Centre for Medical Image Computing

SEGMENTATION PART II, COMPUTATIONAL MODELLING & IMAGING BIOMARKER EXTRACTION

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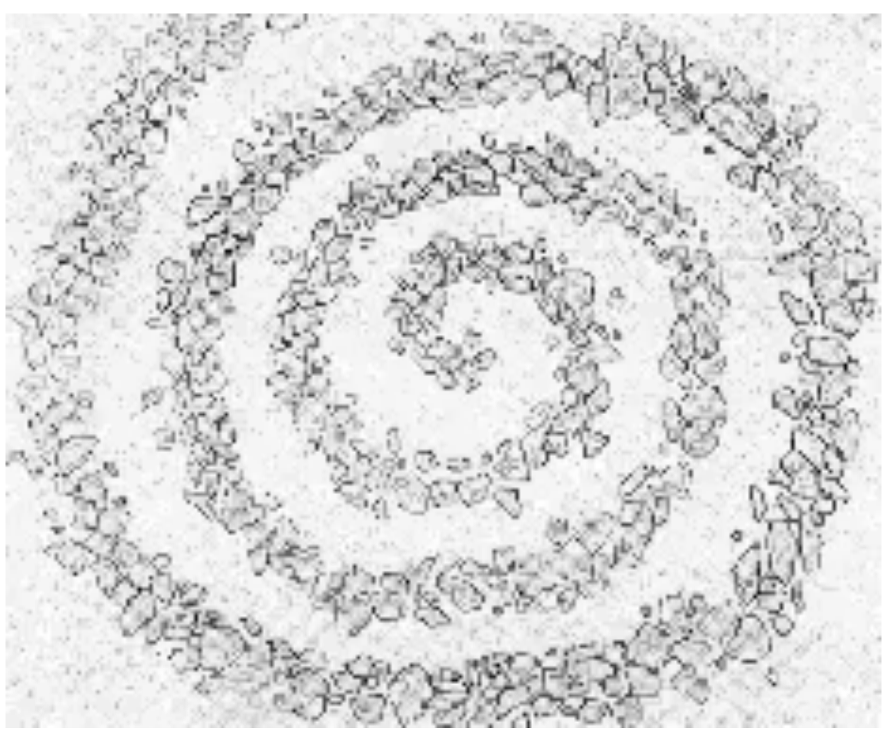
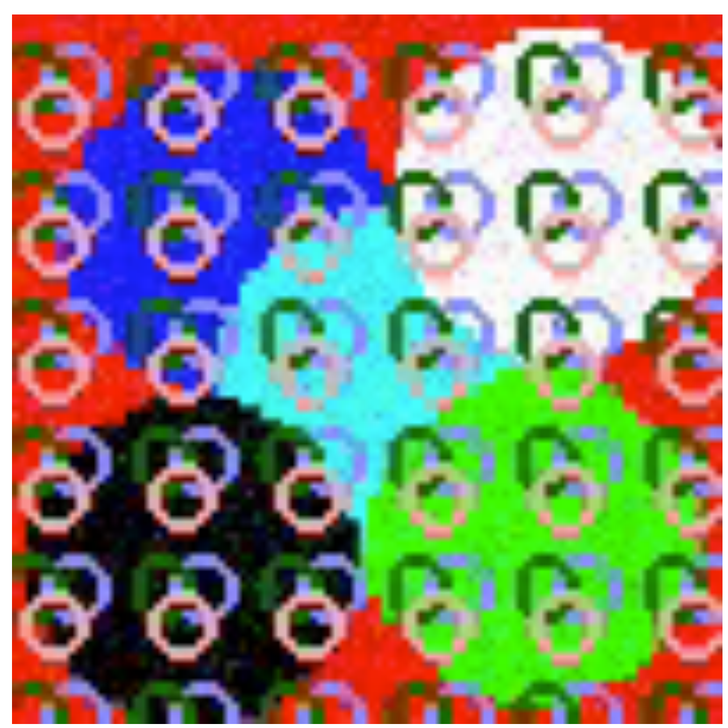
- Segmentation II
  - Level Sets
  - Label Fusion
- Computational neuroanatomy/Biomarker extraction
  - Cross-sectional
    - Groupwise
    - VBM/TBM
    - CTE
  - Longitudinal
    - Atrophy (Volume/BSI)
  - DTI ROI analysis

LEVEL SETS

Level Set Method

- Contour evolution method
- Initially proposed by J. Sethian and S. Osher, 1988
- Problems with “snake-type” methods
  - Self-intersection
  - Changes in topology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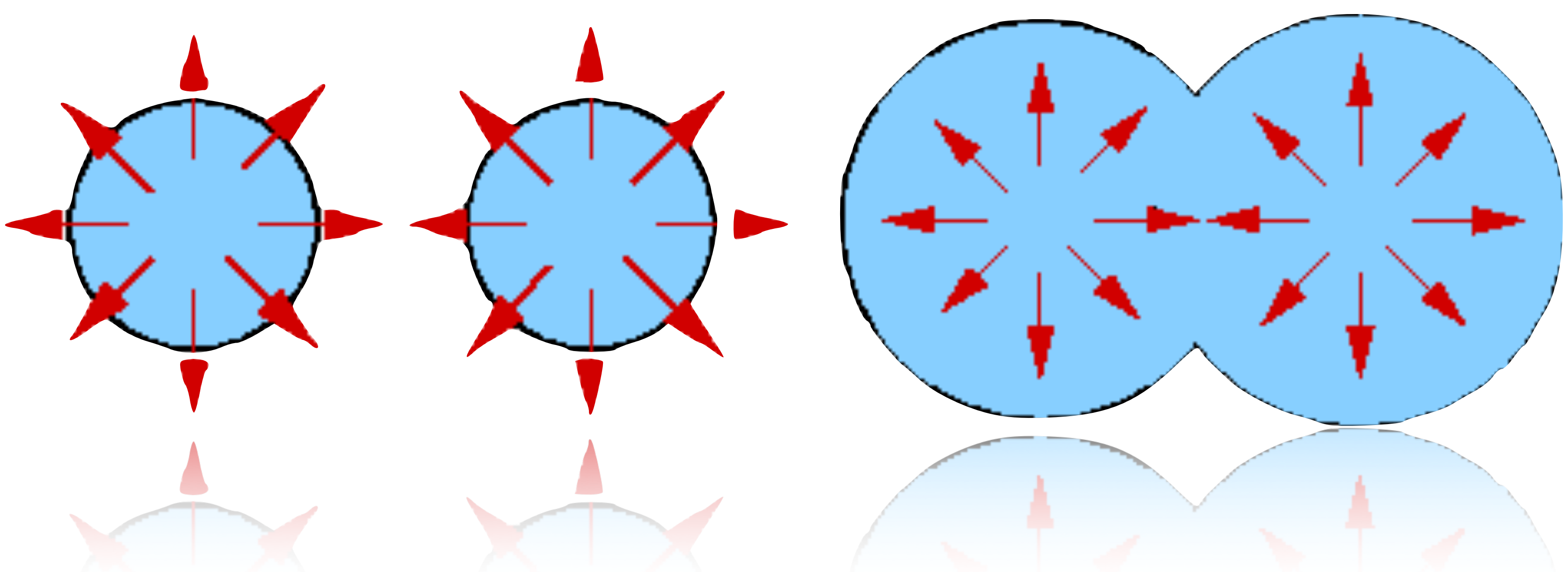
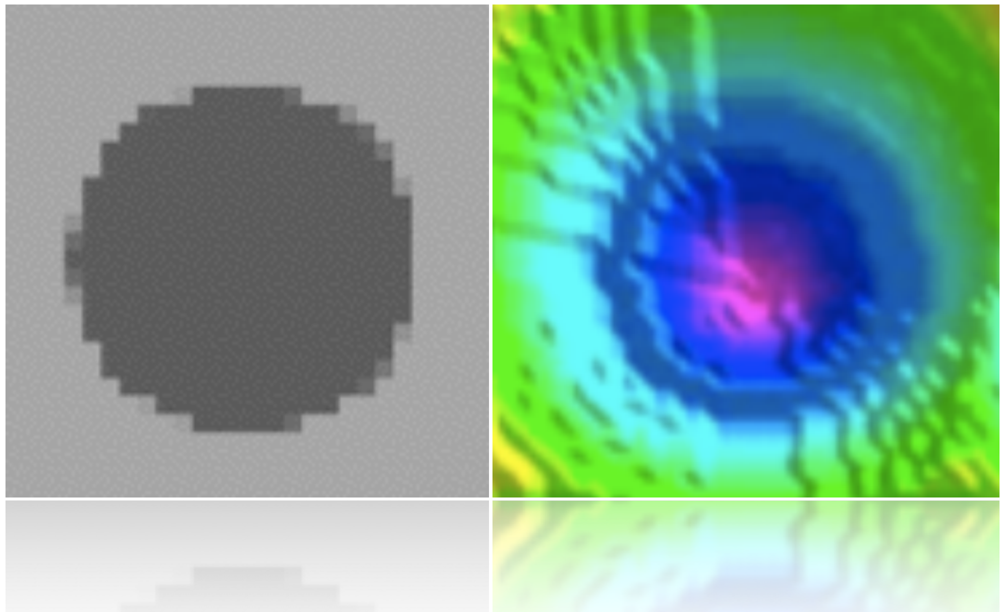


Level Set Method

- Define problem in “1 dimension above” the dimensionality of the problem
  - 2D problem → 3D Level set formulation
  - 3D problem → 4D Level set formulation

- Define level set function $z=(x,y,t=0)$
  - Where the (x,y) plane contains the contour,
  - z = e.g. signed Euclidean distance transform value



Level Sets - Some Maths

- Represents the curve in the form of an implicit surface:

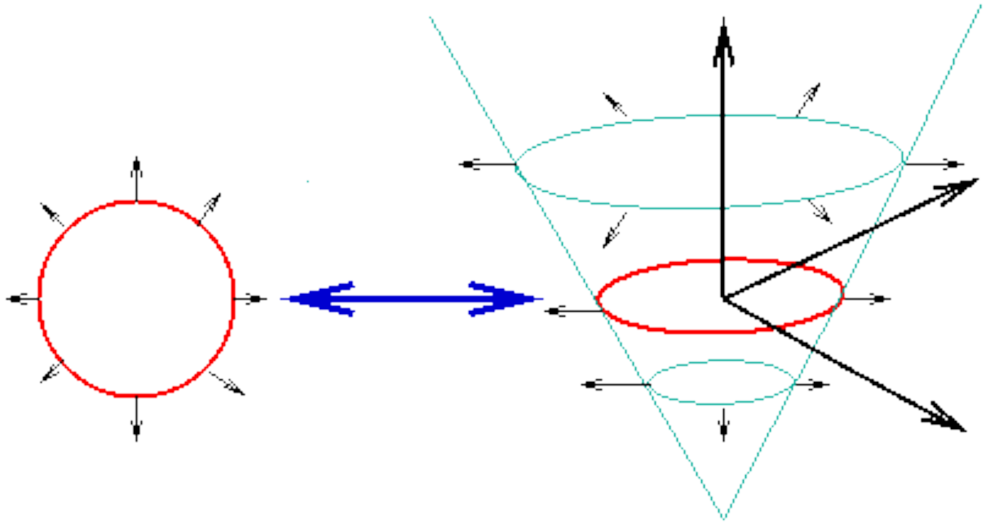
$$T(x,y) = t \qquad\qquad \phi(x,y,t)$$

- The initial contour gives the level set "starting conditions"

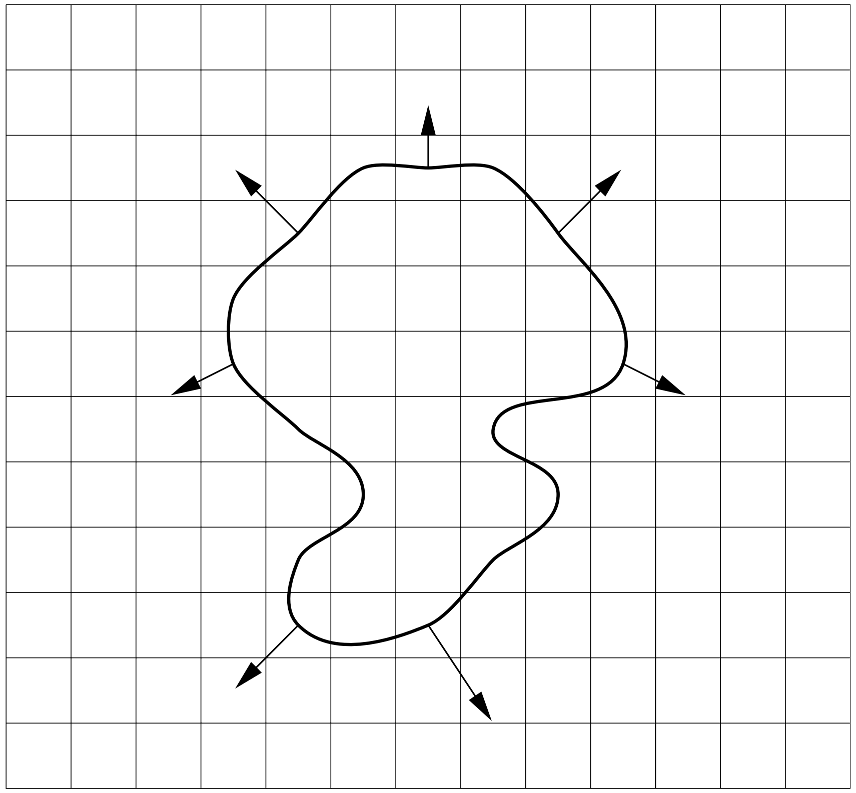
$$\Gamma(t) = \{(x,y) | T(x,y) = t\}$$

$$\Gamma(t) = \{(x,y) | \phi(x,y,t) = 0\}$$

$$z = r^2 = x^2 + y^2$$



Boundary Value Formulation - Fast Marching Method



- Speed has to be positive F>0
- Front always move in one direction:
  - "outwards" or "inwards"
- The position of the advancing front is computed by the arrival time *T(x,y) at each (x,y) position*
- *distance=rate*time*

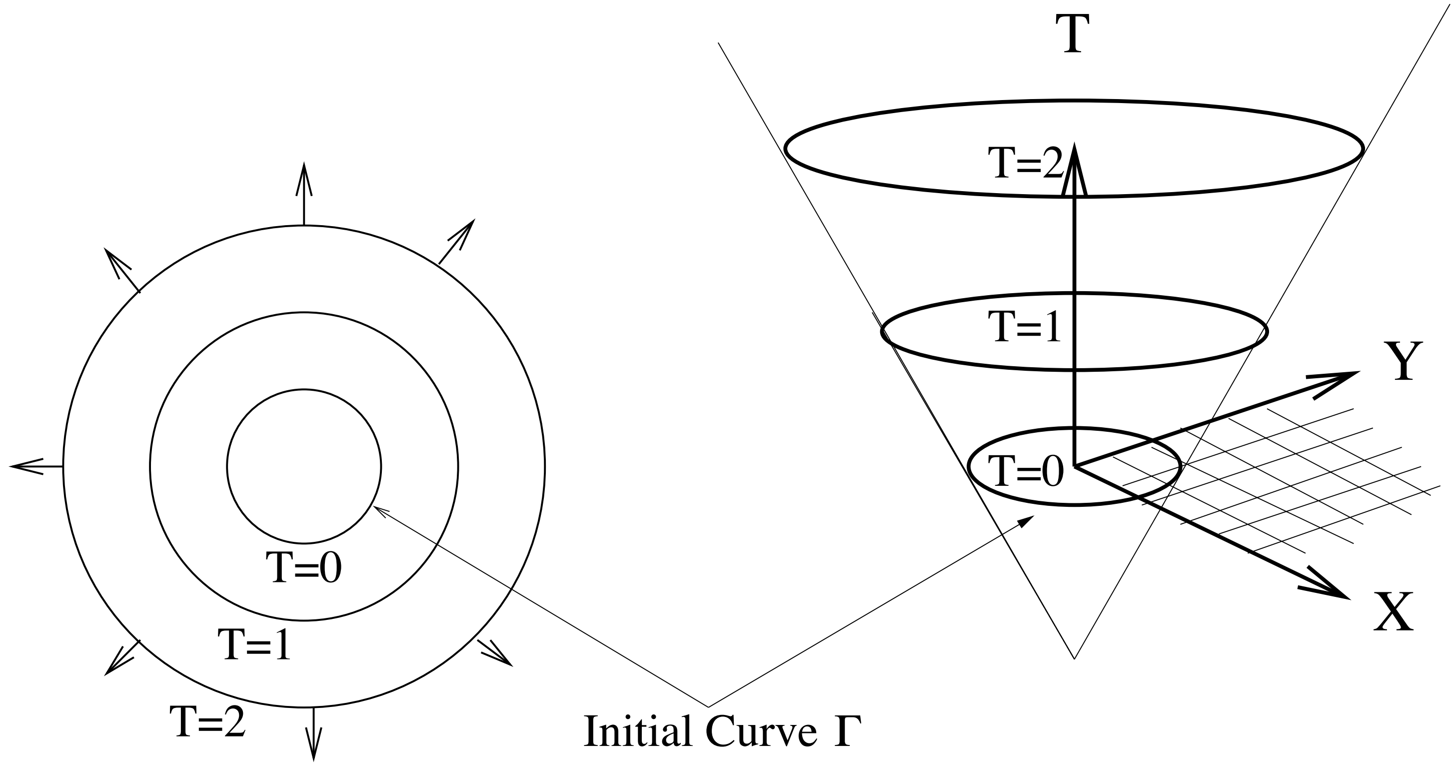
$$1 = F\,\frac{dT}{dx}.$$

$$|\nabla T|F = 1, \qquad\qquad T = 0 \text{ on } \Gamma,$$

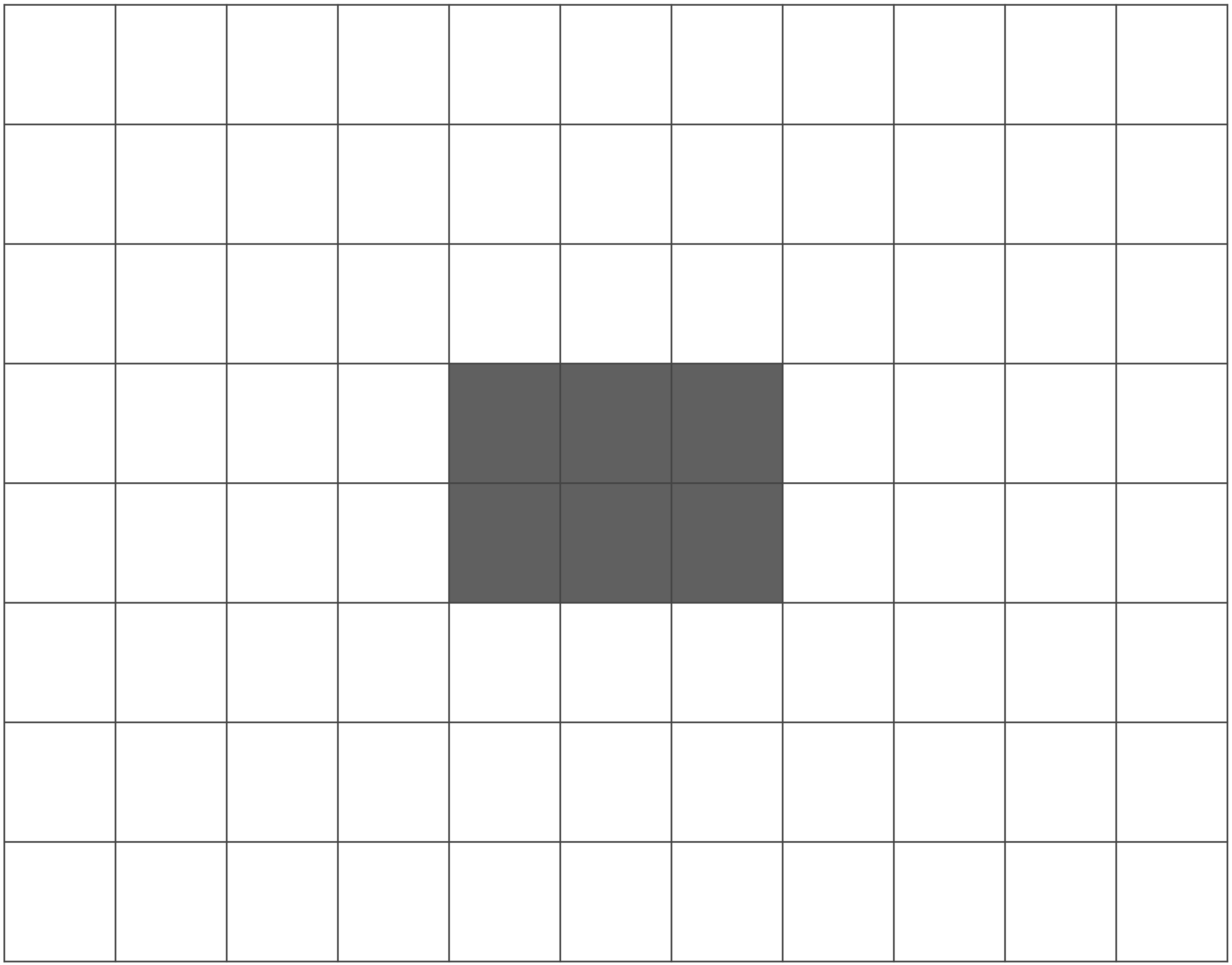
- *with* ∇T *orthogonal to the level set*

Boundary Value Formulation - Fast Marching Method

$$\begin{bmatrix} \max(D^{-x}_{ijk}T, -D^{+x}_{ijk}T, 0)^2 \\ +\max(D^{-y}_{ijk}T, -D^{+y}_{ijk}T, 0)^2 \\ +\max(D^{-z}_{ijk}T, -D^{+z}_{ijk}T, 0)^2 \end{bmatrix}^{1/2} = \frac{1}{F_{ijk}}$$

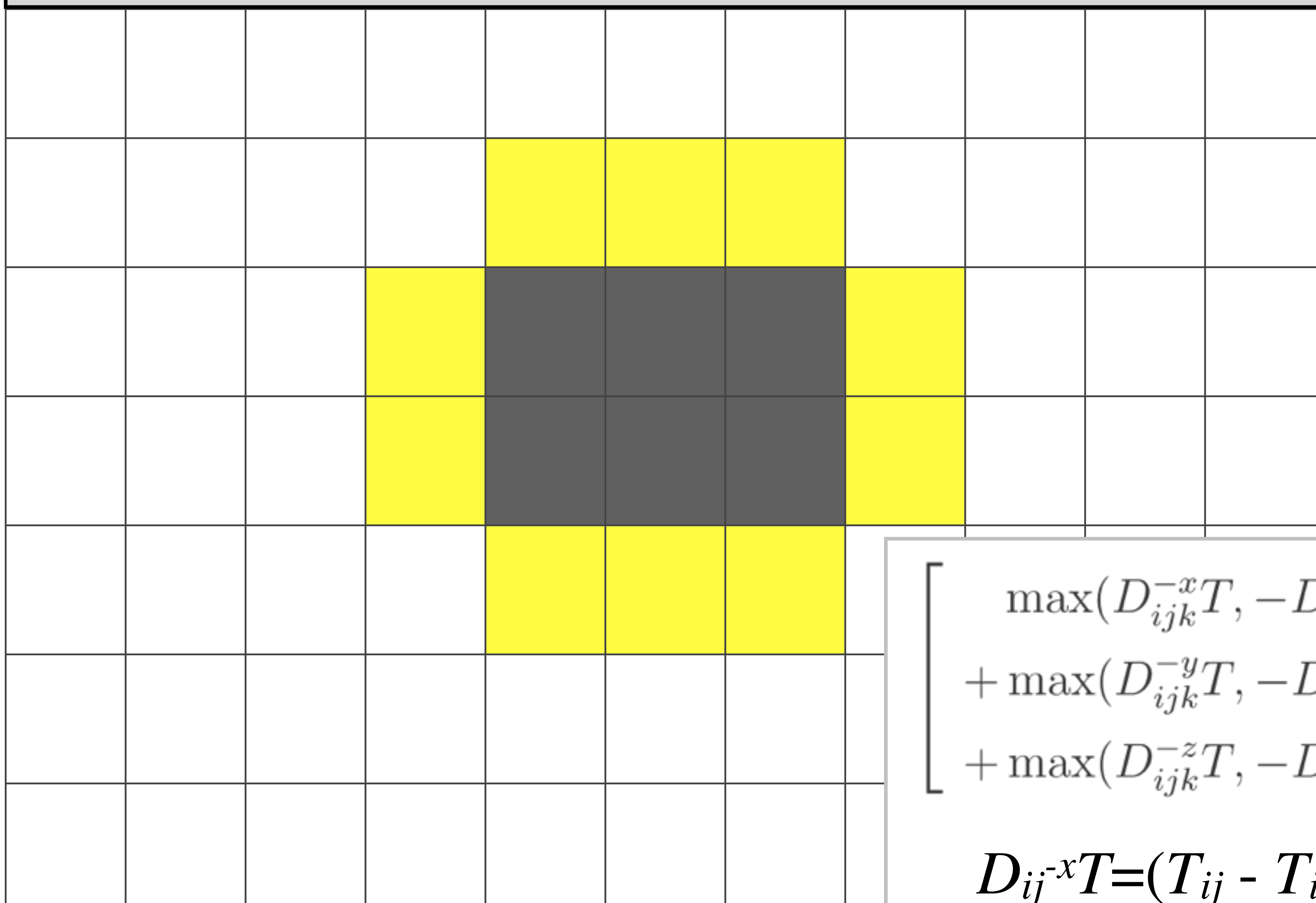


Fast Marching Method - implementation



Fast Marching Method - implementation

Solve Eikonal equation for the yellow voxels

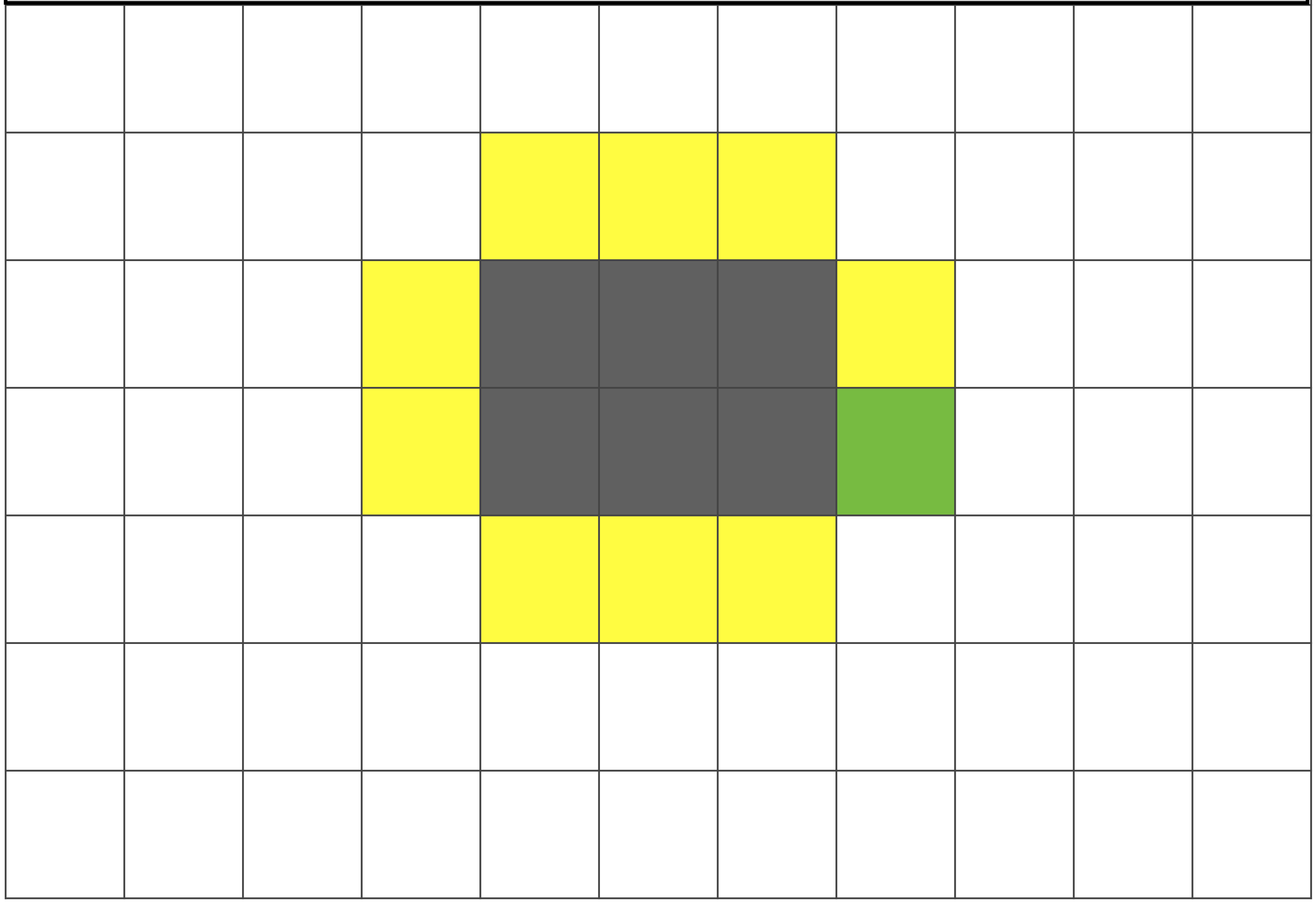


$$\left[\begin{array}{c} \max(D^{-x}_{ijk}T, -D^{+x}_{ijk}T, 0)^2 \\ +\max(D^{-y}_{ijk}T, -D^{+y}_{ijk}T, 0)^2 \\ +\max(D^{-z}_{ijk}T, -D^{+z}_{ijk}T, 0)^2 \end{array}\right]^{1/2} = \frac{1}{F_{ijk}}$$

$$D_{ij}^{-x}T = (T_{ij} - T_{i-1,j})/(x_i - x_{i-1})$$

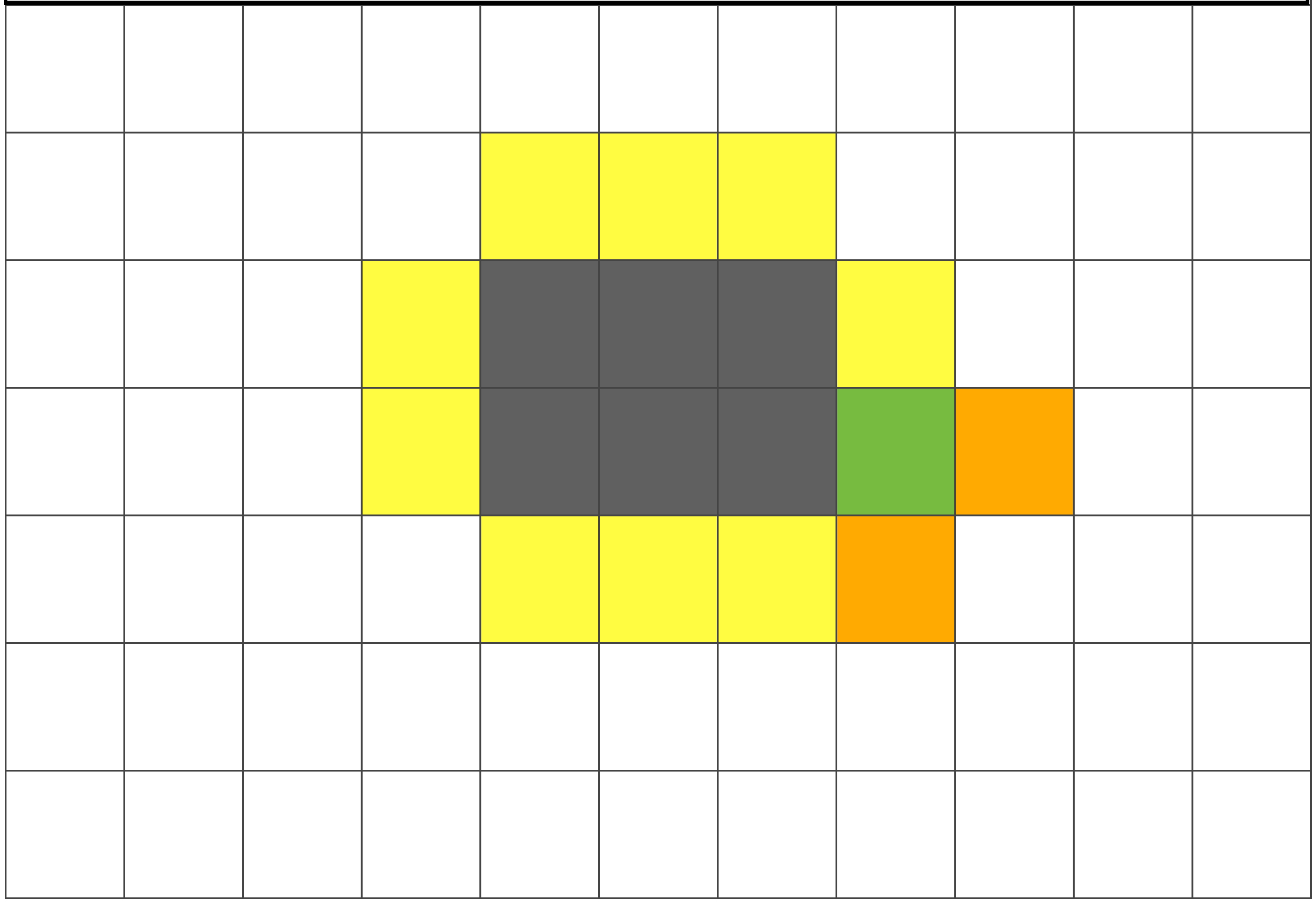
Fast Marching Method - implementation

When one voxel is calculated, add its neighbours to the cue and mark them as “NarrowBand”



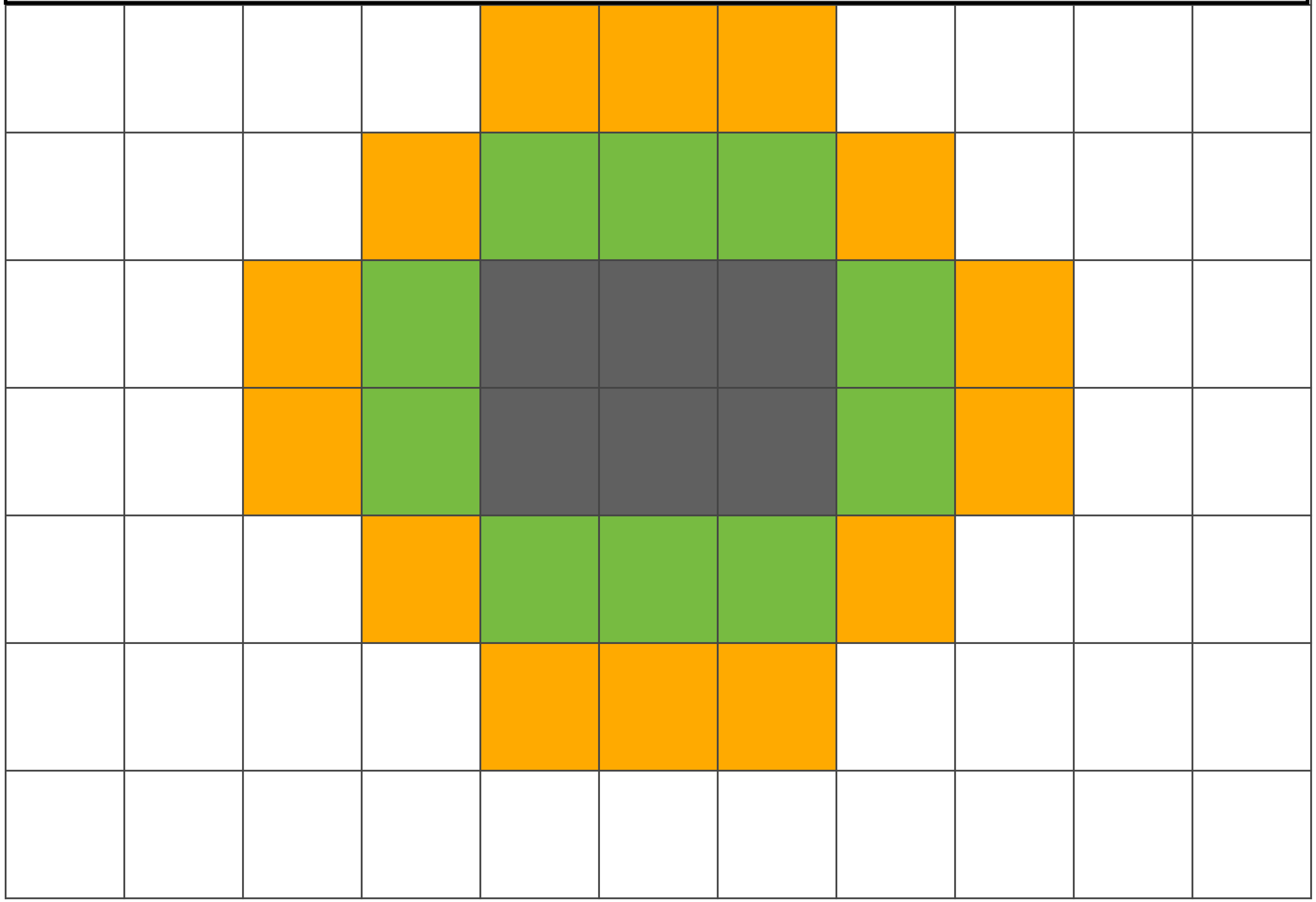
Fast Marching Method - implementation

Orange voxels are marked as “NarrowBand” and the green voxel is marked as “Solved”



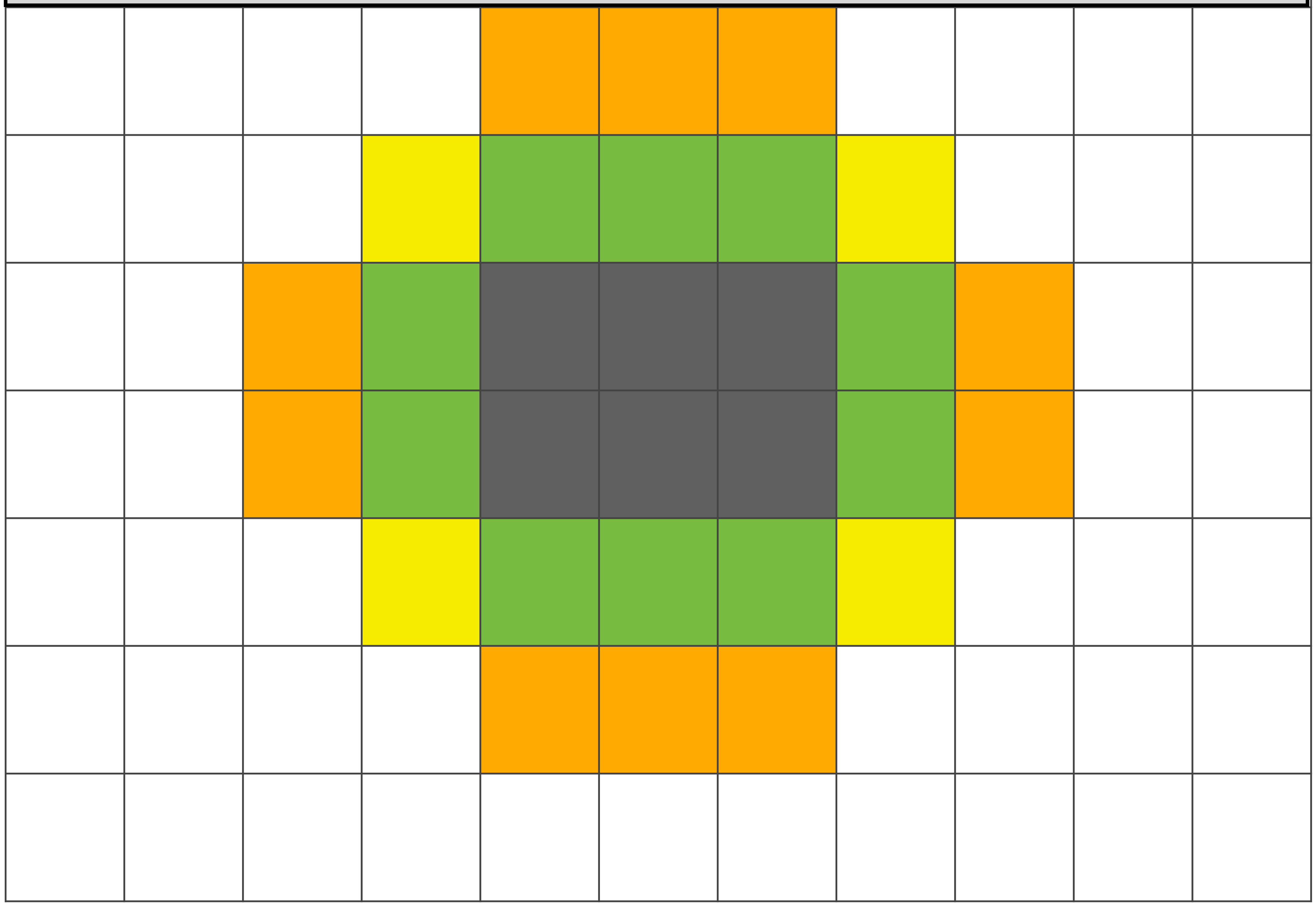
Fast Marching Method - implementation

Solve all the yellow voxels and add all their neighbours to the "NarrowBand" list



