Image Segmentation

Quantitative and Functional Imaging

BME 4420/7450

Fall 2022

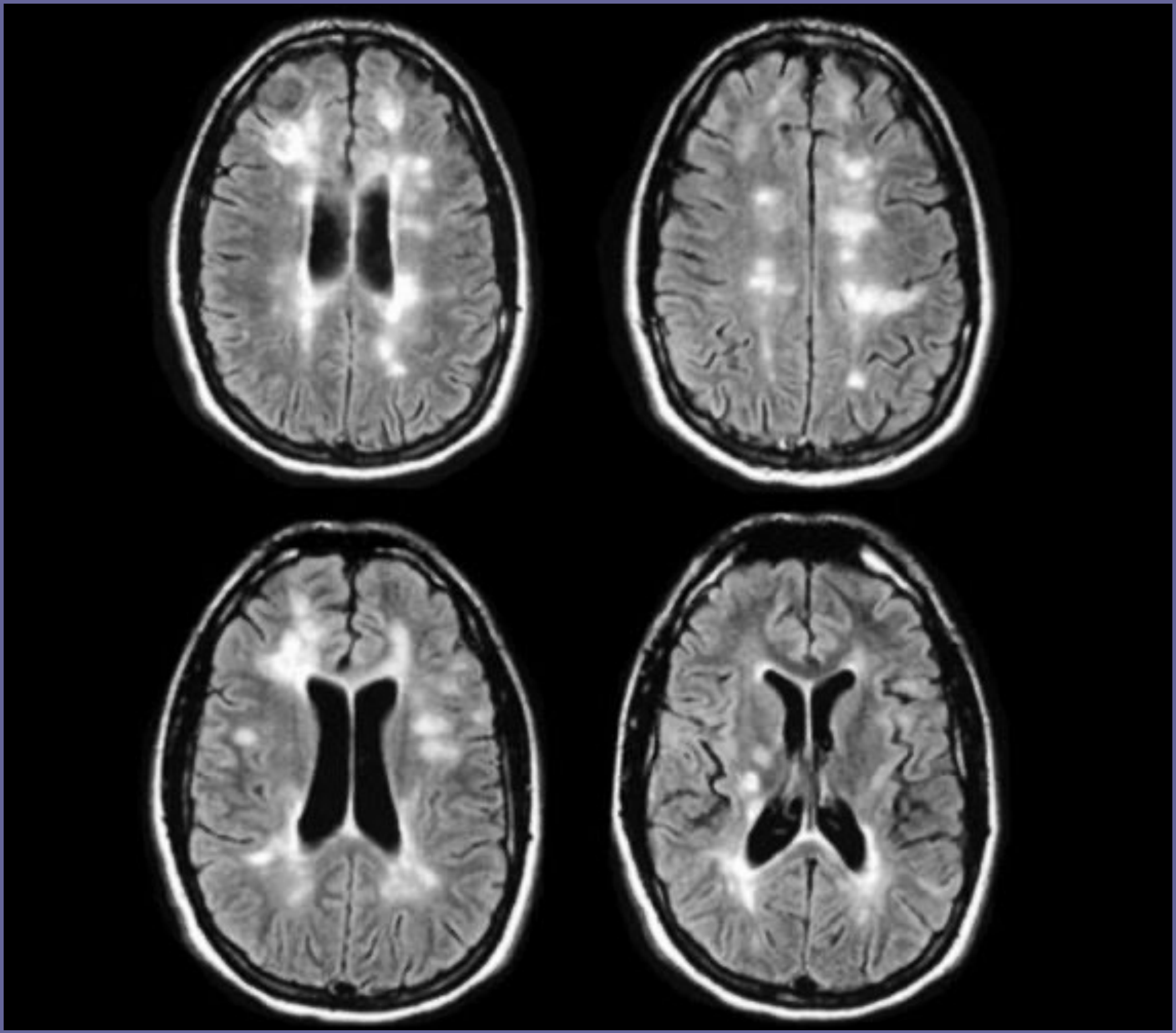
Image segmentation

- What is segmentation and why is it important?
  - Multiple sclerosis (MS) disease burden
  - Deep brain stimulation (DBS) targeting
- Approaches
  - Manual tracing
  - Thresholding
  - Region growing
  - Edge-based methods
  - Multi-spectral methods
- Examples
  - Visualization
  - Brain volumetry
  - Lesion detection in Multiple Sclerosis
- Designing a segmentation-based clinical trial

Image segmentation

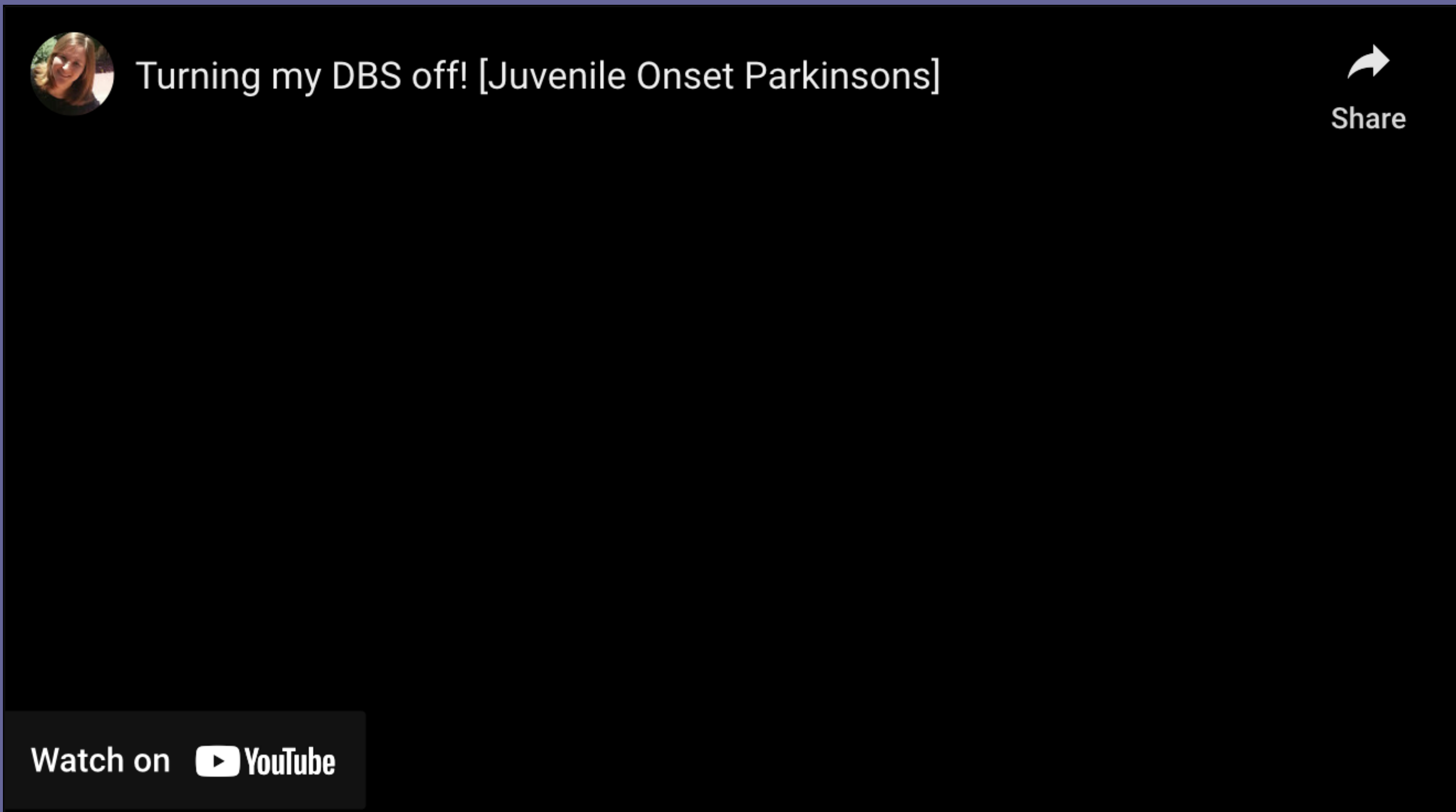
- Partitioning an image into homogeneous regions
  - Classification
- First step in
  - Localization (targeting)
  - Volume measurement
  - Shape analysis
  - Signal averaging over an anatomical structure
  - Visualization
- Why is this useful in medicine?

Brain lesions in Multiple Sclerosis:
Can we use imaging data to quantify disease severity?



https://case.edu/med/neurology

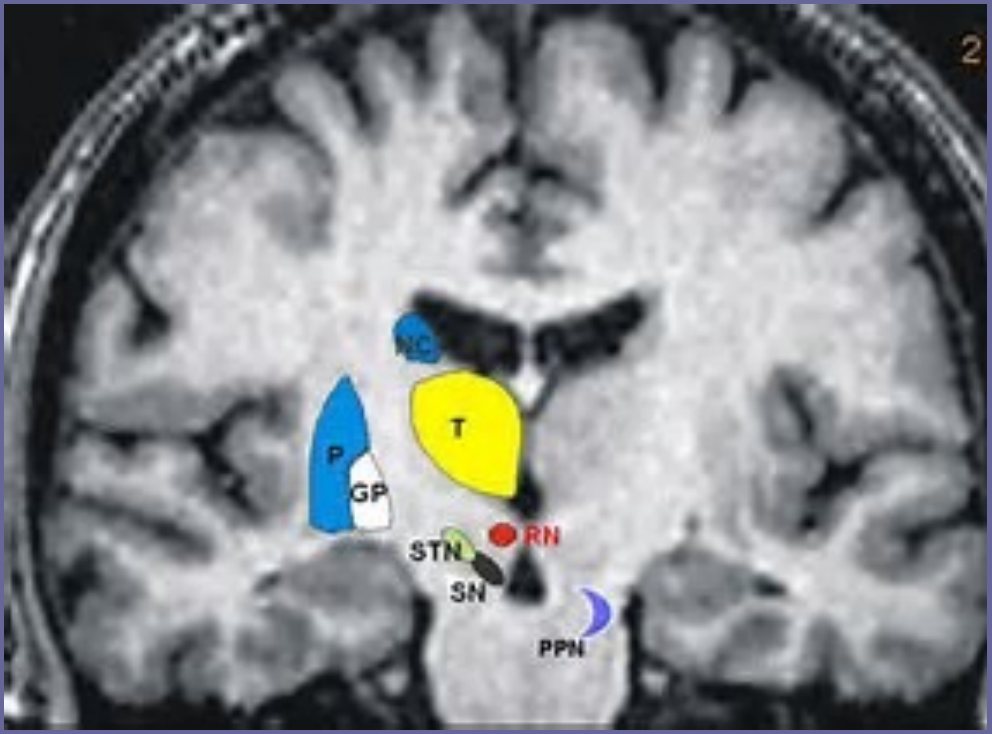
Deep Brain Stimulation (DBS)



https://www.youtube.com/watch?v=ZQ5gAzVjPVM

Targeting for Deep Brain Stimulation

- Electrical stimulation relieves symptoms of
  - Parkinson's Disease
  - Essential Tremor
  - Depression
- To place the electrode, surgeons need to know where the target neurons are.
- Accuracy should be ~1mm



