How a toolkit of diverse MS lesions segmentation methods can support the translation to the clinic

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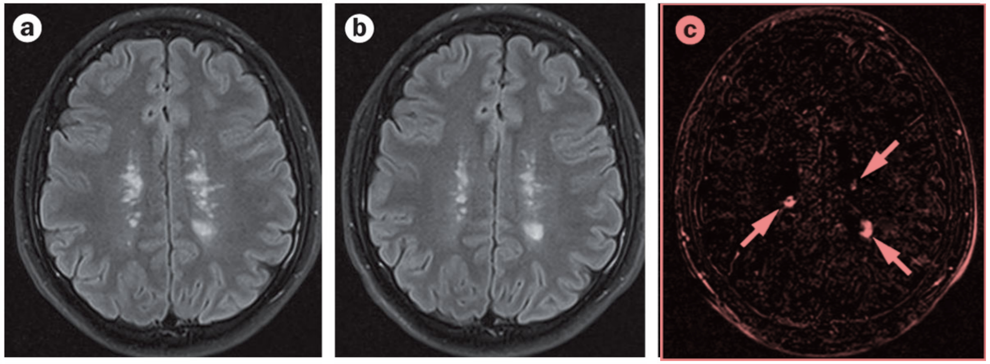
Introduction

- Multiple Sclerosis (MS):
  - Chronic inflammatory-demyelinating CNS disease
  - Lead to acute handicap in young adults (high prevalence in Brittany)
  - Most frequent CNS disease in young adults

- MRI for MS lesion evaluation:
  - clinical diagnosis
  - disease progression
  - treatment monitoring



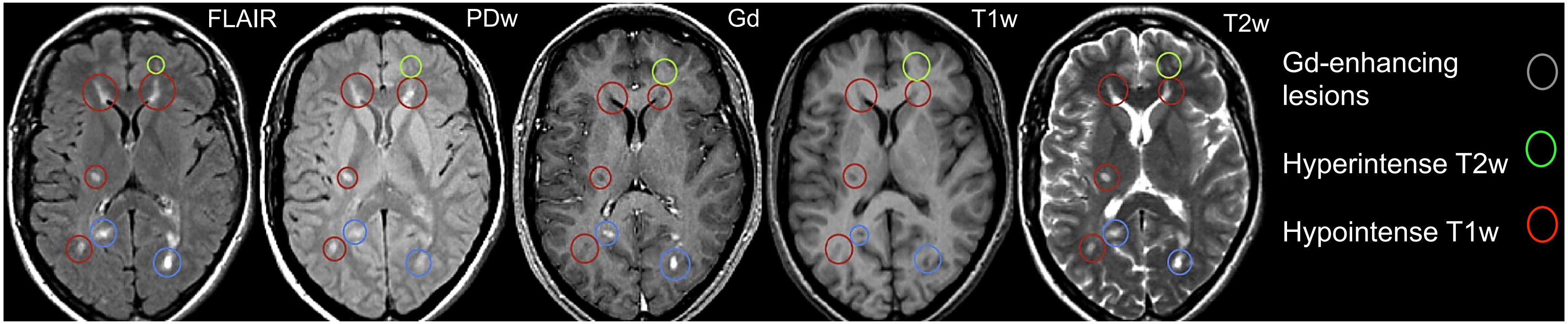
Wattjes, M. P. *et al.* (2015)

Nature Reviews | Neurology

- Segmentation Methods:
  - guiding clinicians in the medical decision process
  - manual segmentation:
    - time consuming task
    - intra- inter- expert variability

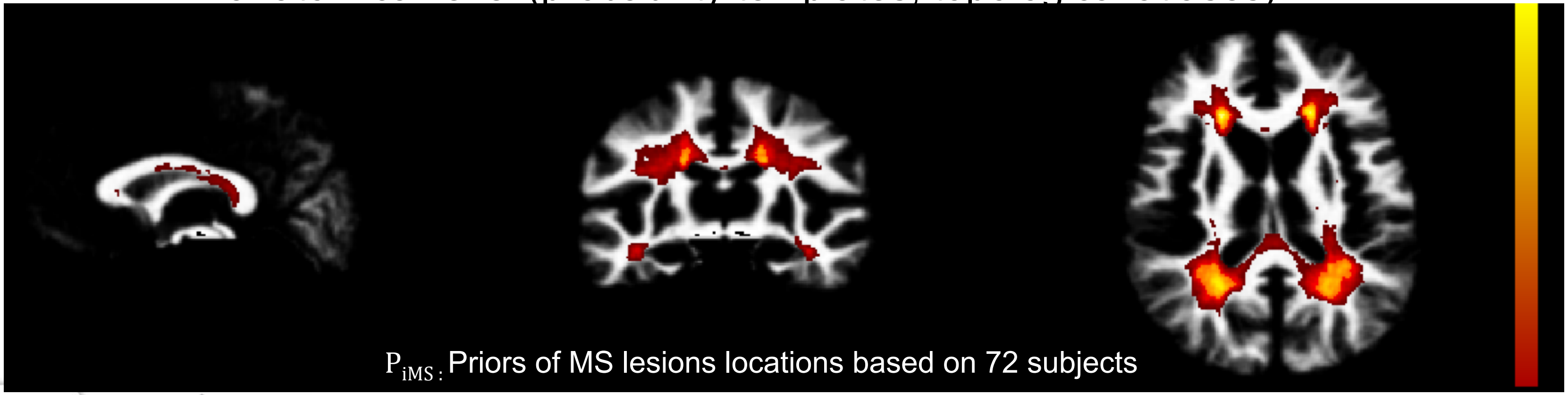
Introduction

- Automatic Segmentation methods:
  - Multimodal intensity information



From: Garcia-Lorenzo et al. Review of automatic segmentation methods of WM lesions on conventional MRI. Medical Image Analysis, 2013.

  - Spatial information:
    - local neighborhood level (e.g. MRF, Graph Cut)
    - anatomical level (probability templates, topological atlases)



Automatic Segmentation Methods in Visages

MICCAI 2016 Athens

Participants		Approach	Sequences
Roura et al.	U	*Rules & Level Sets*	*T1w,FLAIR*
VISAGES	U	***EM initialized Graph Cut***	***T1w,T2w,FLAIR***
VISAGES	U	***Atlas based comparison***	***T1w,T2w,PDw,FLAIR***
McKinley et al.	S	*Deep Dag-like Convolutional Network*	*FLAIR*
Valverde et al.	S	*Convolutional Network of 3D patches*	*T1w,T2w,PDw,FLAIR*

S Supervised

U Unsupervised

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Commowick O et al. *MSSEG Challenge Proceedings MS Lesions Segmentation Challenge Using a Data Management and Processing Infrastructure, 2016.*

International Symposium on BIOMEDICAL IMAGING: From Nano to Macro
April 16-19, 2015

Participants		Approach	Sequences
CMIC	S	*Multimodal patch matching*	*T1w,T2w,PDw,FLAIR*
VISAGES	U	***EM initialized Graph Cut***	***T1w,T2w,FLAIR***
IMI & PVG	S	*Random Forest*	*T1w,T2w,PDw,FLAIR*
ITT MADRAS	S	*n3 Convolutional Neuronal Network*	*T1w,T2w,PDw,FLAIR*
MSmetrix	U	*Hierarchical EM*	*T1w, FLAIR*
VISAGES	S	***Dictionary Learning***	***T1w,T2w,FLAIR***

