



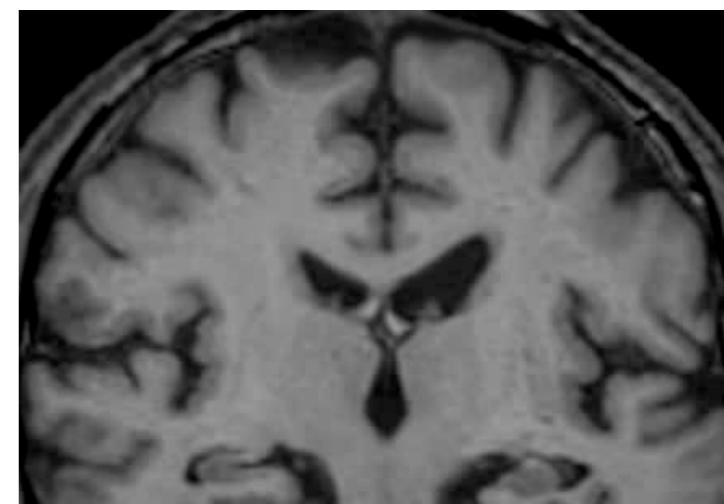
Centre for Medical Image Computing  
Centre for Medical Image Computing

# Information Processing for Medical Imaging

***IPMI Module - MPHYGB06***

*Marc Modat - [m.modat@ucl.ac.uk](mailto:m.modat@ucl.ac.uk)*

**University College London**



# Centre for Medical Image Computing

- ~ 50 post docs & 50 PhD students



- Healthcare
  - Screening
  - Diagnosis
  - Guiding and monitoring therapy
- Pharmaceutical Industry
  - Imaging biomarkers
- Medical Research
  - Neurology
  - Oncology
  - Cardiology

Image acquisition  
Image reconstruction  
Image segmentation  
Image registration/fusion  
Image guided interventions  
Atlas generation  
Group statistics  
Biological function  
Modelling  
Shape  
Biomechanics  
Motion  
Biological function  
Classification

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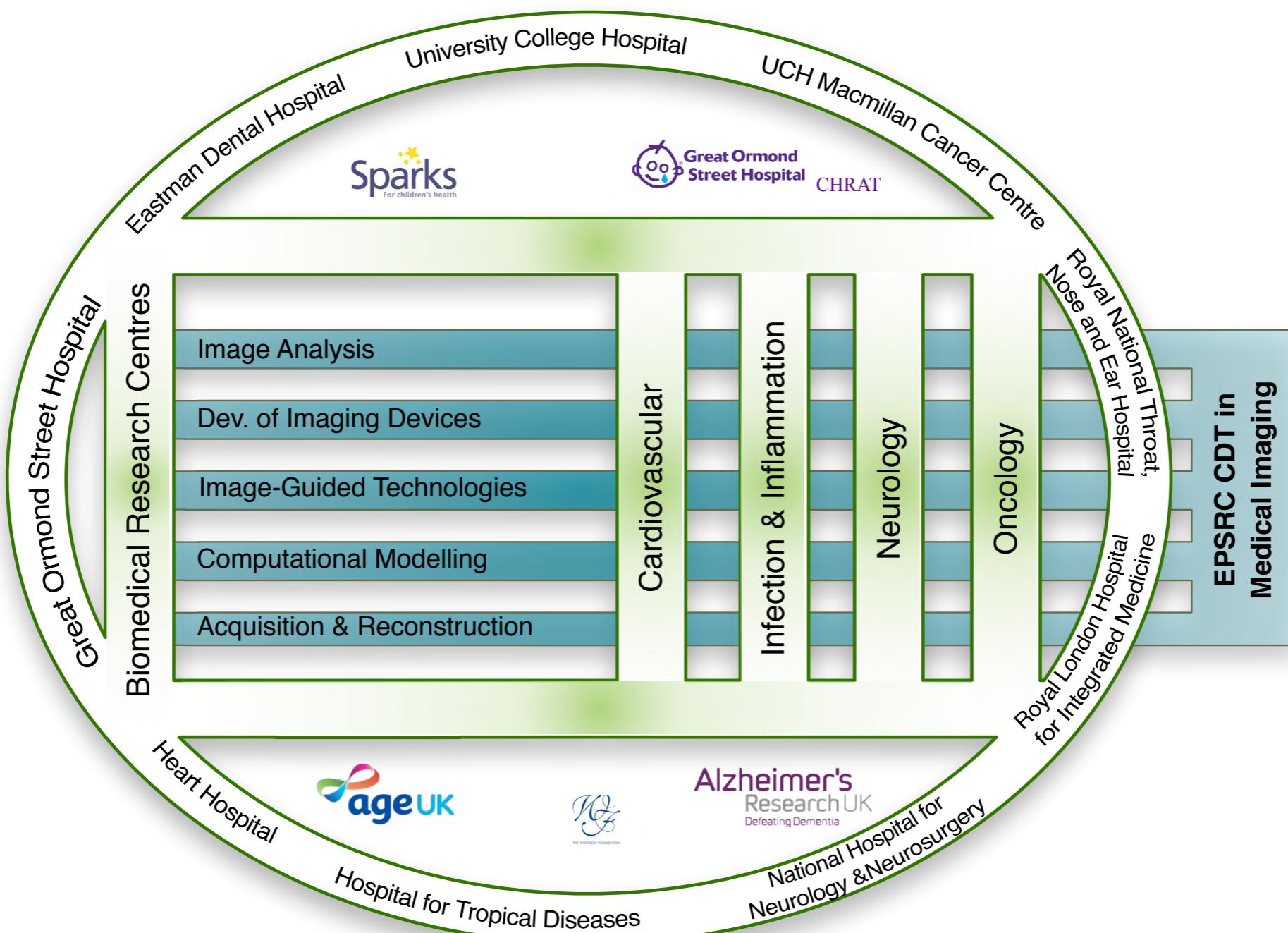
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Doctoral Training in  
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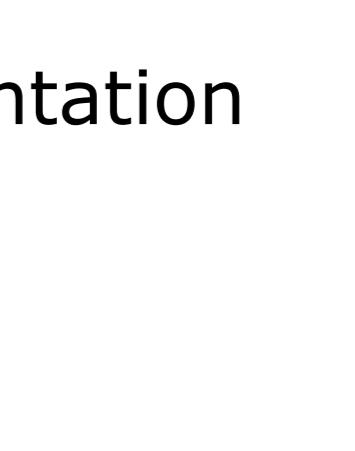
## EPSRC Centre for Doctoral Training in Medical Imaging



Our vision is to train the translational imaging research leaders of the future, filling a critical gap identified in academia, pharmaceutical and medical devices industries, while delivering internationally competitive research. Our innovative training has a strong focus on new image acquisition technologies, novel data analysis methods and integration with computational modelling.



# Structure of the module

- Lecturers
  - Maria A Zuluaga (statistical shape modelling)  
[maria.zuluaga@ucl.ac.uk](mailto:maria.zuluaga@ucl.ac.uk)
  - M Jorge Cardoso (segmentation)  
[m.jorge.cardoso@ucl.ac.uk](mailto:m.jorge.cardoso@ucl.ac.uk)
  - Marc Modat (registration)  
[m.modat@ucl.ac.uk](mailto:m.modat@ucl.ac.uk)
- Assessment
  - 50% Coursework
    - Python code + report
    - Combining medical image registration and segmentation
  - 50% Sat Exam

# Structure of the MPHYGB06 module

- Thursday 15th January
  - 10:00 - 13:00 - Module introduction and Medical Image Registration I (Marc Modat)  
Engineering Front Suite 104
- Thursday 22nd January
  - 10:00 - 13:00 - Medical Image Registration II (Marc Modat)  
Wilkins Gustave Tuck LT
  - 14:00 - 17:00 - Workshop - Medical Image Registration I (Marc Modat)  
Malet Place Eng. 105
- Thursday 29th January
  - 10:00 - 13:00 - Statistical Shape Model (Maria A. Zuluaga)  
Chadwick G08
  - 14:00 - 17:00 - Workshop - Simple ITK (Maria A. Zuluaga)  
Malet Place Eng. 105

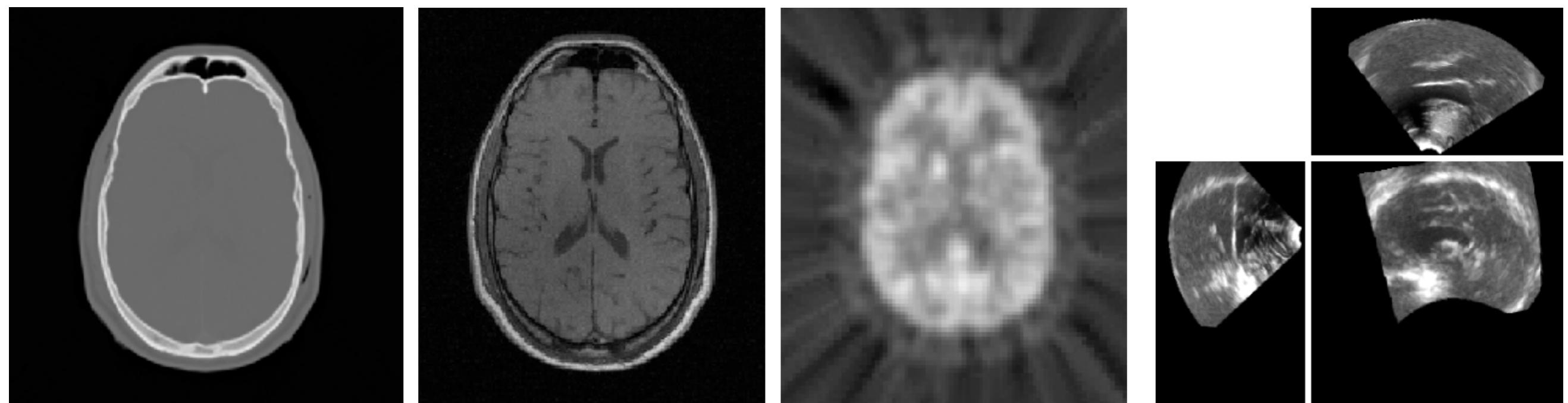
# Structure of the MPHYGB06 module

- Thursday 5th February
  - 10:00 - 13:00 - Medical Image Segmentation I (M. Jorge Cardoso)  
Engineering Front Suite 104
  - 14:00 - 17:00 - Workshop - Medical Image Segmentation I  
(M. Jorge Cardoso)  
Malet Place Eng. 105
- Thursday 12th February
  - 10:00 - 13:00 - Medical Image Segmentation II (M. Jorge Cardoso)  
Engineering Front Suite 104
  - 14:00 - 17:00 - Workshop - Medical Image Segmentation II  
(M. Jorge Cardoso)  
Malet Place Eng. 105
- Thursday 19th February
  - 10:00 - 13:00 - Medical Image Registration III (Marc Modat)  
Engineering Front Suite 104
  - 14:00 - 17:00 - Workshop - Medical Image Registration II (Marc Modat)  
Malet Place Eng 1.04

# Different imaging modalities

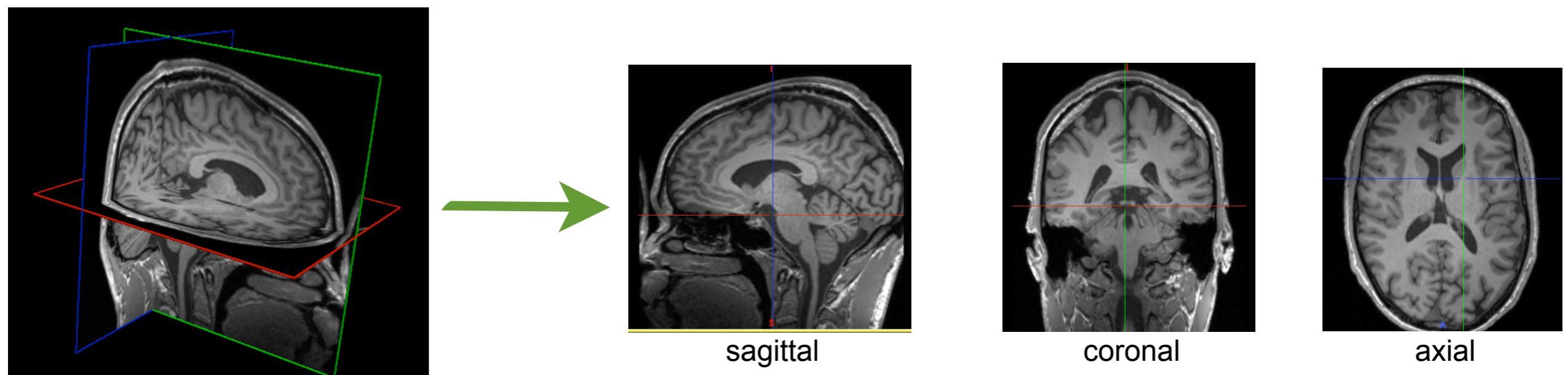
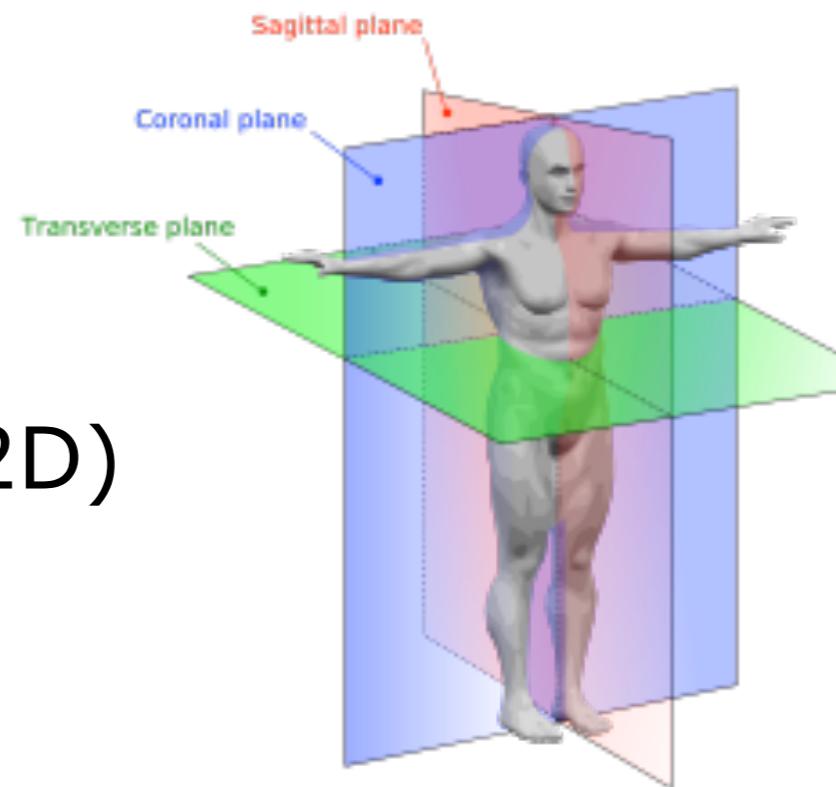
- Some imaging examples
  - 2D and 3D X-ray imaging
  - Micro-CT imaging
  - MRI imaging at 1.5T, 3T and 7T
  - Diffusion imaging
  - Functional MRI
  - Ultrasound imaging
  - PET imaging in dementia and oncology

# Different imaging modalities



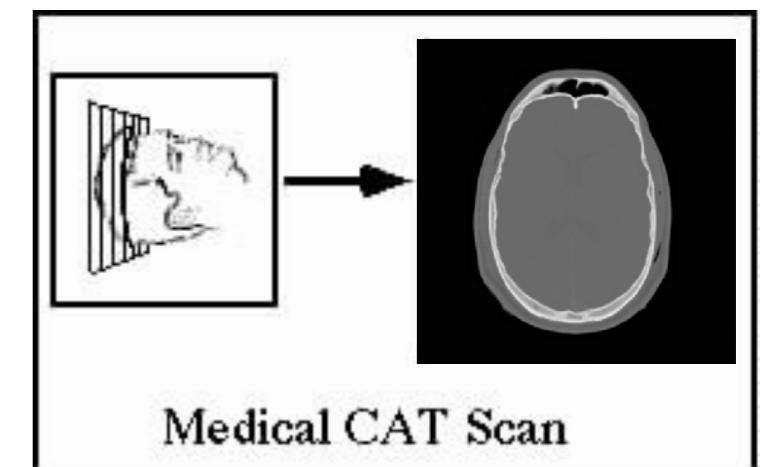
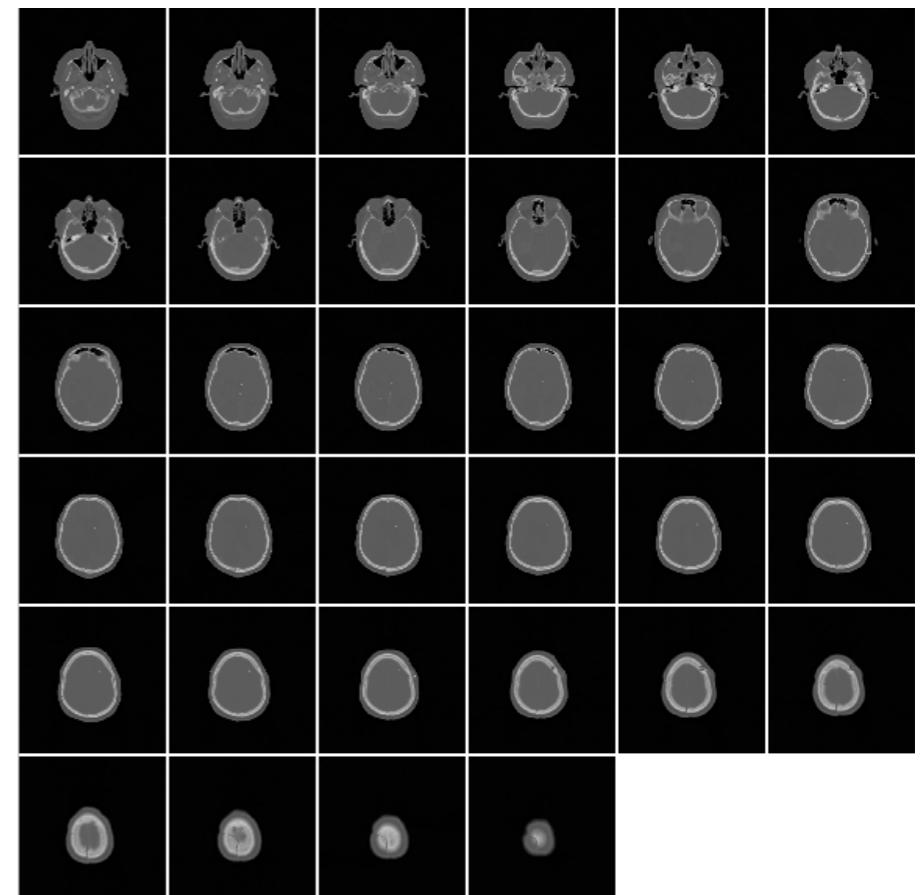
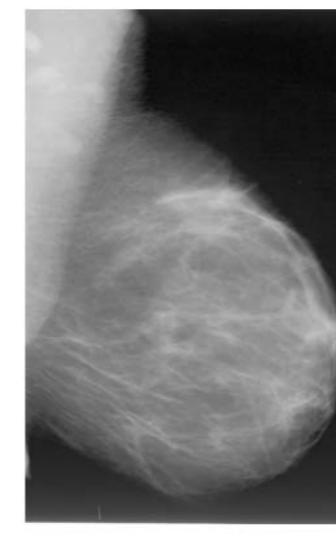
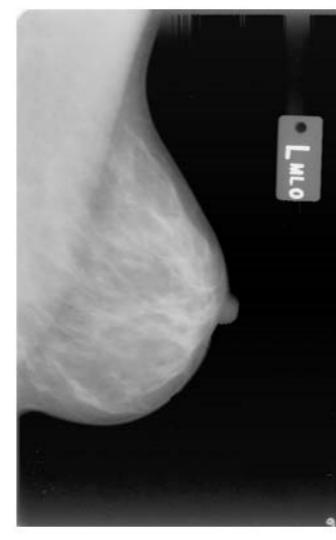
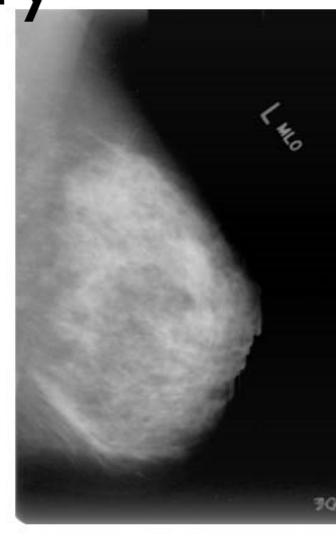
# Medical imaging is mainly in 2D, 3D, 4D...

- We will talk about voxel in 3D (pixel in 2D)

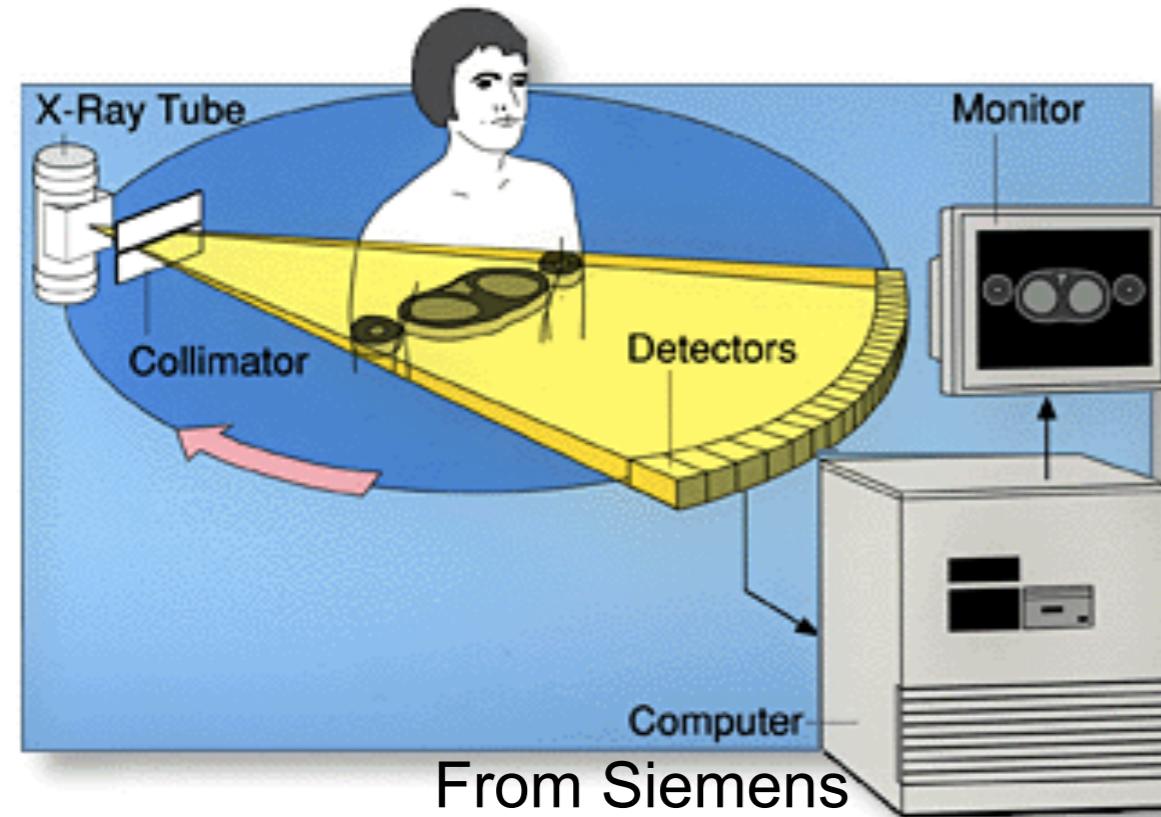


# X-rays

- A beam of high energy electrons crashes into a metal target and x-rays are produced.
- Can traverse the body along straight lines
- Are attenuated by the different tissues
- Be detected and measured outside of the body



# X-ray Computed tomography



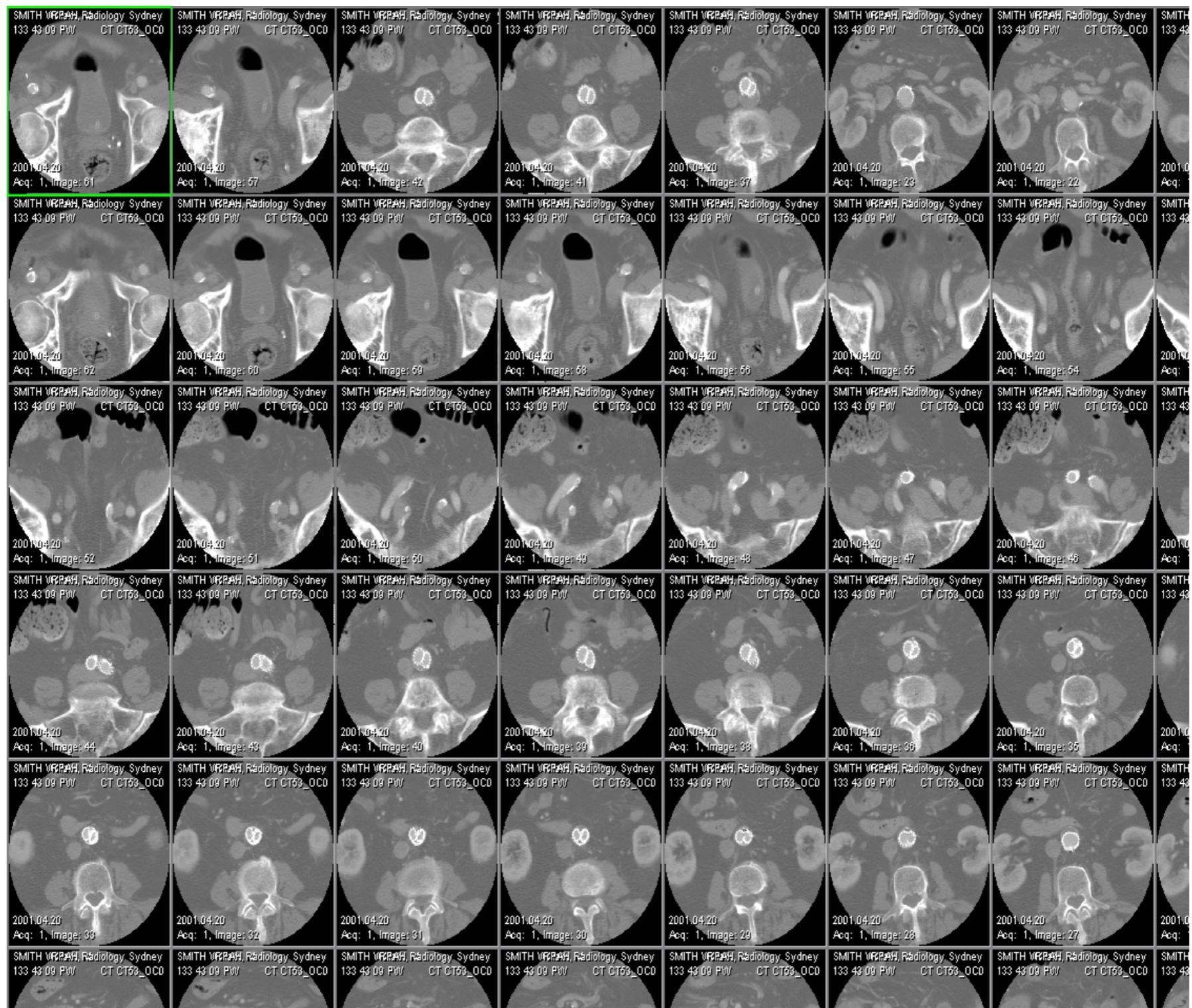
<https://www.youtube.com/watch?v=2CWpZKuy-NE>



