

# Automatic hippocampal box extraction



**Beta-Amyloid**

**Enzymes**

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[Magic-5 Workshop on Medical Imaging  
applications and tools](#)

2-4 December 2009 Istituto Nazionale  
di Fisica Nucleare - Sezione di Genova

# Progress in hippocampal box extraction

1. Code Reorganization (Done)

2. Code Optimization (Done)

3. Descalping (Done)

Significant improvement of normalization (Head Normalization + subsequent Brain normalization).

4. Histogram Normalization (in progress)

5. Hierarchical Clustering (checking)

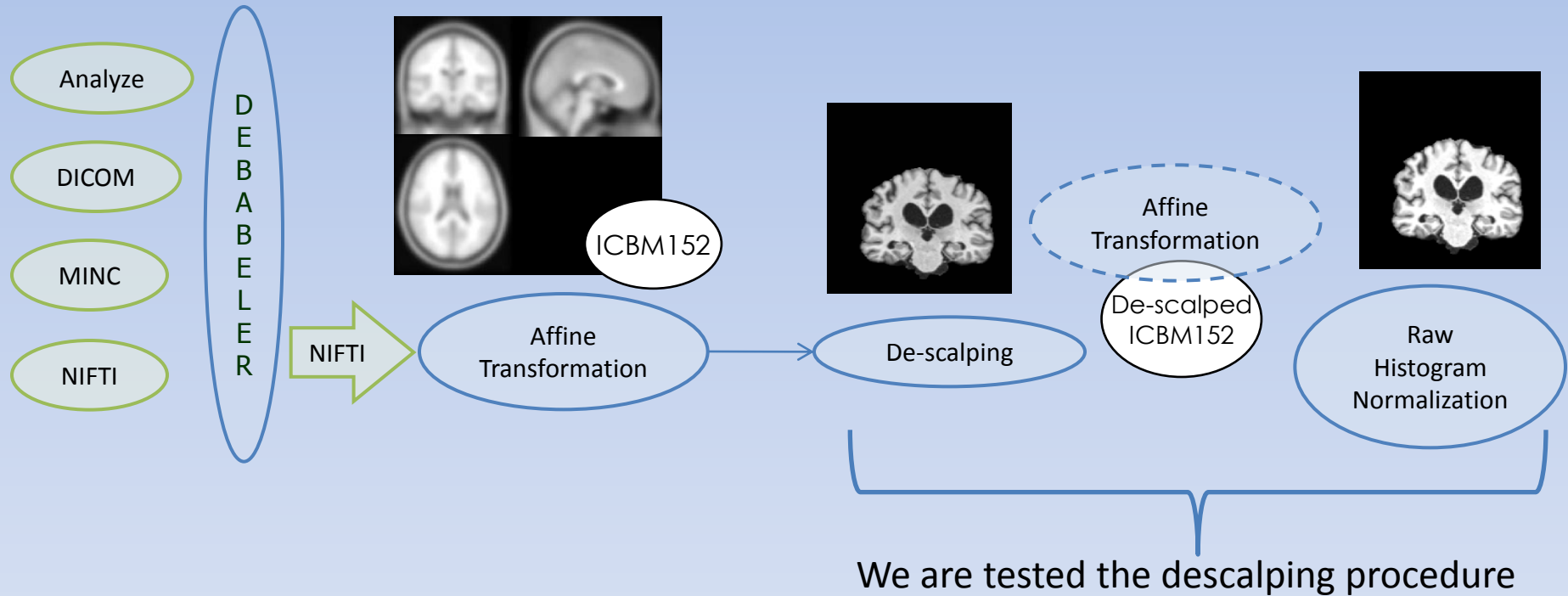
it does not require a priori choose of the number of clusters (k)

6. Best K (in progress)

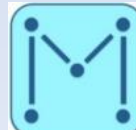
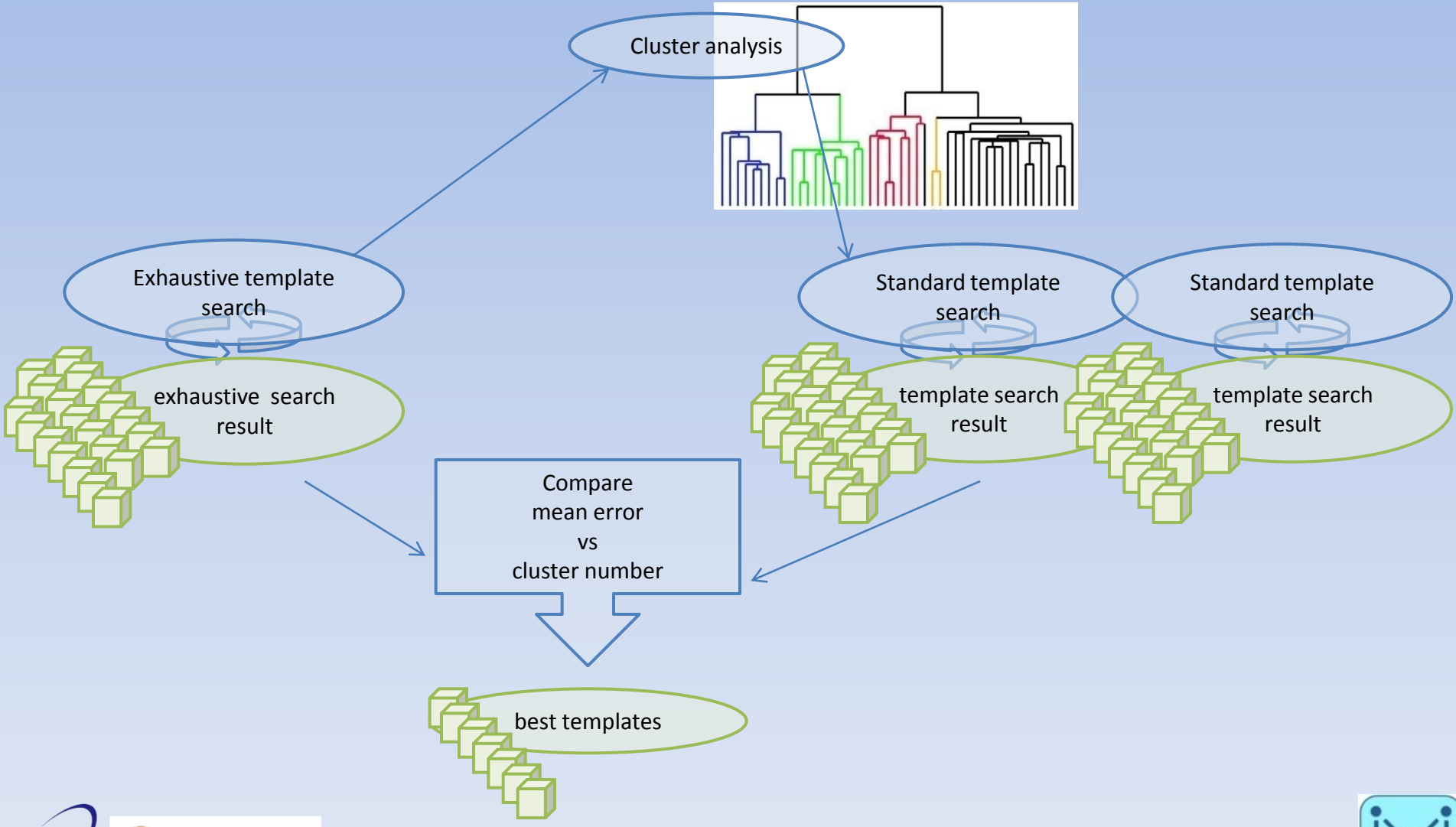
Find the smallest/best value of K according to the average distance of “k-means and Hierarchical boxes” from “exhaustive boxes”



# Algorithm: Descalping and Histogram Normalization



# Algorithm: Hierarchical Cluster Analysis





# Brain extraction (descalping)

In:

K. Boesen, K. Rehm, K. Schaper, S. Stoltzner, R. Woods, D. Rottenberg,

## **Quantitative Comparison of Four Brain Extraction Algorithms, 9th International Conference on Functional Mapping of the Human Brain,**

June 19- 22, 2003, New York, NY. Available on CD-Rom in NeuroImage, Vol. 19, No. 2.

([http://www.neurovia.umn.edu/home/kelly/KB\\_HBM2003.pdf](http://www.neurovia.umn.edu/home/kelly/KB_HBM2003.pdf))

four brain extraction algorithms (BEA) are evaluated (web site links point to the latest versions):

- Statistical Parametric Mapping (SPM), v. 2b (<http://www.fil.ion.ucl.ac.uk/spm/software/spm8/>)
- Brain Extraction Tool (BET), v. 1.2 (<http://www.fmrib.ox.ac.uk/analysis/research/bet/>)
- Minneapolis Consensus Strip (McStrip) (<http://www.neurovia.umn.edu/incweb/>)
- Brain Surface Extractor (BSE), v. 2.99.8 (<http://users.ioni.ucla.edu/~shattuck/brainsuite/cortical-surface-extraction/skull-stripping-with-the-brain-surface-extractor-bse/>)

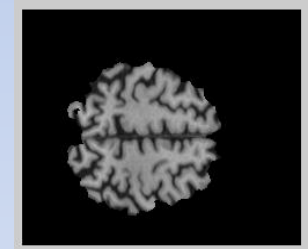
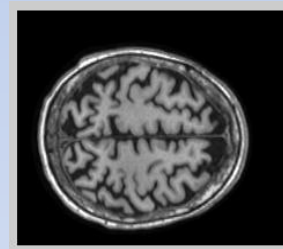
# Brain extraction (descalping)

execution time is measured (no info on the used machine) and quality comparison with manual segmentation is performed:

BEA	Processing Time	Correct Boundary	Pertinent Boundary	Misclassified Tissue
SPM	50 min	42.9%	47.9%	4.0%
BET	<b>40 sec</b>	46.9%	53.7%	10.9%
McStrip	75 min	<b>65.7%</b>	<b>72.7%</b>	<b>2.4%</b>
BSE, Subject-Specific	3-15 min	18.7%	24.3%	5.2%
BSE, Fixed	1 min	17.1%	21.9%	20.2%

The best performance for each metric is colored green.