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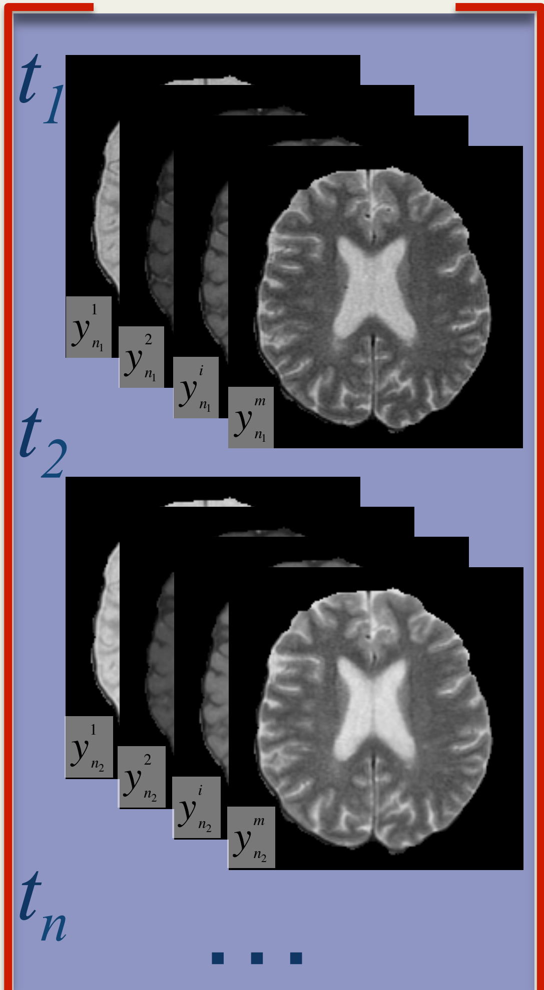
Carass A et al. *Longitudinal multiple sclerosis lesion segmentation: Resource and challenge*, Neuroimage, 2017

Method #1 :MS Lesions as outliers from normal appearing brain tissues



Estimation of "normal" appearances

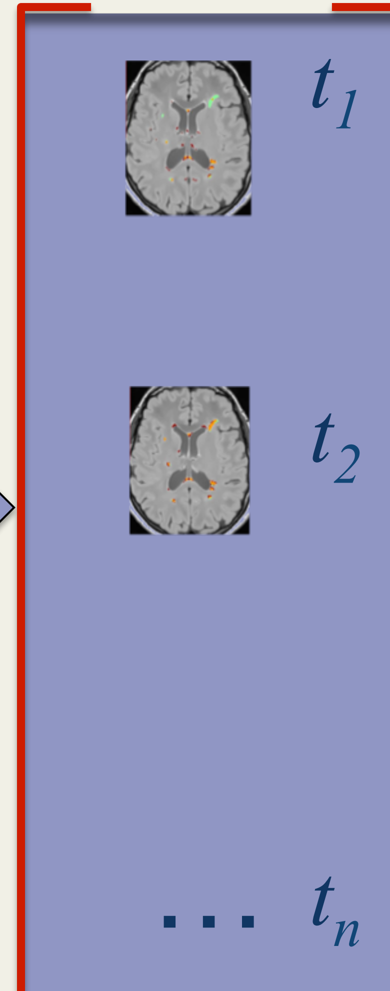
$$\begin{cases} \hat{\theta}_{MLE} = \underset{\theta}{\operatorname{argmax}} \left(\prod_{i=1}^{m} f(y_i|\theta) \right); f(y_i|\theta) = \sum_{j=1}^{n} \left[\alpha_j \cdot \mathcal{N}(\mu_j, \Sigma_j) \right] \\ \hat{\theta}_{TL} = \underset{\theta}{\operatorname{argmax}} \left(\prod_{i=1}^{k} f(y_{sort(i)}|\theta) \right); \left(m/2 < k \le m \right) \end{cases}$$

Identification of "irregular" appearances (e.g. lesions, artifacts)

$$d_i = \min_j \left\{ \sqrt{(y_i - \mu_j)^T \Sigma_j^{-1} (y_i - \mu_j)} \right\} > p\left(t \middle| \aleph^2_n\right)$$

Neuroradiological Expertise
(keep WM lesions only)

$$p_{lesion} = \int_{y_{th}}^{\infty} \mathcal{N}\left(\mu_{WM}^{T2}, \sigma_{WM}^{T2}\right) dy$$



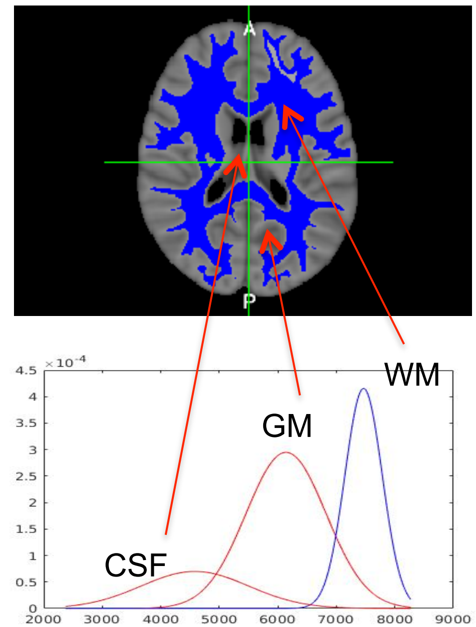
D. Garcia. et al. IEEE-TMI 2011

EM-initialized Graph Cut:

- Estimate NABT 3-class Gaussian Mixture model (multivariate):

$$f(\boldsymbol{y}_i \mid \theta) = \sum_{j=1}^{3} \alpha_j \, N(\mu_j, \Sigma_j)$$

  - Maximum Likelihood principle with Expectation Maximization



NABT probability model, FGM model

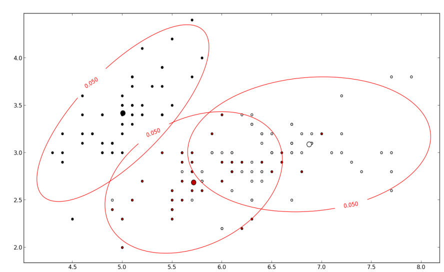
- MS lesions as outliers, Trimmed EM segmentation:

$$\mathrm{TL}(\theta) = \arg\max \prod_{i=1}^{k} f(\boldsymbol{y}_{v(i)} \mid \theta)$$

  - Reject $h = (n-k)/n$ voxels with largest residuals
  - Compute EM segmentation on remaining ones

- Output:
  - Mean μ and covariance Σ of each class j
  - Mahalanobis distances of each voxel to each distribution:

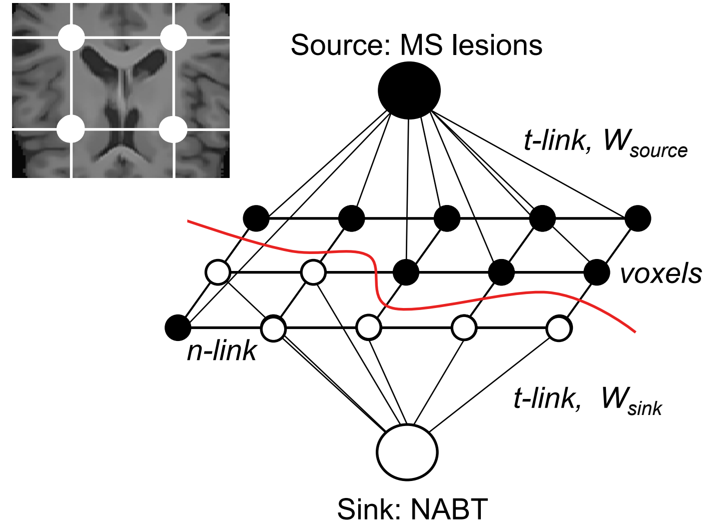
$$d_i = \sqrt{(\boldsymbol{y}_i - \mu_j)^T \Sigma_j^{-1} (\boldsymbol{y}_i - \mu_j)}$$



Mahalanobis distance, 3 classes.

