Topologically Constrained Segmentation of Brain Images with Multiple Sclerosis Lesions

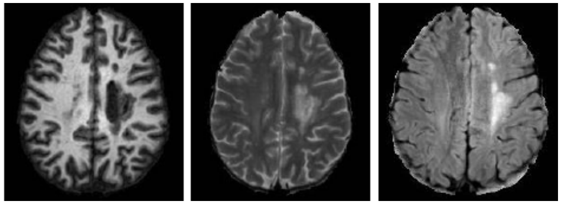
Navid

Navid Shiee[1,2], Pierre-Louis Bazin[1],
Jennifer L. Cuzzocreo[1], Daniel S. Reich[3],
Peter A. Calabresi[3] and Dzung L. Pham[1]

[1]Laboratory for Medical Image Computing
[2]Image Analysis & Communications Laboratory
[3]The Multiple Sclerosis Center
The Johns Hopkins University, Baltimore MD

Multiple Sclerosis (MS)

- A demyelinating disease of the central nervous system
- Commonly leads to inflammatory and atrophic pathology, often causing cognitive impairment
- Primarily expressed as focal lesions in white matter (WM), although can also be found in gray matter (GM)
- Currently does not have a cure
- Role of MR Imaging:
  - Clinical diagnosis
  - Quantitative analysis of MR images makes the measurement and monitoring of lesion load and tissue volumes possible
  - Helpful for patient follow up and evaluation of therapies



Automated MS Lesion Delineation Methods

- Manual delineation of MS lesions :
  - Challenging
  - Time consuming
  - Suffers from inter-rater variability

→ need for automated methods

- Current lesion delineation methods:
  - Modeling Lesions as outliers [Van Leemput et al, 2001][Ait-Ali et al, 2005]
  - Supervised classifiers [Wu et al, 2006][Younes et al 2007]
  - …

Disadvantages: Focus mainly on lesion delineation

If tissue classification :

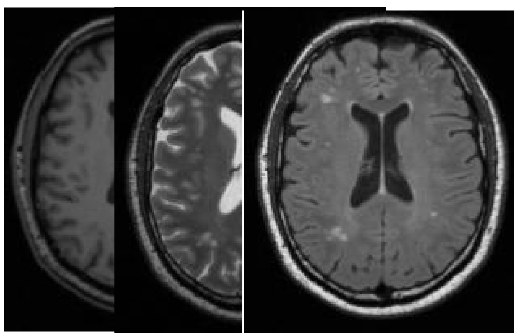
Do not segment sub-cortical structures

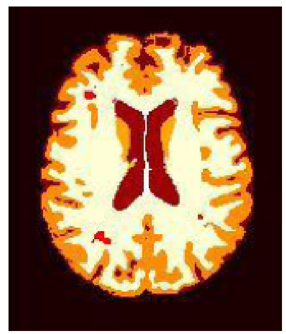
Little use of anatomical knowledge

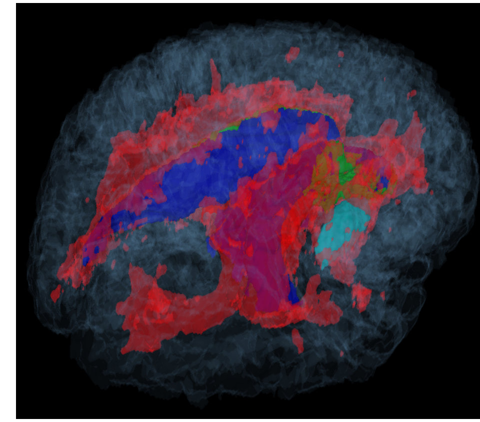
Motivation

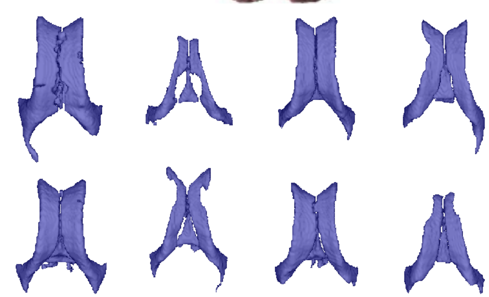
Goal: A method performing:

- MS lesion delineation
- Detailed brain segmentation
- Topologically consistent segmentation









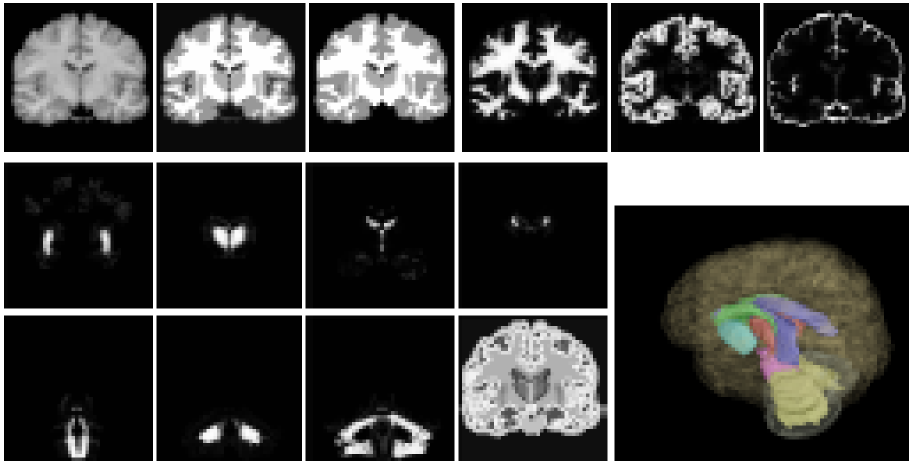
and allowing:

- Cortical surface reconstruction
- Shape analysis
- Diffeomorphic alignment

Statistical and Topological Atlas-based Segmentation in Healthy Brain

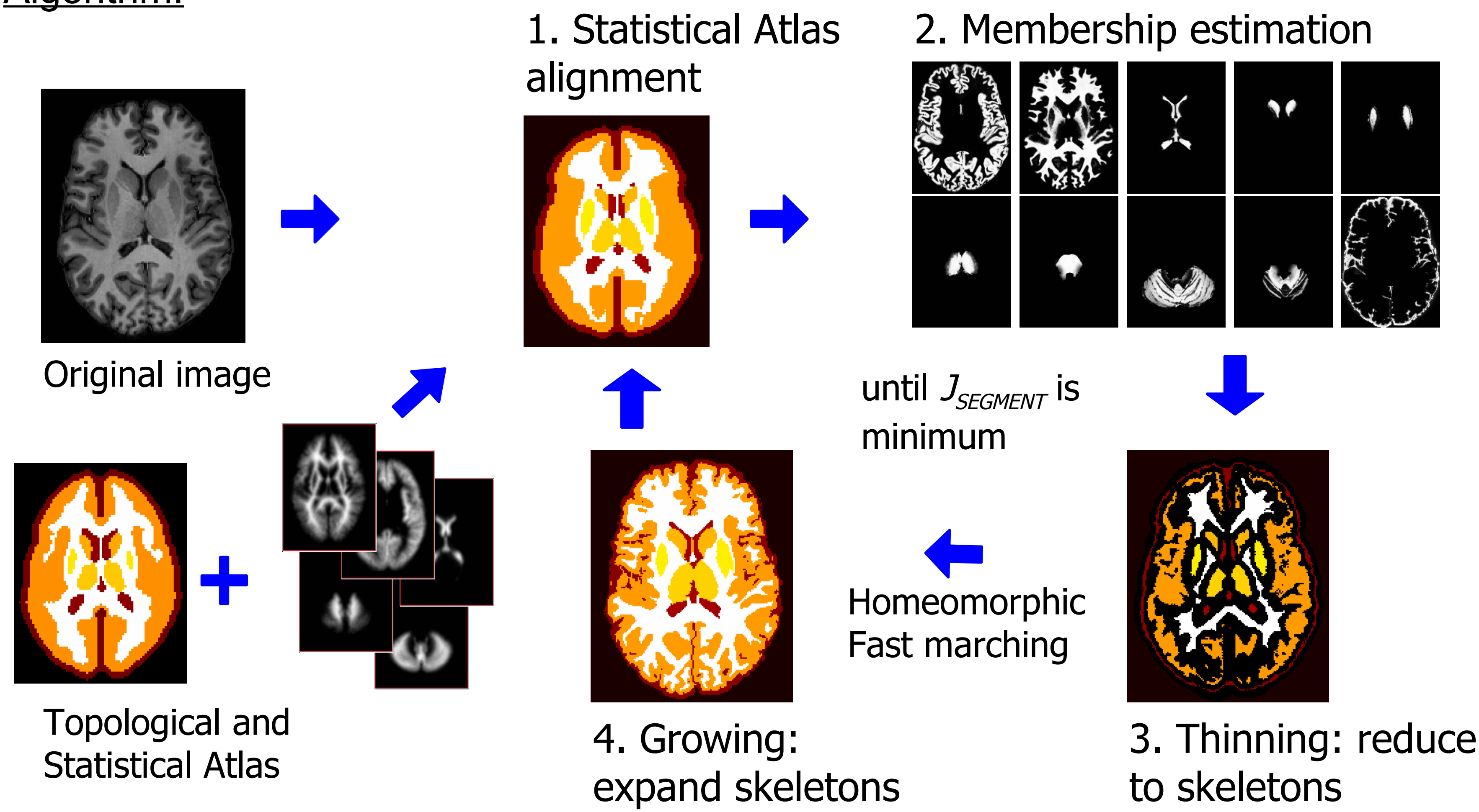
Original method:
[Bazin et al 07]

- Segments the brain into its major structures (cerebral gray and white matter, cerebellar gray and white matter, basal ganglia, ventricles, and brainstem)
- Preserves the brain topology
- Regularizes noise
- Intensity-based technique incorporating information from statistical and topological atlases



Statistical and Topological Atlas-based Segmentation in Healthy Brain

<u>Algorithm:</u>



Statistical and Topological Atlas-based Segmentation in Healthy Brain

Fuzzy Segmentation is obtained by minimizing:

$$J_{SEGMENT} = \sum_{j,k\in C} \frac{1}{r_{jk}} \left(\underbrace{u_{jk}^q \left\| y_j - v_k \right\|^2}_{\textit{Intensity}} + \beta \underbrace{\sum_{l\in N_j, m\in C|_k} u_{jk}^q u_{lm}^q}_{\textit{Smoothing}} + \gamma \underbrace{\sum_{m\in C|_k} w_{km} u_{jk}^q p_{jm}^q}_{\textit{Atlas prior}} \right)$$

Smoothing:
[Pham 01]

$$\sum_{l\in N_j, m\in C|_k} u_{jk}^q u_{lm}^q >> 0 \quad \text{if} \quad \exists m \neq k \,\middle|\, u_{jk} \approx 1, u_{lm} \approx 1$$

Atlas dependency:

$$\sum_{m\in C|_k} w_{km} u_{jk}^q p_{jm}^q >> 0 \quad \text{if} \quad \exists m \neq k \,\middle|\, u_{jk} \approx 1, p_{jm} \approx 1, c_k \approx c_m$$

with $w_{km} = \dfrac{1}{1 + \left\| c_k - c_m \right\|^2 / \delta \left\| c_{\min} - c_{\max} \right\|^2}$