All of the images we have worked on till now (182 nifti files) were processed



As our aim is brain coregistration, it is possible that small mistakes will not affect the final result: this is currently undergoing a full check

How many images suffer from tissue misclassification?

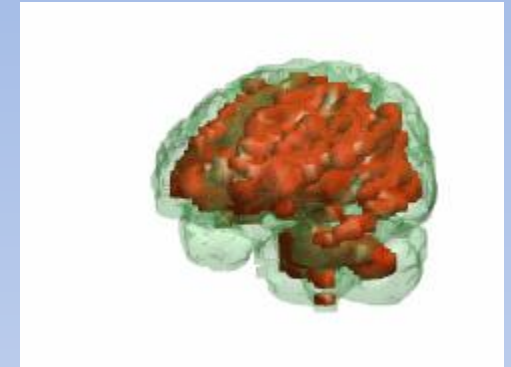
How severe are these errors?

How much will misclassification influence the brain coregistration stage?

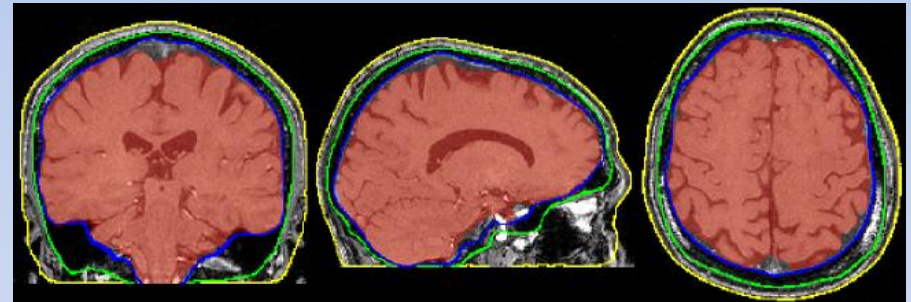
# Descalping

We tested this softwares:

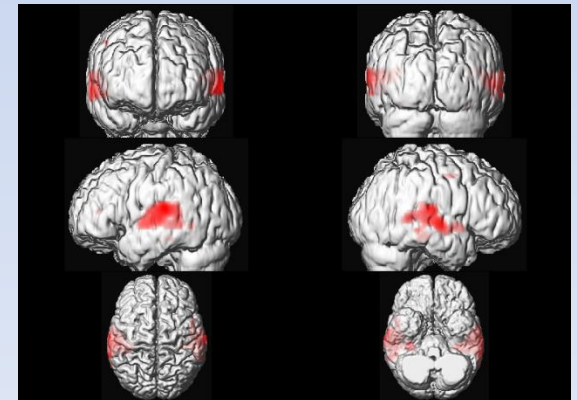
MRI Brain Segmentation (MATLAB)



BET - Brain Extraction Tool



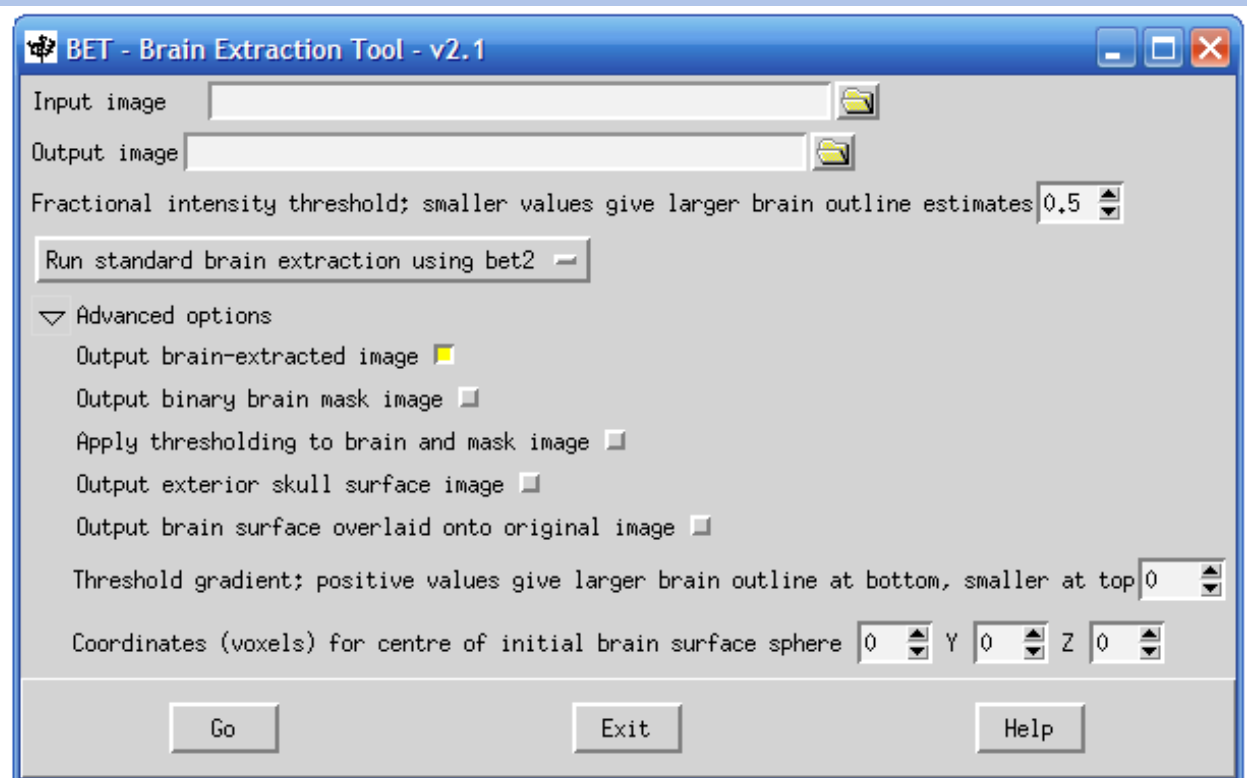
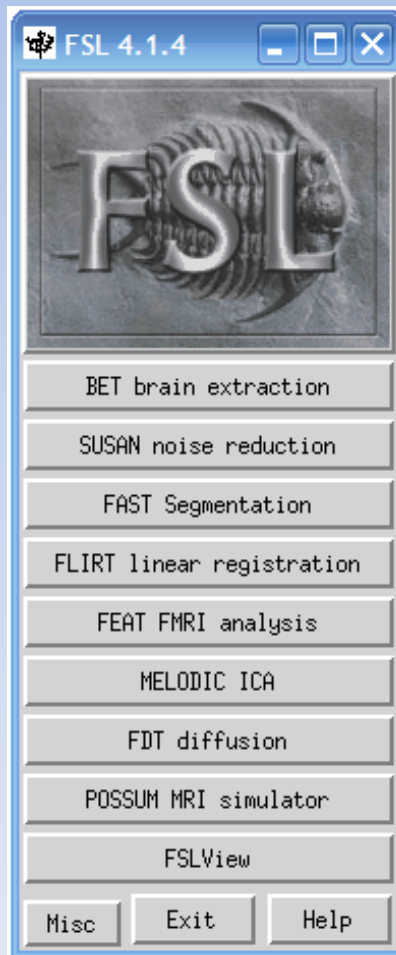
SPM- Statistical Parametric Mapping



# FSL -BET

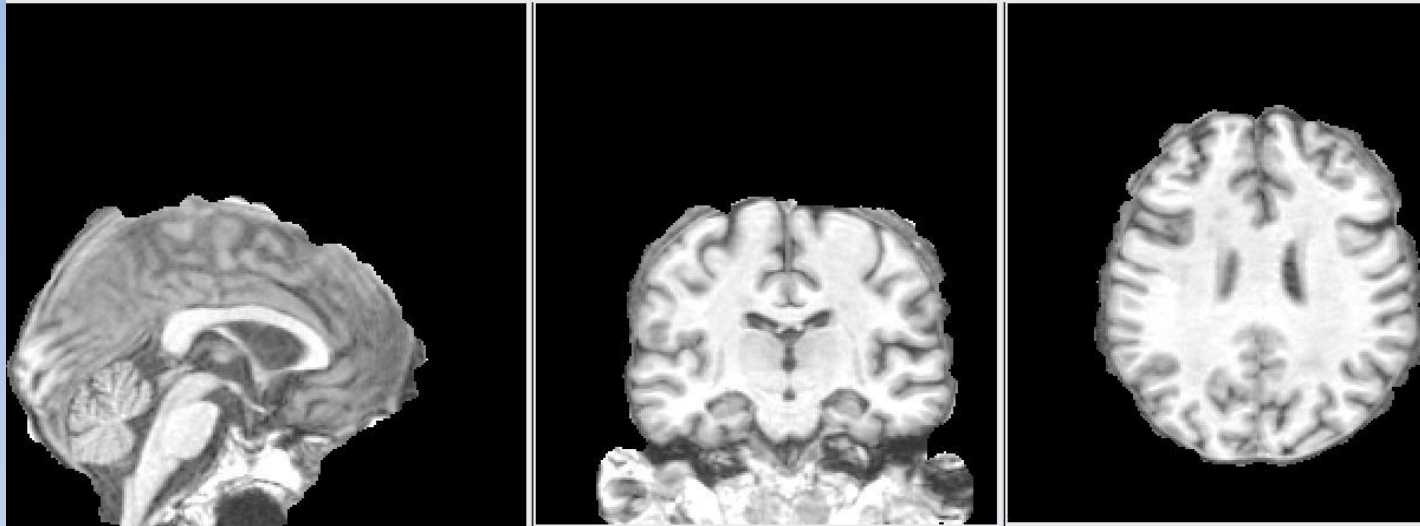
**FSL (FMRIB Software Library):** FSL is a comprehensive library of analysis tools for FMRI, MRI and DTI brain imaging data. FSL is written mainly by members of the [Analysis Group, FMRIB, Oxford, UK](#).