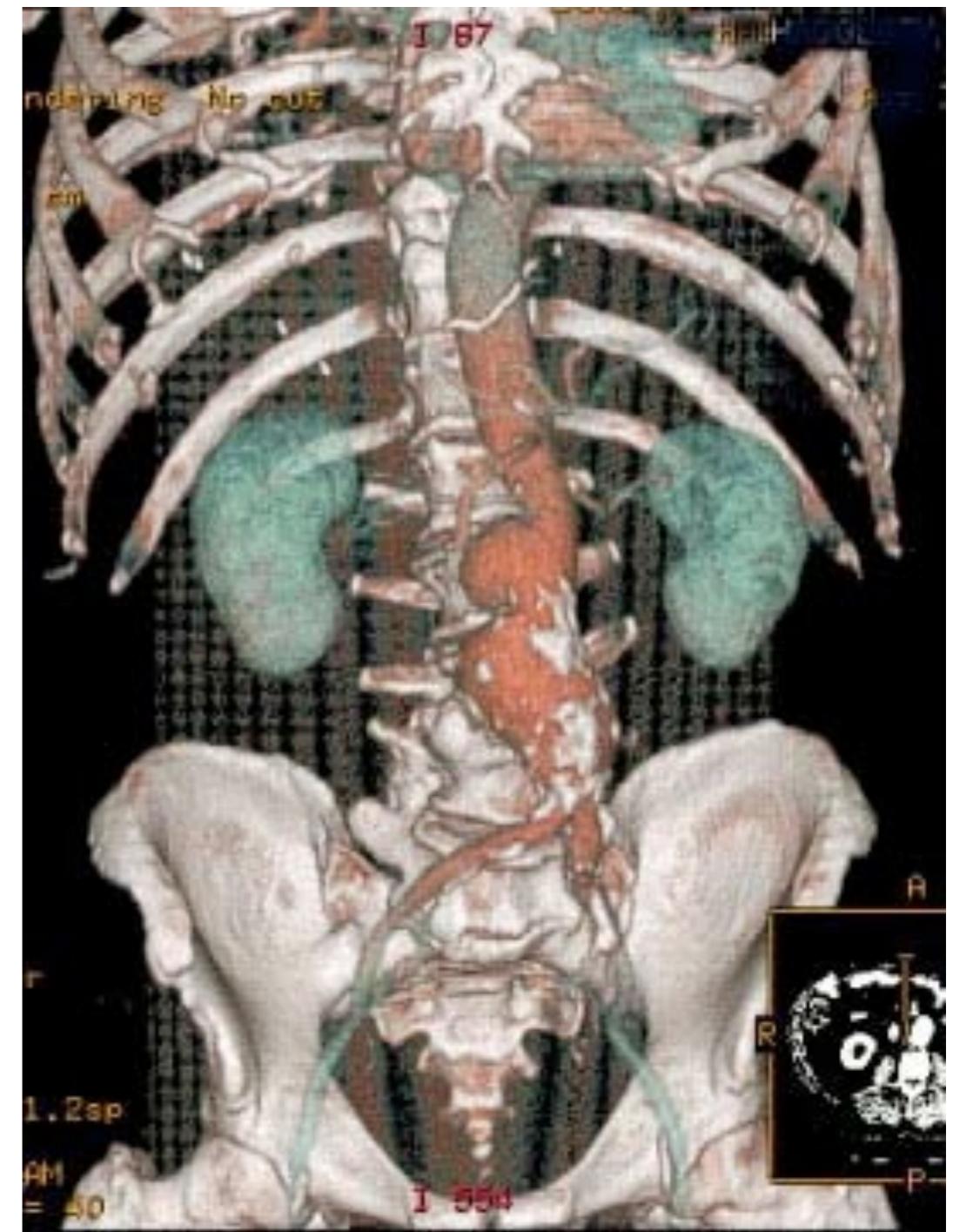
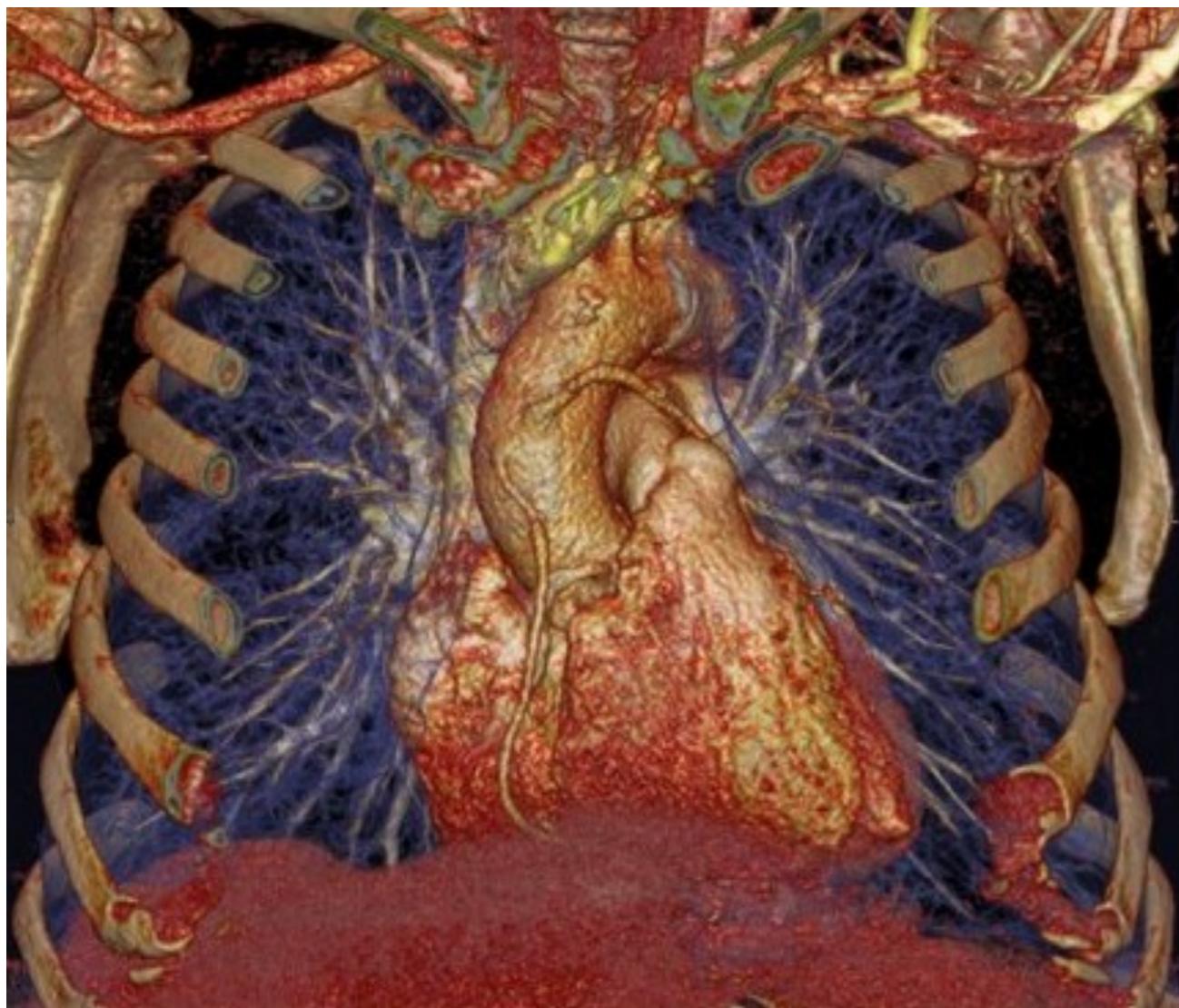
## Nobel prizes:

Roentgen (1901): Discovery of X-rays  
Hounsfield & Cormack (1979): Computed Tomography

# X-ray Computed tomography

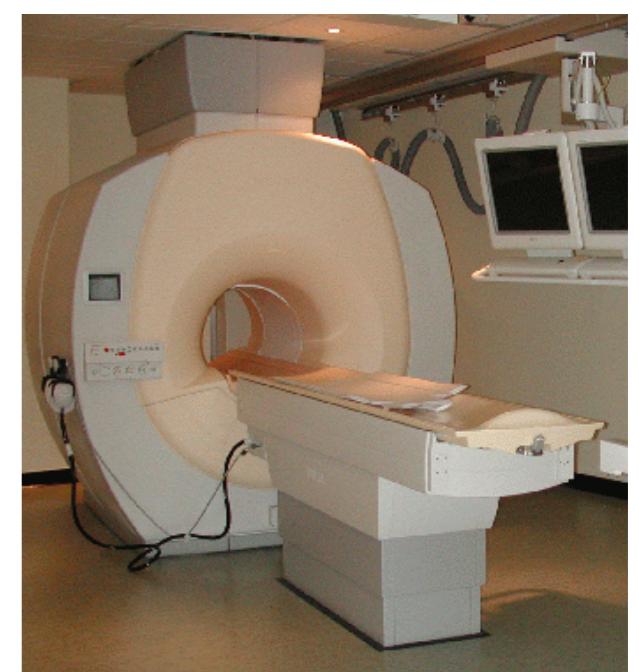
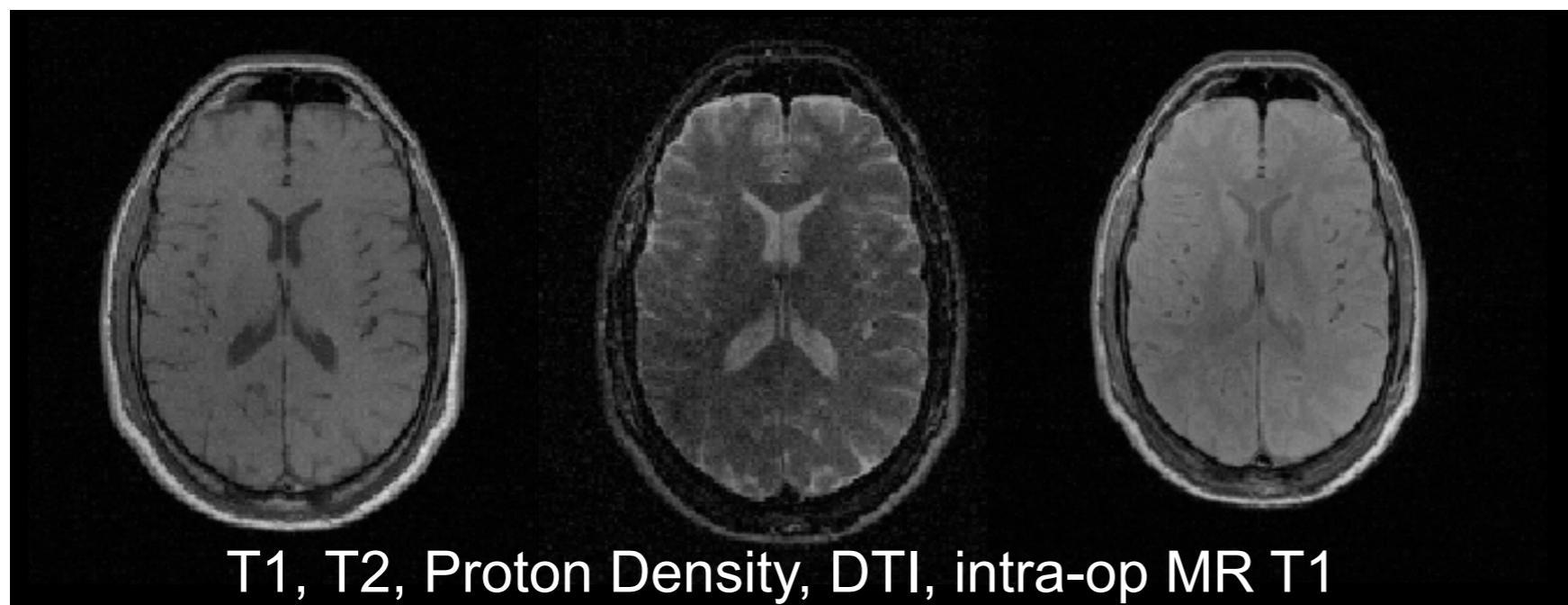


# X-ray Computed tomography

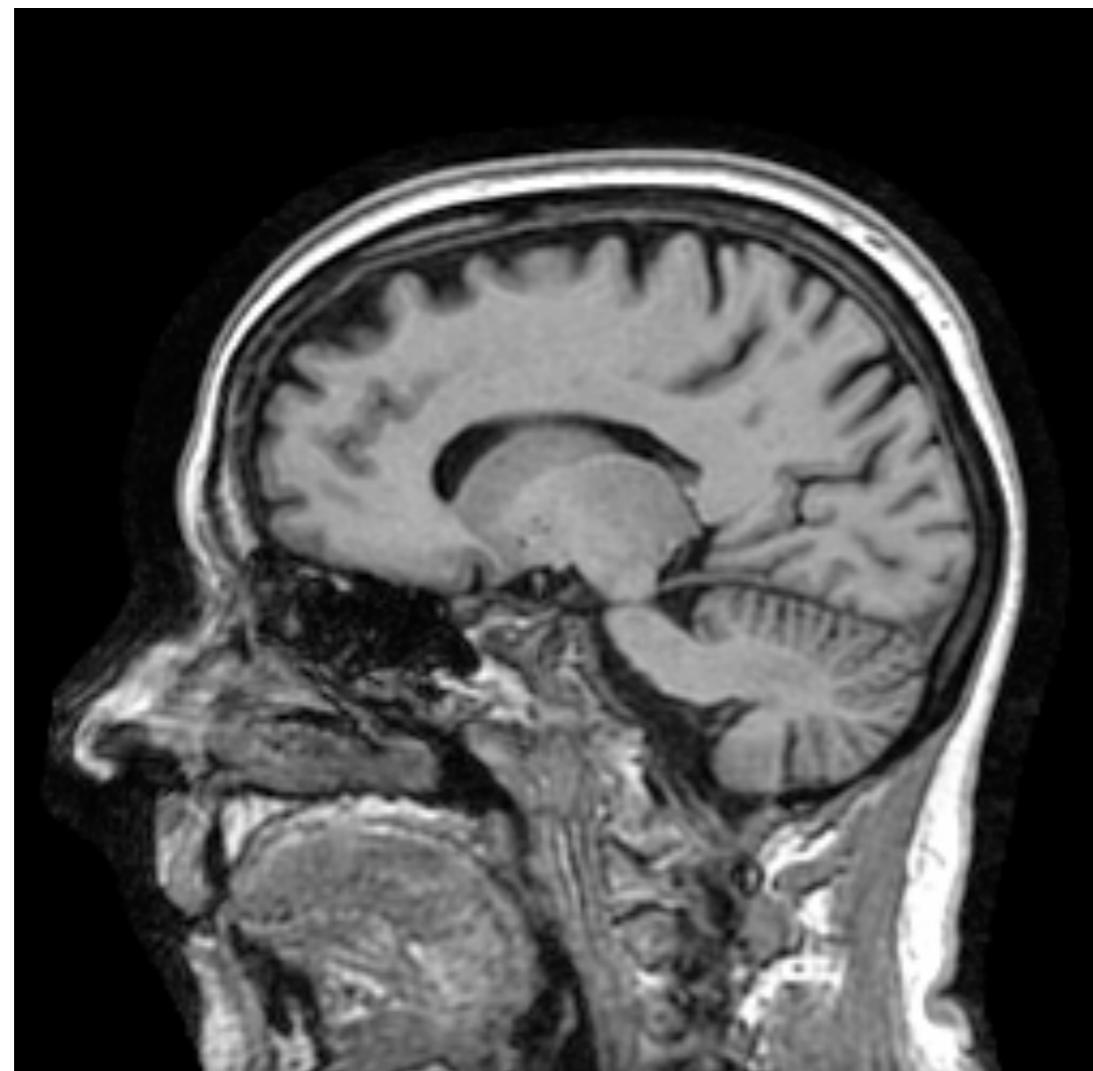


# Magnetic Resonance Imaging (MRI)

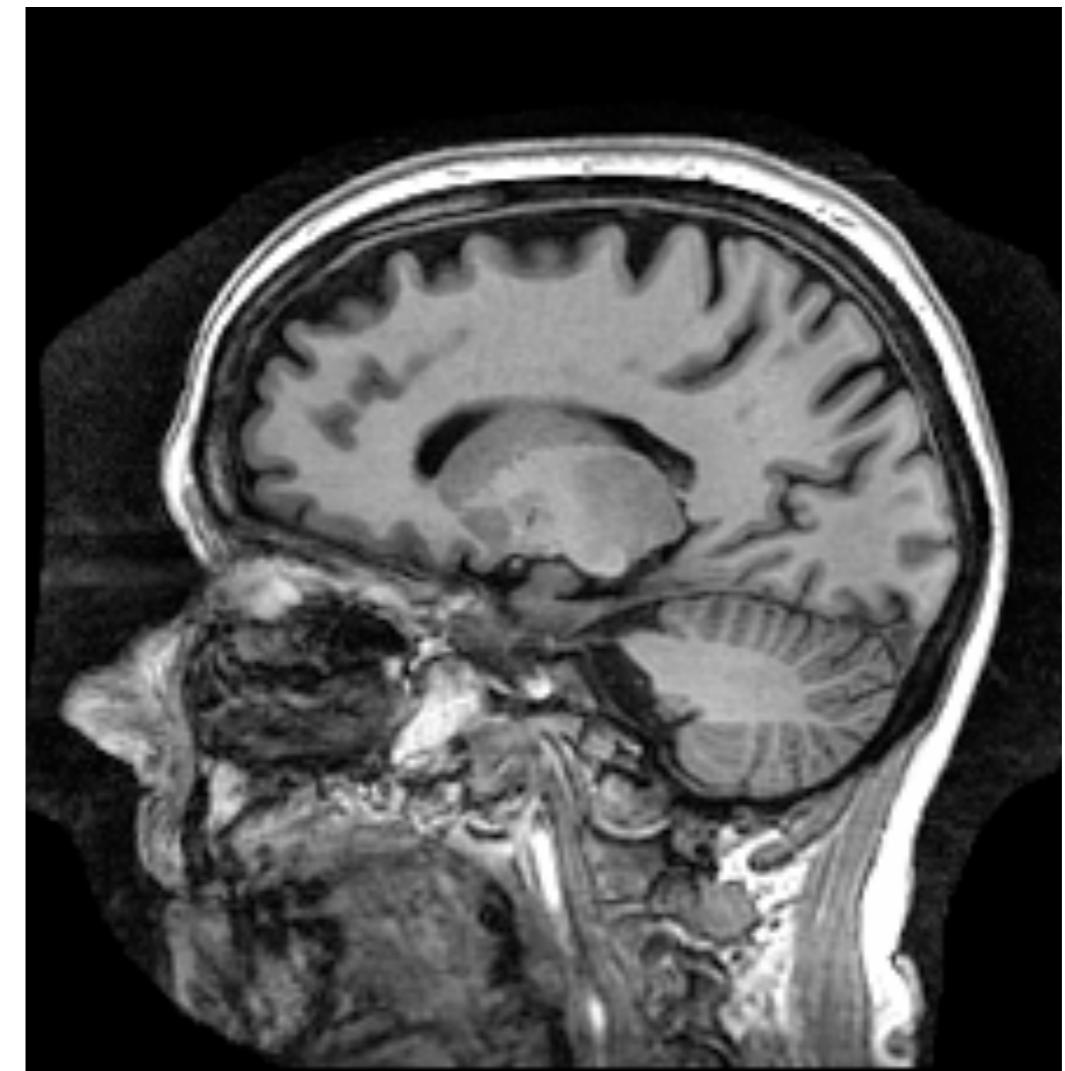
- Based on imaging nuclear spins.
- Excellent soft tissue contrast.
- Non-ionising. Gd contrast is usually safe.
- Image in planes/volumes with any orientation.
- Images often arbitrarily scaled, intensity fluctuations and geometrical distortions.
- low: motion / limited SNR.



# Magnetic Resonance Imaging (MRI)



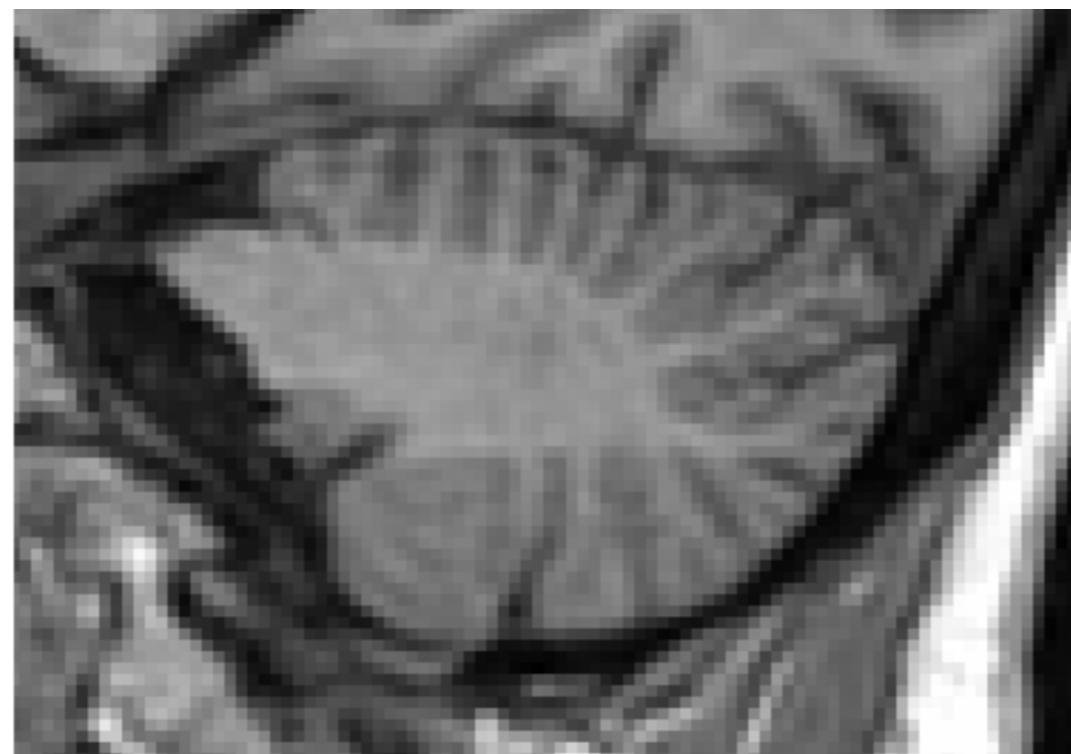
1.5 Tesla  
 $0.94 \times 0.94 \times 1.2$



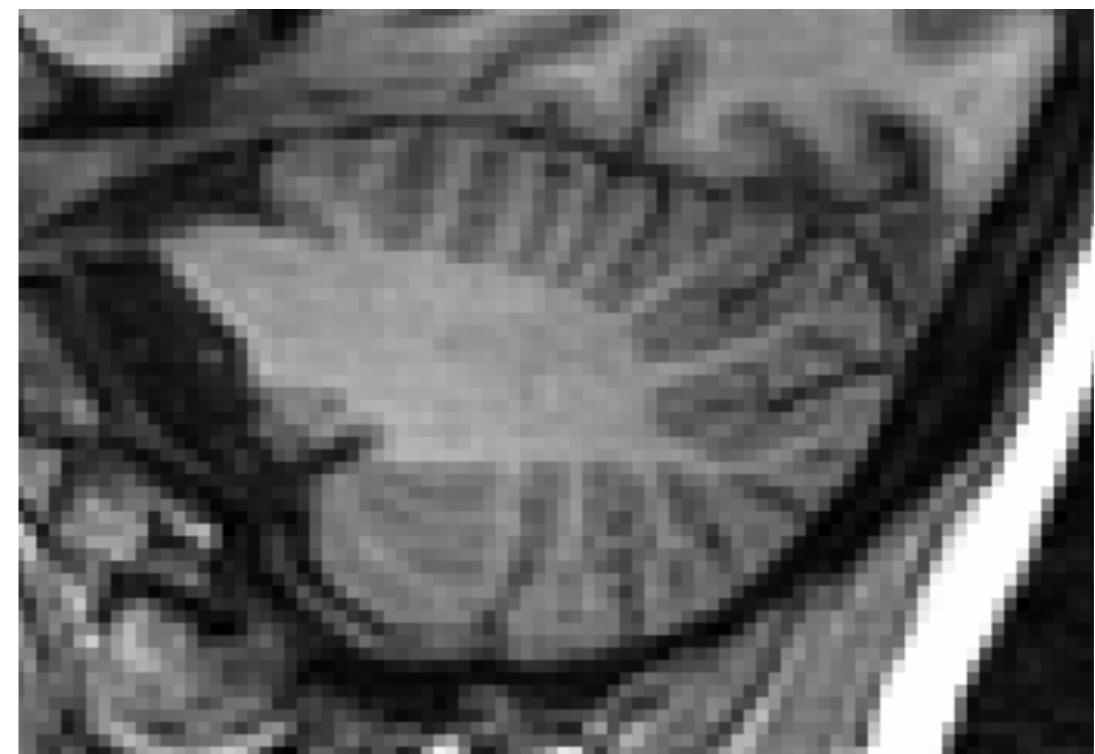
3 Tesla  
 $1.02 \times 1.02 \times 1.2$