Lookfordiagnosis.com

Image segmentation

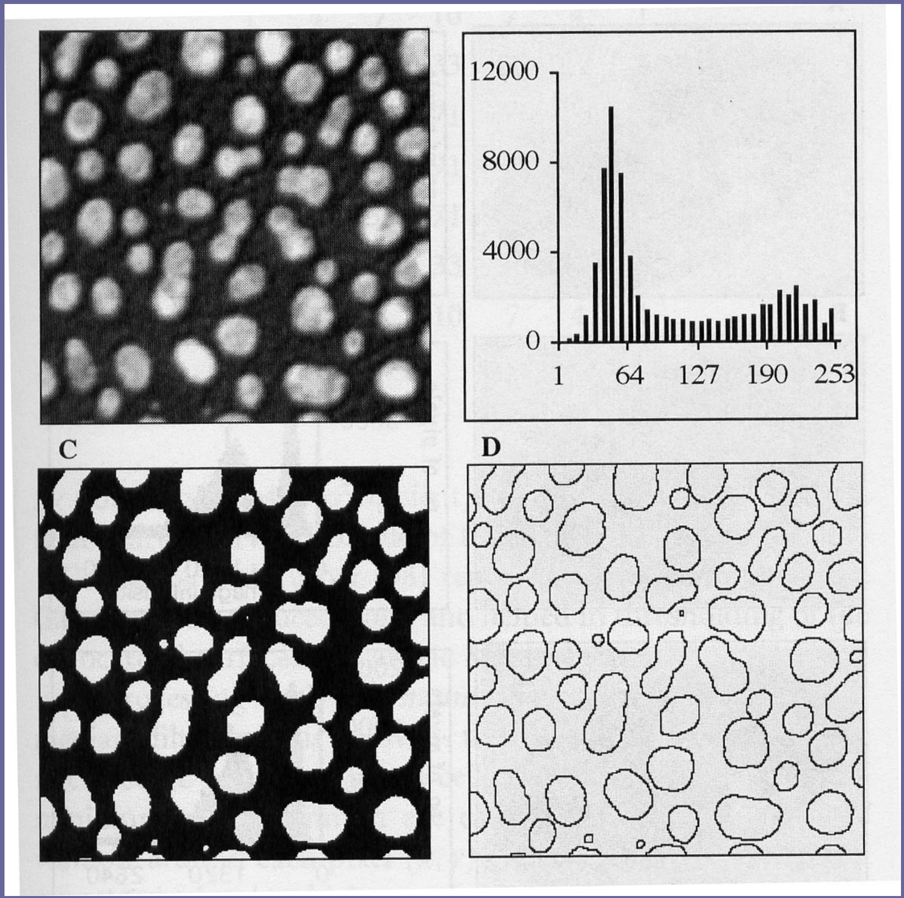
- Partitioning an image into homogeneous regions
  - Classification
- First step in
  - Localization
  - Volume measurement
  - Shape analysis
  - Signal averaging over an anatomical structure
  - Visualization
- Many applications in medicine
- No one approach works well in all situations, so many approaches exist

Thresholding

- Set a ‘threshold’ value
  - Pixels with intensity > threshold
  - Pixels with intensity < threshold
- Result is a binary image (mask)
- Assumes contrast-to-noise ratio (CNR) is high
- Problem: how should the threshold value be chosen?

Threshold selection

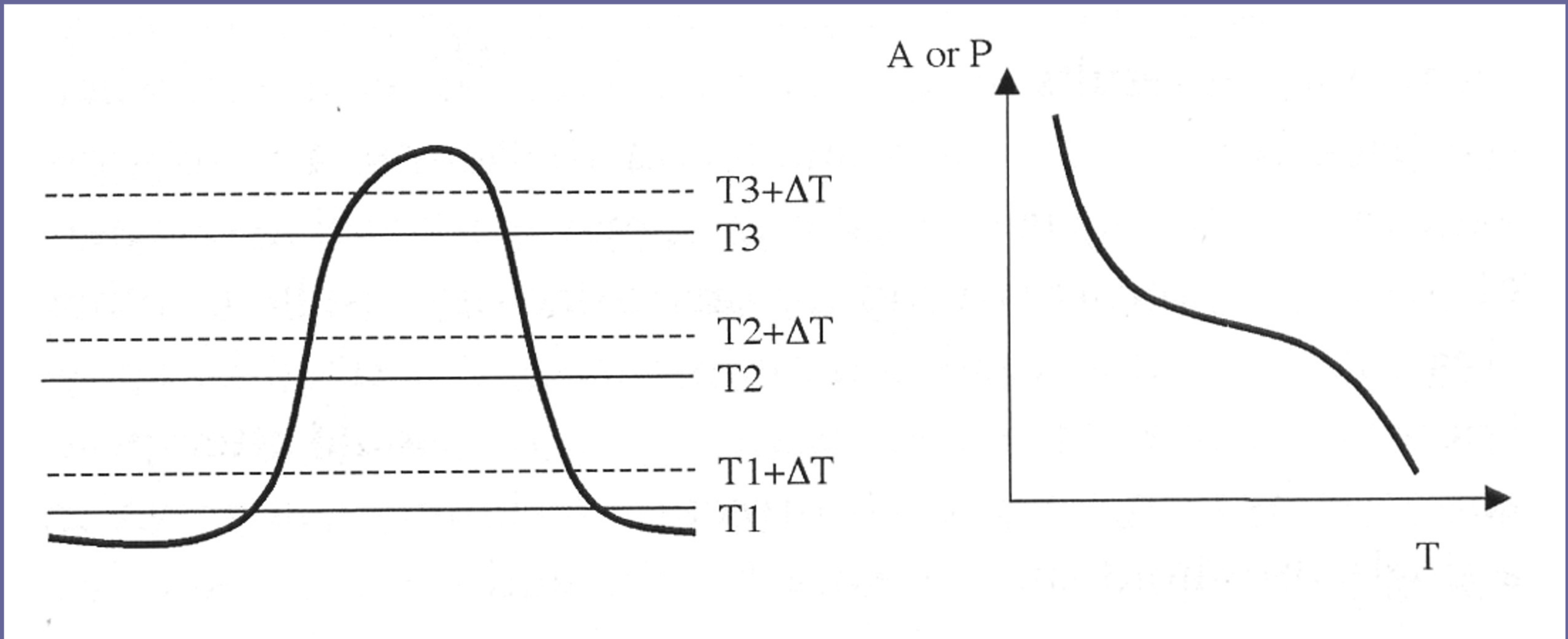
- Based on histogram of pixel intensities
- Works best when intensity histogram is bimodal



Rogowska (2000)

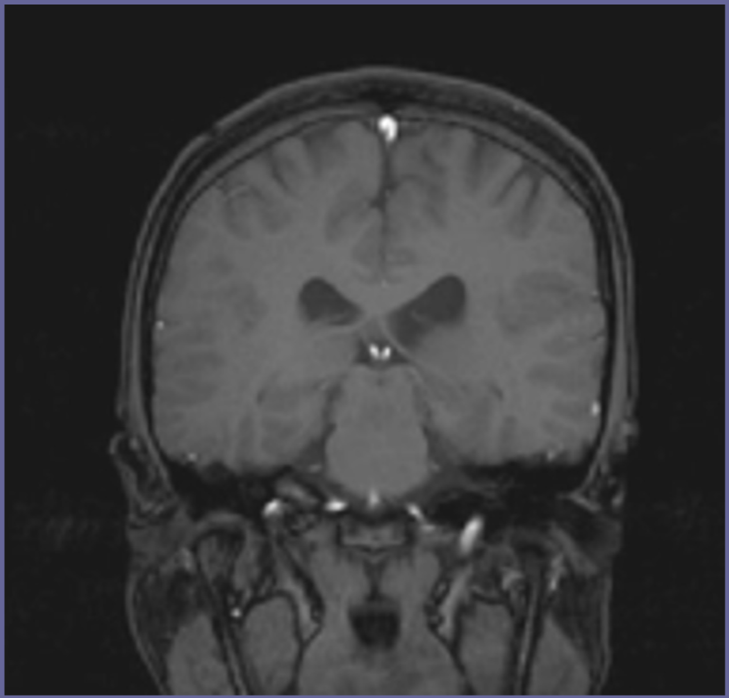
Threshold selection

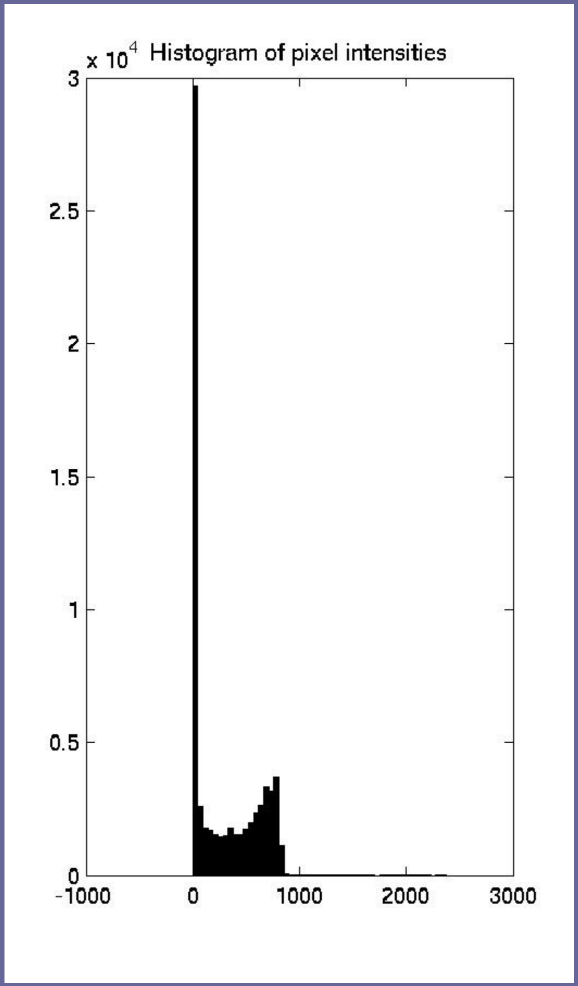
- Choose threshold to minimize dependence of area on threshold



