SPATIAL NORMALIZATION OF BRAIN IMAGES WITH FOCAL LESIONS USING COST FUNCTION MASKING

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3 Pipeline
4 Methodology
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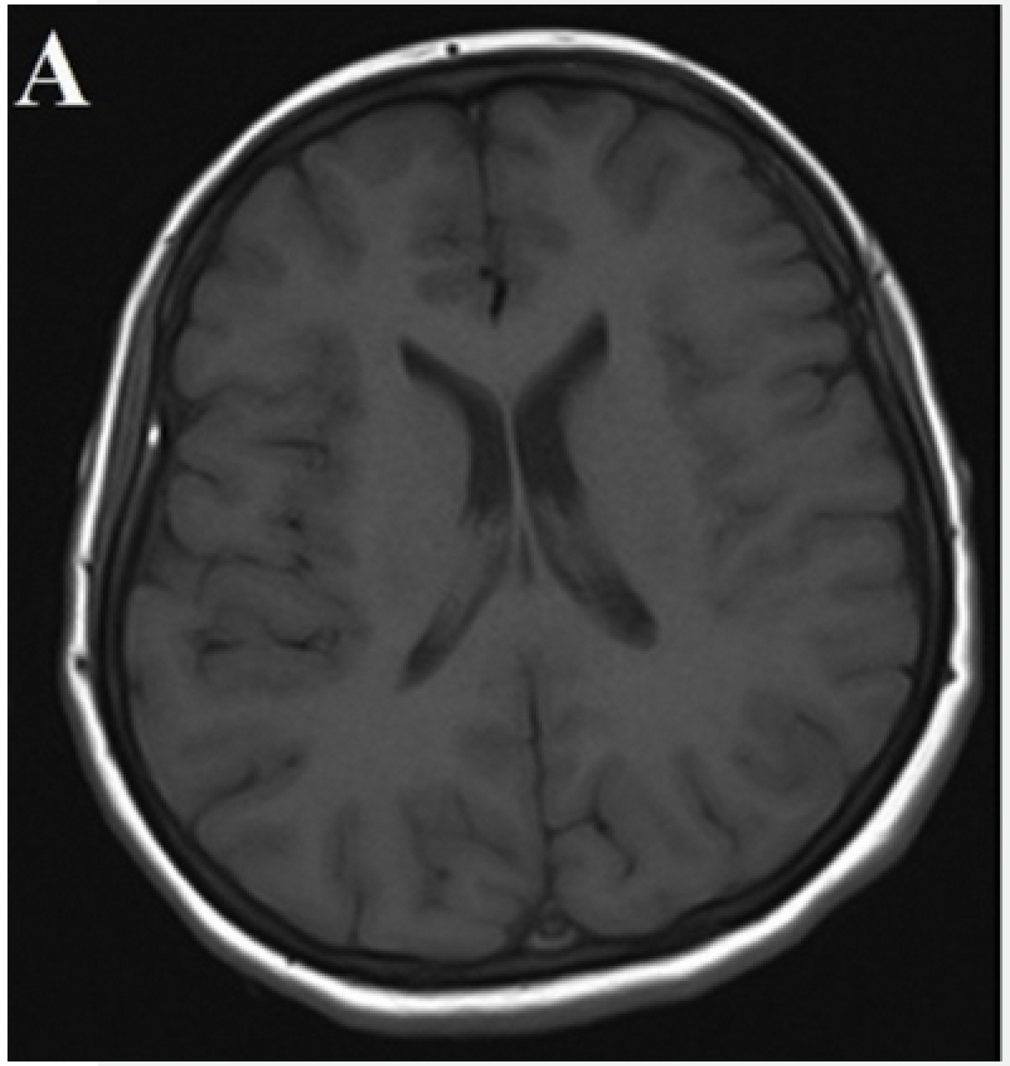
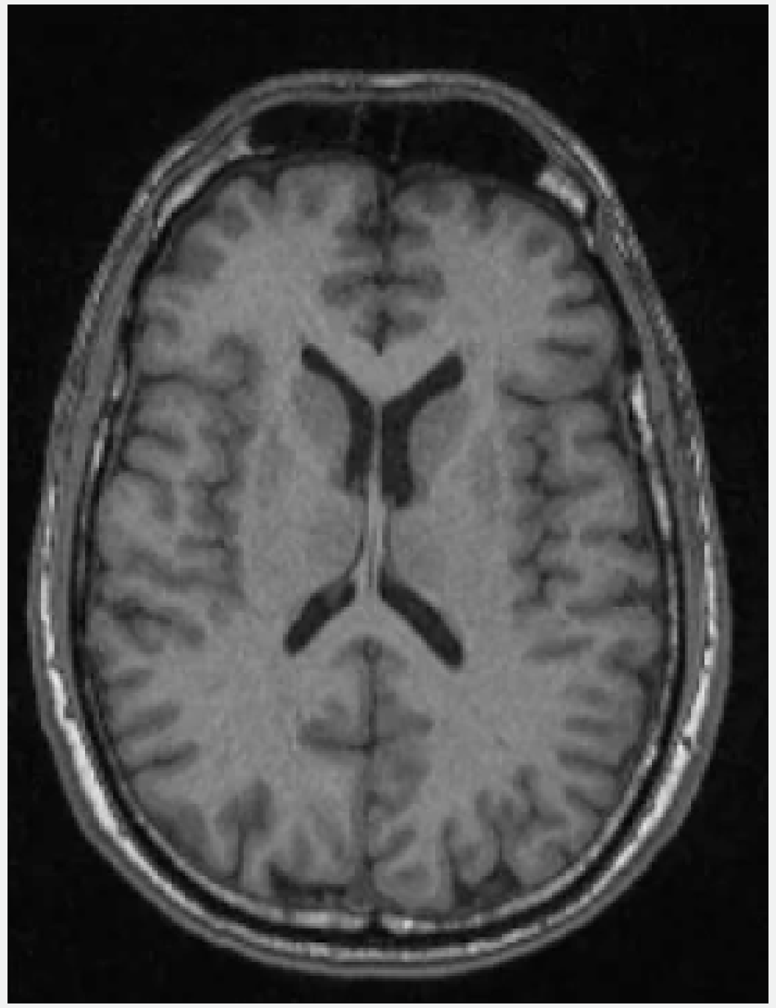
SUPPOSE YOU WERE A DOCTOR...





Spatial Normalization

- A technique used to align brain images to a standard template.
- Helps in comparing anatomical and functional brain data, like the comparison of lesion locations across patients.

INTRODUCTION

Manual Normalization

- Experts manually aligned brain images to templates.
- Time-consuming.
- Requires expert knowledge.
- Limited transformation capabilities.

Automated Normalization

- Uses algorithms to align images based on intensity differences
- Works by minimizing mismatch (cost function) between the brain image and the template.

INTRODUCTION

The Problem with Brain Lesions

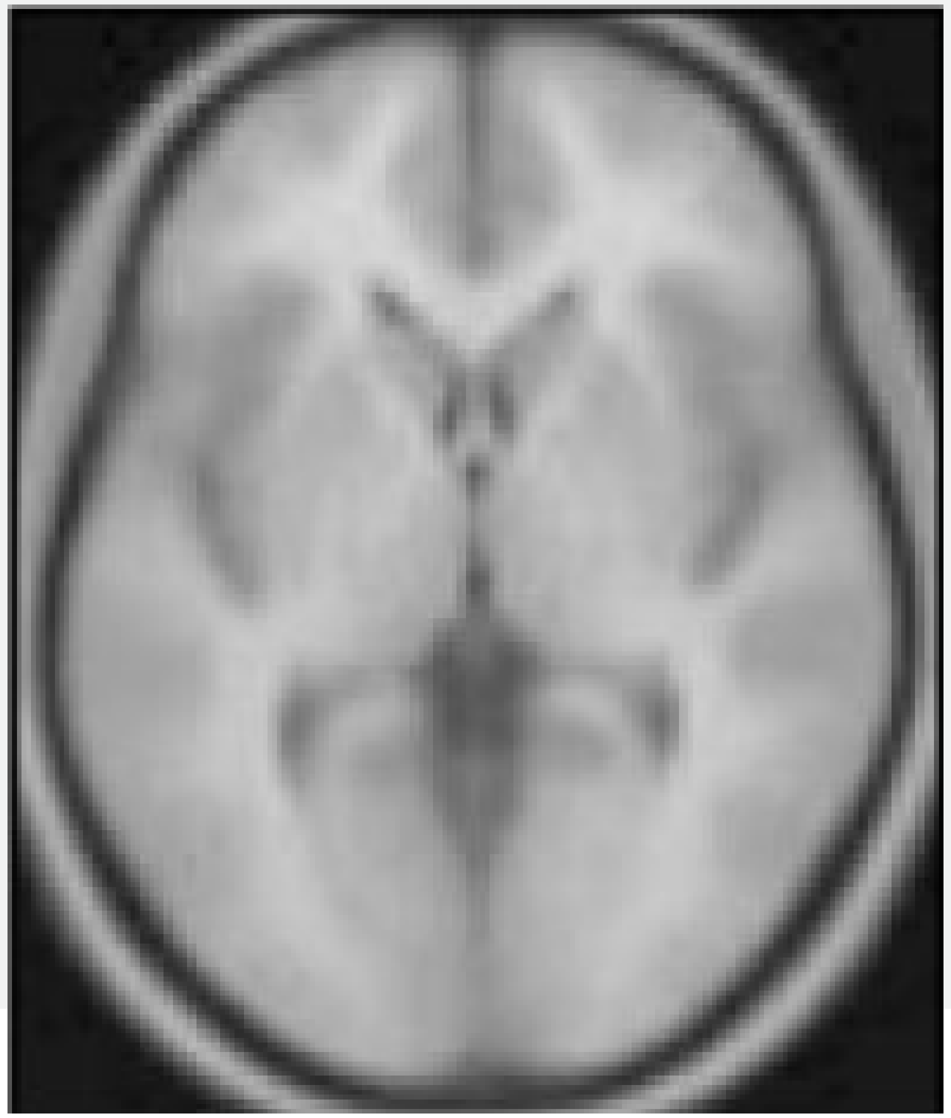
- Lesions have different intensity values, causing high mismatch in cost function.
- Leads to image distortions
    - Especially with nonlinear transformations.