*Images from the ADNI database*

# Magnetic Resonance Imaging (MRI)



1.5 Tesla  
 $0.94 \times 0.94 \times 1.2$

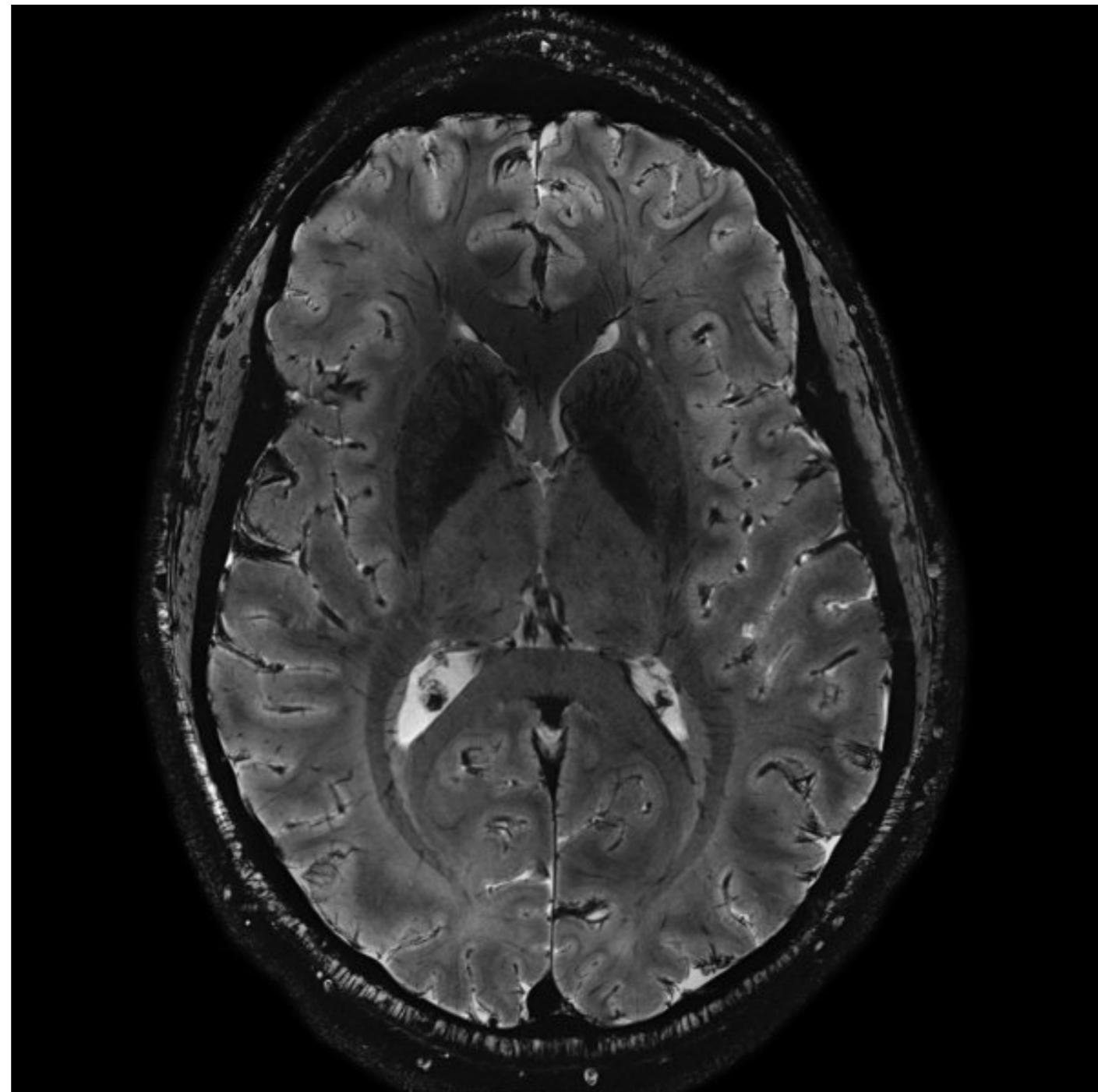


3 Tesla  
 $1.02 \times 1.02 \times 1.2$

*Images from the ADNI database*

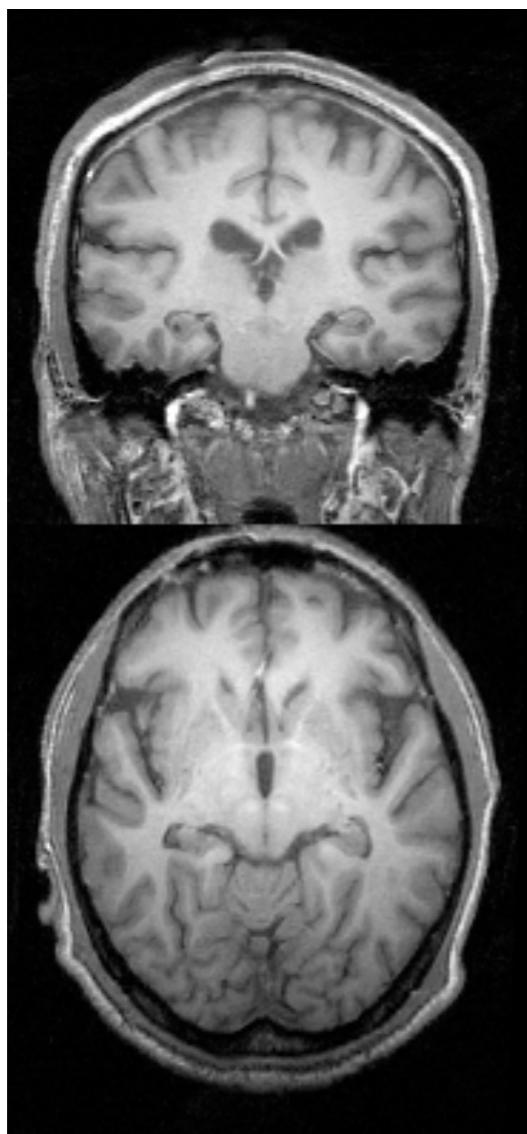
# Magnetic Resonance Imaging (MRI)

- 7T

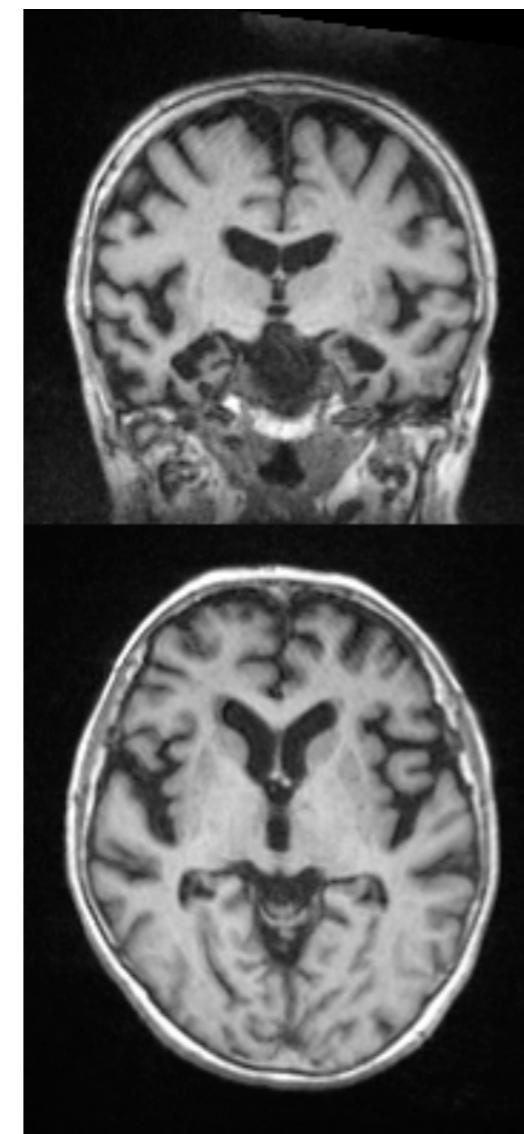


# Magnetic Resonance Imaging (MRI)

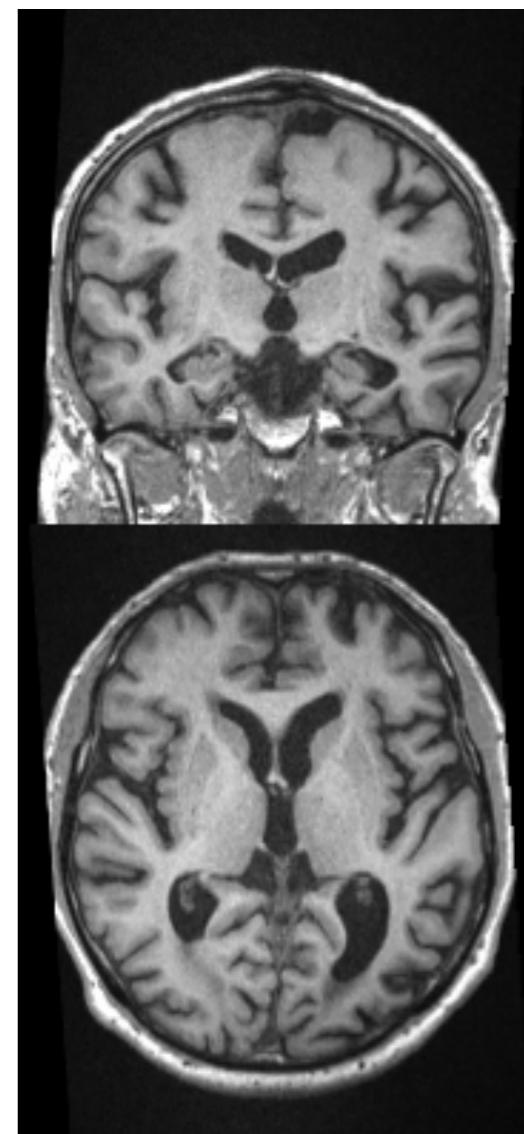
- Structural changes



Normal  
Control



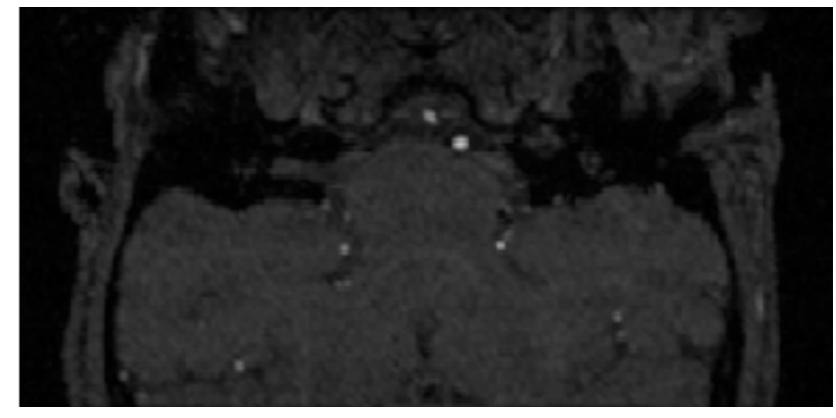
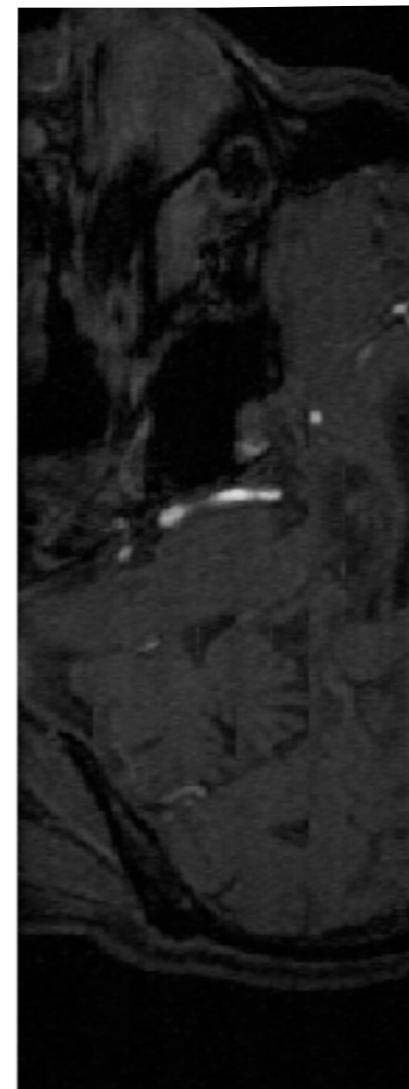
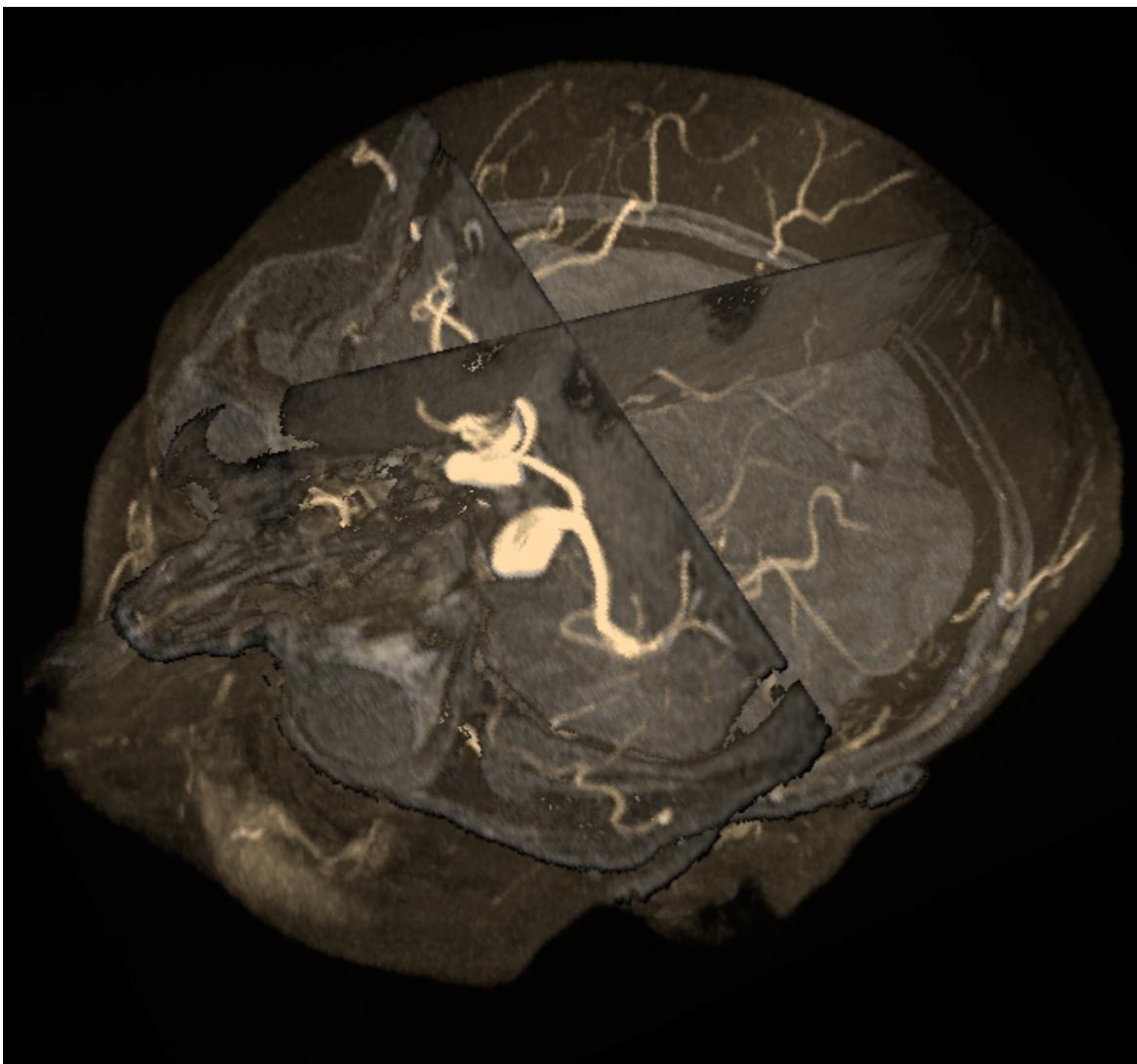
Mild Cognitive  
Impairment



Alzheimer's  
disease

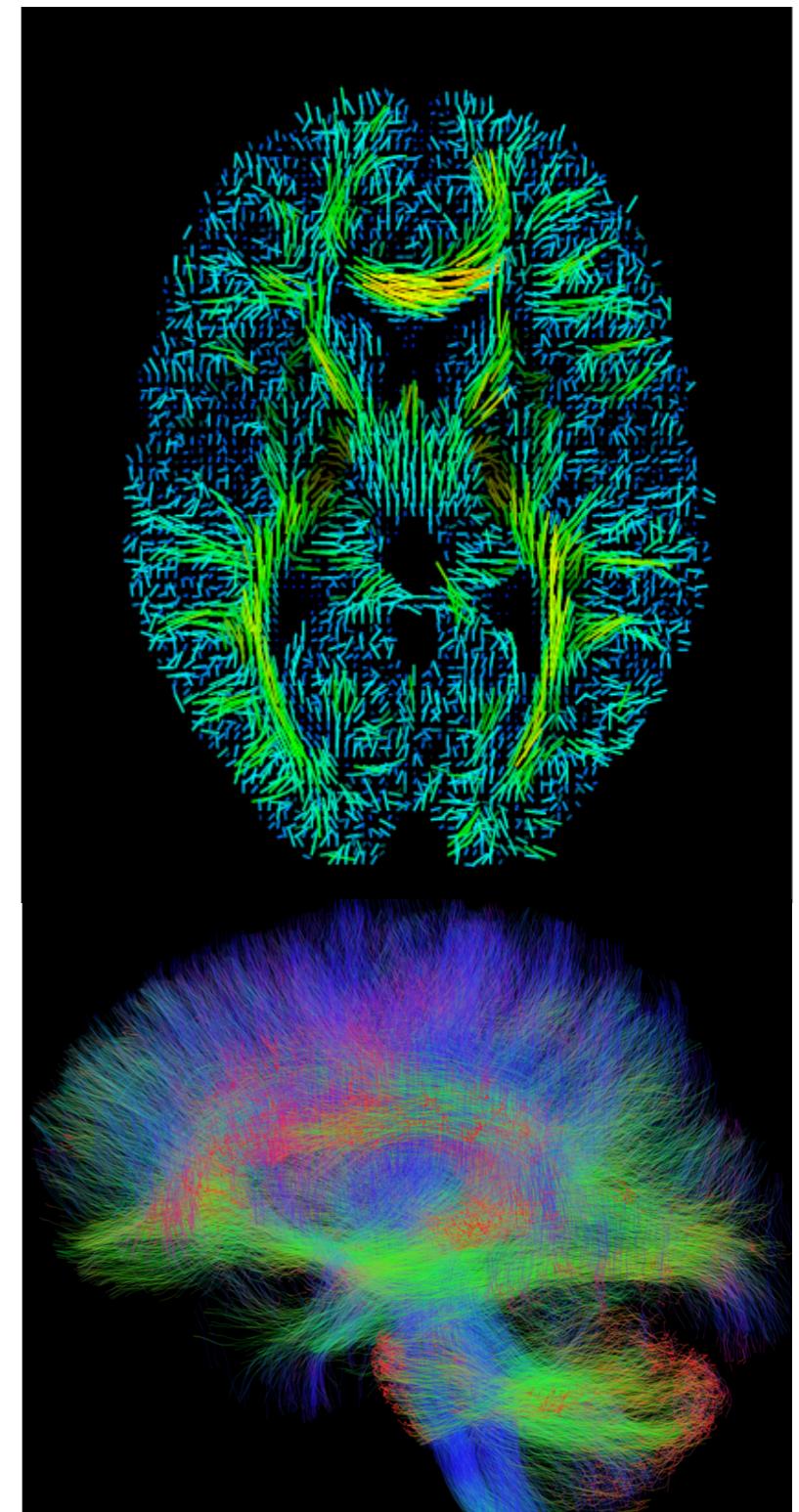
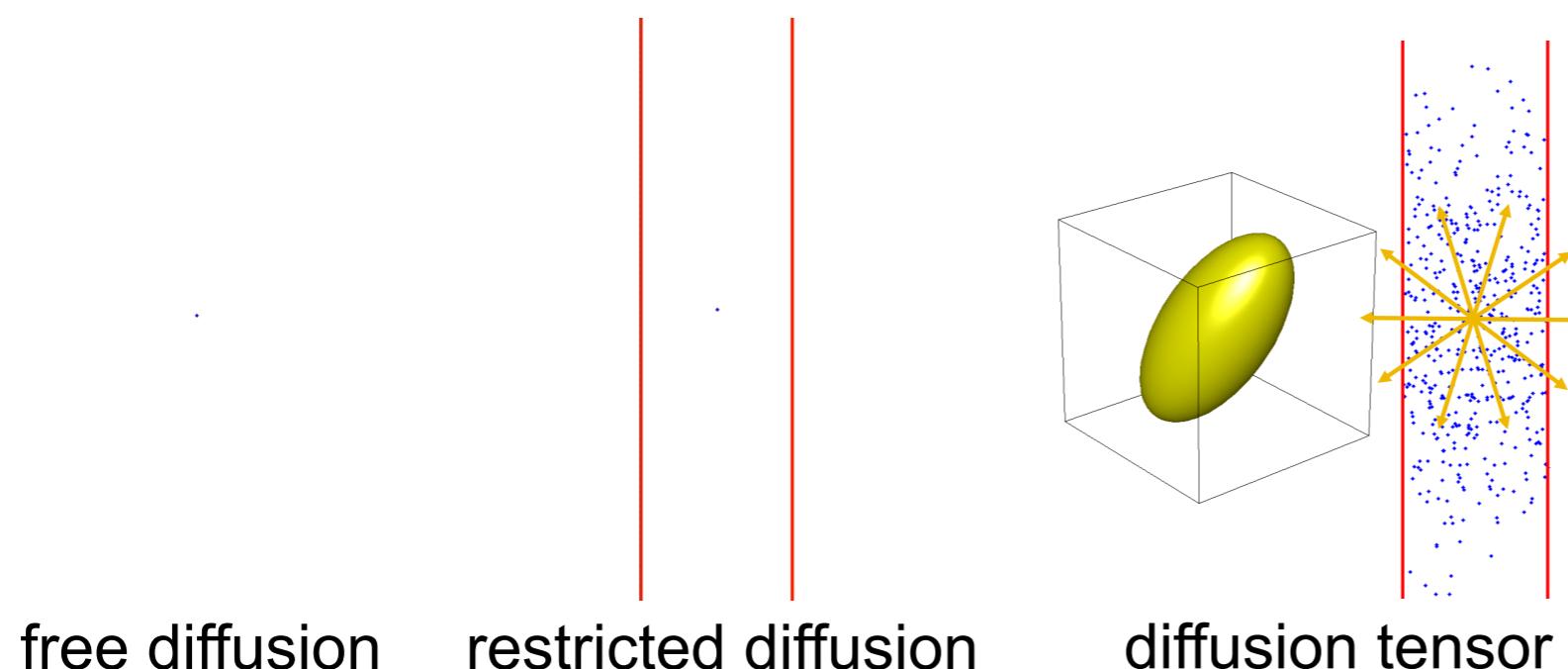
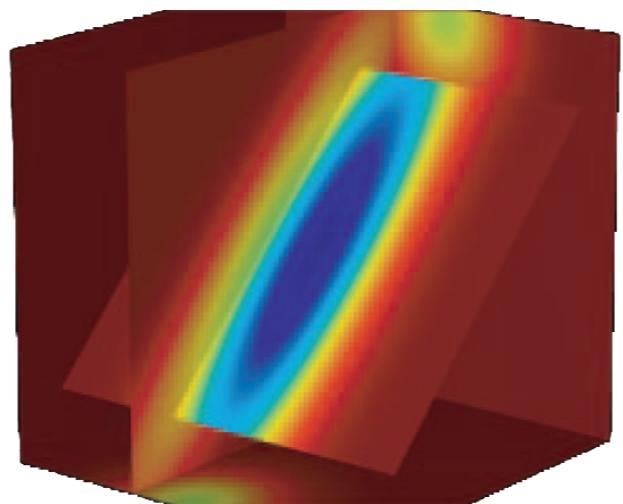
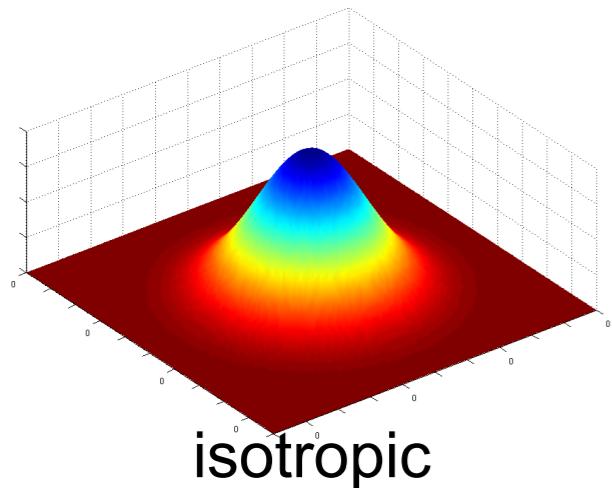
# Magnetic Resonance Imaging (MRI)

- Angiography



# Magnetic Resonance Imaging (MRI)

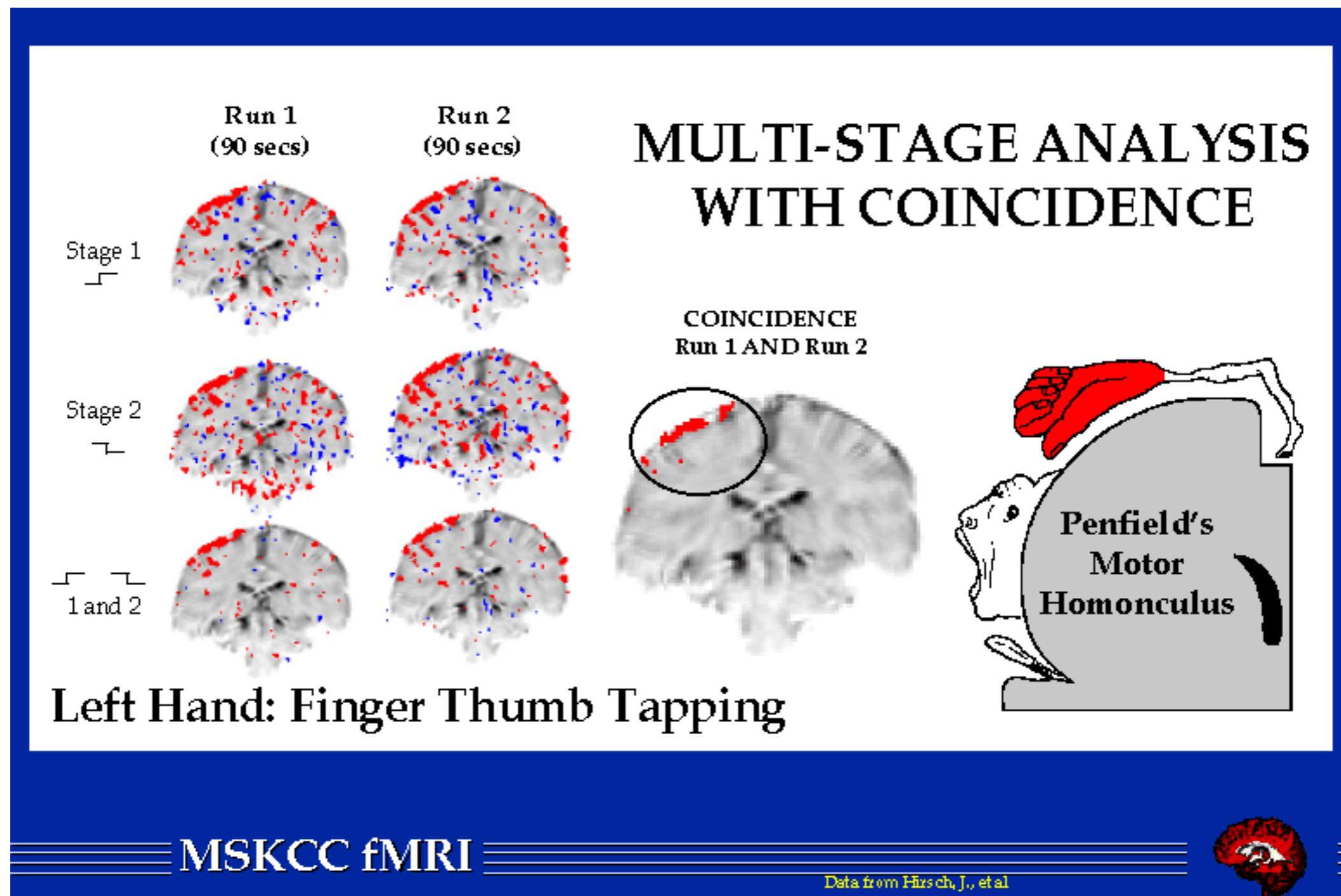
- Diffusion Imaging



# Magnetic Resonance Imaging (MRI)

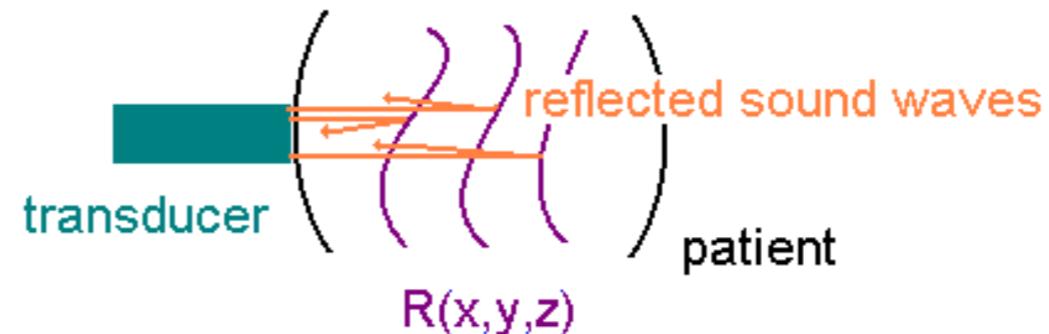
- Functional MRI (fMRI), based on:
  - Mapping changes in brain hemodynamic
  - Movement and flow
  - Blood oxygen level dependant signal: mental operations
- Identification and mapping of brain activity is critical:
  - Brain understanding (cognitive science)
  - Neurodegenerative disease understanding
  - Neurosurgery application
- It does not require injection of radioactive isotopes