**BET (Brain Extraction Tool):** segments brain from non-brain in structural and functional data, and models skull and scalp surfaces.

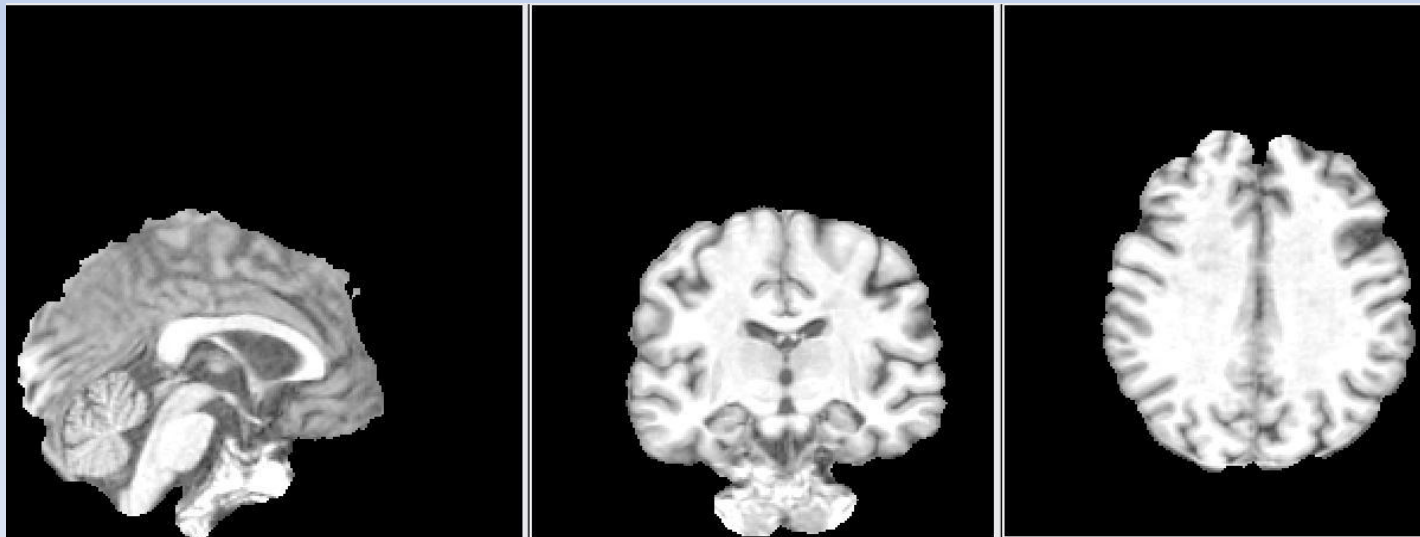




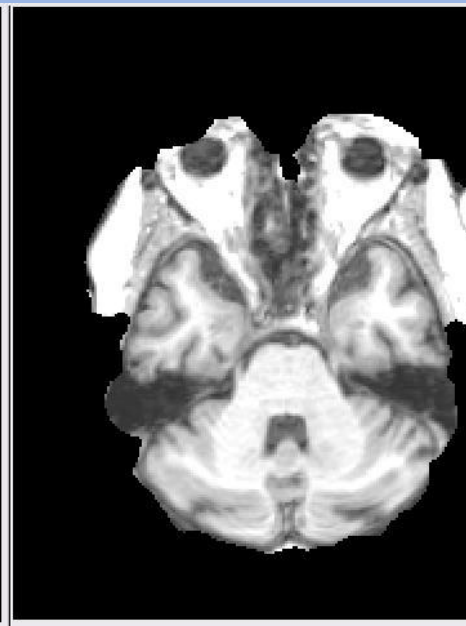
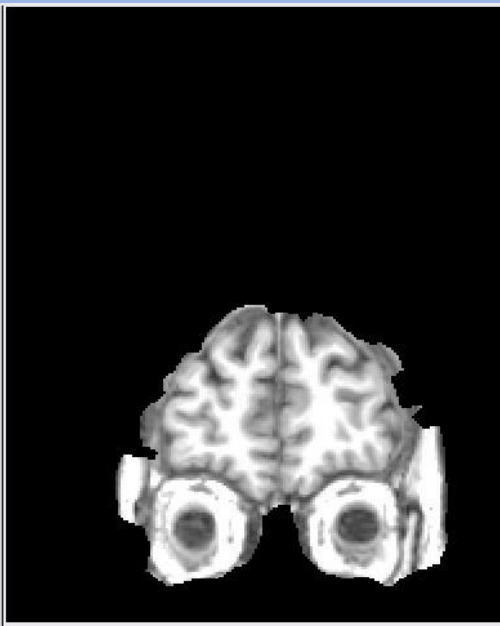
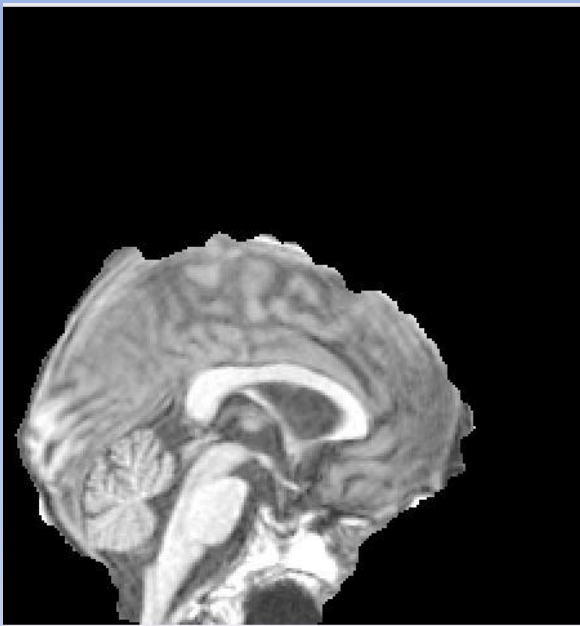
# BET: Results



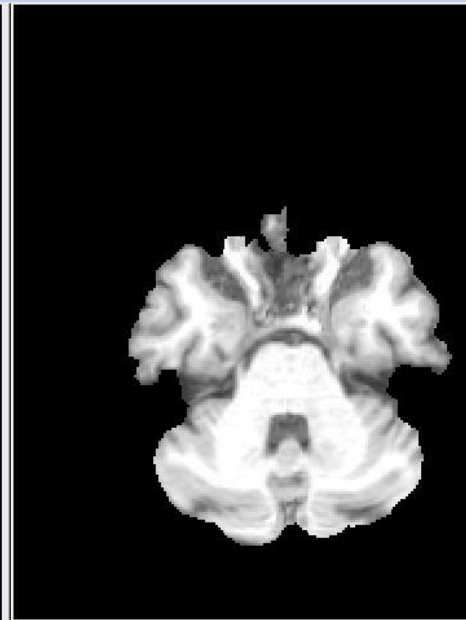
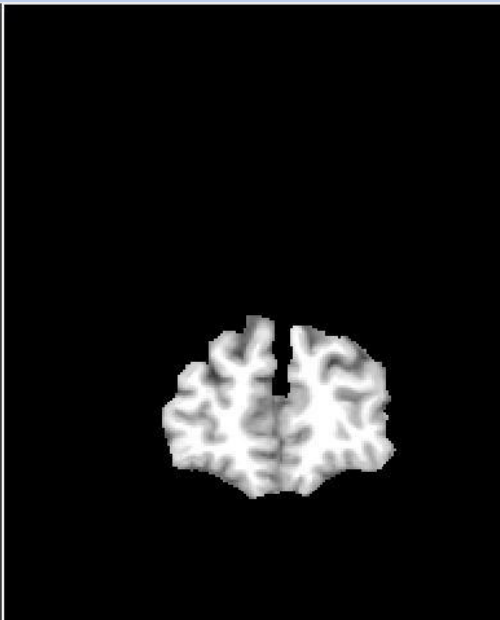
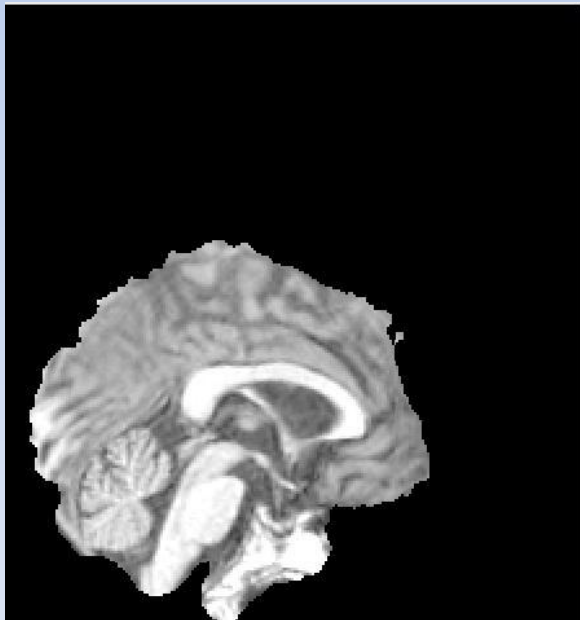
$f = 0.5$