Proposed Solution

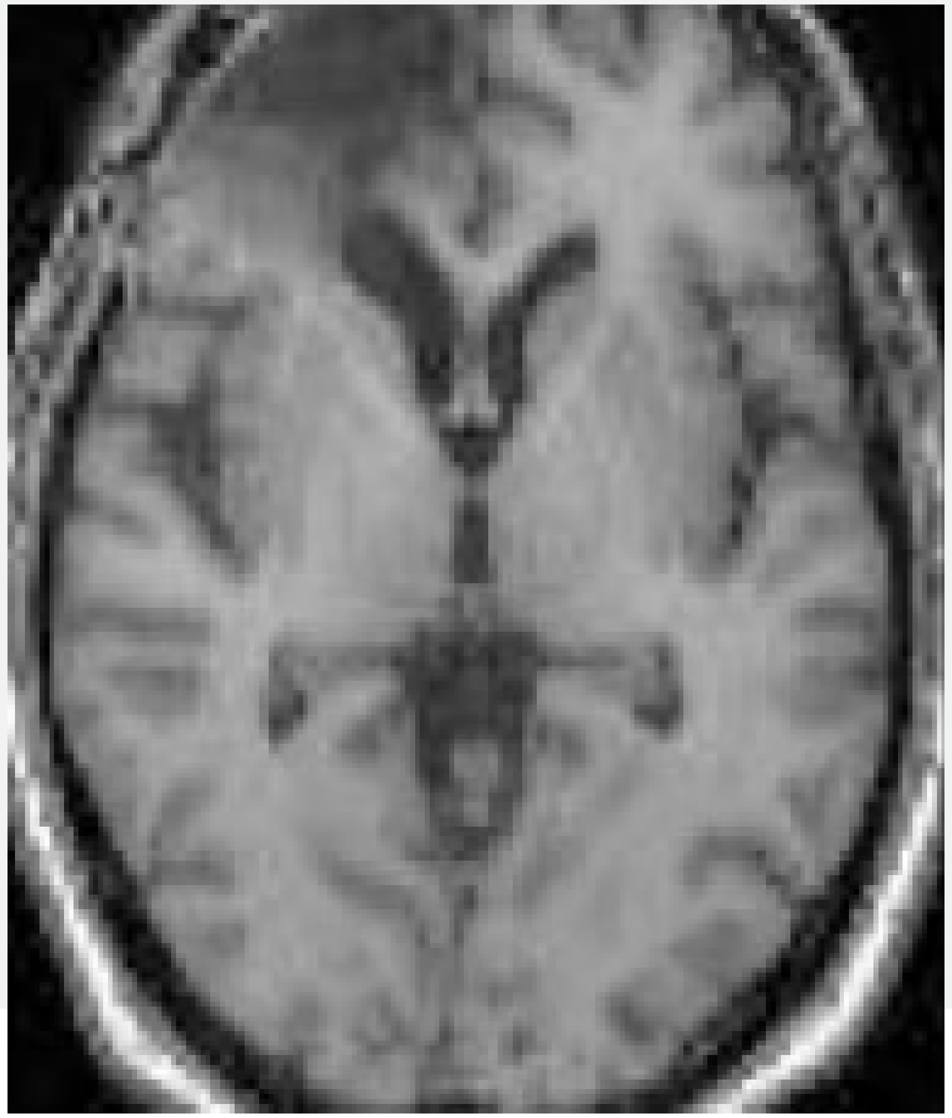
- Mask the lesion area to prevent it from affecting normalization.
- Ensures accurate alignment without distorting brain anatomy
- Improves reliability in functional and anatomical comparisons.