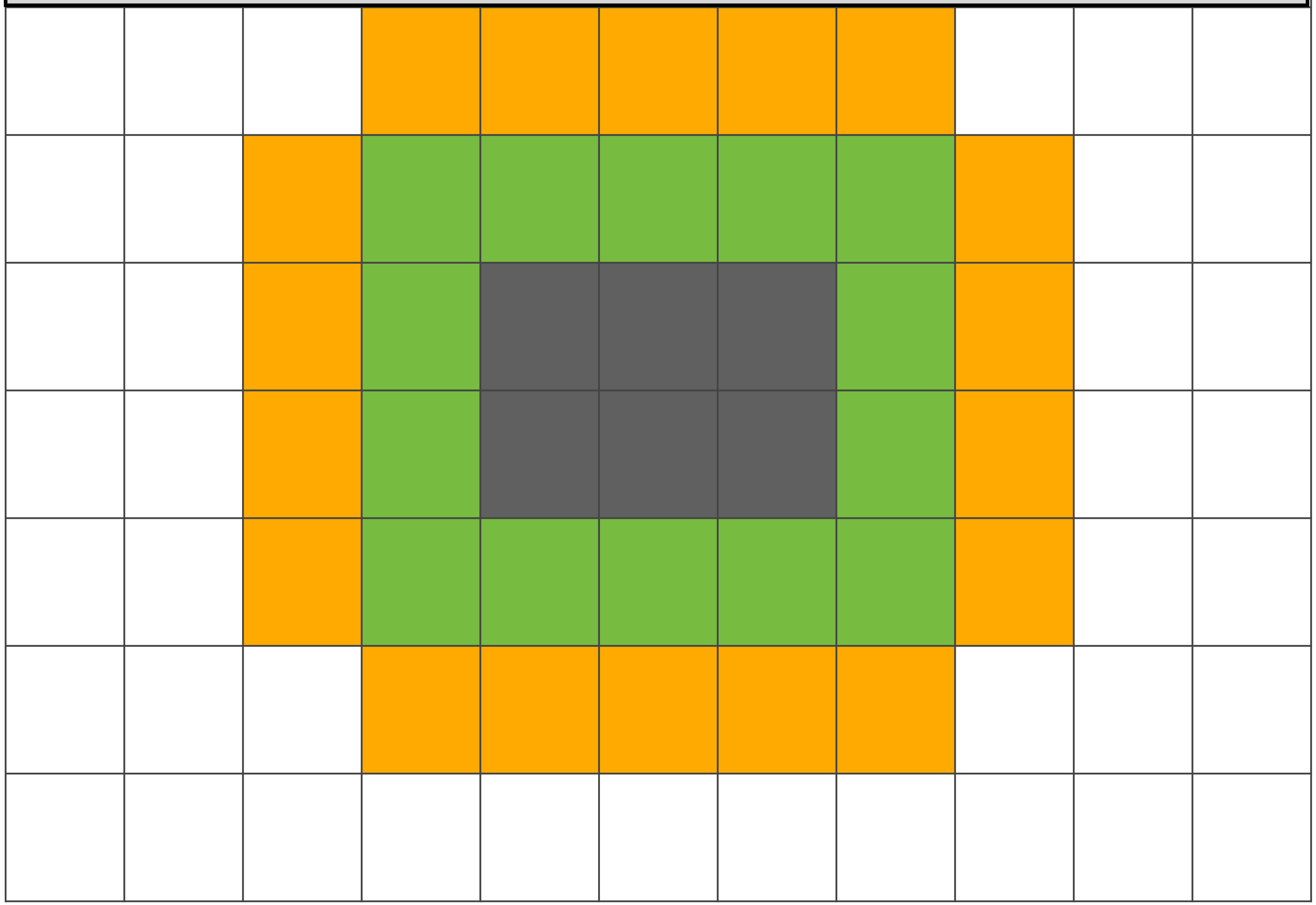
Fast Marching Method - implementation

Solve the “NarrowBand” list.
Select the ones with the smaller T and mark them as “Alive”



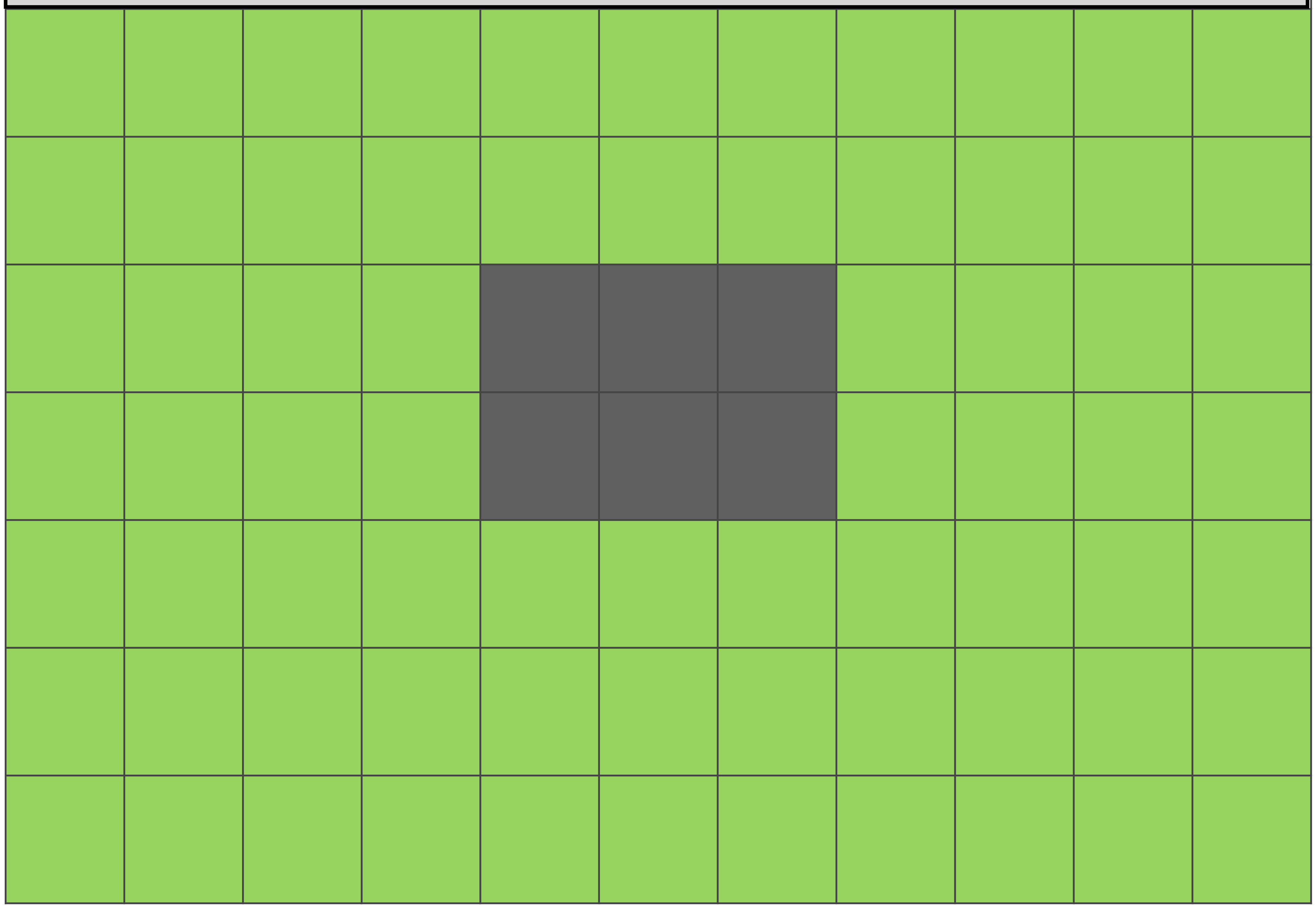
Fast Marching Method - implementation

And add their neighbours to the “NarrowBand” list.
Mark them as “Solved”.



Fast Marching Method - implementation

Keep on doing it until all are marked as solved



Fast Marching Method - Step by Step

- **Initialise Step**

  Alive Points: Let A be the set of all grid points $\{i_A, j_A\}$ the represents the initial curve;

  Narrow Band: Let *NarrowBand* be the set of all grid points neighbours of A.

- **Marching Forwards**

  Begin Loop: Let (i_{min}, j_{min}) be the point in NarrowBand with the smallest value for T.

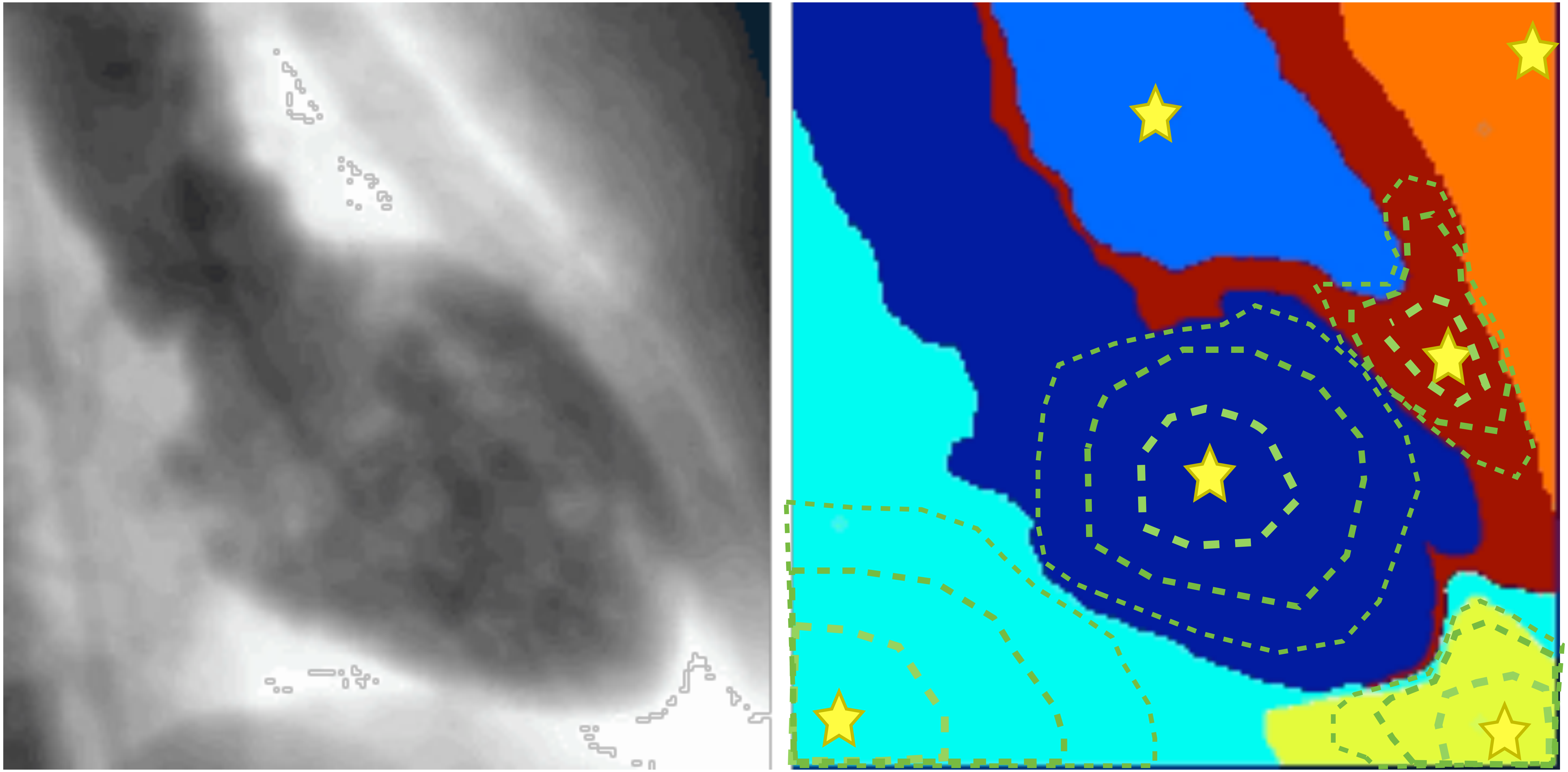
  Add the point (i_{min}, j_{min}) to A *(mark it as "solved")*; remove it from NarrowBand.

  Tag as neighbours any points $(i_{min}-1, j_{min})$, $(i_{min}+1, j_{min})$, $(i_{min}, j_{min}-1)$, $(i_{min}, j_{min}+1)$ that are not yet solved and add them to the NarrowBand

  Recompute the values of T at all neighbours according to discrete Eikonal equation, selecting the largest possible solution to the quadratic equation.

  Return to top of Loop.

How to use it for segmentation



$$1 = F \, \frac{dT}{dx}.$$

Initial Value Formulation - Narrow Band

- Boundary Value Level Set Equation

$$\phi_t + F|\nabla\phi| = 0,$$

$$\text{given} \quad \phi(x, t = 0).$$

- The upwinded finite difference approximations for convection

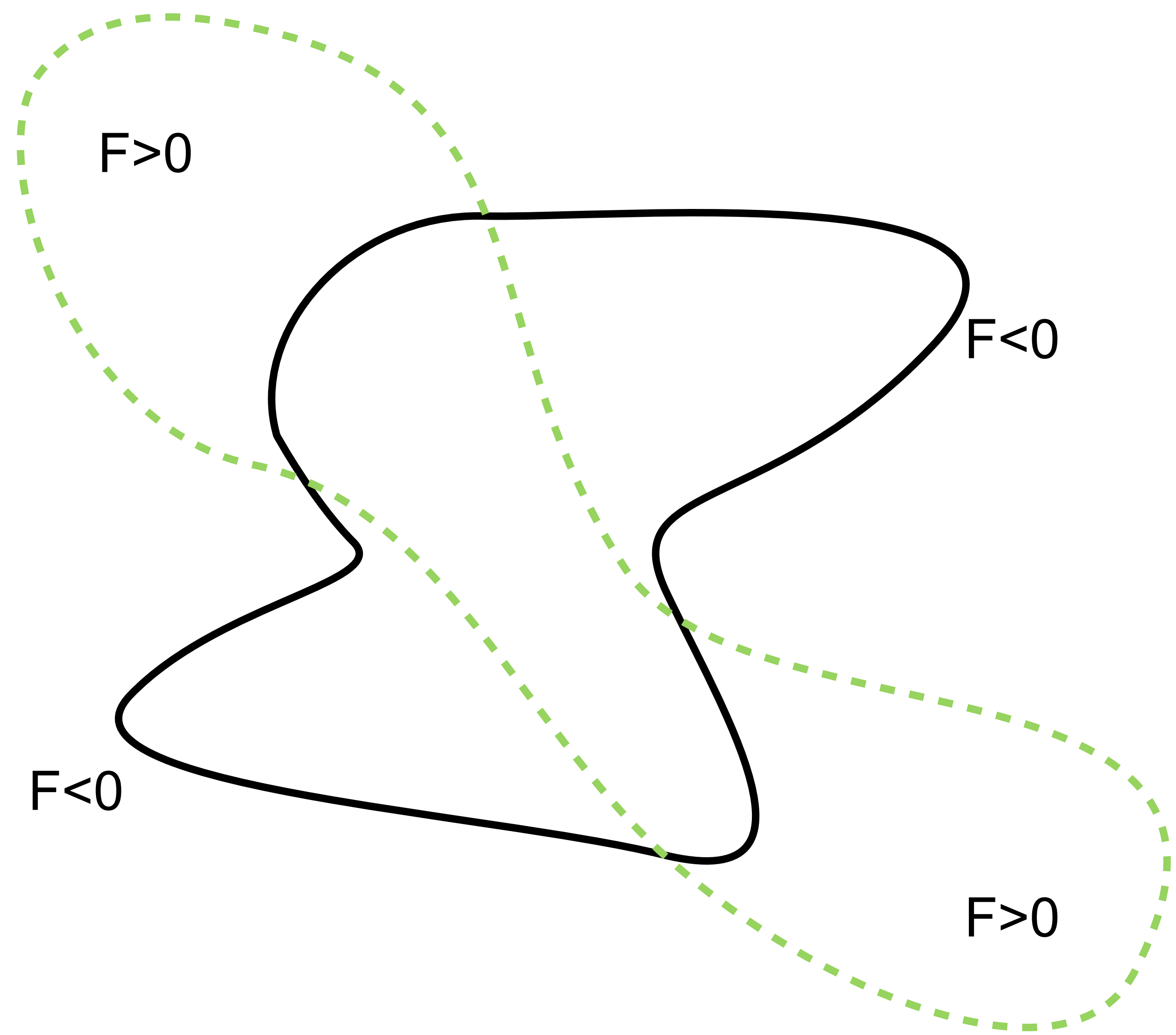
$$\varphi_{ijk}^{n+1} = \varphi_{ijk}^{n} + \Delta t_1 \big(max(F,0)\nabla_{ijk}^{+} + min(F,0)\nabla_{ijk}^{-} \big)$$

$$\begin{aligned}\nabla_{ijk}^{+} = \big[&\max(D^{-x}\phi_{ijk}^{n},0)^2 + \min(D^{+x}\phi_{ijk}^{n},0)^2 + \\ &\max(D^{-y}\phi_{ijk}^{n},0)^2 + \min(D^{+y}\phi_{ijk}^{n},0)^2 + \\ &\max(D^{-z}\phi_{ijk}^{n},0)^2 + \min(D^{+z}\phi_{ijk}^{n},0)^2 \big]^{1/2},\end{aligned}$$

$$\begin{aligned}\nabla_{ijk}^{-} = \big[&\min(D^{-x}\phi_{ijk}^{n},0)^2 + \max(D^{+x}\phi_{ijk}^{n},0)^2 + \\ &\min(D^{-y}\phi_{ijk}^{n},0)^2 + \max(D^{+y}\phi_{ijk}^{n},0)^2 + \\ &\min(D^{-z}\phi_{ijk}^{n},0)^2 + \max(D^{+z}\phi_{ijk}^{n},0)^2 \big]^{1/2}.\end{aligned}$$

Initial Value Formulation - Narrow Band

First Level Set with different F values in different areas

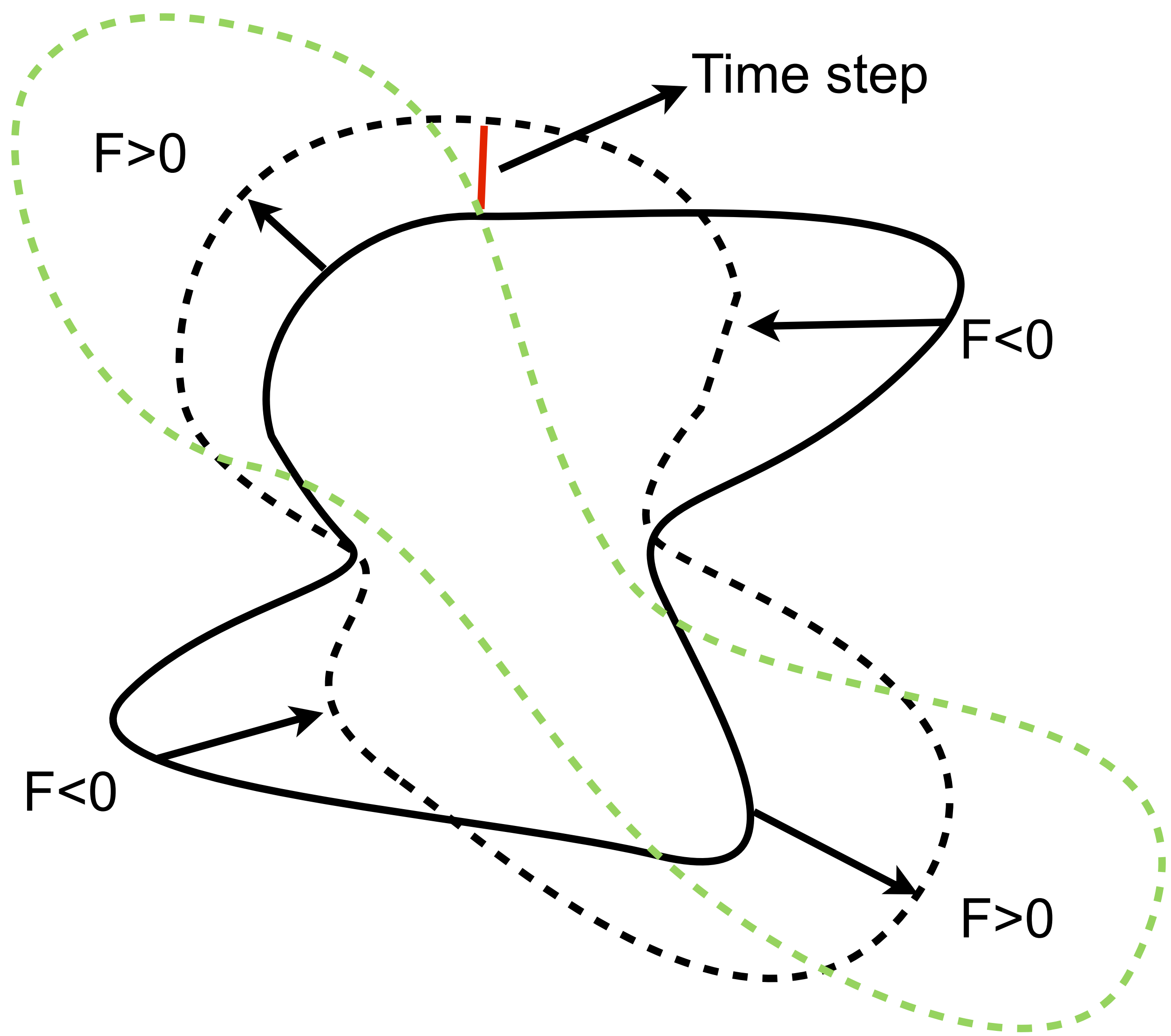


$$\phi_t + F|\nabla\phi| = 0,$$

$$\text{given} \quad \phi(x, t = 0).$$

Initial Value Formulation - Narrow Band

The Level Set evolves a certain amount t

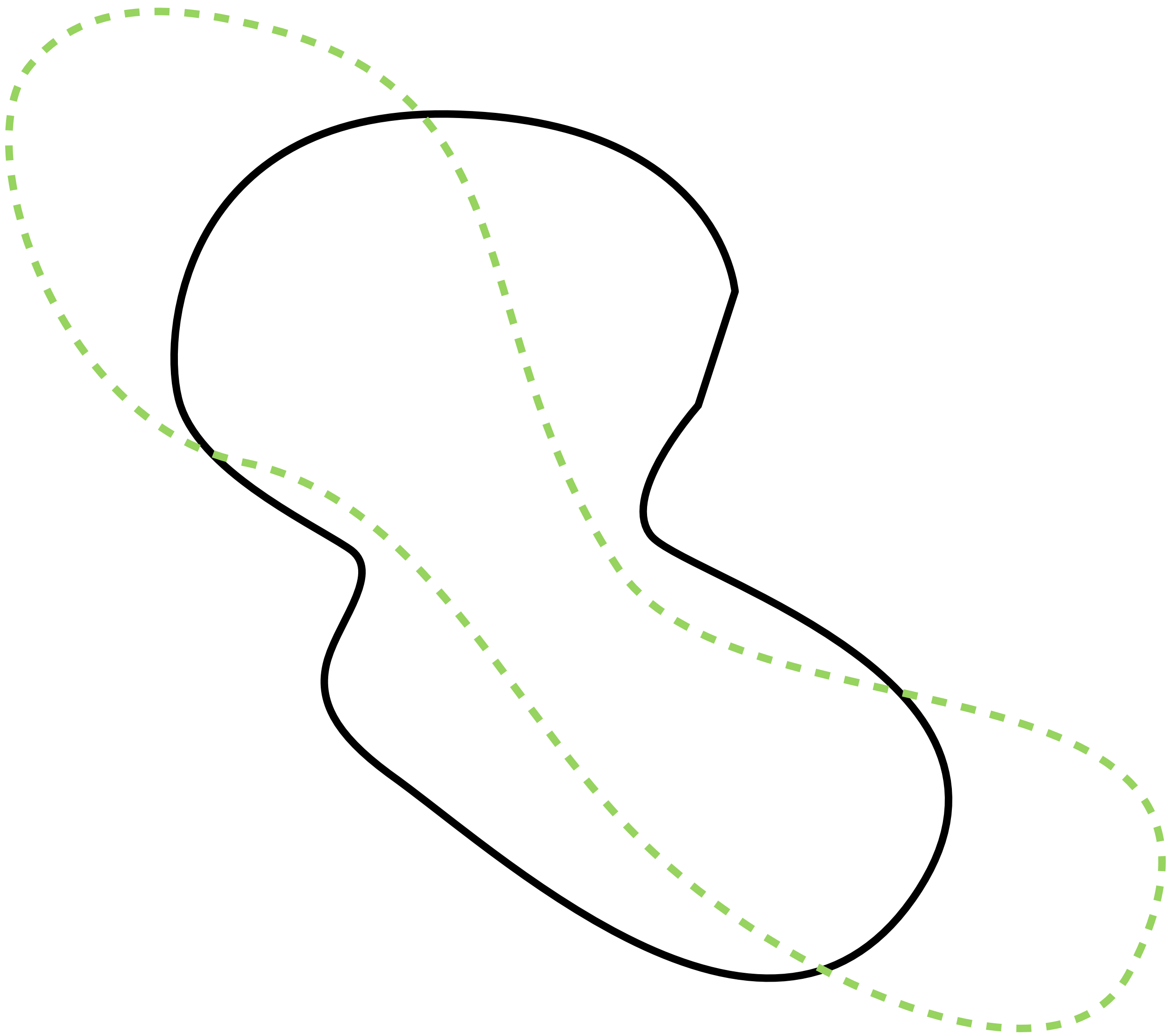


$$\phi_t + F|\nabla\phi| = 0,$$

$$\text{given} \quad \phi(x, t = 0).$$

Initial Value Formulation - Narrow Band

The evolved level set becomes the new zero level set

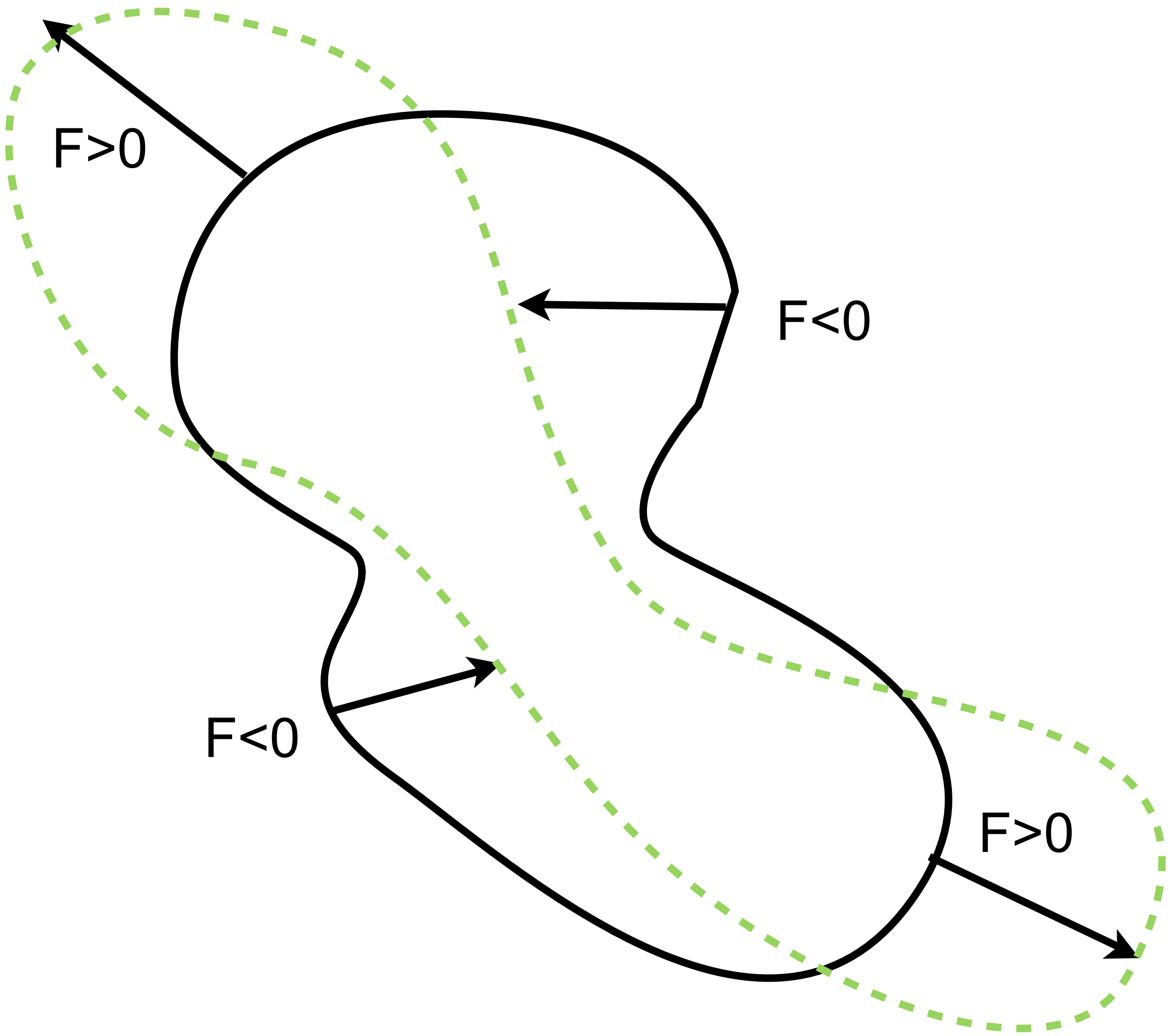


$$\phi_t + F|\nabla\phi| = 0,$$

$$\text{given} \quad \phi(x, t = 0).$$

Initial Value Formulation - Narrow Band

The new level set evolves a geodesic time step t



$$\phi_t + F|\nabla\phi| = 0,$$

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Initial Value Formulation - Narrow Band

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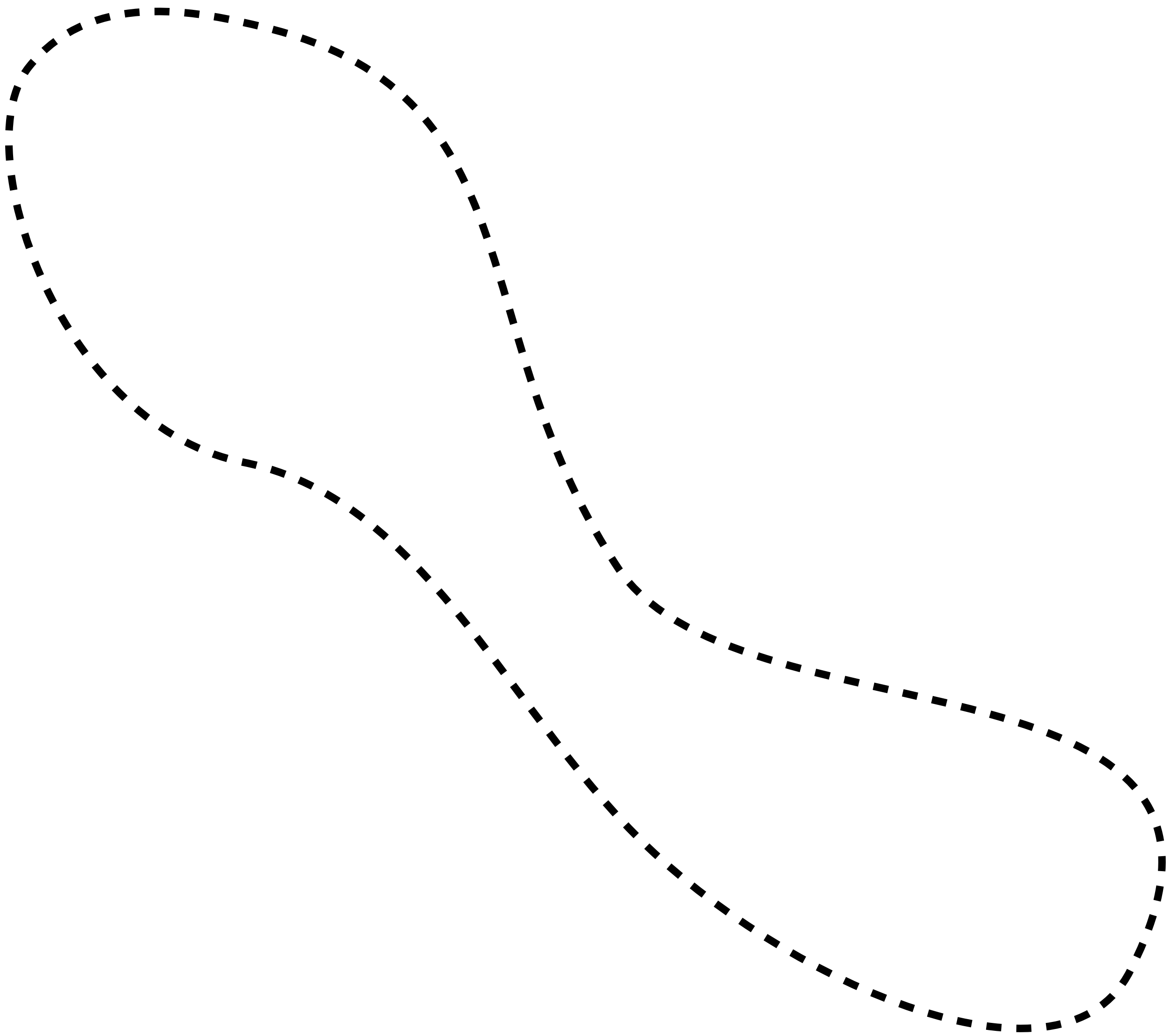

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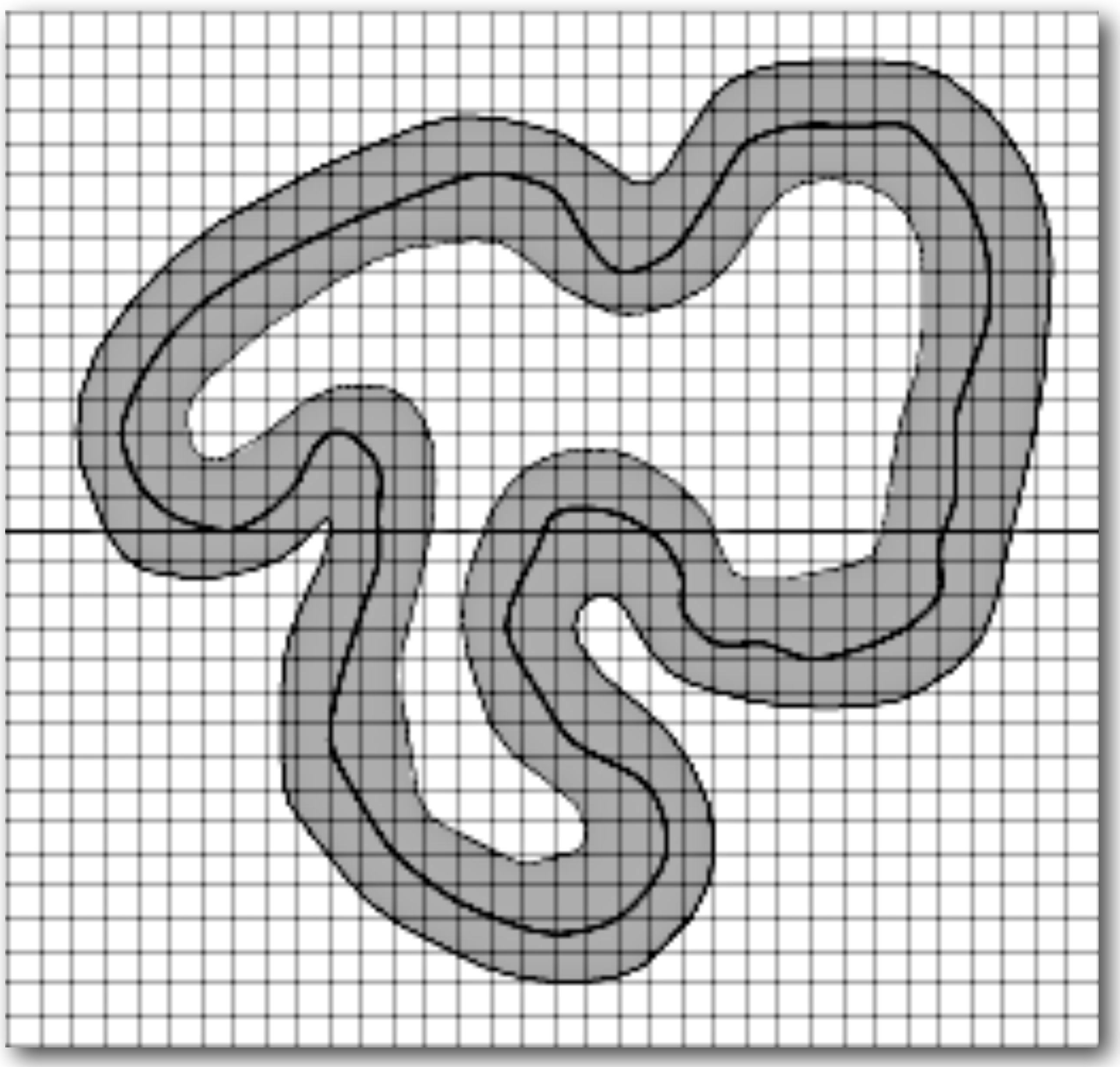
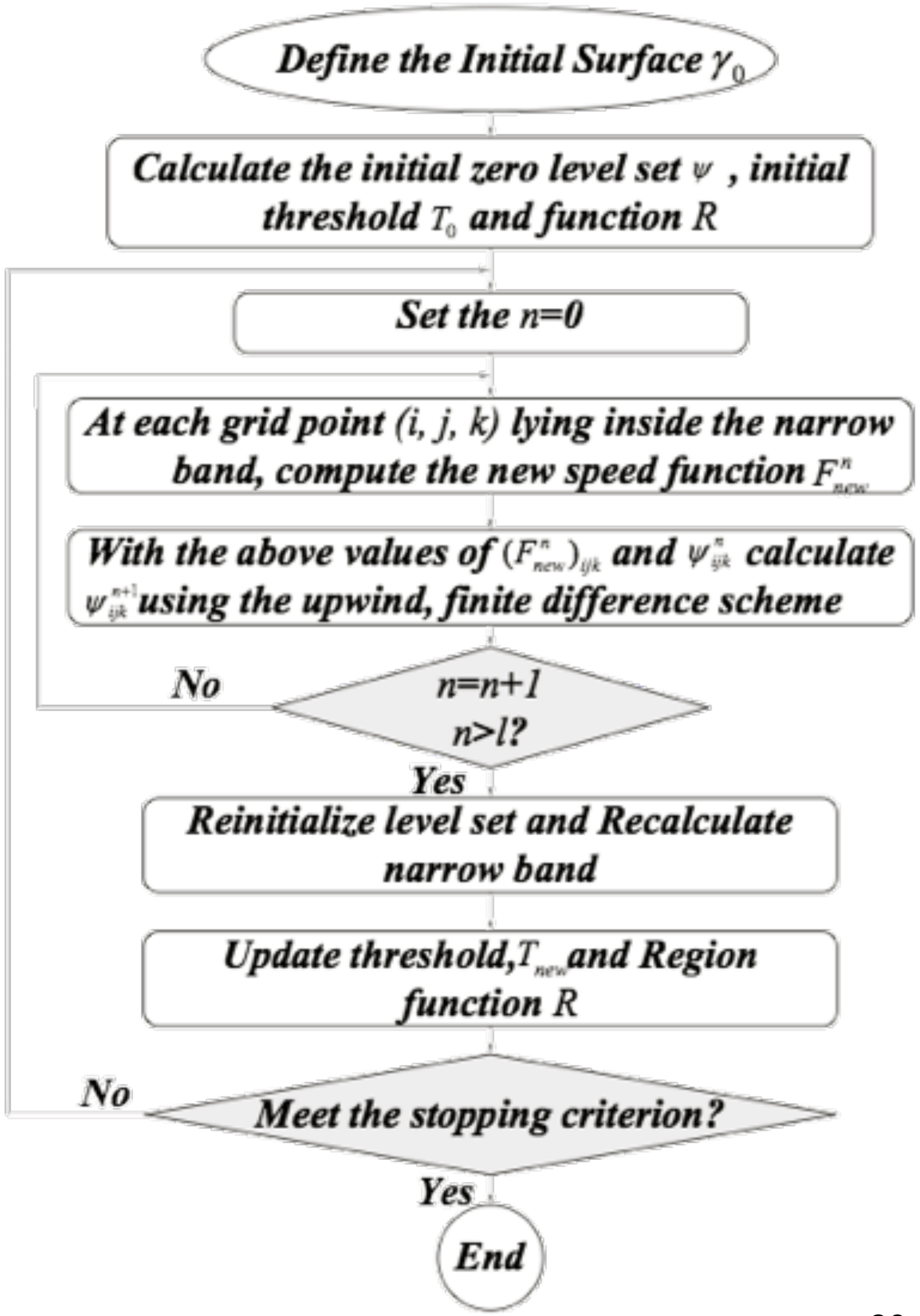