$f = 0.8$

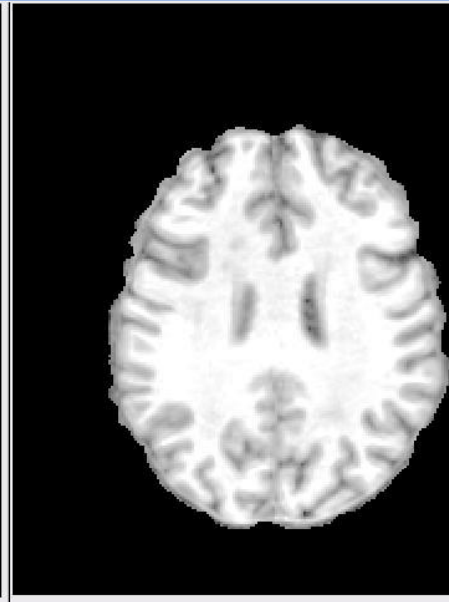
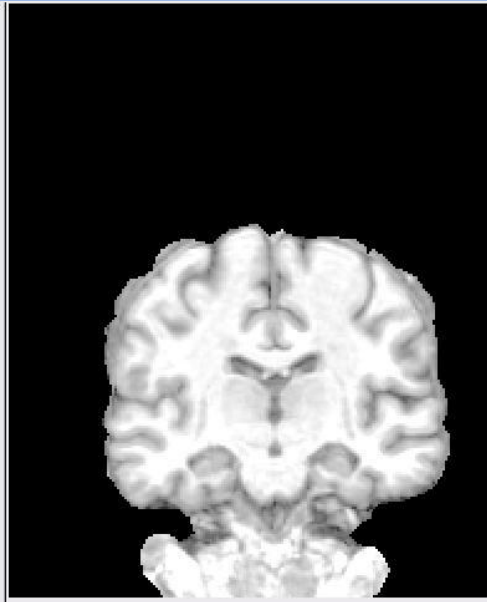
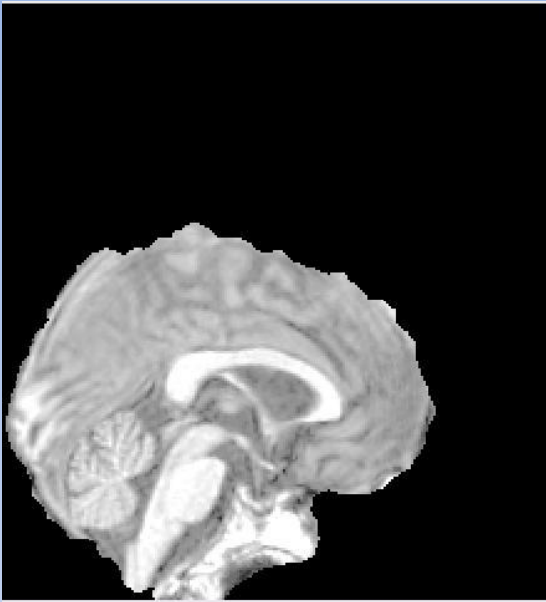


$f = 0.5$

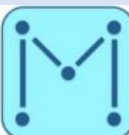
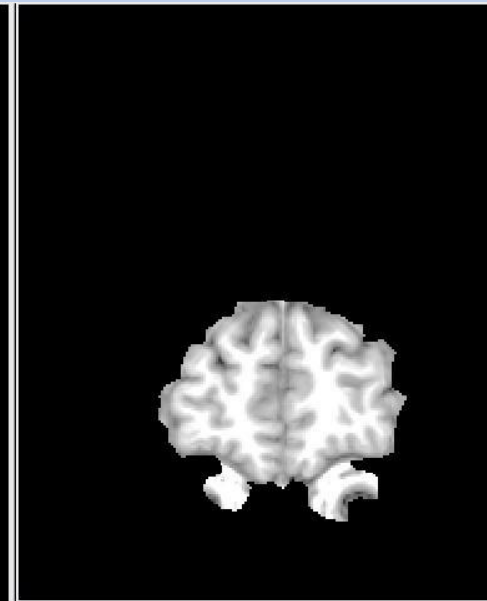
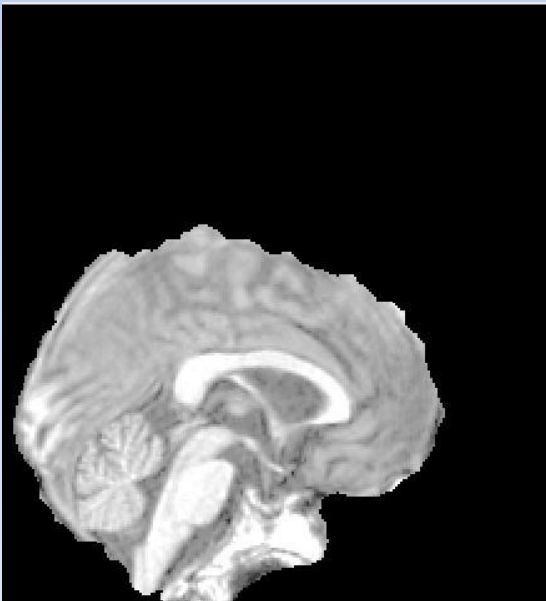


$f = 0.8$





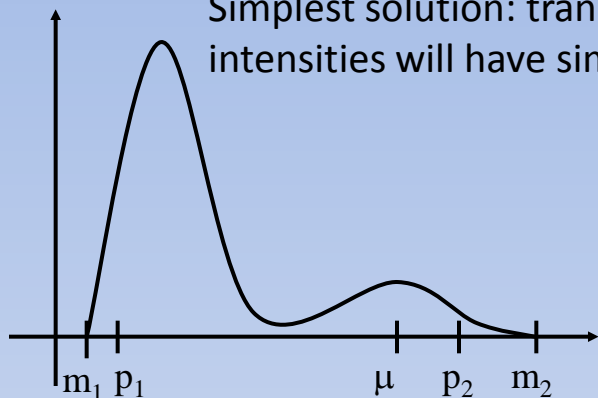
$f = 0.7$



# Histogram standardization

MRI intensities do not have a fixed meaning, not even within the same protocol for the same body region obtained on the same scanner for the same patient.

Simplest solution: transform image histograms by landmark matching, so that similar intensities will have similar tissue meaning.

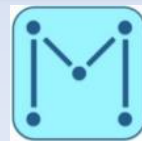
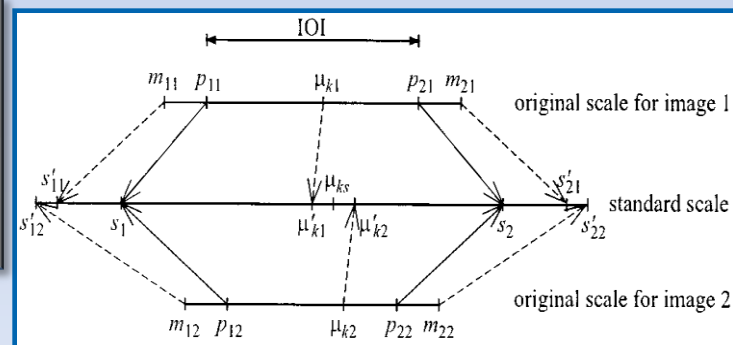


Let be  $pc_1$  and  $pc_2$  the minimum and the maximum percentile value that select a range of intensity of interest (IOI); and let  $s_1$  and  $s_2$  minimum and the maximum value on the standard scale for the IOI.

Consider the percentiles as landmarks  
( $\mu_{1j}, \mu_{2j}, \dots, \mu_{ij}$ )

**Training step:** the landmarks ( $p_{1j}, p_{2j}, \mu_{1j}, \mu_{2j}, \dots, \mu_{ij}$ ) are mapped to the standard scale by mapping the intensities from  $[p_{1j}, p_{2j}]$  to  $[s_1, s_2]$  linearly. then the means of the new mapped landmark locations are calculated.

$$x' = s_1 + \frac{x - p_{1j}}{p_{2j} - p_{1j}} (s_2 - s_1)$$



# OTHER METHODS FOR INTENSITY NORMALIZATION

## MIXTURE GAUSSIANS (MG)

Approximate the intensity histogram by a mixtures of Gaussians.  
Align the mean intensity by the parametric intensity Correction.

## KULLBACK-LEIBLER DIVERGENCE (KLD)

A multiplicative correction field adapts the intensity statistics to a previously created model.  
The parameter field is chosen in a way that the KLD between the model and the template intensity distribution is minimized.

## NON-RIGID REGISTRATION OF JOINT HISTOGRAMS

Find a deformation of the joint histograms of two sets of images with respect to a certain distance measure . If the probability density functions are considered as image, the normalization is treated as a registration problem.  
Adjust the image intensities of the MRI image series by the resulting non-linear correction function.

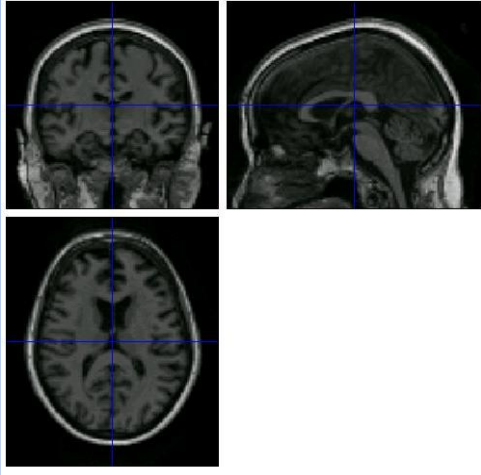
Method	Speed	Applicability	Accuracy
Landmarks	~2sec	average	good
MG	~5min	below average	average
KLD	~30min	average	good
Joint histograms	~1min	good	good