INTRODUCTION

Template



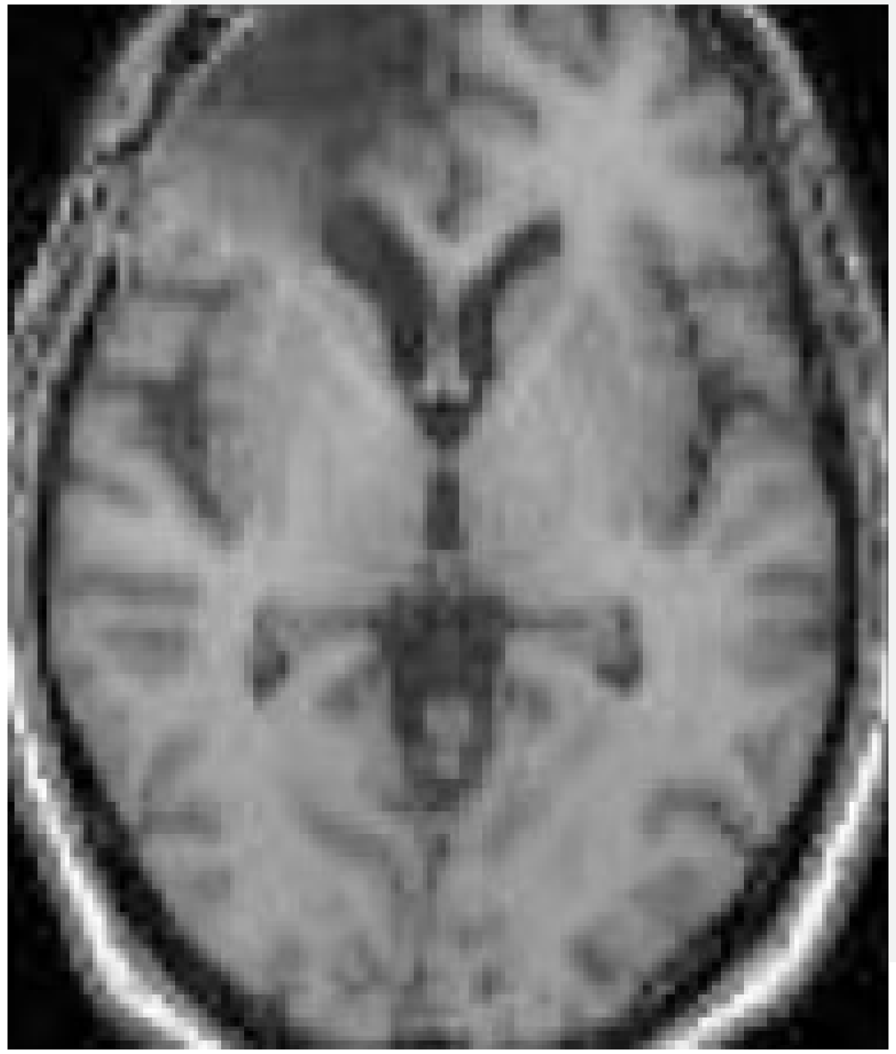
Stroke damage



Cost function

INTRODUCTION

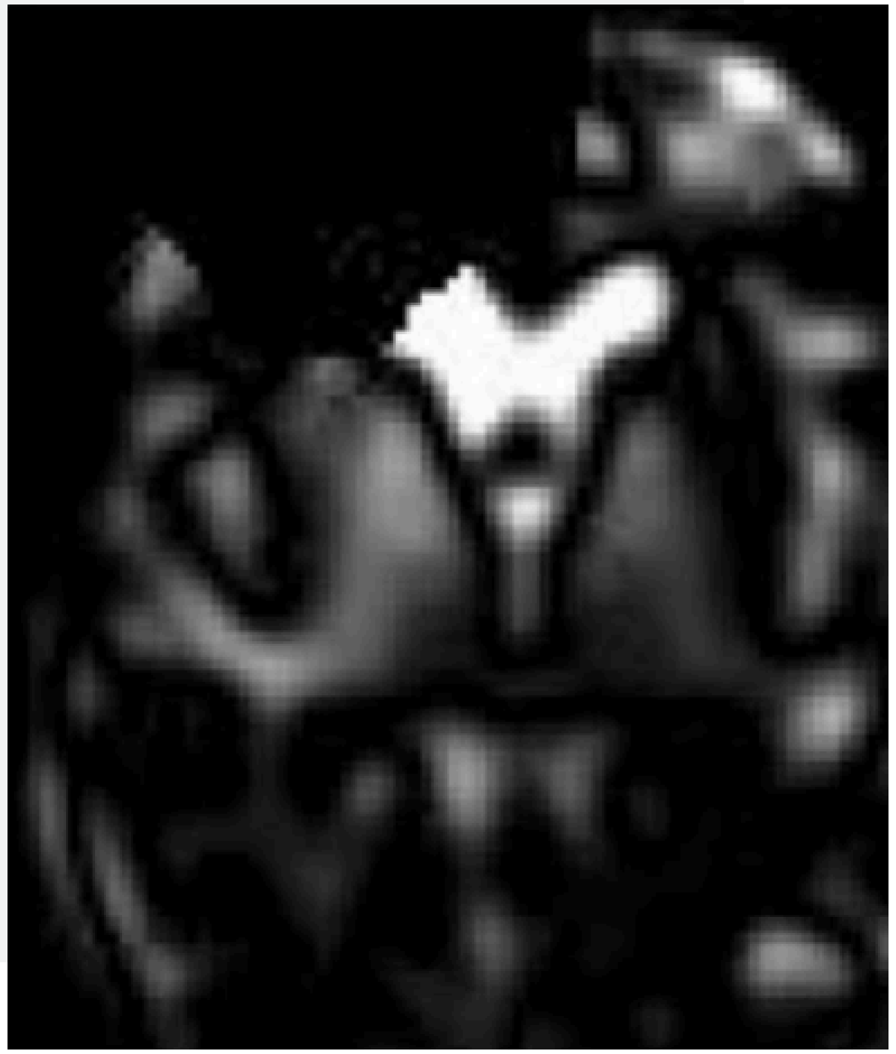
Stroke damage



Lesion definition

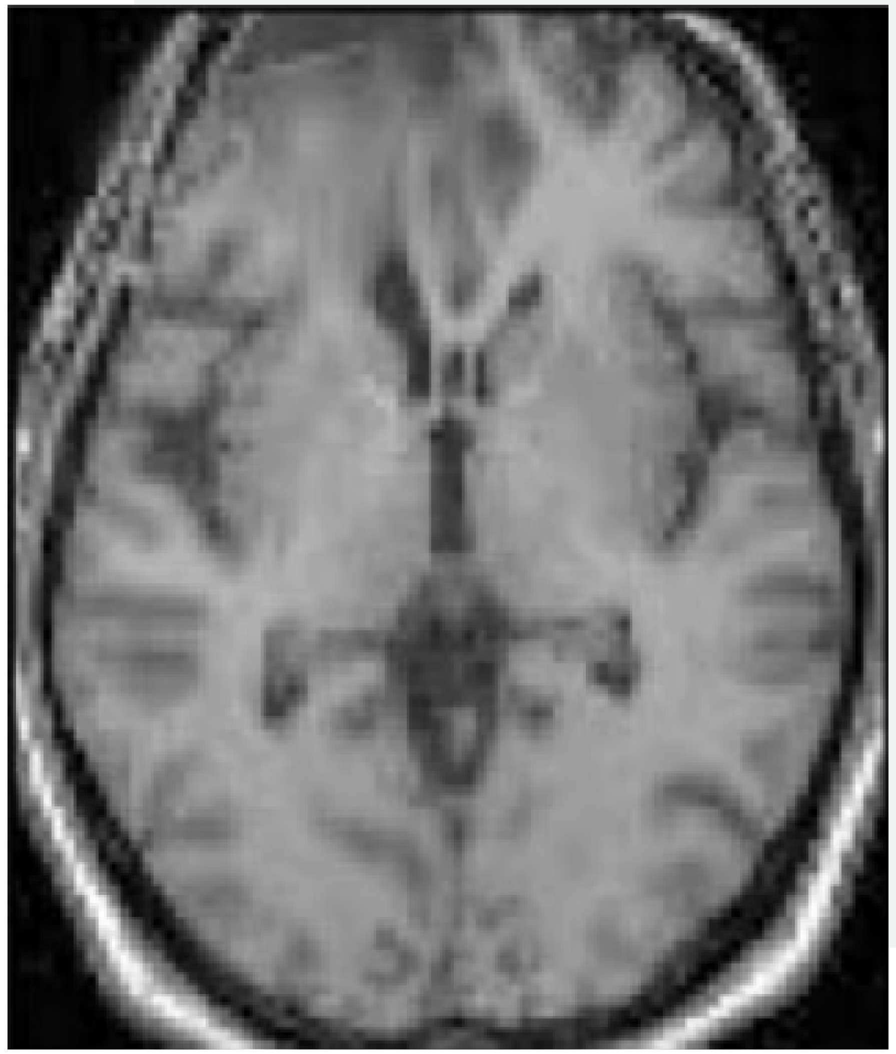
Mask definition

Cost function with mask

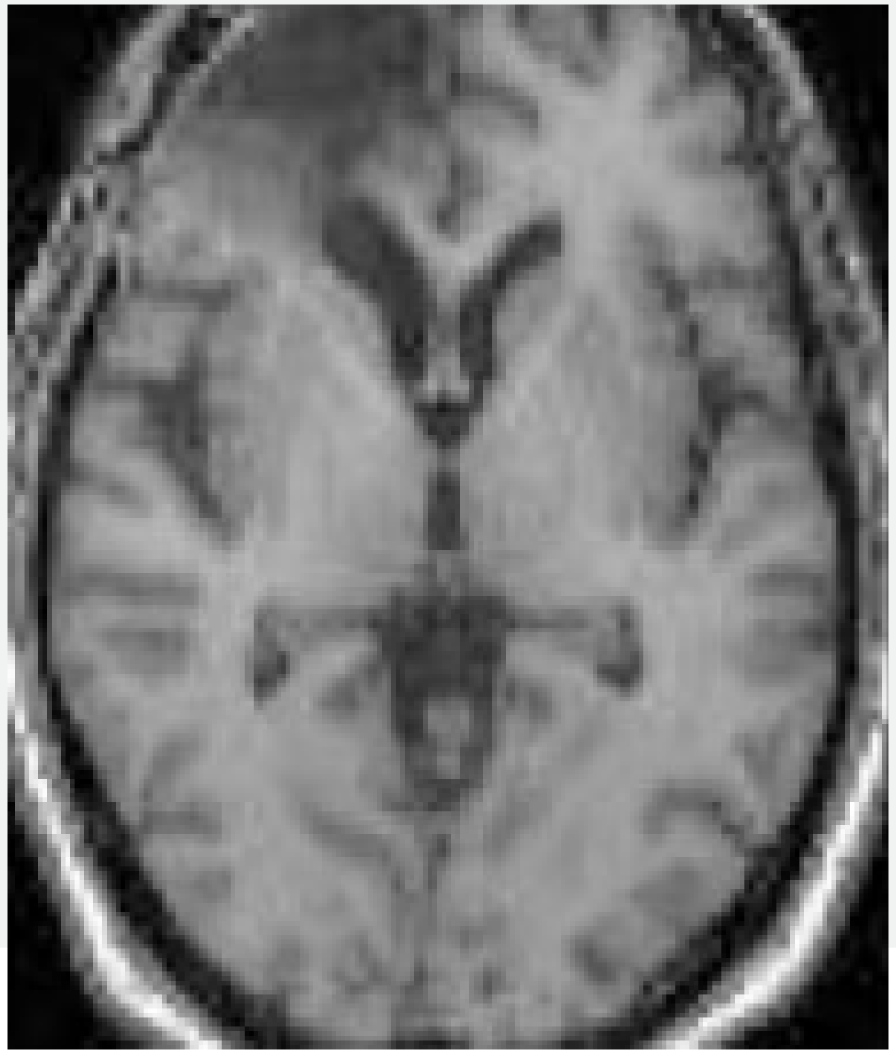


INTRODUCTION

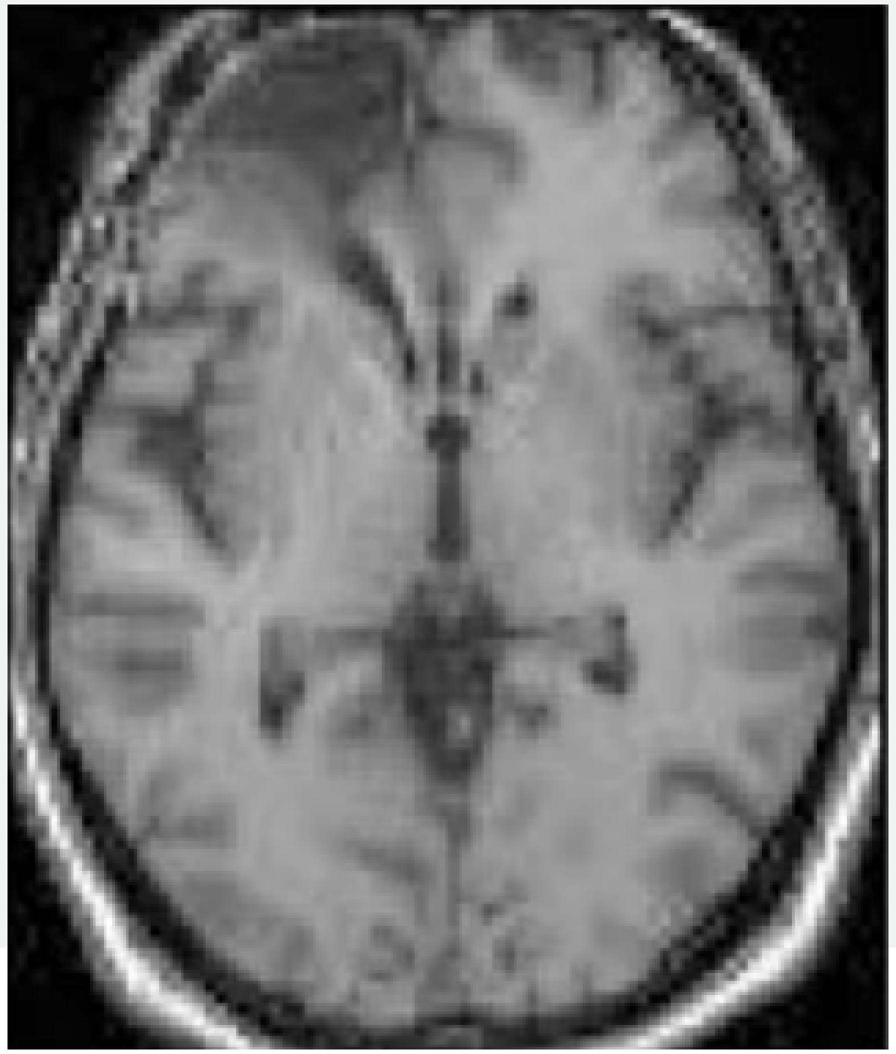
Standard Normalization



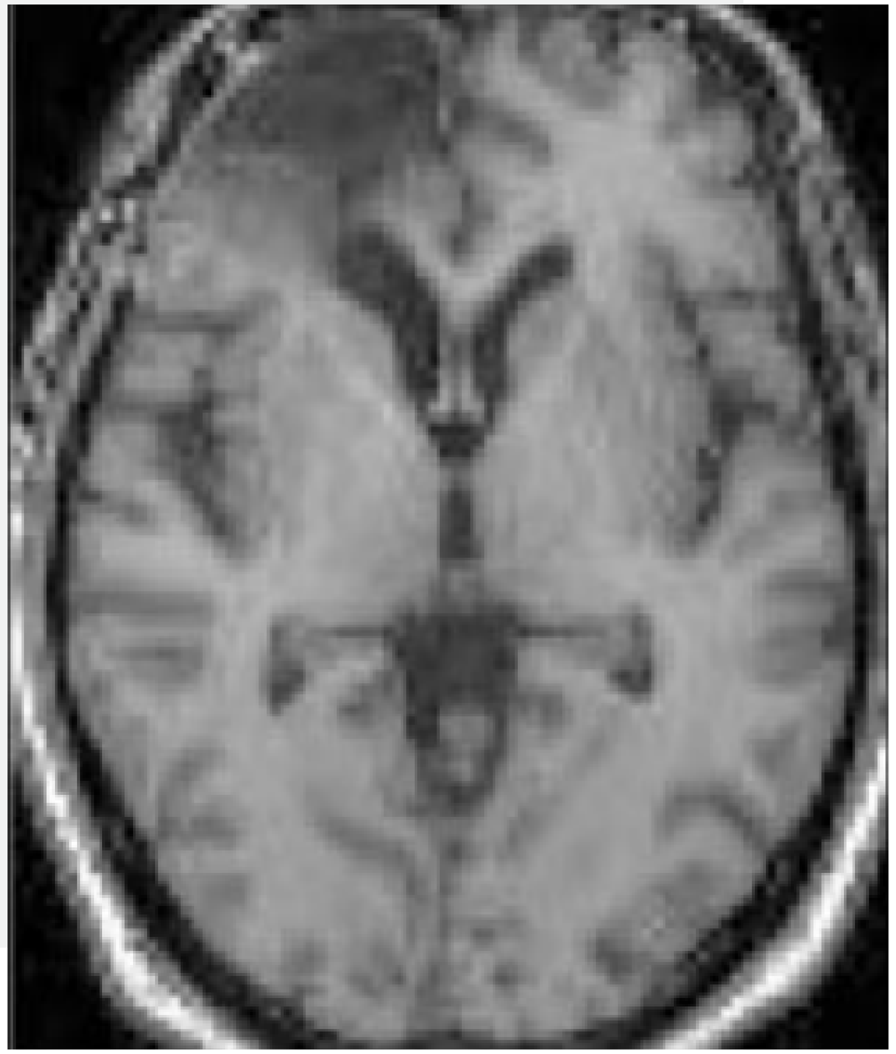
Stroke damage



Cost function masking with affine and nonlinear



Cost function masking with affine only



THEORY

- Algorithm treats the cost function (which we want to minimize) as the sum of the squares of the differences
- First, images are smoothed with an 8-mm isotropic Gaussian filter
- Second, SPM99 weights the optimization for affine and nonlinear steps using a Bayesian approach.

- Affine transformations: translations, rotations, scaling, and shears.

- Nonlinear transformations: Discrete Cosine Transform (DCT)

THEORY - THE OPTIMIZATION PROBLEM

$$d_i(\mathbf{p}+\mathbf{t}) = d_i(\mathbf{p}) + t_1 \frac{\partial d_i(\mathbf{p})}{\partial p_1} + t_2 \frac{\partial d_i(\mathbf{p})}{\partial p_2} \cdots$$

Across voxels