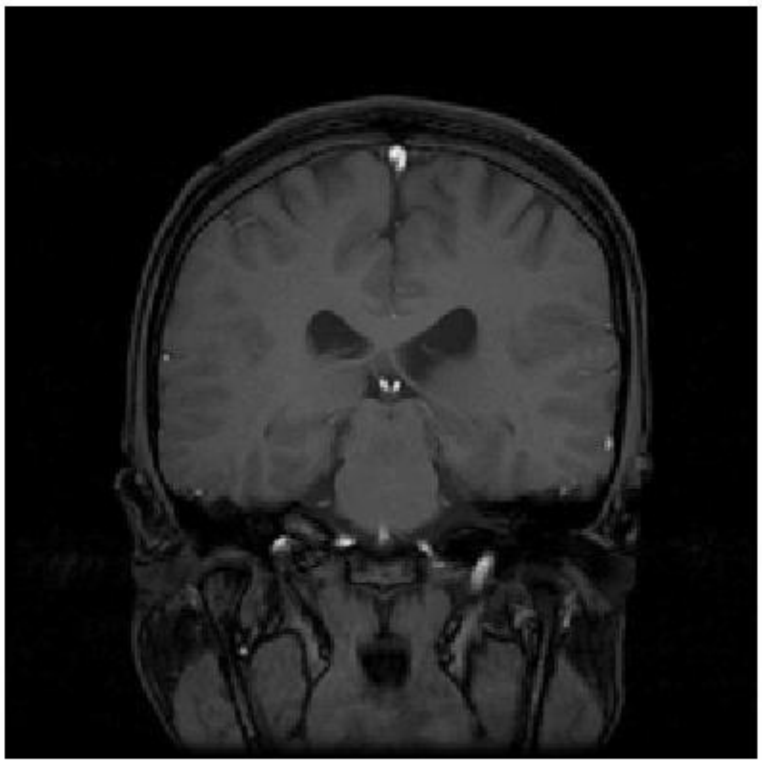
Rogowska (2000)

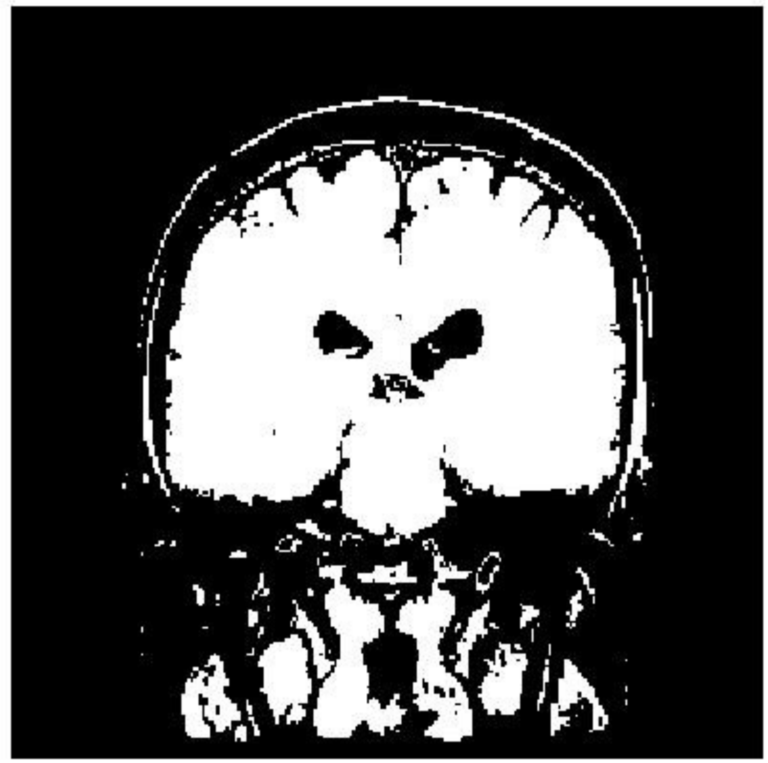
How well does this work in other cases?



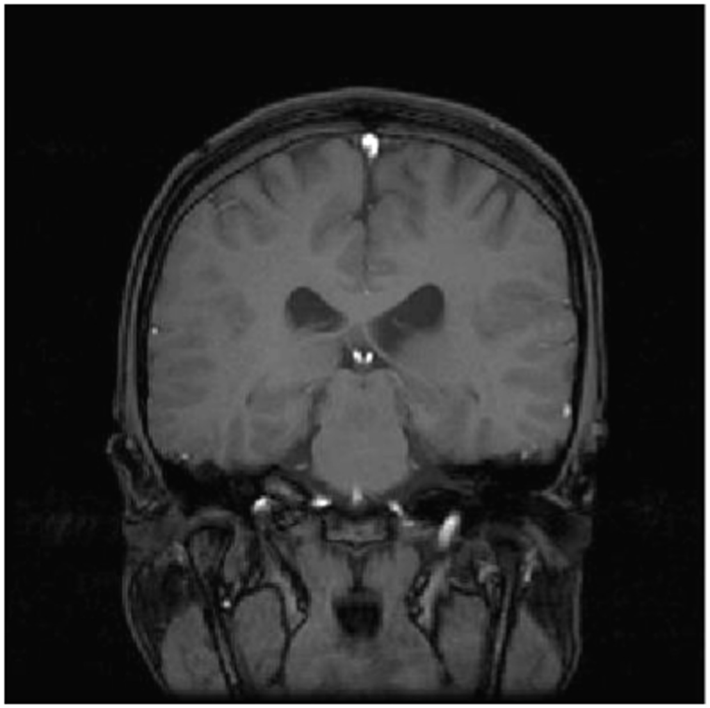


Segment head from background



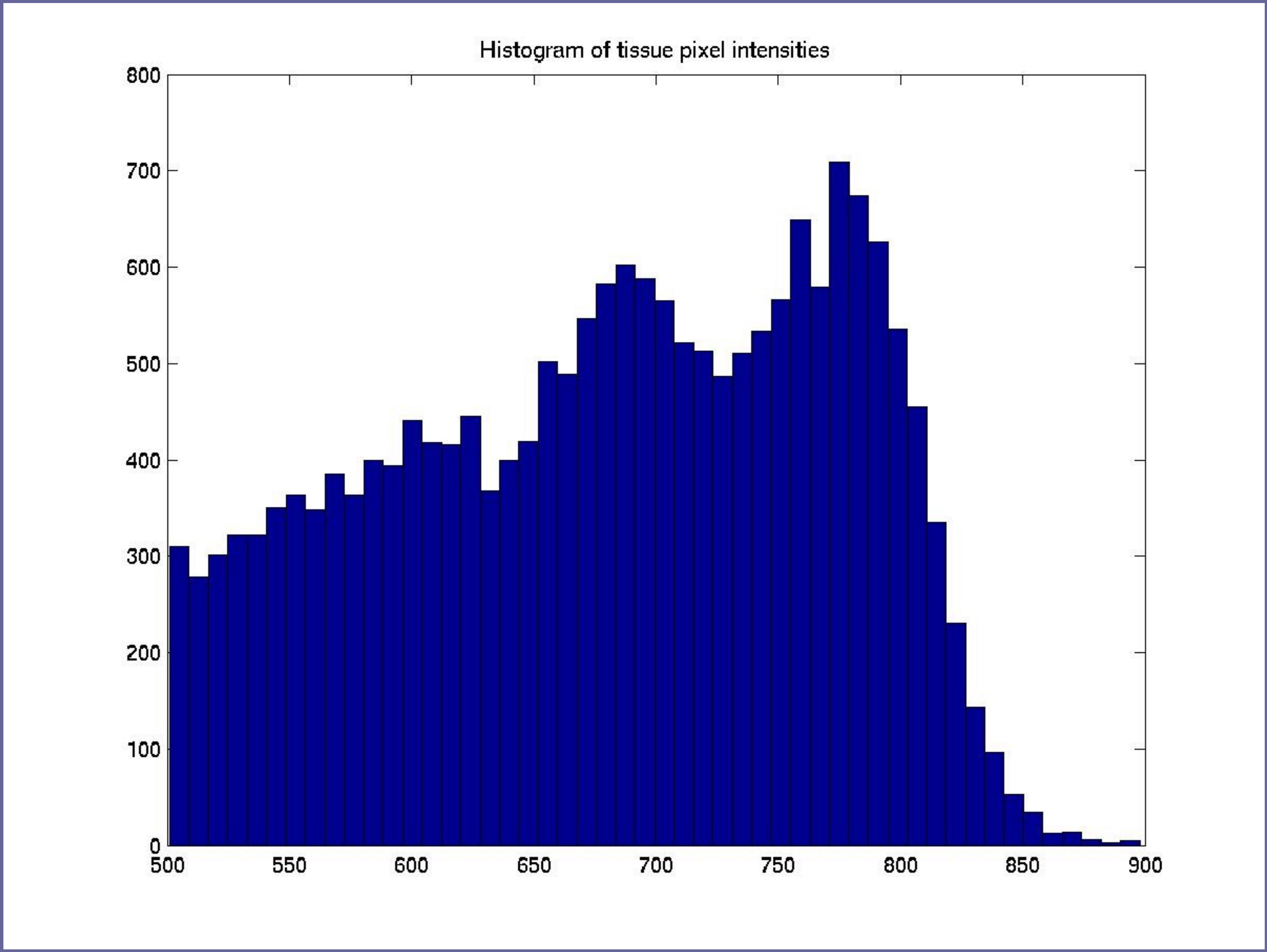


Segmenting white and gray matter



Why doesn't this work so well?

