03	0.78 +- 0.027
	[0.62-0.73]	[0.68-0.79]	[0.70-0.83]
	-	p< 0.0001	p< 0.0001
	0.78 +- 0.030	0.79 +- 0.024	0.83 +- 0.022
	[0.72-0.82]	[0.73-0.84]	[0.78-0.87]
	-	p < 0.011	p< 0.0001
	0.62 +- 0.070	0.72 +- 0.036	0.72 +- 0.038
	[0.48-0.73]	[0.65-0.77]	[0.63-0.79]
	-	p< 0.0001	p<0.7

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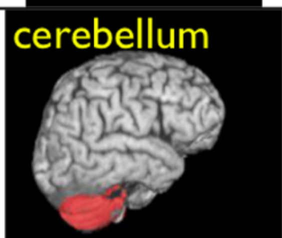
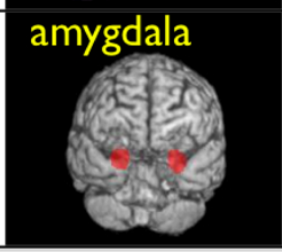
Results and Discussion

Structure	Demons	Elastic XCor > Demons	SyN XCor > Elastic
	0.74 +- 0.026	0.81 +- 0.026	0.85 +- 0.024
	[0.65-0.77]	[0.73-0.84]	[0.79-0.88]
	-	$p< 0.0001$	$p< 0.0001$
	0.89 +- 0.012	0.89 +- 0.011	0.92 +- 0.011
	[0.87-0.92]	[0.88-0.92]	[0.91-0.93]
	-	$p<0.2$	$p< 0.0001$
	0.59 +- 0.053	0.73 +- 0.065	0.74 +- 0.05
	[0.5-0.68]	[0.59-0.81]	[0.63-0.81]
	-	$p<0.0001$	$p<0.24$

Source: Avants et al.

Results and Discussion

- More exact comparison of volume measurements between registration and manual expert (gold standard)
- Sum voxel volumes assigned to each structure
- Only temporal, frontal, and parietal lobes because of differences between elderly and FTD brains

Results and Discussion

- Table 1: Pearson correlations between manual and algorithmic volume measures

Structure	Corr(Man,Syn)	Corr(Man,Elas)	Corr(Man,Demon)
Temporal	0.86	0.69	0.79
Frontal	0.89	0.67	0.71
Parietal	0.71	0.42	0.66

- Table 2: Absolute volume error between manual and algorithmic volume measures

Structure	VolErr(Man,Syn)	VolErr(Man,Elas)	VolErr(Man,Demons)
Temporal	8.4	9.2	8.7
Frontal	11.1	16.1	15.8
Parietal	7.9	9.3	7.9

Results and Discussion

Other results:

- No significant difference between minimum Jacobian of SyN vs Elastic CC
- No significant difference in volumes between FTD and elderly individuals
- Automated methods tend to overestimate volumes
- Though SyN outperforms other methods, still not able to claim accurate reproduction of manual labeling

Criticisms/Application to Project

- Dice statistic threshold is arbitrary
- SyN method not as quick/efficient as authors portray
- Will work well with CT to CT registration
- Maybe fixed post-op image and moving pre-op image more useful
- Volume overestimation better case than underestimation
- Good first step as registration algorithms improve

References

1. Dawant B, Hartmann S, Thirion JP, Maes F, Vandermeulen D, Demaerel P. Automatic 3-D segmentation of internal structures of the head in MR images using a combination of similarity and free-form transformations, part II: methodology and validation on severely atrophied brains. IEEE Trans Med Imaging 1999;18:971–926.

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Dice statistic

$$S(R1,R2)=\frac{2\#(R1\cap R2)}{\#(R1)+\#(R2)},$$