$$\begin{bmatrix} d_1(\mathbf{p}+\mathbf{t}) \\ d_2(\mathbf{p}+\mathbf{t}) \\ \vdots \end{bmatrix} = \begin{bmatrix} d_1(\mathbf{p}) \\ d_2(\mathbf{p}) \\ \vdots \end{bmatrix} + \begin{bmatrix} \frac{\partial d_1(\mathbf{p})}{\partial p_1} & \frac{\partial d_1(\mathbf{p})}{\partial p_2} & \cdots \\ \frac{\partial d_2(\mathbf{p})}{\partial p_1} & \frac{\partial d_2(\mathbf{p})}{\partial p_2} & \cdots \\ \vdots & \vdots & \ddots \end{bmatrix} \begin{bmatrix} t_1 \\ t_2 \\ \vdots \end{bmatrix}$$

$$\mathbf{A} = \begin{bmatrix} -\frac{\partial d_1(\mathbf{p})}{\partial p_1} & -\frac{\partial d_1(\mathbf{p})}{\partial p_2} & \cdots \\ -\frac{\partial d_2(\mathbf{p})}{\partial p_1} & -\frac{\partial d_2(\mathbf{p})}{\partial p_2} & \cdots \\ \vdots & \vdots & \ddots \end{bmatrix}$$

$$\mathbf{t} = \begin{bmatrix} t_1 \\ t_2 \\ \vdots \end{bmatrix} \quad \mathbf{b} = \begin{bmatrix} d_1(\mathbf{p}) \\ d_2(\mathbf{p}) \\ \vdots \end{bmatrix}$$

THEORY - THE OPTIMIZATION PROBLEM

We can solve the equations to give the parameter changes t that minimize the sum of the squared image differences across voxels:

$$\mathbf{t} = (\mathbf{A}^\top \mathbf{A})^{-1} \mathbf{A}^\top \mathbf{b} = \arg \min_{\mathbf{t} \in \mathbb{R}^p} \|\mathbf{b} - \mathbf{A}\mathbf{t}\|_2^2$$

This estimate of t allows an iterative scheme

For any iteration n, the parameters p are updated as follows:

$$\mathbf{p}^{(n+1)} = \mathbf{p}^{(n)} + \mathbf{t}$$

The iterations proceed until the sum of squared difference is minimized.