Statistical and Topological Atlas-based Segmentation in Healthy Brain

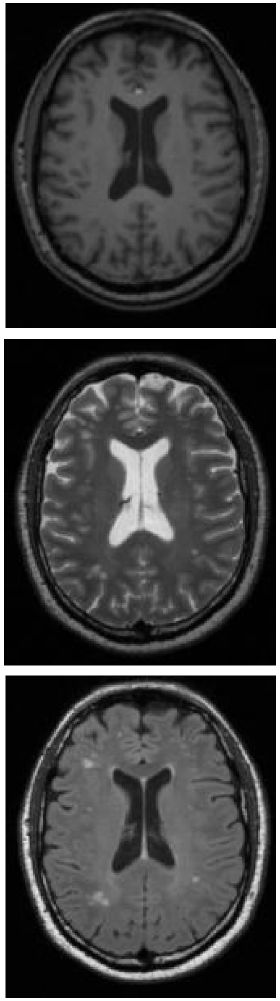
$$J_{SEGMENT} = \sum_{j,k\in C} \boxed{\frac{1}{r_{jk}}} \left(u_{jk}^{q} \left\| y_j - v_k \right\|^2 + \beta \sum_{l\in N_j, m\in C|_k} u_{jk}^{q} u_{lm}^{q} + \gamma \sum_{m\in C|_k} w_{km} u_{jk}^{q} p_{jm}^{q} \right)$$

- r_{jk} is the *relationship function* penalizing against inconsistent membership configurations with the topology atlas

$$r_{jk} = \begin{cases} 1 & for\ j\ in\ k\ or\ a\ structure\ bordering\ k \\ \frac{1}{2} & for\ j\ in\ a\ structure\ bordering\ a\ structure\ adjuacent\ to\ k \\ 0 & otherwise \end{cases}$$

→ Lowers influence of unwanted structures

Application to Multiple Sclerosis

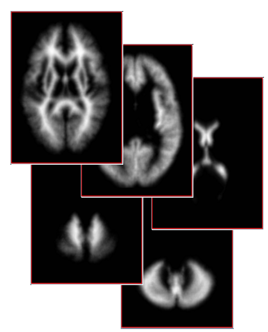


- Multi-channel images:
  Combine multiple contrasts weighted by SNR

$$u_{jk}^{q}\left\|y_j - v_k\right\|^2 \rightarrow u_{jk}^{q}\sum_i \omega_i \left\|y_j^i - v_k^i\right\|^2$$

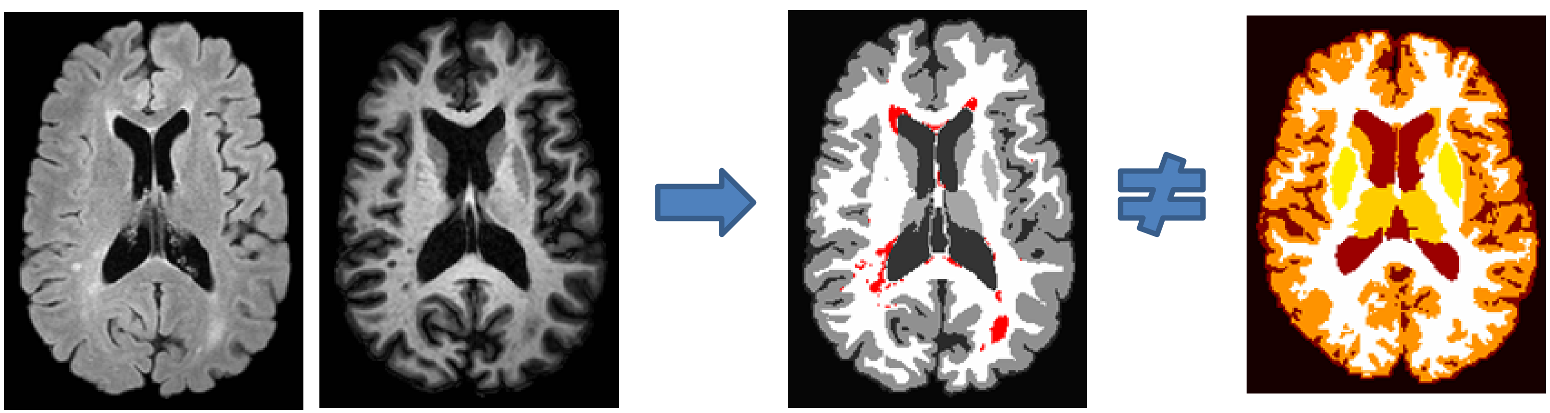
with $\omega_i = \dfrac{\sigma_i^{-2}}{\sum_c \sigma_c^{-2}}$ where $\sigma_i^2 = \dfrac{\sum_{jk} u_{jk}^q \|g_j^i I_j^i - c_k^i\|^2}{\sum_{jk} u_{jk}^q}$

- Lesions:
  Add a lesion class to the atlas

 +  + Lesion prior ?

Effect of Lesions on Topology

- Lesions *can occur anywhere* in WM resulting in:
  - Lesions cannot be modeled topologically
  - A statistical atlas cannot be associated to lesions
  - Arbitrary appearance of lesion in WM change the topology of WM



- But lesions *always occur in WM* which means:

WM + Lesion has the same topology as healthy WM

Lesions in Topology Preserving Framework

Modification needed to adapt the method to lesions:

Lesions are likely where WM is likely

- use the WM statistical atlas for lesion class (set $p_{j,lesion} = p_{j,WM}$)
- set $w_{lesion,WM} = 0$