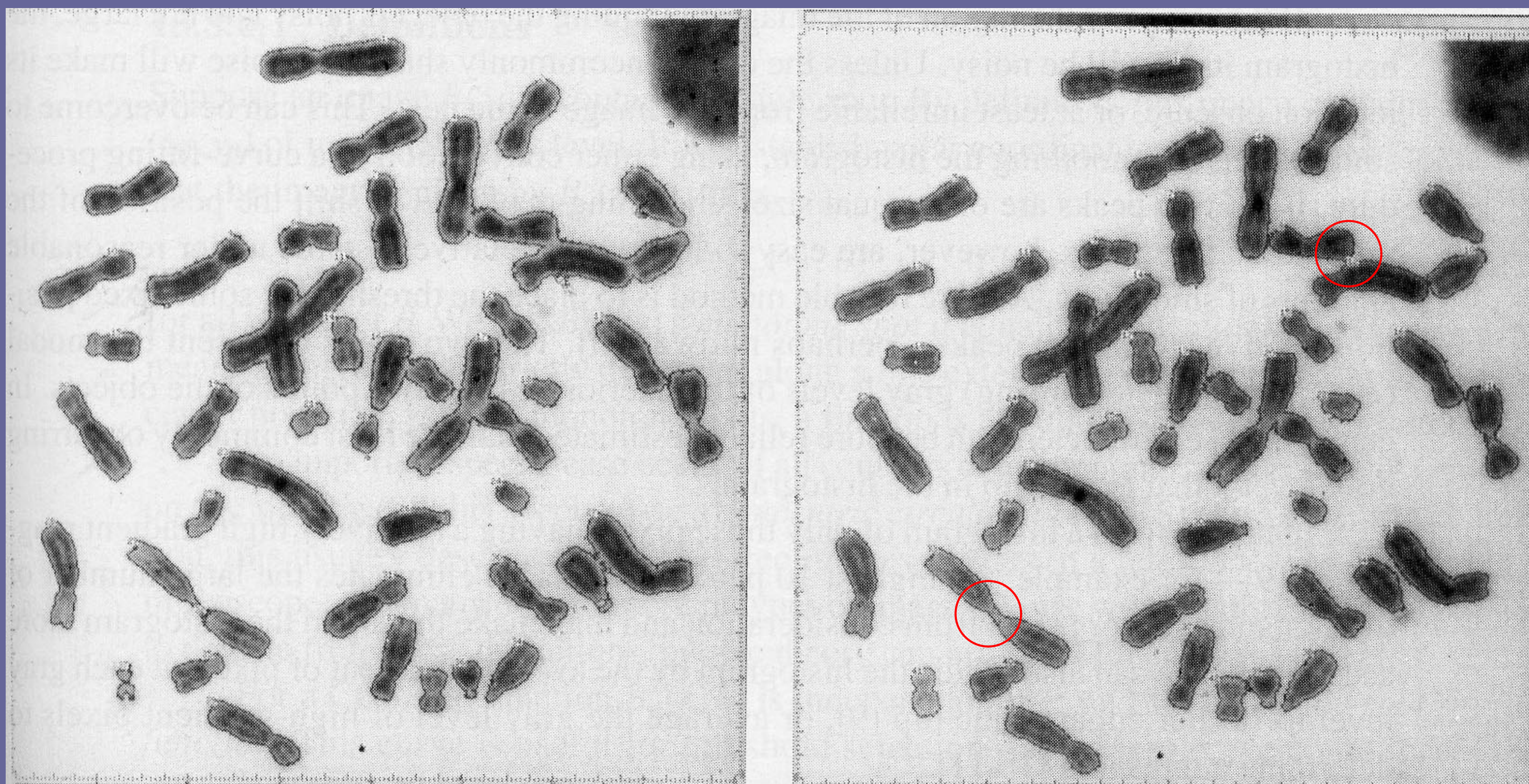
White and gray matter intensities overlap



Improved thresholding

- Use *adaptive* threshold
  - Threshold varies across the image
  - Calculated separately within sub-regions of an image
- Correct non-uniform sensitivity in image (adjust intensity values)

Effects of adaptive thresholding



Castleman (1996)

Global threshold   Adaptive threshold

Region growing

- Start at a single pixel (the *seed* point)
- Check the neighboring pixels
  - If the neighbor has nearly the same intensity, include it in the growing region
  - *Homogeneity criterion*
- Repeat until no more pixels can be added
- Yields a nearly uniform, connected region
- Problem: how to pick homogeneity criterion?

Edge-based methods

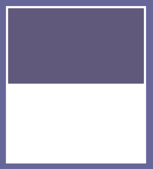
- Find boundaries between uniform regions
- Edges can be identified using the gradient of image intensity
- For an image intensity described by *f(x,y)* the magnitude of the gradient is

$$|G| = \sqrt{G_x^{\,2} + G_y^{\,2}} = \sqrt{\left(\frac{\partial f}{\partial x}\right)^2 + \left(\frac{\partial f}{\partial y}\right)^2}$$

Gradient calculation

- Calculate gradient by convolving image with a small matrix
  - Compares intensity on each side of the current pixel
- Examples are the Sobel edge operators:

$$G_x = \begin{pmatrix} -1 & 0 & 1 \\ -2 & 0 & 2 \\ -1 & 0 & 1 \end{pmatrix} \qquad G_y = \begin{pmatrix} -1 & -2 & -1 \\ 0 & 0 & 0 \\ 1 & 2 & 1 \end{pmatrix}$$



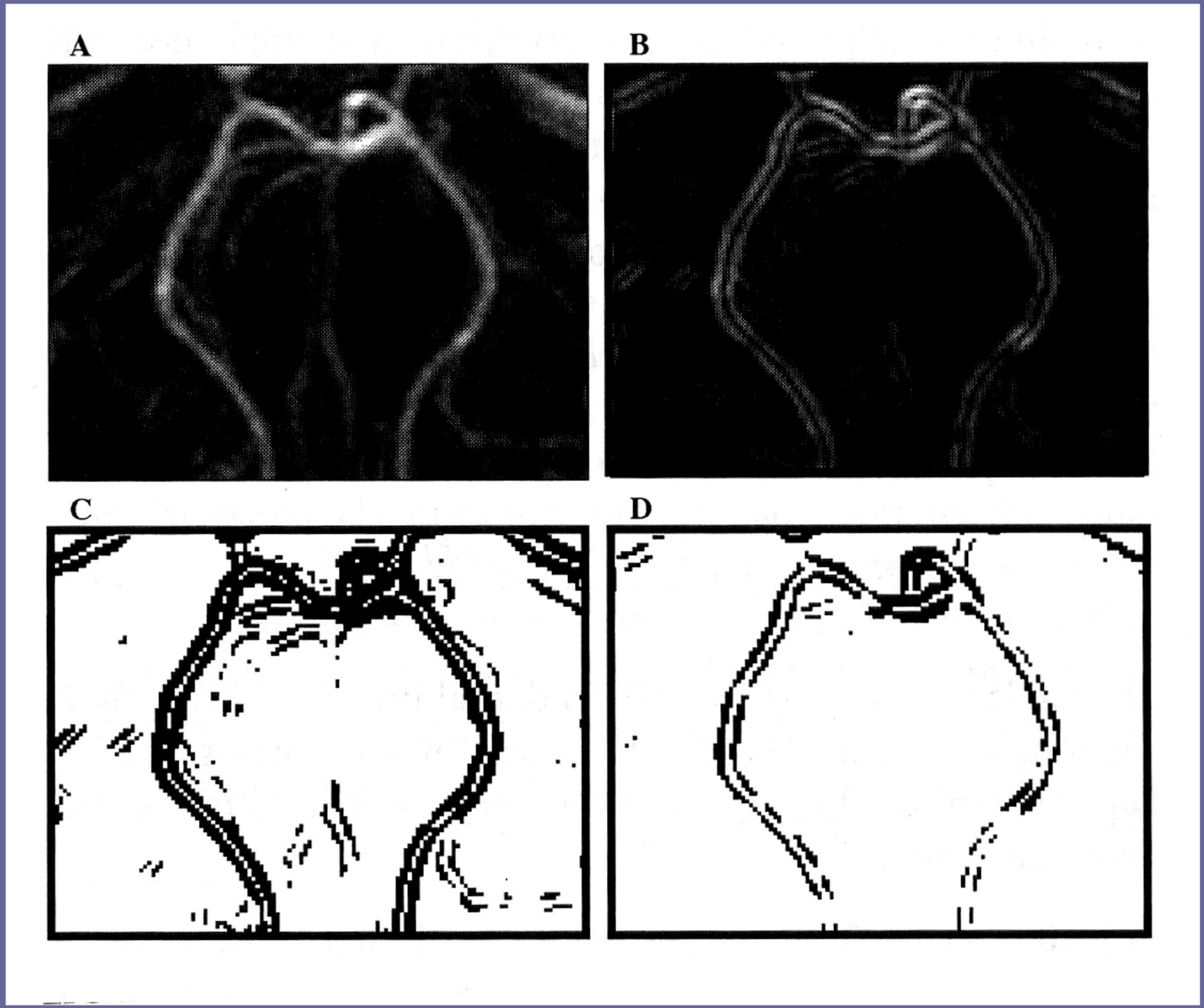
Edge detection

- Intensity gradient image is thresholded to find most significant edges
- Problems:
  - Edges may not be continuous
  - Sensitive to noise
- Often edge detection must be preceded by image smoothing (to reduce noise)