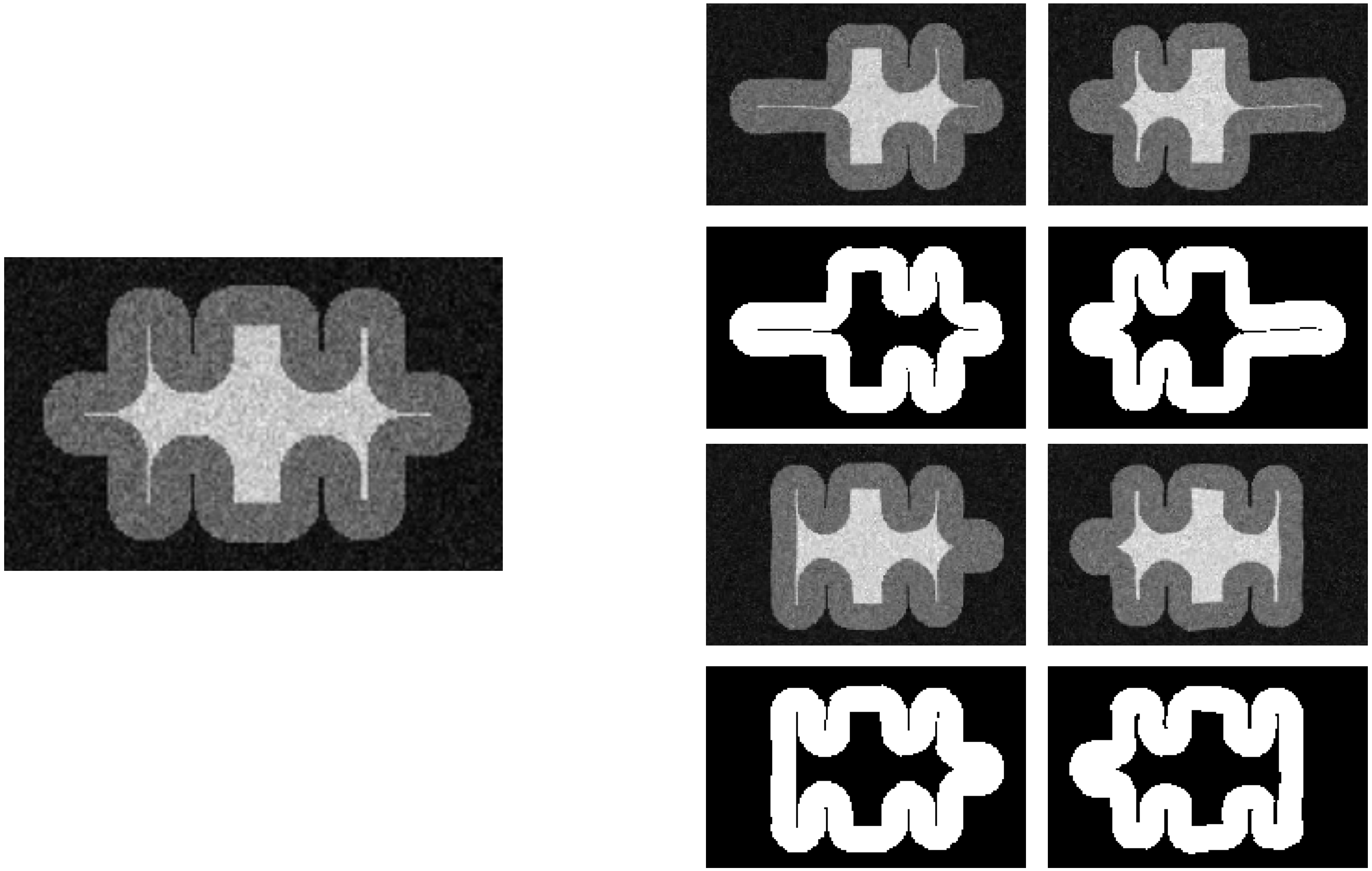
Recap

BOUNDARY VALUE FORMULATION	INITIAL VALUE FORMULATION
$\lvert\nabla T\rvert F = 1,$	$\phi_t + \nabla\phi(x(t),t)\cdot x'(t) = 0$
$\Gamma(t) = \{(x,y) \vert T(x,y) = t\}$	$\Gamma(t) = \{(x,y) \vert \phi(x,y,t) = 0\}$
F is static and positive	Spatially and time varying F

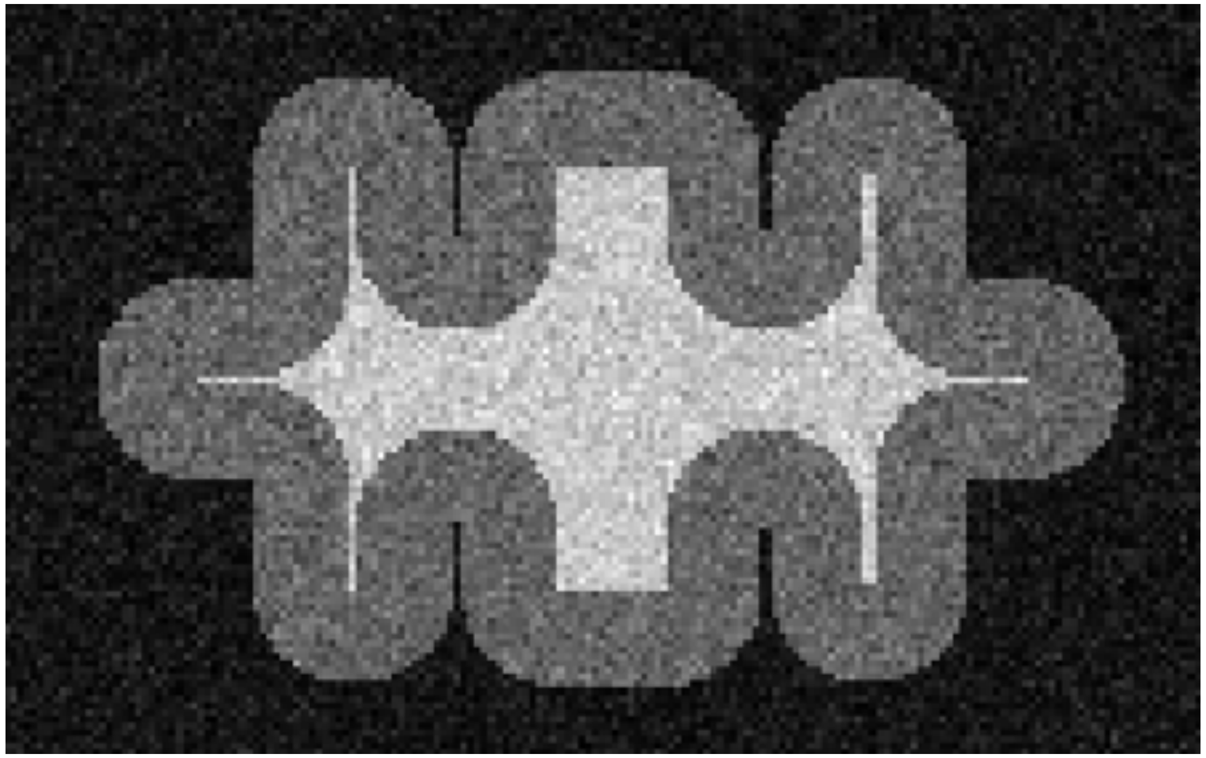
LABEL FUSION

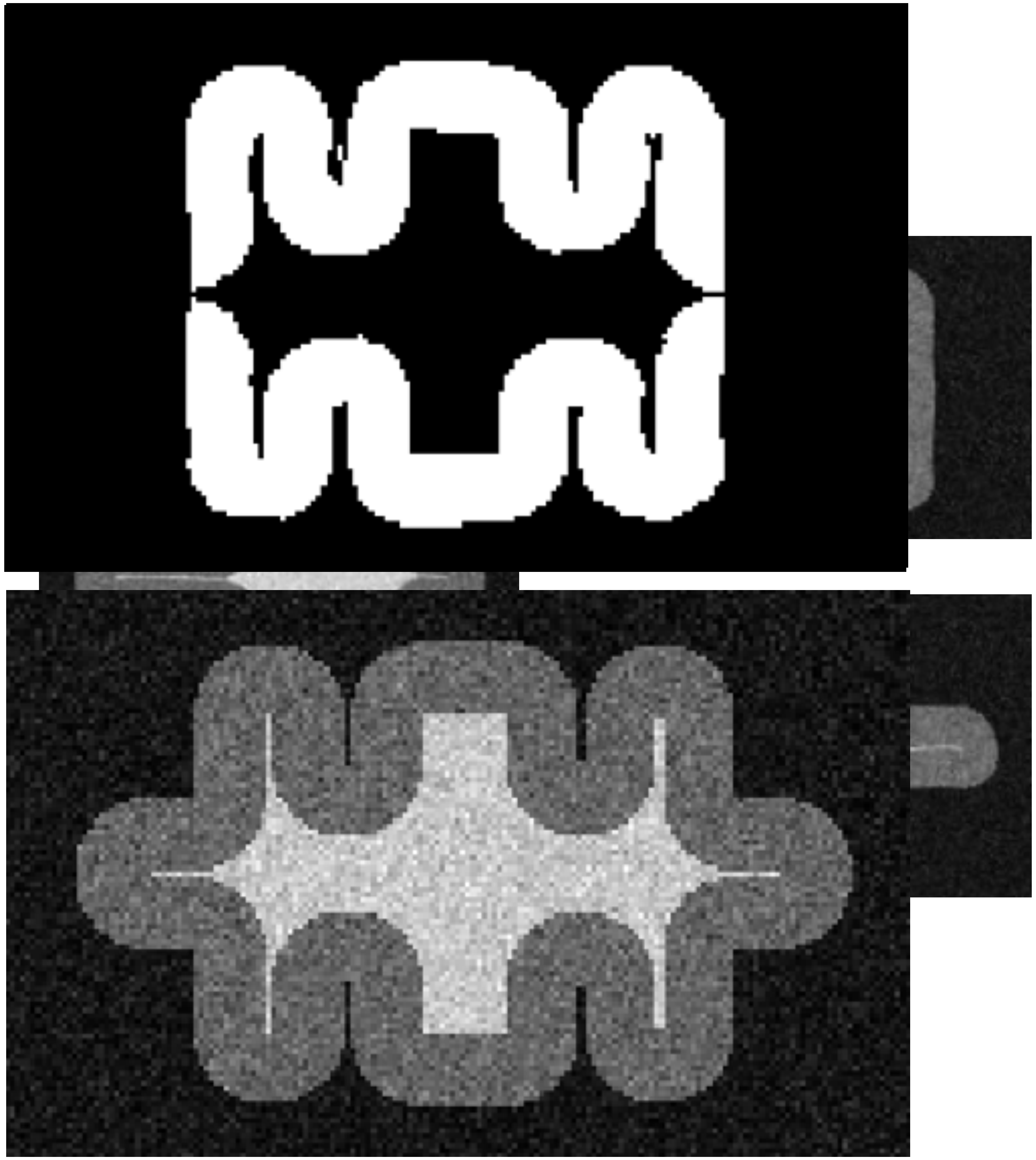
Fusion and Ranking methods

- Types of fusion:
  - Voting: Majority Voting, Weighted Voting, SIMPLE
  - Probabilistic: STAPLE, Spatial-STAPLE, STEPS



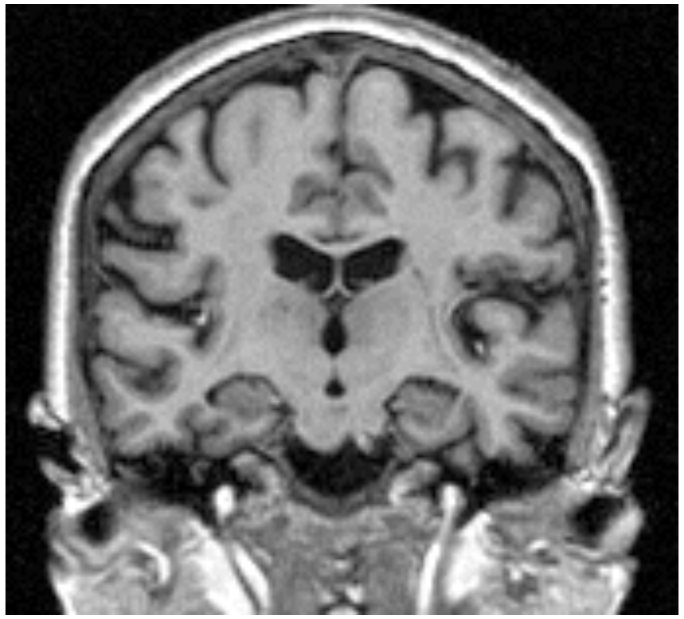
How does label fusion works



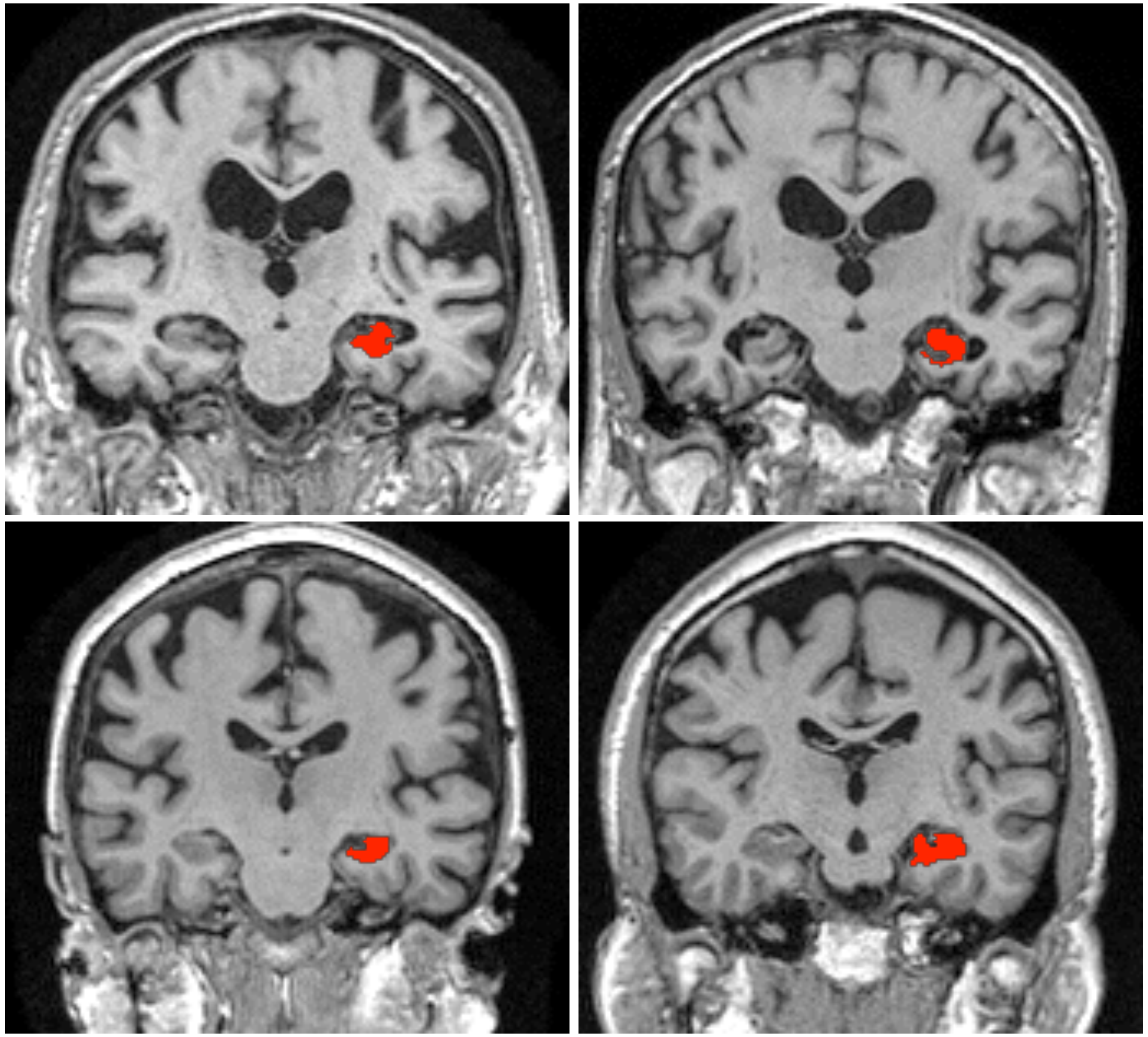


Label Fusion

- Segmentation propagation
  - Example - Hippocampus segmentation



Unseen image



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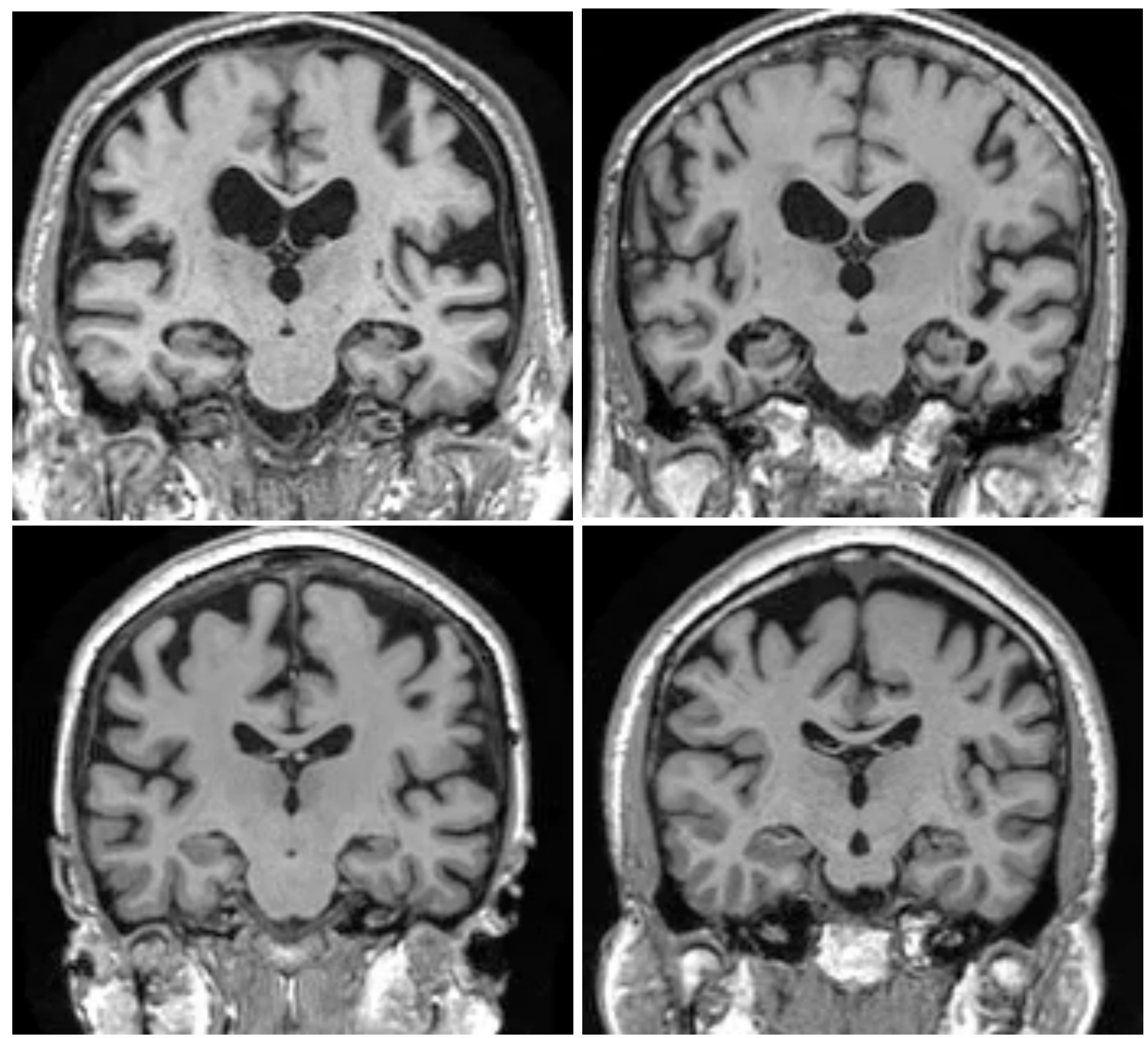

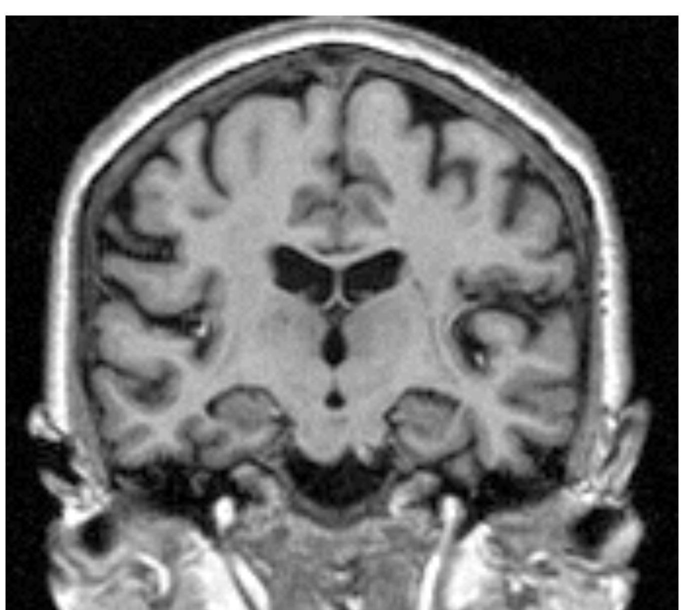

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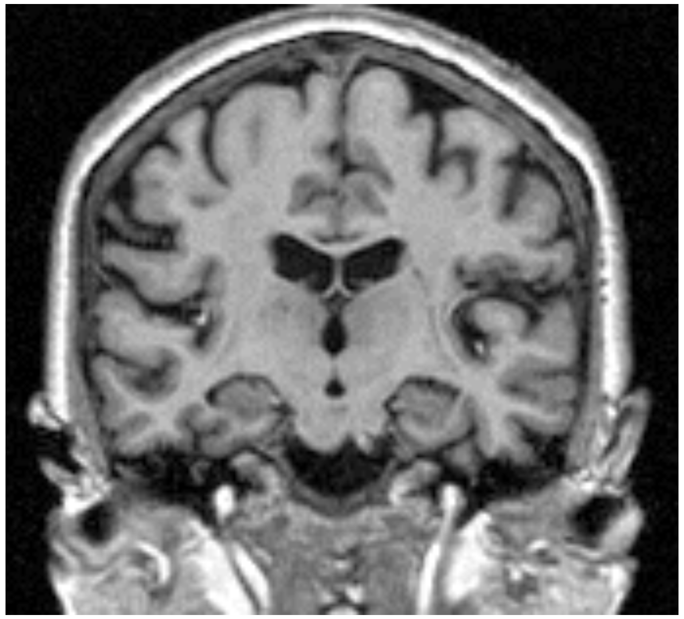

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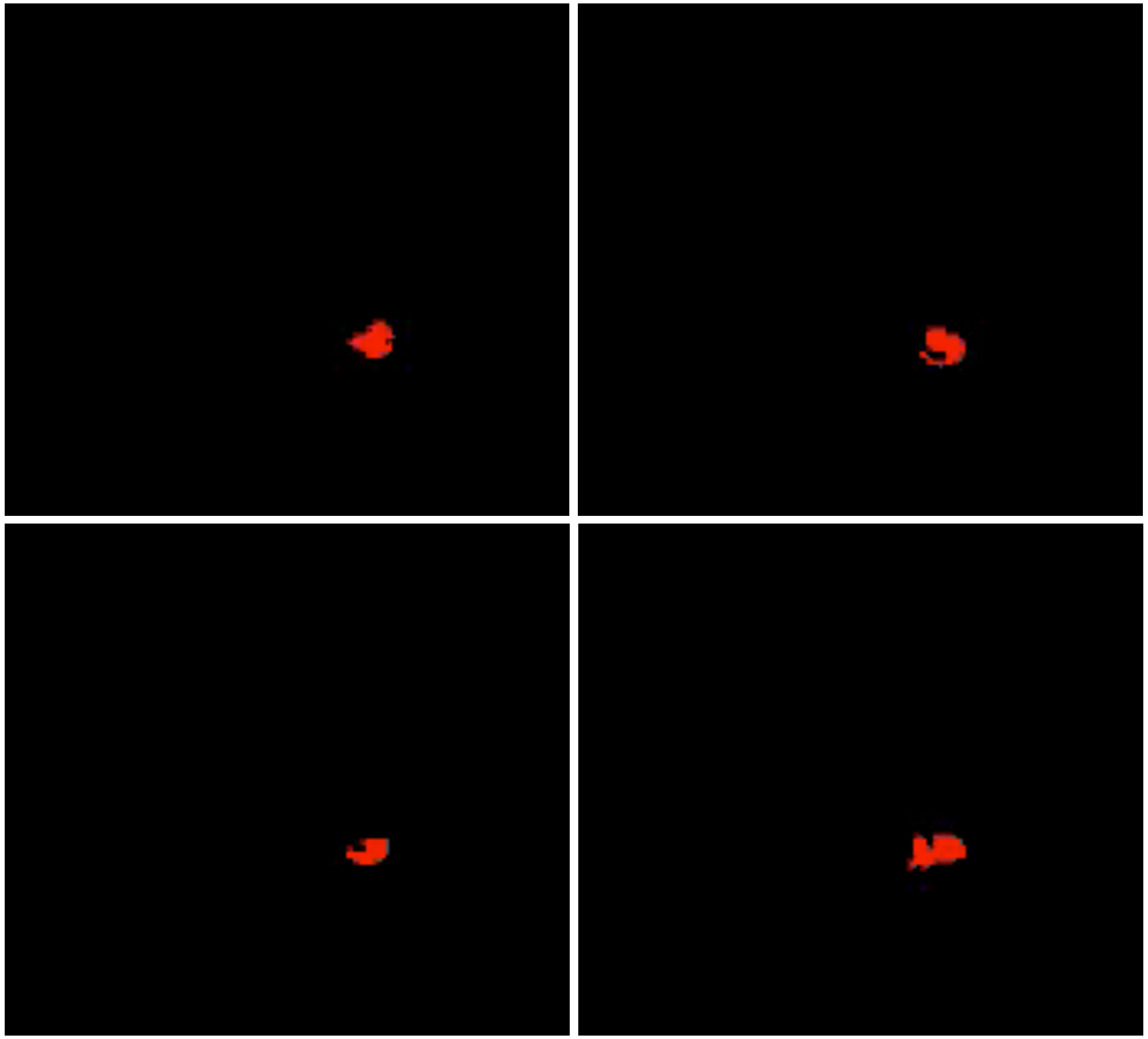

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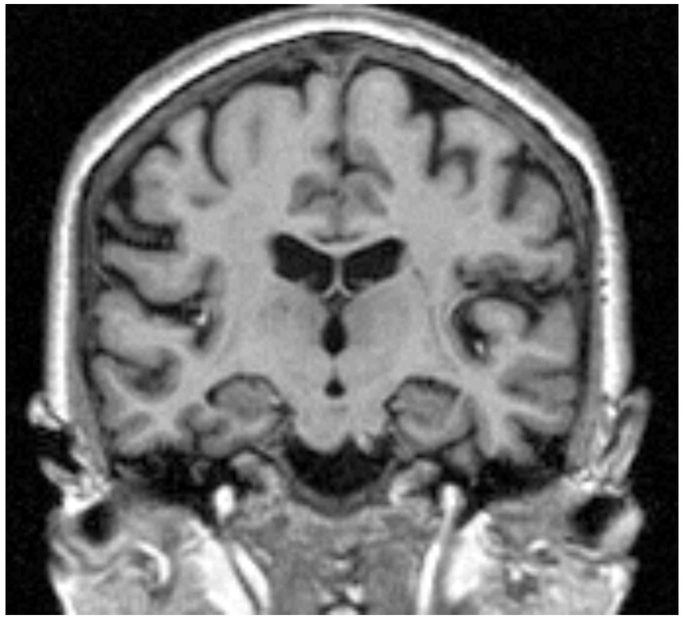

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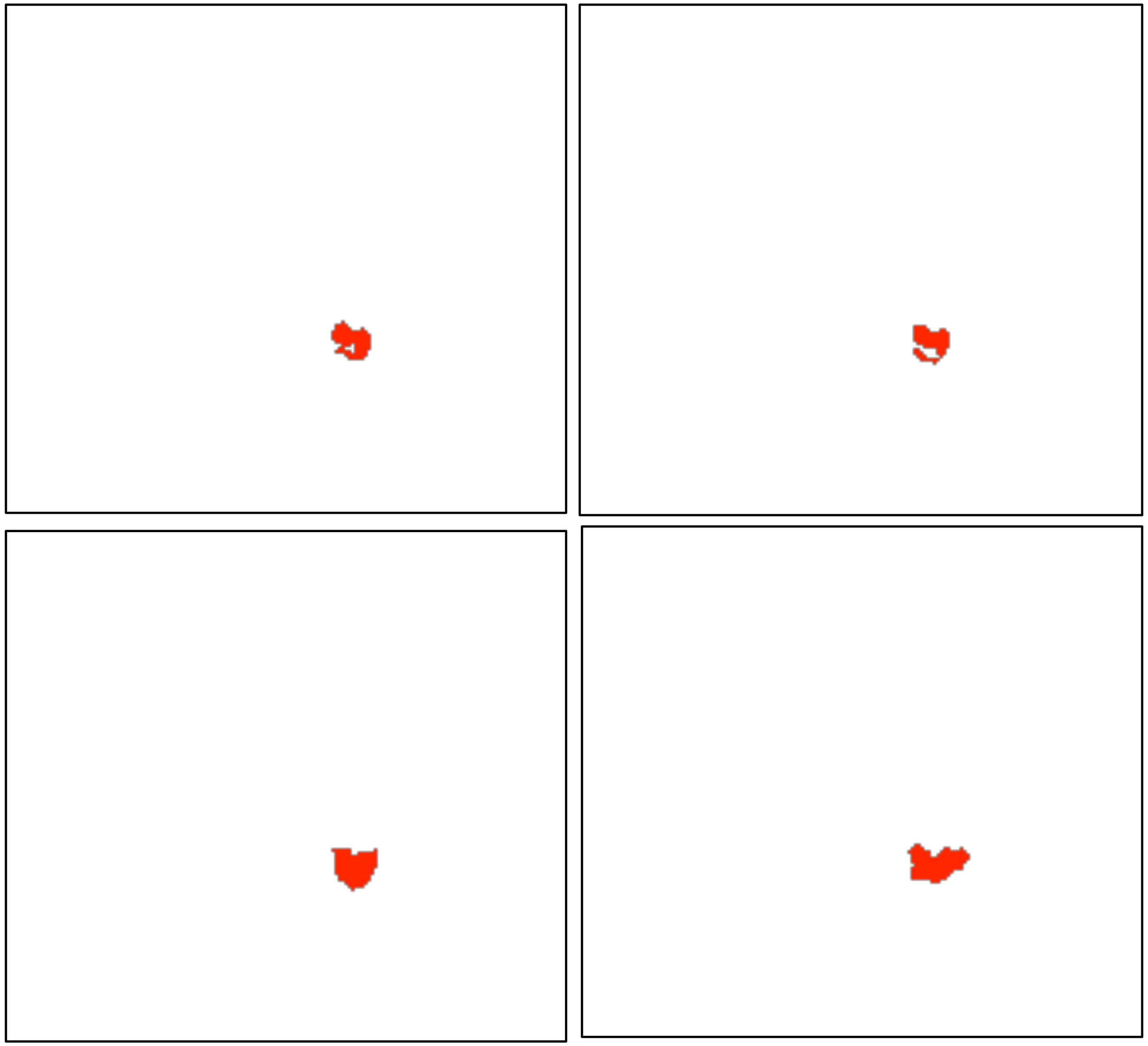

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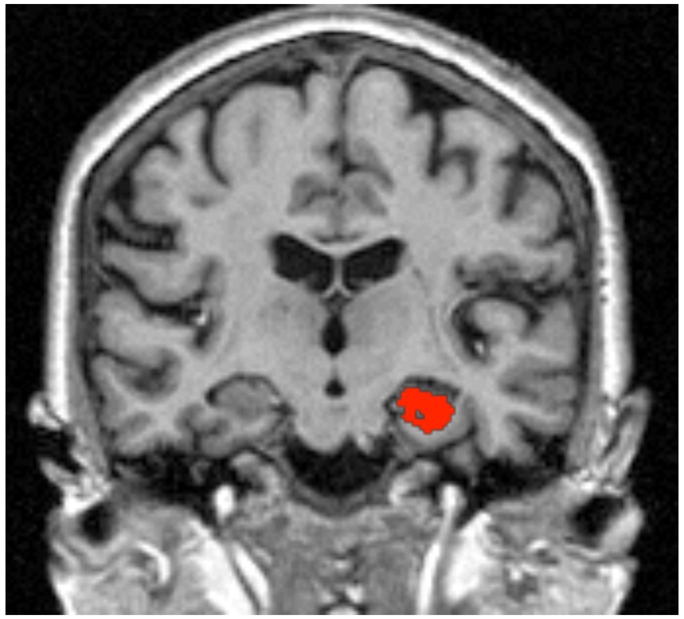

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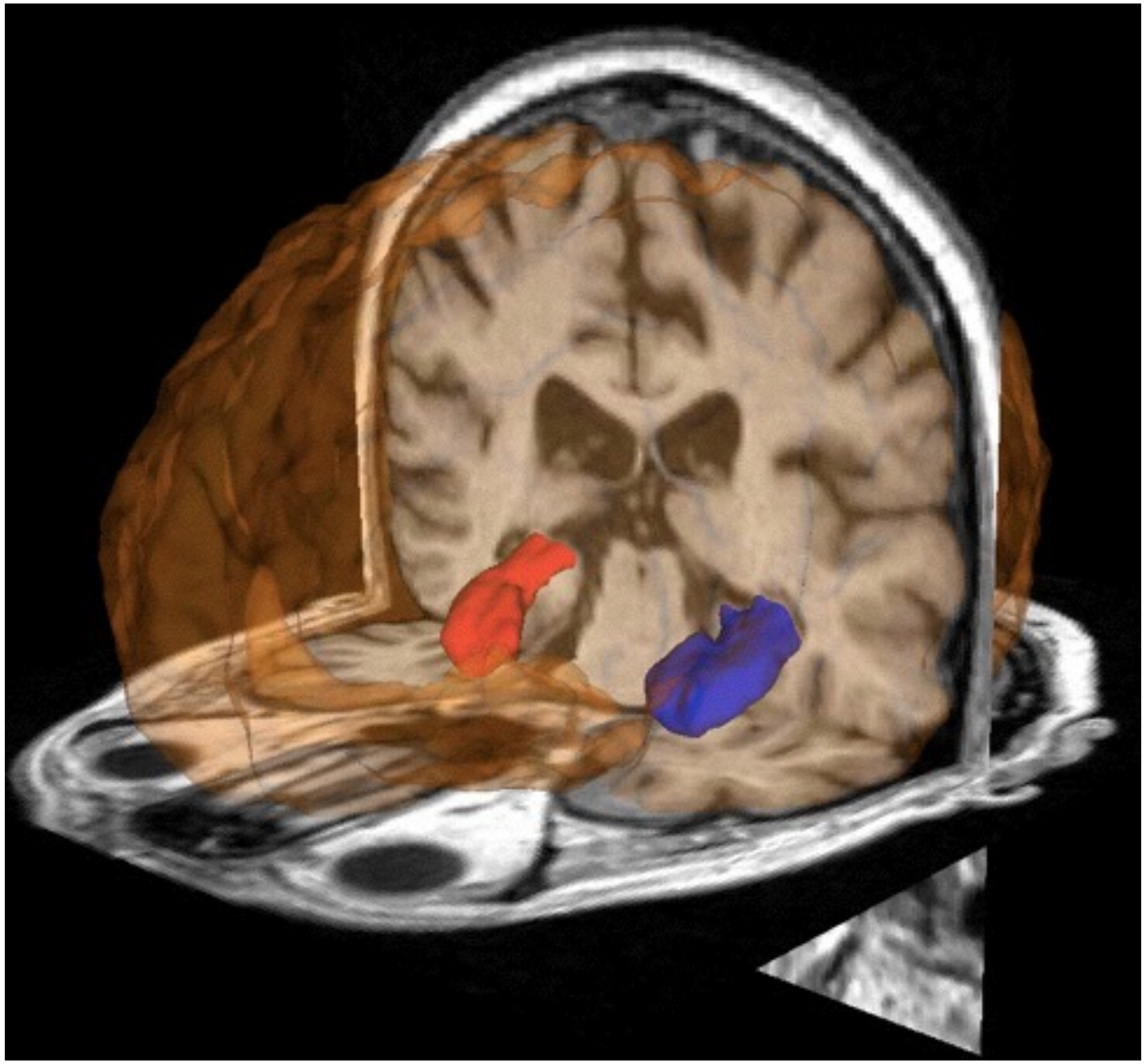


Sources of Error

1. Manual segmentation
   – Fix: STAPLE, SIMPLE

2. Correlation between errors
   – Fix: Wang et al. 2013

3. Registration accuracy/Varying morphology
   – Fix: Weighted-Voting, STEPS, Non-local-STAPLE

4. Registration Uncertainty
   – Still unsolved

The 1st problem - Manual segmentation

- Humans are not perfect at segmenting an object
- Variability introduced due to:
  - Inter-rater variability
  - Intra-rater variability
  - Stress/Focus of the human rater
  - Number of coffees per day ?!