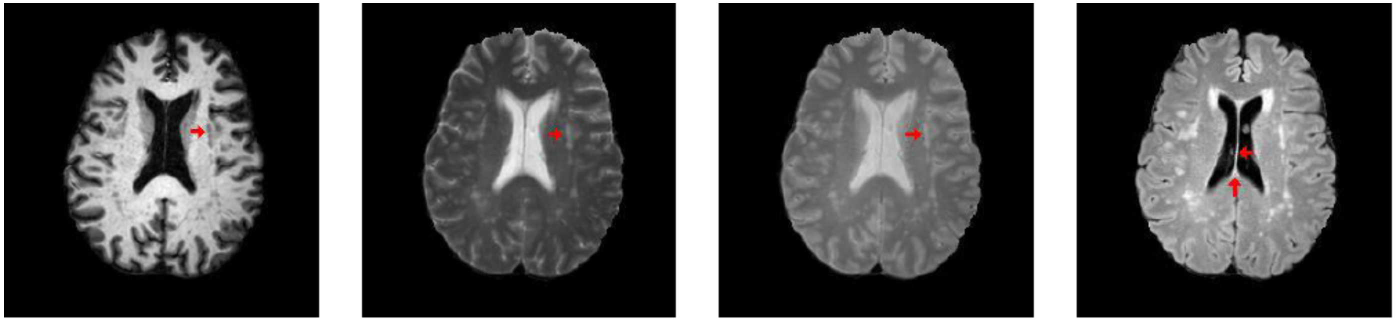
Topology applies to {WM+Lesions}

- In thinning and growing steps use $u_{j,WM} + u_{j,lesion}$ to modulate the fast marching speed function
- After computing hard segmentation, separate lesion and WM based on the membership functions

Stabilization of lesions centroids;

$$c_{lesion}^{new} = (1-\lambda)c_{lesion}^{new} - \lambda\, c_{lesion}^{previous}$$

Intensity and False Positives



T1 T2 PD FLAIR

- Lesions look like GM on T1, like CSF on T2 and PD and like boundary of ventricles on FLAIR
- Intensity-based techniques suffer from large amount of false positives
- Boundary of ventricles, GM and sub-cortical structures with WM are common area of false positives
- Using the computed hard segmentation, the *relationship function* for lesion can be modified

Reducing False Positives

- Lesions are less likely near to Ventricle and GM (cortical and sub-cortical):

$$\tilde{r}_{j,lesion} = \begin{cases} (\frac{d^2_{j,VEN}}{d^2_{max,VEN}})r_{j,wm} & d_{j,VEN} \leq d_{max,VEN}, \\ (\frac{d^2_{j,GM}}{d^2_{max,GM}})r_{j,wm} & d_{j,GM} \leq d_{max,GM} \text{ and } d_{j,VEN} > d_{max,VEN}, \\ r_{j,wm} & \text{otherwise.} \end{cases}$$

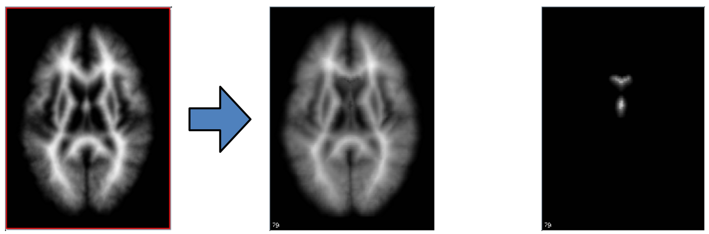
- GM is less likely near to Ventricles:

$$\tilde{r}_{j,gm} = \begin{cases} (\frac{d^2_{j,VEN}}{d^2_{msx,VEN}})r_{j,gm} & d_{j,VEN} \leq d_{max,VEN}, \\ r_{j,gm} & \text{otherwise.} \end{cases}$$

with $d_{j,class}$ the distance from *j* to *class*

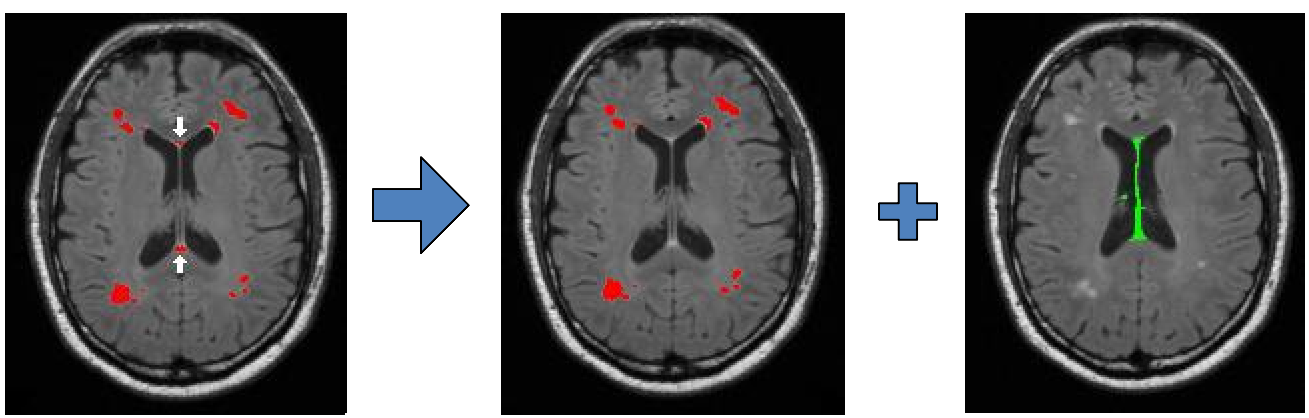
Reducing False Positives

- Lesions are less likely in inter-ventricular region:

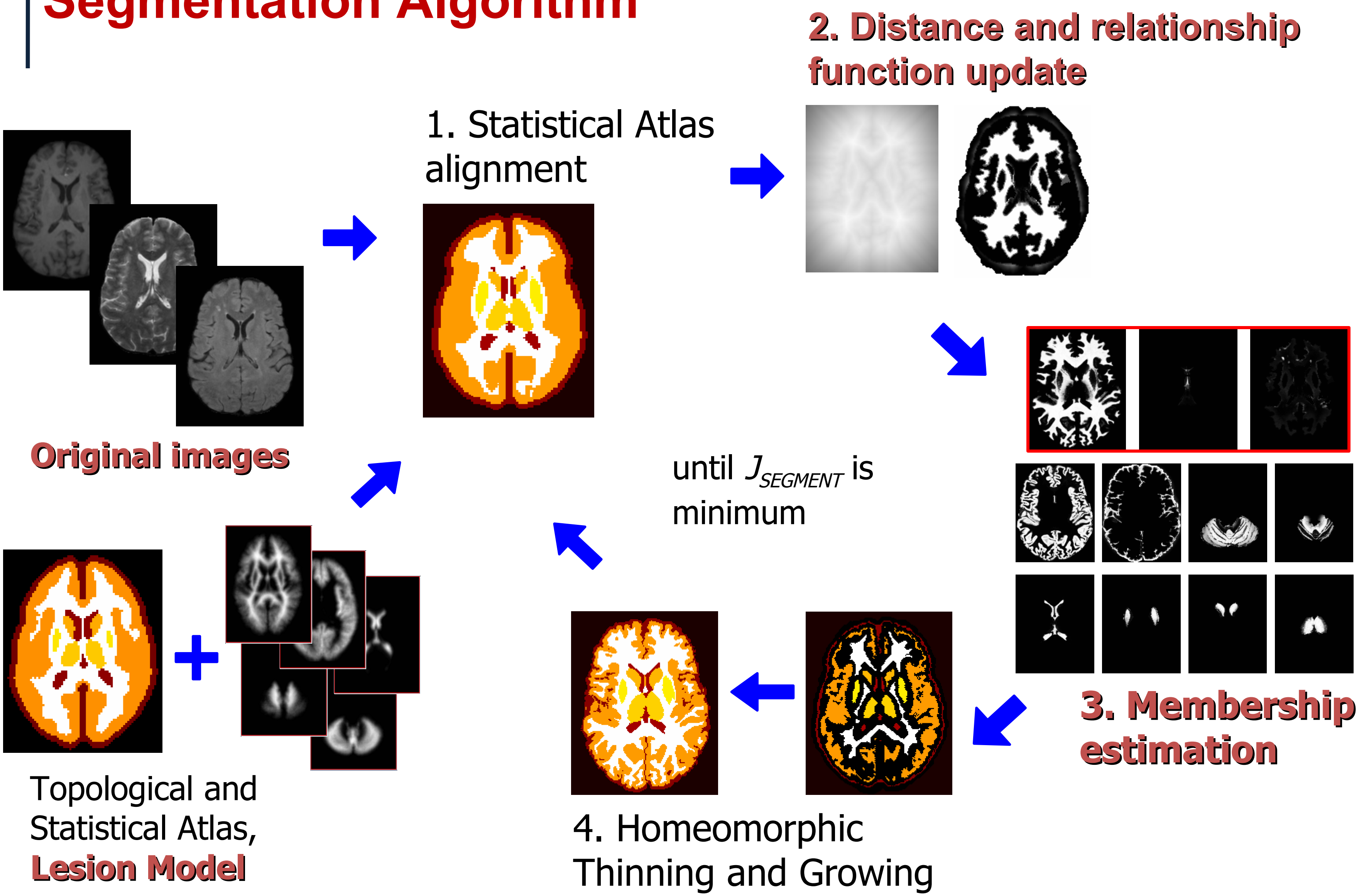


Inter-ventricular WM class

$$\tilde{r}_{j,lesion} = \begin{cases} \left(\dfrac{d^2_{j,WM_{int}}}{d^2_{max,WM_{int}}}\right)\tilde{r}_{j,lesion} & d_{j,WM_{int}} \leq d_{max,WM_{int}}, \\ \tilde{r}_{j,lesion} & \text{otherwise.} \end{cases}$$