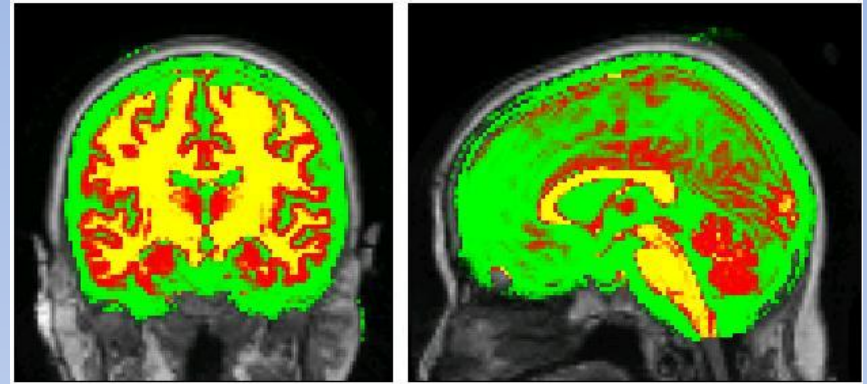
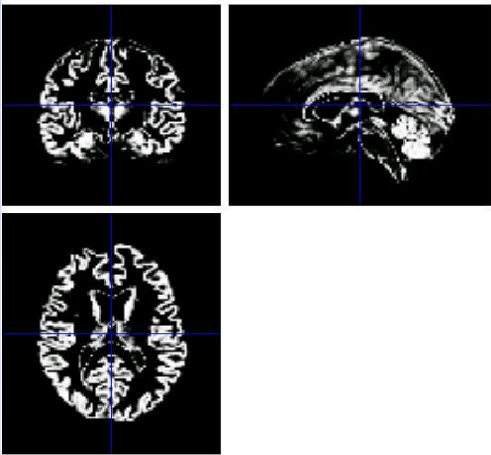


# SPM 8

Image normalized on ICBM 152



Segmentation - Gray Matter



Red -> Grey matter

Yellow -> White matter

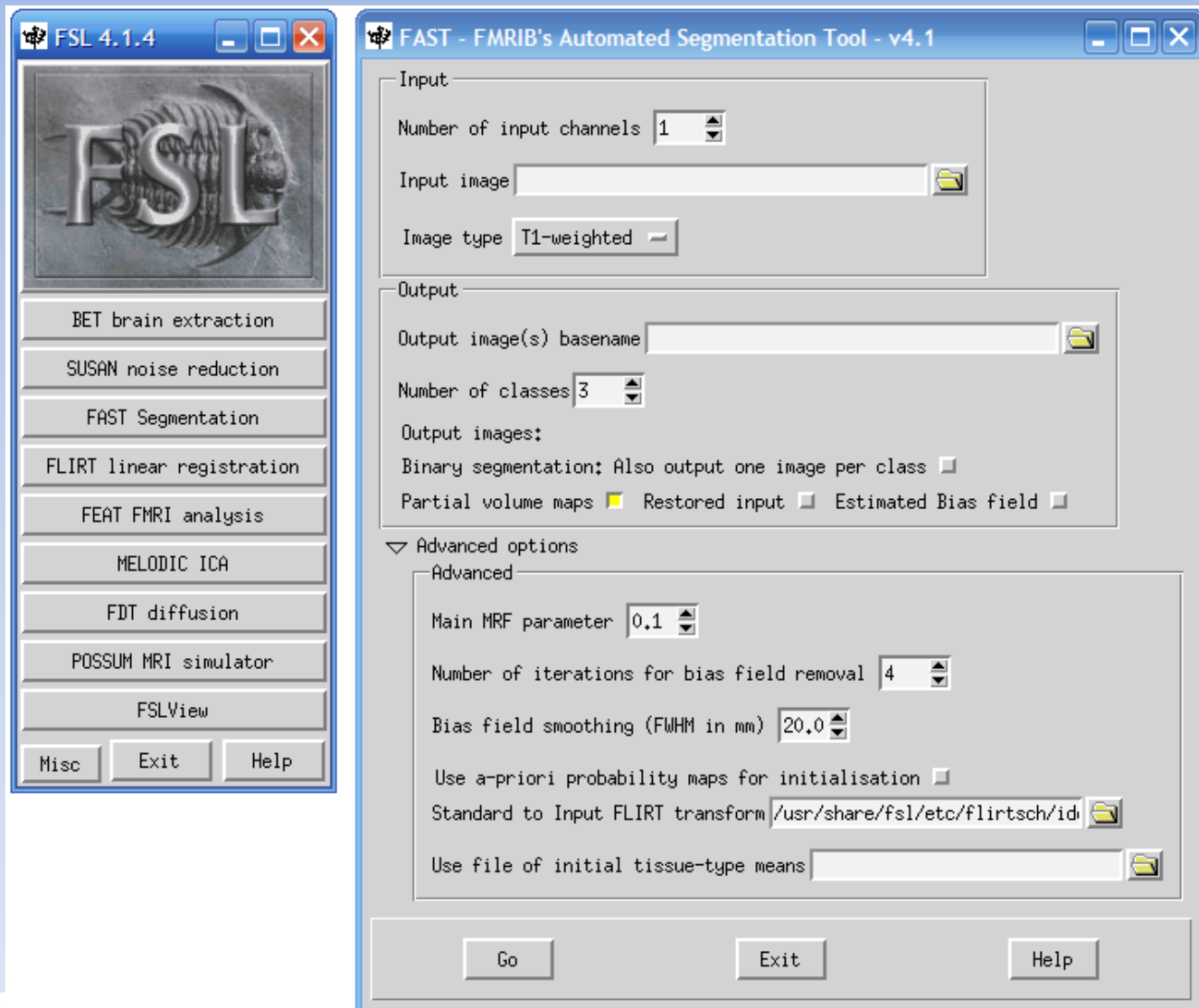
Green -> CSF

Operation whit SPM 8 on Image ADNI :

- Coregistration whit ICBM 152;
- Bias Corrected;
- Segmentation.



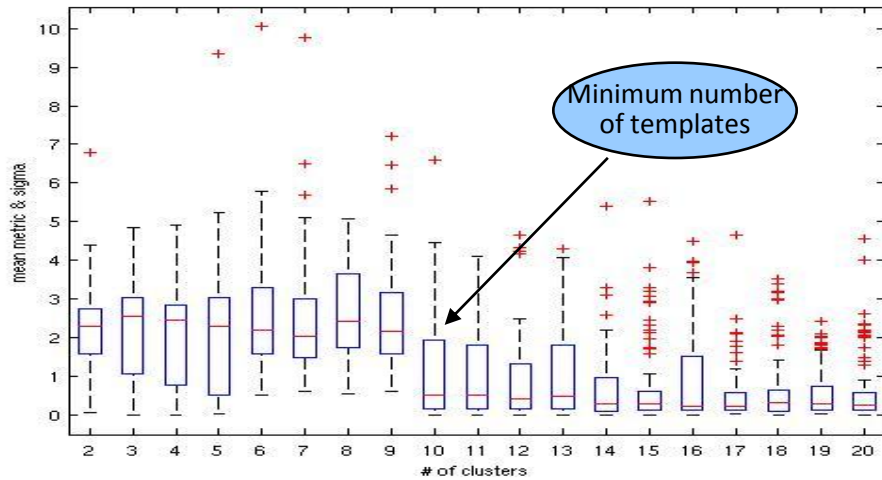
FAST (FMRIB's Automated Segmentation Tool): brain segmentation (into different tissue types) and bias field correction.



# Best K K-means Clustering

79 ADNI

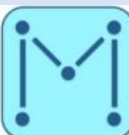
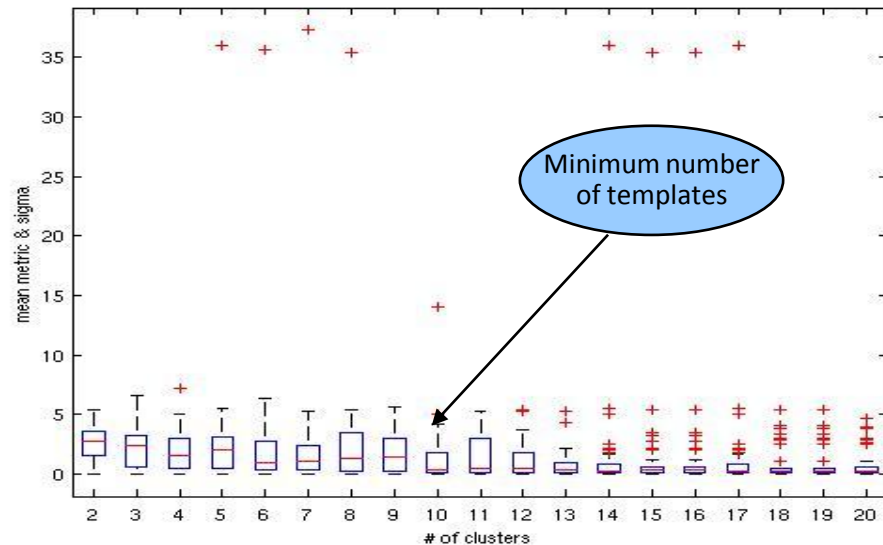
Exhaustive extraction (fourth Calvin's template), validation of clusterization results.