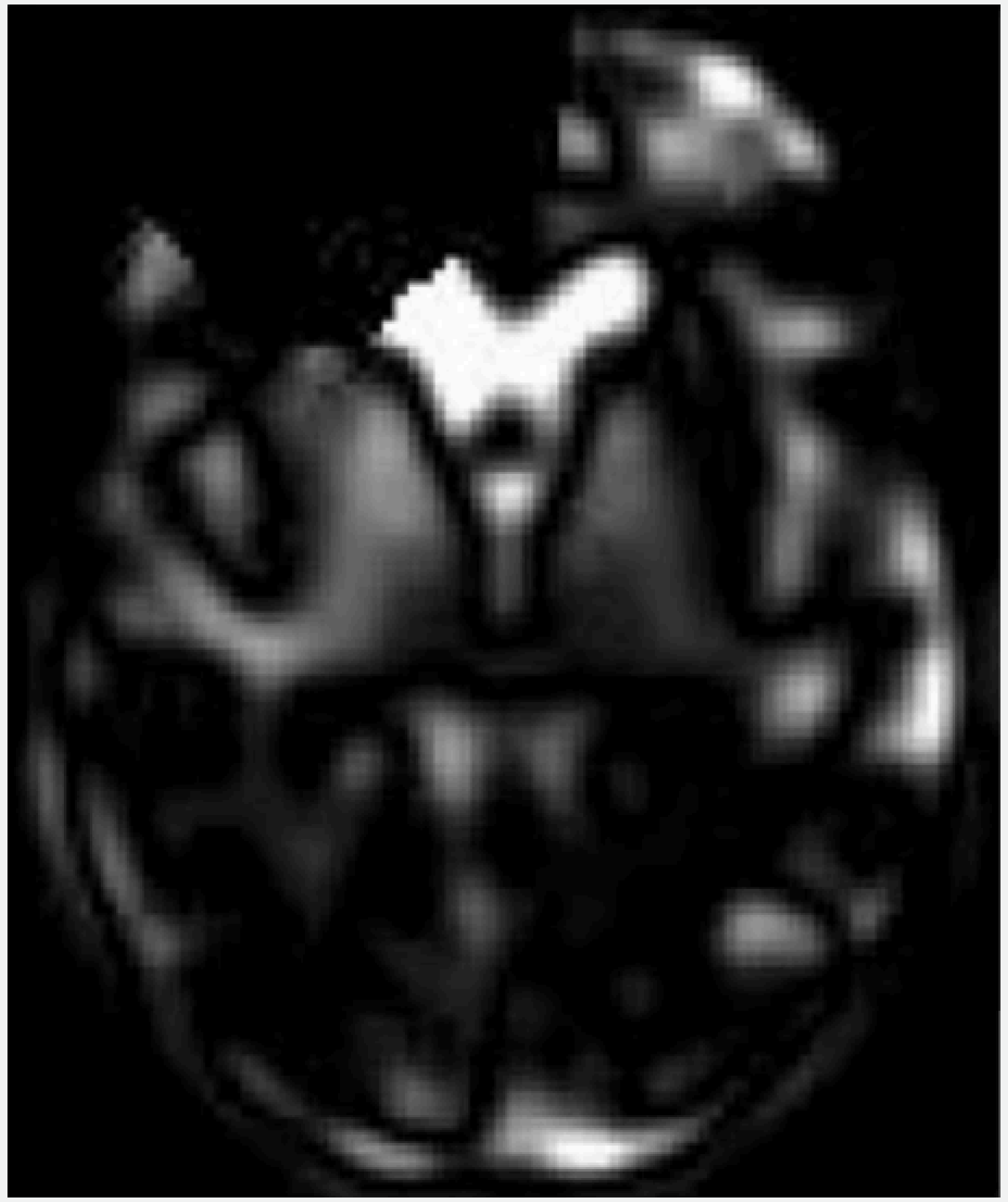
THEORY - LESION AREA MASKING

Matrix A is modified using weights w at each voxel i

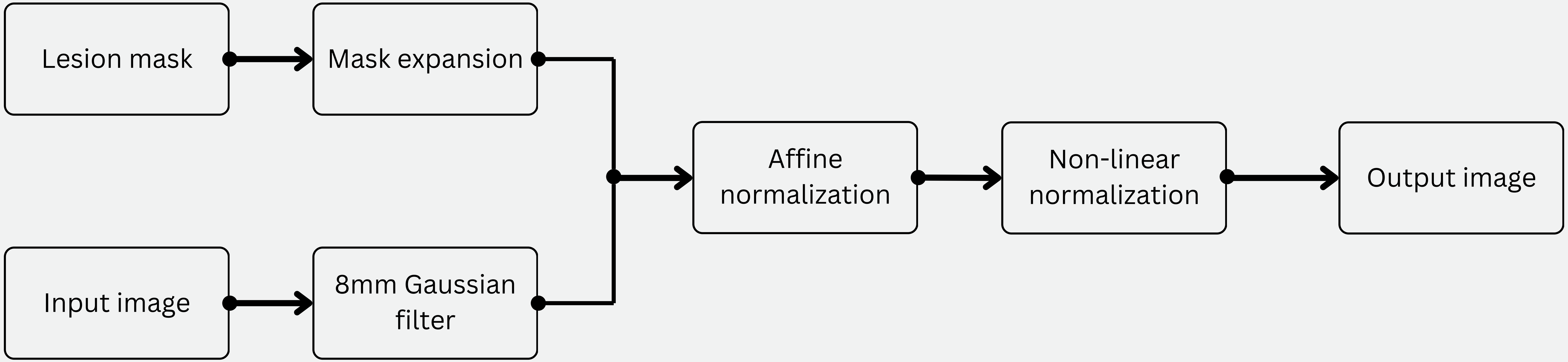
$$\mathbf{A} = \begin{bmatrix} -\frac{\partial d_1(\mathbf{p})}{\partial p_1} w_1 & -\frac{\partial d_1(\mathbf{p})}{\partial p_2} w_1 & \cdots \\ -\frac{\partial d_2(\mathbf{p})}{\partial p_1} w_2 & -\frac{\partial d_2(\mathbf{p})}{\partial p_2} w_2 & \cdots \\ \vdots & \vdots & \ddots \end{bmatrix}$$

- w = 1 for normal brain regions (included in the optimization)
- w = 0 now for lesioned regions (excluded from cost function calculation)
- The mask sets the cost function to zero in the lesioned area and it no longer influences the optimization

THEORY - LESION AREA MASKING



PIPELINE: OVERALL METHOD



METHODOLOGY

1. How different cost masks affect the resulting normalization?
2. How can we modify the cost mask if we smooth the source image before normalization?
3. How this method compares to the “perfect” affine-only transform in a healthy brain? (quantitative comparison)
4. How to analyze the normalization qualitatively?

METHODOLOGY: DATASET

x10 lesions

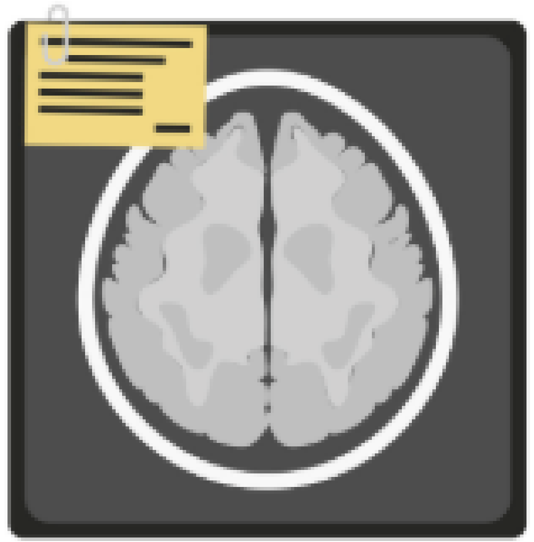
- 10 MRIs with lesions
- 4 professionals to identify the region of the lesion as accurately as possible



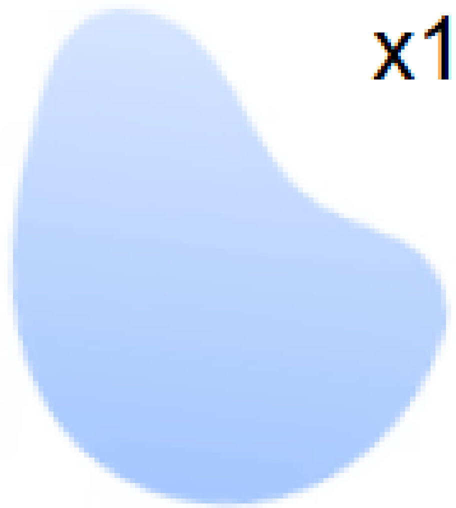

METHODOLOGY: DATASET

Original lesion

METHODOLOGY: DATASET



x10 healthy



Pretend to be
the ground truth

Different segmentations
of the lesions

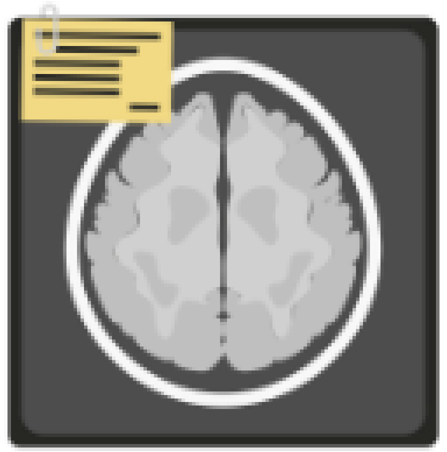
- The artifical lesion is added to the healthy brain
- A scale factor is used to match the intensity of pixels

$$s = \frac{\text{MaskedMean}(\text{normal image})}{\text{MaskedMean}(\text{lesion image})}$$

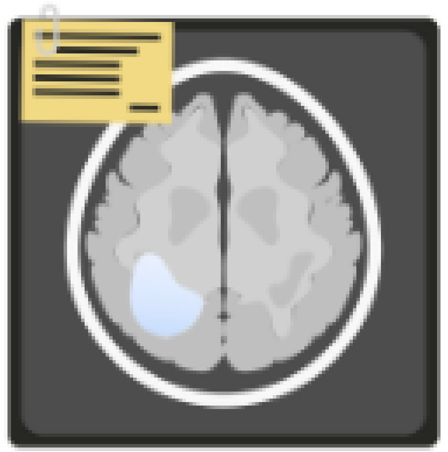
- Now, we can create a new image with a simulated lesion

METHODOLOGY: DATASET

How different cost masks affect the resulting normalization?



Healthy



Simulated lesion

Different masks

METHODOLOGY: DATASET

- If we smooth the source image, the lesion signal will spread to a larger region
- We will enlarge the mask region!
- By how much?

$$\mathrm{ld}_i = \begin{cases} 1 & \text{voxel } i \text{ is in lesion} \\ 0 & \text{otherwise} \end{cases}$$

- We smooth ld (lesion definition), getting sld (smooth lesion definition)
- sld has values in [0, 1]

METHODOLOGY: DATASET

$$\mathrm{ld}_i = \begin{cases} 1 & \text{voxel } i \text{ is in lesion} \\ 0 & \text{otherwise} \end{cases}$$

- We smooth ***ld*** (lesion definition), getting ***sld*** (smooth lesion definition)
- ***sld*** has values in [0, 1]
- Define a threshold t, then consider the ***pnm*** (processed normalization mask). The smaller the threshold, the bigger the mask

$$\mathrm{pnm}_i = \begin{cases} 1 & \mathrm{sld}_i \leq t & \text{voxel } \textbf{outside} \text{ lesion} \\ 0 & \text{otherwise} & \text{voxel } \textbf{inside} \text{ lesion} \end{cases}$$