EM-initialized Graph Cut:

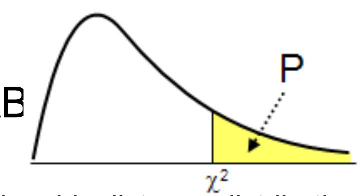
- Image as a Graph:
  - Weight of a n-link represents voxels similarity
  - Compute the optimal cut between MS lesions and background



- t-links weights:
  - χ^2 p-value$_{Mahalanobis}$: probability not to fit into NAB
  - MS lesions have high p-value$_{Mahalanobis}$

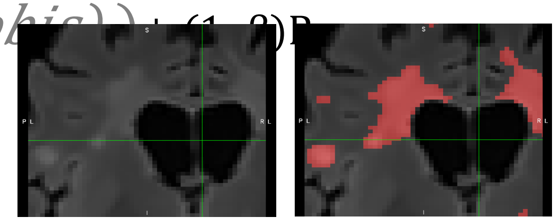
$$W_{sink} = \beta(1 - \min(p\text{-value}_{Mahalanobis})) + (1-\beta)P$$

Intensities prior Spatial prior



Mahalanobis distance distribution, p-value

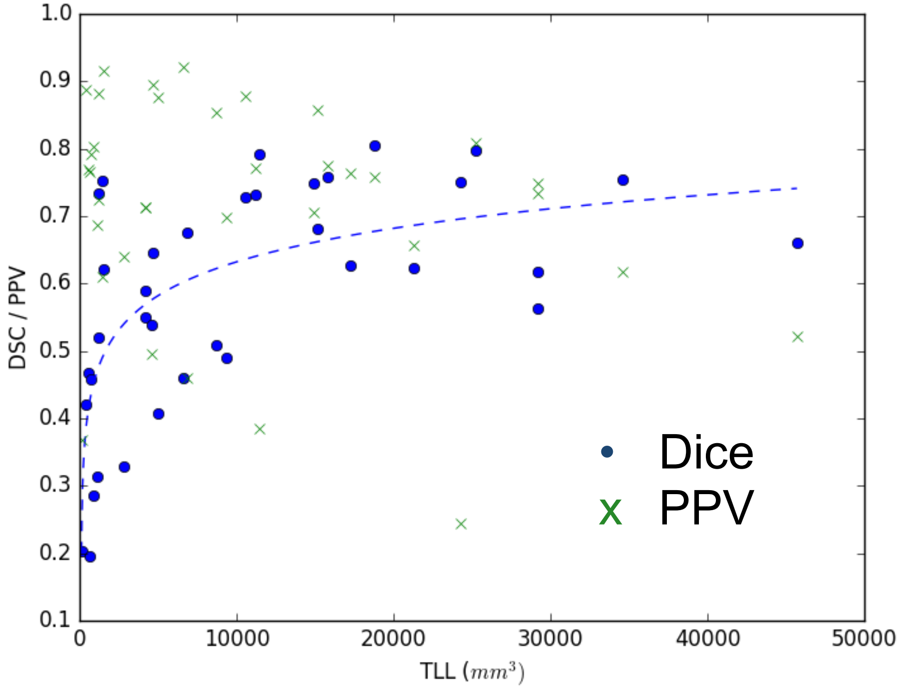
  - Distinguish from other outliers using hyperintensity
    - $W_{source} = \min\{p\text{-value}_{Mahalanobis}, W_{T2W}, W_{FLAIR}\}$

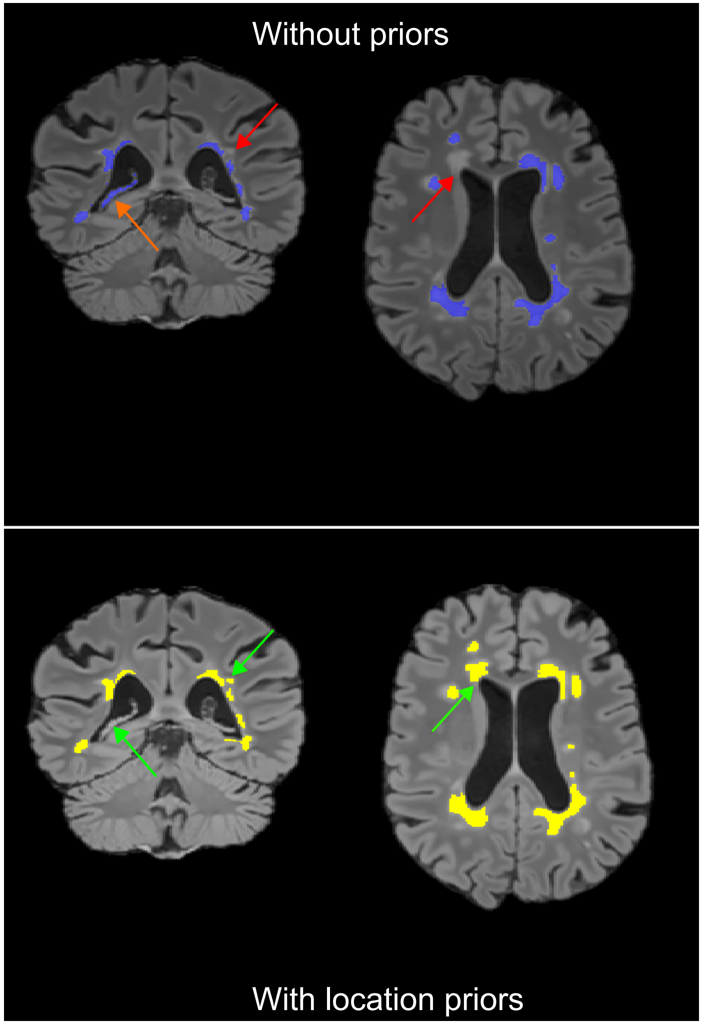


MS hyperintensity, FLAIR mage

EM-initialized Graph Cut:

- Limitations: tuning of parameters for different lesion loads.
- Accuracy increases with TLL
- Priors can improve accuracy