- One has to model the accuracy of the human rater:
  - Global Sensitivity/Specificity: STAPLE
  - Local Sensitivity/Specificity: COLATE
  - Consensus Dice score: SIMPLE

The 1st problem - STAPLE

- We want to maximise the log likelihood of the complete data of this problem (D,T) given the set of parameters (p, q) representing the sensitivity and specificity of the rater

- By definition

$$(\hat{p},\hat{q}) = \arg\, max_{p,q} ln f(D,T|p,q)$$

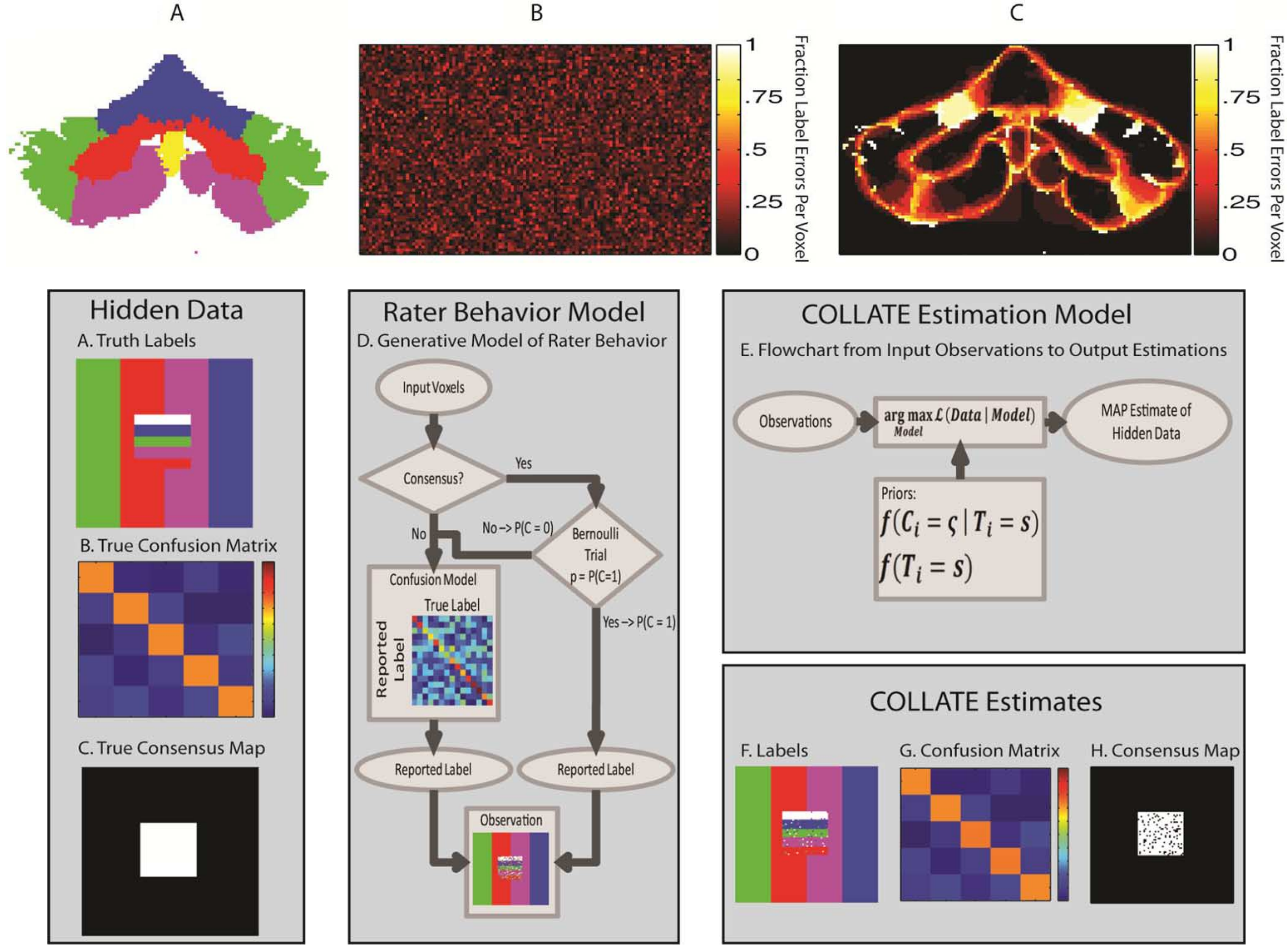
$$\boxed{p_j} = Pr(D_{ij} = 1|T_i = 1)$$
$$\boxed{q_j} = Pr(D_{ij} = 0|T_i = 0)$$

$$a_i^{(k-1)} \equiv f(T_i = 1) \prod_j f(D_{ij}|T_i = 1, p_j^{(k)}, q_j^{(k)})$$

$$b_i^{(k-1)} \equiv f(T_i = 0) \prod_j f(D_{ij}|T_i = 0, p_j^{(k)}, q_j^{(k)})$$

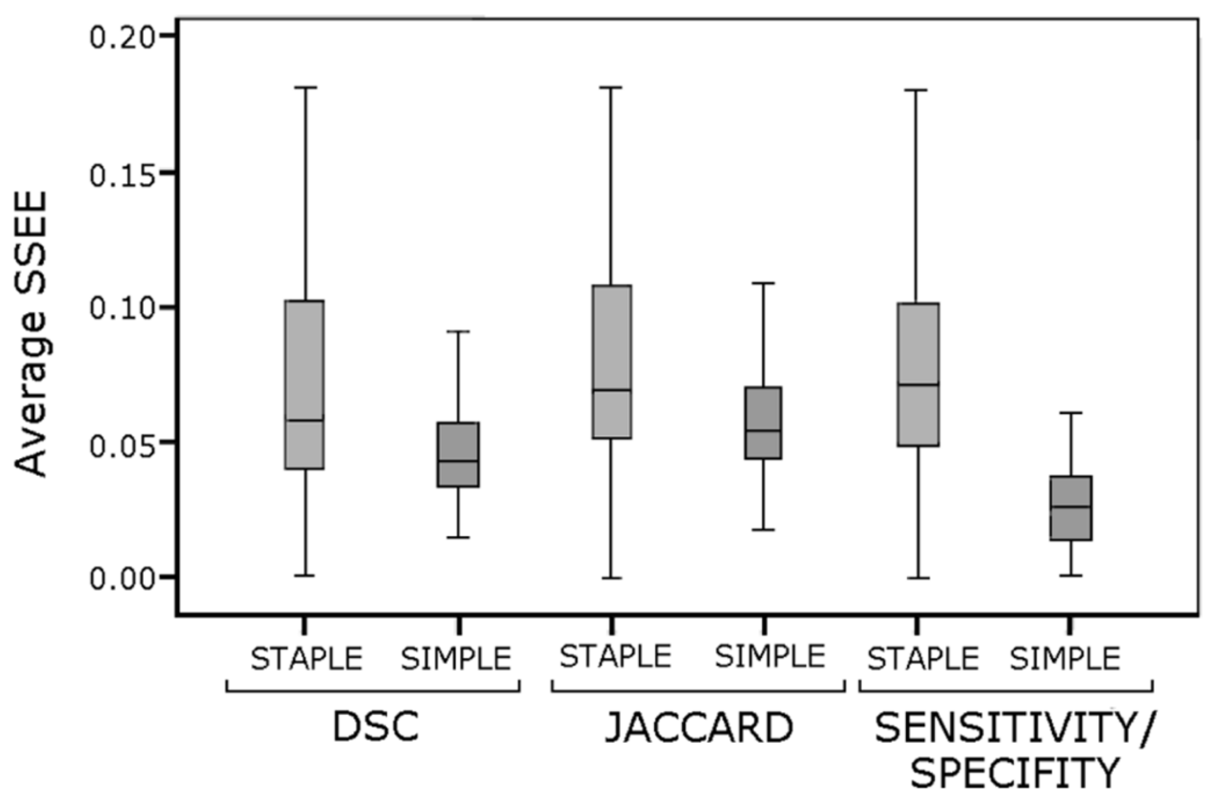
The 1st problem - COLLATE

- Local Sensitivity/Specificity: COLLATE (Asman et al.)
  - Extends the global p_j and q_j to voxels, i.e. p_{ji}, q_{ji}



The 1st problem - SIMPLE

- Consensus Dice score: SIMPLE
  - Estimates the Dice score between the propagated segmentation and the current estimate of the consensus
  - Uses Dice as a weight to reestimate the consensus



The 2nd problem - Correlation between errors

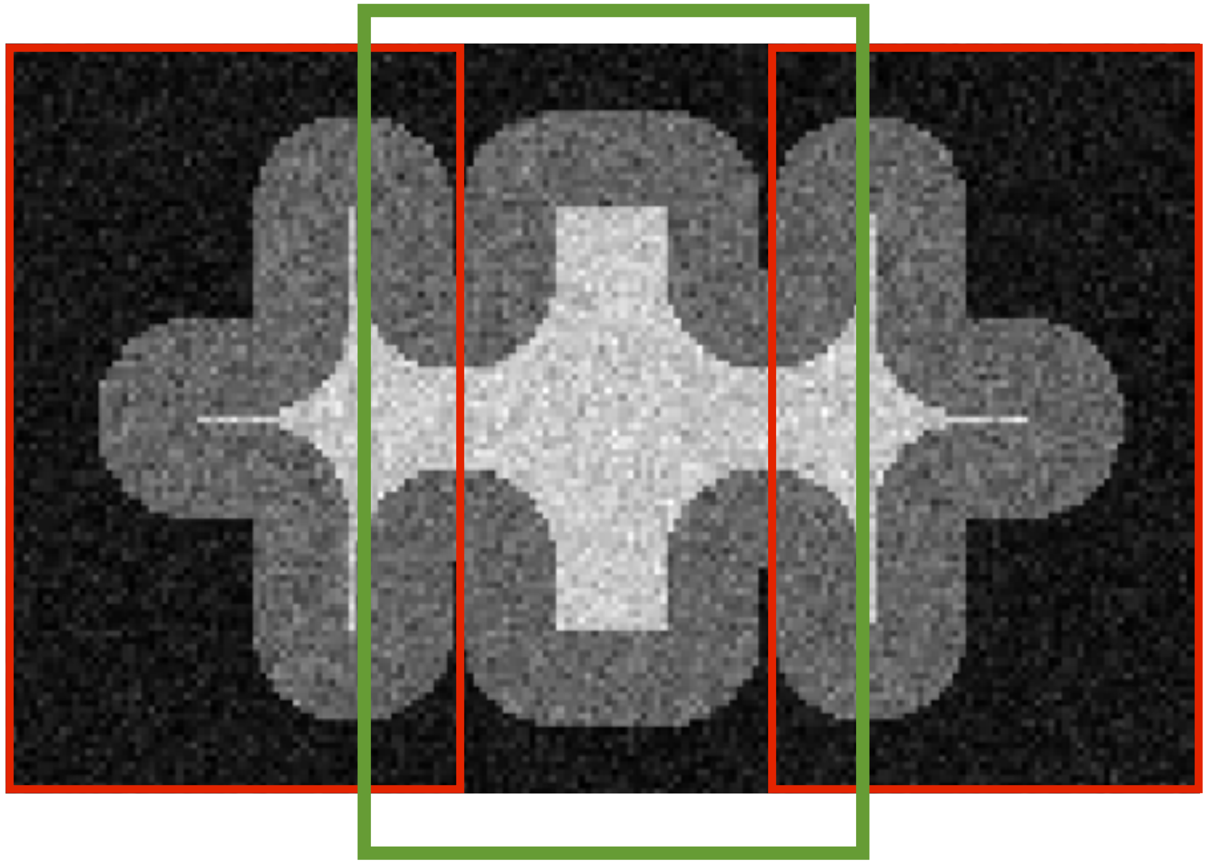
- Consensus Dice score
  - Wang et al. 2013
  - If the errors between two raters are correlated, then they should have a lower weight in the final segmentation result:
    - i.e. if both raters produce the same segmentation locally
  - They also find what areas are prone to error, and the use ADABOOST to correct for it

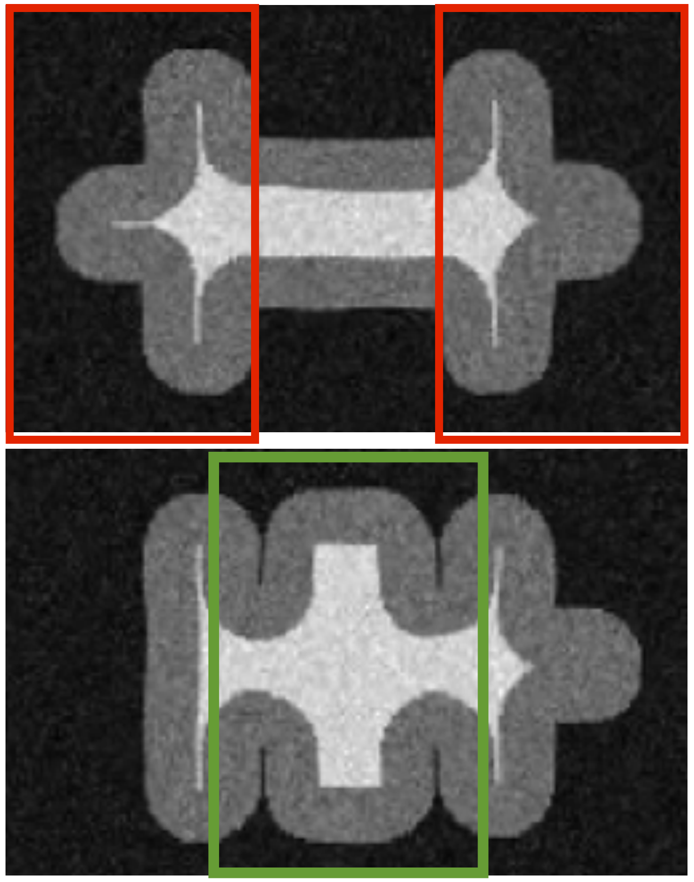
- If tho images look similar after registration, then the registration worked fine
  - –Weighted-Voting (Aljabar et al., Yushkevich et al.)
  - –STEPS (Cardoso et al.)
  - –Non-local-STAPLE (Asman et al.)

- One defines how similar the images are using an image similarity term
  - NCC (Aljabar et al.)
  - LNCC (Cardoso et al.)
  - L2 norm (Asman et al.)
  - Ranked similarity (Yushkevich et al.)

The 3rd problem - Registration accuracy/Morphology

- Templates have different morphologies





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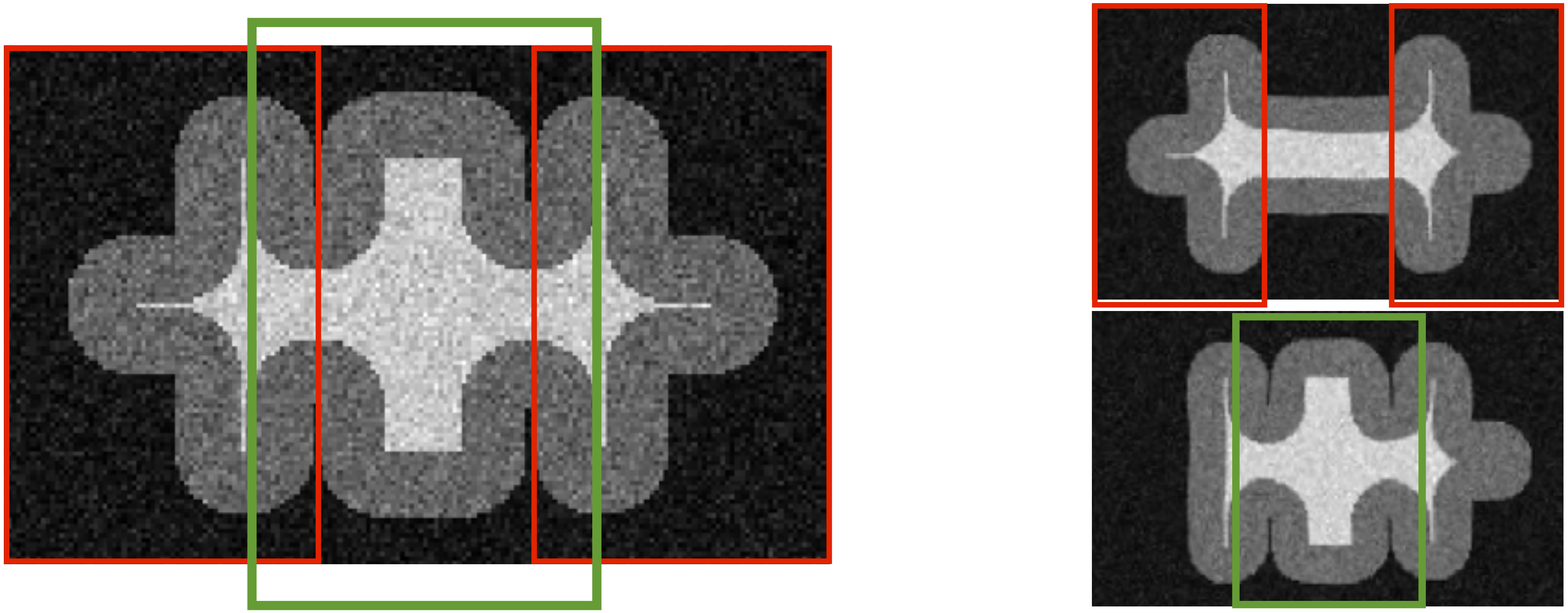

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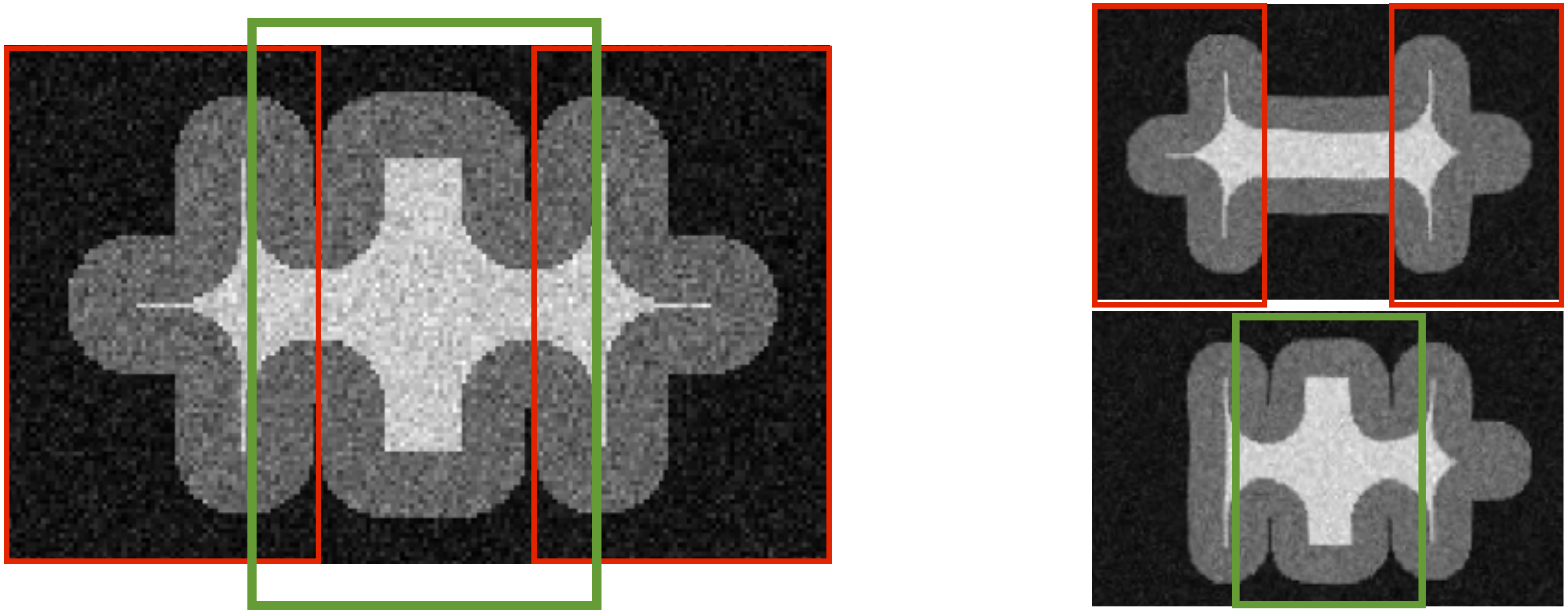
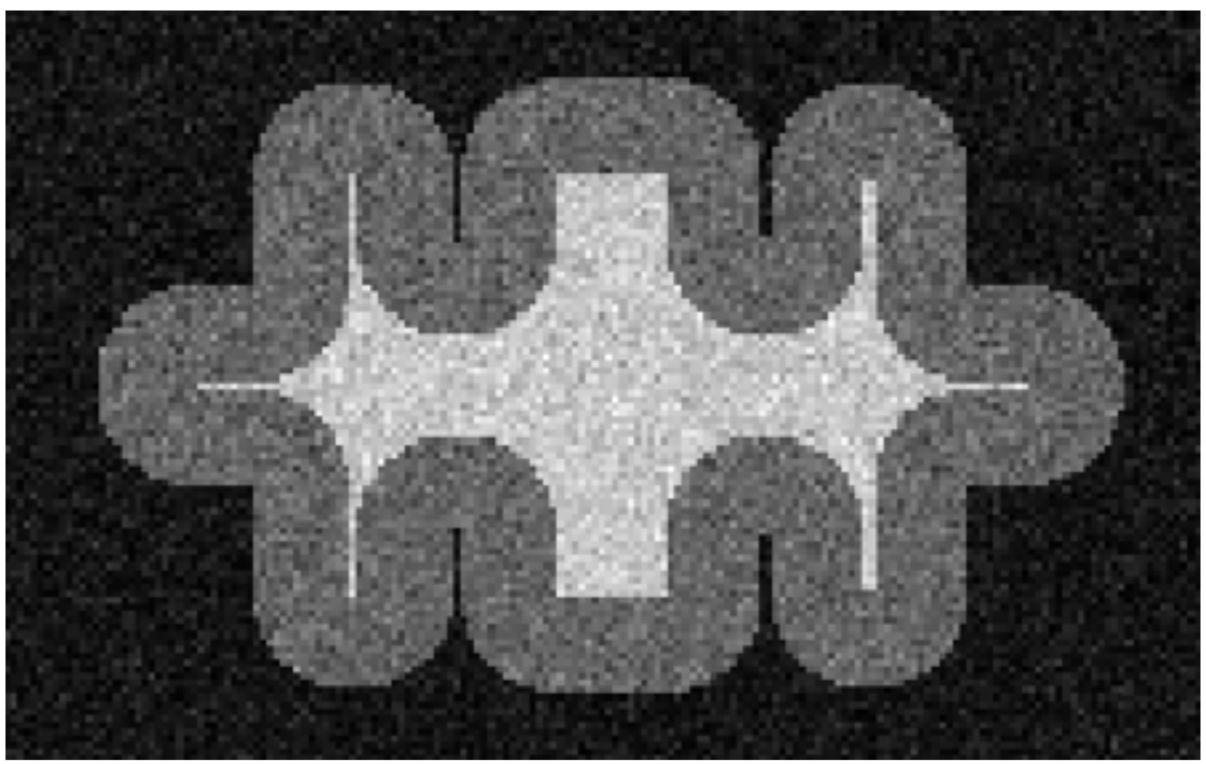
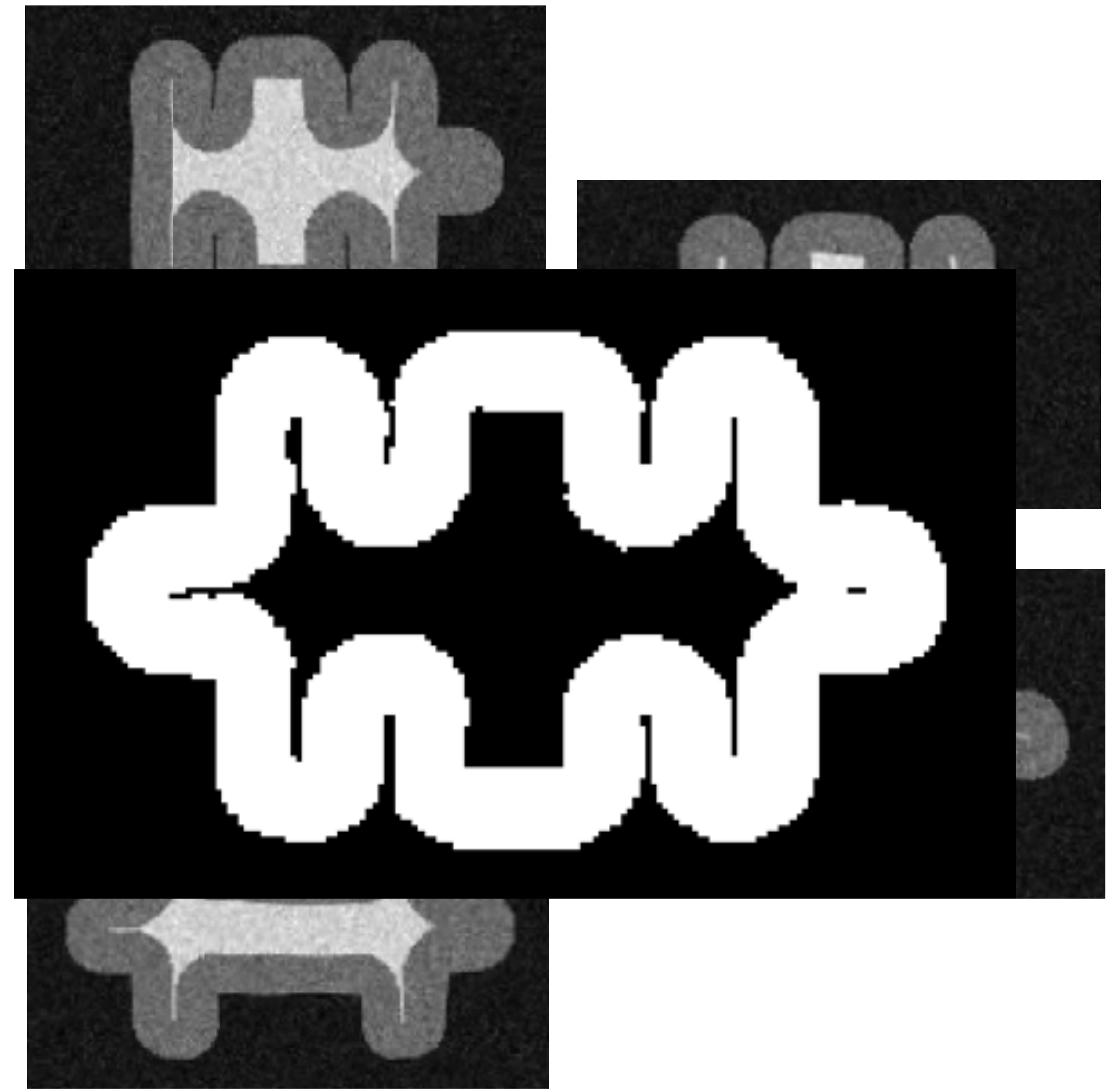


The 3rd problem - Registration accuracy/Morphology





The Weighted voting

- Weighted sum of labels

$$\mathcal{L}_i(\vec{v}) = \frac{\sum W_{ij}(\vec{v})\mathcal{L}_{i;}(T_{ij}(\vec{v}))}{\sum W_{ij}(\vec{v})},$$

Weights are described as some global/local image similarity where $W_{ij}=1$ means the two mapped locations are similar, while $W_{ij}=0$ means the two locations are different.

The STEPS algorithm

- Compared to STAPLE, the only thing that changes is:

$$(\hat{p}, \hat{q}) = \arg\, max_{p,q} ln f(D, T | p, q)$$

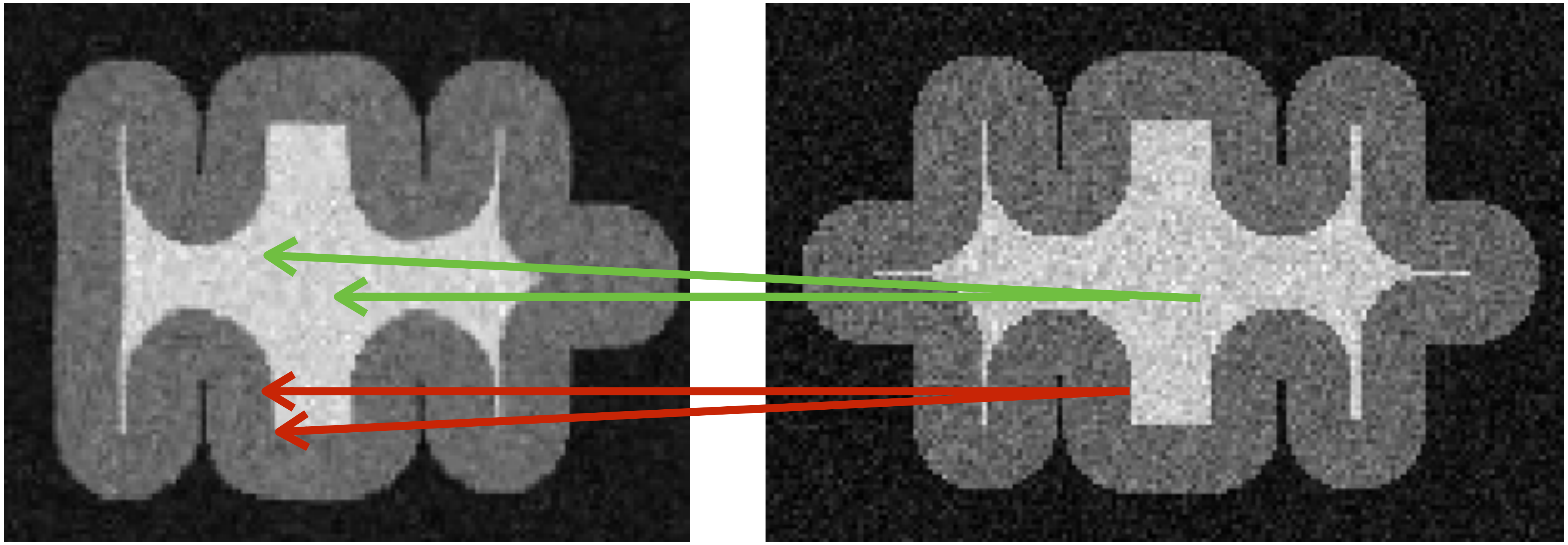
$$p_j = Pr(D_{ij} = 1 | T_i = 1)$$
$$q_j = Pr(D_{ij} = 0 | T_i = 0)$$

$$a_i^{(k-1)} \equiv f(T_i = 1) \prod_{\boxed{j \forall L_{ij} = 1}} f(D_{ij} | T_i = 1, p_j^{(k)}, q_j^{(k)})$$

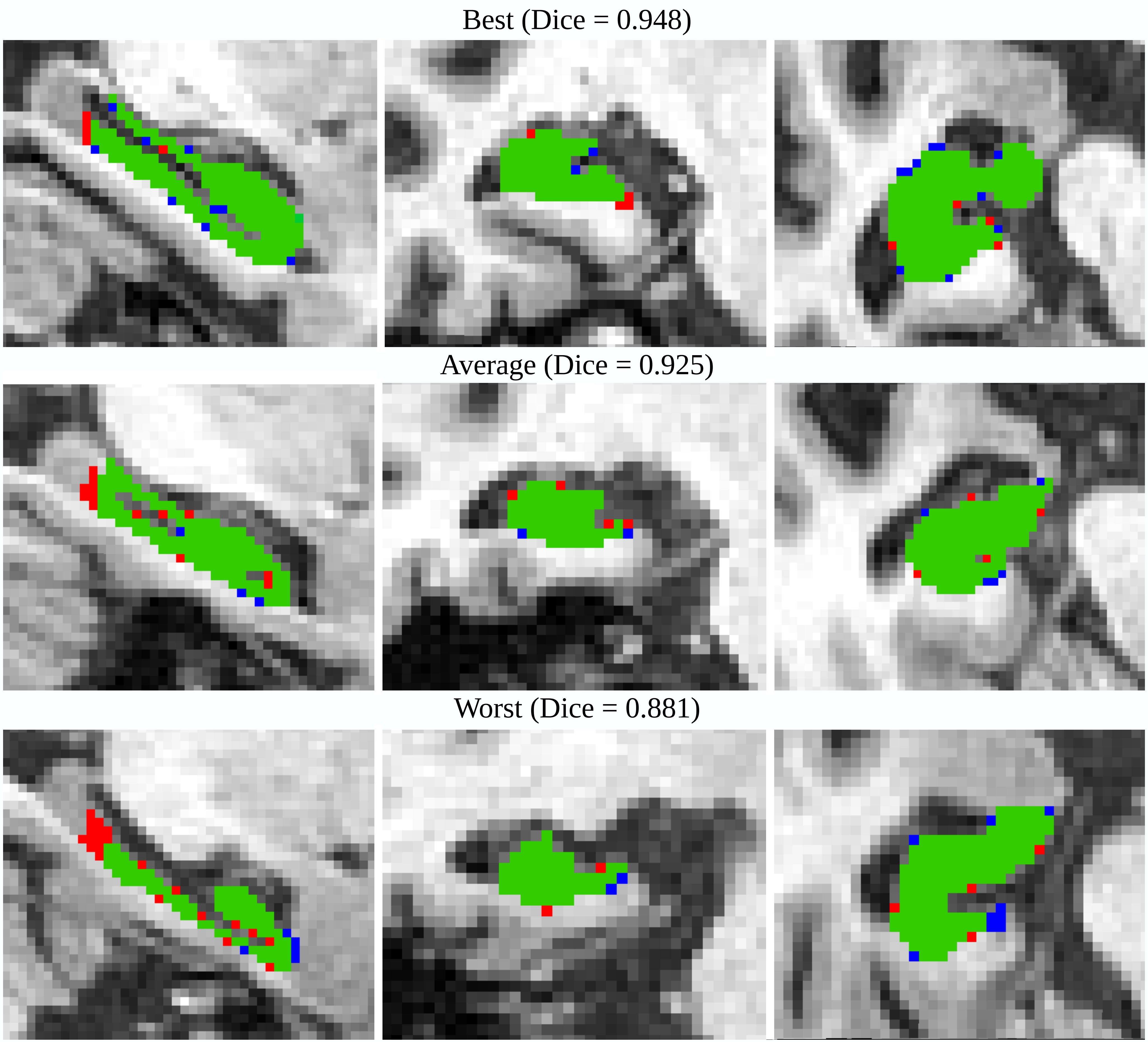
$$b_i^{(k-1)} \equiv f(T_i = 0) \prod_{\boxed{j \forall L_{ij} = 1}} f(D_{ij} | T_i = 0, p_j^{(k)}, q_j^{(k)})$$

The 4th problem - Registration uncertainty

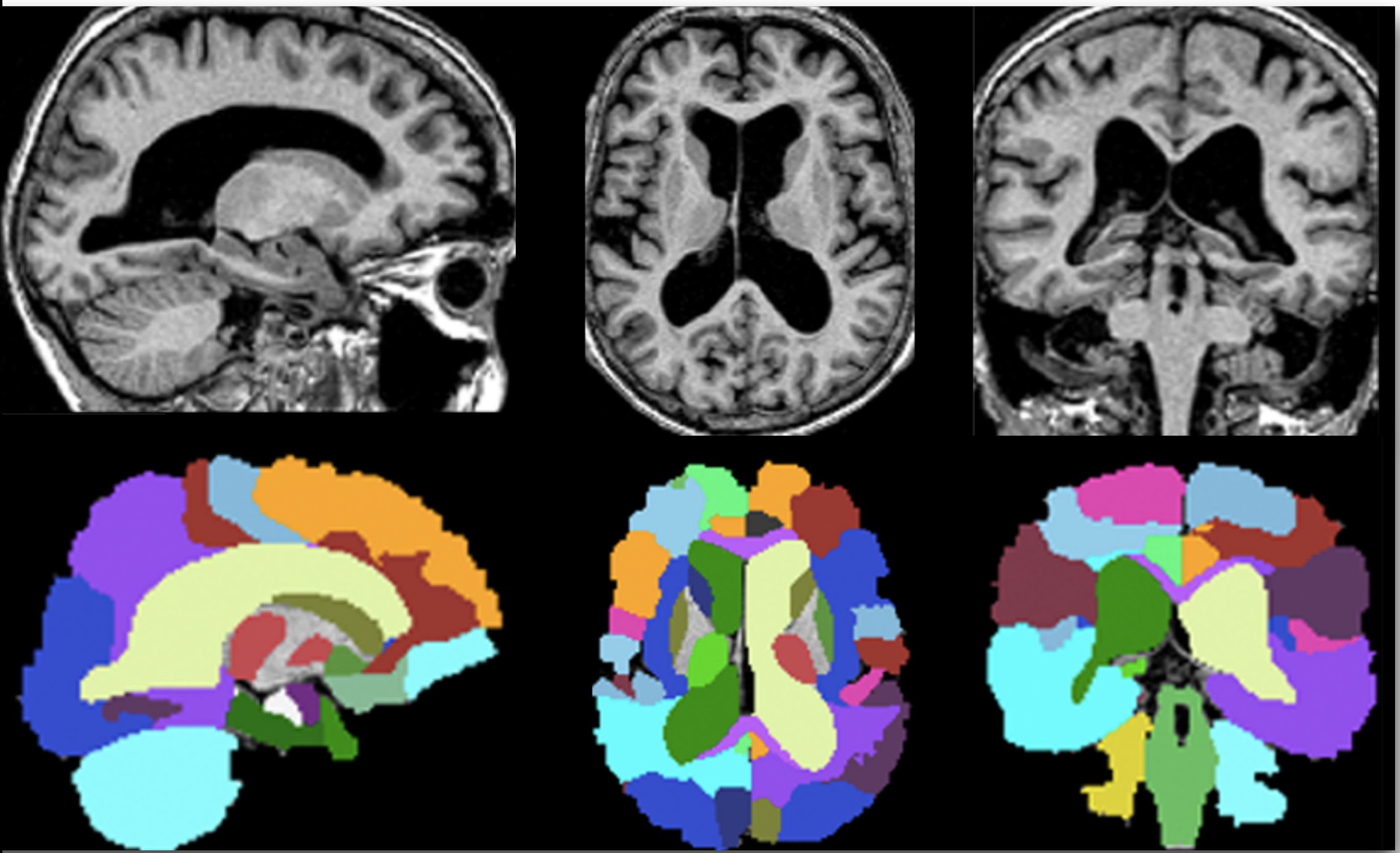
- Do images provide good enough matching?
- Is there a 1-to-1 correspondence?
- What happens in areas without contrast?