# Magnetic Resonance Imaging (MRI)



# Ultrasound Imaging (US)

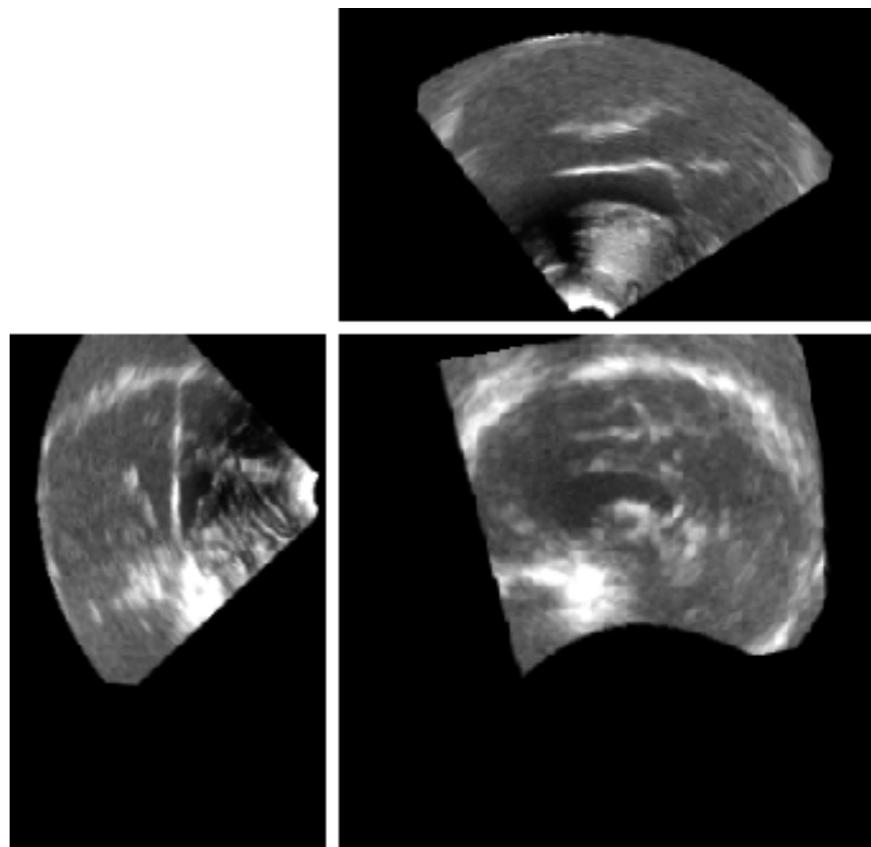
- Image based on:
  - Reflected waves
  - Tissue composition
  - Movement and flow



- A pulse is propagated and its reflection is received, both by the transducer
- Key assumption:
  - Sound waves have a nearly constant velocity of ~1500 m/s in H<sub>2</sub>O
  - Sound wave velocity in H<sub>2</sub>O is similar to that in soft tissue
  - Thus, echo time maps to depth

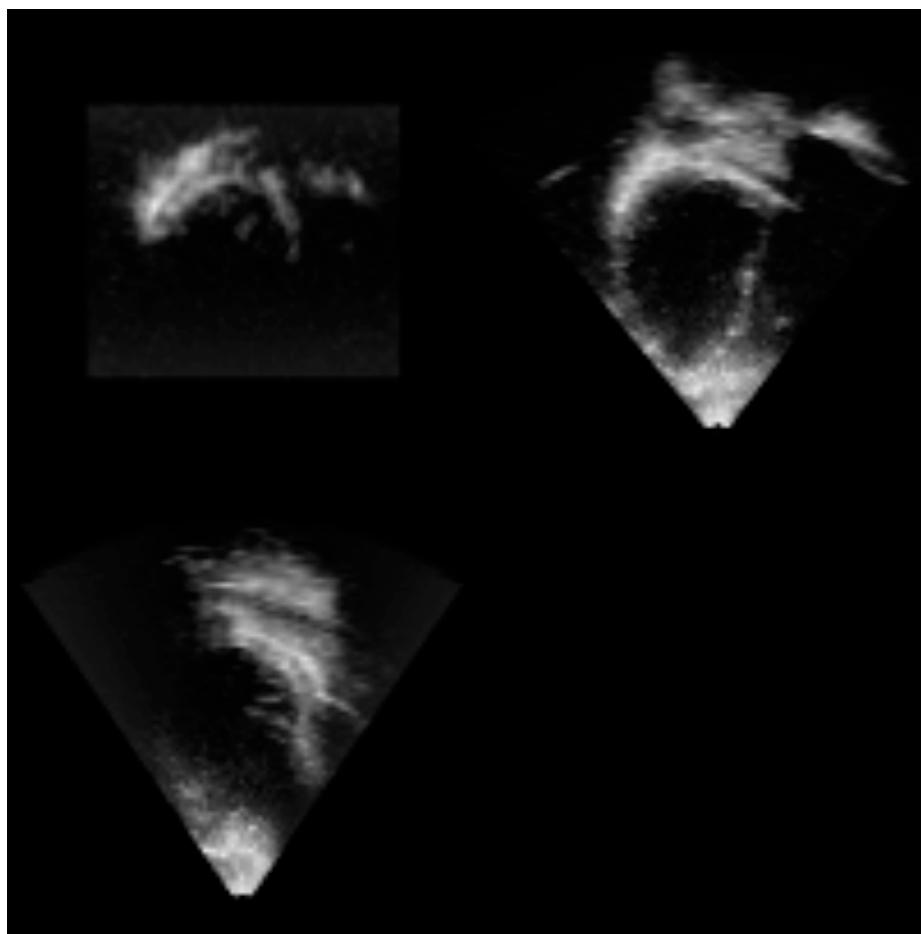
# Ultrasound Imaging (US)

- Advantages:
  - Cheap, safe, portable “bed side”, compact
  - Real-time imaging
- Weaknesses:
  - Images very operator dependent
  - Does not penetrate bone
  - Limited viewing angles
  - Image quality issues

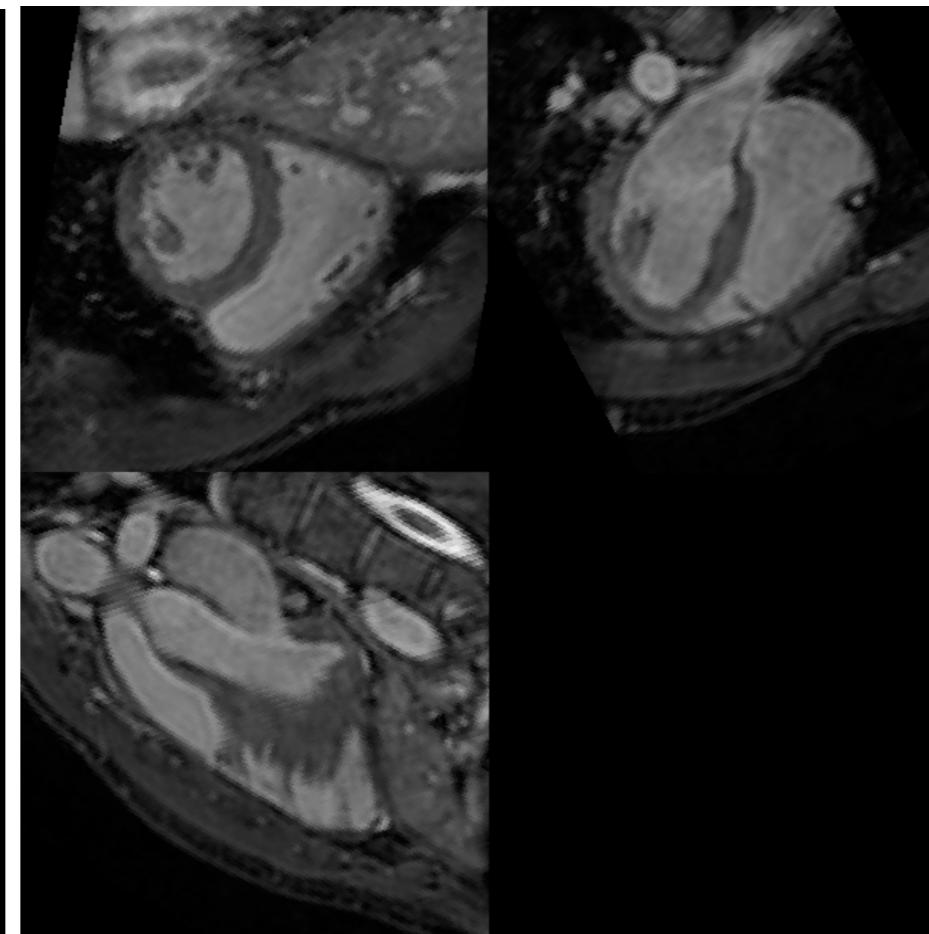


# Ultrasound Imaging (US)

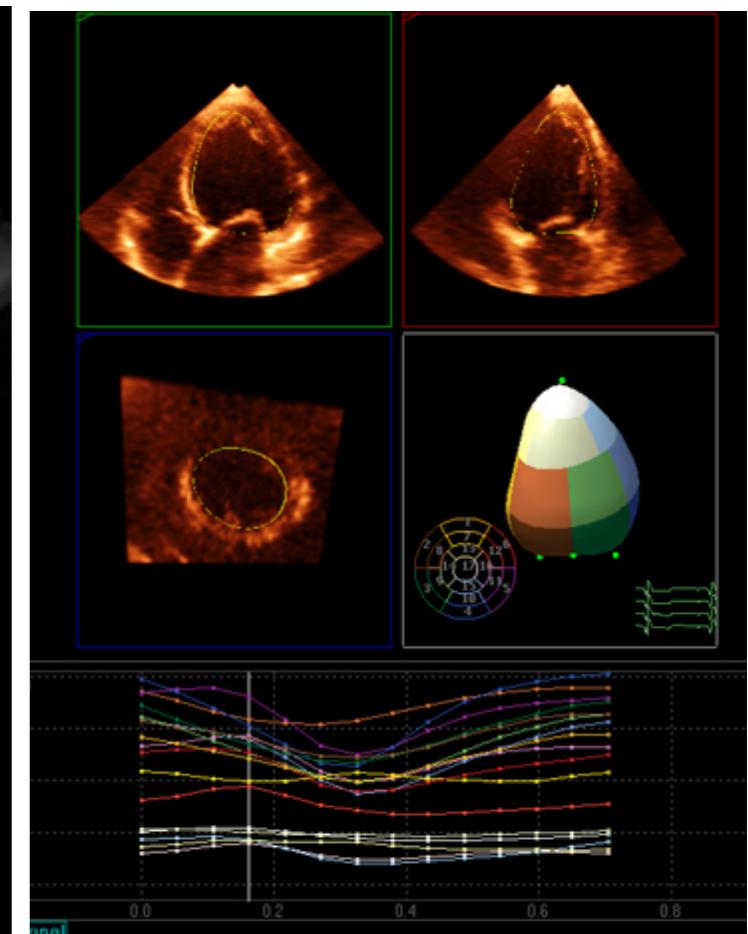
- Heart imaging example



3D ultrasound of the heart



MRI of the heart

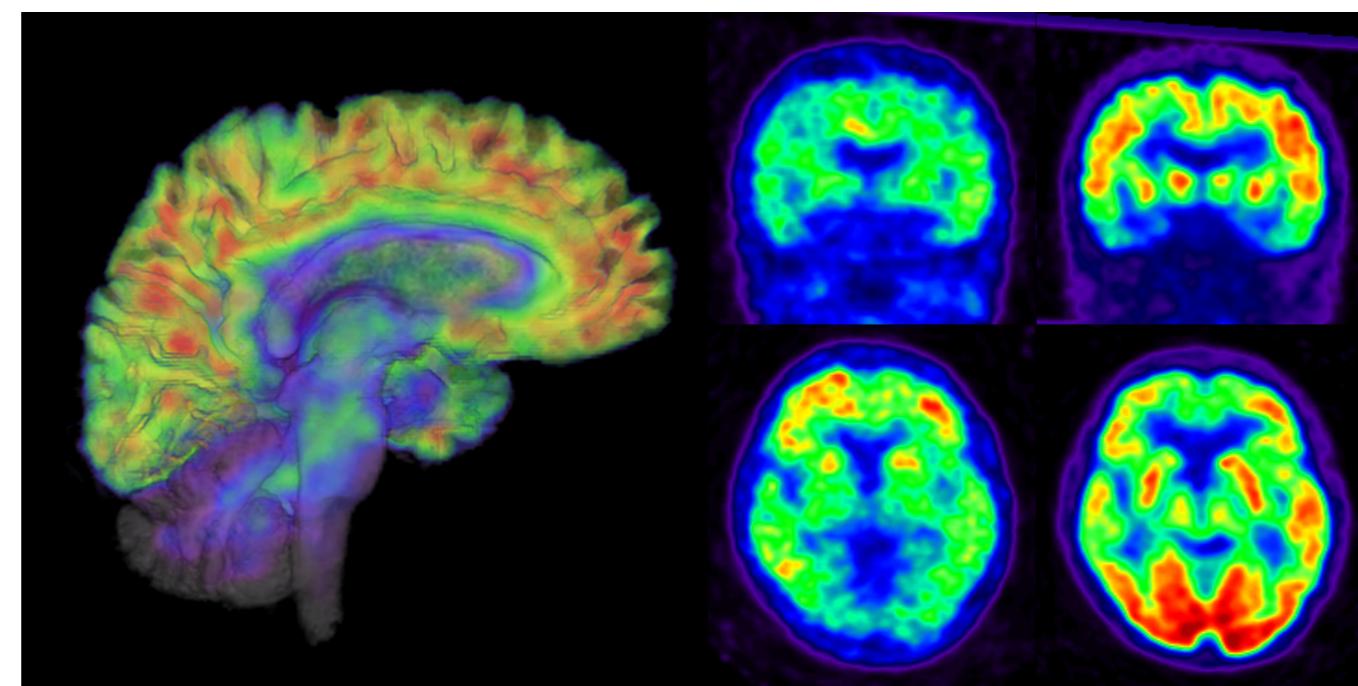


4D heart analysis

# Positron Emission Tomography (PET)

- Image based on:
  - Radioactive isotope attached to metabolic marker (injected tracer: radionuclide)
  - Gamma radiation
  - Tissue biochemistry

Each patient is given a minute amount of a radioactive pharmaceutical that closely resembles a natural substance used by the body.

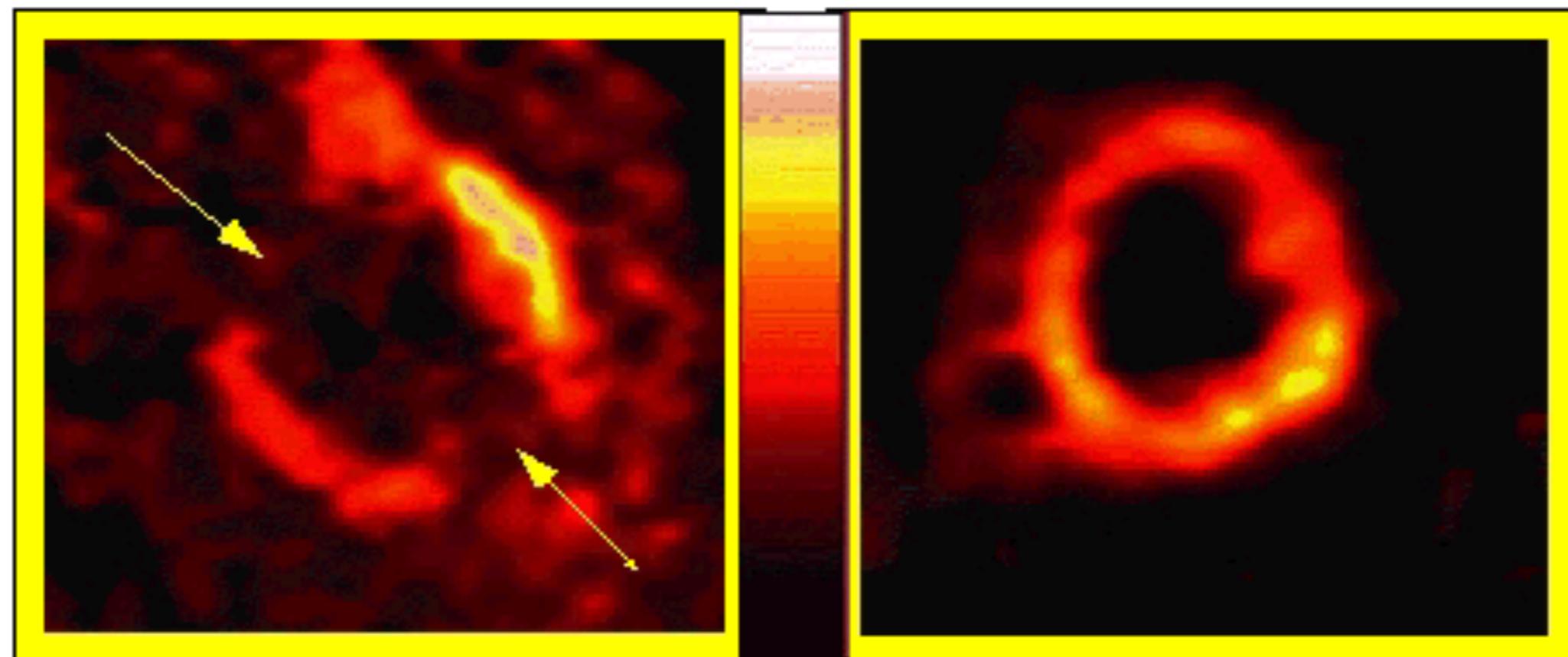


# Positron Emission Tomography (PET)

- Tracer (FDG) concentrates in areas with increased glucose metabolism
- Non specific uptake also seen in the kidneys, bladder, liver
- PET imaging can also show the region of the brain that is causing a patient's seizures
- Useful in evaluating degenerative brain diseases such as Alzheimer's, Huntington's, and Parkinson's

# Positron Emission Tomography (PET)

- Example

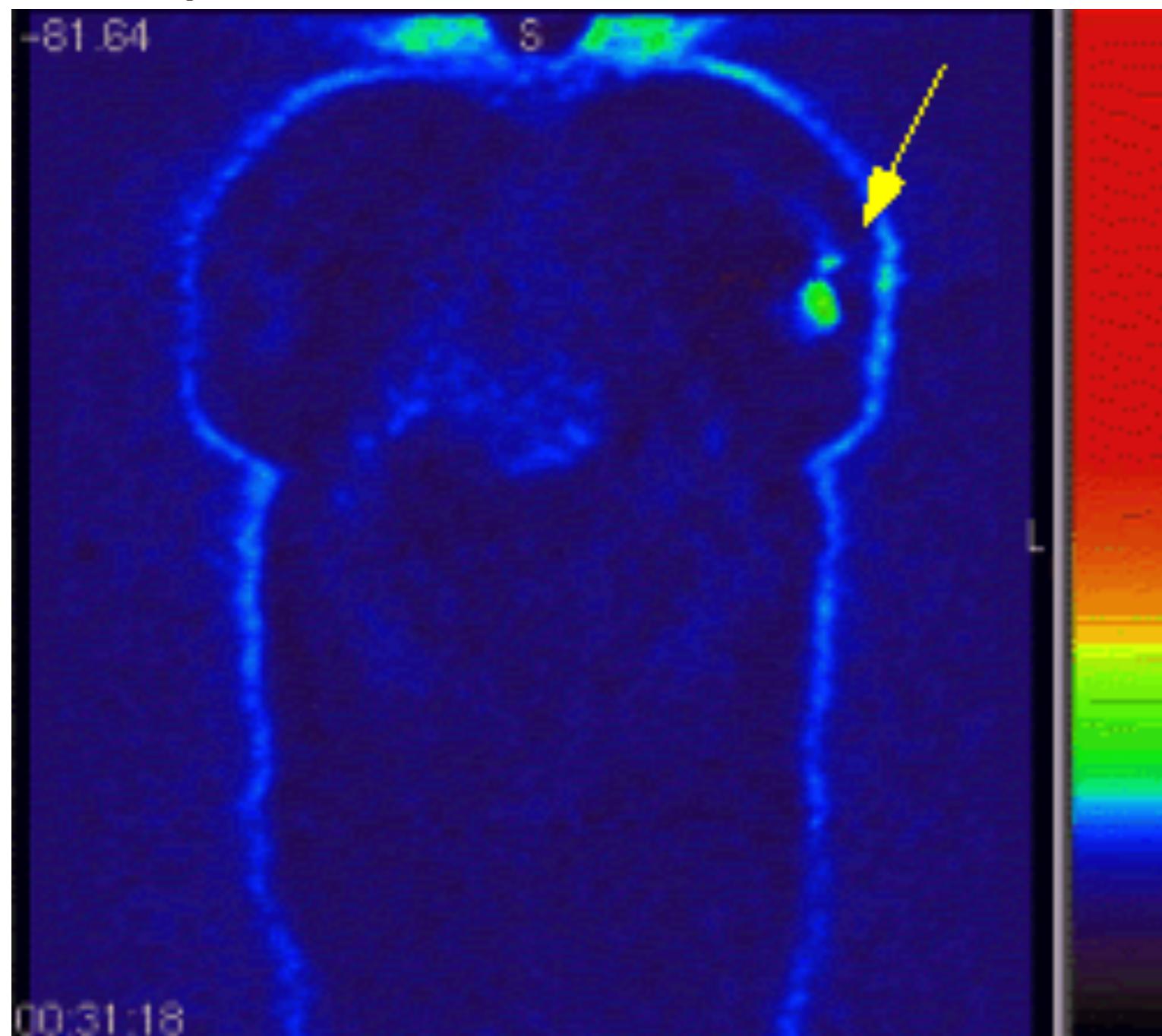


myocardial infarction  
(heart attack)

normal heart

# Positron Emission Tomography (PET)

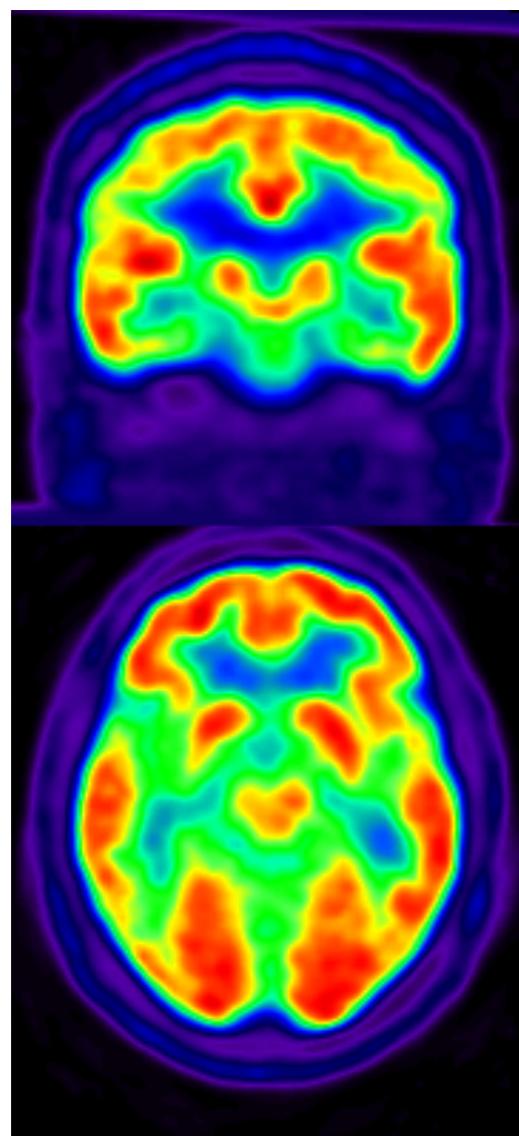
- Example



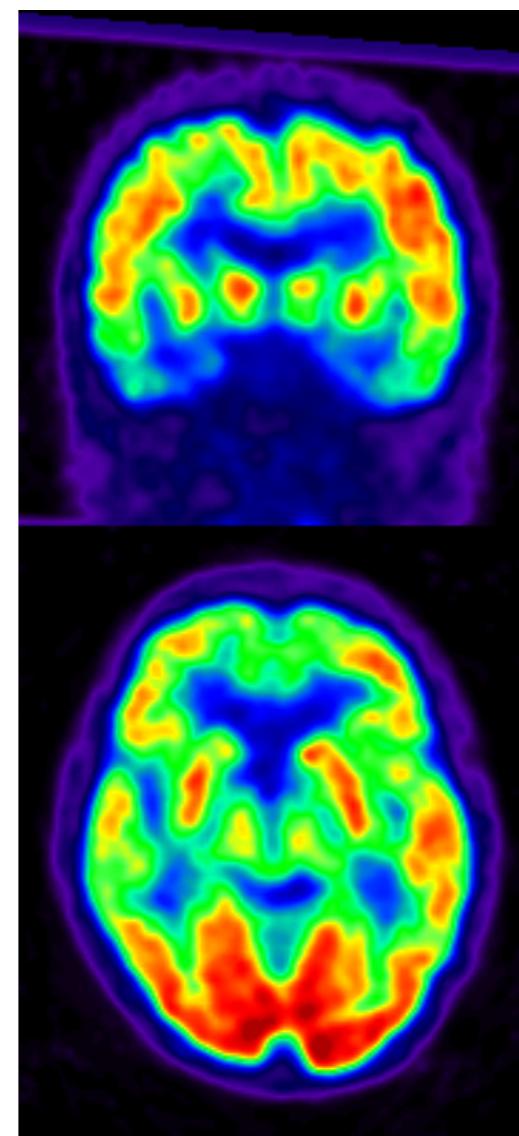
Malignant breast mass that was not revealed by conventional imaging techniques such as CT, MRI, and mammogram.