Edge detection using the Sobel operator

Original

Edges



Low threshold

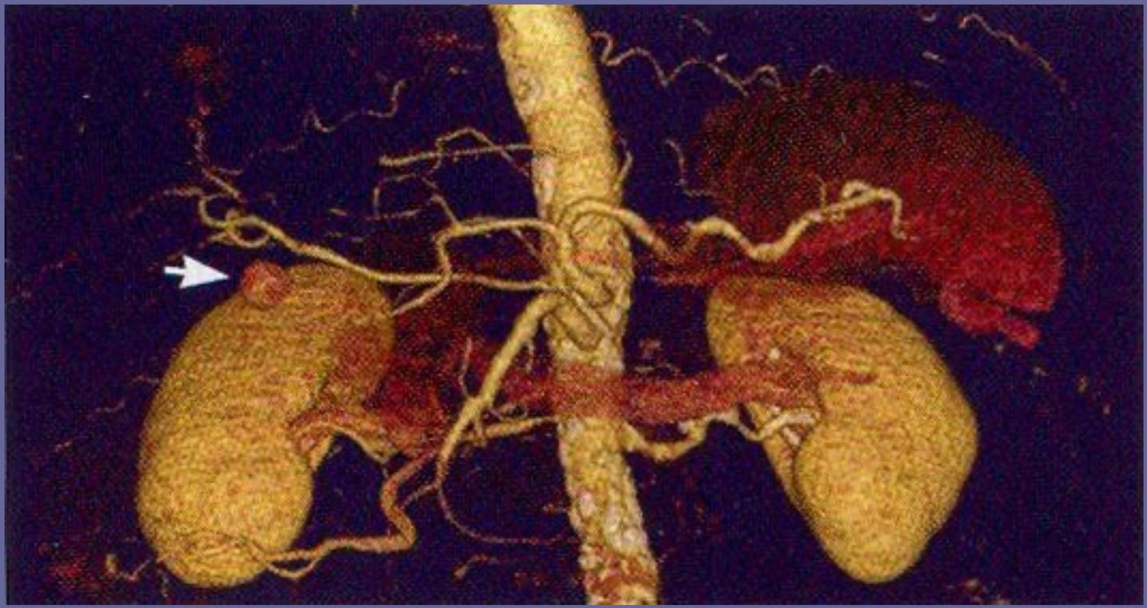
High threshold

Rogowska (2000)

Example I: Visualization

- Appearance of segmented structures can be altered to highlight the anatomy of interest
- Surfaces rendered in 3D to show spatial relationships
- Guide to treatment

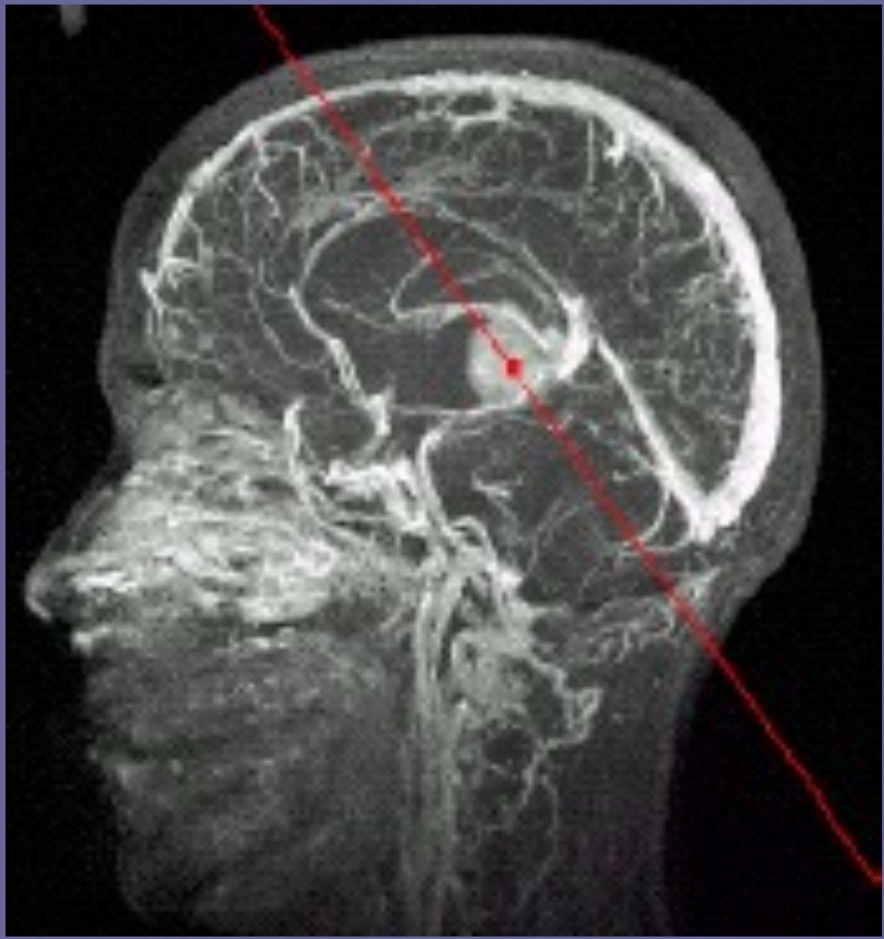
Urinary tract calcification



Prokop & Galanski, 2003

Surgical planning

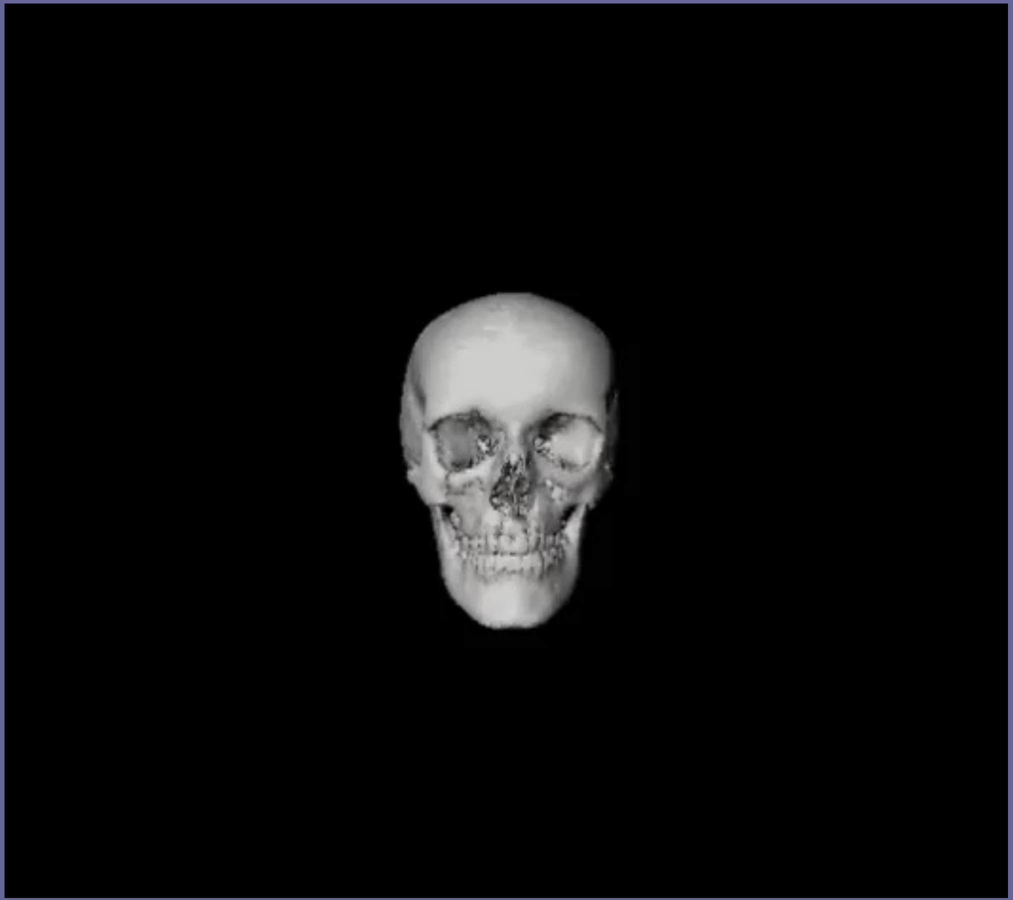
- Guide biopsy needle to deep structures
- Avoid damaging vessels or critical brain tissue on the way
- Update image information intra-operatively (image-guided surgery)