Segmentation Algorithm



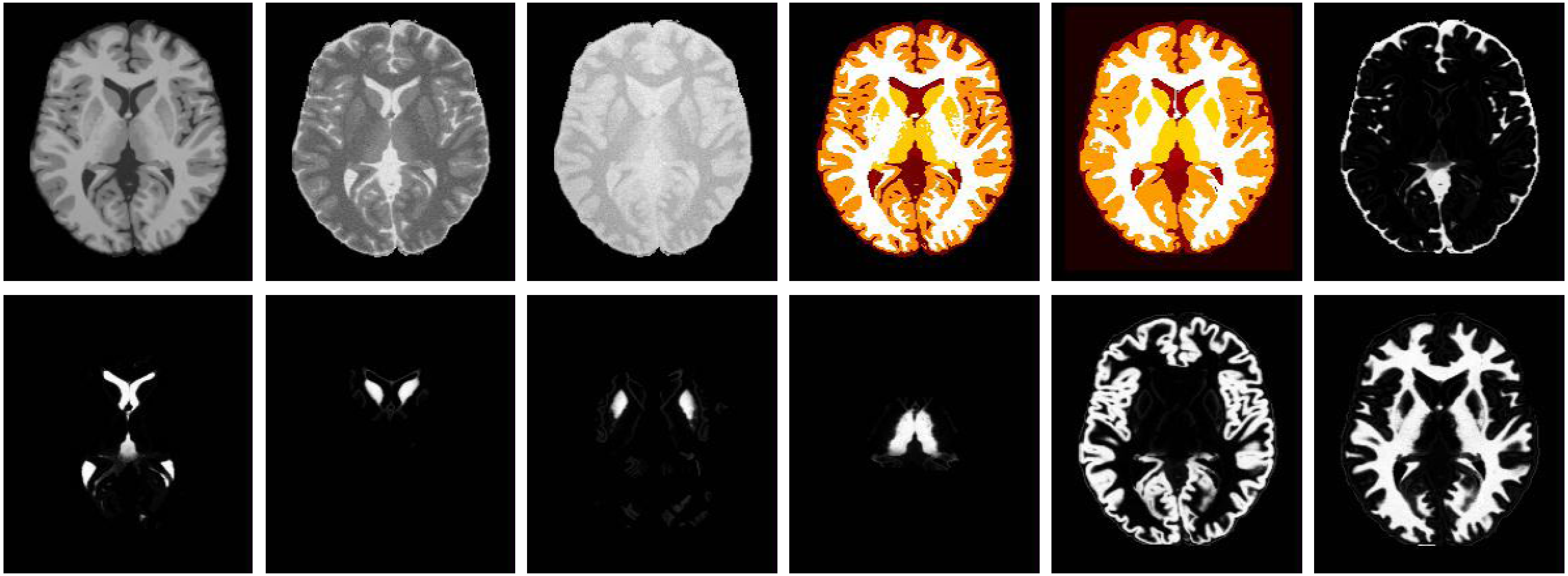
Validation on Brainweb MS phantom

- T1, T2 and PD images (no FLAIR)
- Simulated images with or without lesions

Without lesions: only $6.37 \times 10^{-4}\%$ voxels classified as lesion

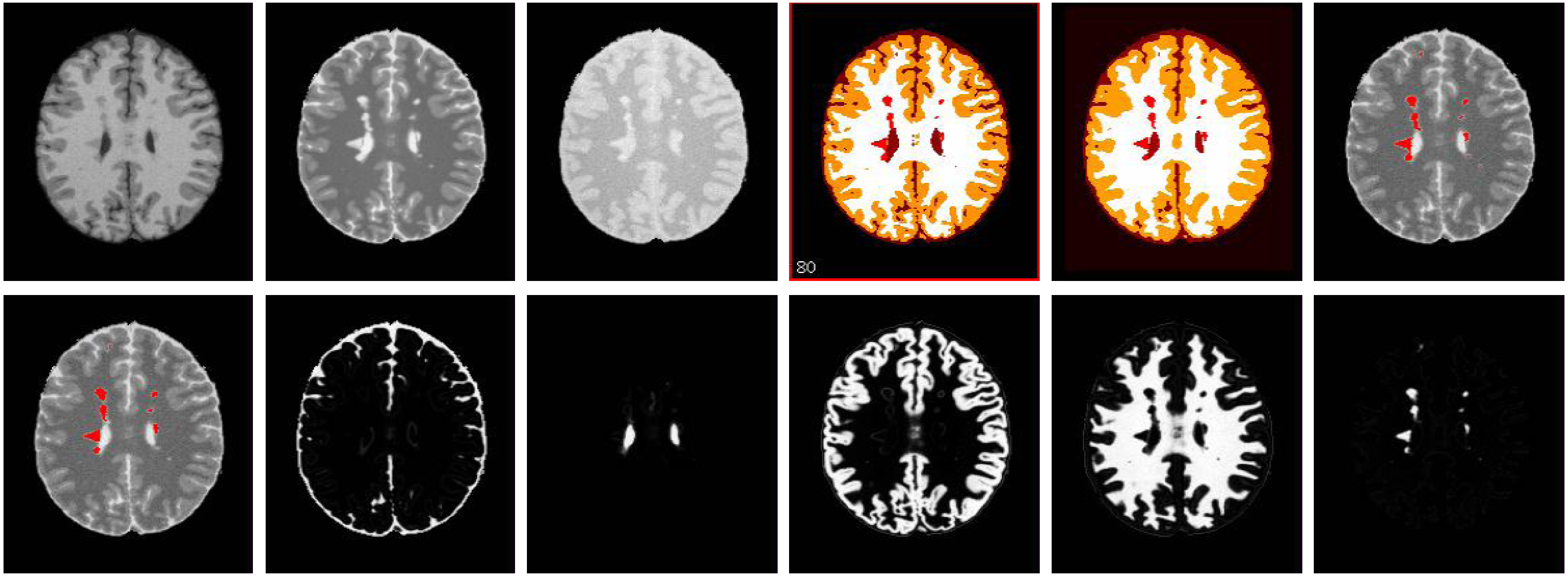
Noise	Tissues			Structures						
	WM	GM	CSF	WM-CR	GM-CR	CBS,	GM-CB	Sub-cortical	Vent	Lesion
1%	0.916	0.903	0.901	0.929	0.901	0.728	0.869	0.777	0.873	0.717
3%	0.912	0.900	0.900	0.925	0.899	0.720	0.871	0.774	0.879	0.720
5%	0.901	0.894	0.896	0.920	0.890	0.708	0.849	0.751	0.882	0.700
7%	0.897	0.885	0.893	0.901	0.882	0.696	0.842	0.726	0.884	0.658
9%	0.898	0.882	0.851	0.911	0.884	0.698	0.857	0.726	0.885	0.591
Mean	0.905	0.893	0.888	0.917	0.891	0.710	0.858	0.751	0.881	0.677
St.Dev	0.009	0.009	0.021	0.011	0.009	0.014	0.012	0.025	0.005	0.054
Healthy Brain	0.919	0.906	0.903	0.932	0.902	0.723	0.865	0.789	0.855	-

Validation on Brainweb MS phantom (slice with no lesion)



Example segmentation of the phantom with 3% noise

Validation on Brainweb MS phantom (slice with lesions)