# Positron Emission Tomography (PET)

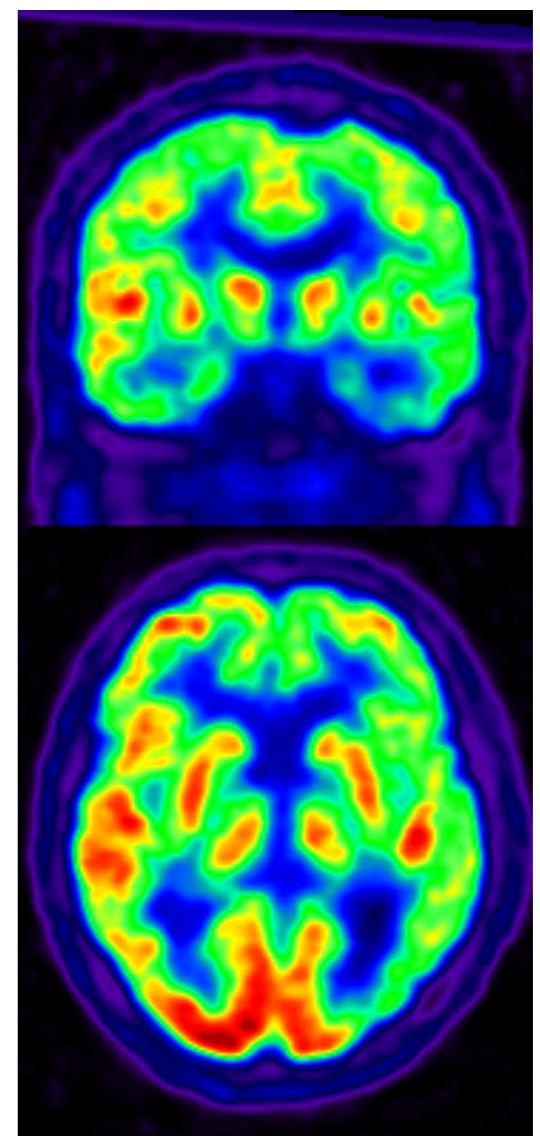
- FDG PET



Normal  
Control



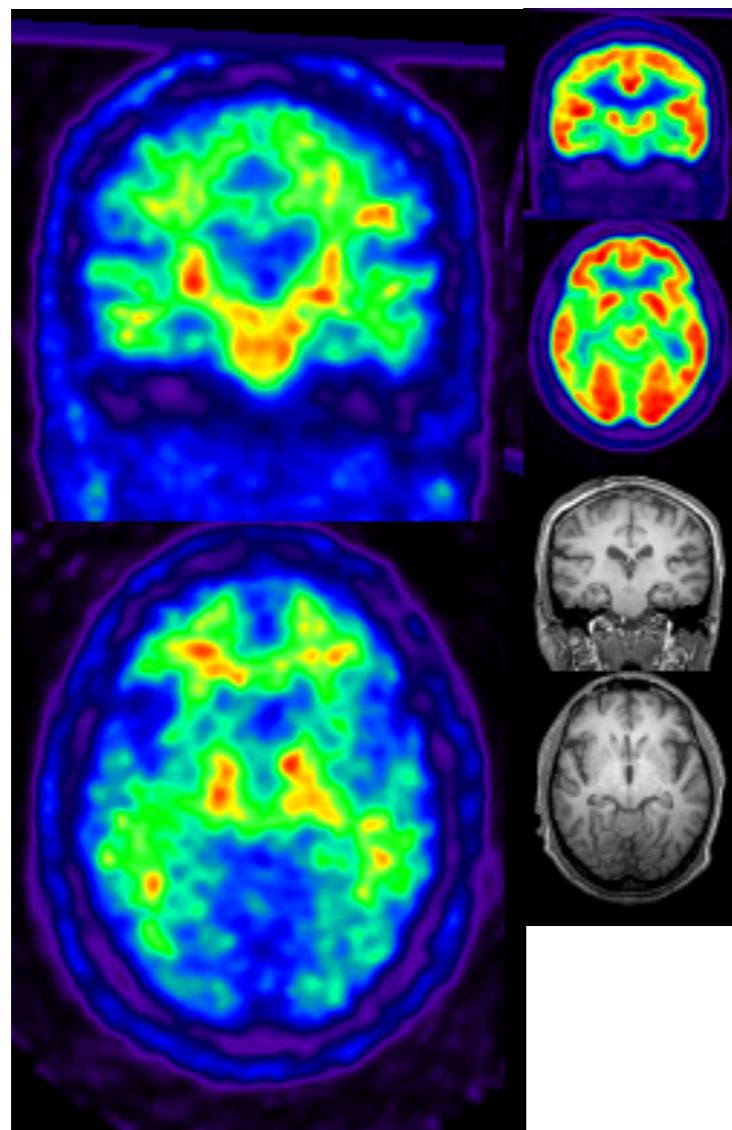
Mild Cognitive  
Impairment



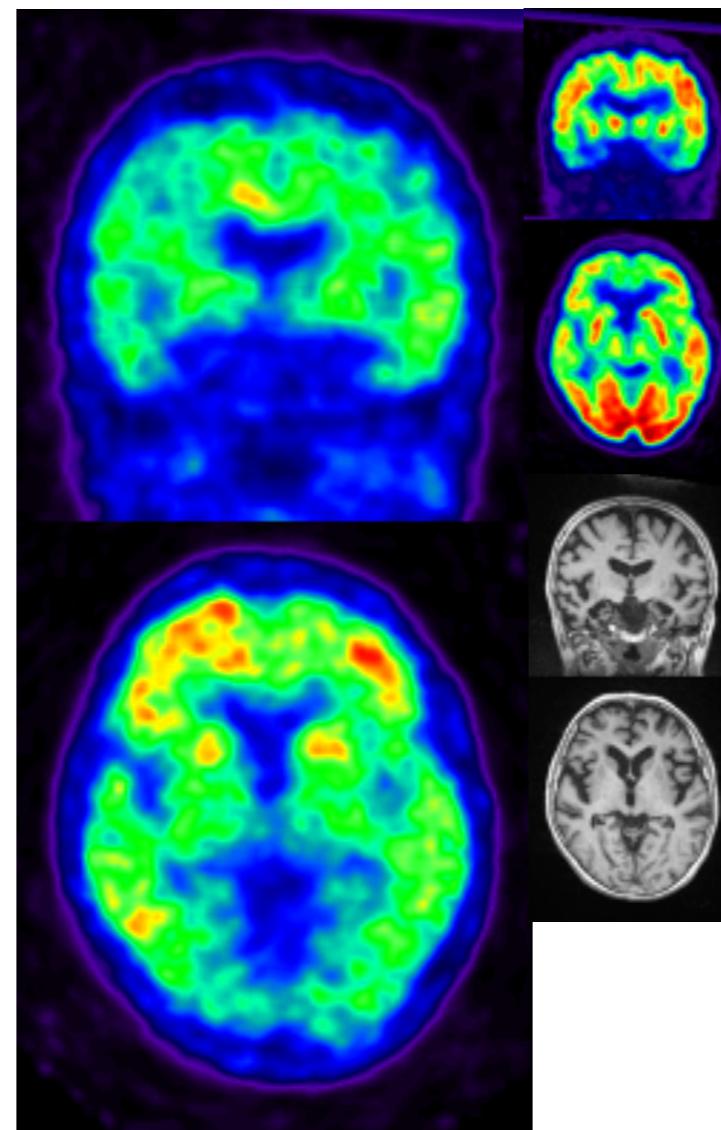
Alzheimer's  
disease

# Positron Emission Tomography (PET)

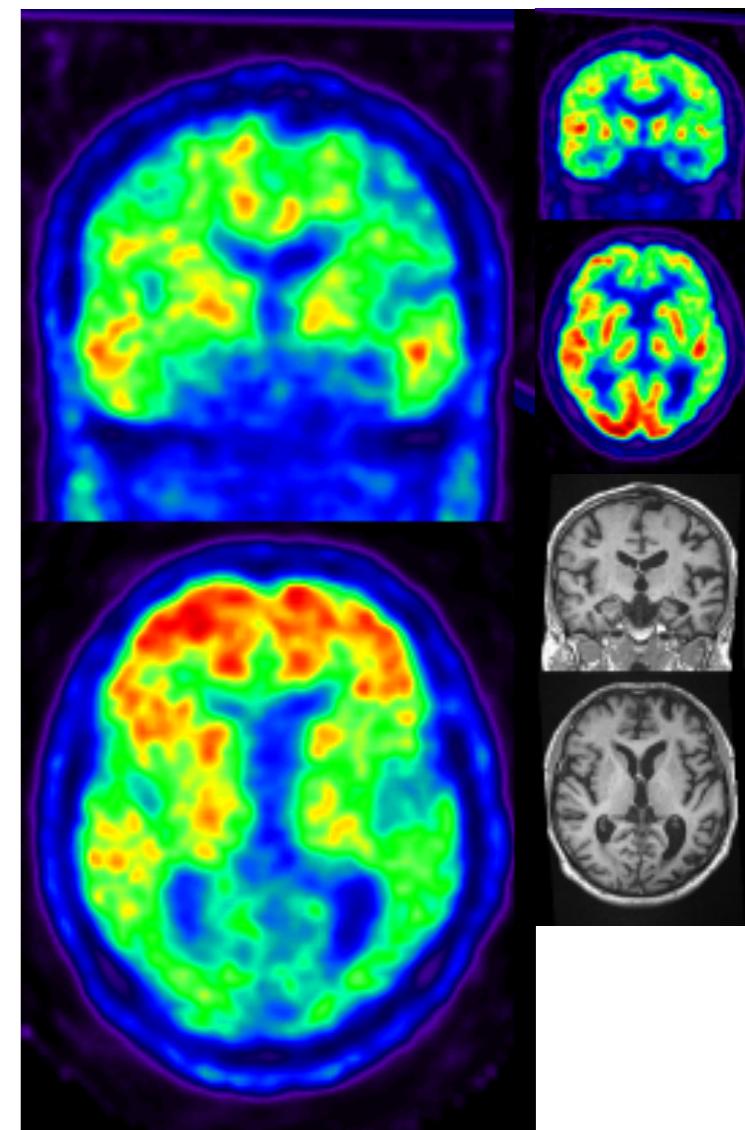
- PIB PET



Normal  
Control



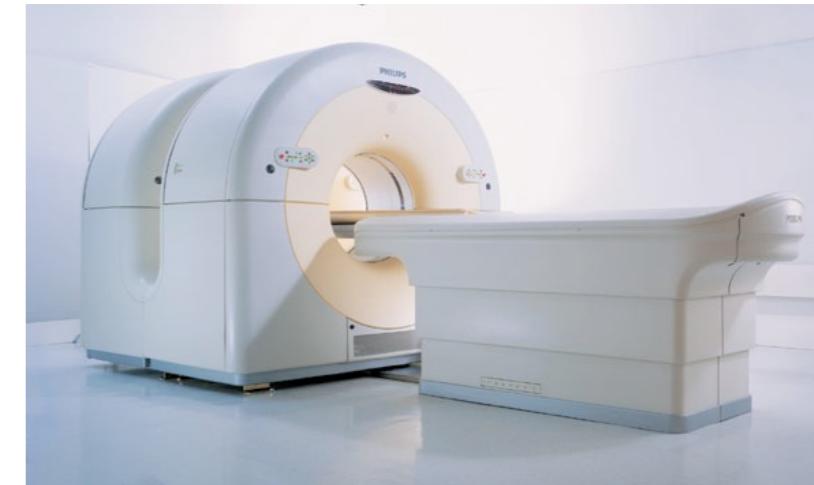
Mild Cognitive  
Impairment



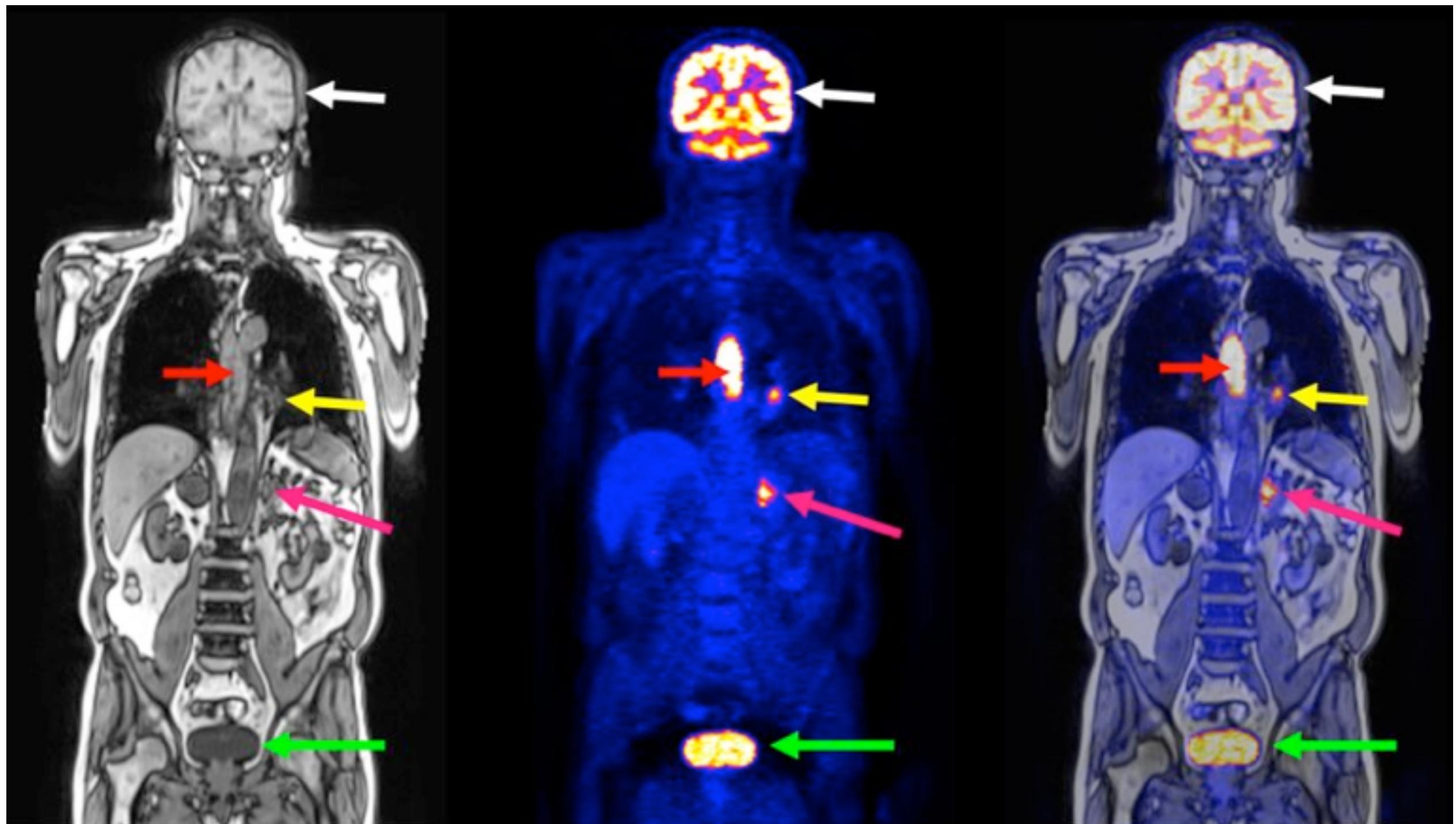
Alzheimer's  
disease

# Combined PET-CT

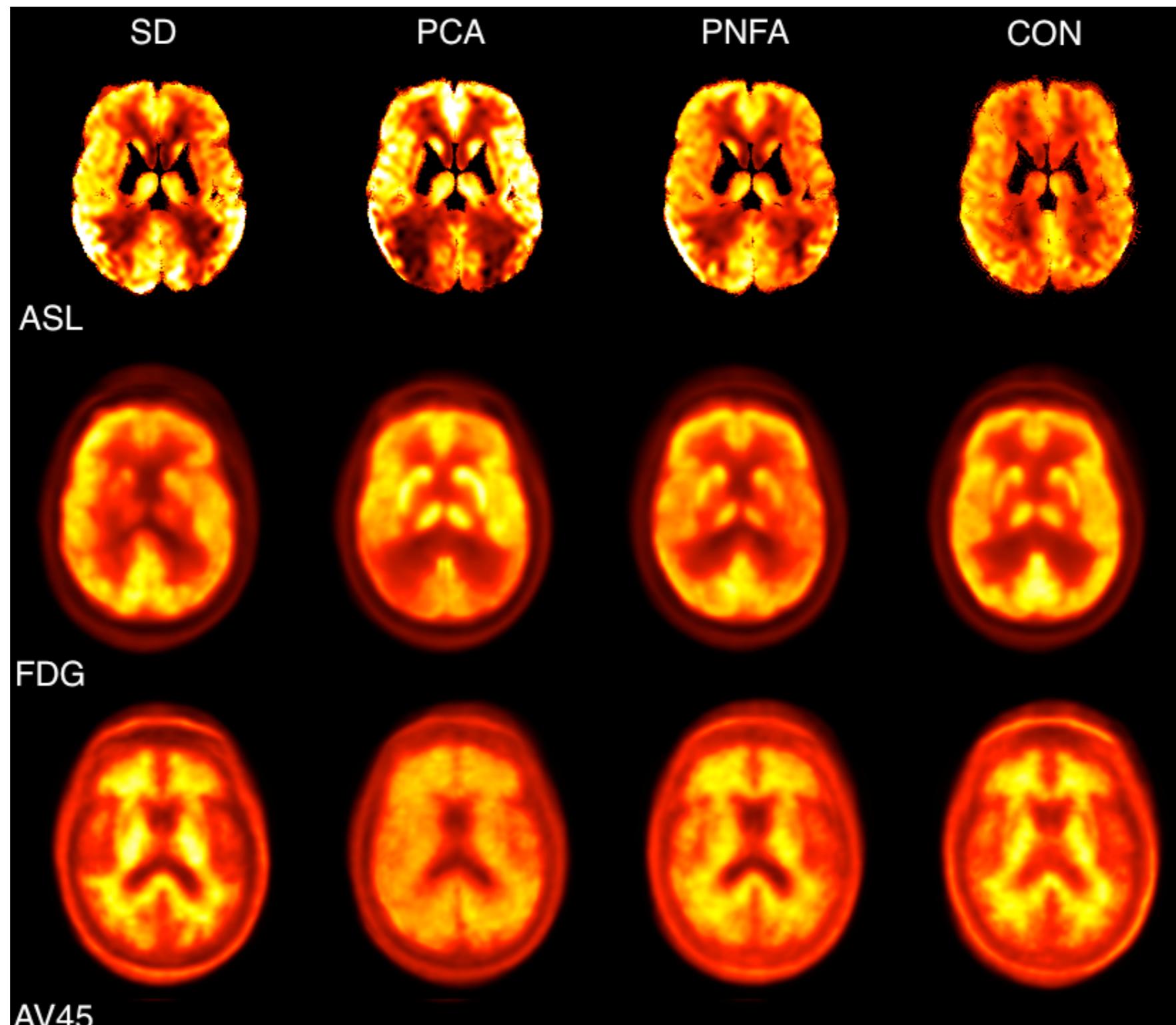
- Combining Structure and Function has many diagnosis and screening advantages



# Combined PET-MR



# Combined PET-MR



# Clinical Applications

	<b>Chest</b>	<b>Abdomen</b>	<b>Head</b>
X-Ray/ CT	+ widely used + CT	– needs contrast + CT - excellent	+ X-ray - is good for bone – CT - bleeding trauma
Ultrasound	– Mostly heart	+ excellent – problems with gas	– poor
Nuclear	+ extensive use in heart	Merge with CT	+ PET
MR	+ growing cardiac applications	+ minor role	+ standard

# Clinical Applications

	<b>Cardiovascular</b>	<b>Skeletal / Muscular</b>
X-Ray/ CT	+ X-ray – Excellent, with catheter-injected contrast	+ strong for skeletal system
Ultrasound	+ real-time + non-invasive + cheap – but, poorer images	– not used
Nuclear	+ functional information on perfusion	+ functional - bone marrow
MR	+ getting better High resolution Myocardium viability	+ excellent

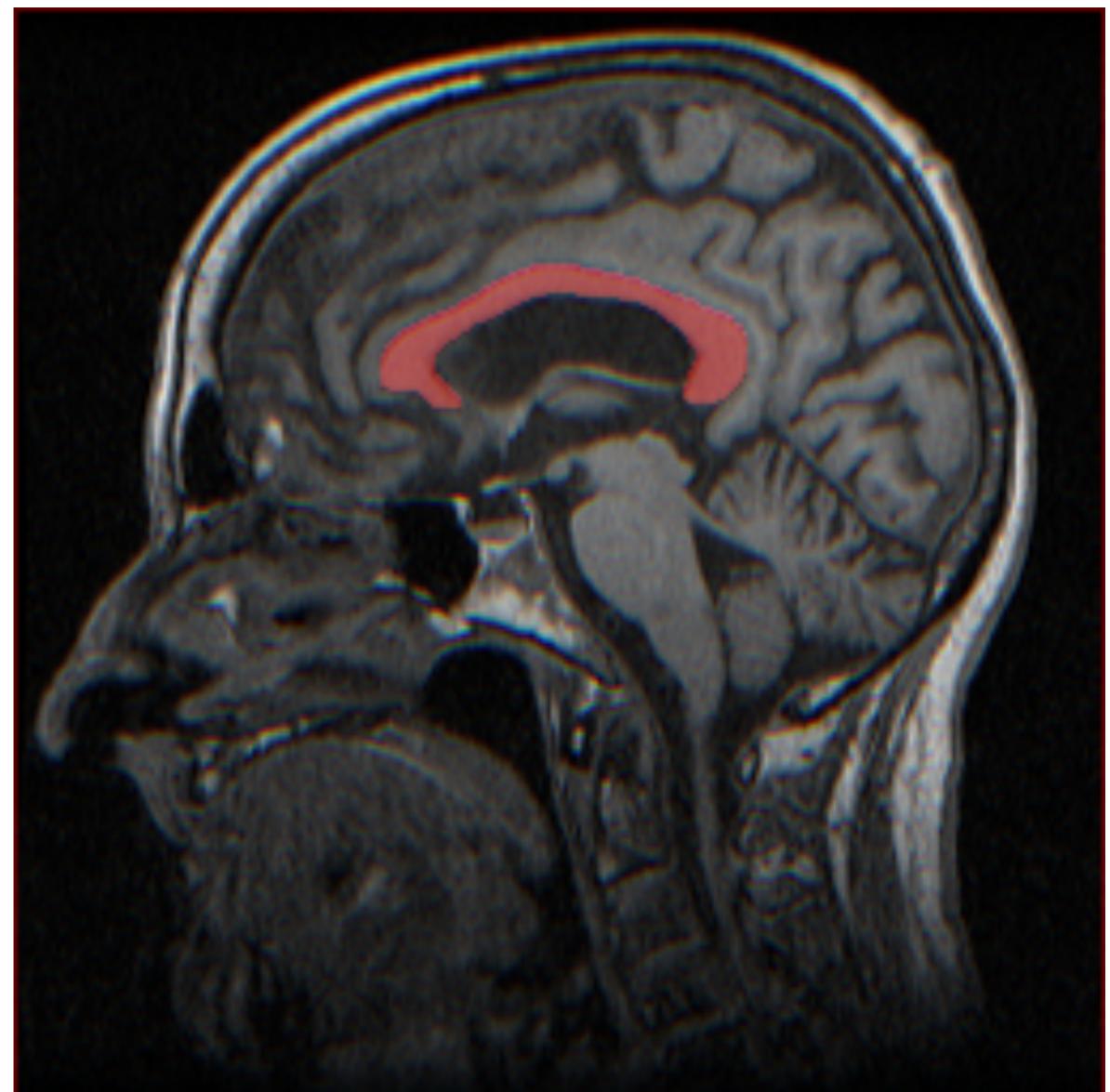
# Methods

# What is segmentation?

- “Delineating and assigning a label to a biological structure”

A wide variety of techniques have been proposed

No magic segmentation for all images

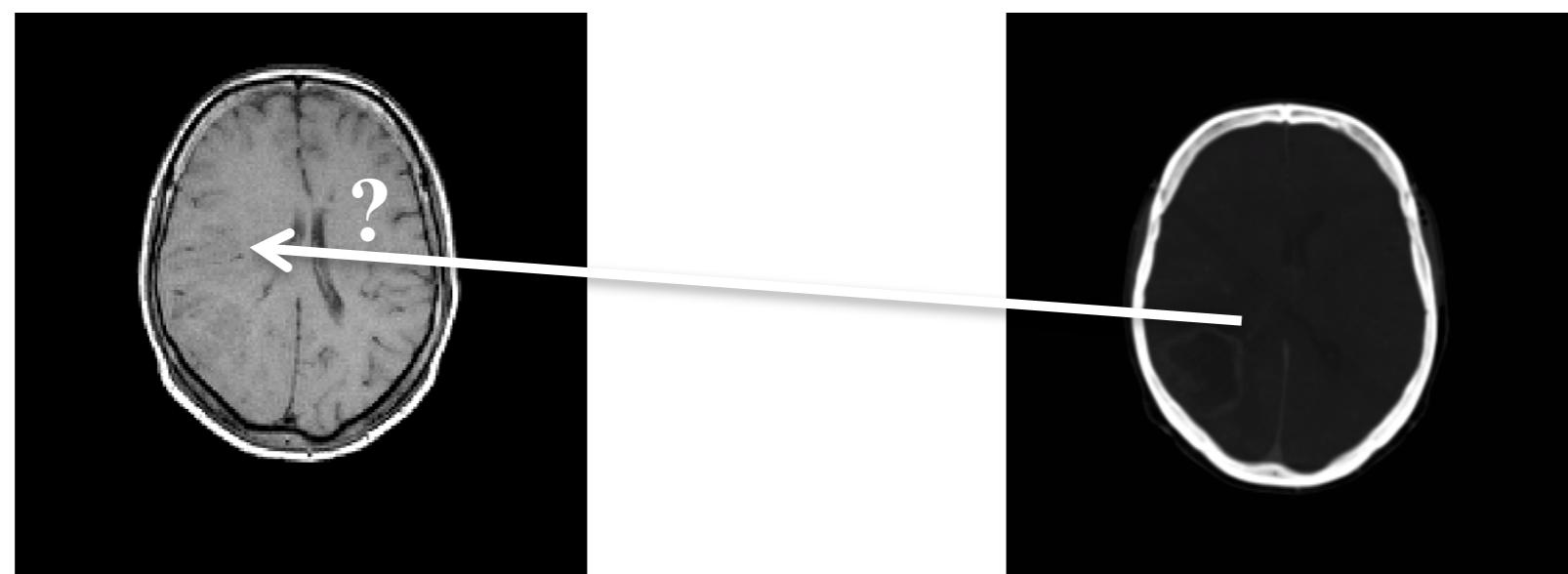


# Segmentation: Matrix Classification

	<b>Pixel-based</b>	<b>Region-based</b>	<b>Model-based</b>
<b>Structural</b>	Thresholding Edge-based	Watershed	Graph-searching
<b>Statistical</b>	Clustering	Markov Random Fields Split and Merge	Histogram-based
<b>Hybrid</b>	Statistical Atlas	Region Growing	Deformable Model Atlas Warping

# What is registration?

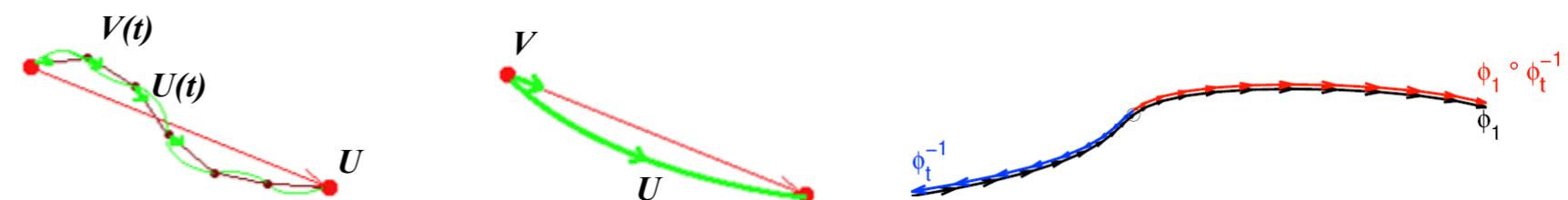
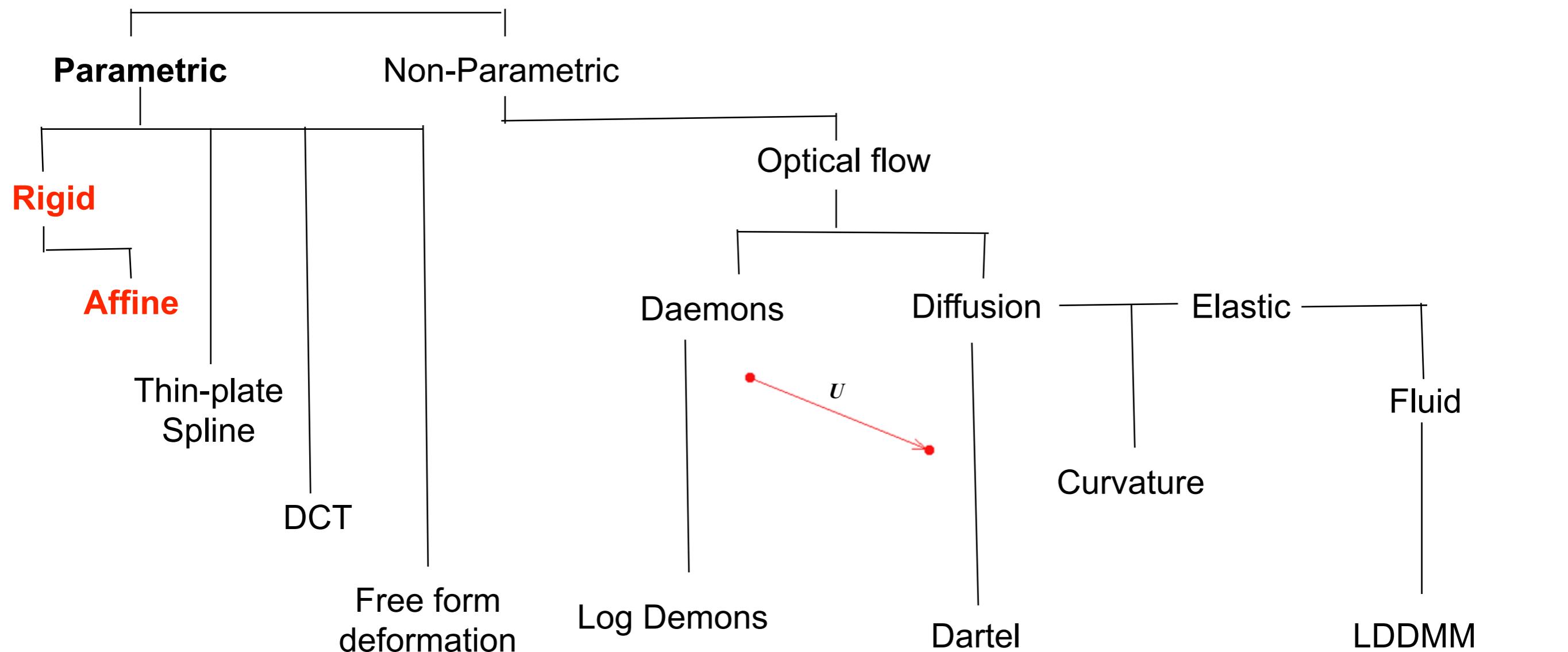
- “Registration is the process of mapping between coordinates in one space and those in another, to achieve biological, anatomical or functional correspondence”.