Suetens, 2002

Surgical planning

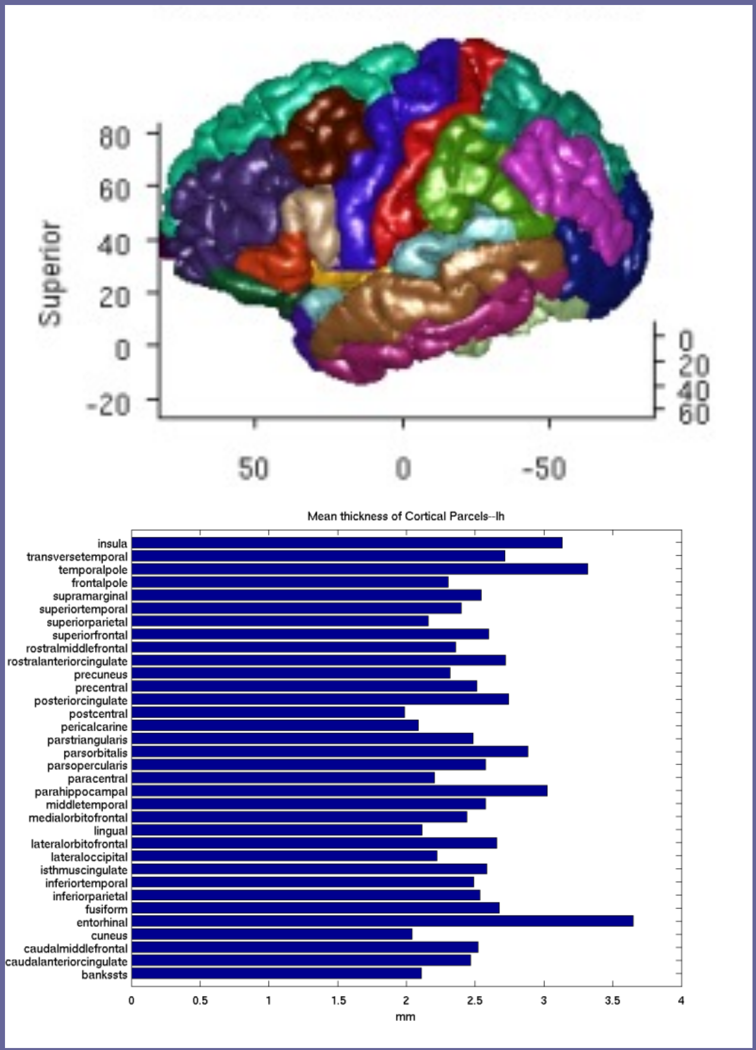
- 3D modeling allows preoperative evaluation and rehearsal
- Software is similar to flight simulators
- Haptics integrates tactile feedback



Suetens, 2002

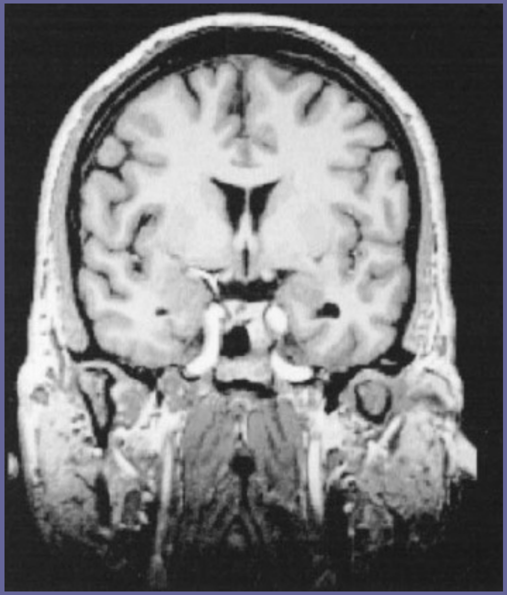
Example II: cortical parcellation

- Automatically define cortical regions
- Measure parcel area, thickness, and volume
- Relies on segmenting the cortex from white matter and CSF/skull
- Performed by popular software packages (FreeSurfer, for example)



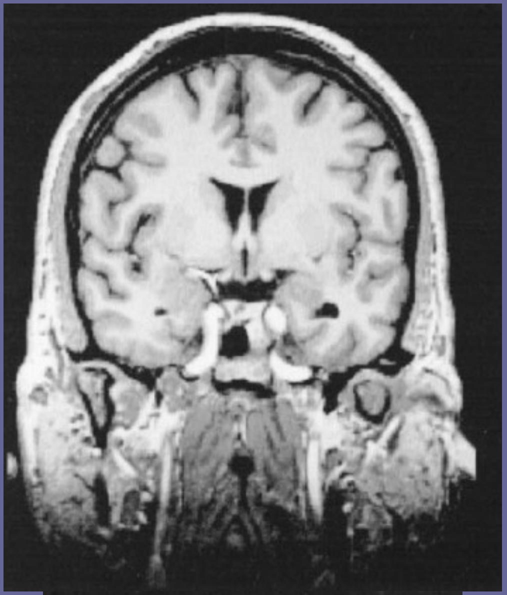
Computational steps

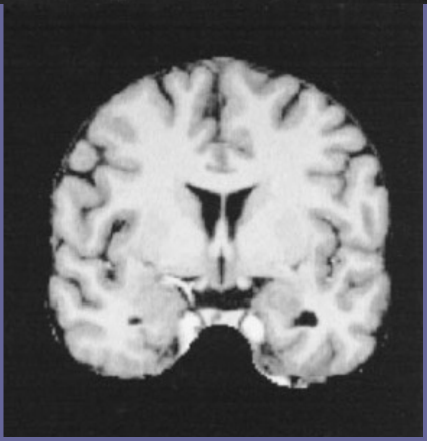
- Suppose we want to measure the thickness of the cortex (i.e., gray matter)
- How can we deal with
  - Spatially-dependent sensitivity?
  - Image warping?
  - Folded surface of brain?
  - Identifying parcels?

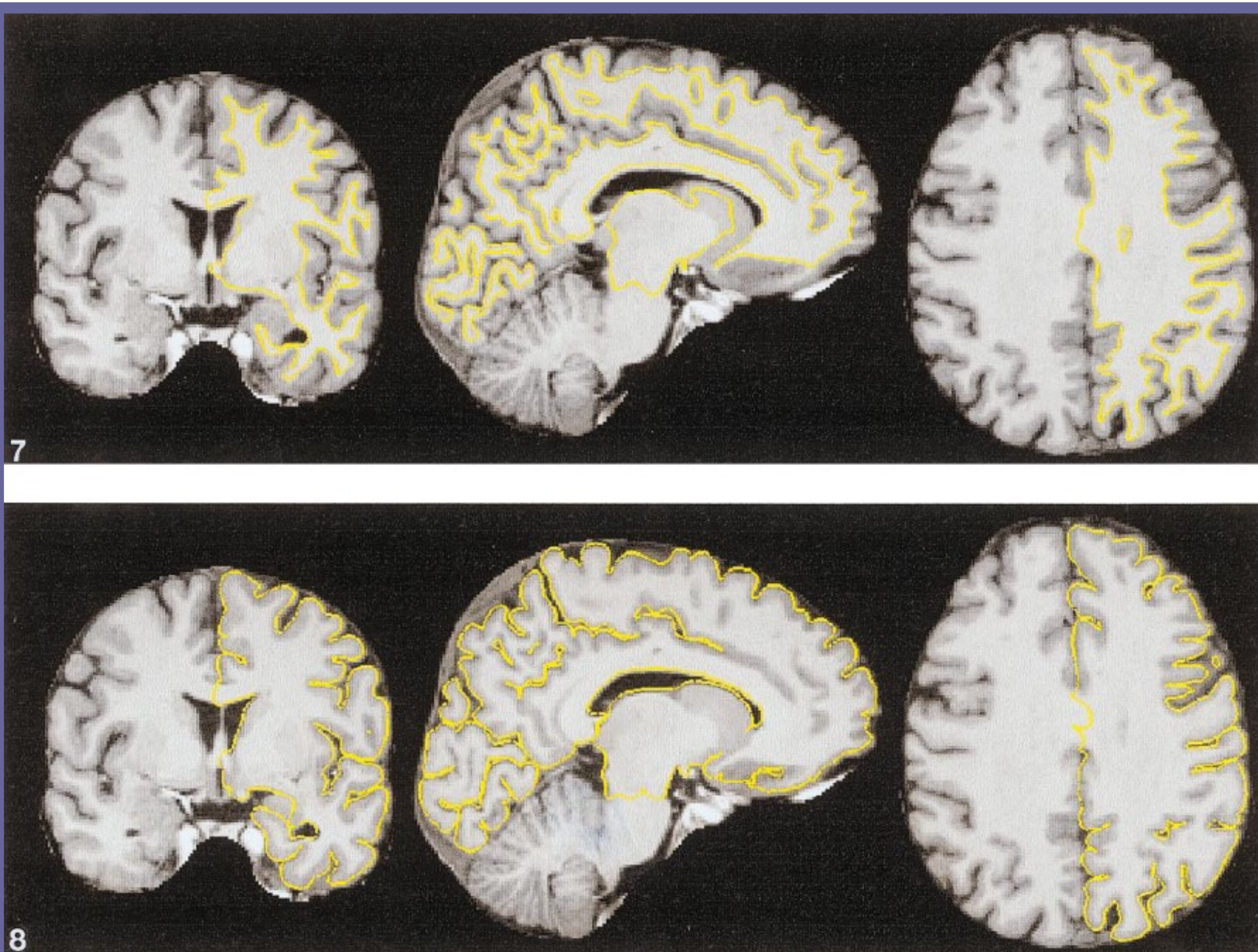


Computational steps (examples)

- Remove intensity variations across image to simplify segmentation
- Remove the skull and extracranial tissues from image ("skull-stripping")
- Gray matter/white matter/CSF segmentation
- Separate hemispheres from each other and subcortical structures (assume spherical topology)
- Tessellate gray and white matter surfaces



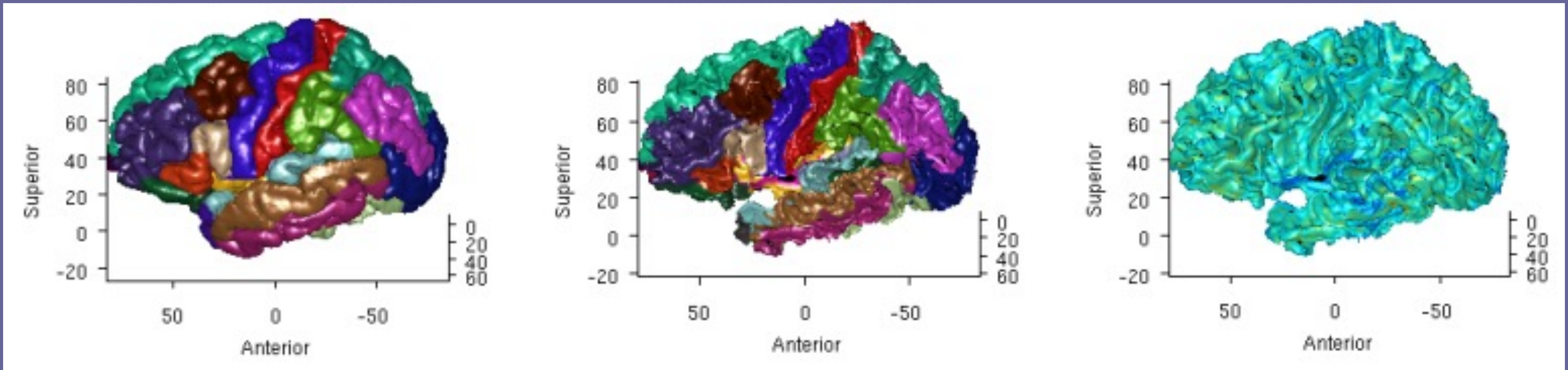




Dale et al (1999)