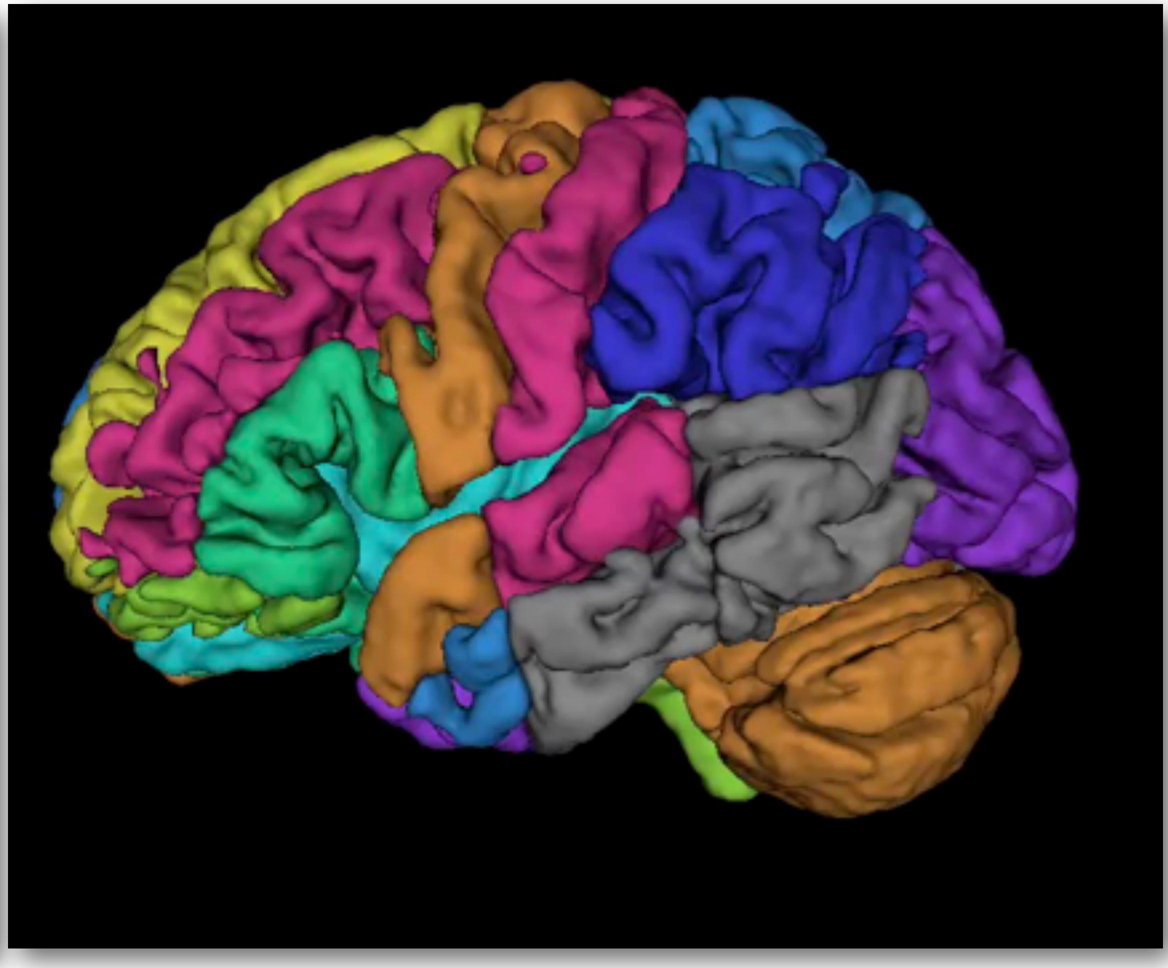


Hippocampal Segmentation in AD patients



Multi Structure: Segmentation results



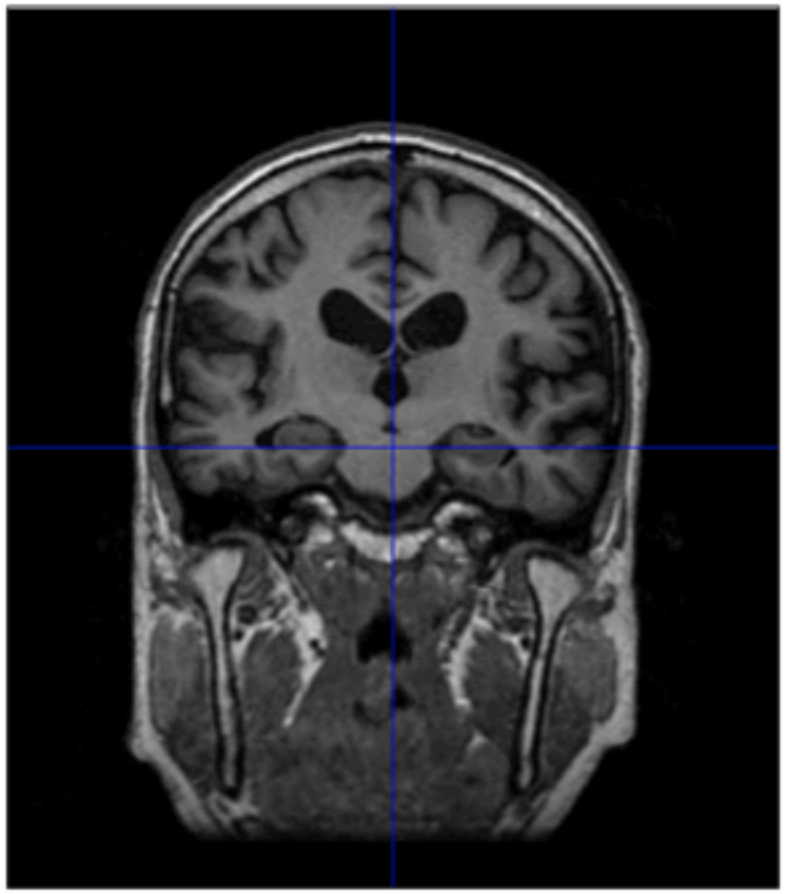


COMPUTATIONAL NEUROANATOMY & IMAGING BIOMARKER EXTRACTION

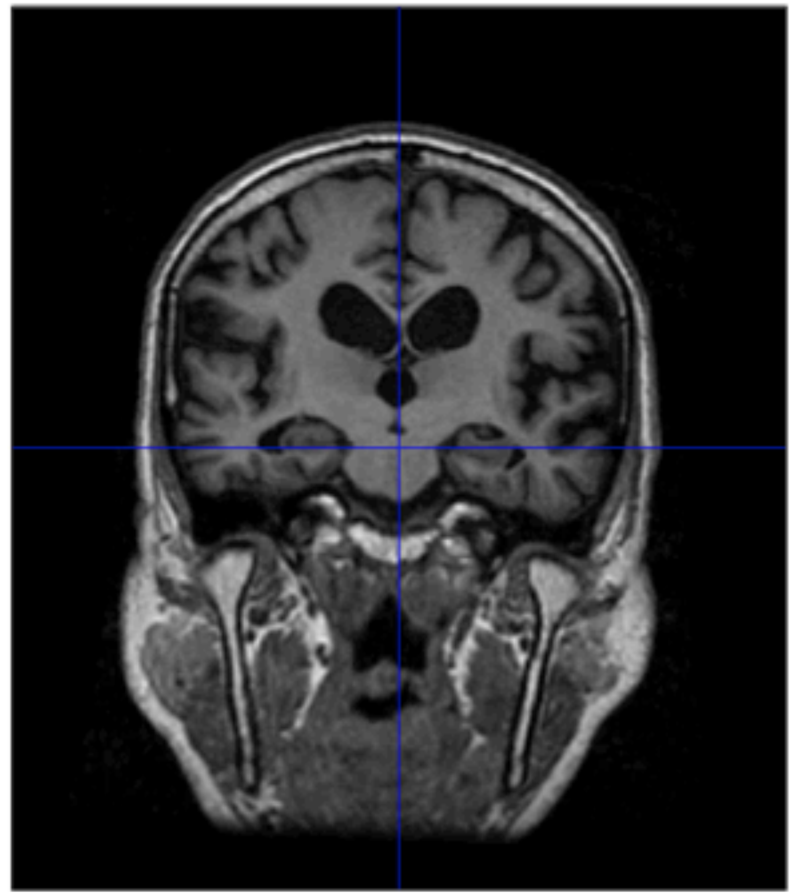
Aims of computational neuroanatomy

- Many interesting and clinically important questions might relate to the shape or local size of regions of the brain
- For example, whether (and where) local patterns of brain morphometry help to:
  - Distinguish schizophrenics from healthy controls
  - Understand plasticity, e.g. when learning new skills
  - Explain the changes seen in development and ageing
  - Differentiate degenerative disease from healthy ageing
  - Evaluate subjects on drug treatments versus placebo

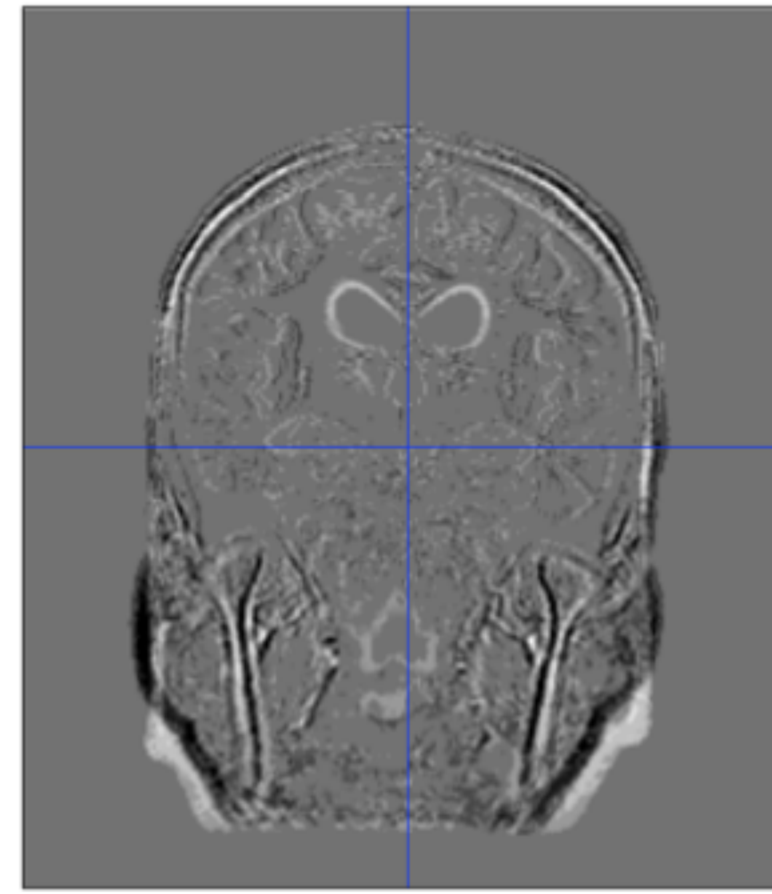
Alzheimer's Disease example



Baseline Image
Standard clinical MRI
1.5T T1 SPGR
1x1x1.5mm voxels



Repeat image
12 month follow-up
rigidly registered

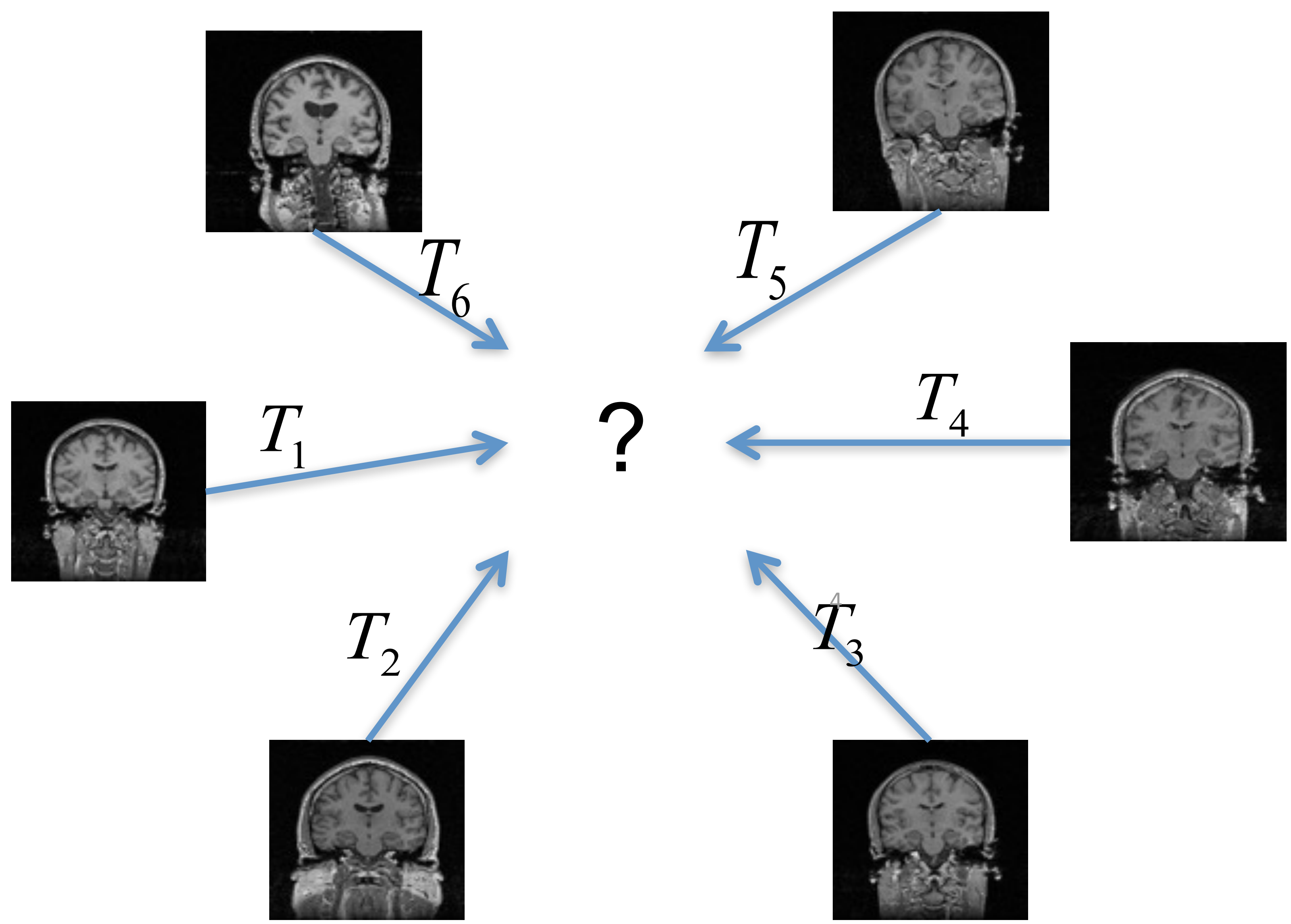


Subtraction image

GROUPWISE ALIGNMENT

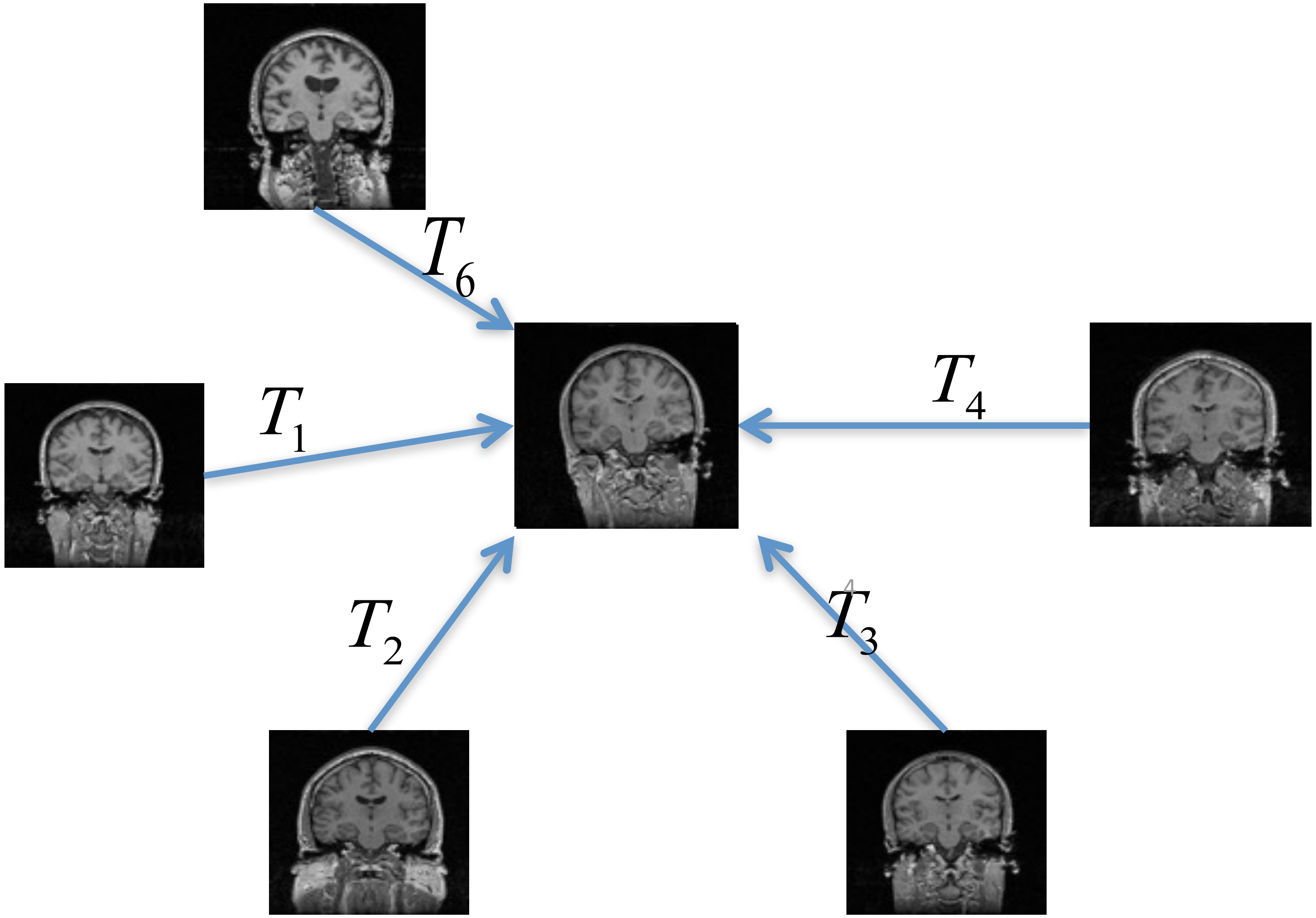
Groupwise (overall picture)

$$\max_{T_1,\ldots,T_N} \sum_{n=1}^{N} IS\left(I_n(T_n(x));\mu(x)\right)$$



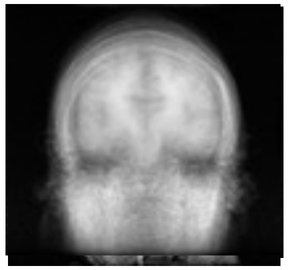
Groupwise (Iterative process)

- Rigid Alignment
  - Because it's rigid, it does not introduce bias in towards a specific morphology



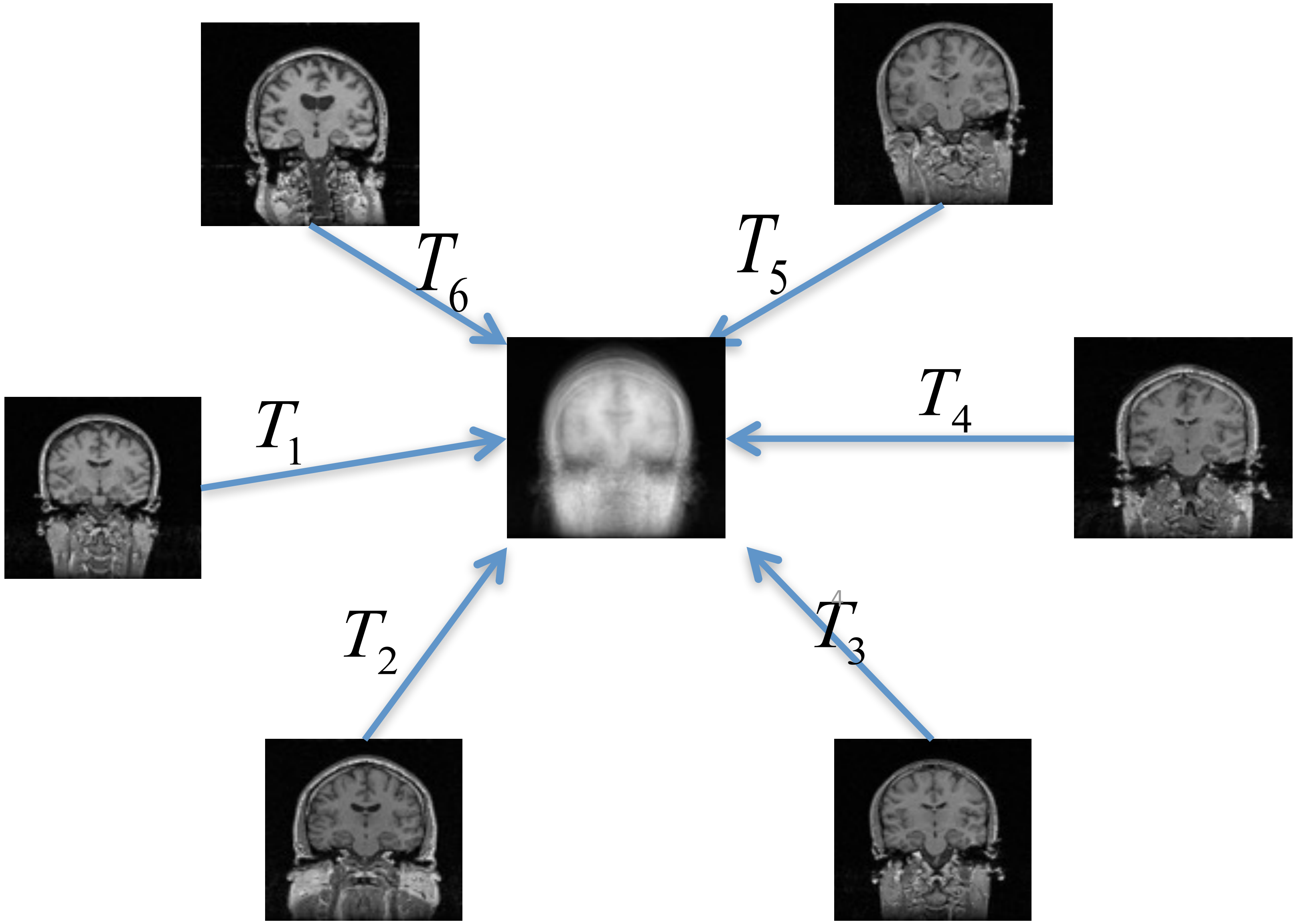
Groupwise (Iterative process)

- Congealing (averaging)



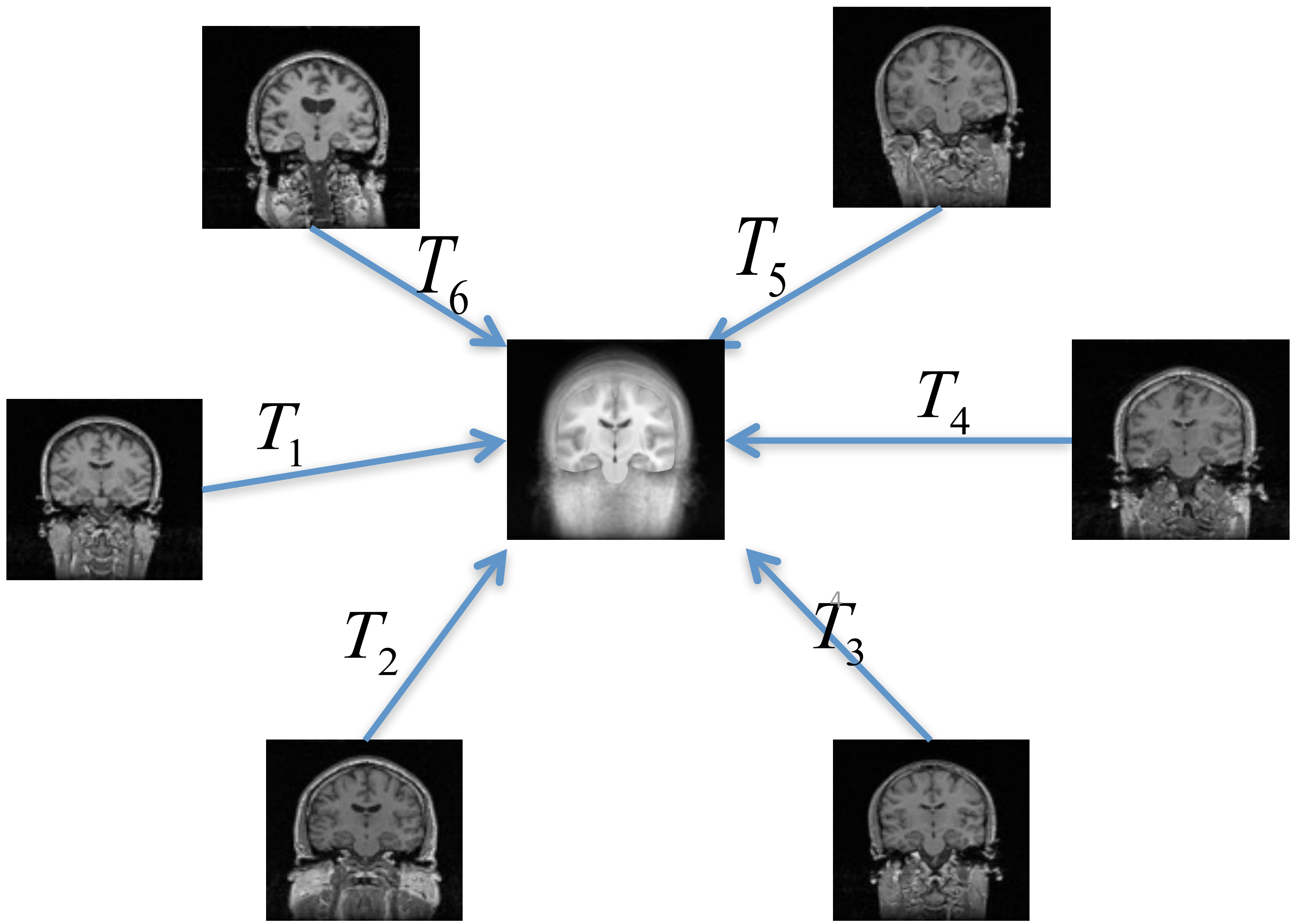
Groupwise (Iterative process)

- Affine Alignment + Congealing
  - Because it's now registered to an "average image", it does not introduce bias in towards a specific morphology



Groupwise (Iterative process)

- Non-Rigid Alignment + Congealing
  - The image become increasingly sharper
  - Sharper average ⇒ Better Registration ⇒ Sharper average

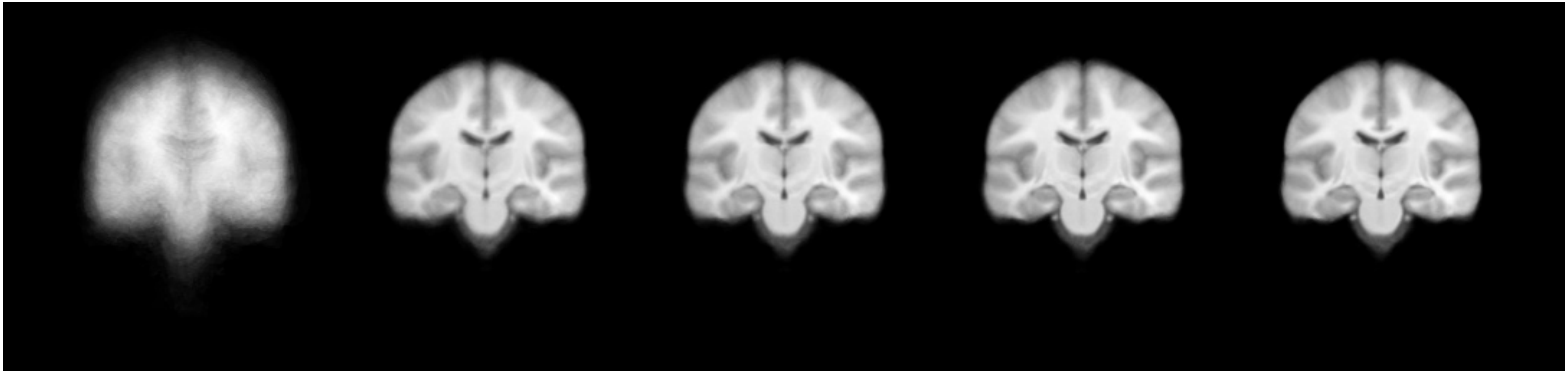


Groupwise (choices...)

- Optimisation procedure:
  - Iterative (rigid, affine, affine, nrr, nrr, nrr, nrr, ...)
    - like most people do, but less optimal
  - Joint
    - like most people would like to do, but computationally/memory intensive

$$\max_{T_1,\ldots,T_N} \sum_{n=1}^{N} IS\left(I_n(T_n(x)); \mu(x)\right)$$

- Choice of mapping parameterisation
  - Small vs large-world deformations
    - See next registration lecture



No Reg   Affine   NRR it1   NRR it2   NRR it3

VBM

How can we exploit this idea?

VBM overview

- Unified segmentation and spatial normalisation

↓

- Optional modulation with Jacobian determinant

↓

- Optional computation of tissue totals/globals

↓

- Gaussian smoothing

↓

- Voxel-wise statistical analysis

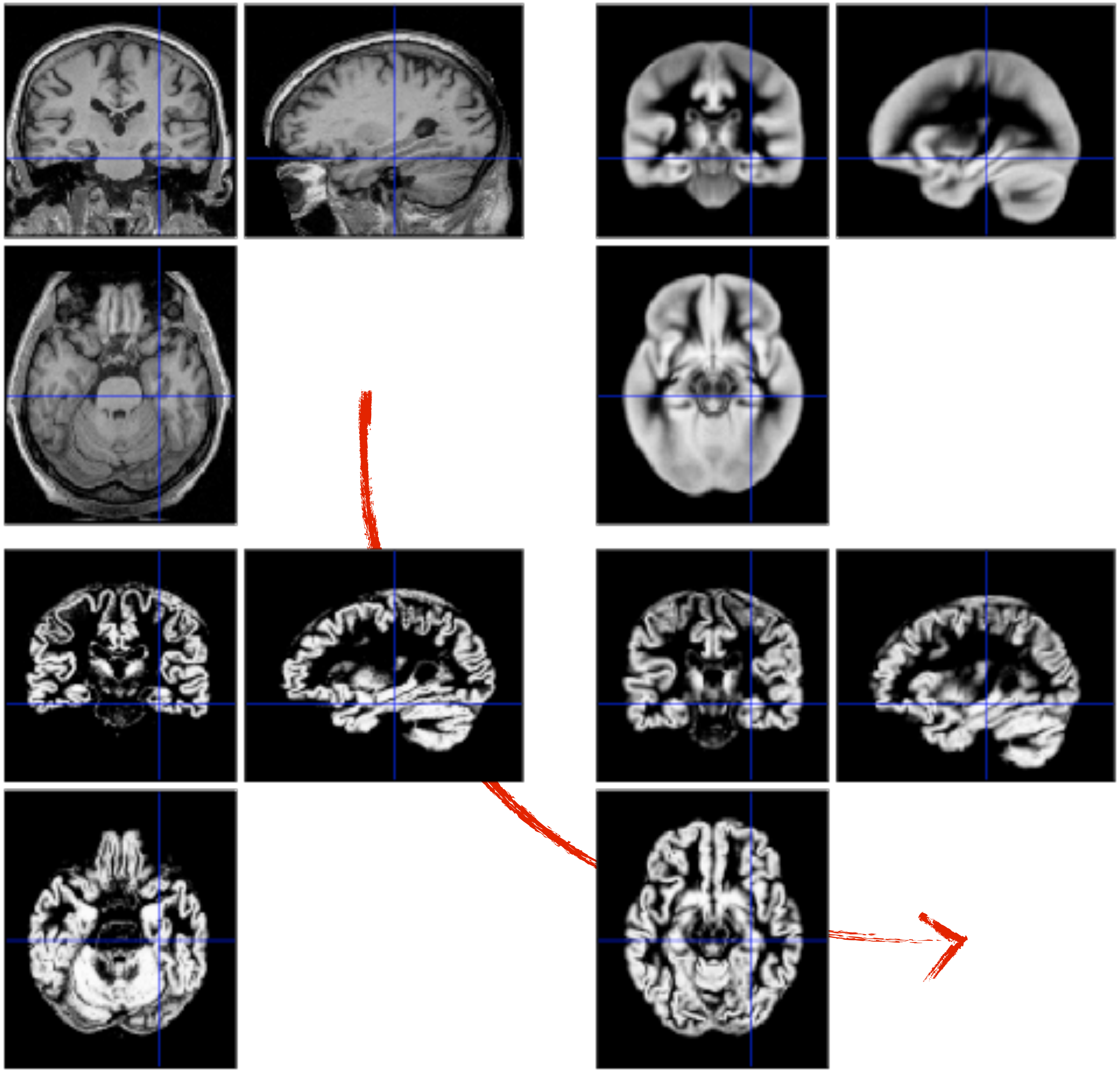
VBM in pictures

Segment

Normalise (GW)

Modulate (?)

Smooth



VBM in pictures

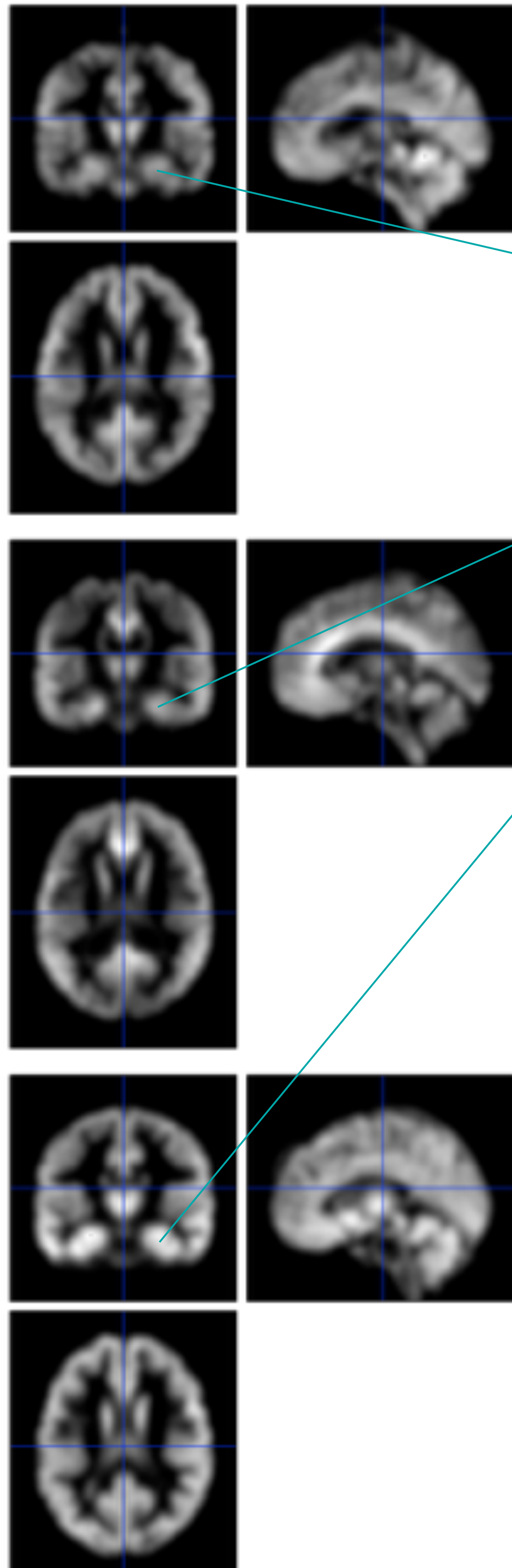
Segment

Normalise

Modulate (?)

Smooth

Voxel-wise statistics



$$\begin{bmatrix} a1xyz \\ a2xyz \\ \vdots \\ aNxyz \end{bmatrix} = Y = X\beta_{xyz} + e_{xyz}$$

$$e_{xyz} \sim N(0, \sigma^2_{xyz} V)$$

$$X = \begin{bmatrix} 1 & 0 \\ 1 & 0 \\ \vdots & \vdots \\ 0 & 1 \\ 0 & 1 \end{bmatrix}$$

VBM in pictures

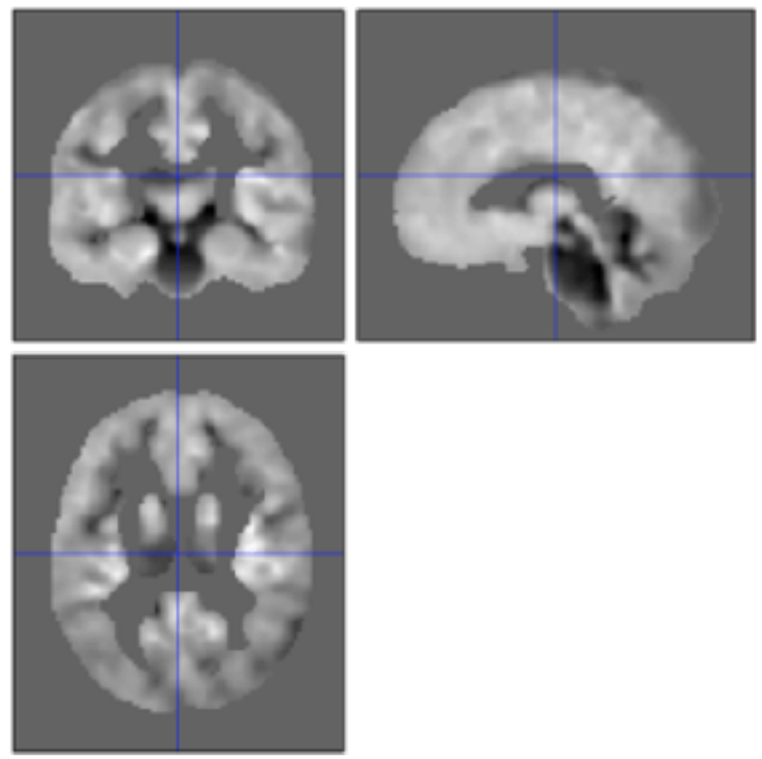
Segment

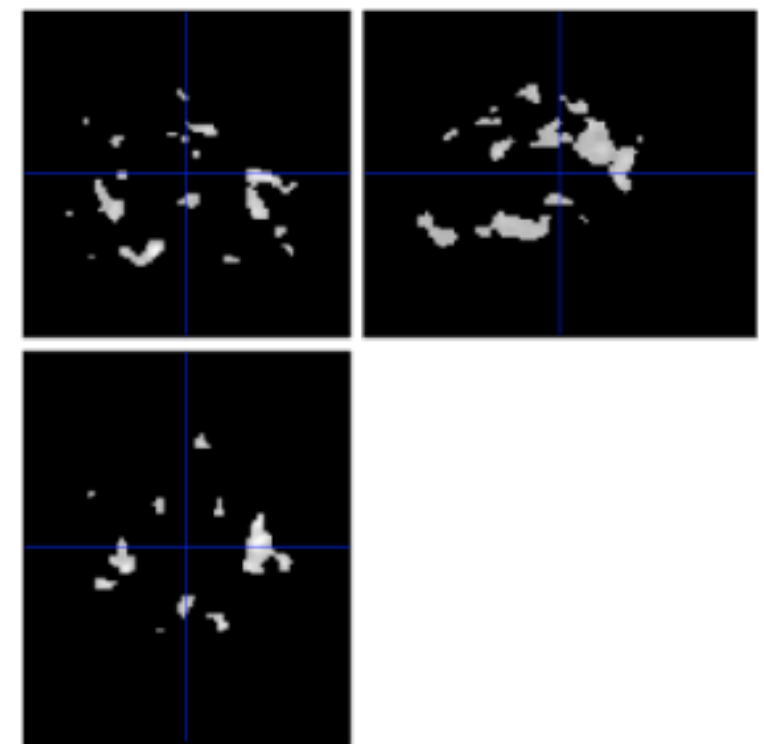
Normalise

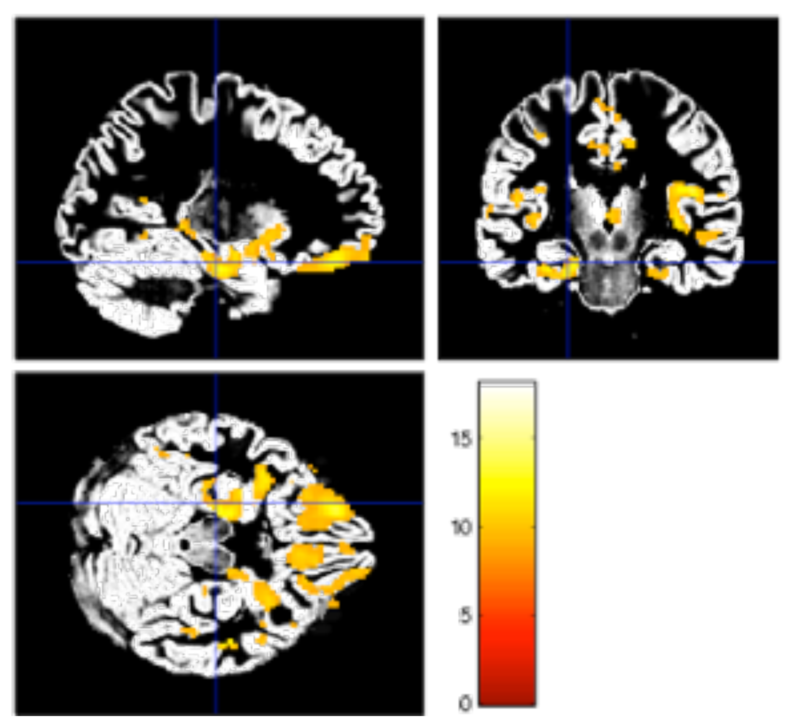
Modulate (?)