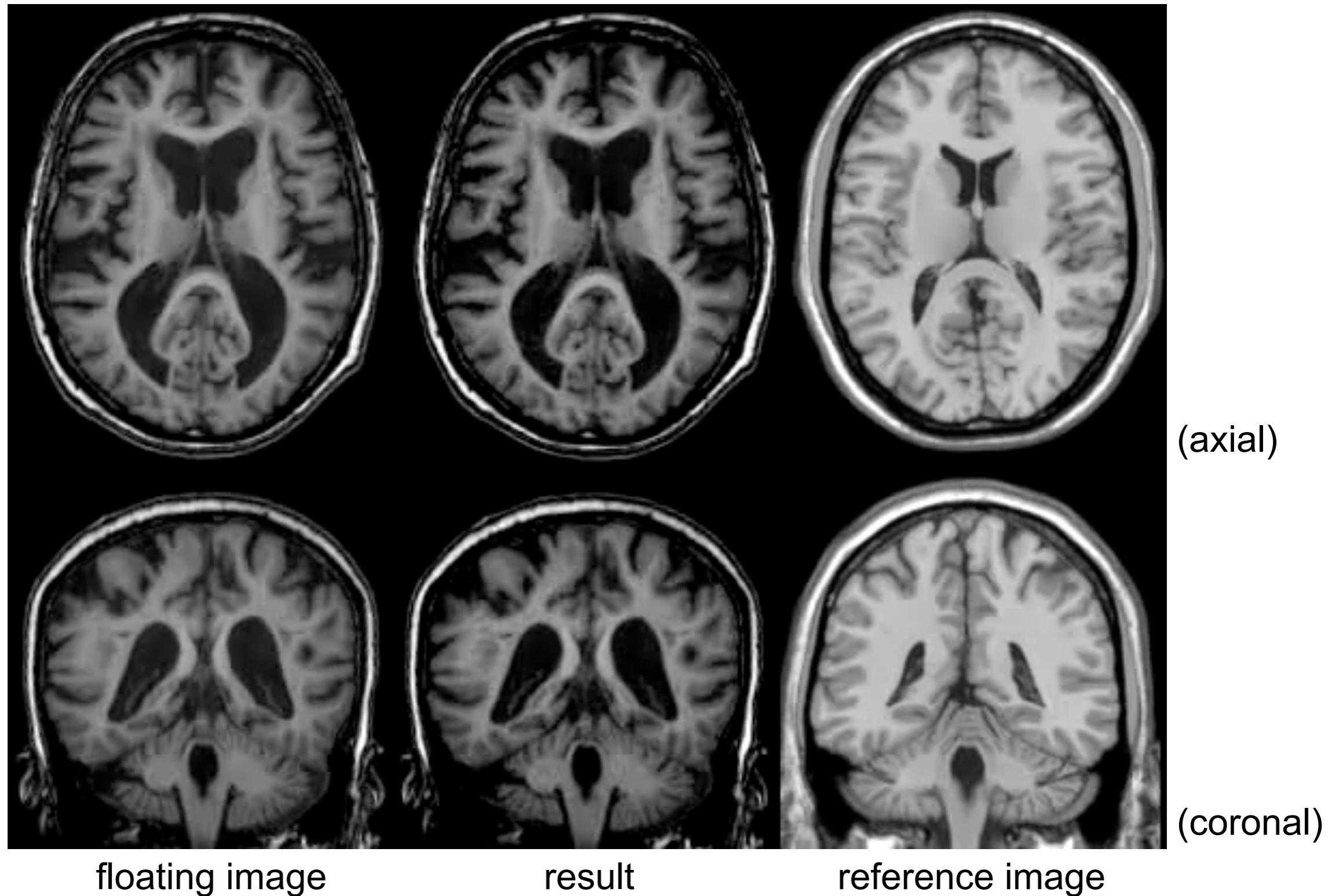
# Why do we need registration?

- Quantitatively compare scans of the same subjects done at different times or with different modalities.
- Pre-/Post- surgery/treatment.
- Compare MR/CT/PET/SPECT.
- Correct for patient motion in dynamic imaging.
- Estimate change over time (tumour progression, atrophy).
- Quantitatively compare scans of different subjects.
- Compare normal subjects with abnormal subjects.
- Construct population models of anatomical variation.
- Fit generic models to individual subjects.

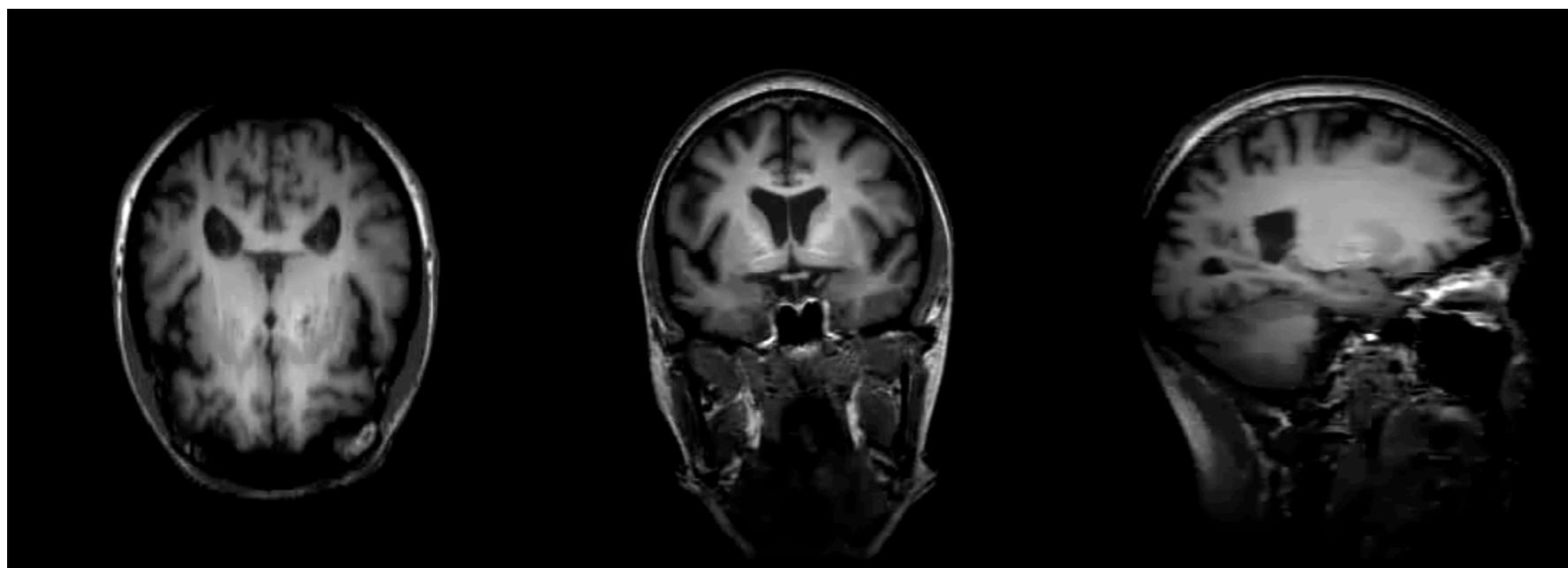
# A taxonomy of reg. algorithms



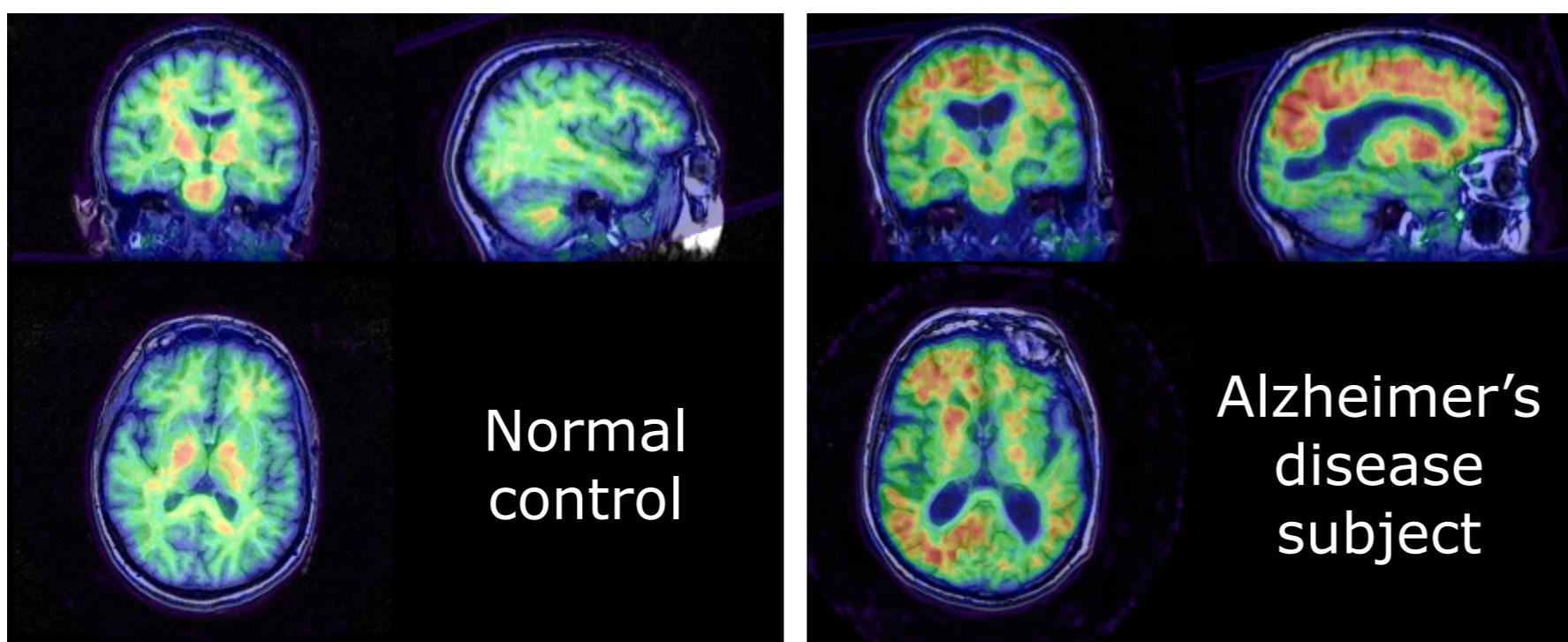
# Registration example



# Registration example



Registration process of PET and MR of the same patient



# Registration application examples

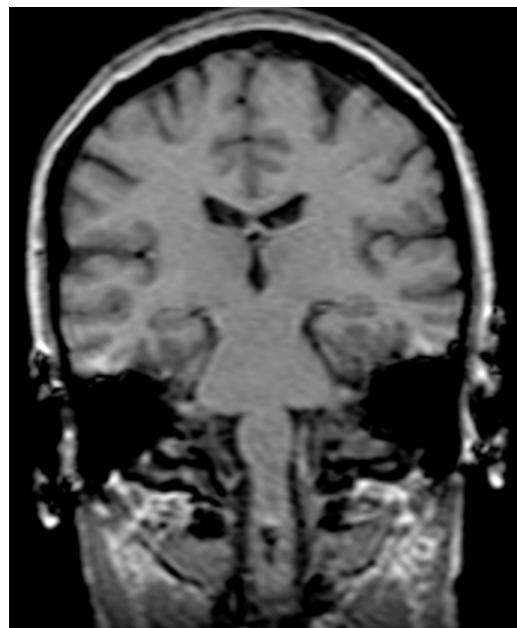
- Some (of many) clinical applications
  - Measurement of atrophy in Alzheimer's disease
  - Measurement of lesion volume in Multiple Sclerosis
  - MRI-US for surgery image guidance
  - Intraoperative MRI
  - Tumour growth modelling
  - Breathing motion modelling for radiotherapy guidance
  - MRI-US prostate biopsy guidance
  - Motion correction in contrast enhanced MRI
  - Preterm imaging
  - Genotype-Phenotype imaging
  - Research software at CMIC

# Alzheimer's Disease: the most common cause of dementia

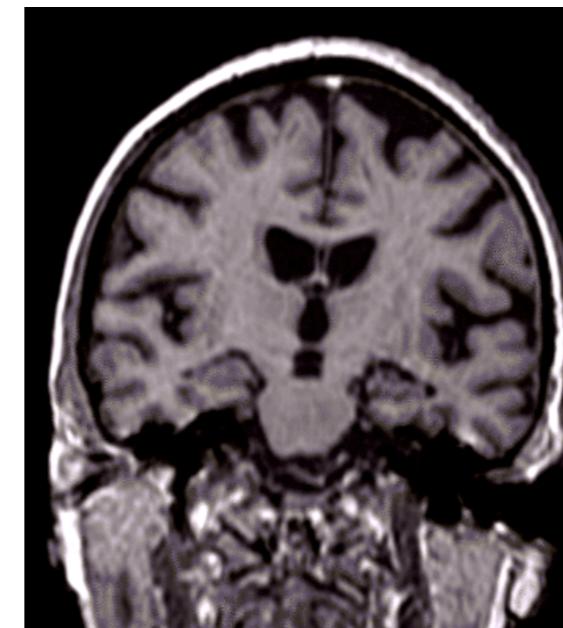
- Alzheimer's disease (AD) affects more than 18 million people worldwide
- If onset was delayed by 5 years, the number of cases worldwide would be halved
- According to the Amyloid cascade hypothesis, accumulation of A $\beta$  in the brain is the primary influence driving AD pathogenesis (Hardy, Science'92)
- Early detection of abnormal Amyloid deposit could help detect AD before neurons death and cognitive decline

# Alzheimer's Disease: the most common cause of dementia

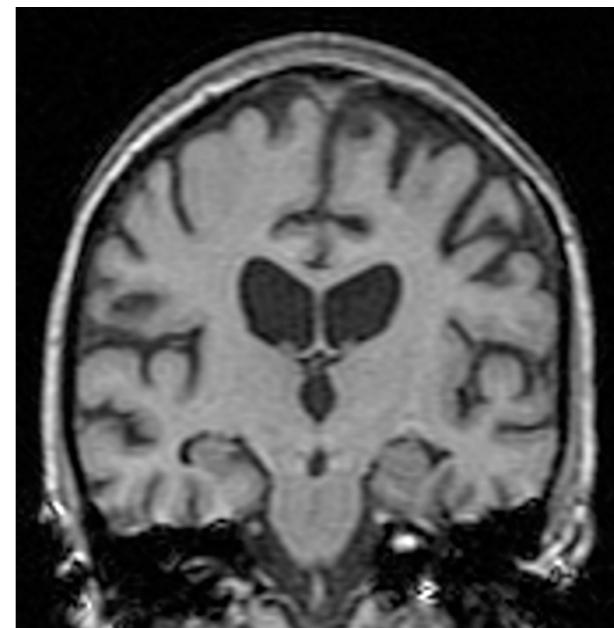
- Changes at a cellular level have macroscopic consequences that might be detectable with Magnetic Resonance Images (MRIs).



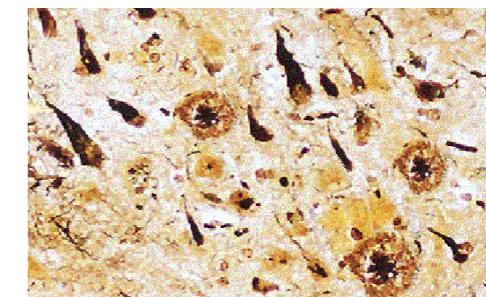
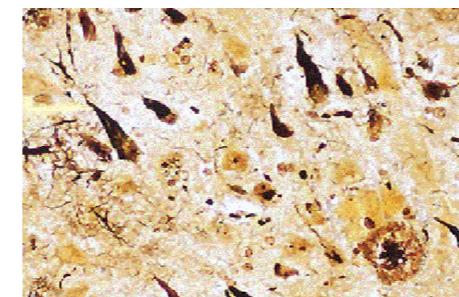
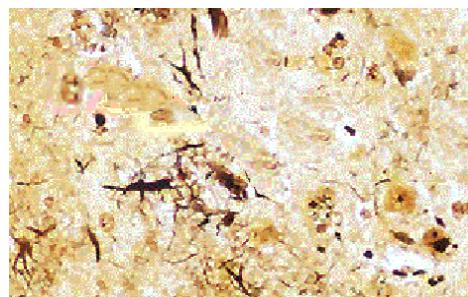
Pre-symptomatic



Diagnosis

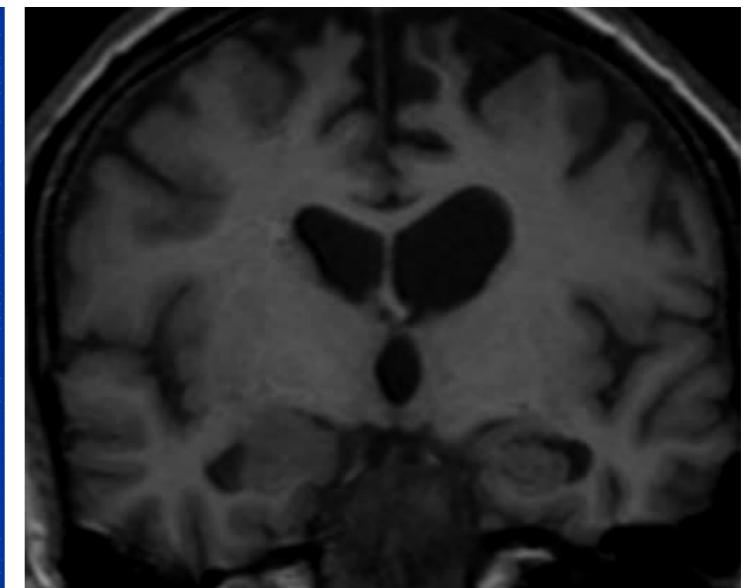
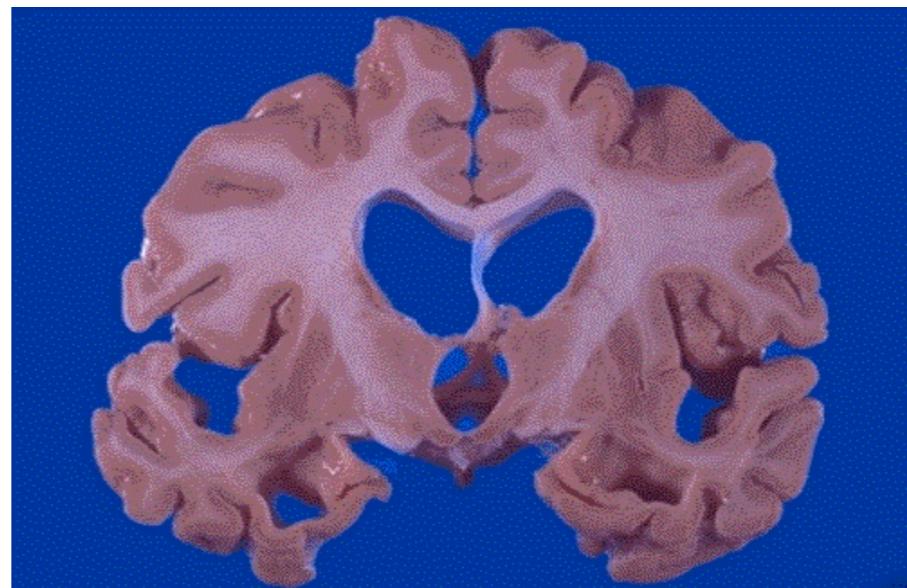
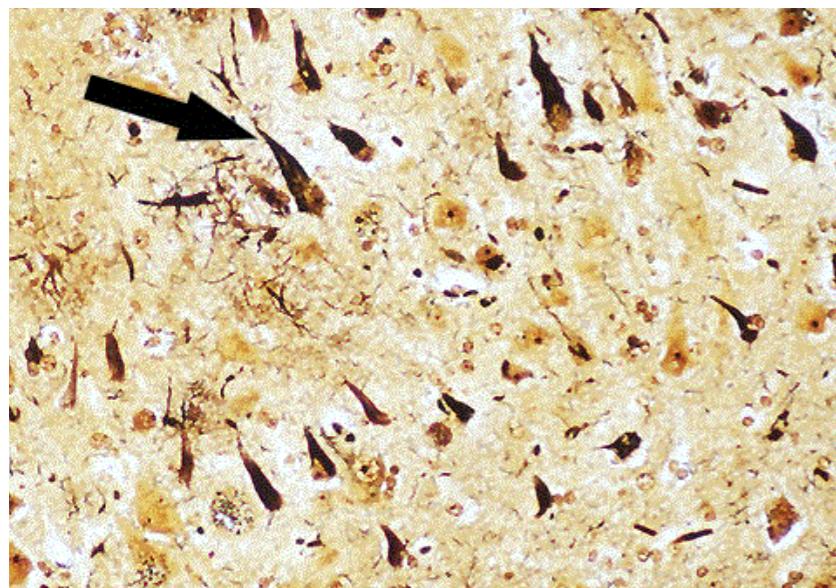


Dementia

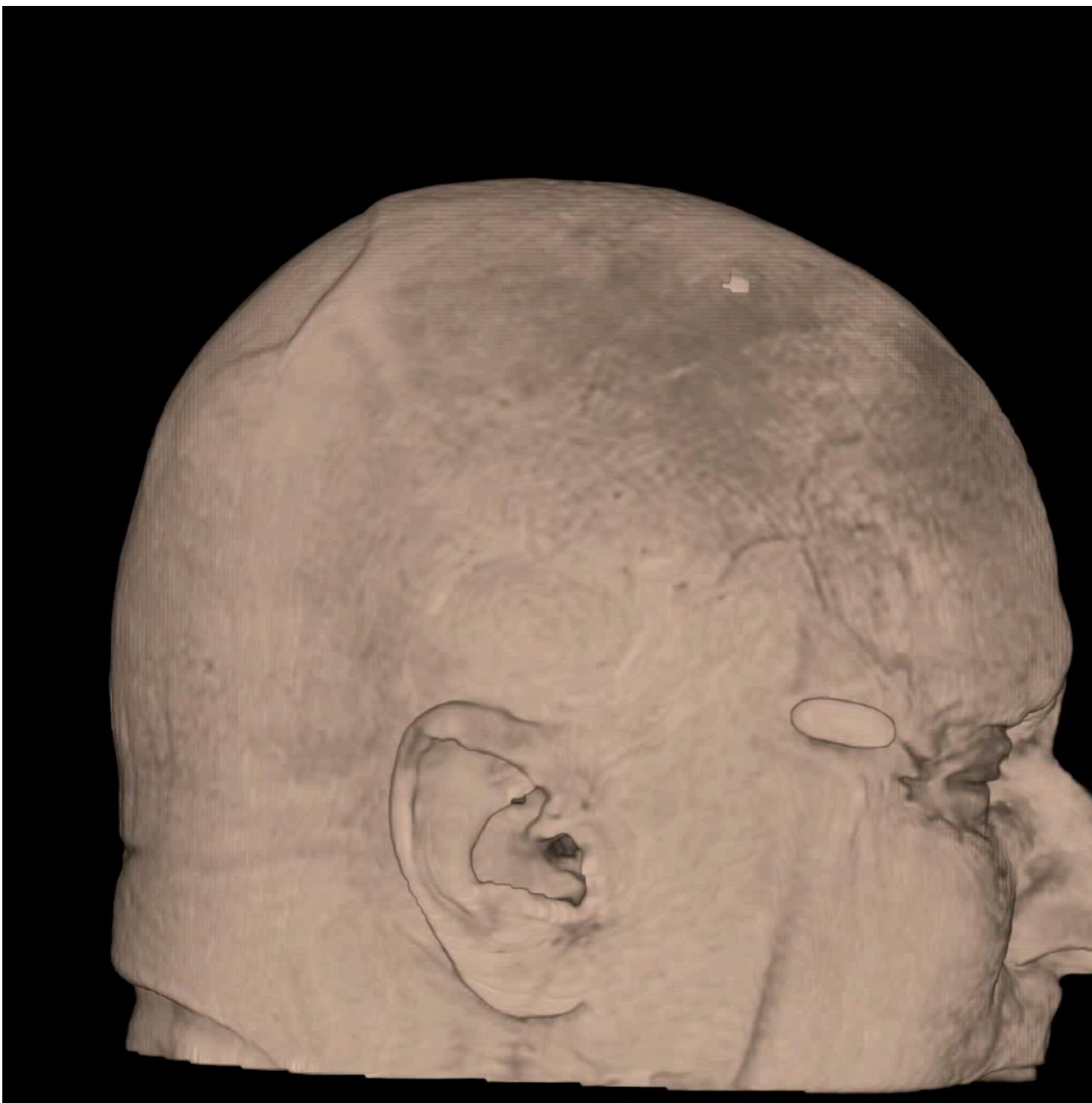


# Cerebral atrophy

- AD = amyloid plaques, neurofibrillary tangles, synaptic, dendritic, neuronal & axonal loss... and atrophy
- Can we measure atrophy using MRI?  
Using 4D MRI: 3D MRI + time