Classify points on cortical surface

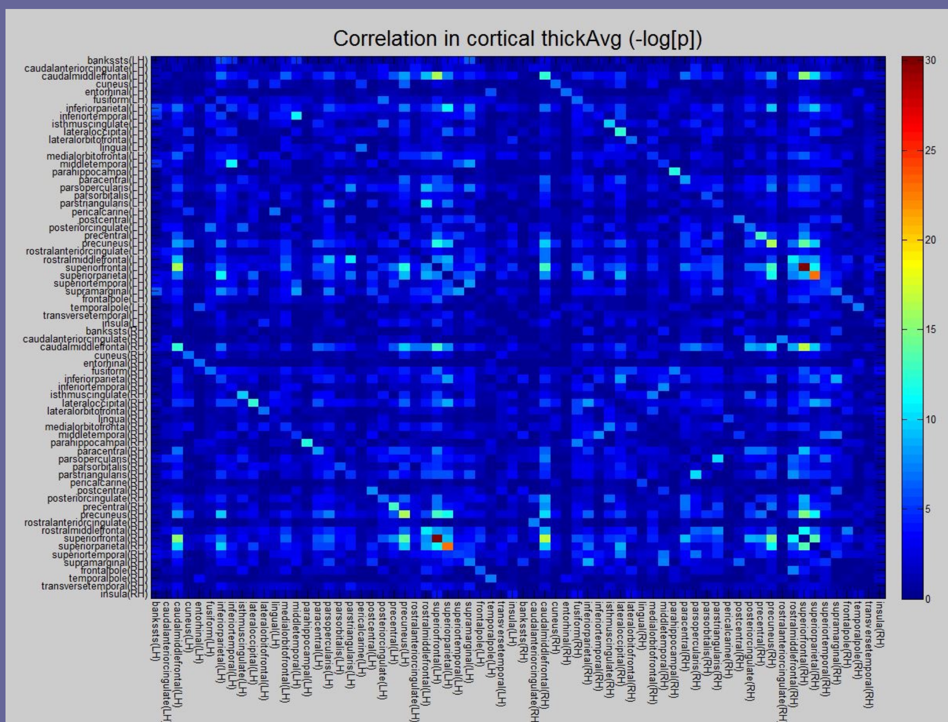
- The surface is modeled as a deformable surface
  - Balance smoothness with intensity-matching
- Labels are added using a reference atlas



Cortical surface　　White matter surface　　GM/WM CNR

Quantify cortical properties by parcel

- Measure thickness of cortex in each region
- Correlate thickness variations in a large group of subjects

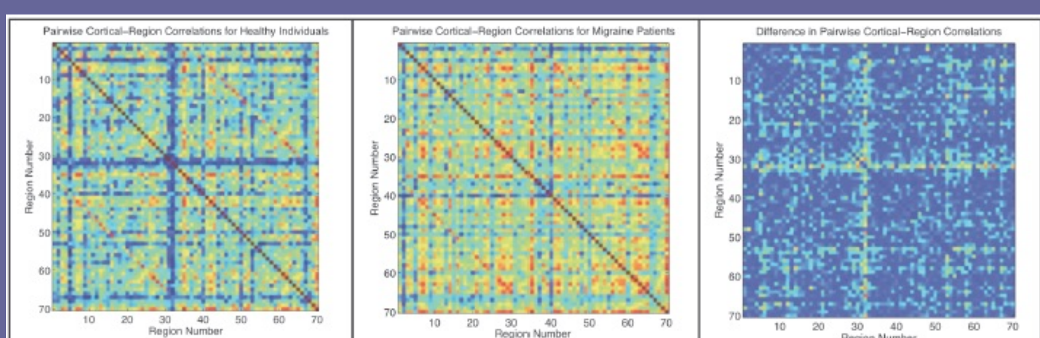


Large values in the correlation matrix indicate cortical regions that tend to vary together

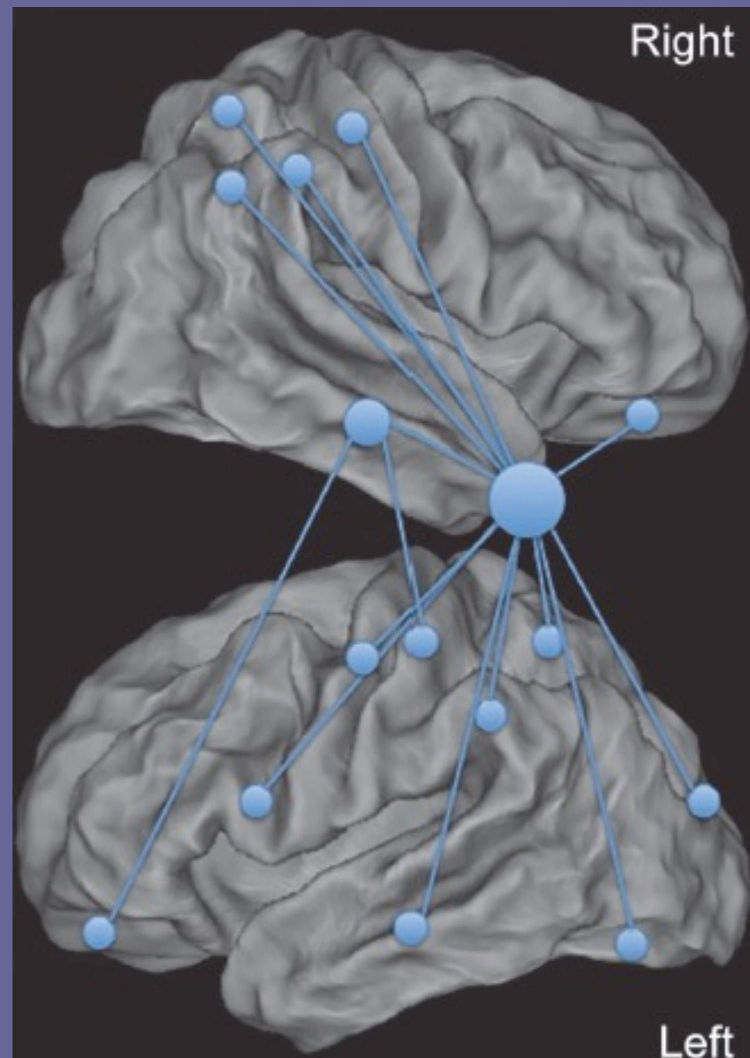
Evidence that the regions are involved in the same networks

Structural Connectivity

- Identify networks of regions that co-vary in GM thickness
- How are these affected by disease?
- Example: migraine
- Cause or effect of migraines?



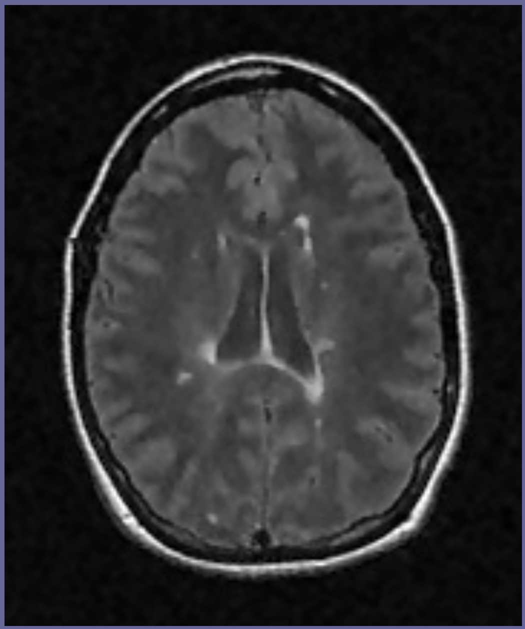
Healthy Migraine Difference



Schwedt et al, PLOS One (2015)