Method #2 : Atlas-based comparison segmentation

- **Approach**: MS lesions as outliers to normal control subjects

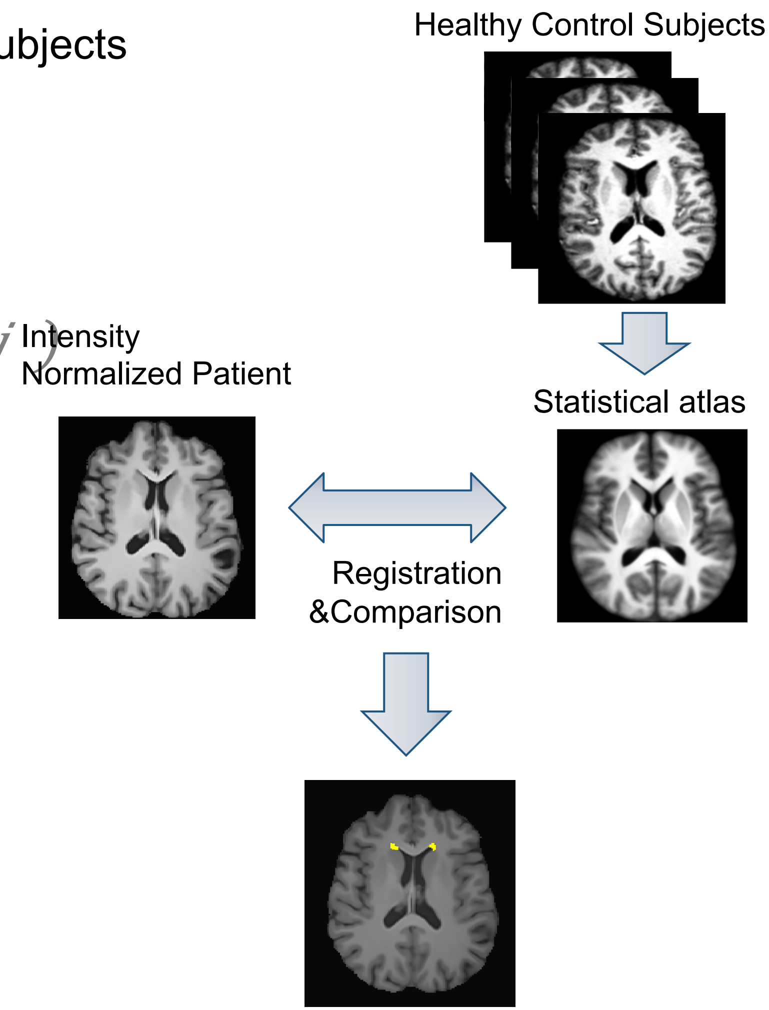
- Intensity normalization:
  - Estimate NABT 3-class GM model (multivariate):

$$f(y_i|\theta) = \sum_{j=1}^{3} \alpha_j N(\mu_j, \Sigma_j)$$

    - using Notsu et al. γ-loss EM robust to outliers

  - Output: Mean μ and covariance Σ of each class
    - Linear regression on means for normalization

- Output: intensity-normalized image patients

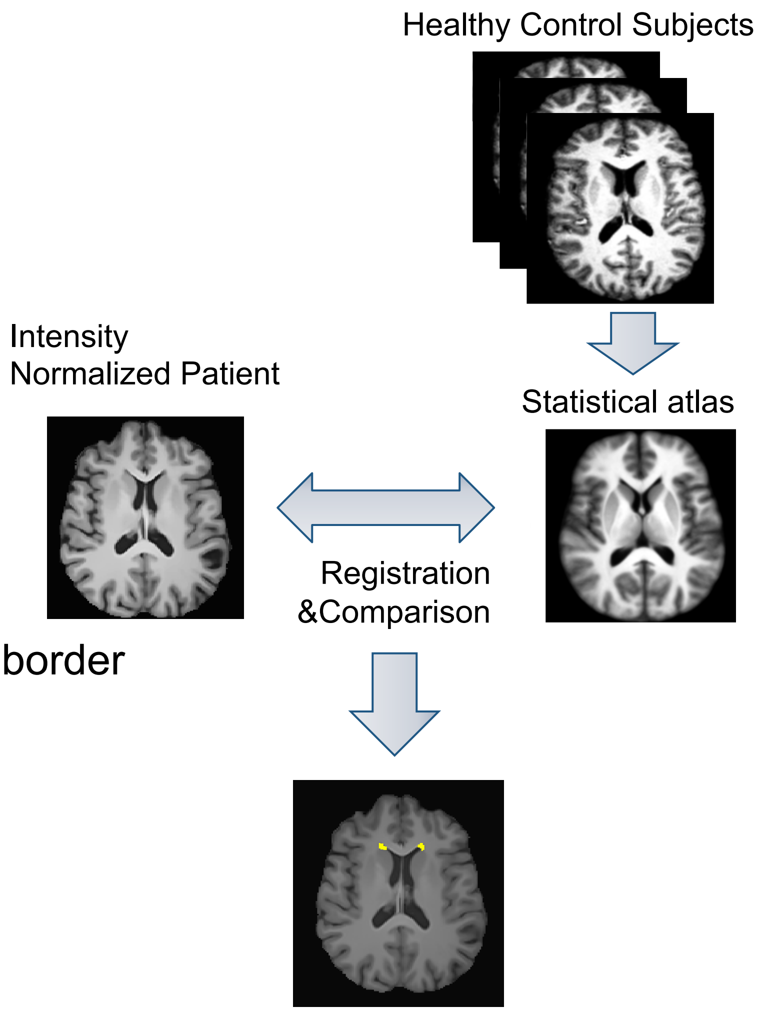


Atlas-based comparison segmentation

- **Three steps segmentation:**
  - Registration on healthy controls
    - Non-linear registration

      Voxel-wise computation (Mahalanobis distance)
    - Patient vs Controls mean and variance

      Derivation of p-value of abnormality presence
    - Corrected for multiple comparisons
  - Post-processing :
    - remove lesions too small or touching the brain border
    - keep lesions inside a probable lesions mask
  - Towards a locally multivariate approach
    - A contrario approach [Maumet et al. Neuroimage 2016]



Machine learning: Probabilistic One Class SVM for Automatic Detection of MS Lesions

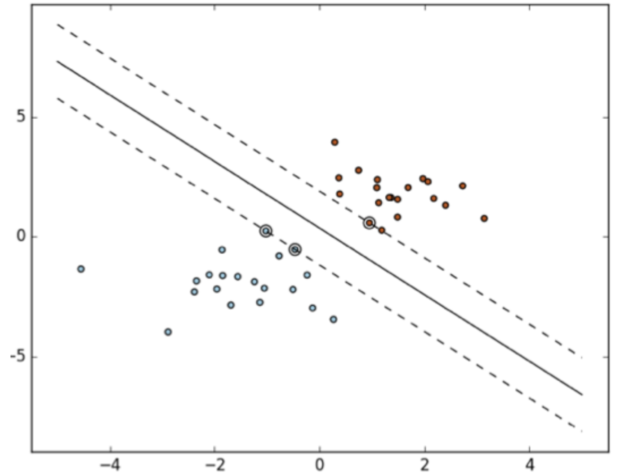
Goal: Propose an automatic framework for MSL Detection based on multichannel MRI patch based information

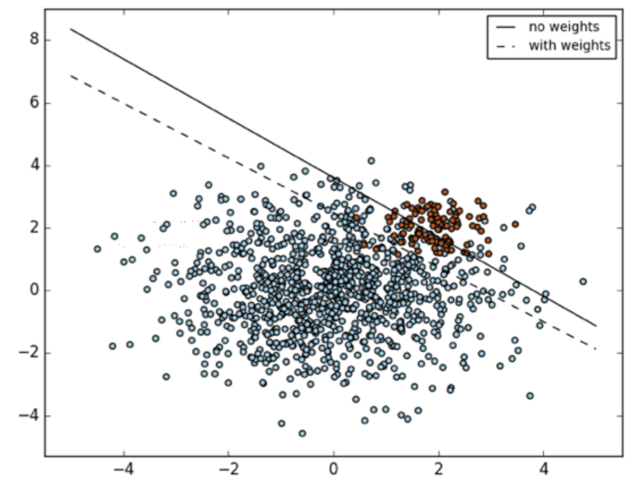
State-of-the-art machine learning algorithms:

- SVM [Vapnik et al.1995], Logistic Regression [Zhang et al.2002], Neural Network…
- Works well in practice when training examples in classes are balanced

If not ?