Example segmentation of the phantom with 3% noise

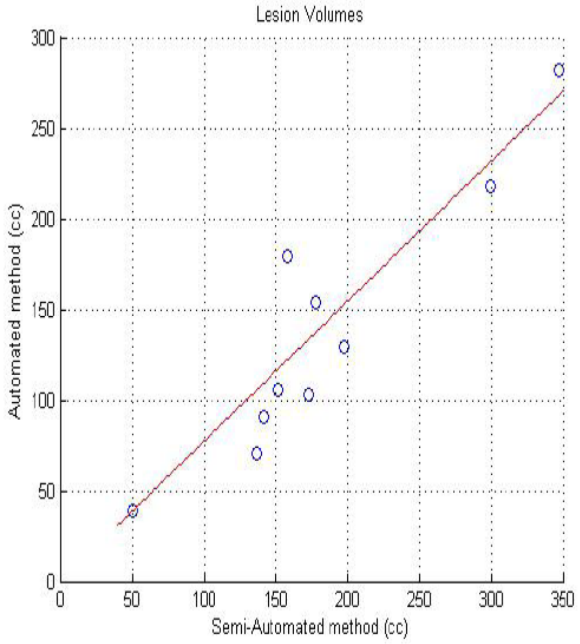
Validation on Real Images

- Dataset of 10 real MR images acquired from MS patients
- T1, T2 and FLAIR with slice thickness of 2.2mm

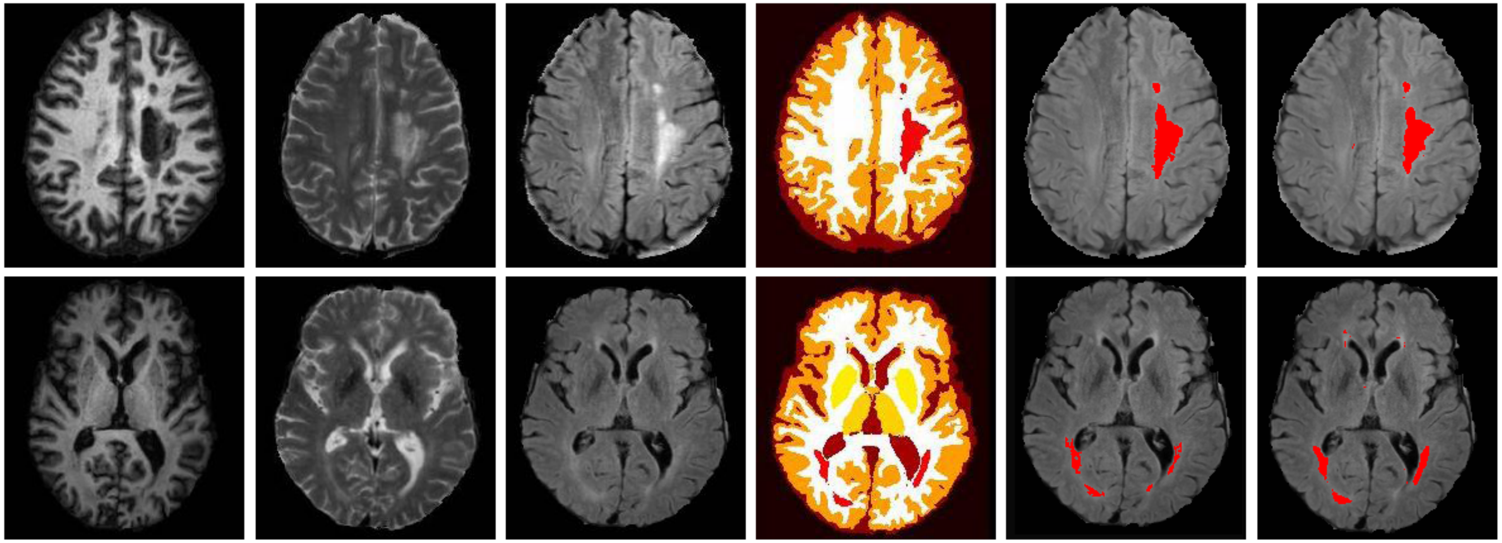
- Ground Truth from an expert-guided thresholding on FLAIR
- A subset of images was manually delineated by another human expert