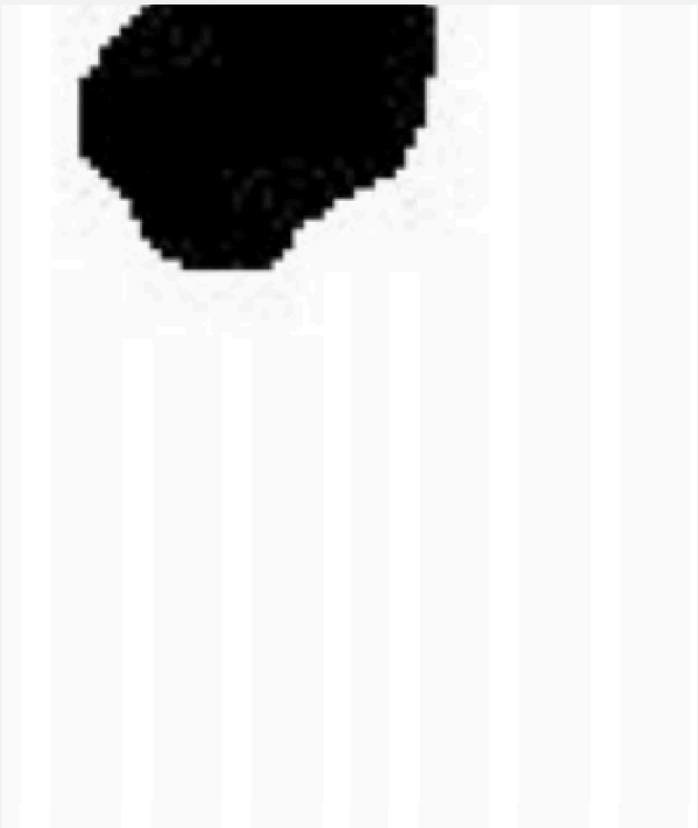
METHODOLOGY: DATASET

$$\mathrm{ld}_i = \begin{cases} 1 & \text{voxel } i \text{ is in lesion} \\ 0 & \text{otherwise} \end{cases}$$

$$\mathrm{pnm}_i = \begin{cases} 1 & \mathrm{sld}_i \leq t \\ 0 & \text{otherwise} \end{cases}$$

voxel **outside** lesion

voxel **inside** lesion



METHODOLOGY: DATASET

How can we modify the cost mask if we smooth the source image before normalization?

$$\mathrm{pnm}_i = \begin{cases} 1 & \mathrm{sld}_i \leq t \\ 0 & \text{otherwise} \end{cases}$$

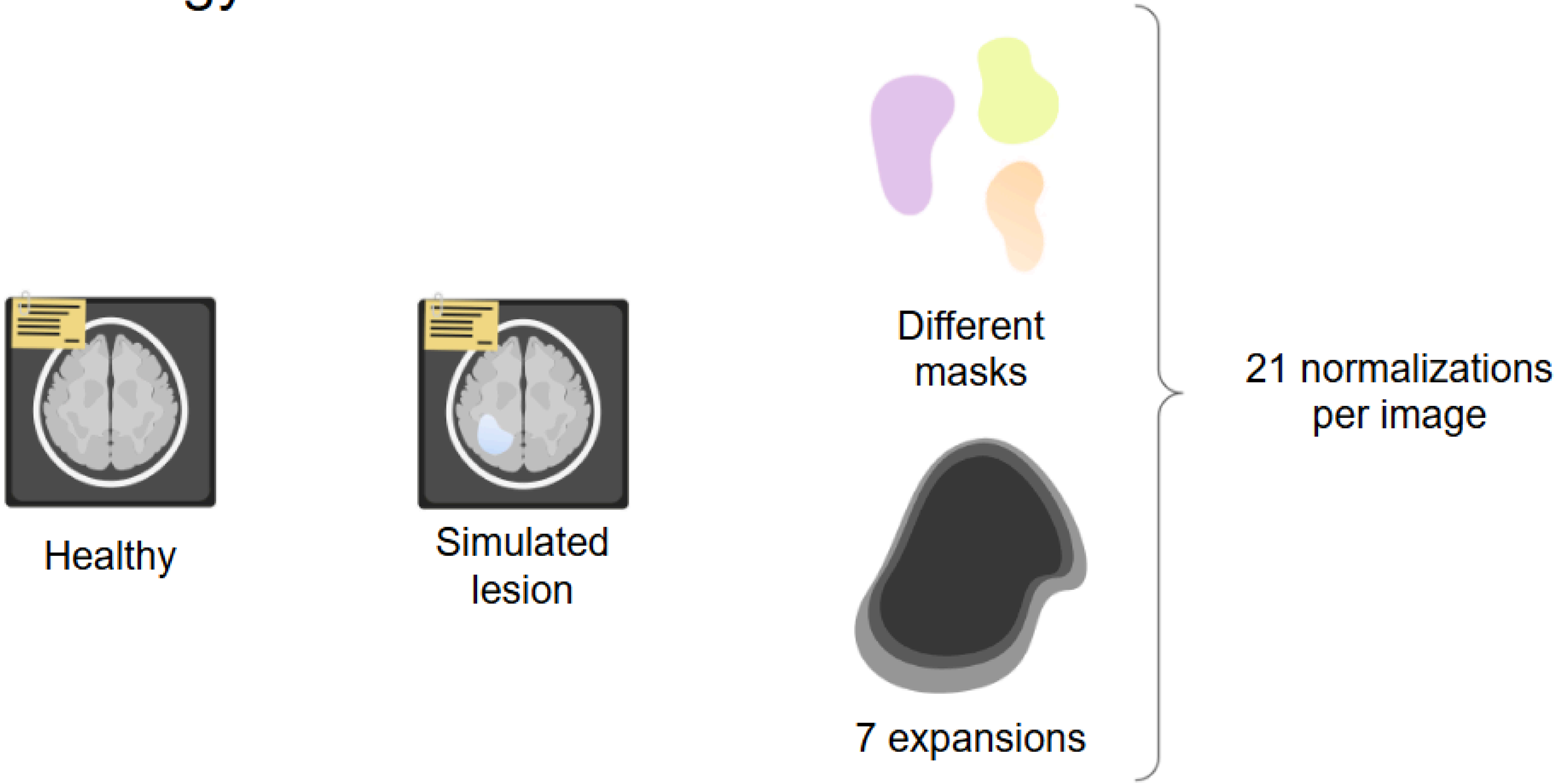
voxel **outside** lesion

voxel **inside** lesion

Threshold (%)	25	10	5	1	0.1	0.001	0.0001
Increase (mm)	2.3	4.3	5.5	7.7	9.6	10.1	10.2

METHODOLOGY: DATASET

Methodology: dataset



METHODOLOGY: NORMALIZATION COMPARISON

How this method compares to the “perfect” affine-only transform?

- Suppose we have two normalizations: ***a*** and ***b***
- We define the displacement distance in a voxel ***i***:

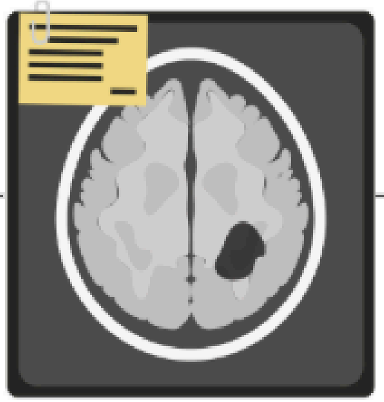
$$d_i^{a,b} = \sqrt{(x_i^a - x_i^b)^2 + (y_i^a - y_i^b)^2 + (z_i^a - z_i^b)^2}$$

- Low displacement distance means that the normalizations agree
- An overall metric on the similarity between two normalizations is the ***Root Mean Square***

$$\mathrm{RMS}_{a,b} = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(d_i^{a,b})^2}$$

METHODOLOGY

How to analyze the normalization qualitatively?



Affine-only

Affine + non-linear + cost function masking (4 masks)

x10 lesions

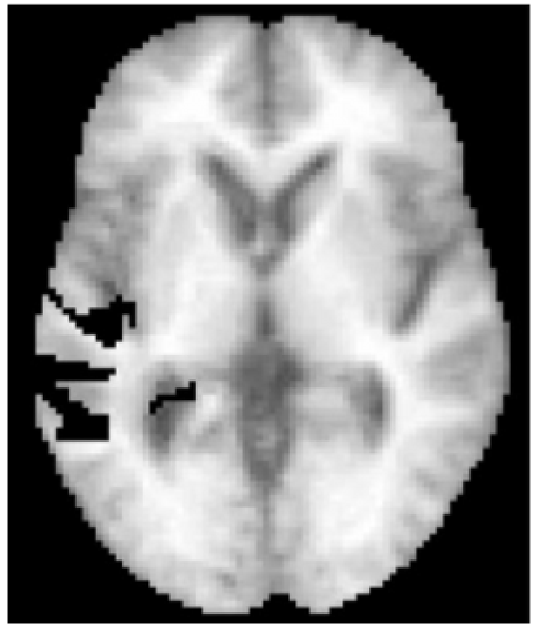
- Check if lesion generated distortions and if its location is consistent
- Then, apply the same parameters to the ***mask*** (***ld***) giving the normalized lesion definition (***nld***) and check if it maintains shape, size, consistency

METHODOLOGY: SIMILARITY BETWEEN NORMALIZATION

How to analyze the normalization qualitatively?