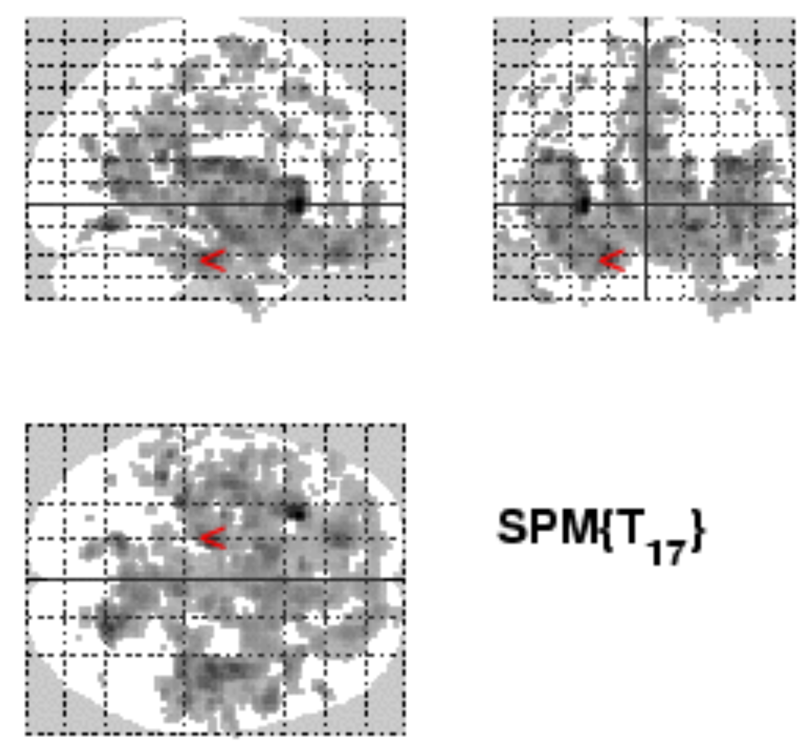
Smooth

Voxel-wise statistics



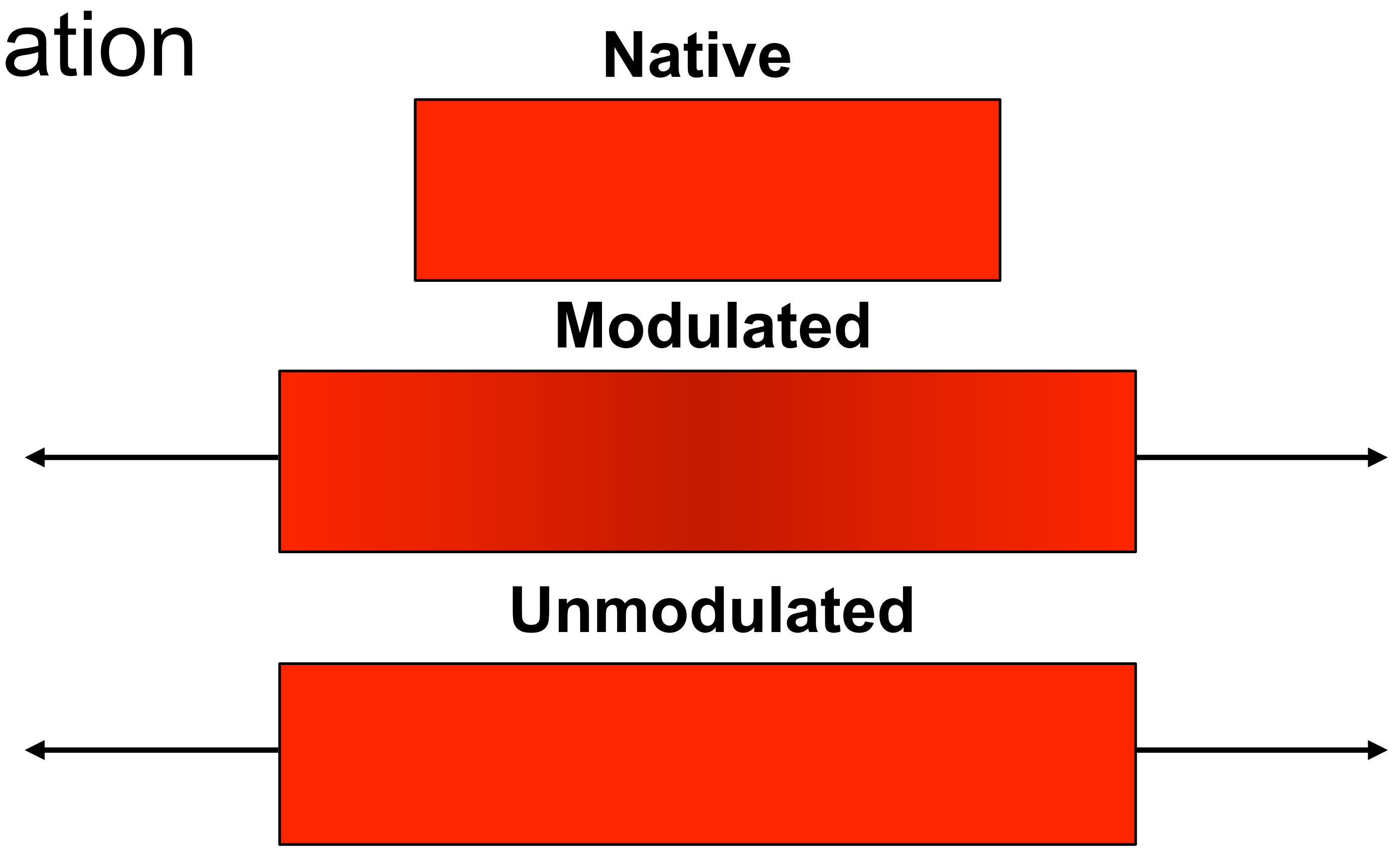






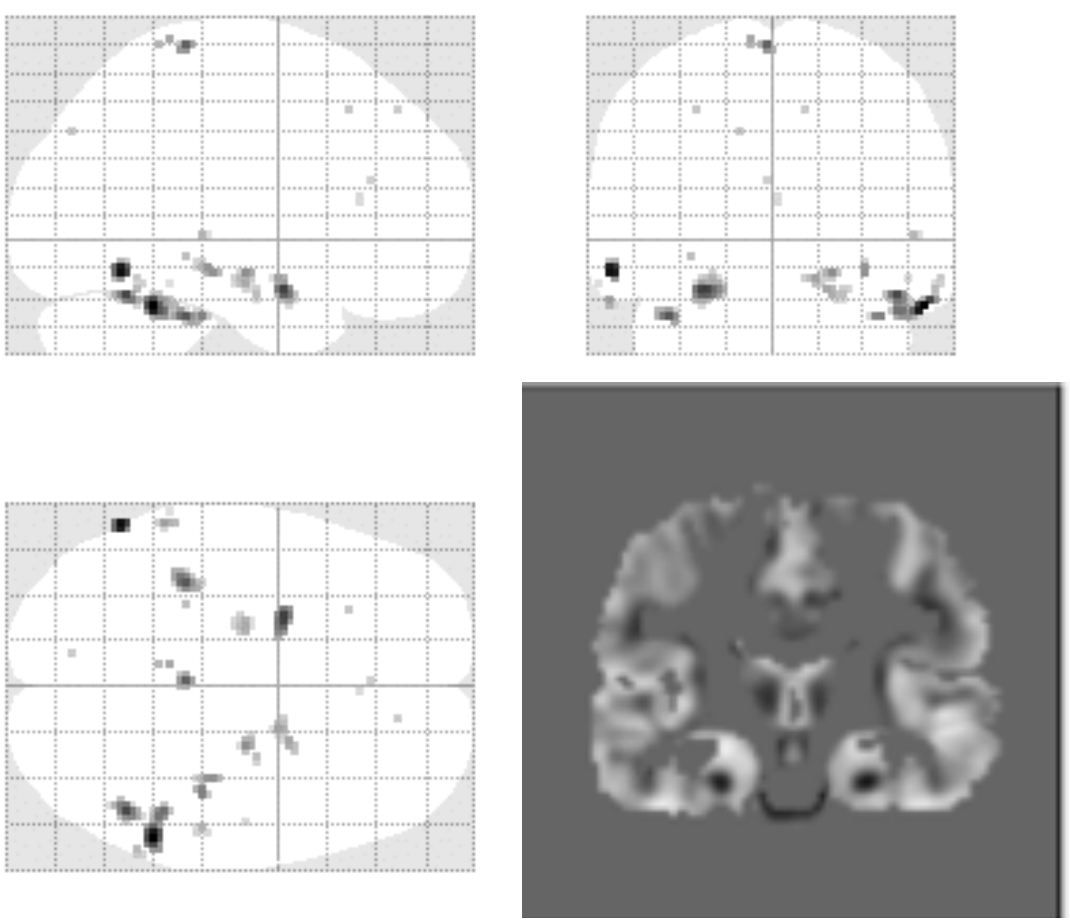
Decisions, decisions... and a few problems

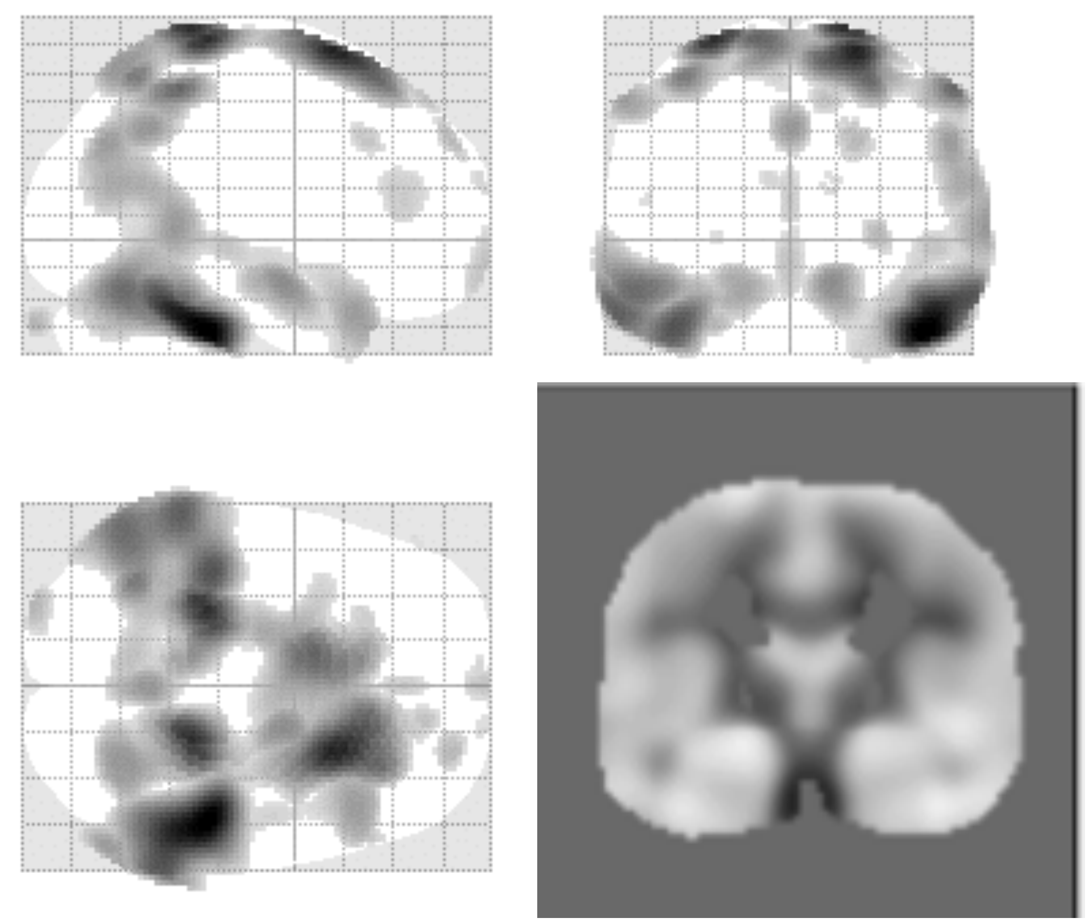
- Whether to modulate
  - Yes: Preserves regional volume
  - No: Preserves concentrations
- Adjusting for total GM or Intracranial Volume
- How much to smooth
- Limitations of linear correlation
- Statistical validity



Problems: Smoothing

- Between 7 and 14mm is probably best
  - (lower is okay with better registration techniques)
- The results below show two fairly extreme choices, 5mm on the left, and 16mm, right



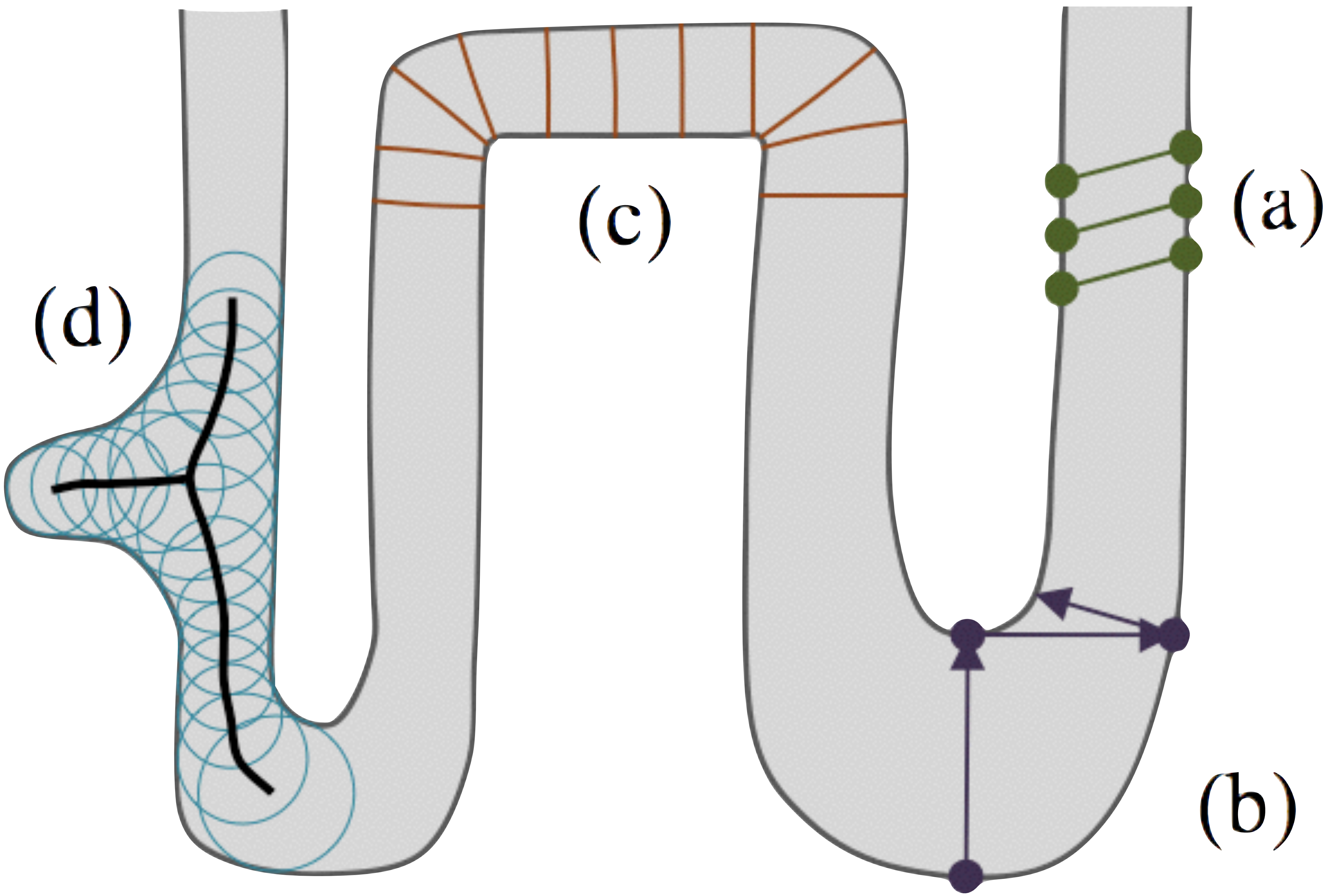


Variations on VBM

- TBM
  - "All modulation, no gray matter"
    - Jacobian determinant: Davatzikos et al. (1996) JCAT 20:88-97
- DBM
  - Cao and Worsley (1999) Ann Stat 27:925-942
  - Ashburner et al (1998) Hum Brain Mapp 6:348-357
- Other "variations" on TBM
  - Chung et al (2001) NeuroImage 14:595-606
- And also... other statistical analysis/correction strategies

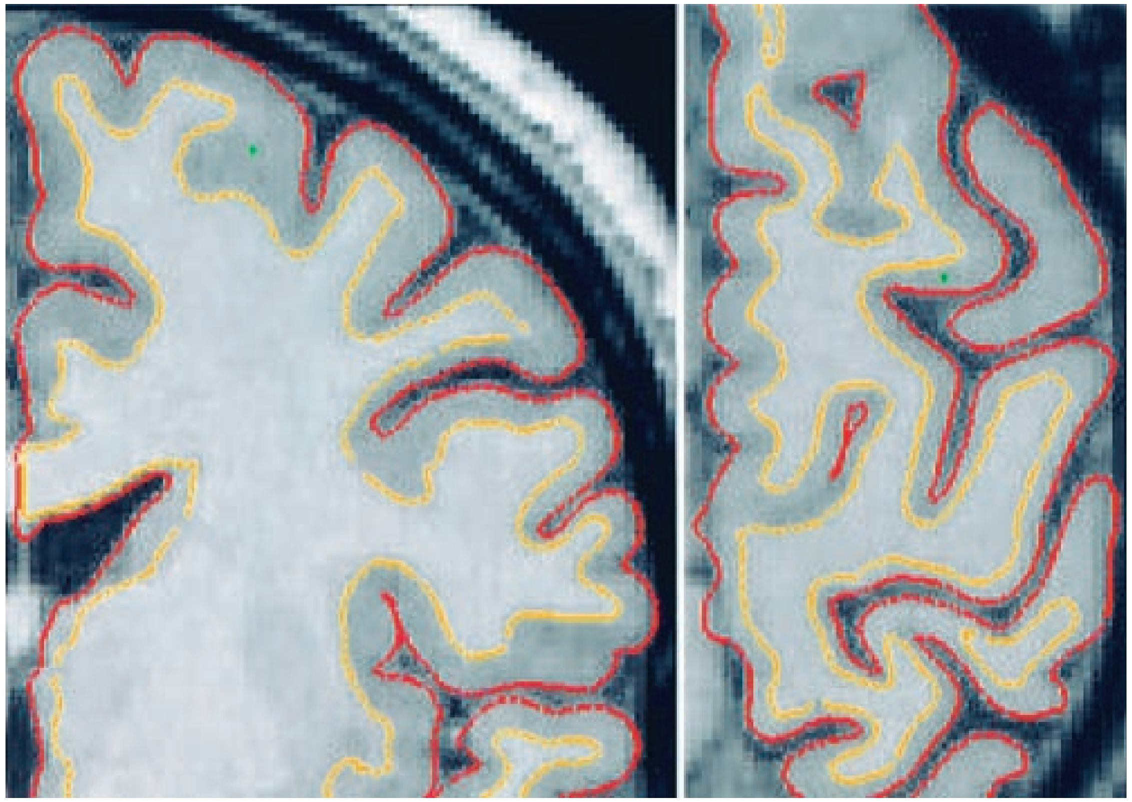
CORTICAL THICKNESS

Cortical Thickness



Surface Based CTE

- Most well known packages:
  - Freesurfer
  - Cruise
- Fits 2 surfaces to the cortex
- Types of surfaces
  - Coupled (example a)
    - Thickness is just a node distance
  - Independent (example a)
    - Thickness has to be approximated by casting a line perpendicular to the surface



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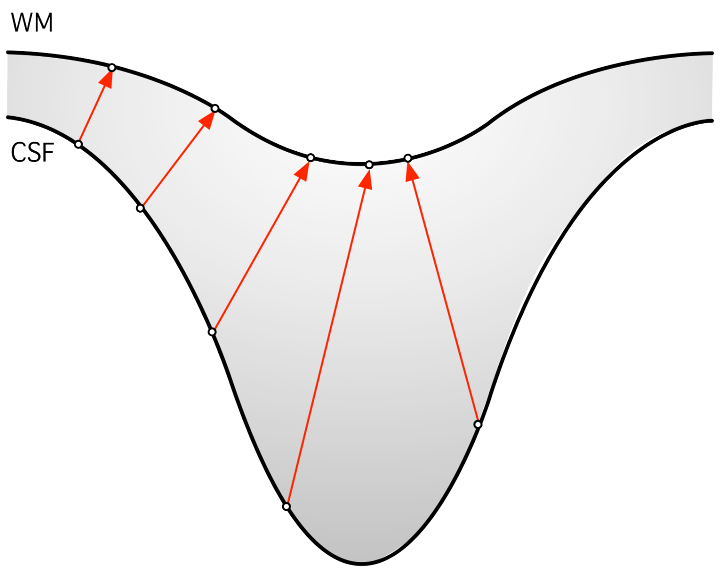

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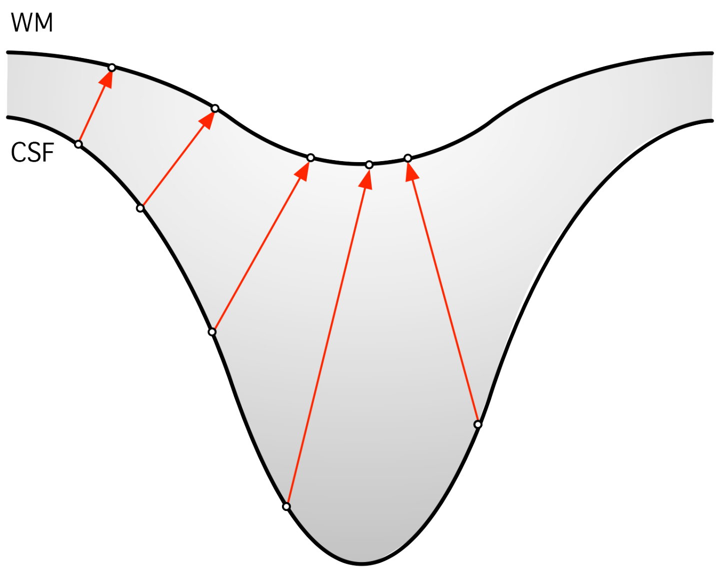

  - Independent (example a)
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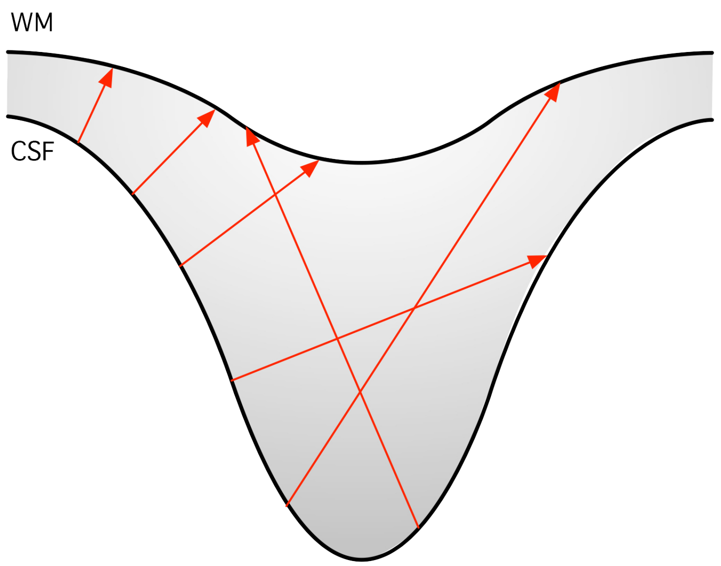
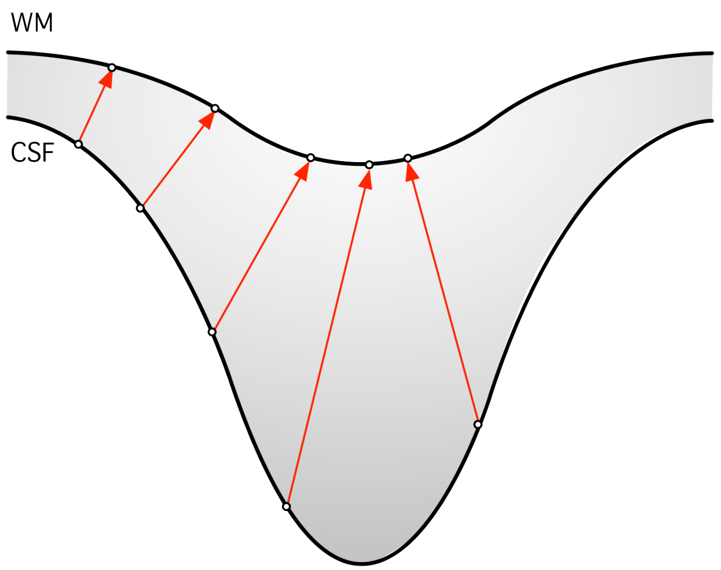
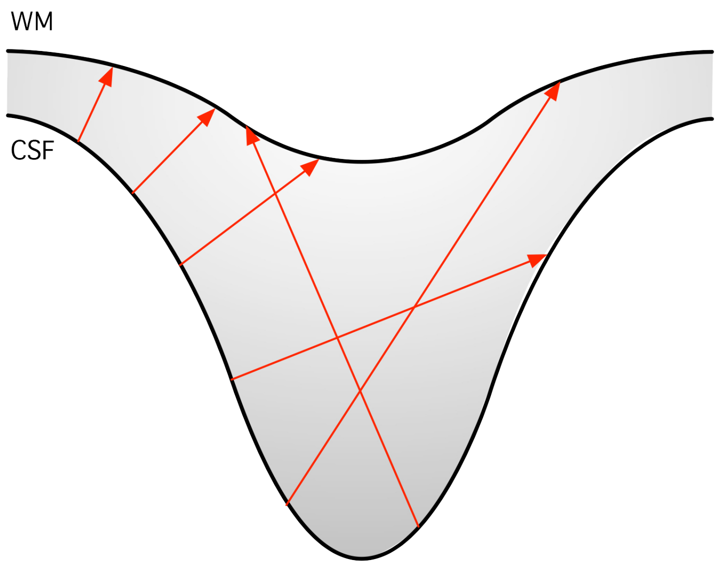


Surface Based CTE

- Advantages
  - Curvature constrains
  - Sub-voxel precision
  - Inter-subject comparison

- Disadvantages
  - Curvature constrains
  - Optimisation
  - Time
  - Sliding in coupled curves
  - Approximated distance in independent curves

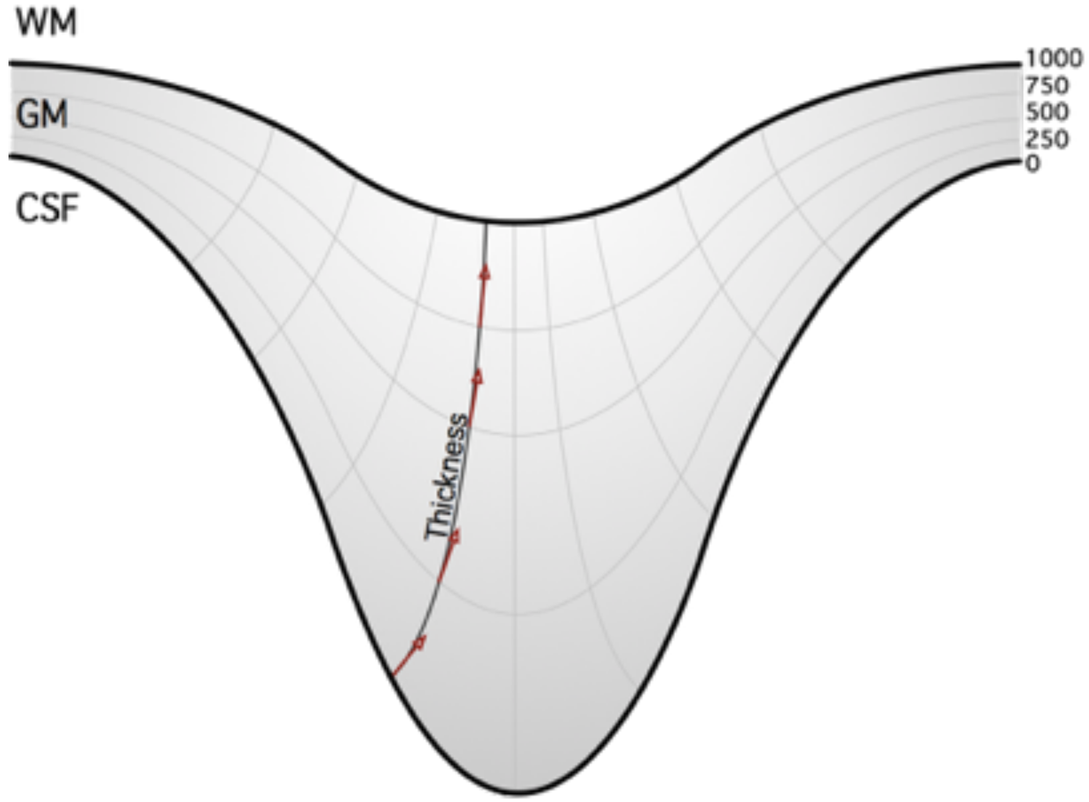


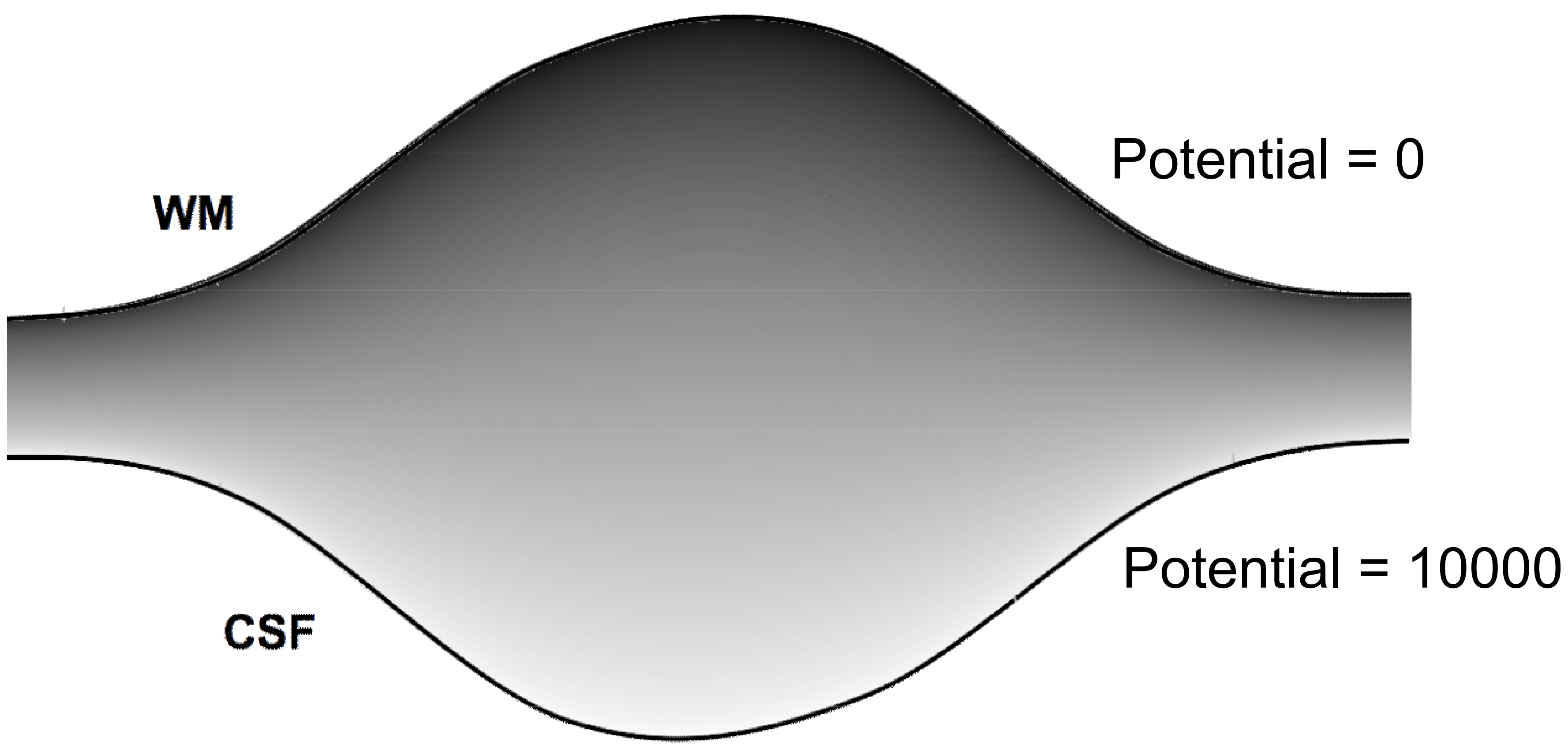


Voxel Based CTE (Laplace equation)

- Solves the Laplace equation between 2 regions (example c)
- Integrates the distance by following the perpendicular to the Laplace equation's isolines

$$\nabla^2\phi = 0$$



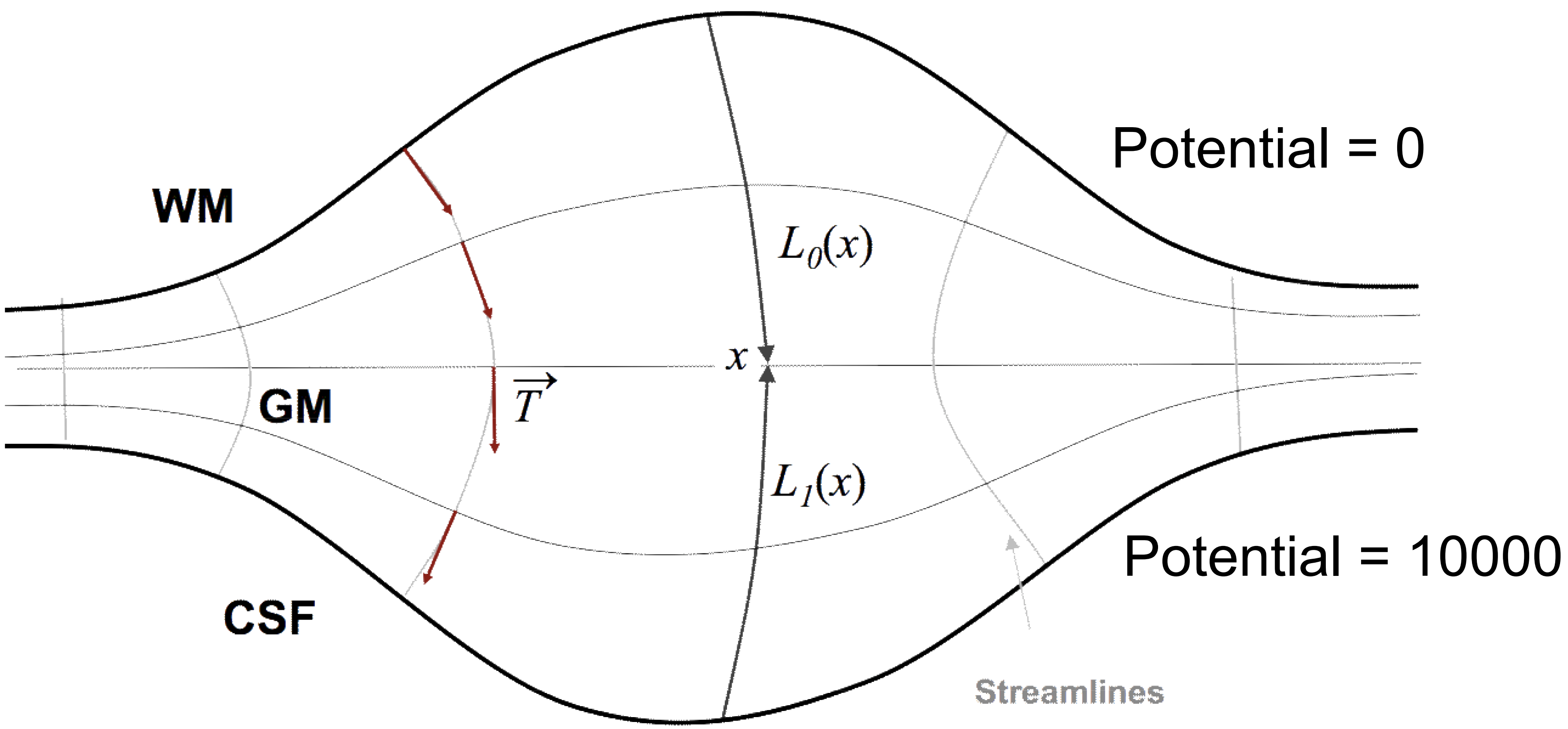


Voxel Based CTE (Laplace equation)

$$Thick = L0 + L1.$$

$$\nabla L \cdot T = f$$

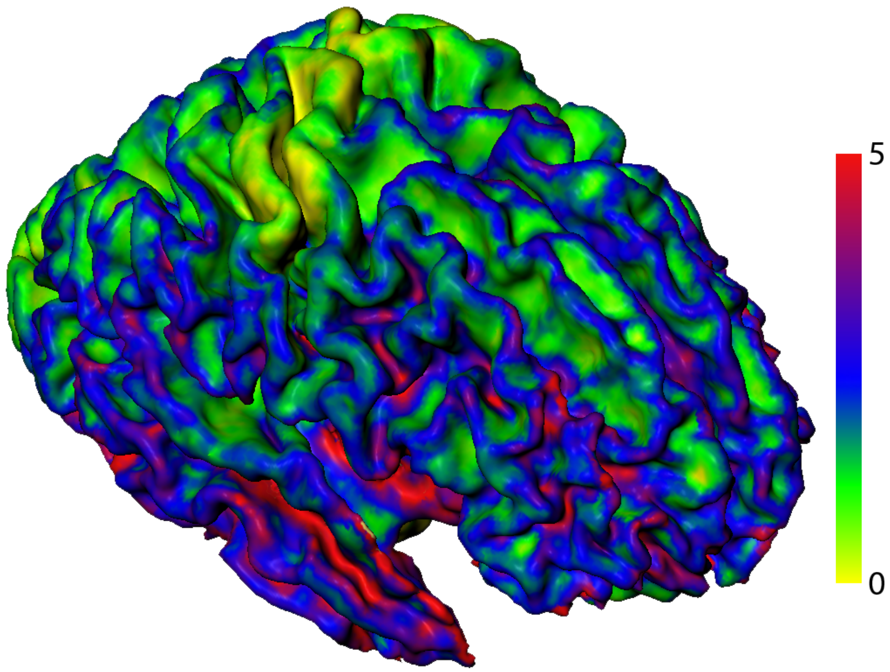
$$L0_{(x,y,z)} = \frac{1}{(a_y a_z|T_x| + a_x a_z|T_y| + a_x a_y|T_z|)}\Big[f_{(x,y,z)} a_x a_y a_z + a_y a_z|T_x| * L0_{(x \mp a_x, y, z)} + a_x a_z|T_y| * L0_{(x, y \mp a_y, z)} + a_x a_y|T_z| * L0_{(x, y, z \mp a_z)}\Big]$$