# Cerebral atrophy



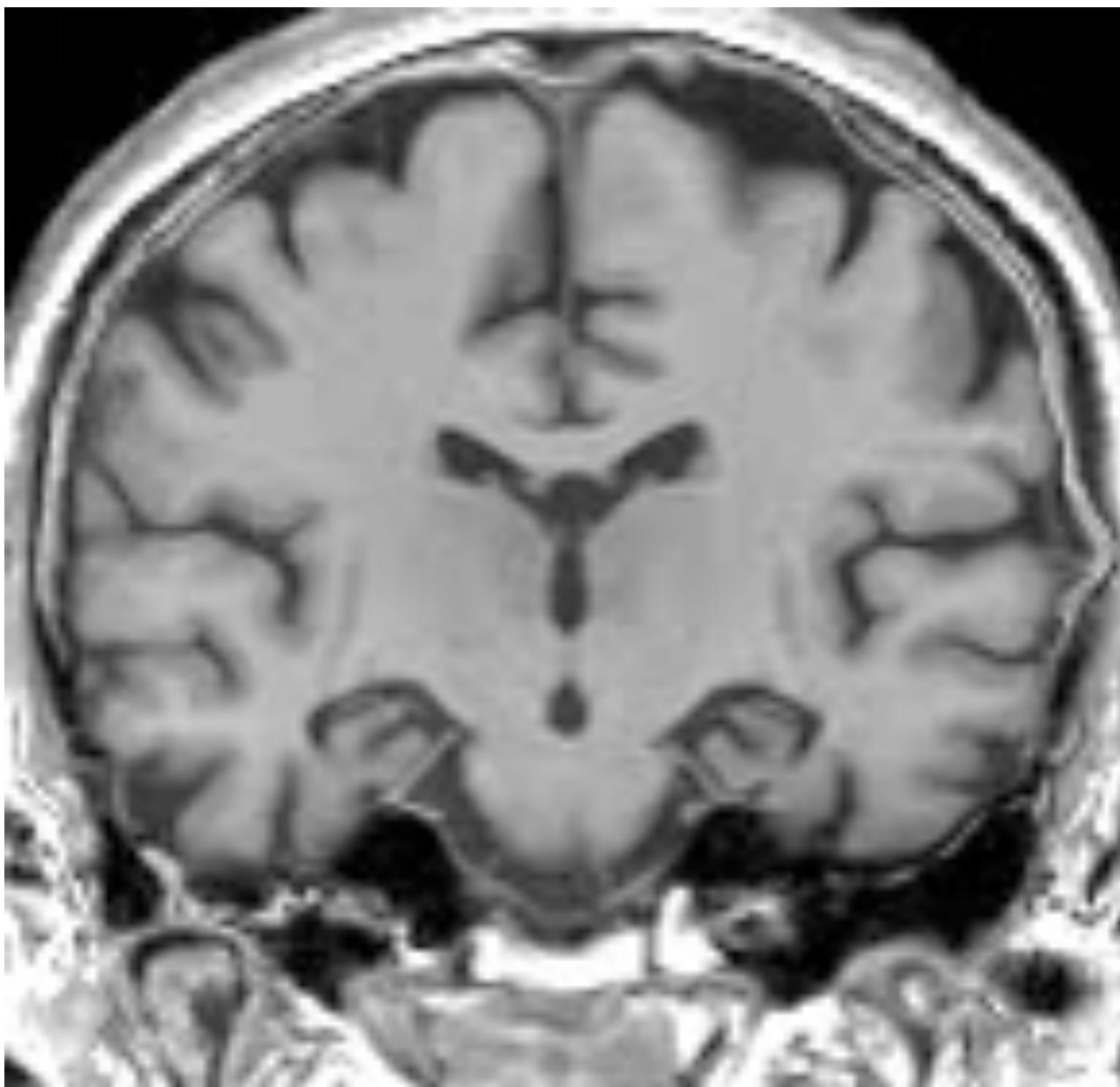
*Volume changes occurring  
over two years*

Simulated using two T1-  
weighted MRIs  
*Baseline and 2 year follow-up*

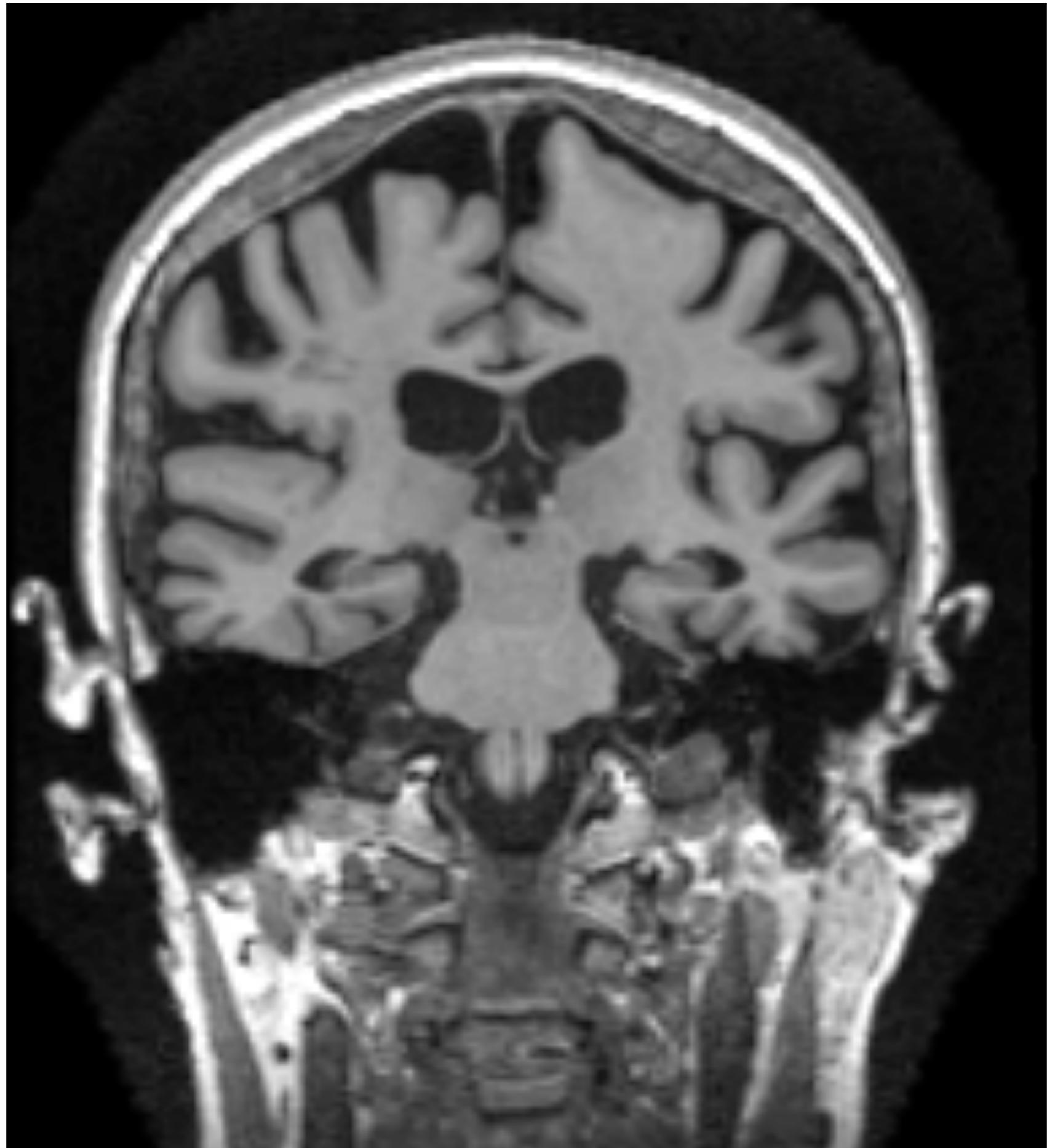
Male - 68 years old at baseline  
Alzheimer's disease diagnosed

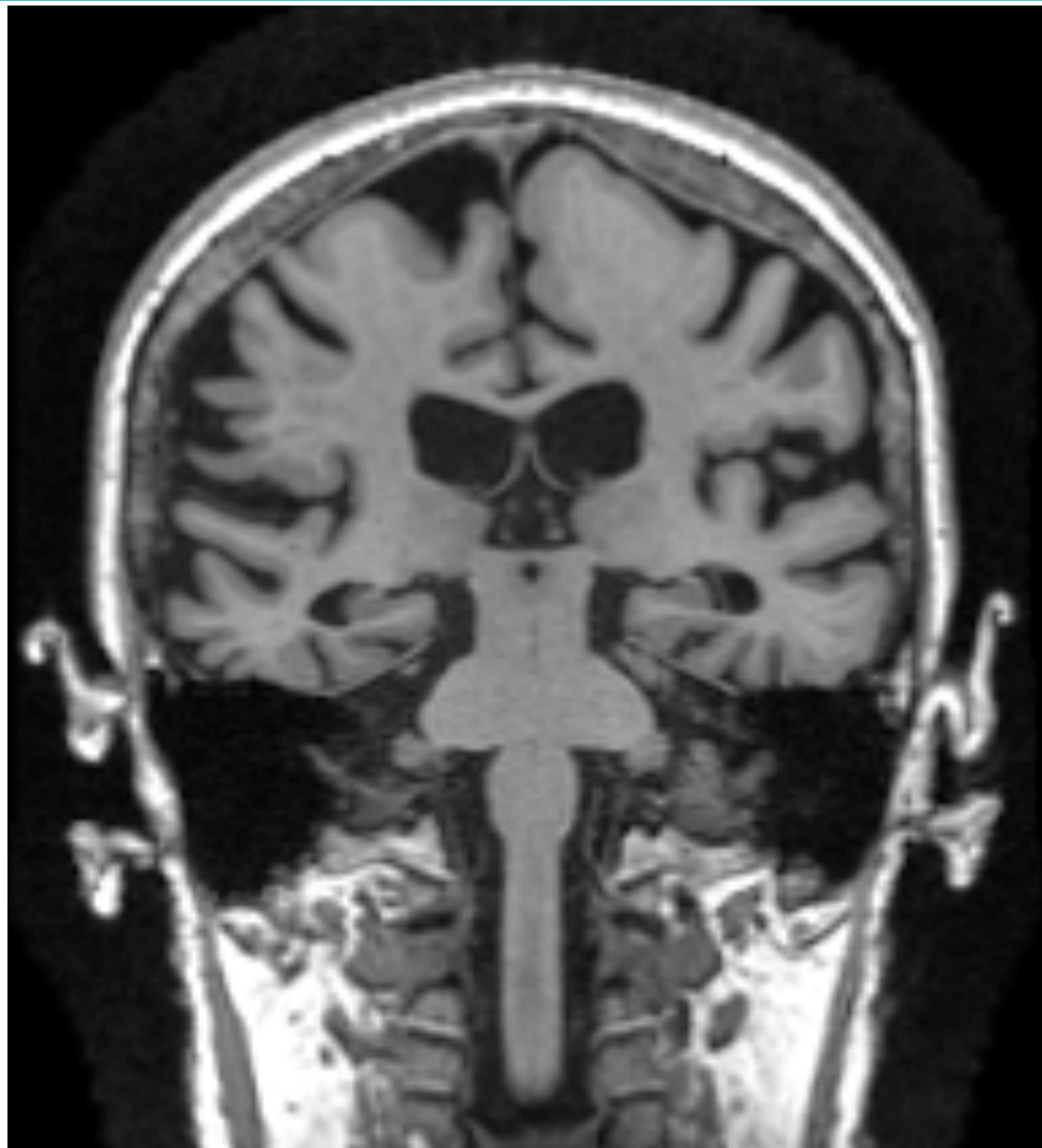
Subject from the ADNI database

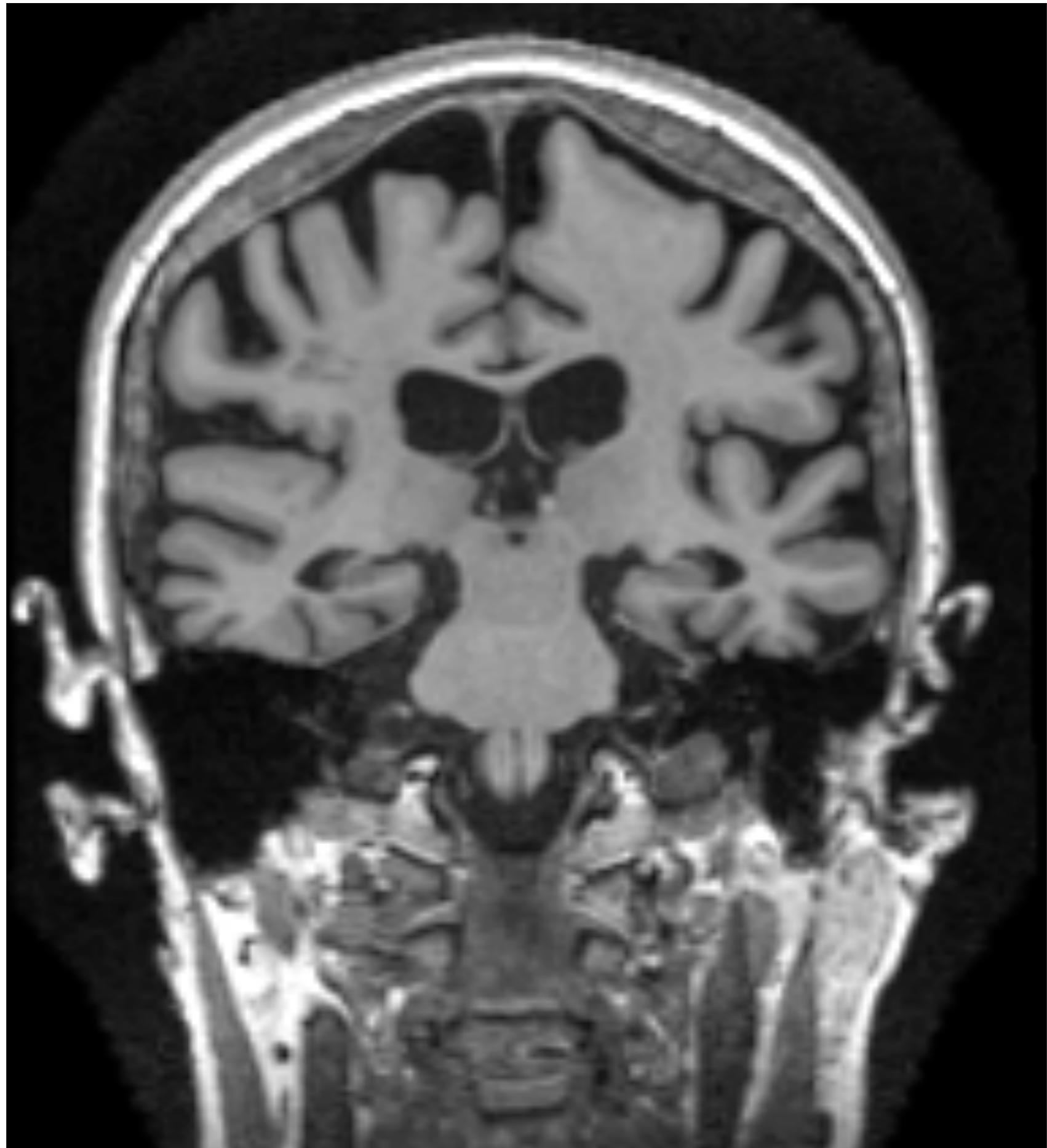
# Cerebral atrophy

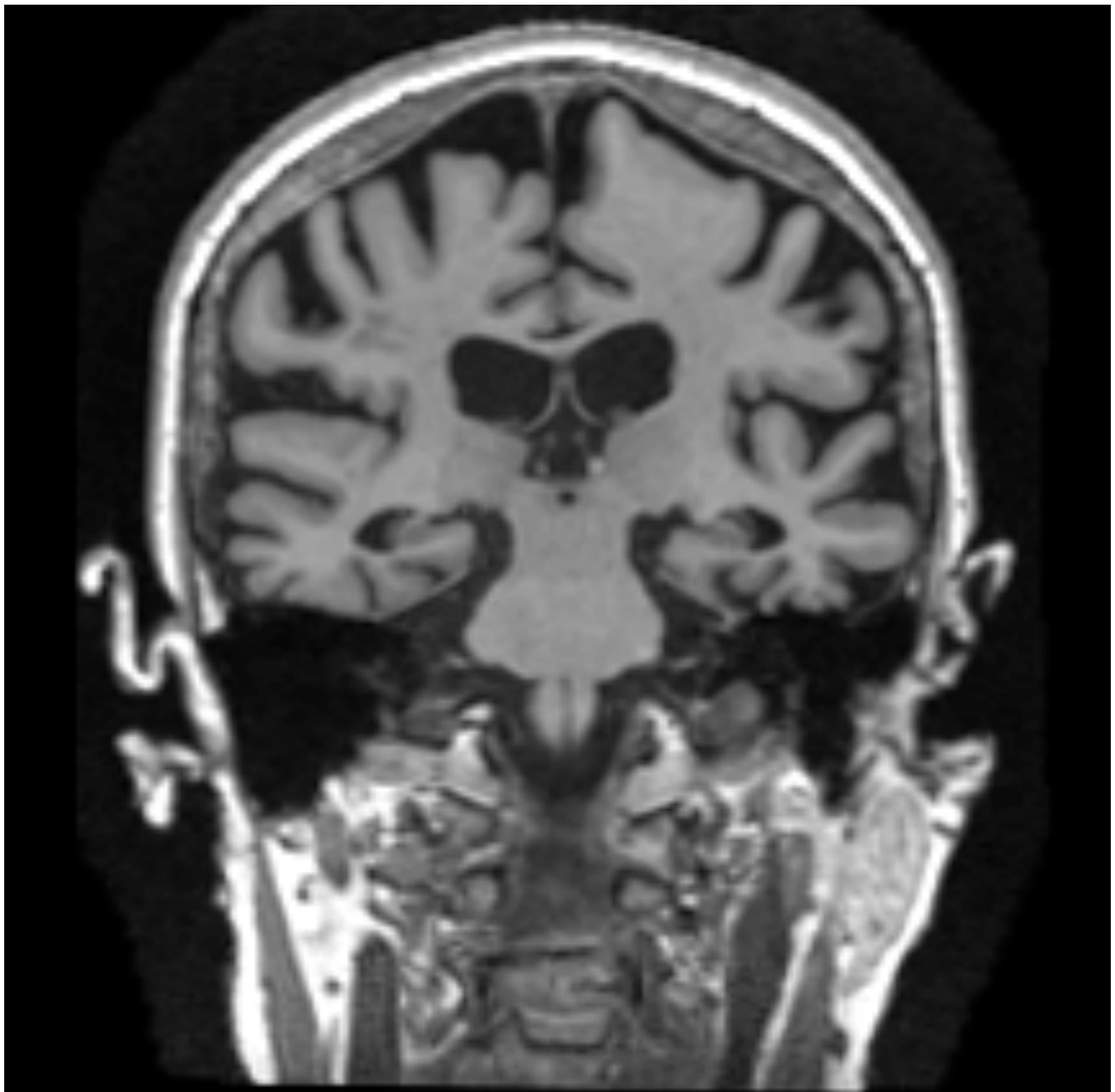


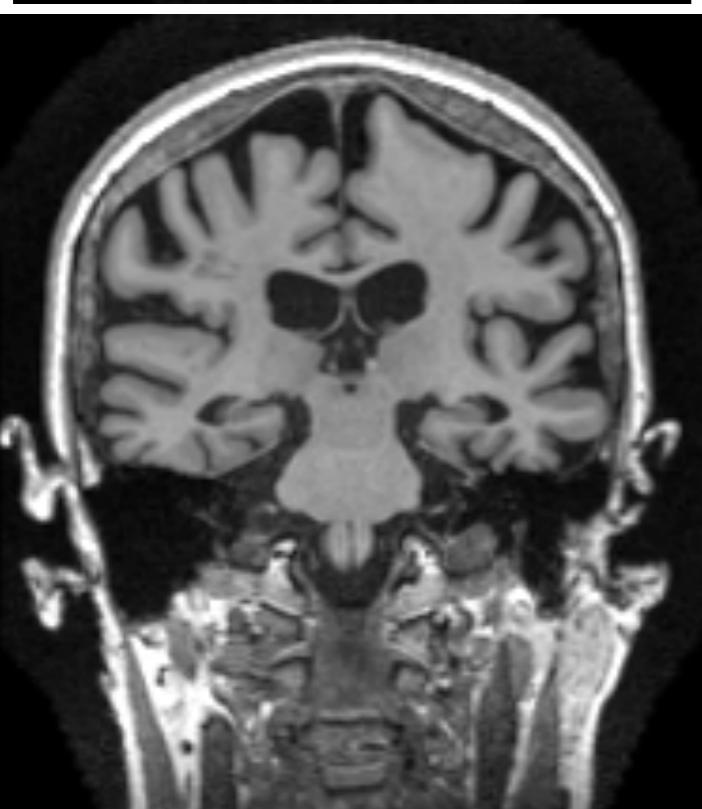
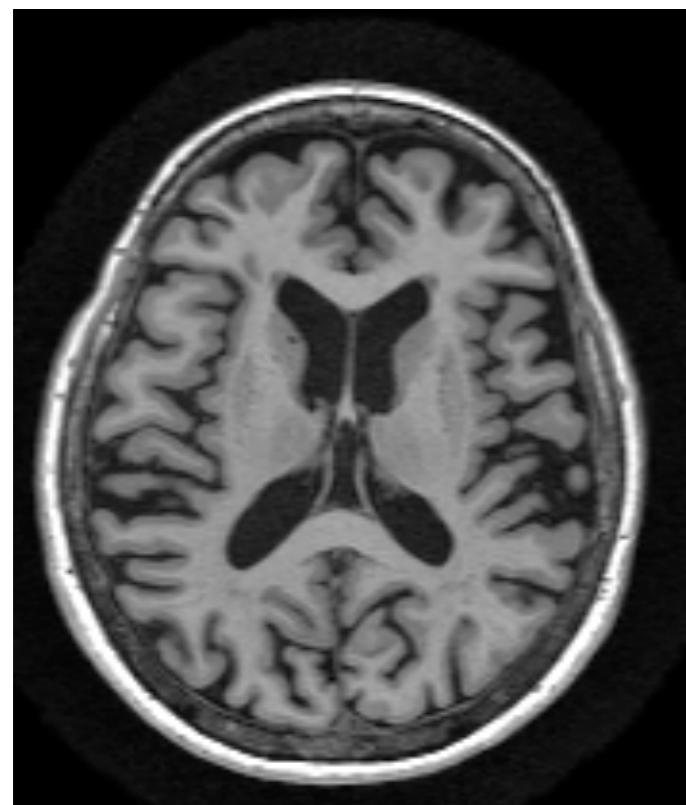
*Brain evolution over 12 years (2000-2012)*



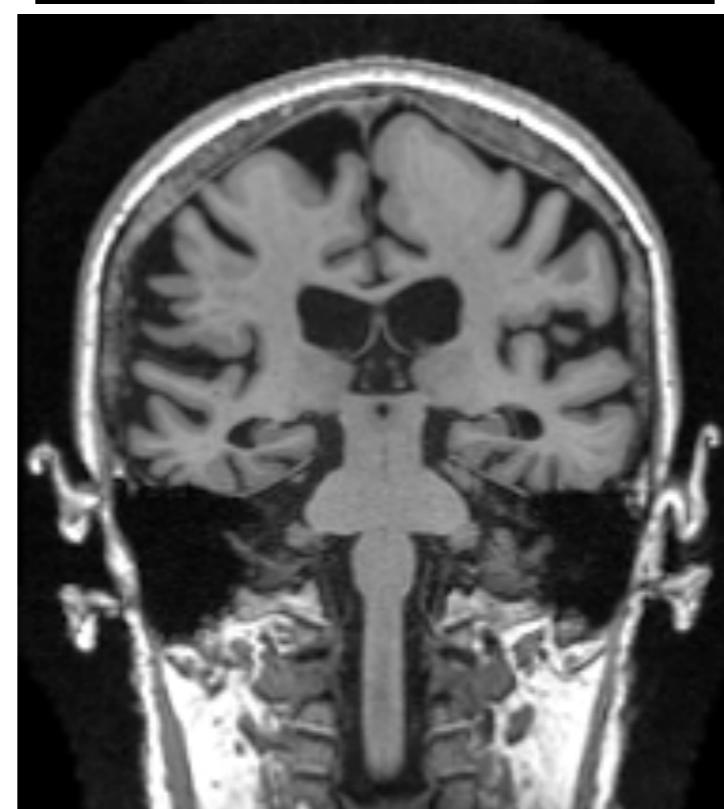
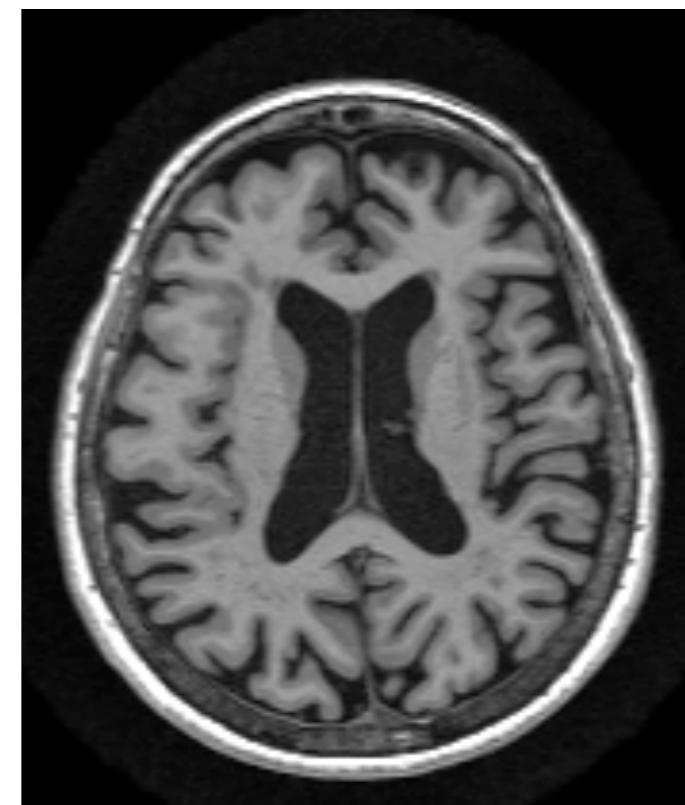