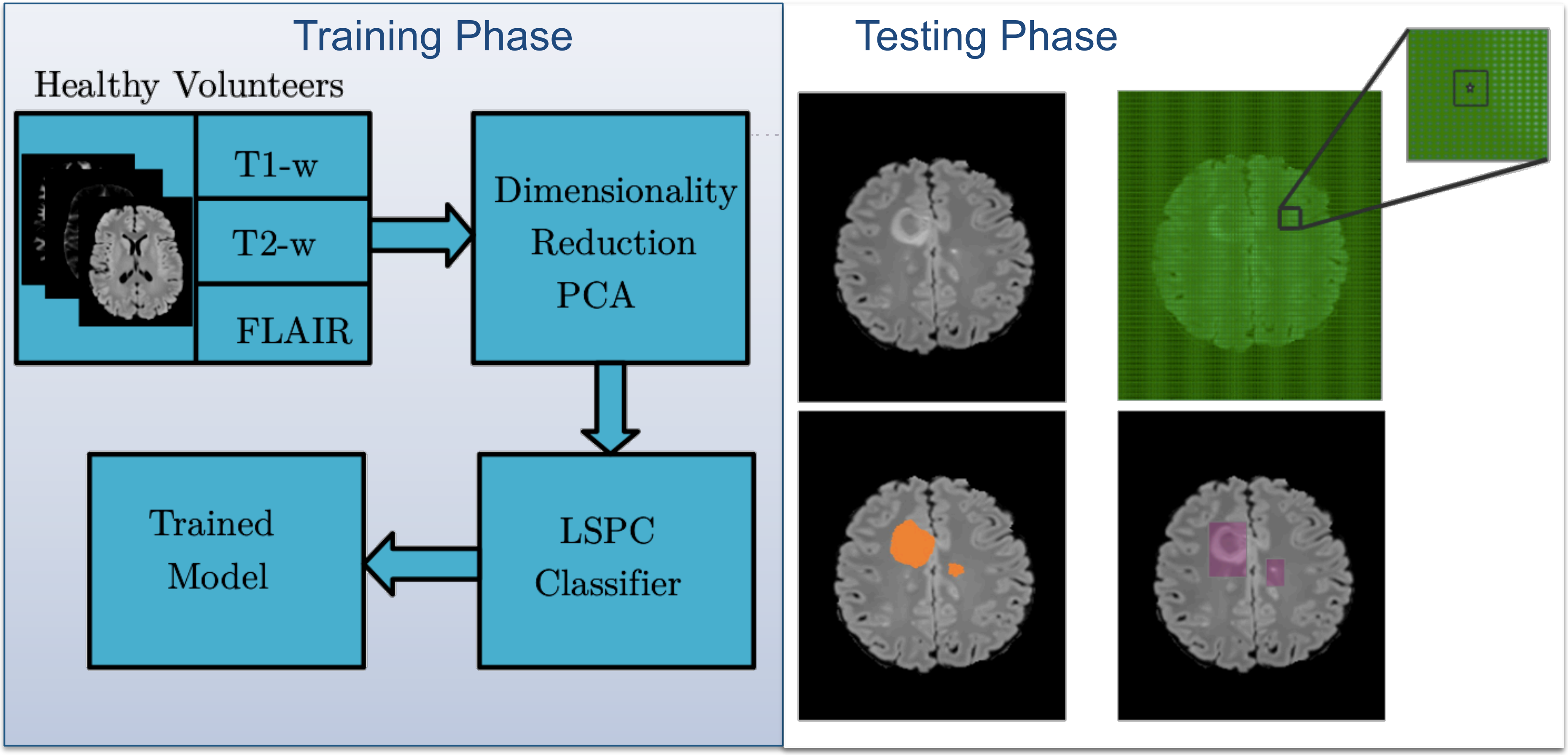
- Class Imbalance ⇒ under-/over-fitting of the Classifier [Chawala 2005]
- Class imbalance between Normal Brain Tissues and MS lesions
- Solution : A higher misclassification penalty on the minority class (MS lesion)





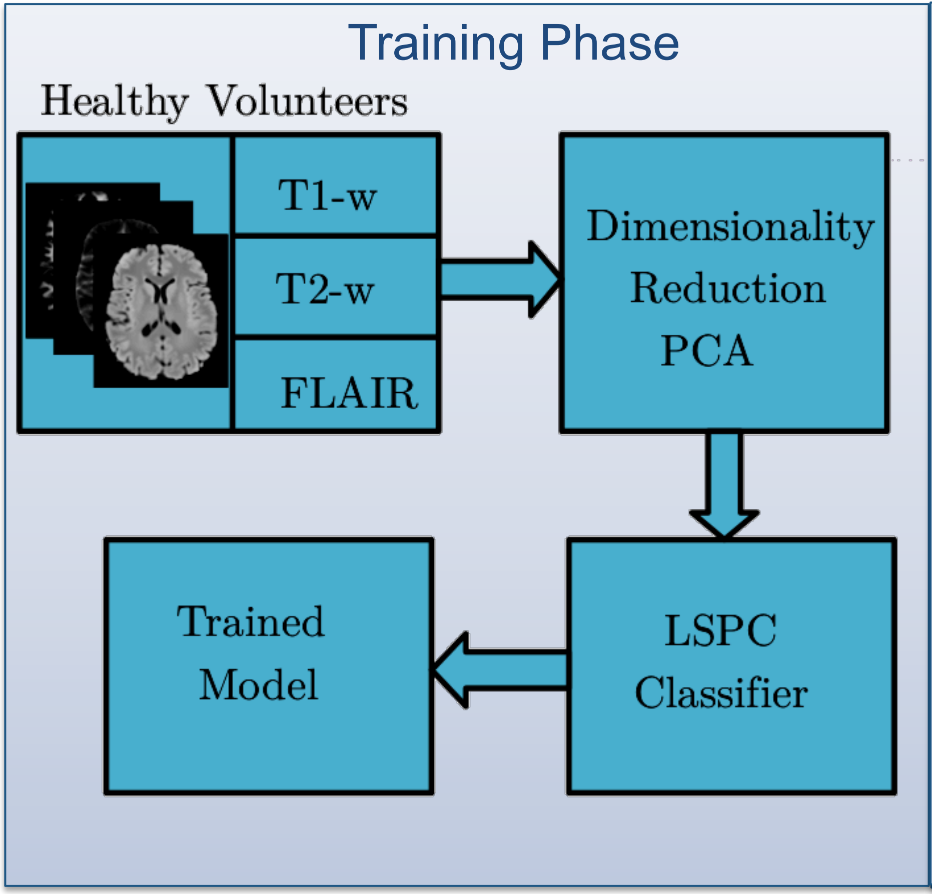
Toy example of SVM for balanced and unbalanced classes, Courtesy : www.scikit-learn.org.