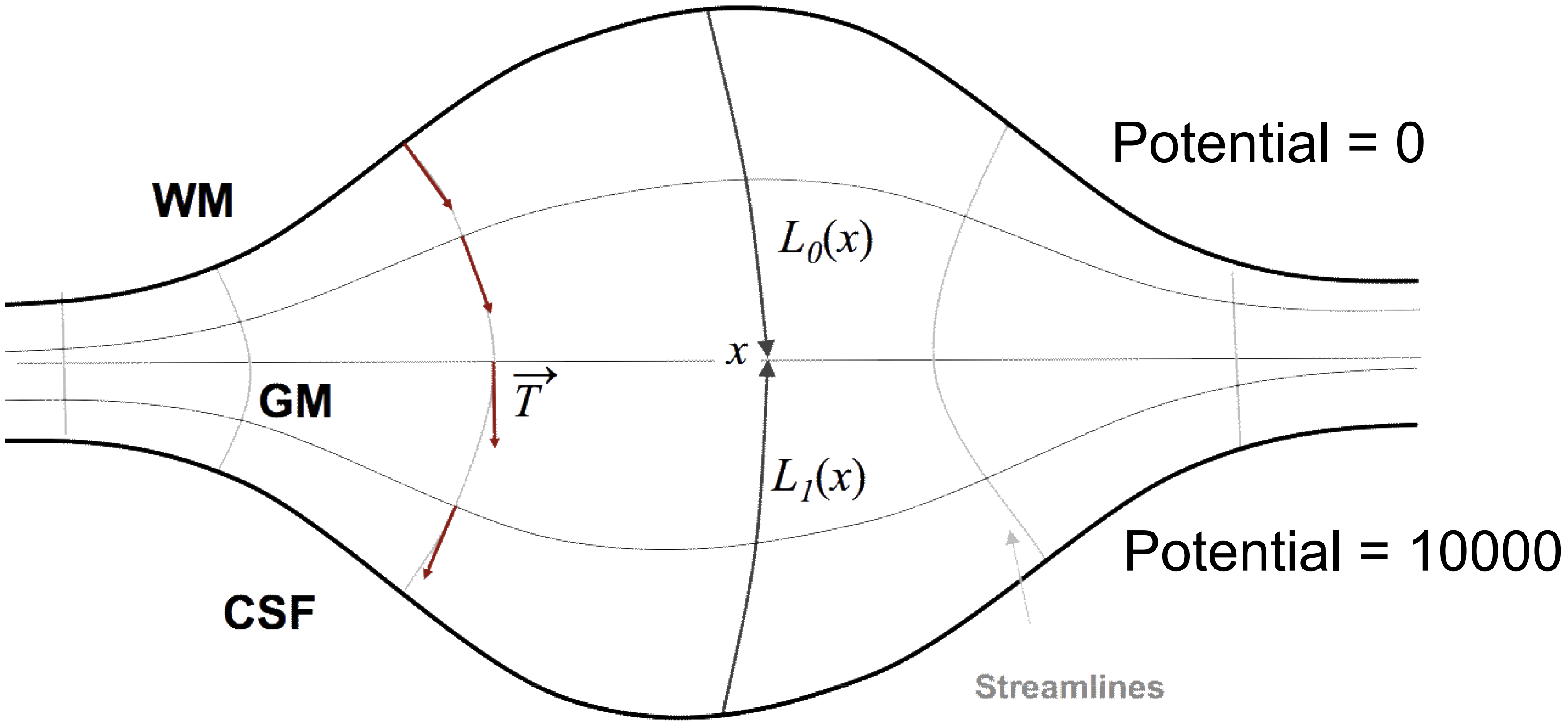


Voxel Based CTE (Laplace equation)

- Advantages
  - One-to-one correspondence
  - Well behaved

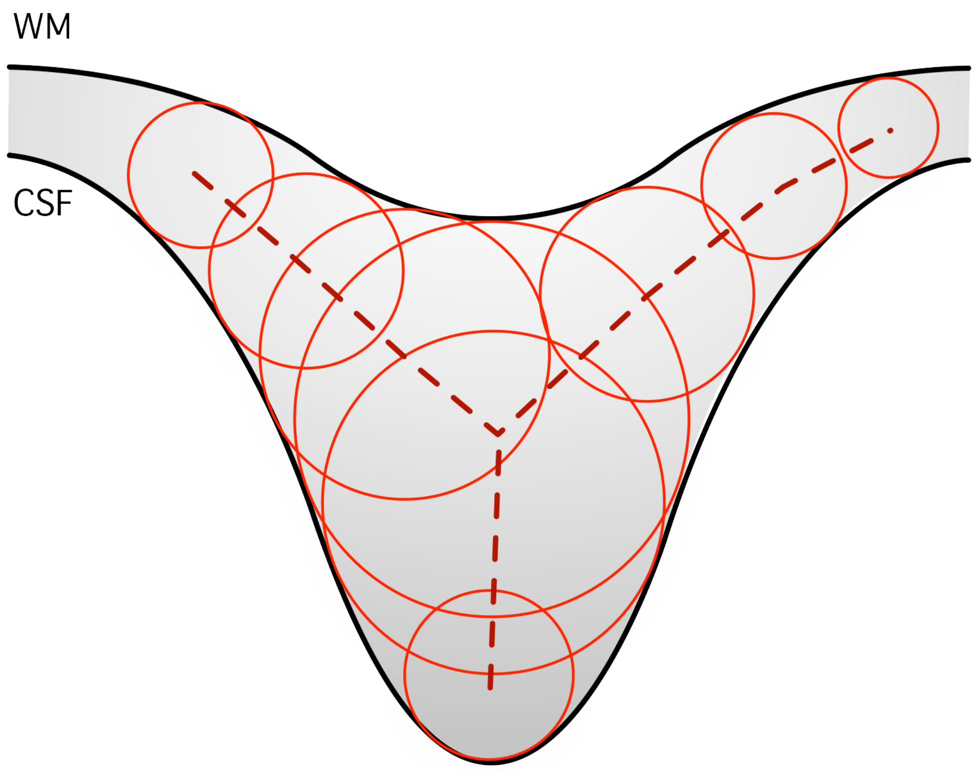
- Disadvantages
  - Does not implicitly take PV into account
  - Topology correctness





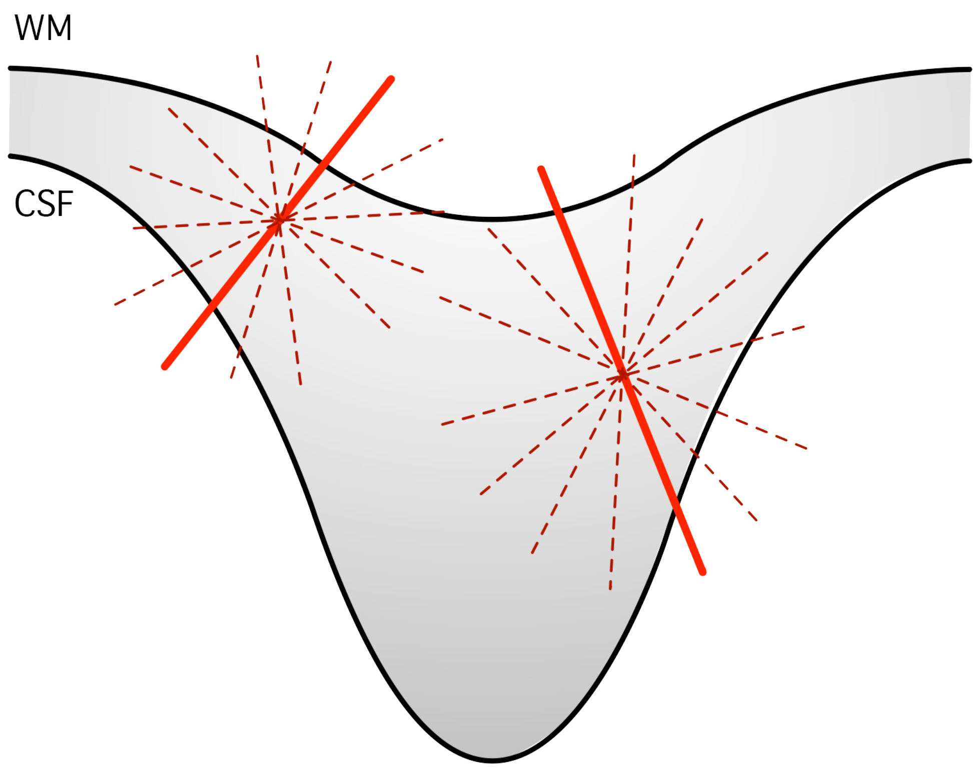
Voxel Based CTE (Maximum Spheres)

- Maximum Spheres (example d)
  - At each point in the cortex, find the largest size sphere that fits within the cortex
  - Advantages:
    - Deals relatively well with closed sulci
  - Disadvantages:
    - Binary images only
    - Branching effect



Voxel Based CTE (Line Integral)

- Line Integral
  - At each point in the cortex, find the direction that minimises the integral of the GM segmentation
  - Advantages:
    - takes PV into account
  - Disadvantages:
    - Problems with sulci
    - Discretisation



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  - At each point in the cortex, find the direction that minimises the integral of the GM segmentation
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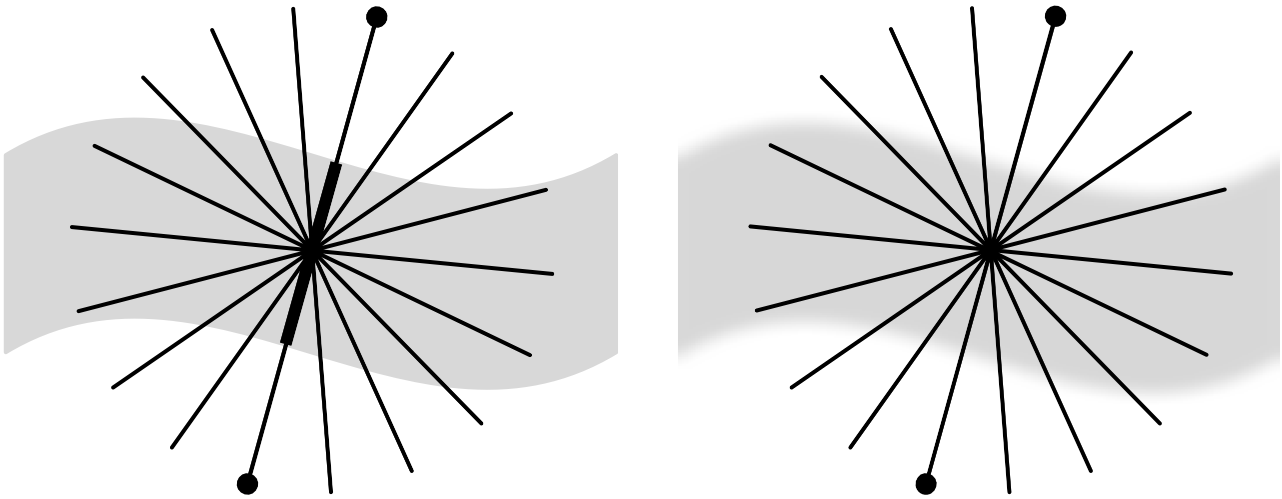
    - takes PV into account
  - Disadvantages:
    - Problems with sulci
    - Discretisation

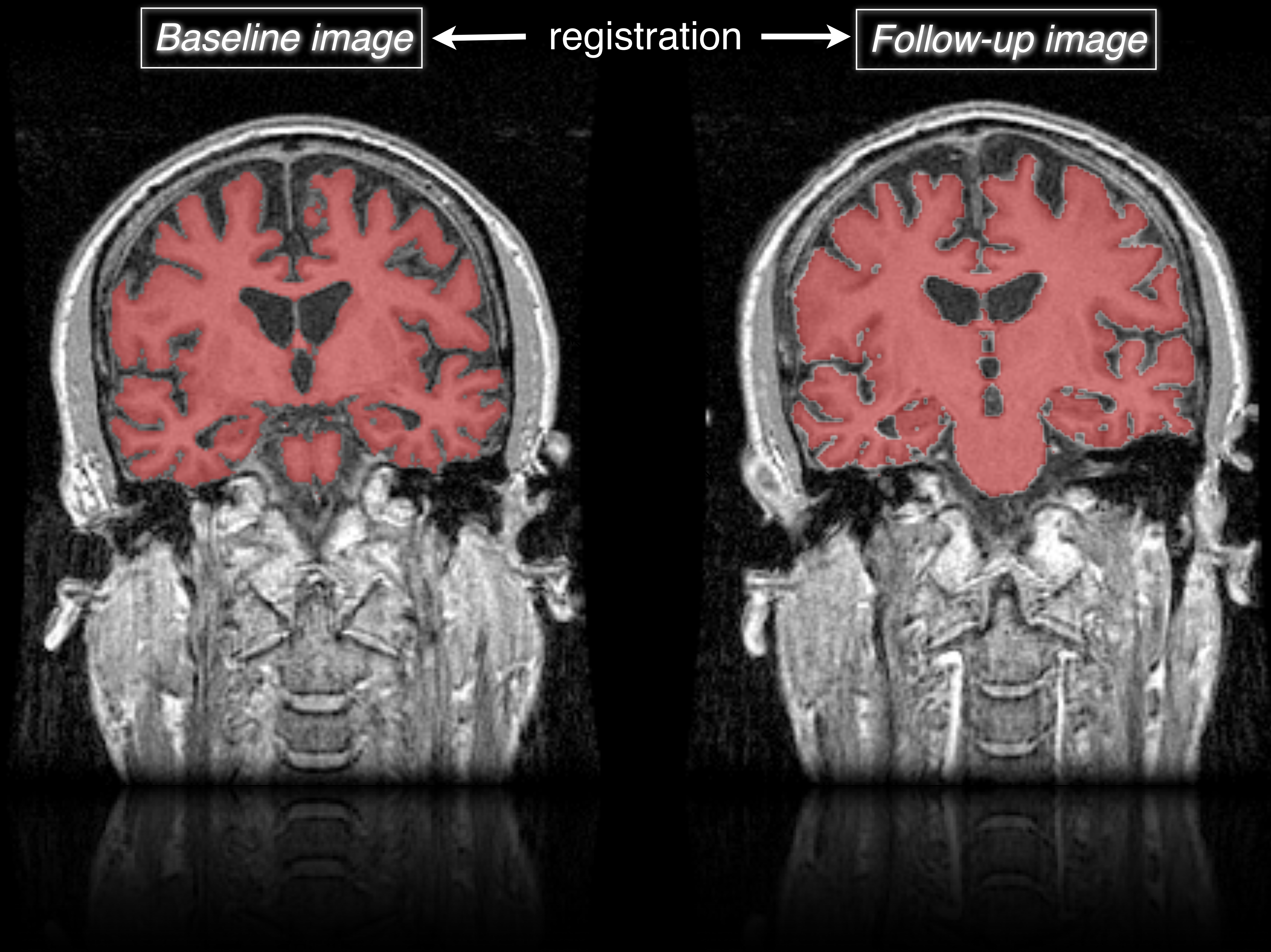
$$T(\vec{x}) := \min_{l \in L_{\vec{x}}} \int_{l} P(\vec{r})\,dl,$$



(a) (b)

ATROPHY ESTIMATION (VOLUME CHANGE)

Extracting imaging biomarkers: measuring cerebral atrophy



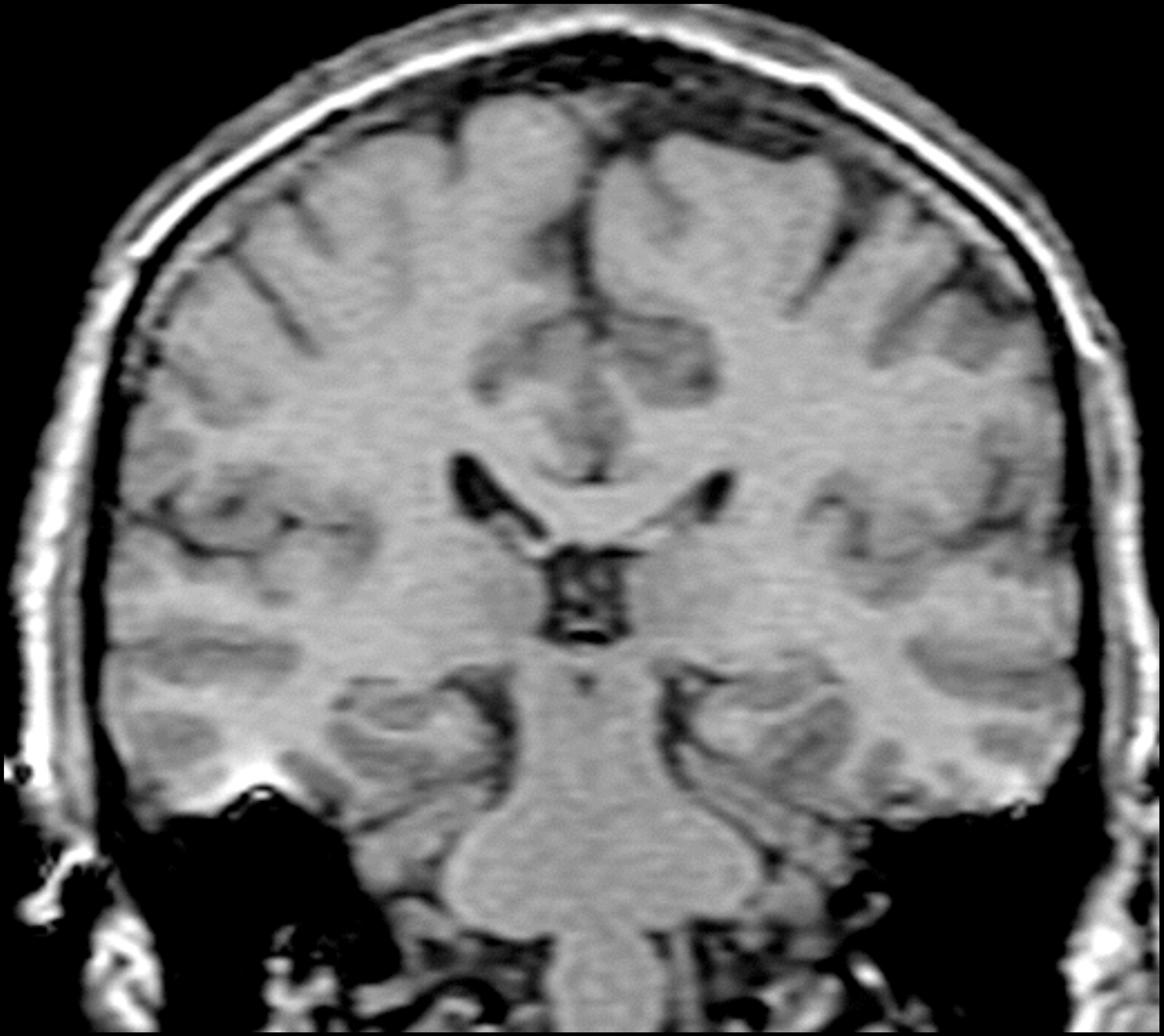
MRI and Biomarkers: Dealing with Artefacts

- Instrument/Scanner:
  - Geometric distortion.
    - Magnetic gradient non-linearity (grad warp artefact).
    - Magnetic gradient drift (scaling effect)
  - Intensity distortion/inhomogeneity.
    - Inhomogeneity in B0 or RF pulses,
    - non-uniform receiver sensivity,
- Subject:
  - "Ghost effect".
    - Motion/movement.
  - "Streaks effect"
  - Pulsatile flow in carotid arteries.

Once everything is corrected for... and QC...

MCI

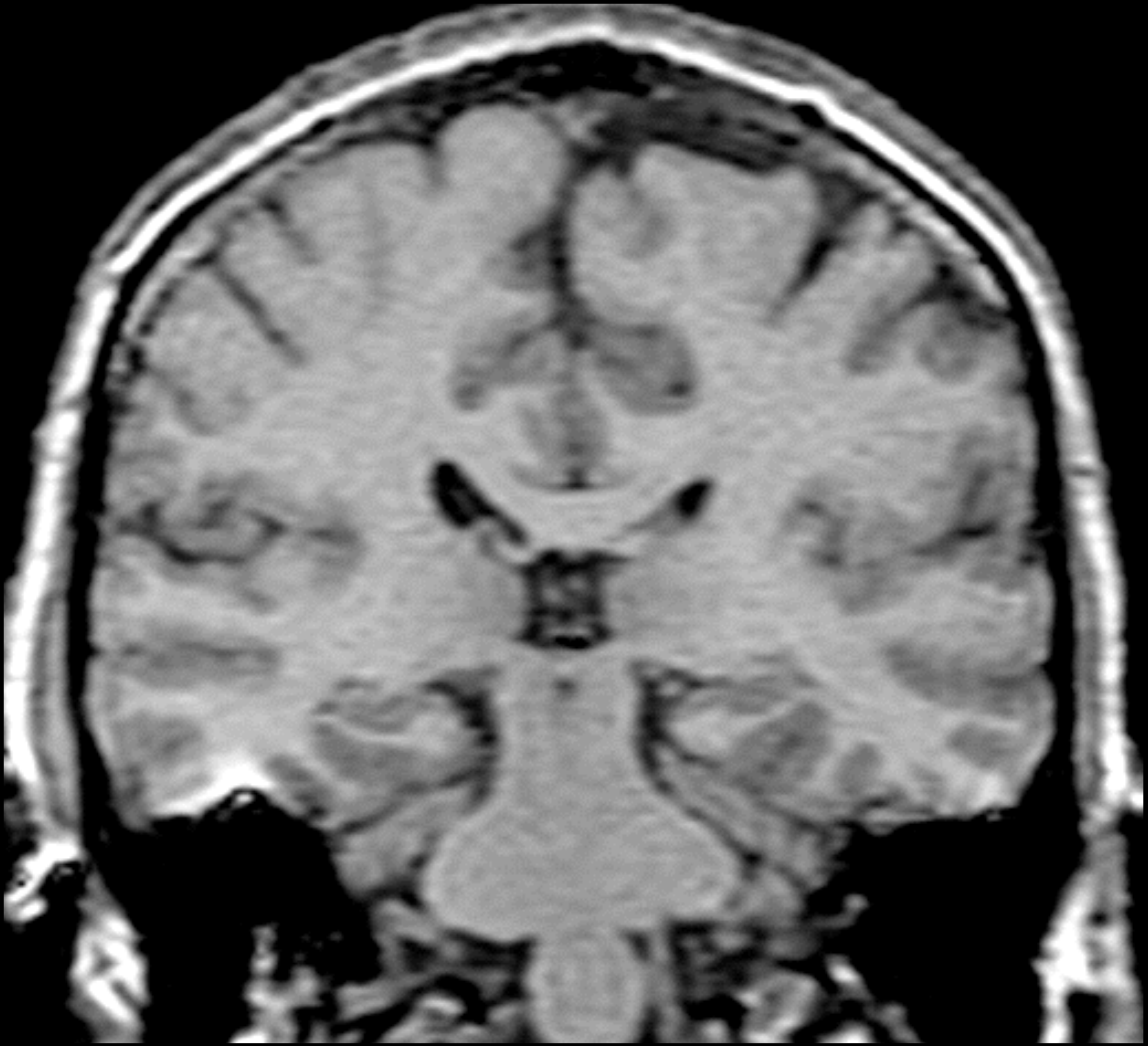
Scan 1



... Registered... and QC again...

MCI

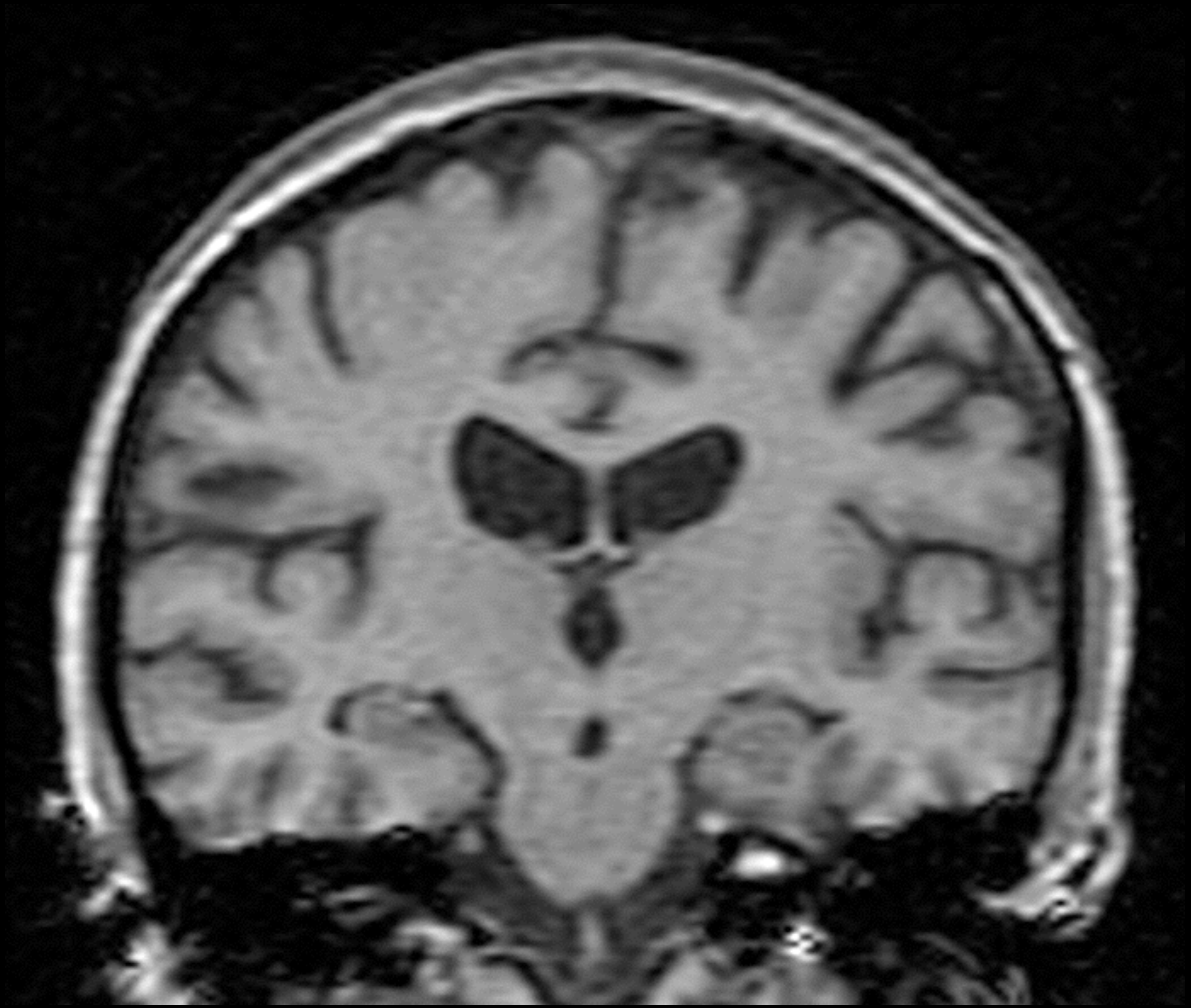
Scan 2



Again, once everything is corrected for... and QC...

MCI-AD

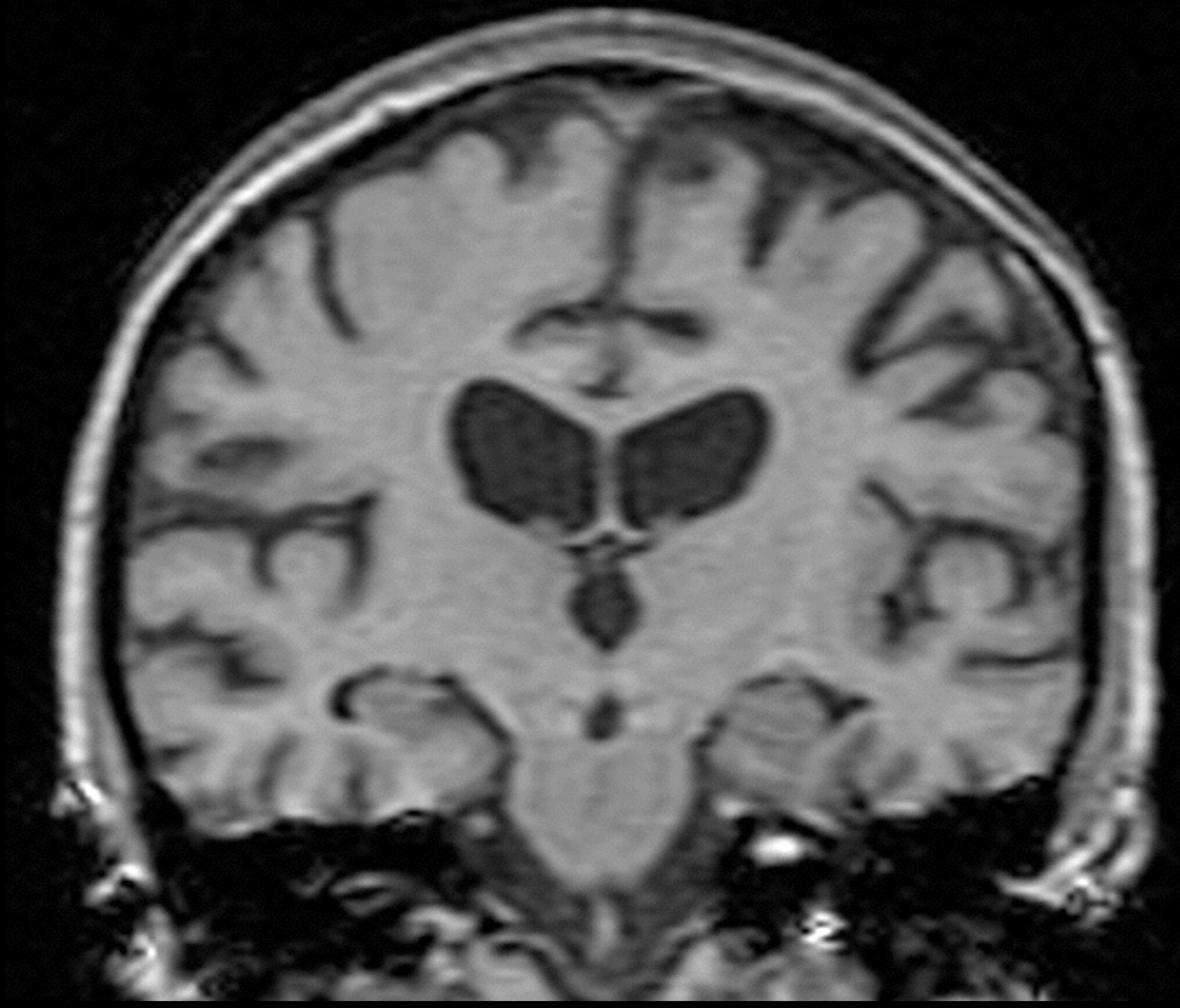
Scan 1



... Registered... and QC again...

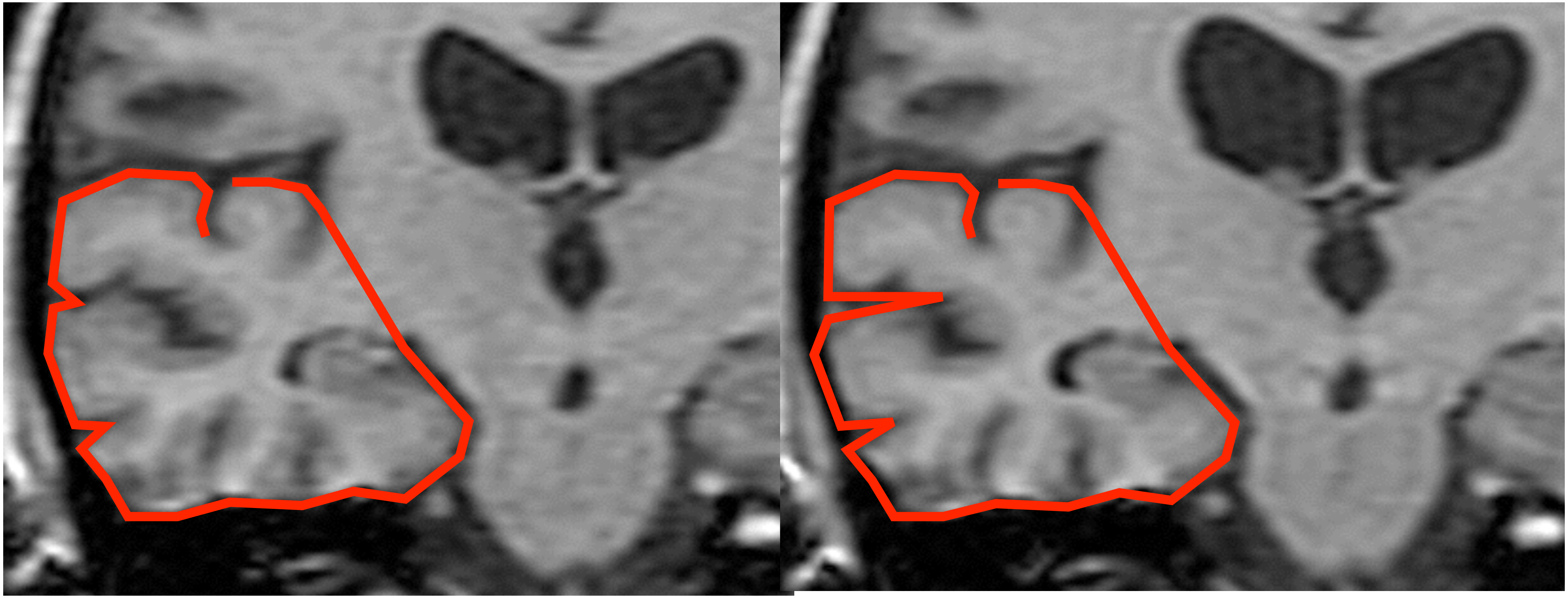
MCI-AD

Scan 2



Direct Volume and why it can be problematic

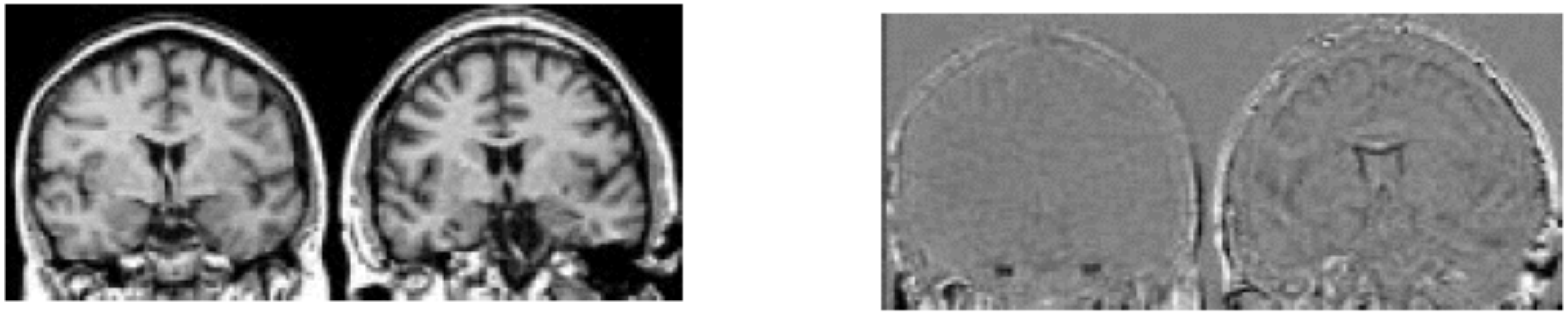
- Still very much used by many groups
  - Simple, practical, easy
- However, volume difference methods depends directly on the manual/ automated segmentations, which includes segmentation errors



ATROPHY ESTIMATION - BSI

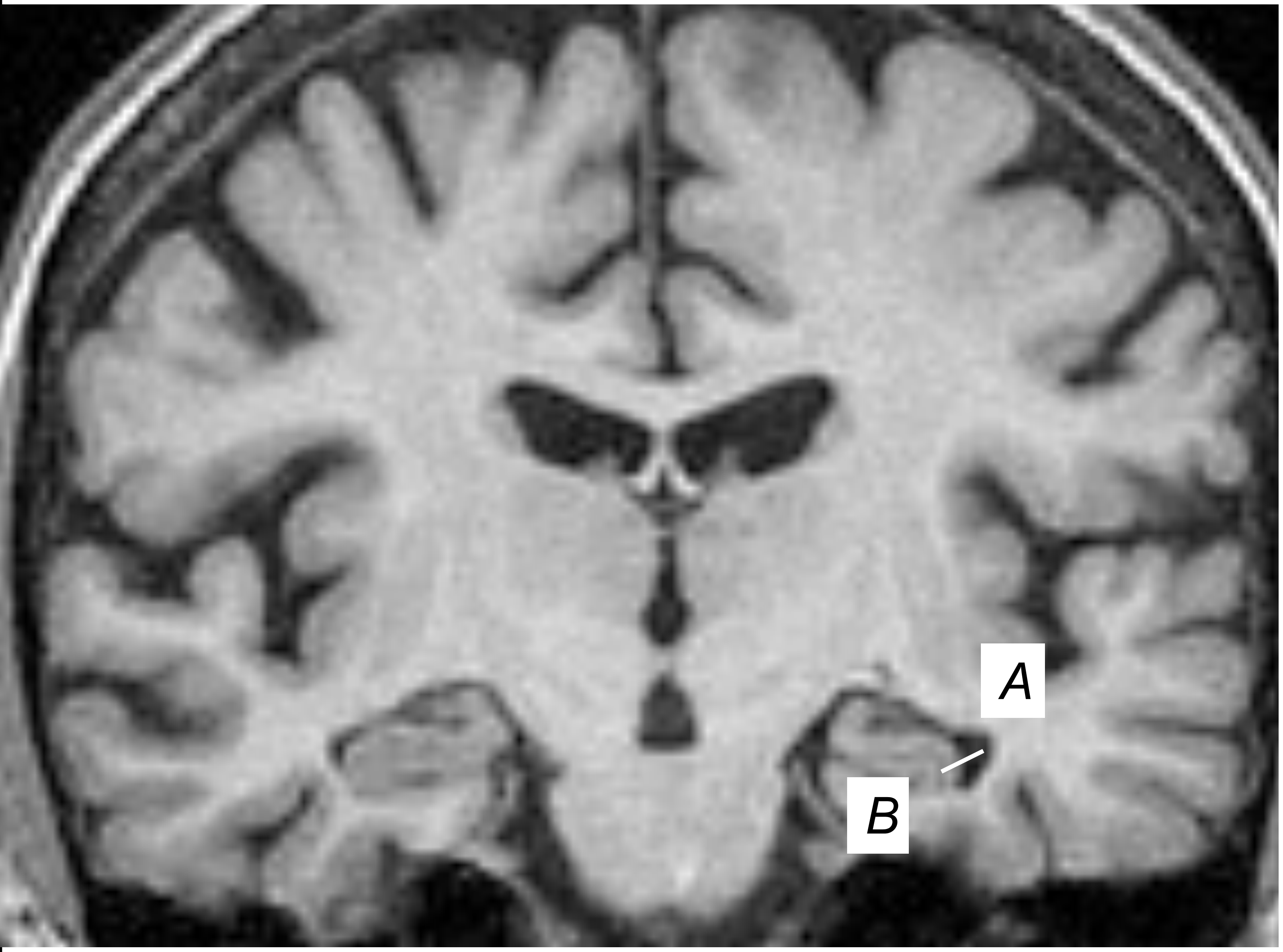
BSI Background

- BSI measures the brain volume change between two serial MR images.
- BSI currently being used as outcome measure in several phase 2 and 3 clinical trials.
- Based on the observation that a volume change is associated with a boundary shift.
  - Volume change $\Rightarrow$ boundary shift $\Rightarrow$ intensity change
- We can measure the change in volume by measuring the intensity change between baseline & repeat images
  - Volume change $\Leftarrow$ boundary shift $\Leftarrow$ intensity change

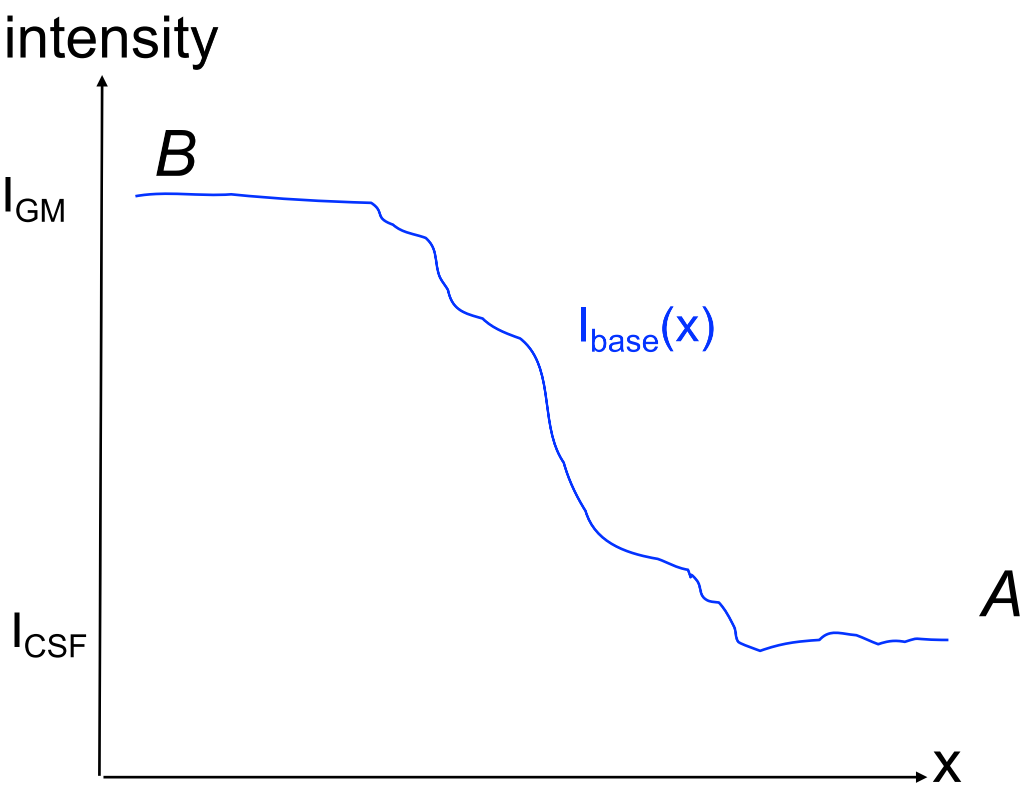


(a) (b) (c) (d)

What is the BSI?