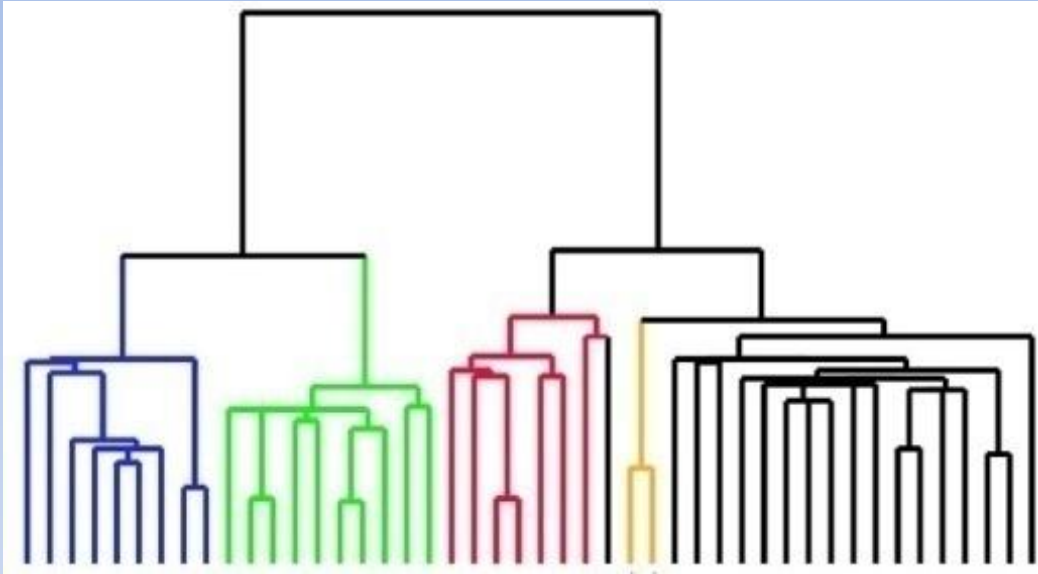
132 ADNI

Extraction error as a function of the number of clusters

The distance is calculated combining box angles and coordinates



# Hierarchical clustering



## Metrics:

Euclidean distance

Manhattan distance

Mahalanobis distance

## linkage:

Complete linkage

$$\max \{ d(a, b) : a \in A, b \in B \}.$$

Minimum or single linkage

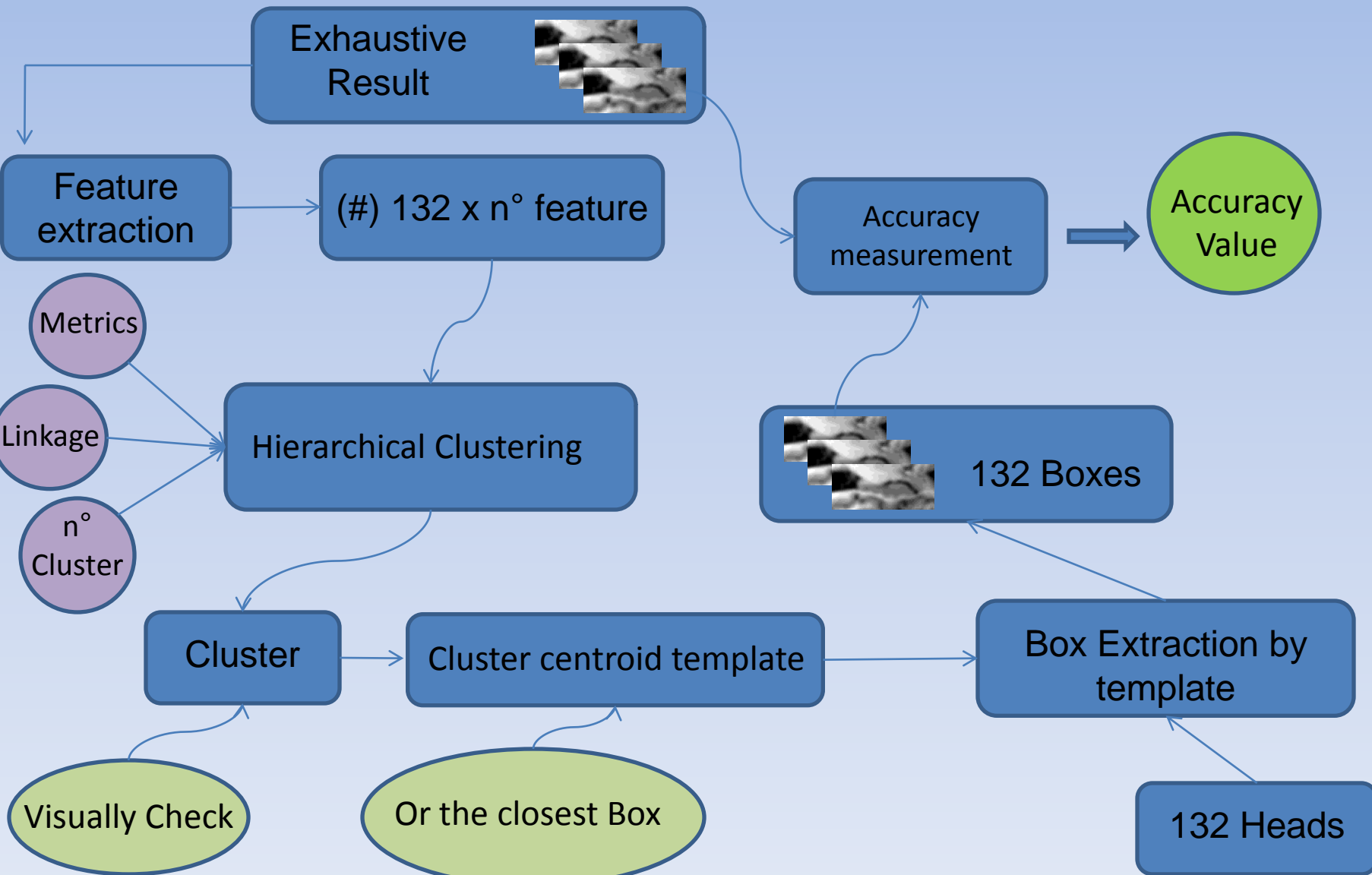
$$\min \{ d(a, b) : a \in A, b \in B \}.$$

Average linkage

$$\frac{1}{|A||B|} \sum_{a \in A} \sum_{b \in B} d(a, b).$$

Loop over possible metrics and linkages, each time getting a box-extraction accuracy value.

How to choose cluster representatives? virtual (Centroid) or real (element of clusters)





# Hierarchical clustering

Test on 132 boxes

```
distances = {'euclidean'; 'seuclidean'; 'cityblock'; 'minkowski'; 'cosine';  
            'correlation'; 'spearman'; 'hamming'; 'jaccard'; 'chebychev'};  
  
methods = {'single'; 'complete'; 'average'; 'weighted';  
          'centroid'; 'median'; 'ward'};
```

$C = \text{COPHENET}(Z, Y)$

If the clustering is valid, the linking of objects in the cluster tree should have a strong correlation with the distances between objects in the distance vector. The cophenet function compares these two sets of values and computes their correlation, returning a value called the cophenetic correlation coefficient. The closer the value of the cophenetic correlation coefficient is to 1, the better the clustering solution. Thus, it is a measure of how faithfully the tree represents the dissimilarities among observations.