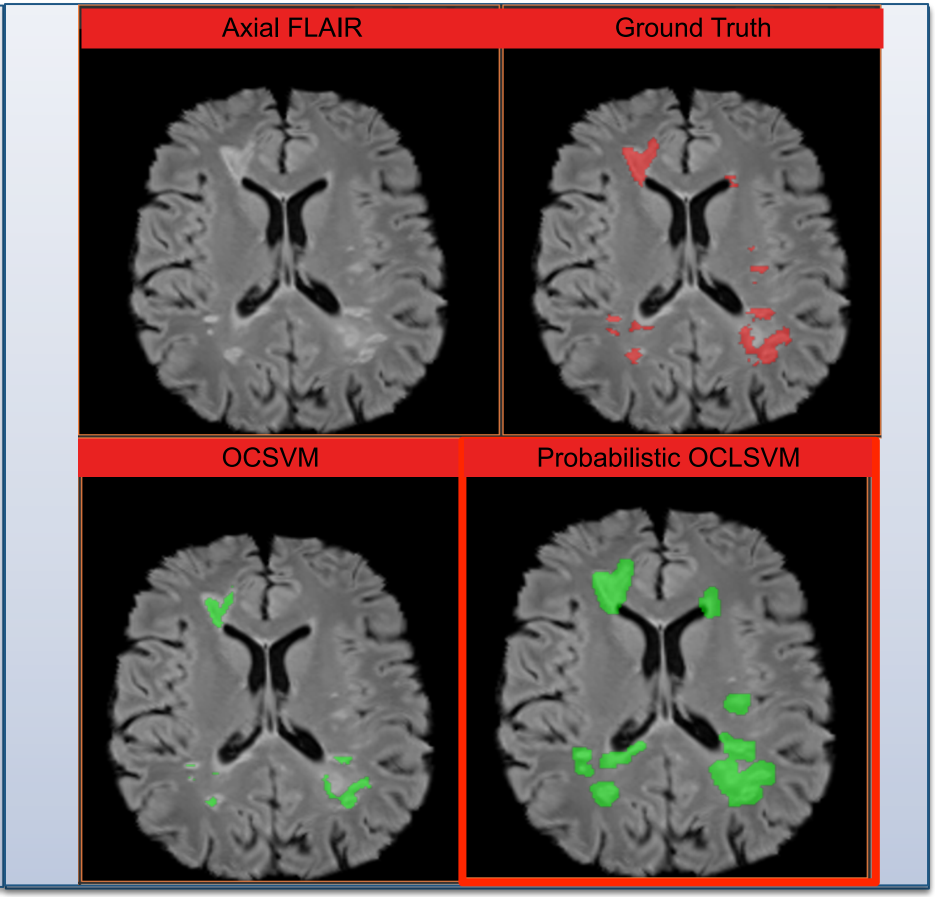
Method #3 : Probabilistic One Class SVM for Automatic Detection of MS Lesions



[Karpate et al, 2015]: Probabilistic One Class Learning for Automatic Detection of MS Lesions. Proceedings of ISBI 2015

Method #3 : Probabilistic One Class SVM for Automatic Detection of MS Lesions

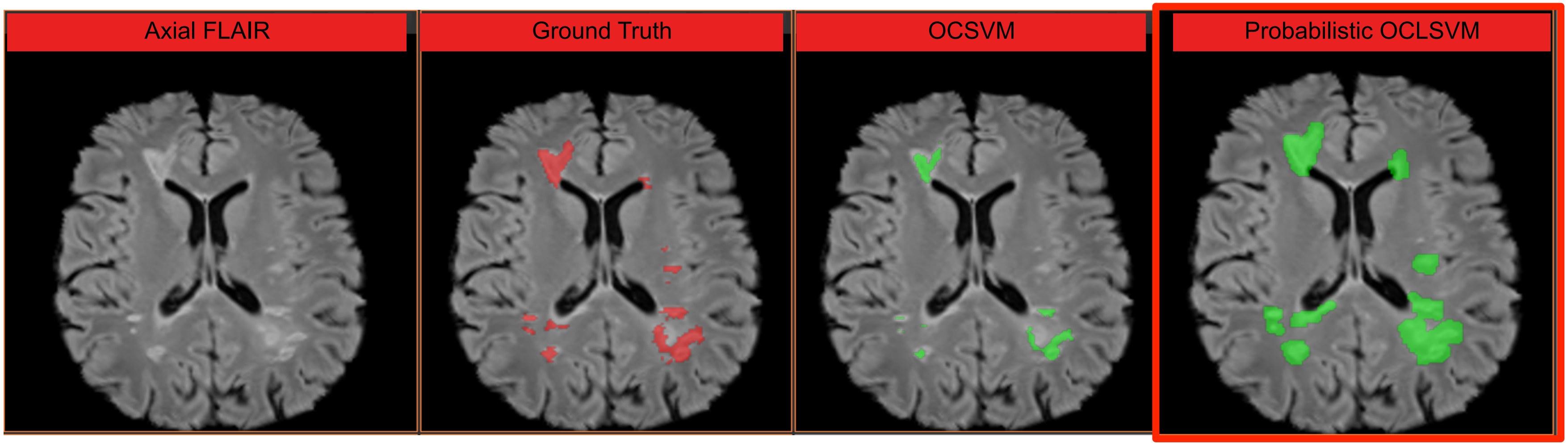




[Karpate et al, 2015]: Probabilistic One Class Learning for Automatic Detection of MS Lesions. Proceedings of ISBI 2015

Method #3 : Probabilistic One Class SVM for Automatic Detection of MS Lesions

- Goal: Robust detection of lesions as deviation from normal appearing tissues
- Challenge: overcome learning approaches problems with MS lesions
  - Two-class imbalance problem (much more normal samples than lesions)
- Contributions:
  - Robust spatio-temporal multi-modal intensity normalization for T1-Gd and longitudinal MS lesion detection
  - One class learning for lesion detection from multidimensional MRI
    - Dimensionality reduction of the feature space
    - Lesions modeled as the complementary of the normal class
    - Testing by comparing patient patches characteristics to the pdf of the normal class

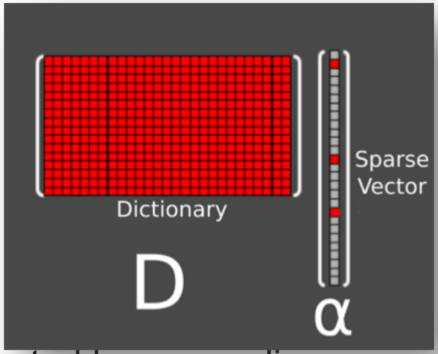


[Karpate et al. 2015]: Probabilistic One Class Learning for Automatic Detection of MS Lesions. Proceedings of ISBI 2015

Method #4 : Detection of MS lesions via competitive Dictionary Learning

- Goal: New sparse representation and dictionary learning method for classification
- Challenge: competitive dictionary learning
  - One dictionary per class, classification decision based on reconstruction error
  - Representative Dictionary Learning : good for denoising, inpainting, … How to optimize DL for classification
- Sparse Representation: SR represents signals using linear combination of few basis elements in a set of redundant basis functions:
  - SR is an optimization problem (ε is an approximation error):

$$min_\alpha \|\alpha\|_0 \;\; s.t. \; \mathbf{x} = \mathbf{D}\alpha \;\; or \;\; \|\mathbf{x} - \mathbf{D}\alpha\|_2^2 \leq \varepsilon$$



- Related Dictionary learning (DL) : Finds D such that each signal can be represented by sparse linear combination of its atoms:

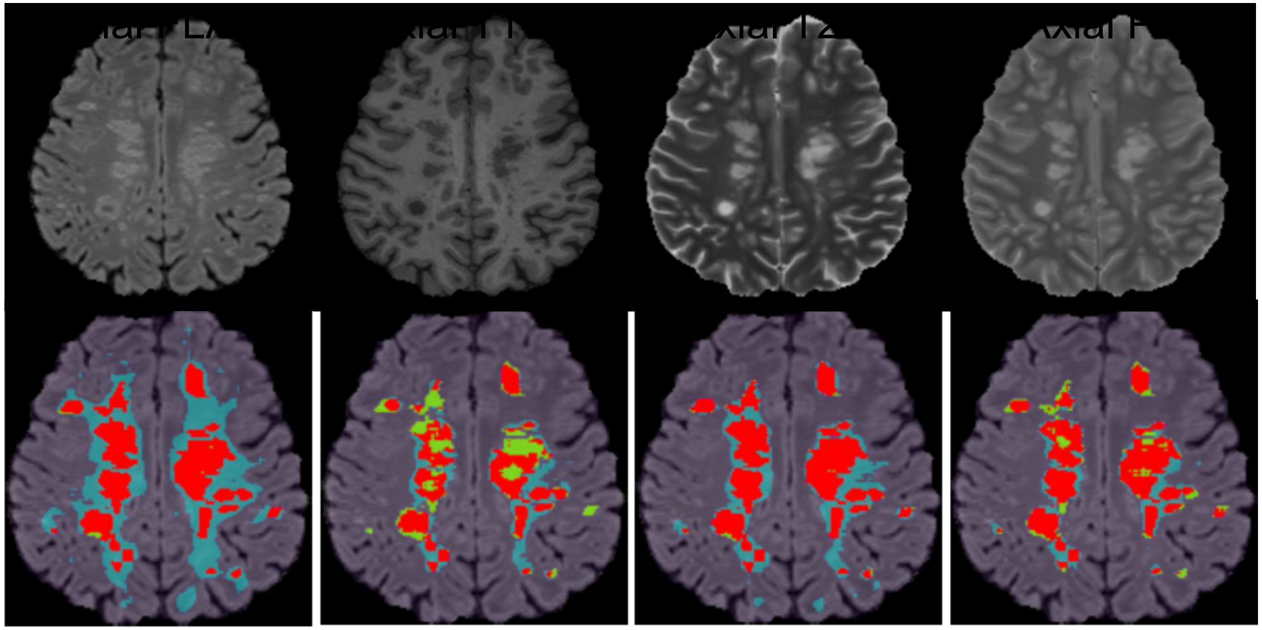
$$\min_{\mathbf{D}^c, \{\alpha_i^c\}_{i=1,..,m}} \sum_{i=1}^{m} \|\mathbf{x}_i^c - \mathbf{D}^c\alpha_i^c\|_2^2 + \lambda \|\alpha_i^c\|_1$$

  - Classification using DL: find k classes such as : $k = \underset{c}{\text{argmin}} \|\mathbf{y} - \mathbf{D}^c\alpha^c\|_2^2$

[Deshpande et al, 2015]: Classification of Multiple Sclerosis Lesions using Adaptive Dictionary Learning. Computerized Medical Imaging and Graphics, (*Dec.*), 2015

<u>Method #4</u> : Detection of MS lesions via competitive Dictionary Learning

- *Goal*: New sparse representation and dictionary learning method for classification
- *Contribution*:
  - Adaptation of dictionary size to a class complexity: improved over standard DL or discriminative methods
  - Detection of MS Lesions by classification on multimodal MRI images



(a) Two dictionaries with 5000 atoms for healthy and lesion classes

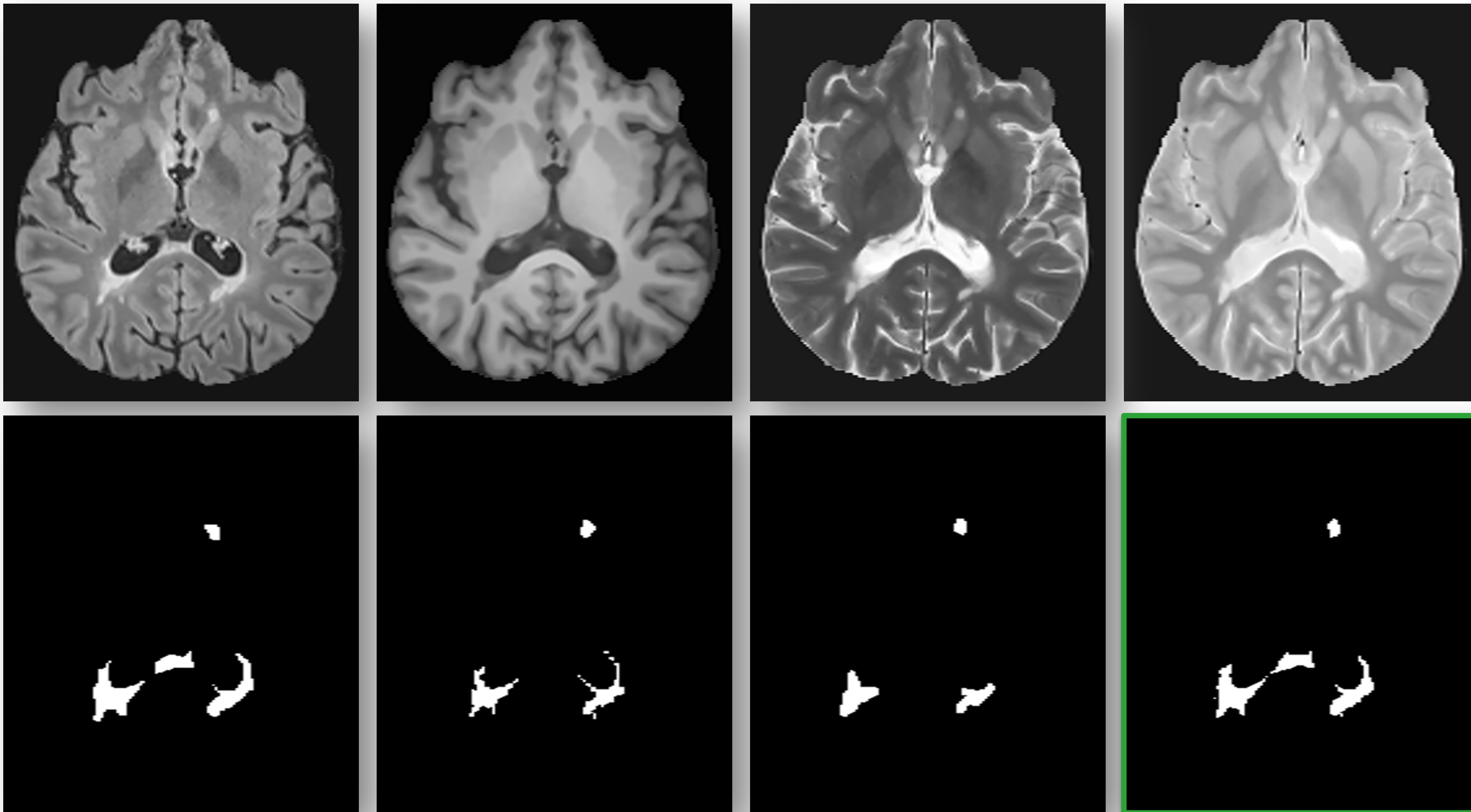
(b) Two dictionaries with 5000 atoms for healthy and 1000 for lesion class

(c) Four dictionaries with 2000 atoms for WM, GM, CSF and lesion class

(d) Four dictionaries with 2000 atoms for each tissue, and 1000 for lesion class

[Deshpande et al, 2015]: Classification of Multiple Sclerosis Lesions using Adaptive Dictionary Learning. Computerized Medical Imaging and Graphics, (*Dec.*), 2015