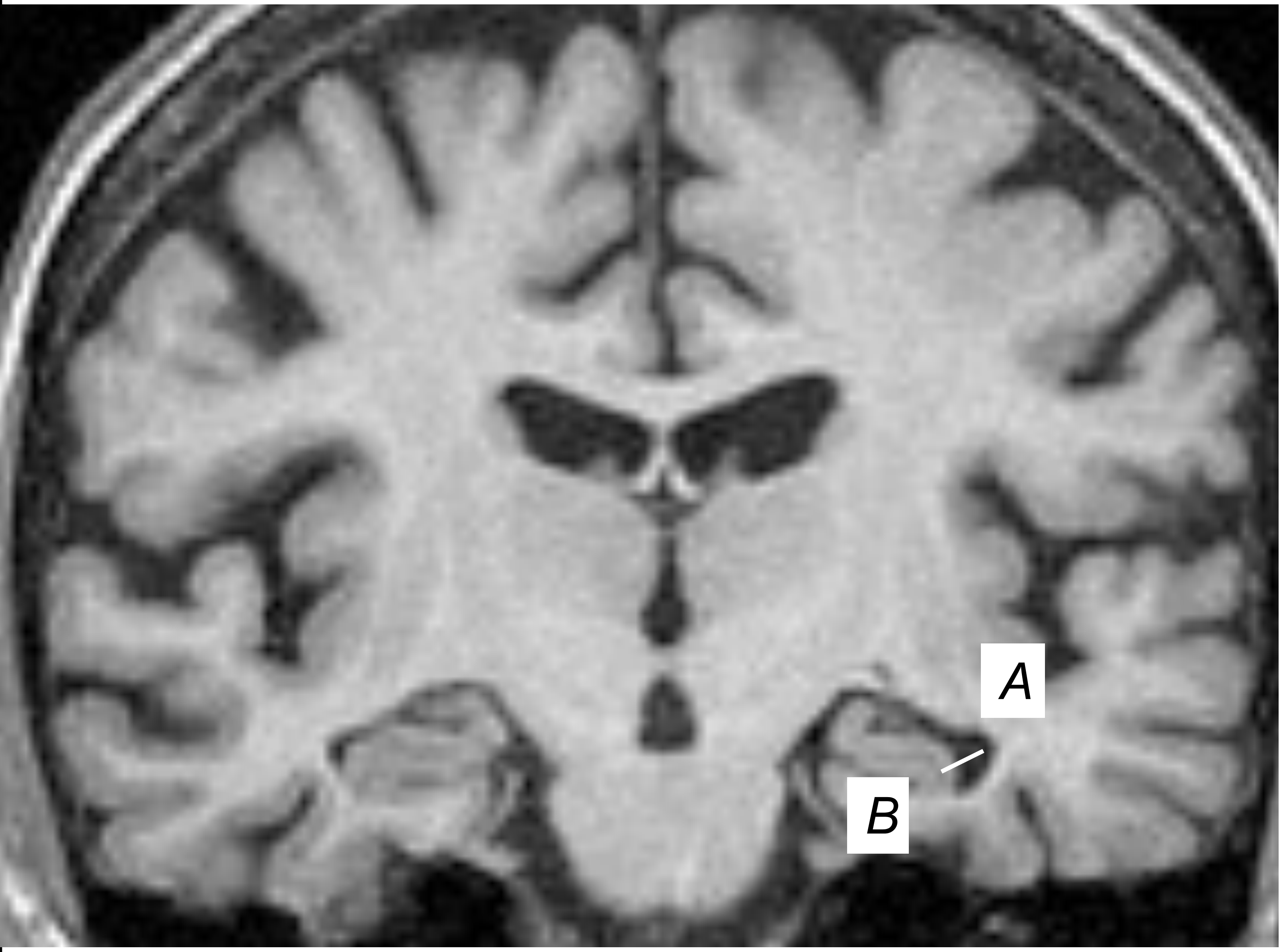


Baseline scan

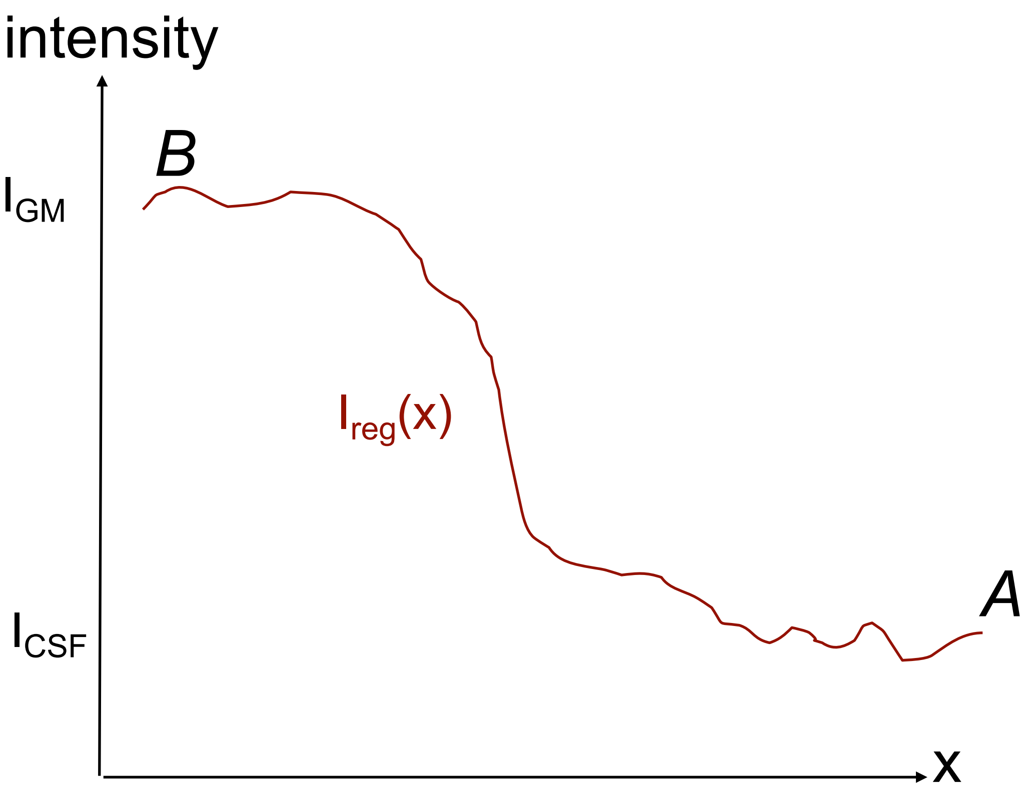


Intensity change from *A* to *B*

What is the BSI?



Registered repeat scan



Intensity change from *A* to *B*

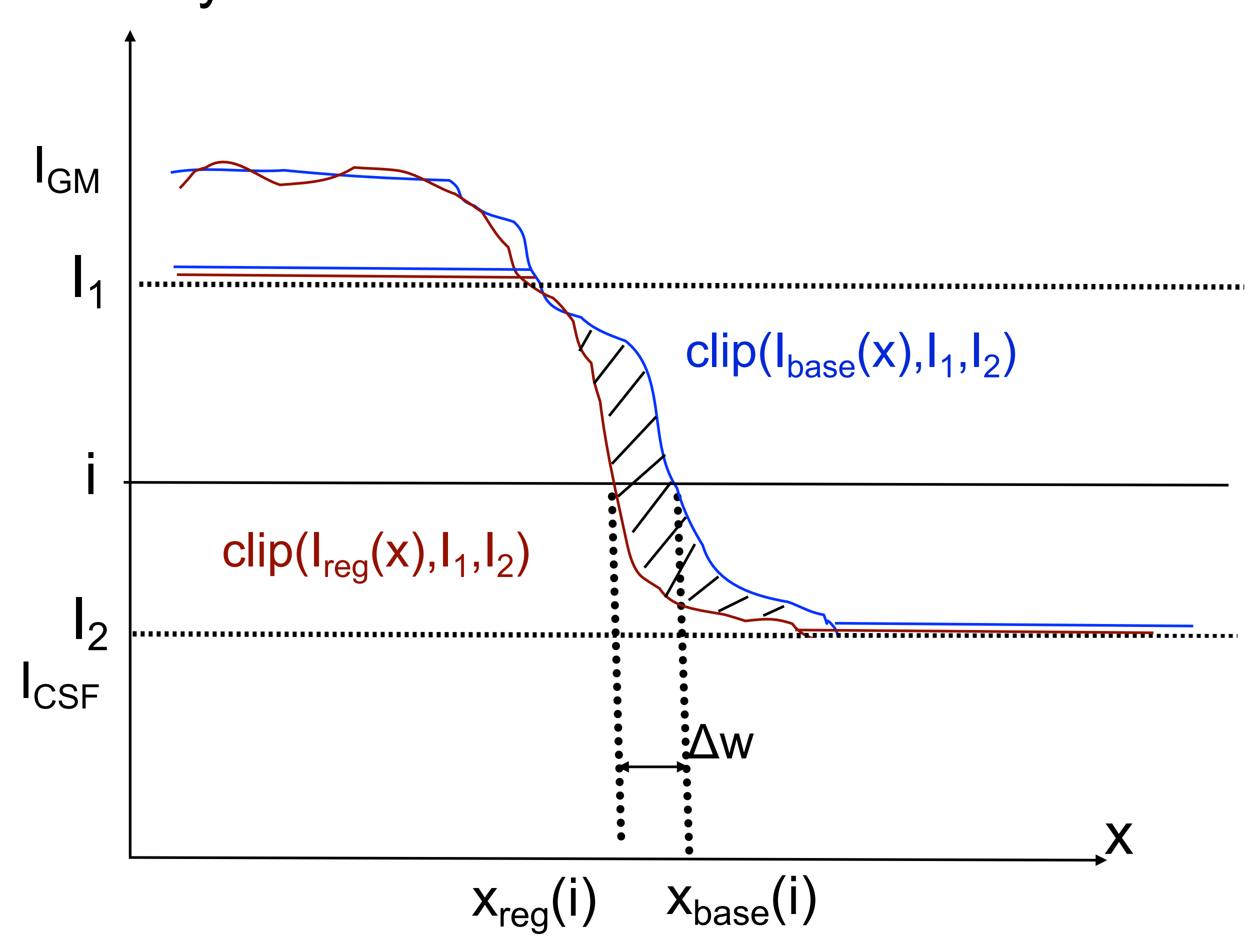
What is the BSI?

$$BSI = \frac{1}{I_1 - I_2} \int_{boundary} [clip(I_{base}(x), I_1, I_2) - clip(I_{reg}(x), I_1, I_2)]dx$$

$$where\ I_{CSF} \leq I_2 \leq I_1 \leq I_{GM}$$

$$clip(a, I_1, I_2) = \begin{cases} I_2 & a < I_2 \\ a & I_2 \leq a \leq I_1 \\ I_1 & a > I_1 \end{cases}$$

- The chosen window is quite often appropriate as BSI is a robust measure.
- Differential bias between baseline and follow-up can affect the measure.



K.K. Leung, M.J. Clarkson, J.W. Bartlett, S. Clegg, C.R. Jack, M.W. Weiner, N.C. Fox, S. Ourselin. "Robust atrophy rate measurement in Alzheimer's disease using multi-site serial MRI: tissue-specific intensity normalisation and parameter selection." Neuroimage 2010 Apr 1;50(2):516-23.

Requirements/Problems with the BSI

- Intensity Normalisation:
  - Problem:
    - Images have to be intensity normalised.
    - Normally done through image segmentation.
    - Minor errors introduce normalisation problems, and thus, introduce large variations.
  - Solution:
    - Longitudinal segmentation algorithms can reduce these errors

Requirements/Problems with the BSI

- Bias Field correction:
  - Problem:
    - The two images have to be corrected for bias field.
    - Errors in this correction result in the existence of a differential bias between images.
  - Solution:
    - An extra differential bias field correction step is necessary to correct for residual bias.

Requirements/Problems with the BSI

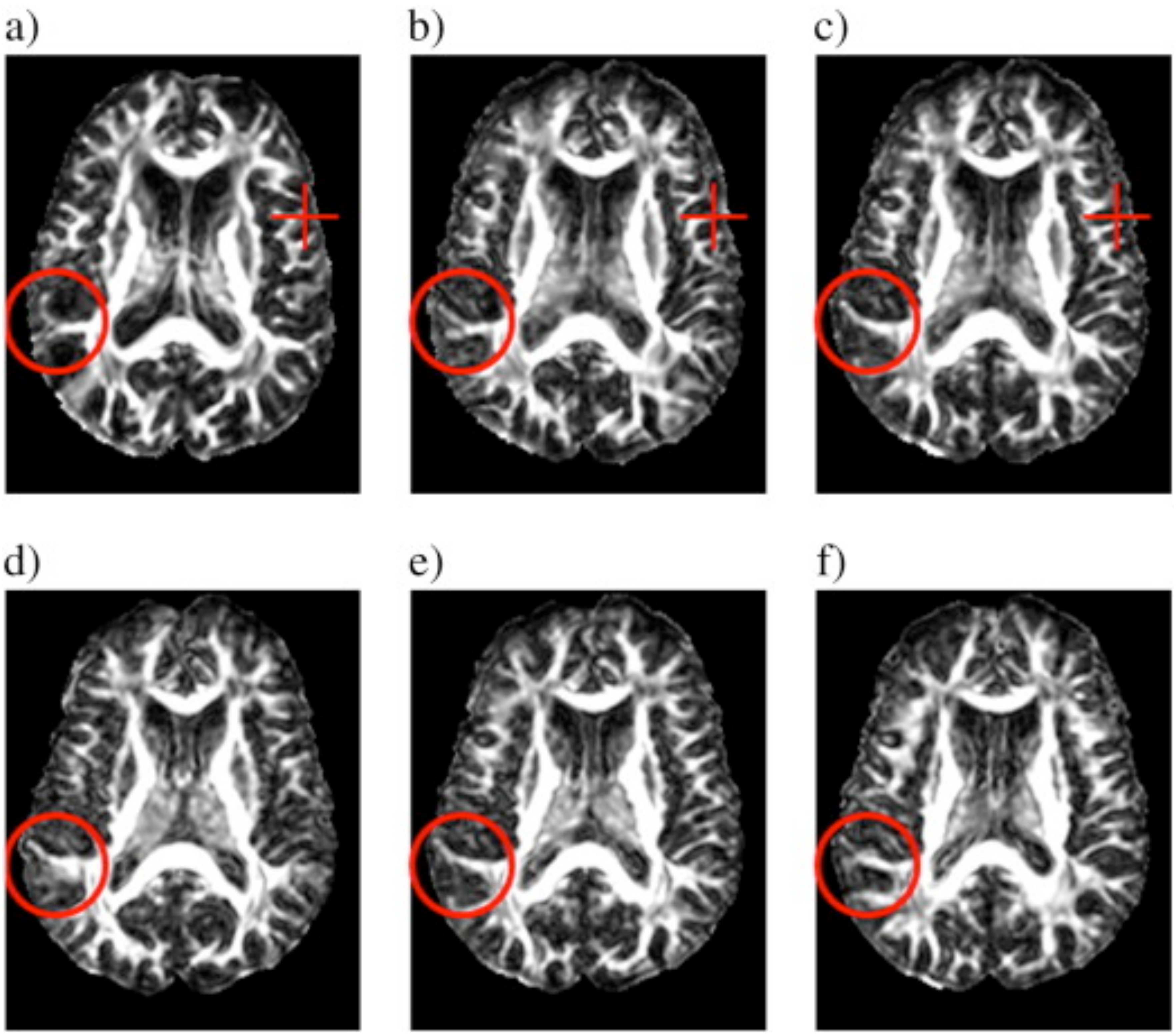
- Symmetry:
  - Problem:
    - The two time points need to be aligned with each other
    - If a specific direction (TP1-TP2, or TP2-TP1) is chosen for analysis, then a directional bias can be introduced.
  - Solution:
    - The alignment should be done to a mid point.
    - Both time point images should be resampled in the same manner.

DTI analysis

DTI analysis

- WM damage has been reported in multiple pathologies using DTI
- Cross-sectional studies using DTI can show a decline in WM tract integrity
- Longitudinal DTI studies on fibber tract changes are still rare.
- Most studies use manually defined ROIs on WM tracts at each TP
- Registration of longitudinal DTI can provide a framework for measuring a common ROI across all time-points

DTI analysis using FA



DTI ROI analysis

- Segment and parcelate T1w MRI

↓

- Register T1 and DTI of each patient

↓

- Resample the segmentation to the DTI

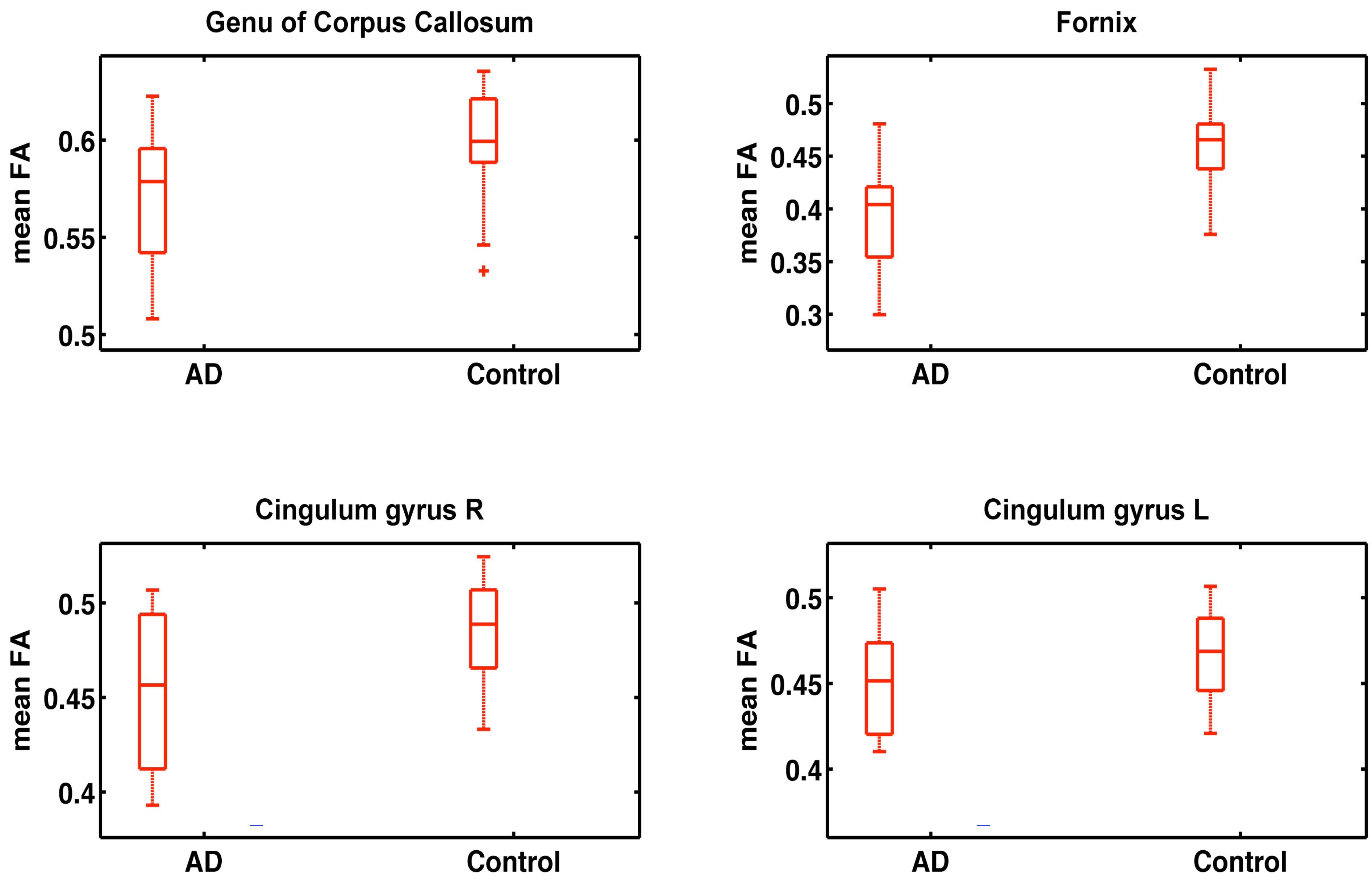
↓

- Obtain some metric of interest from the DTI (e.g. FA, MD)

↓

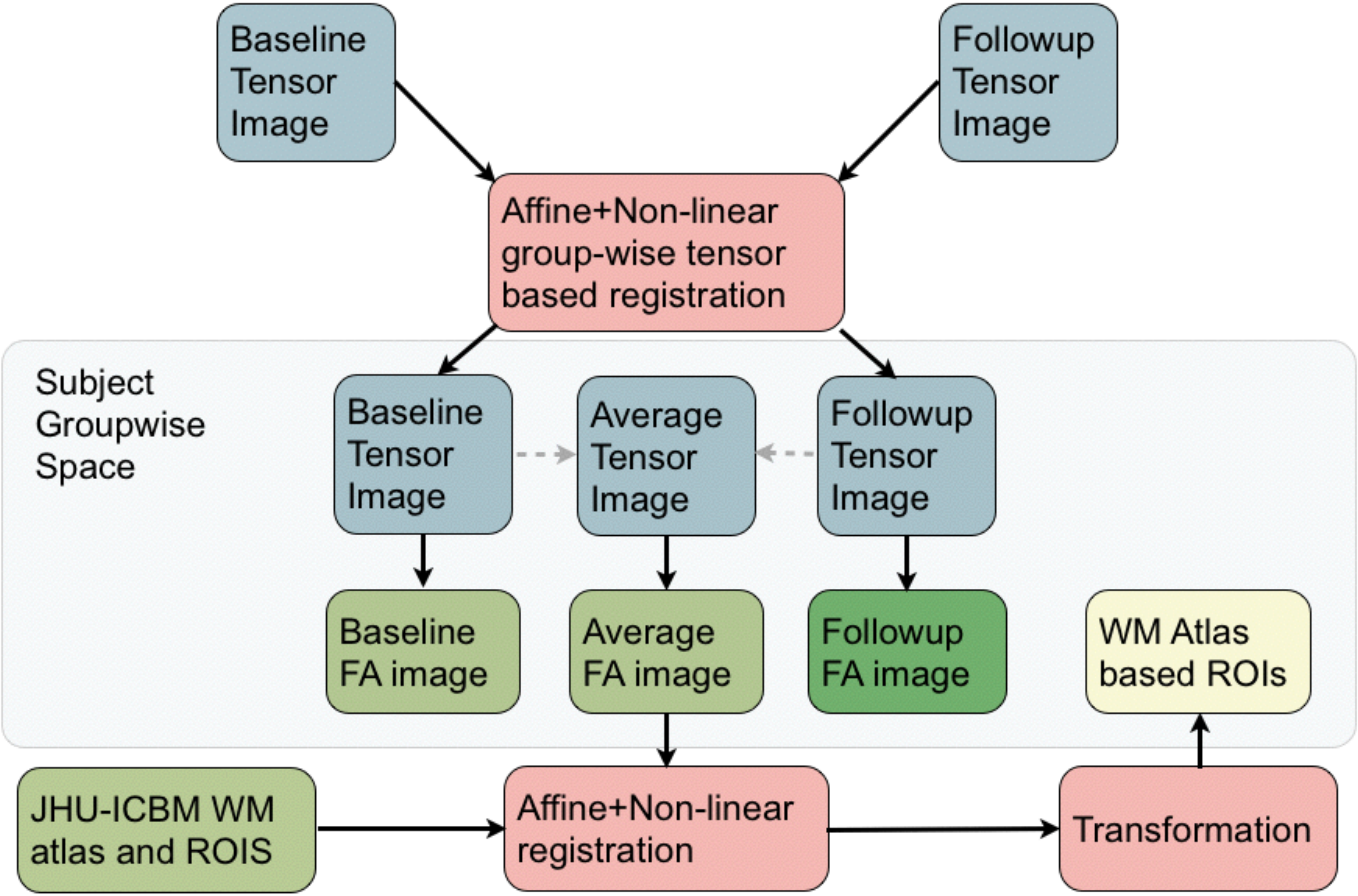
- Calculate average metric values per region

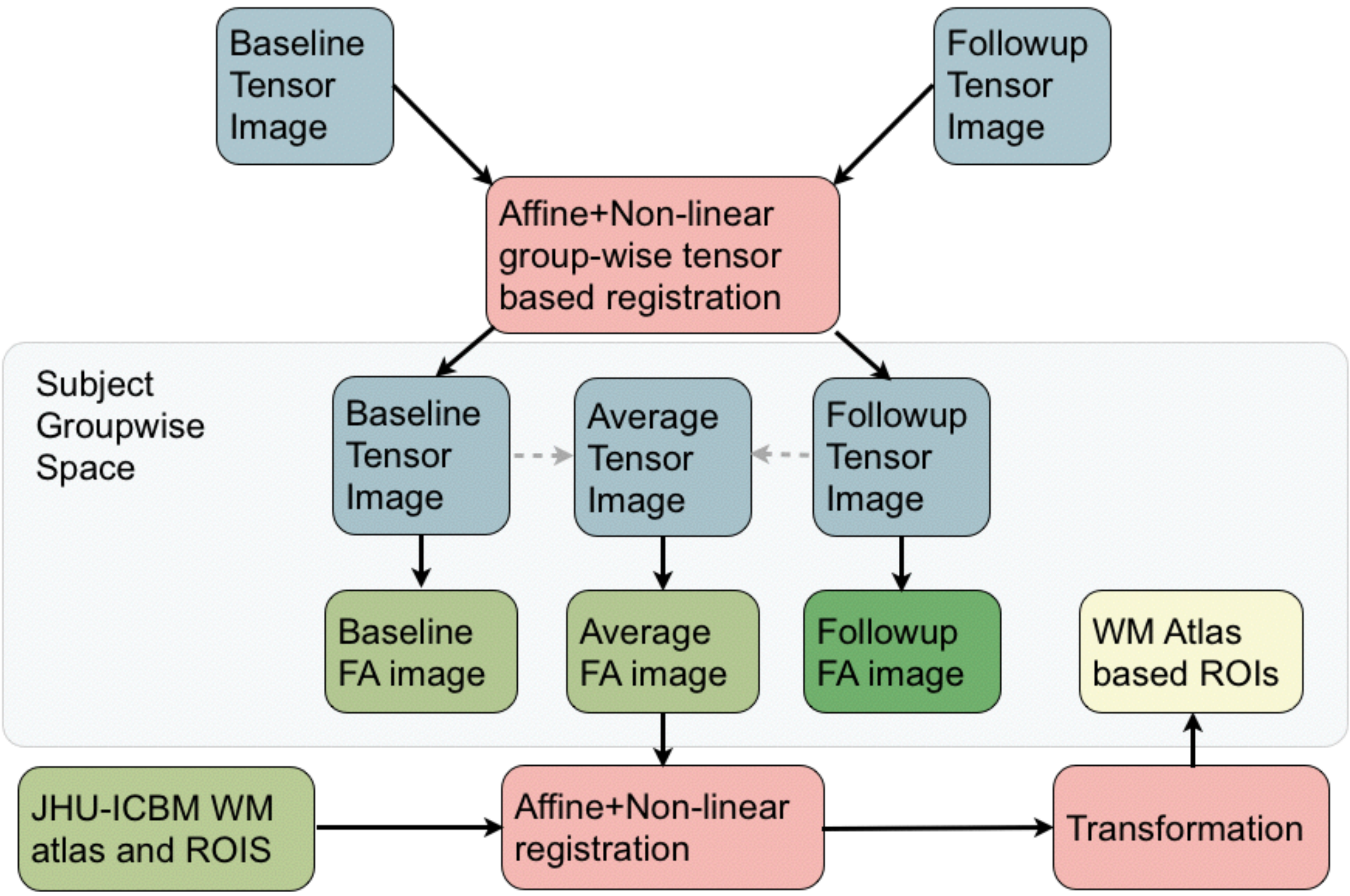
Results/advantages/disadvantages

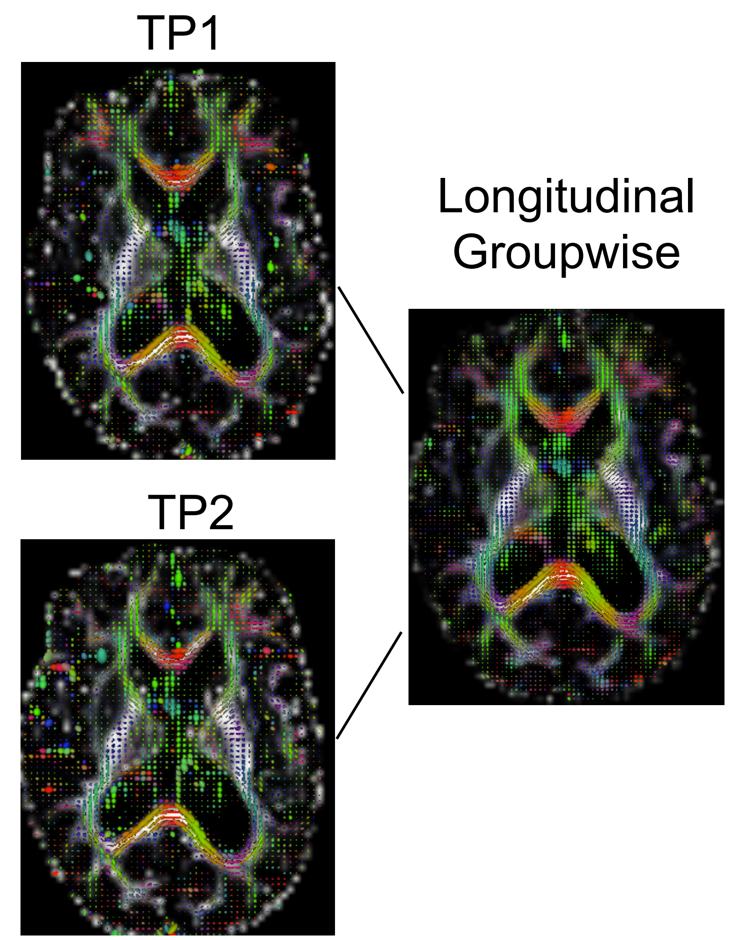


- Advantages:
  - Methodologically simple
  - Interpretable
  - Good for cross-sectional studies
- Disadvantages:
  - Registration dependent
  - Lacks robustness
  - Only for cross-sectional studies

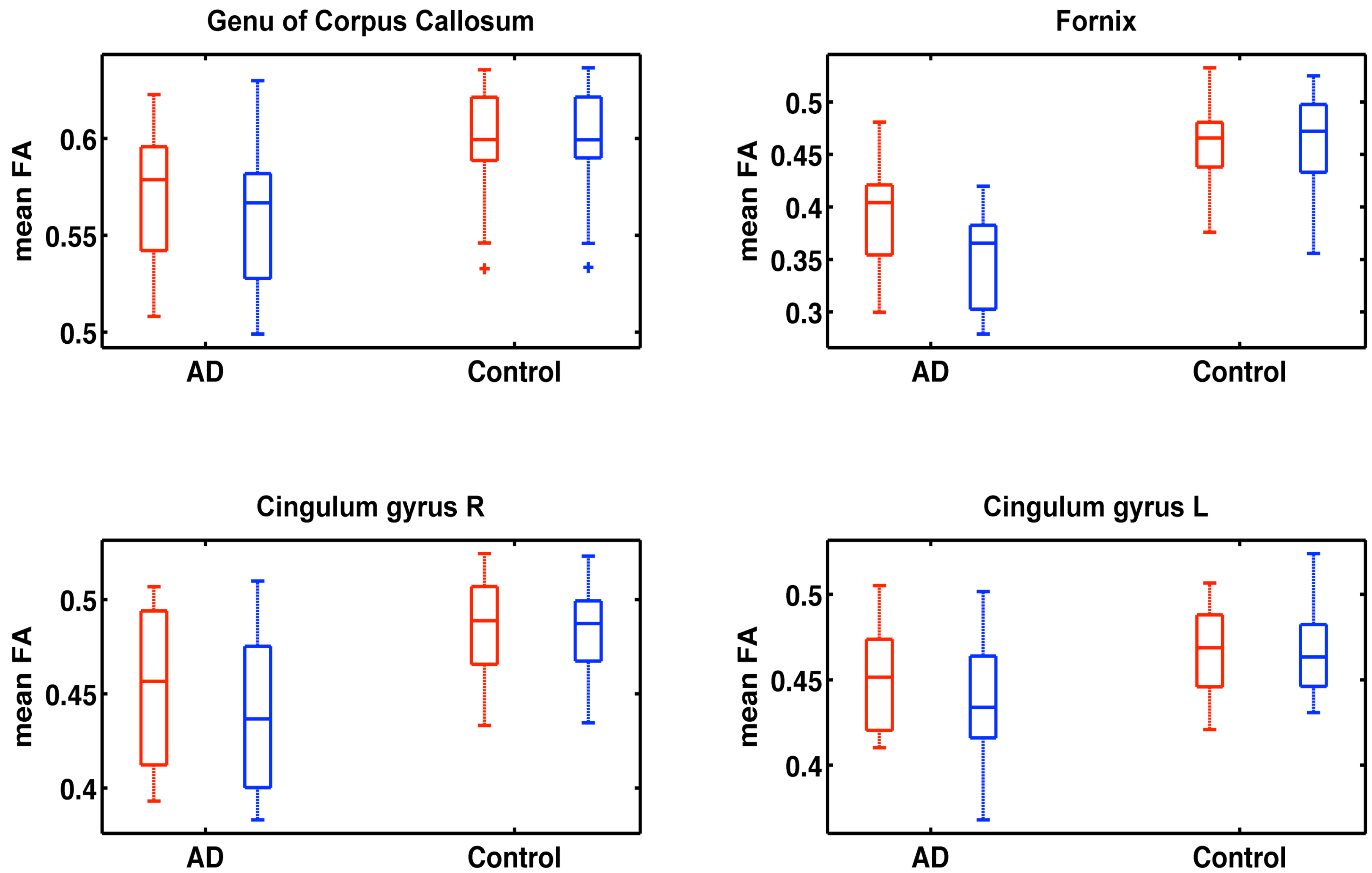
DTI ROI analysis: longitudinal extension




Baseline Tensor Image
Followup Tensor Image
Affine+Non-linear group-wise tensor based registration
Subject Groupwise Space
Baseline Tensor Image
Average Tensor Image
Followup Tensor Image
Baseline FA image
Average FA image
Followup FA image
WM Atlas based ROIs
JHU-ICBM WM atlas and ROIS
Affine+Non-linear registration
Transformation


TP1
TP2
Longitudinal Groupwise

Results/advantages/disadvantages



- Advantages:
  - Methodologically still simple
  - Interpretable
  - Good for longitudinal-sectional studies

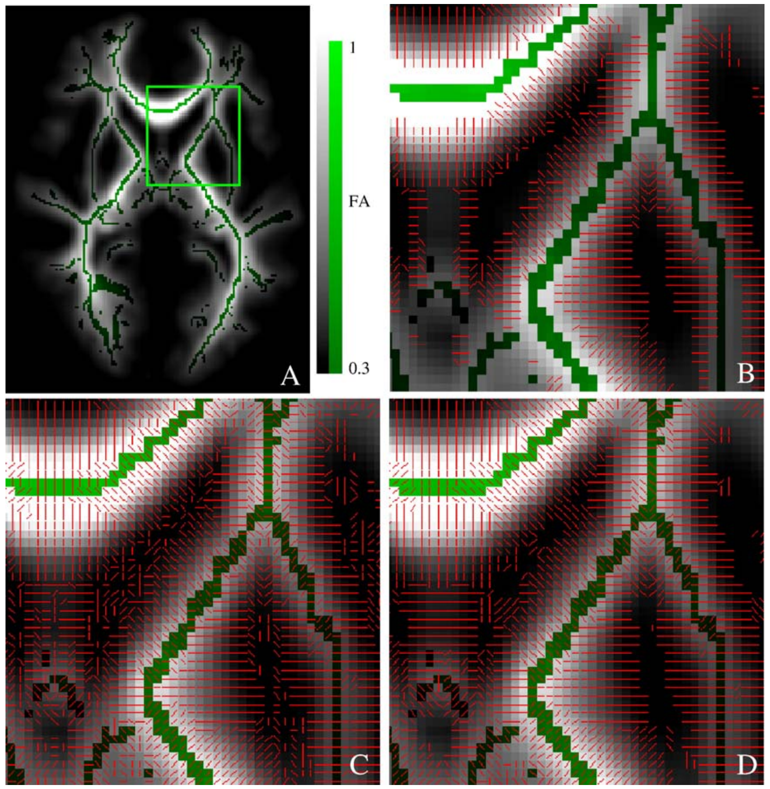
- Disadvantages:
  - Registration dependent

“Voxel-based” DTI analysis: TBSS

- Groupwise registration of DTI is difficult
  - Tracts might not align

- TBSS approach avoids some of these problems by “searching” for the tracts in case of miss-alignment

- Steps for TBSS:
  - FA Groupwise
  - Skeletonisation
  - FA search
  - Statistics



QUESTIONS??