- For each of the 5 normalizations, compute a weighted mean across all lesions. The weights sj are the masked means of each of the images in a given set.
- Only voxels where nldi = 0 were considered.
- Voxels with less than 6 samples were considered as 0.

$$y_{ij}^{m} = \begin{cases} y_{ij}/s_j & \text{if } \ nld_{ij} = 0 \\ 0 & \text{otherwise} \end{cases}, \quad mn_i = \begin{cases} \sum_{j=1}^{10} y_{ij}^{m}/n_i^{m} & \text{if } \ n_i^{m} > 5 \\ 0 & \text{otherwise} \end{cases}.$$

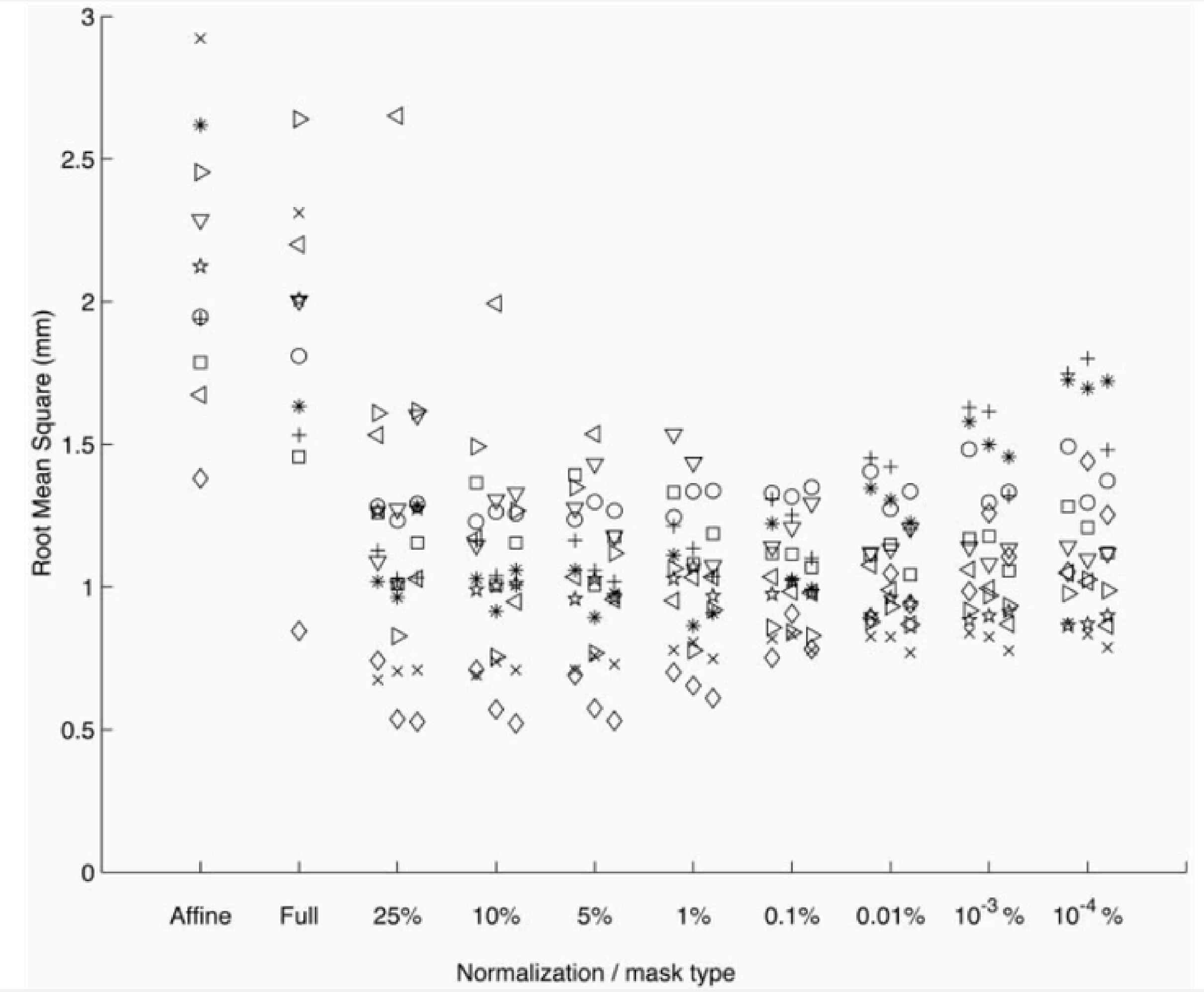


METHODOLOGY: VARIANCE IMAGE

- Let ti be the value of voxel i in the template image and let st be the mean of all voxels in the template
- Then, we can compute the mean squared difference between the normalized lesion images and the template, yielding the variance image
- We can then qualitatively see where the image varies the most
- Measure of similarity between normalizations and the template

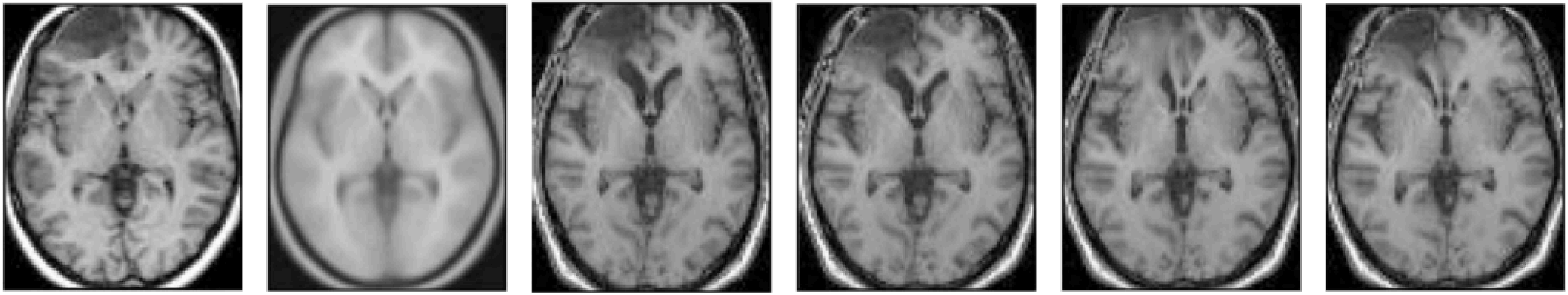
$$d_{ij}^{m} = \begin{cases} y_{ij}/s_j - t_i/s_t & \text{if } \ nld_{ij} = 0 \\ 0 & \text{otherwise} \end{cases}, \quad v_i = \begin{cases} \sum_{j=1}^{10} (d_{ij}^{m})^2/(n_i^m - 1) & \text{if } \ n_i^m > 5 \\ 0 & \text{otherwise} \end{cases}$$

RESULTS



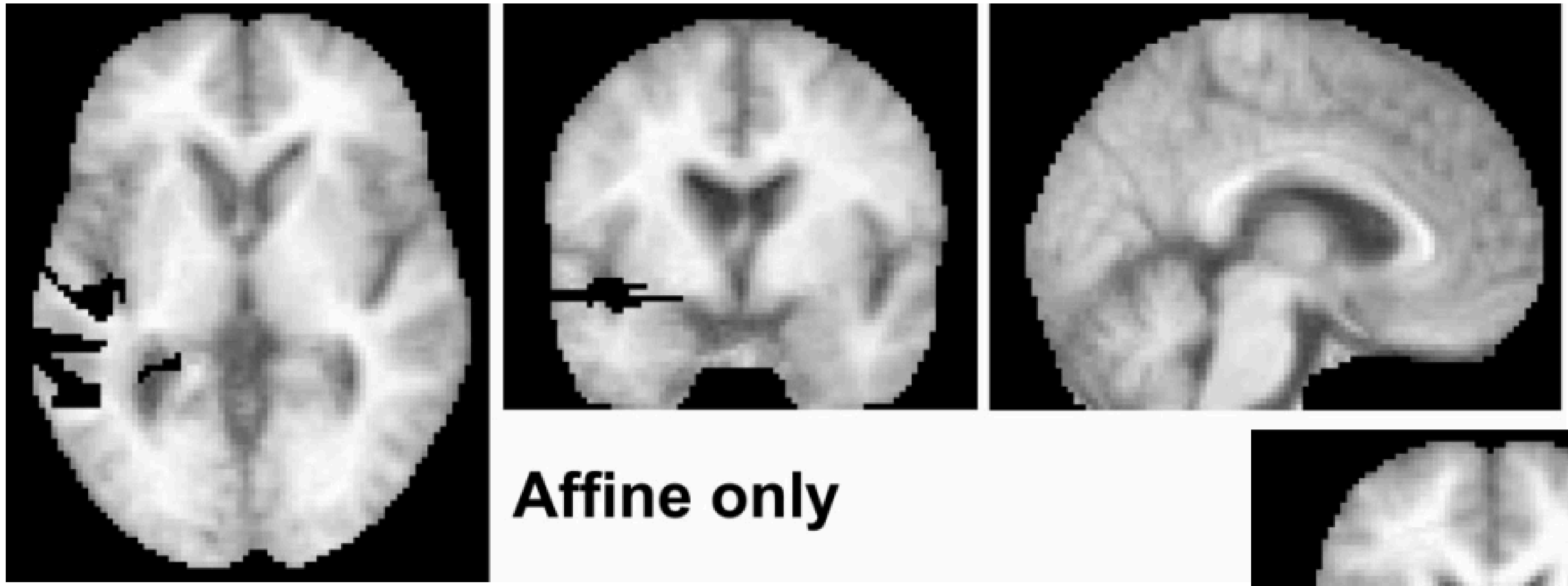
- We can see the RMS for each configuration of the simulated lesions
- The RMS compares the normalization of the simulated lesion and the healthy counterpart
- For each threshold, we have 3 columns: one for each mask set
- Ideally, we want low RMS and a low variance between images
- The threshold of 0.1% performs well