$\Sigma method_i$: Merging MS lesions Annotations



Automatic Annotations

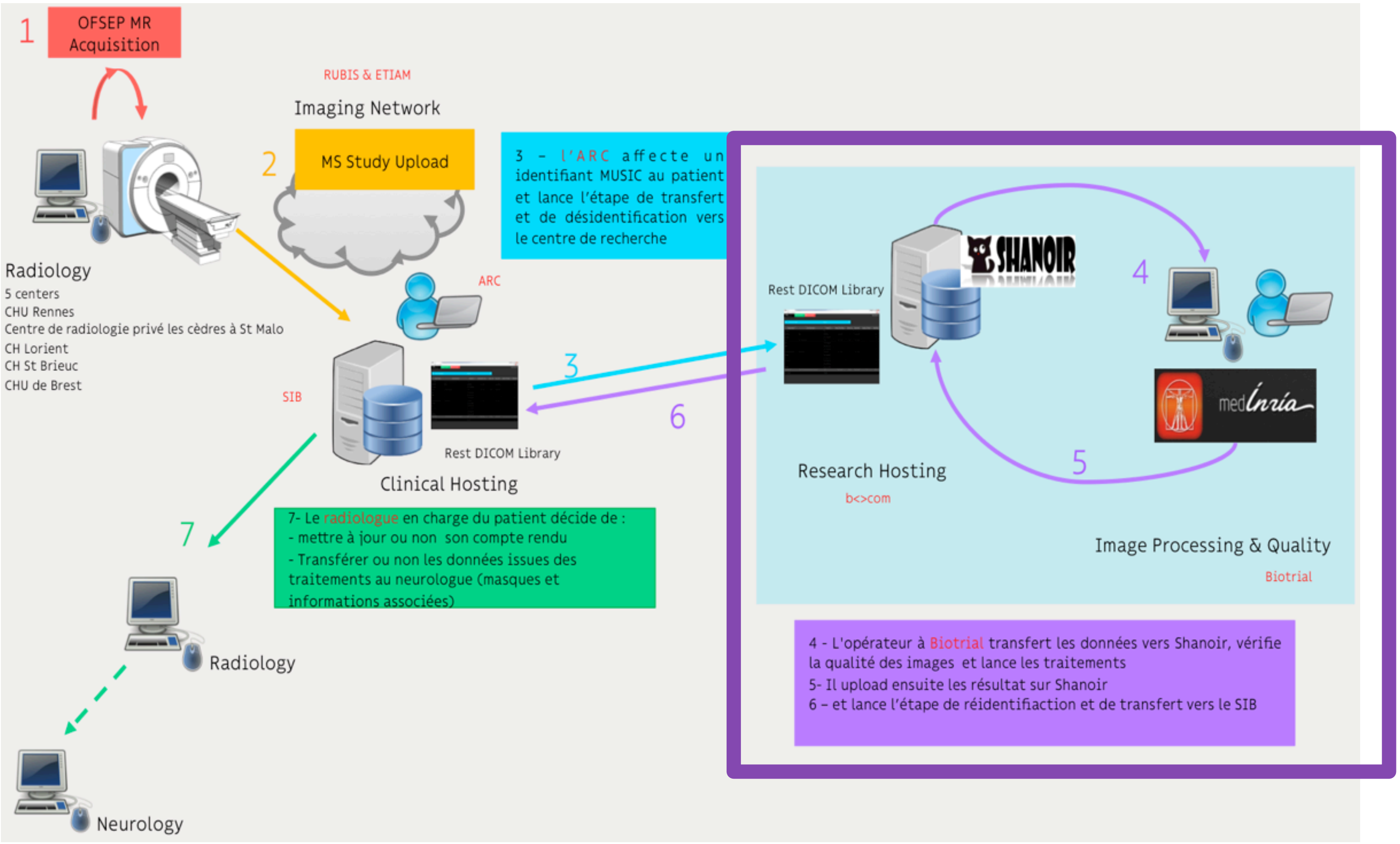
Consensus
(LOP STAPLE*)

Akhondi-Asl A, Hoyte L, Lockhart ME, Warfield SK. *A Logarithmic Opinion Pool Based STAPLE Algorithm For The Fusion of Segmentations With Associated Reliability Weights,* IEEE Trans Med Imaging. 2014

Conclusions

- Challenges:
  - Multicenter datasets, Availability (MICCAI challenges)
  - Several manual segmentations (STAPLE,…)
  - Accuracy: Multiple metrics (DSC, F1,…)
  - Robustness: Large multicenter database (MUSIC) – combination of methods to compensate for limitations of each methods
  - ???

MUSIC étape 4 : analyse des images

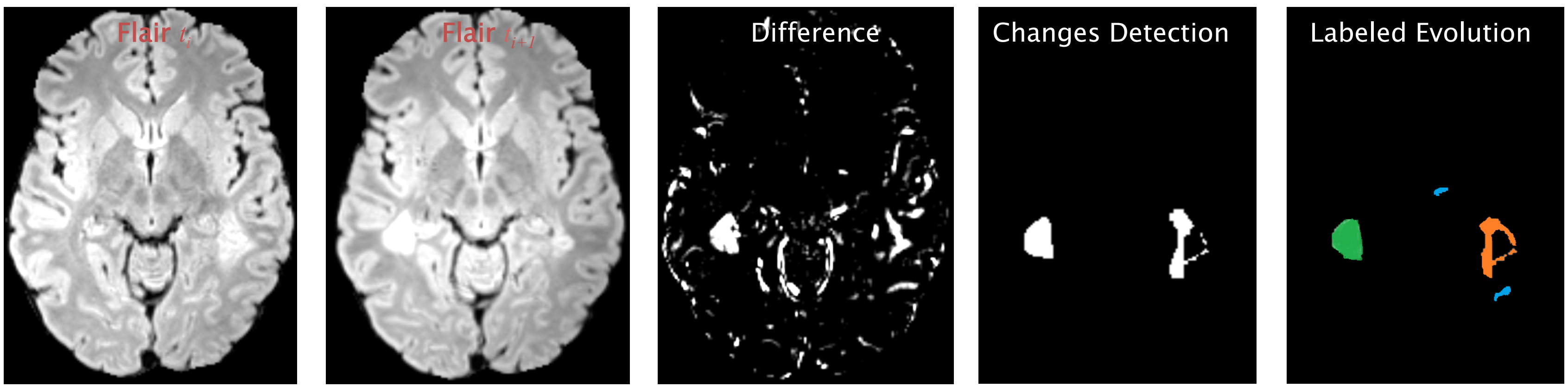


MUSIC étape 4 : analyse des images

Contrôle qualité des images

Segmentation des lésions

Détection de l’évolution des lésions



Basées sur algorithmes développés au laboratoire

Etape 4 : une étape délicate…

Validation et amélioration de l'outil de segmentation

- **Financement d'un poste d'ingénieur de recherche pendant 2 ans**
- **PHRC inter-régional obtenu en 2016**

ETUDE POCADIMS

Performance d'un outil d'aide au diagnostic des lésions visualisées en IRM dans le diagnostic et le suivi de la SEP (CADIMS) en pratique clinique

Objectif principal

Evaluer, en aveugle, la performance diagnostique de l'outil CADIMS du projet MUSIC pour la détection de lésions de SEP sur des IRM cérébrales réalisées en pratique courante en comparaison à un consensus d'expert.