- Pierson Correlation Coefficient (R^2) and DSC has been computed

	R^2	DSC
Auto vs GT	0.772	0.506
Inter-rater	0.847	0.531

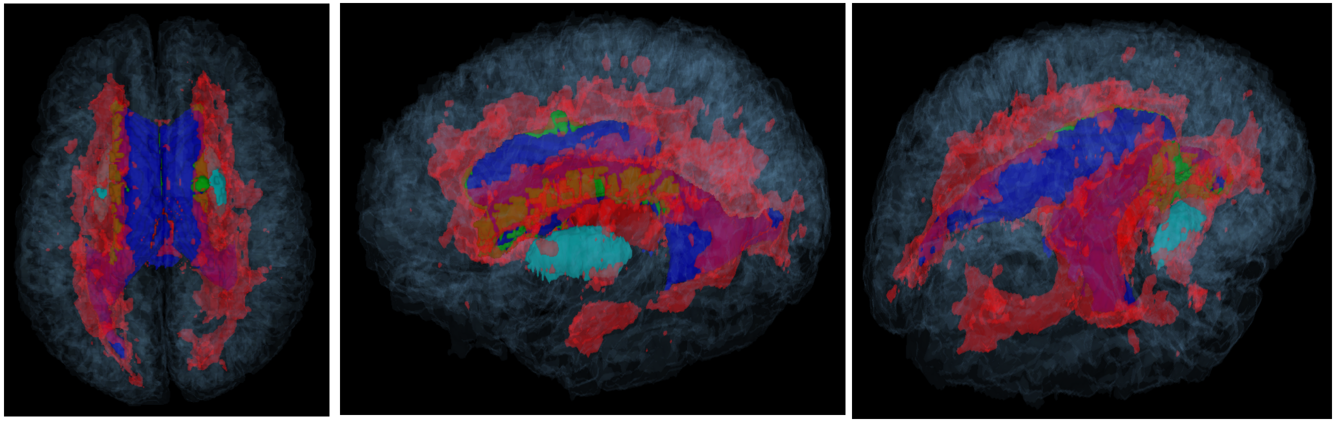


Validation on Real Images

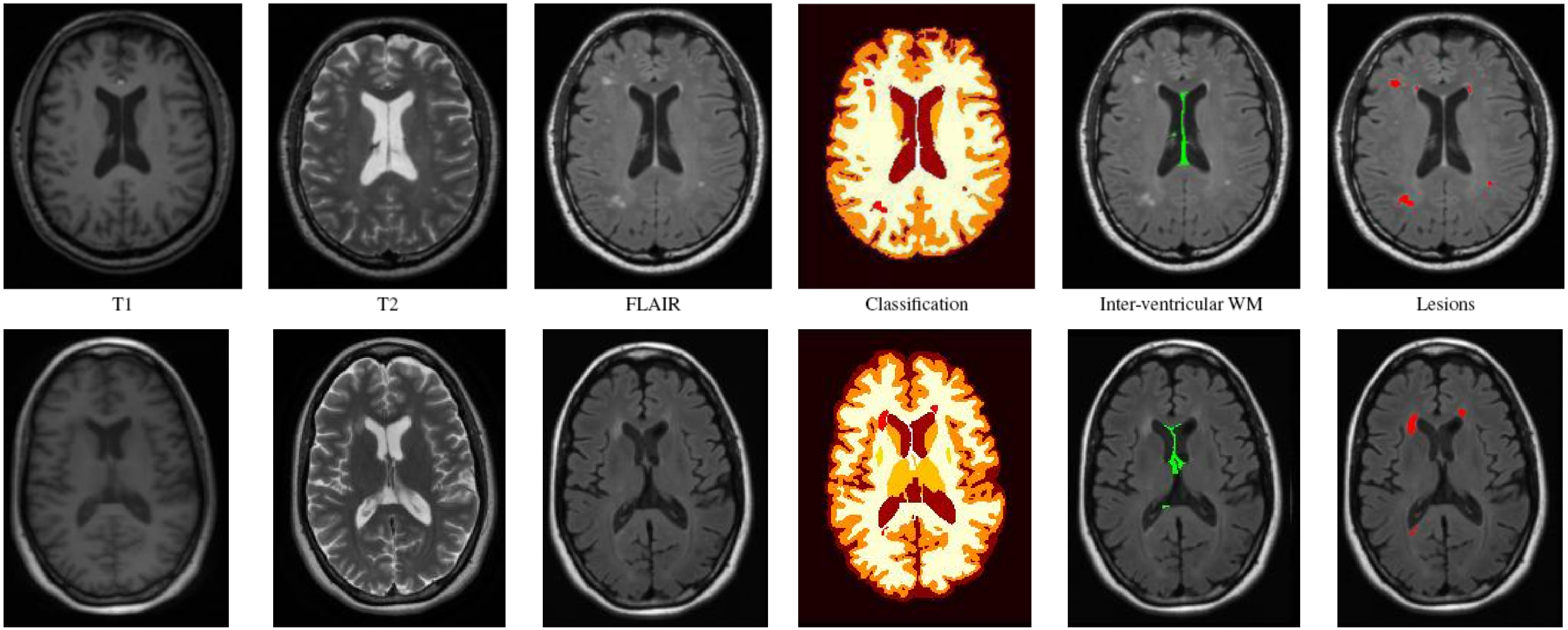


T1 T2 FLAIR Hard Classsification Ground Truth Automated

3D surface renderings showing the relations between structures and lesions



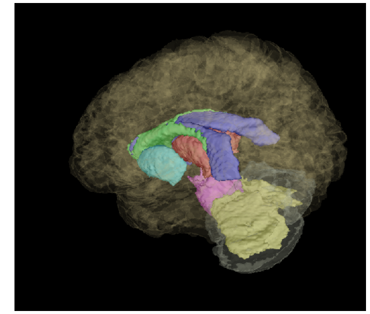
Segmentation Grand Challenge



Third place!

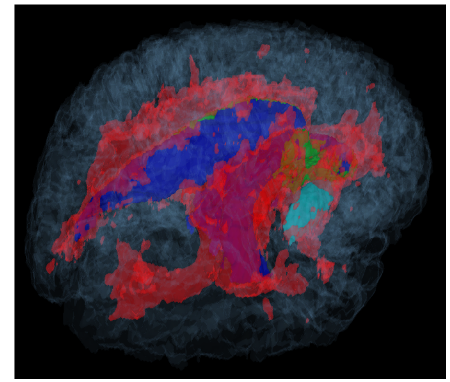
Ground Truth	UNC Rater								CHB Rater									STAPLE		
All Dataset	Volume Diff. [%]	Score	Avg. Dist. [mm]	Score	True Pos. [%]	Score	False Pos. [%]	Score	Volume Diff. [%]	Score	Avg. Dist. [mm]	Score	True Pos. [%]	Score	False Pos. [%]	Score	Total	Specificity	Sensitivity	PPV
All Average	69.6	90	7.1	85	49.8	80	74.3	64	84.2	88	7.9	84	55.4	83	68.8	68	80	0.9824	0.4249	0.6102
All UNC	61.8	91	7.9	84	46.4	78	67.4	69	121.3	82	11.6	76	59.9	85	68.5	68	79	0.9824	0.4655	0.6000
All CHB	75.3	89	6.5	87	52.2	81	79.2	61	57.6	92	5.3	89	52.2	81	69.1	68	81	0.9825	0.3958	0.6176

Conclusion



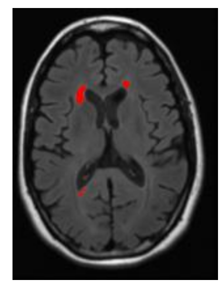
Fully automated WM MS lesion segmentation:

- Anatomy of healthy brain respected



- Main brain regions segmented

- Topology, relationships encode anatomical knowledge about lesions



- Enable use of advanced morphometric techniques for MS population:
    - Volumetric Analysis
    - Cortical Thickness Analysis
    - Diffeomorphic shape Analysis