RESULTS: SIMULATED LESIONS

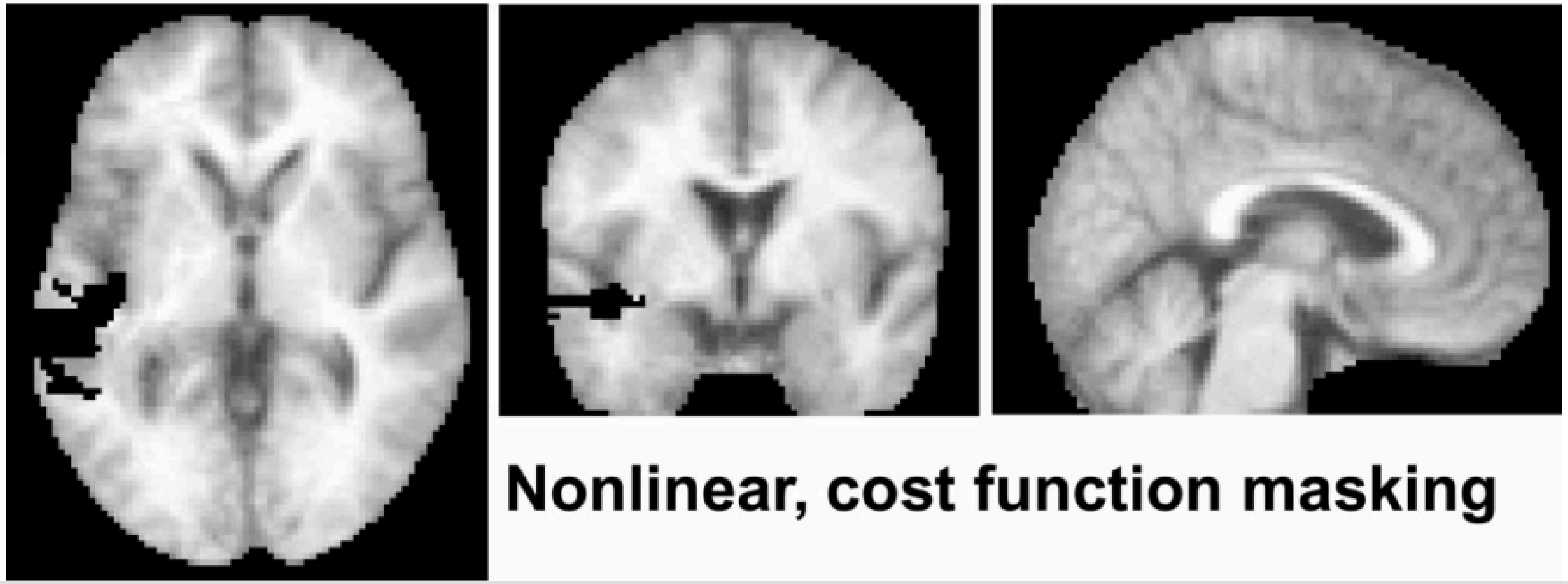


Simulated lesion | Template | Affine | Affine with masking | Affine + non-linear | Affine + non-linear with masking

RESULTS: MEAN IMAGE WITH REAL LESIONS

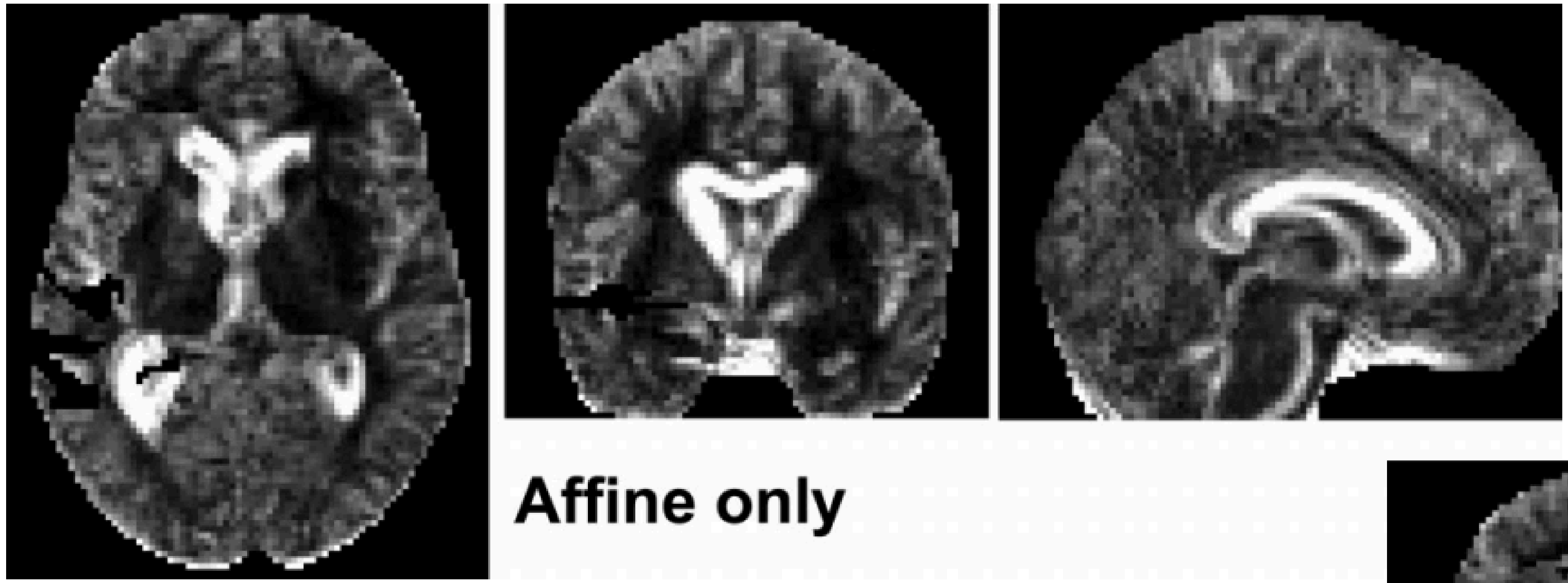


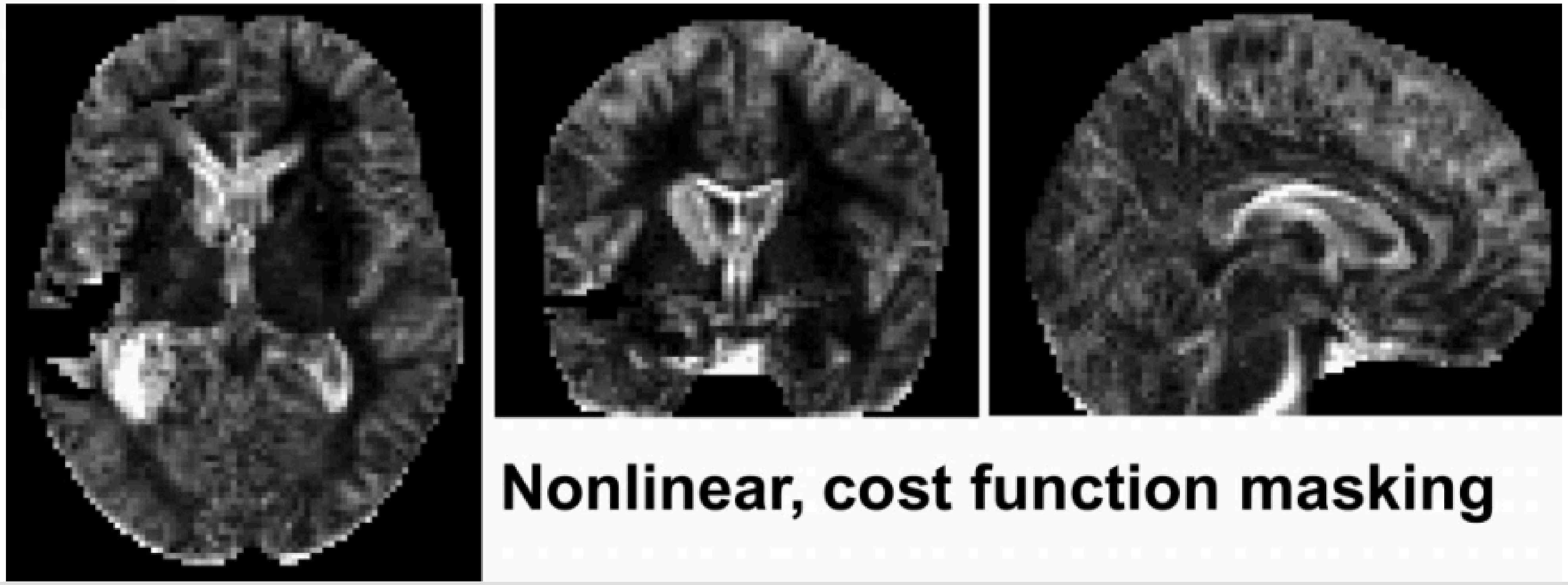
Affine only



Nonlinear, cost function masking

RESULTS: VARIANCE IMAGE WITH REAL LESIONS





DISCUSSION: ADVANTAGES OF COST FUNCTION MASKING:

- Even affine transformation is improved because the masking reduces the bias of the lesion
- We can use non-linear transformations without severe distortions
- Little differences for different masks at 0.1% threshold
- May help in functional imaging studies

DISCUSSION: LIMITATIONS OF COST FUNCTION MASKING

Requires manual input - The user must define the lesion area manually, which makes the process more time consuming (about 30 minutes per scan)

Does not work well with large bilateral lesions (but is robust to big unilateral lesions)

CONCLUSION AND INSIGHTS

Would you feel ar ease implementing it?
Affine: yes; Nonlinear: no.

Would you recommend trying it on other data or applications?
Yes. Other body regions, stellite imaging and general pre-processing tools

What part did you find most difficult to understand? Methodology: low precision on definitions, unclear symbols and variables, poor overall cohesion.

THANK YOU

QUESTIONS AND ANSWERS