% 0.931100 jaccard average

% 0.909639 jaccard single

% 0.908437 hamming average

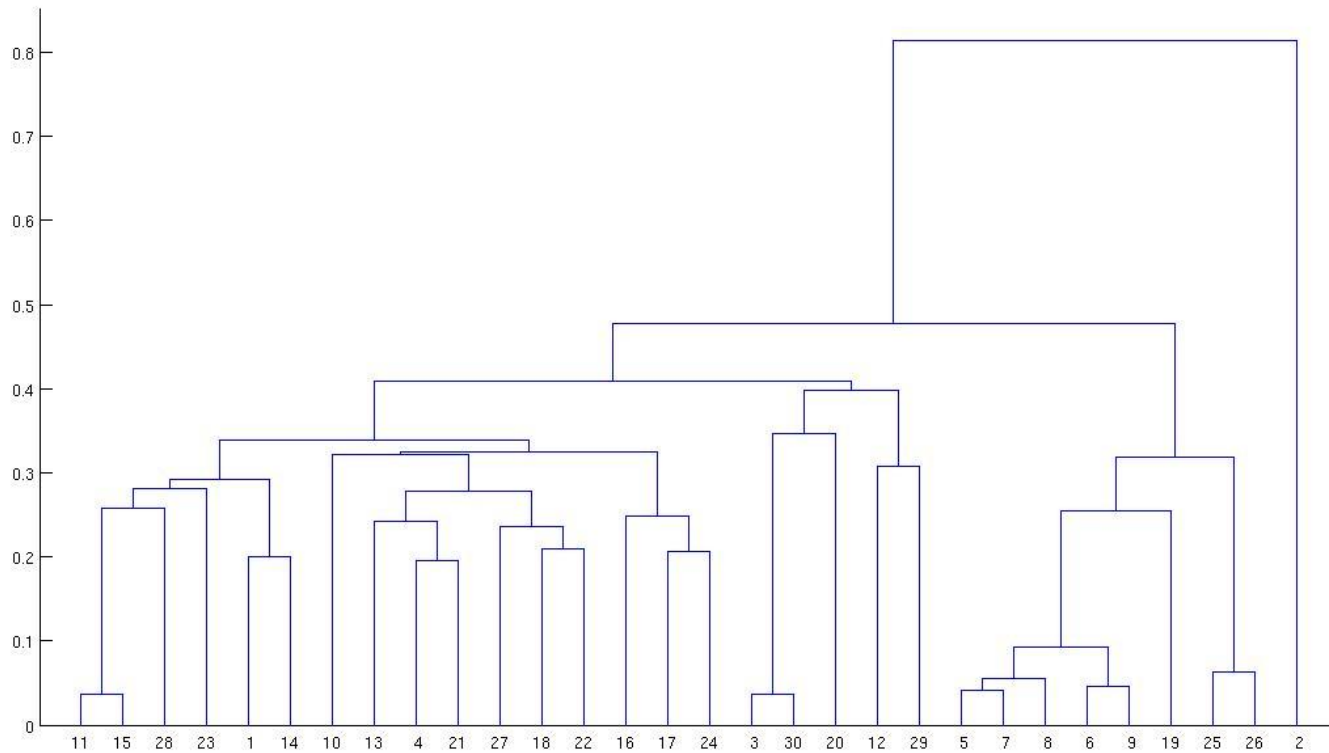
% 0.897070 correlation average

% 0.892561 spearman average

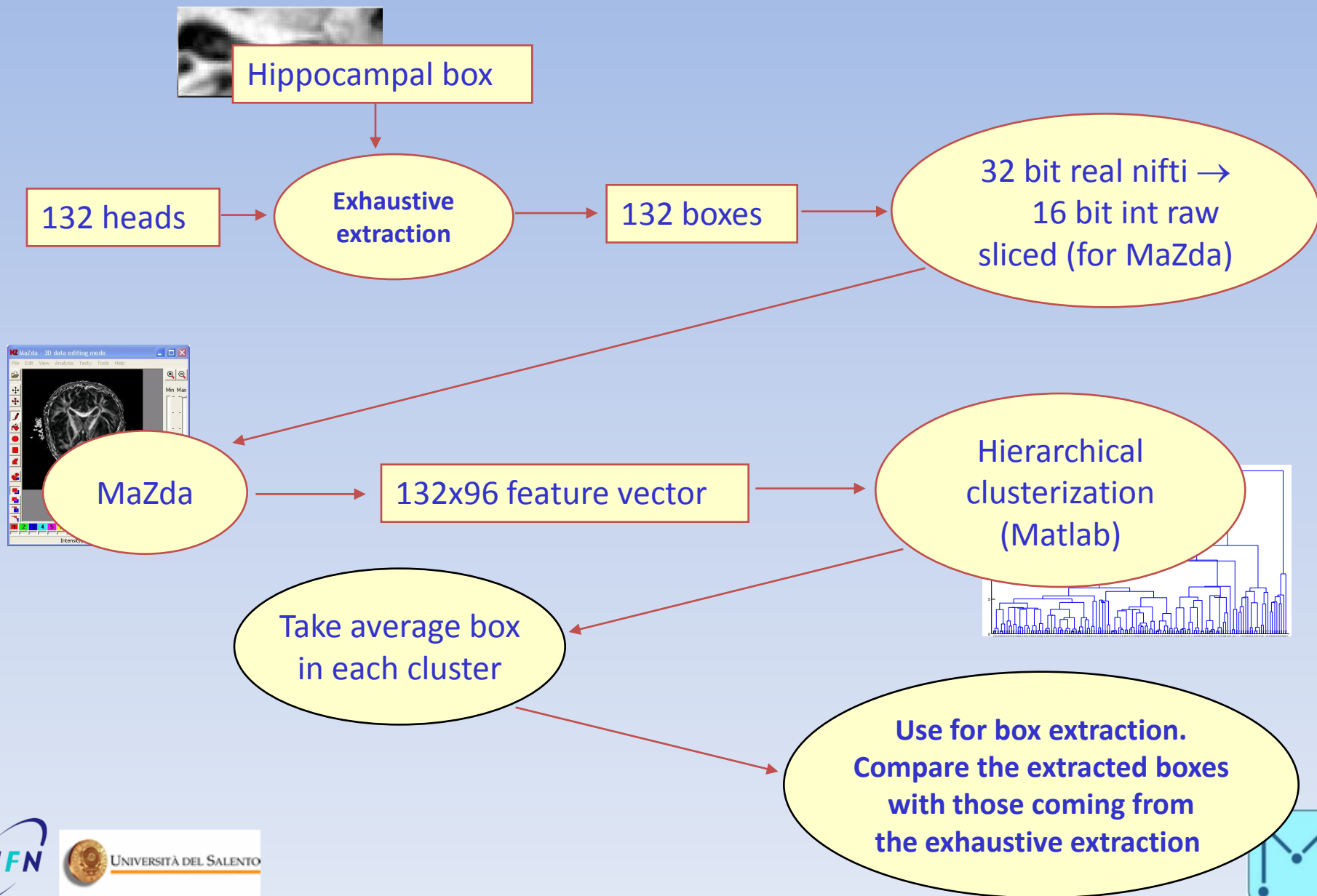
...

# Dendrogram obtained with jaccard distance and average linkage

132 ADNI



# Hierarchical clustering by texture features (MaZda/Matlab)



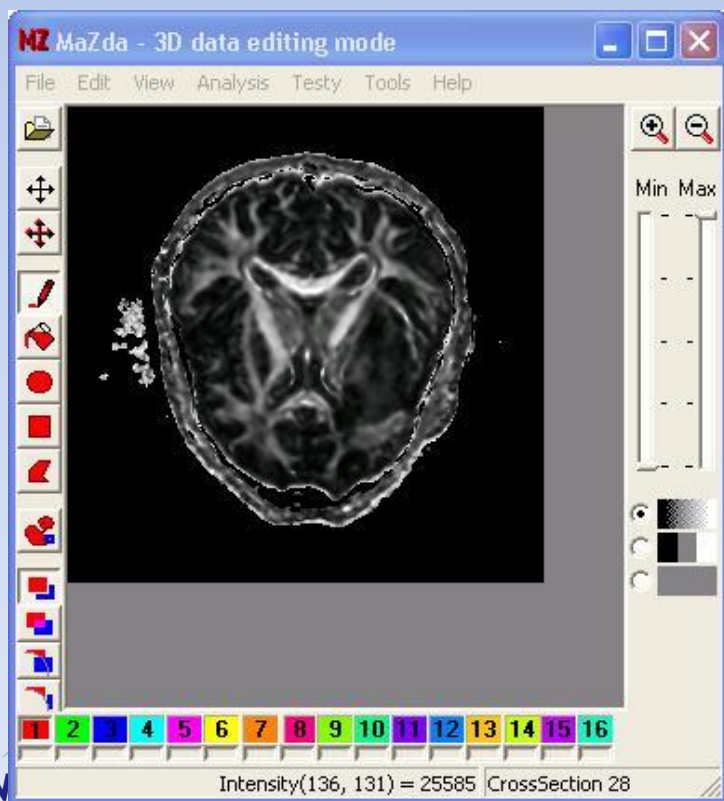
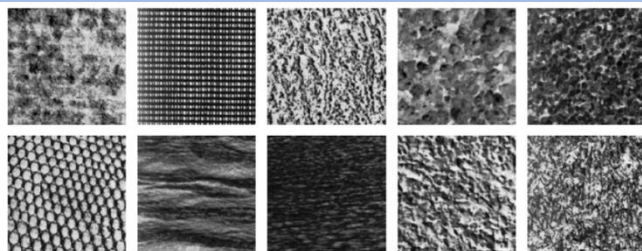
# Texture features: MaZda 4.6 for feature calculation

Statistical class: histogram

cooccurrence matrix

run-length matrix

absolute gradient



MZ Report

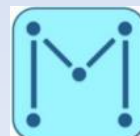
File Feature selection Tools

2006-1-24 13\_33\_32

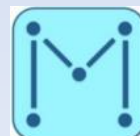
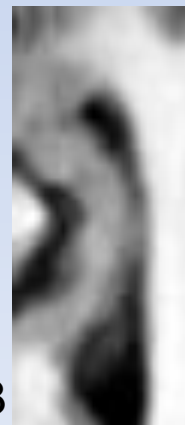
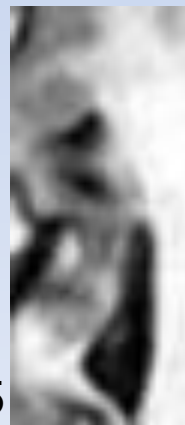
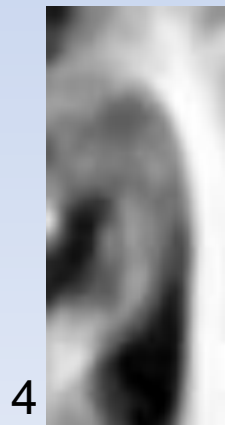
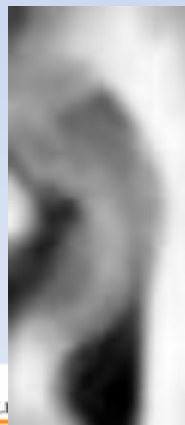
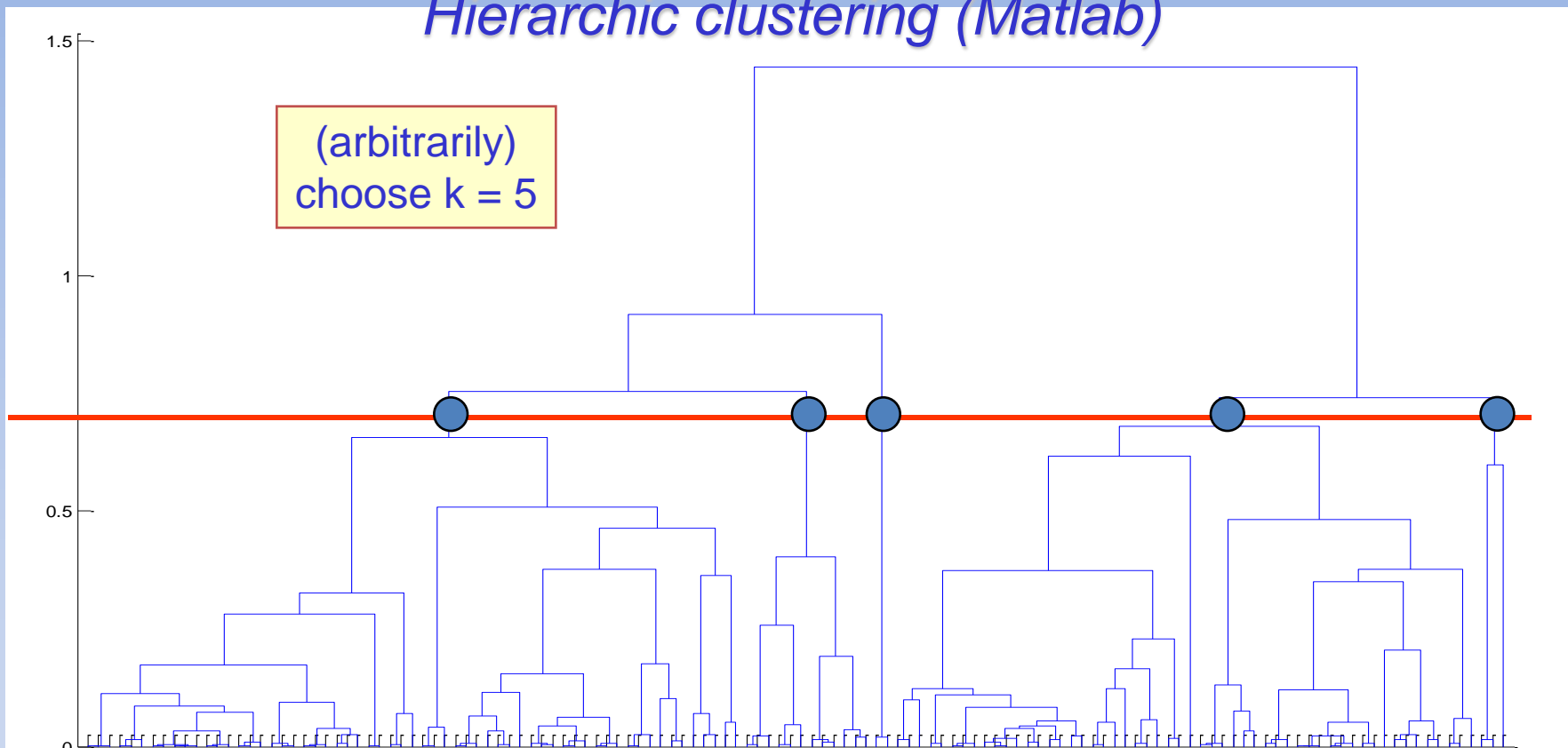
Image File: TEXT0324.IMA  
ROI File: newdraw.roi  
Image size: 256 x 256  
Min. lum.: 1  
Max. lum.: 1240  
Bits/pixel: 11