Example III: Measuring lesion volume in multiple sclerosis

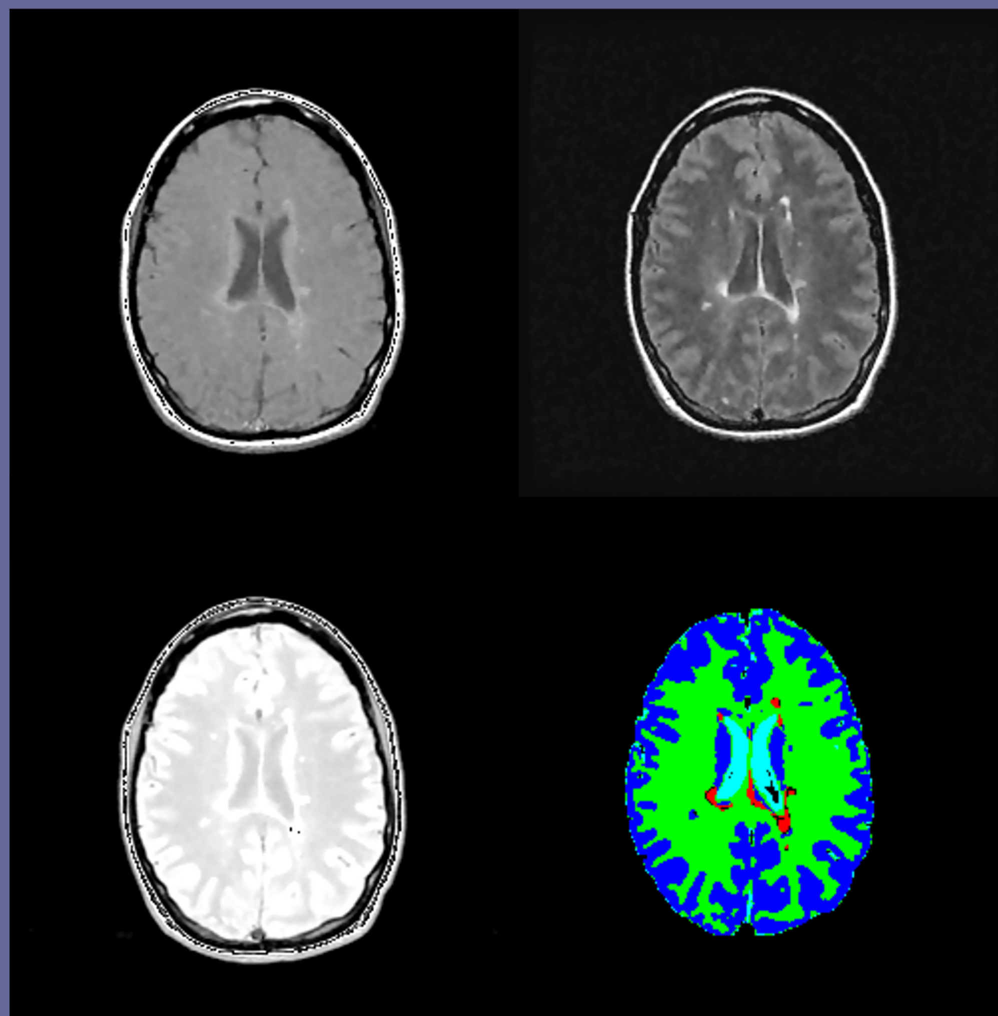
- Immune system attacks myelin
- Interferes with action potential transmission
- Inflammation -> long T2
- Demyelination -> long T1



Segmenting brain lesions from normal tissue

T_1 weighting

T_2-weighting

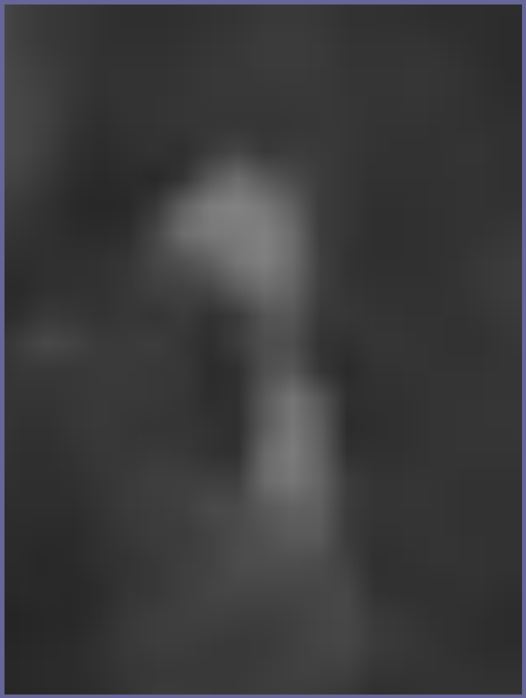


M_0 weighting

Segmented

Approaches to measuring lesion volume

- Hand tracing, slice by slice
  - Low reproducibility
- Intensity thresholding
- Contour following/edge detection
- Cluster analysis
- Multispectral cluster analysis



Reproducibility: Problems with manual segmentation

expedited publication

Interferon beta-1b is effective in relapsing-remitting multiple sclerosis.

II. MRI analysis results of a multicenter, randomized, double-blind, placebo-controlled trial

D.W. Paty, MD; D.K.B. Li, MD; the UBC MS/MRI Study Group*;
and the IFNB Multiple Sclerosis Study Group*

Article abstract—We performed yearly MRI analyses on 327 of the total 372 patients in a multicenter, randomized, double-blind, placebo-controlled trial of interferon beta-1b (IFNB). Clinical results are presented in the preceding companion paper. Baseline MRI characteristics were the same in all treatment groups. Fifty-two patients at one center formed a cohort for frequent MRIs (one every 6 weeks) for analysis of disease activity. The MRI results support the clinical results in showing a significant reduction in disease activity as measured by numbers of active scans (median 80% reduction, $p = 0.0082$) and appearance of new lesions. In addition, there was an equally significant reduction in MRI-detected burden of disease in the treatment as compared with placebo groups (mean group difference of 23%, $p = 0.001$). These results demonstrate that IFNB has made a significant impact on the natural history of MS in these patients.

NEUROLOGY 1993;43:662-667

Paty DW, Li DK (Neurology, 1993)

Does the drug treat MS?

- Disease severity = lesion volume
- Does the drug decrease lesion volume?
- Manual segmentation of lesions
  - One operator
- Decreased lesion area for placebo group in year 3!
  - What happened?

Table 3. Number of MRIs available and median change in total lesion area by MRI (mm^2) by treatment group

Time point	Measurement	Placebo	IFNB 1.6 MIU	IFNB 8 MIU
Baseline	Area	2,611	2,750	2,392
1 year	N	111	113	107
	Median change	152.5	45.2	–72.0
2 years	N	99	103	96
	Median change	305.1	142.0	–13.0
3 years (end point)	N	112	115	109
	Median change	198.7	0.0	–118.9

A consistently reproducible step change occurred in the areas measured during the third year. This reduction in area traced probably resulted from a conservative approach by the technician in tracing the margin of the lesions. Because the same step change occurred in all scans analyzed at the third year, it did not affect the intergroup differences, which continued to be highly significant statistically. This problem in consistency does, however, point out the difficulty of performing such a study over a number of years.

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  - Operator changed eyeglasses prescription

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Multi-spectral methods

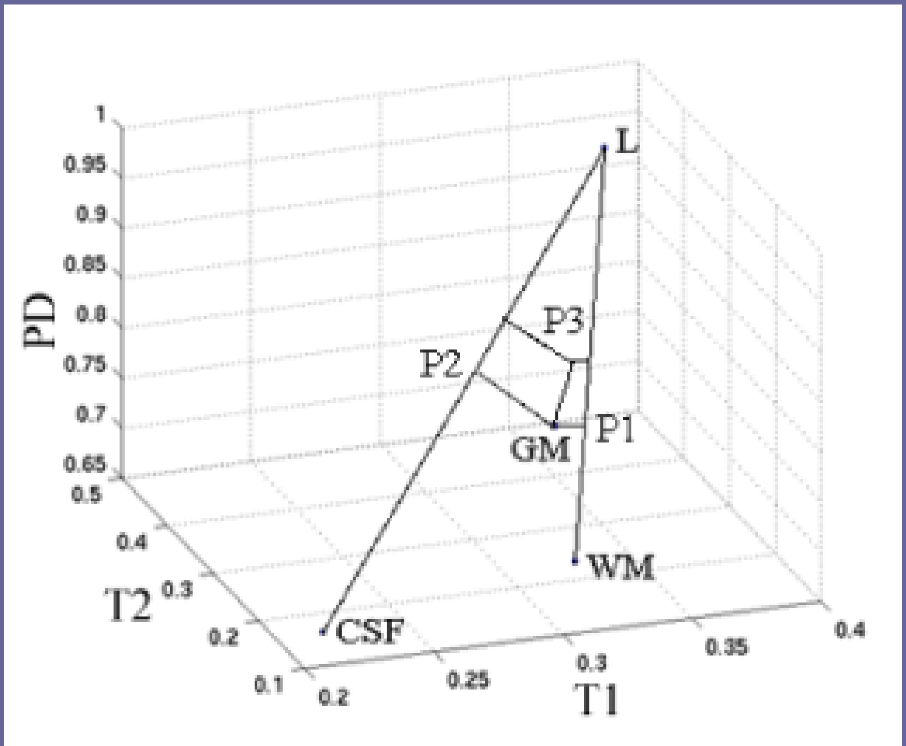
- In a gray scale image, pixels can differ in intensity (one dimension)
- Images can be acquired with more than one source of contrast
  - T_2-weighting
  - T_1-weighting
  - Proton density (M_0) weighting
- Intensity of two different tissues can differ in any or all of these images

Feature space

- The intensities can be thought of as coordinates in a multidimensional *feature* space
  - One dimension for each source of contrast
- Each pixel in the combined data set has a single position in the feature space
- Pixels in the same type of tissue *cluster* in feature space
- Sorting points into clusters is equivalent to segmentation

Multispectral segmentation

- Plot pixel as a position in (T_1-w,T_2-w,M_0-w) space
- Define 'training' points
- Use a statistical rule to decide class of unknown points



Pixel locations in feature space

Designing a segmentation-based clinical trial

- Imagine you have just been hired to run the analysis of a clinical trial for a drug that may improve cardiac contractility.
- The drug will be evaluated using MRI data from 1000 cardiac imaging exams over a year
- How would you carry out the analysis?

Study design decisions

www.teepublic.com

1. Accuracy vs. precision
   – Which is more important?
2. What sensitivity is required?
   – Sensitivity is expensive!
   – What is the minimum change you should be able to measure?
3. Choosing an analysis strategy is solving an optimization problem
   – What should be optimized?
4. Analysis strategy
5. What are the costs involved in your strategy?
6. Is a negative result something to avoid?

Summary

- Segmentation divides an image into discrete, relatively homogeneous regions
- There are several classes of strategies for automatically (numerically) segmenting an image
  - The best strategy will depend on the properties of the image
- Common applications are segmenting structures in the nervous and cardiovascular systems
- Segmentation is often the first step in
  - Localization
  - Visualization
  - Volumetrics
  - Studying effects of disease

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- A.M. Dale, B. Fischl, and M.I. Sereno. Cortical Surface-Based Analysis I: Segmentation and Surface Reconstruction. NeuroImage 9: 179-194 (1999).
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