Normalisation = 3 sigma  
Histogram analysis = No  
CD matrix analysis = Yes, Dimensions = 6 x 6, Distances = 1 2  
RL matrix analysis = No  
Gradient analysis = No

Feature name	1	2	3	4	5
• _Area	2009	2009	2009	2009	0
• _MinNorm	844	917	920	-44	0
• _MaxNorm	1262	1120	1161	224	0
• _Area_S(1,0)	3916	3916	3916	3916	0
✓ S(1,0)AngScMom	0.0023138	0.0012696	0.0011695	0.0010423	0
✓ S(1,0)Contrast	111.26	168.72	183.72	154.75	0
✓ S(1,0)Correlat	0.40151	0.11395	0.074166	0.28962	0
✓ S(1,0)SumOfSqs	92.952	95.206	99.218	108.92	0
✓ S(1,0)InvDfMom	0.151	0.10729	0.089699	0.10168	0
✓ S(1,0)SumAverg	64.985	64.484	64.497	64.555	0
✓ S(1,0)SumVanc	260.55	212.11	213.15	280.93	0
✓ S(1,0)SumEntrp	1.7154	1.7537	1.7586	1.8173	0
✓ S(1,0)Entropy	2.8212	3.0052	3.0375	3.0704	0



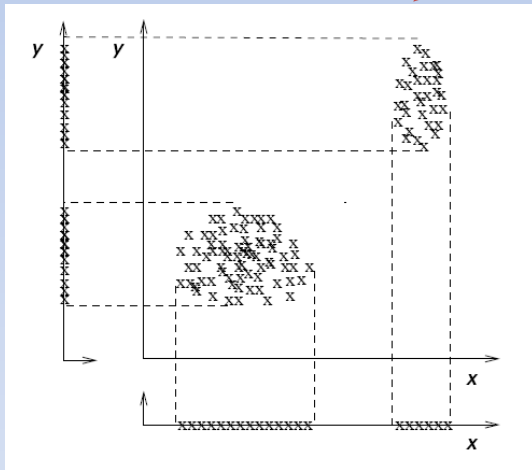
# Hierarchical clustering (Matlab)



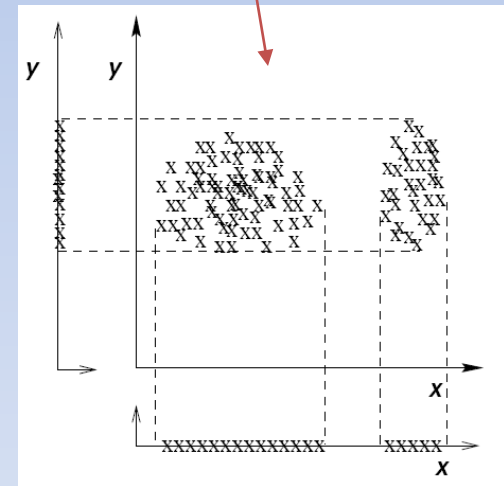


# May feature redundancy mislead clustering?

1. In unsupervised learning, we are not given class labels. Which features should we keep? Why not use all the information we have?
2. Some of the features may be redundant, some may be irrelevant, and some can even misguide clustering results (especially when there are more irrelevant features than relevant ones)
3. Select the most “interesting” subspace with the minimum number of features



x, y are redundant



y is irrelevant

Dy & Brodley, “Feature Selection for Unsupervised Learning”  
Journal of Machine Learning Research 5 (2004) 845–889

# Conclusions

- |  |  |
|--|--|
| 1. Descalping (Done)                     | BET or SPM ???   |
| 2. Histogram Normalization (in progress) | Atlas Segmentation + Histogram Standardization (percentile method) |
| 3. Hierarchical Clustering (checking)    | Automatic software in progress                                     |
| 4. Best K (in progress)                  |  |

## Suggestions

Check of head population

Medical classification of our boxes

Other possible methods to calculate the distance: exhaustive extraction vs template extraction

# Haralick texture features

$$AngScMom = \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i, j)^2$$

$$Contrast = \sum_{n=0}^{N_g-1} n^2 \sum_{\substack{i=1 \\ |i-j|=n}}^{N_g} \sum_{j=1}^{N_g} p(i, j)$$

$$Entropy = - \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i, j) \log(p(i, j))$$

$$DifEntrp = - \sum_{i=1}^N p_{x-y}(i) \log(p_{x-y}(i))$$

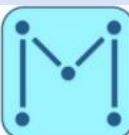
$$SumEntrp = - \sum_{i=1}^{2N} p_{x+y}(i) \log(p_{x+y}(i))$$

IMAGE				
0	0	0	0	0
4	1	6	4	2
3	1	3	2	7
5	1	2	7	7
4	2	7	7	7

COM								
	0	1	2	3	4	5	6	7
0	6	0	0	0	0	0	0	0
1	0	0	1	0	1	0	0	1
2	0	1	0	0	0	1	1	2
3	0	0	0	2	0	0	0	1
4	0	1	0	0	0	0	1	1
5	0	0	1	0	0	0	0	0
6	0	0	1	0	1	0	0	0
7	0	1	2	1	1	0	0	2

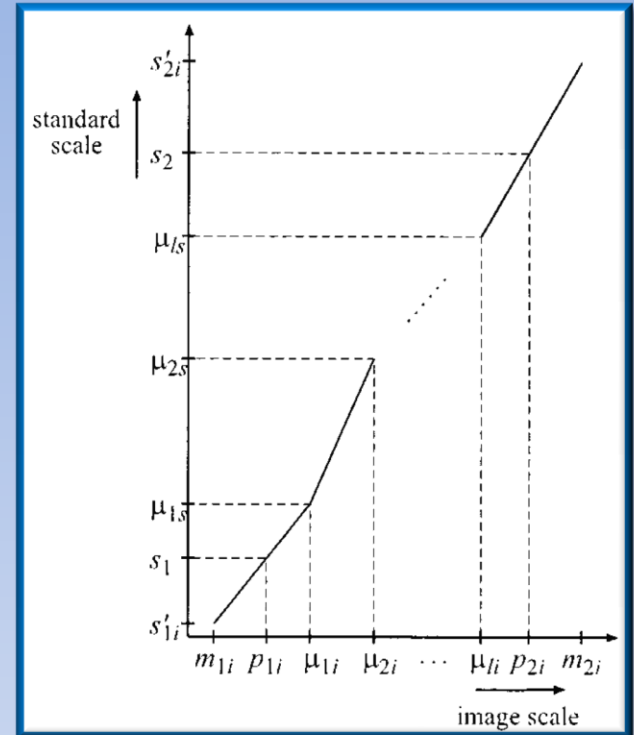
$$SumAverg = \sum_{i=1}^{2N} ip_{x+y}(i)$$

$$p_{x+y}(k) = \sum_{i=1}^N \sum_{\substack{j=1 \\ i+j=k}}^N p(i, j)$$

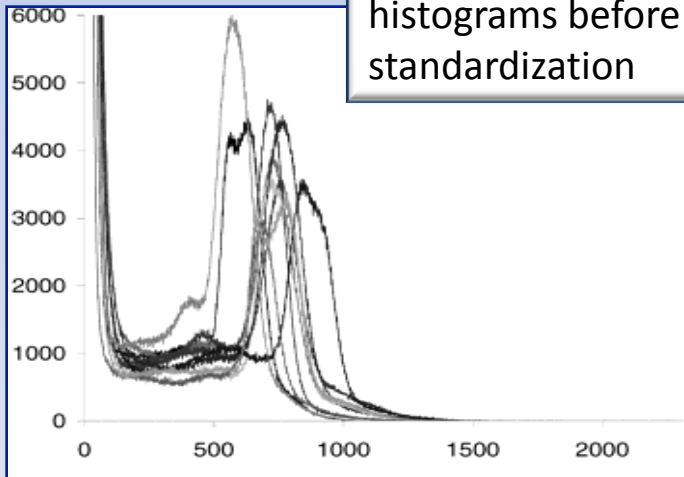


**Trasformation step:** for any image the actual landmark location  $\mu_{ks}$  are matched to  $\mu_{ks}$  by doing several separate linear mapping.

$$\tau_{V_i} = \begin{cases} \left[ \mu_{ks} + (x - \mu_i) \frac{s_1 - \mu_{ks}}{p_{1i} - \mu_i} \right] & \text{if } m_{1i} \leq x \leq \mu_{ki} \\ \left[ \mu_{ks} + (x - \mu_i) \frac{s_2 - \mu_{ks}}{p_{2i} - \mu_i} \right] & \text{if } \mu_{ki} \leq x \leq m_{2i} \end{cases}$$



histograms before standardization



histograms after standardization