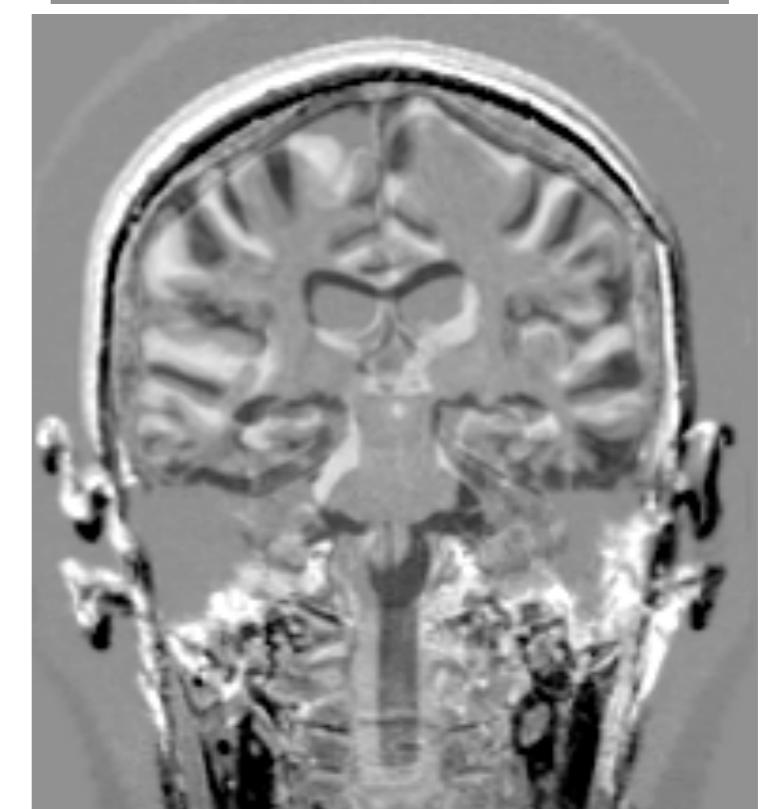
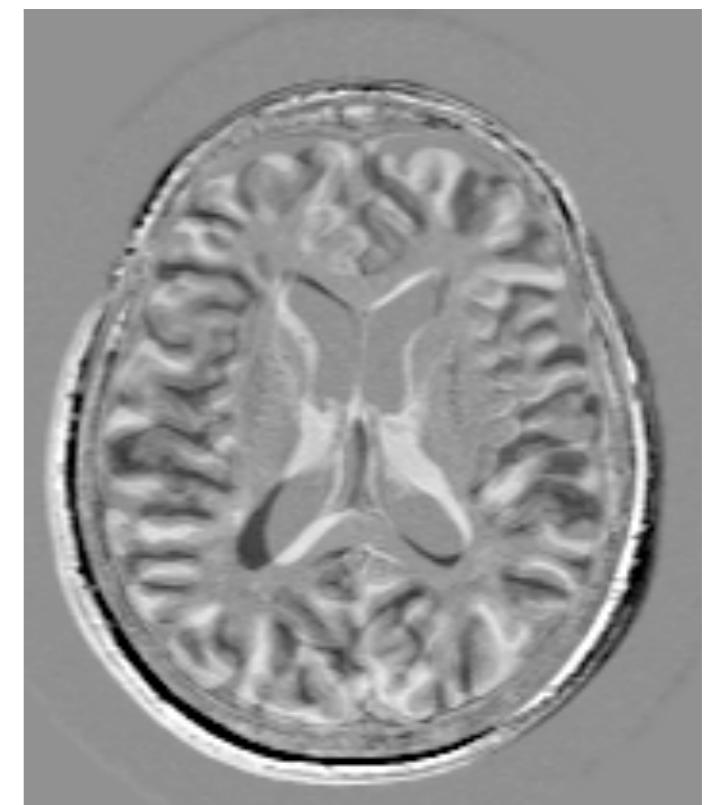




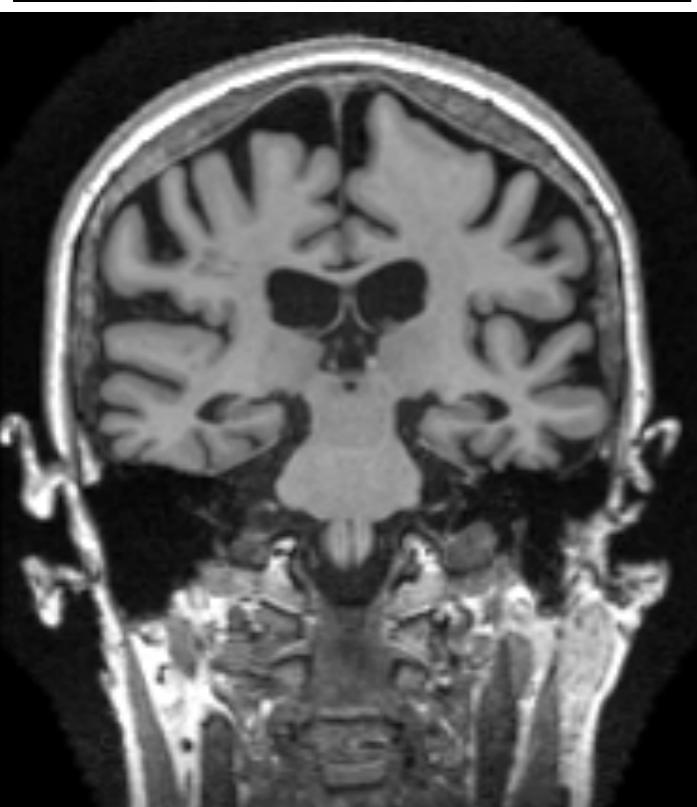
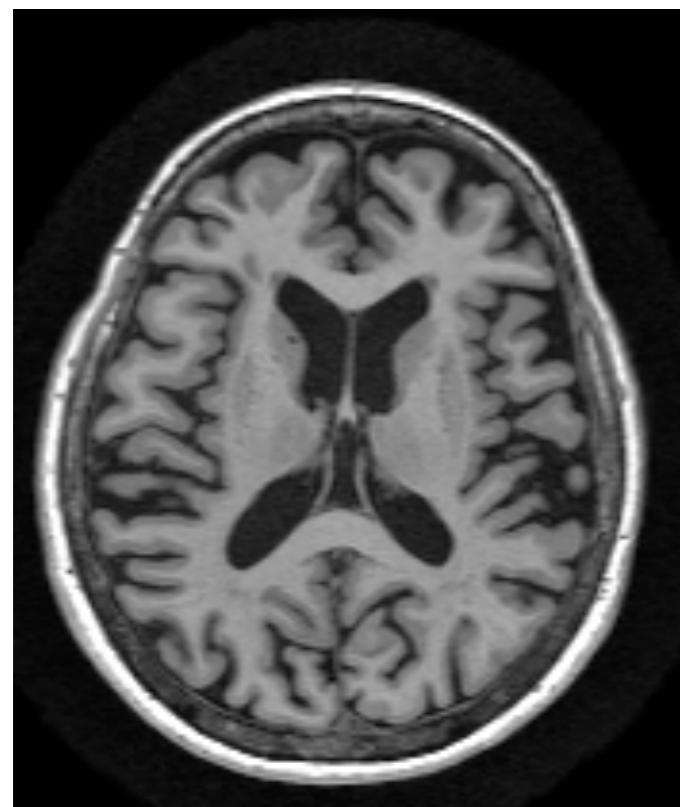
Baseline scan



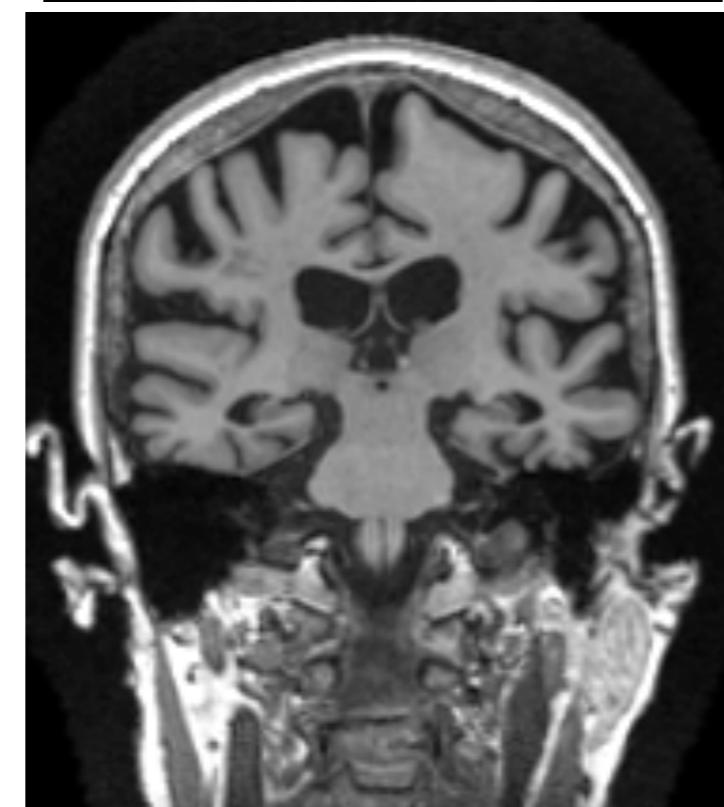
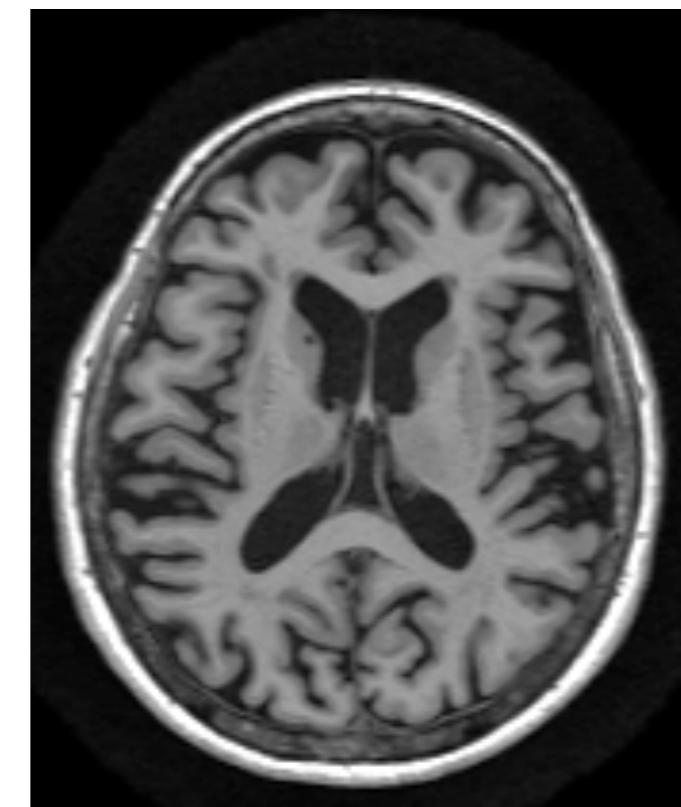
Follow-up scan



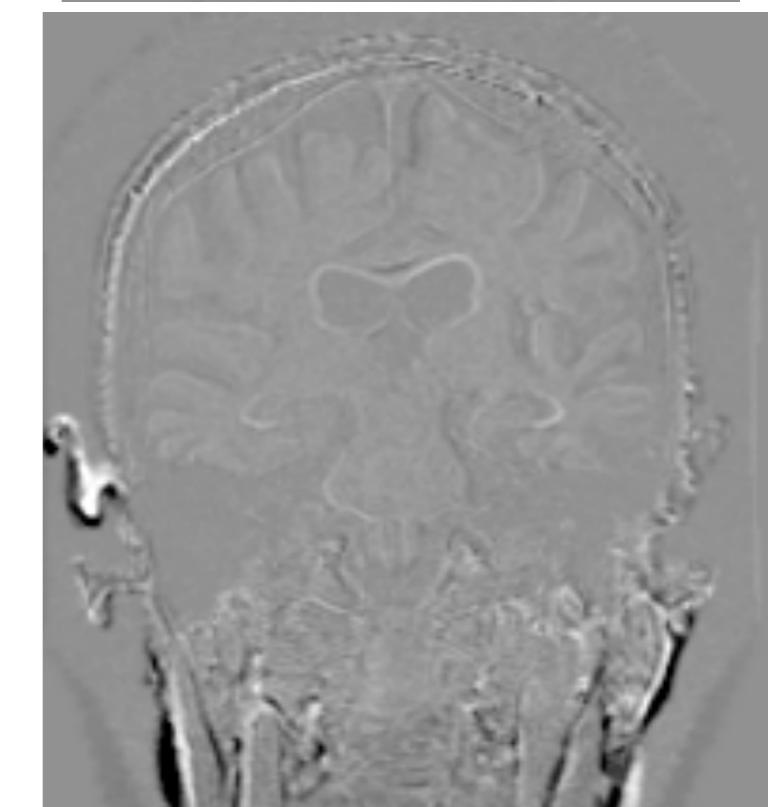
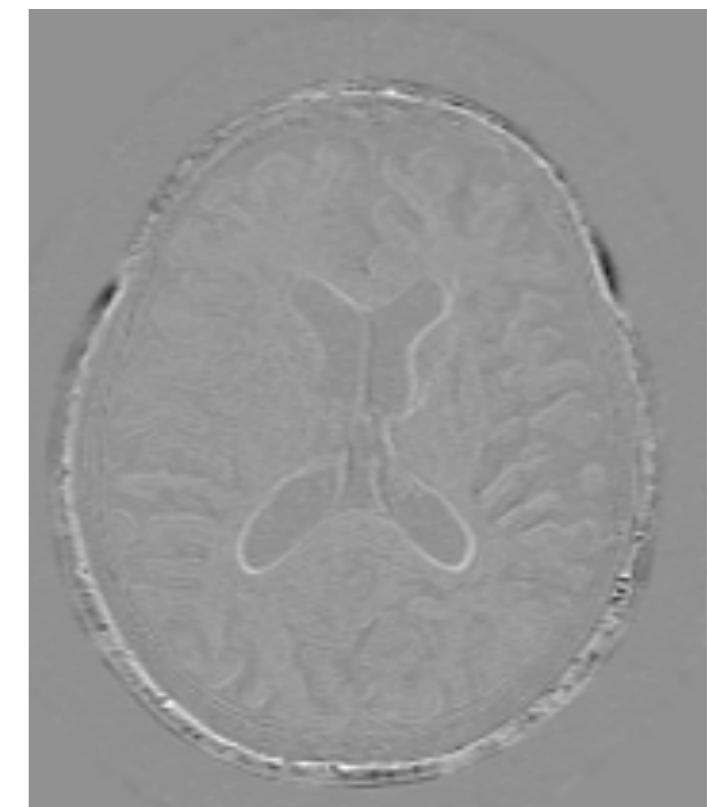
Difference image



Baseline scan

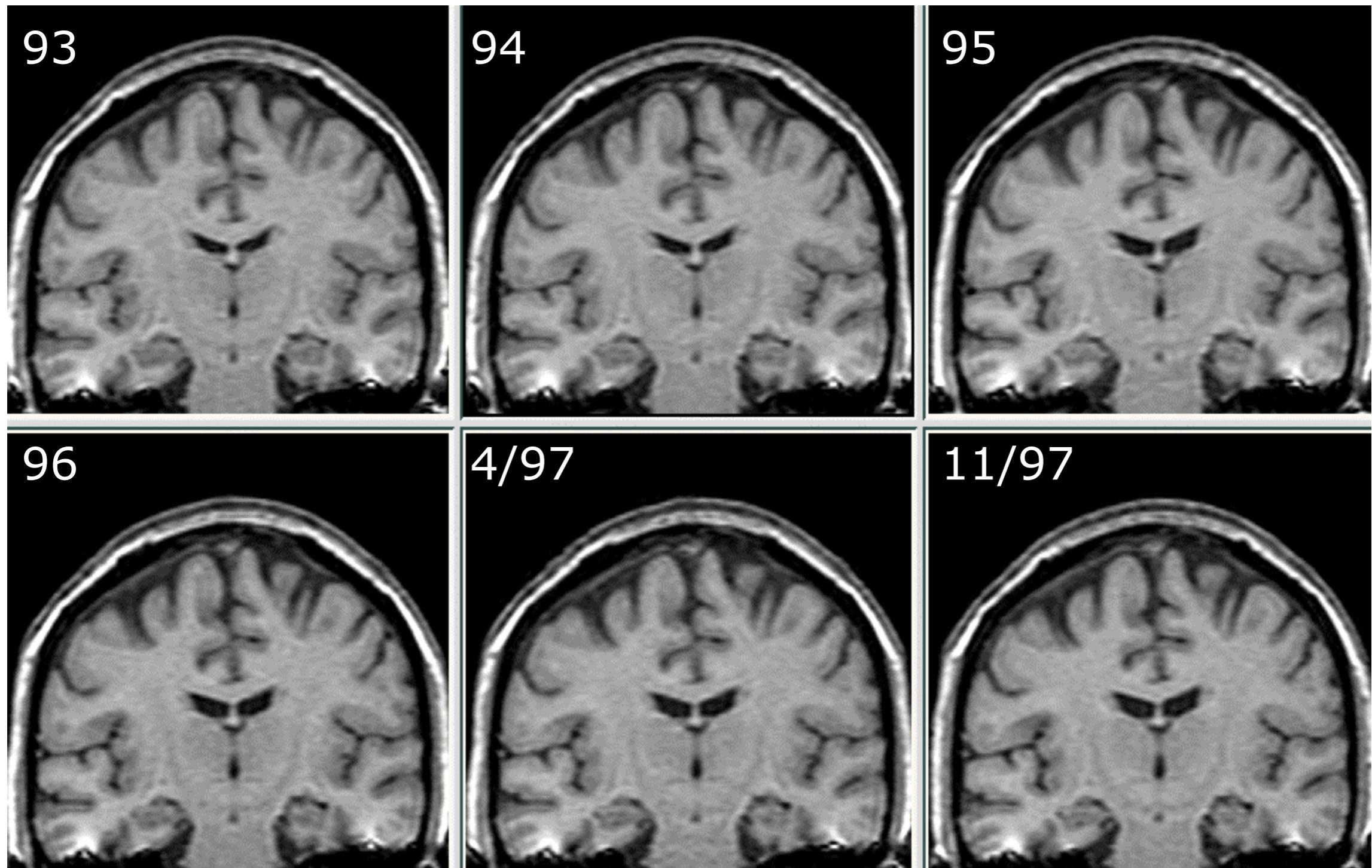


Follow-up scan



Difference image

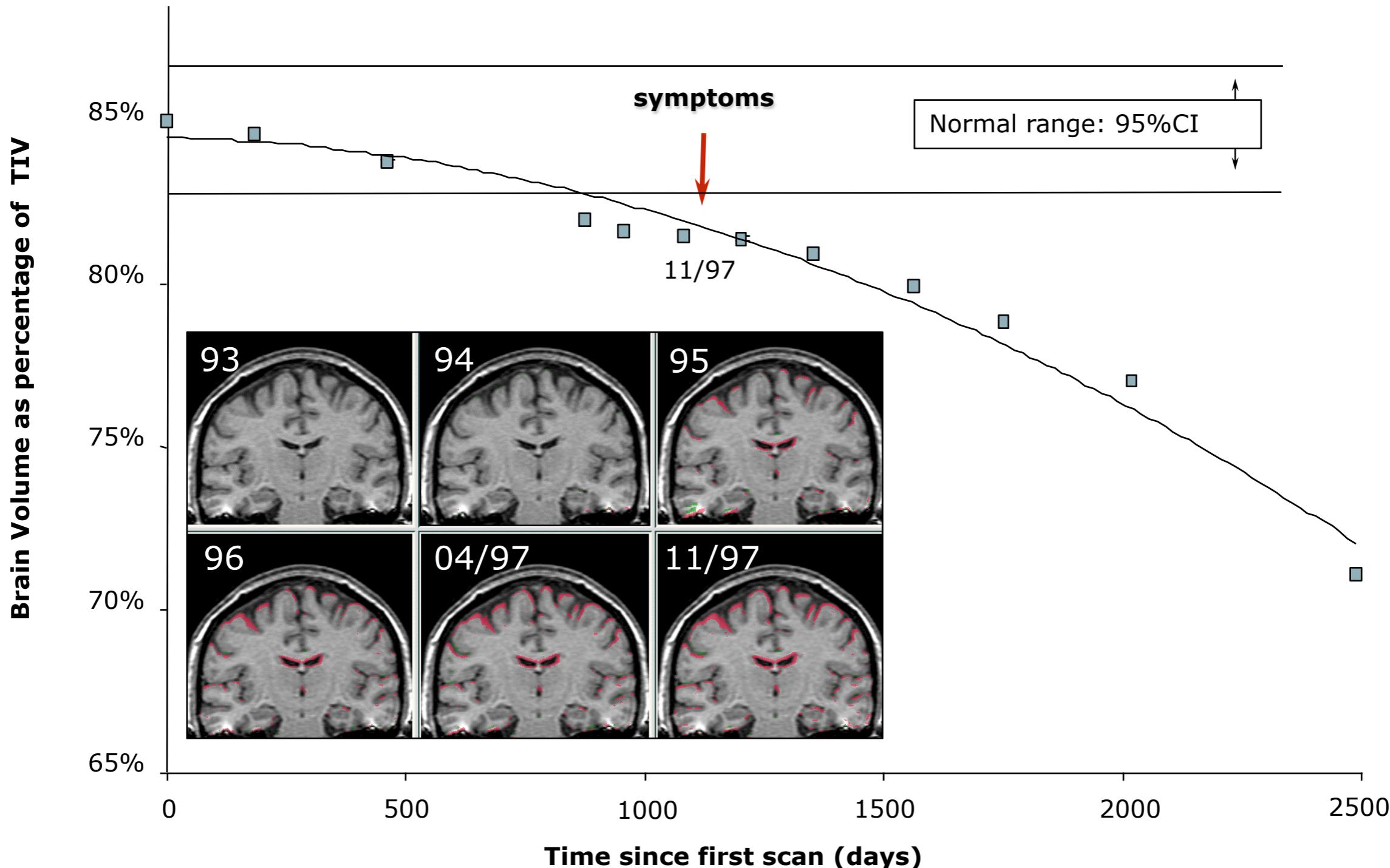
# Brain atrophy - 4-year longitudinal study



AD: At risk subject - serial scans registered to 1993 baseline

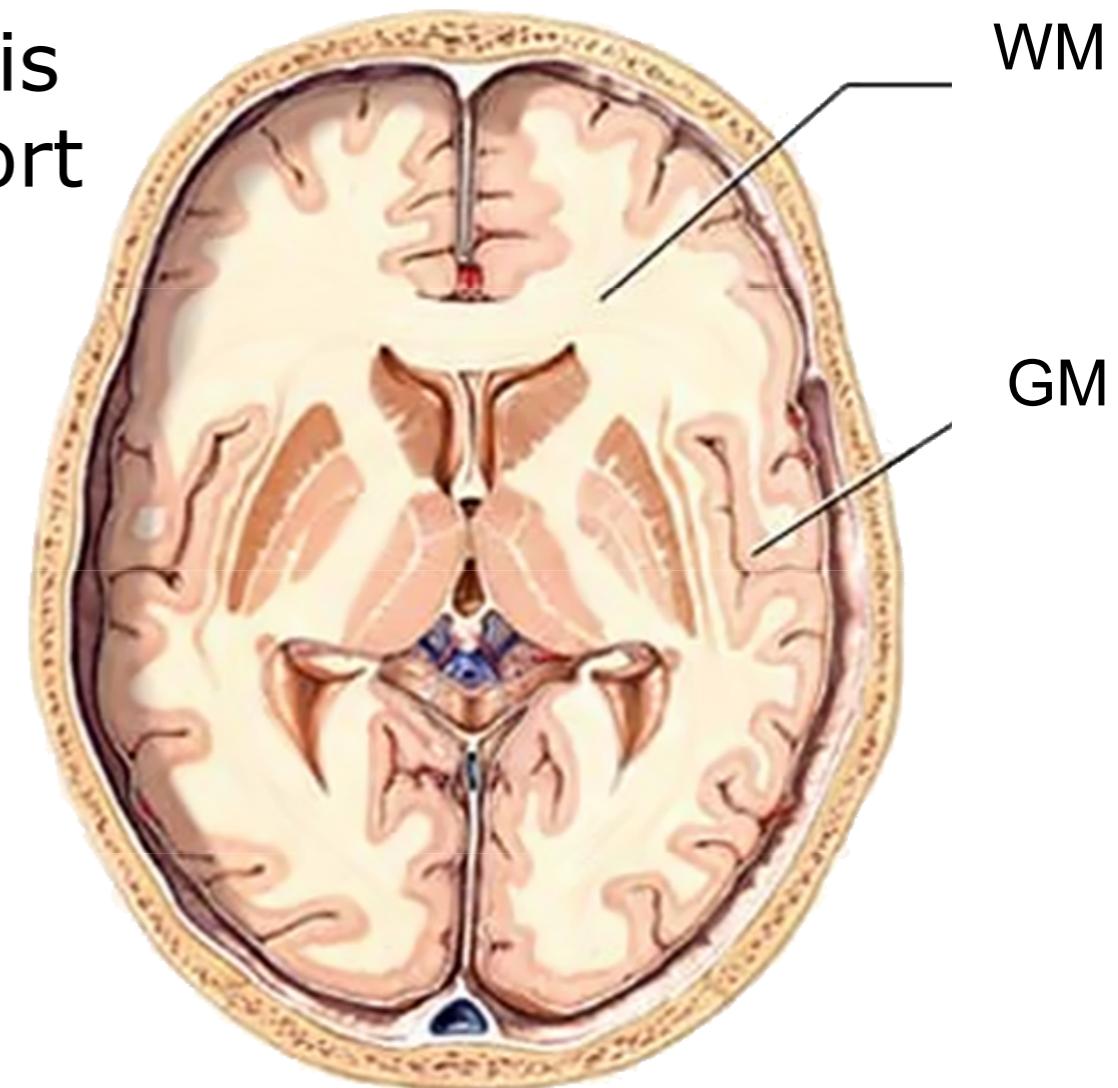
# Brain atrophy

## Detect changes before clinical symptoms



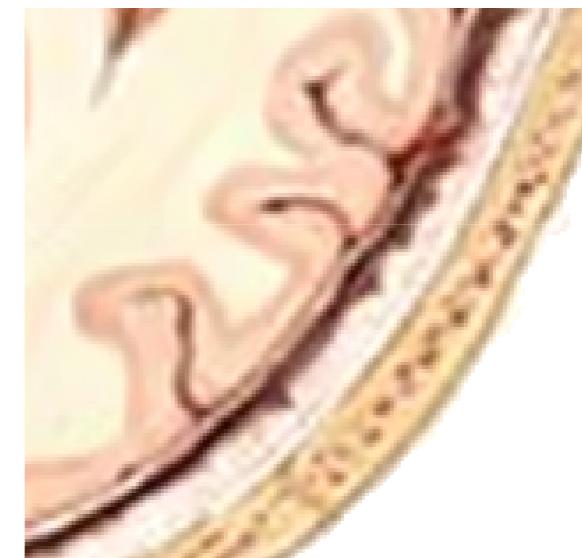
# Cortical thickness

- Cortical thickness is at promising biomarkers for neurodegenerative disease progression.
- Leading to:
  - Earlier and more robust diagnosis
  - Reduction in the size of the cohort for the same statistical power in clinical studies



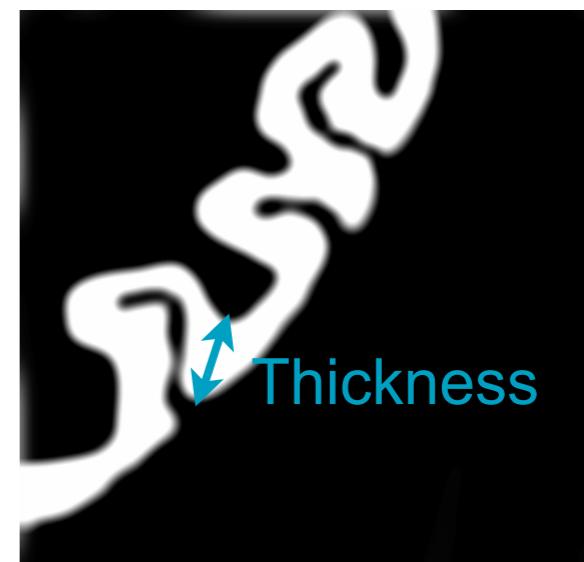
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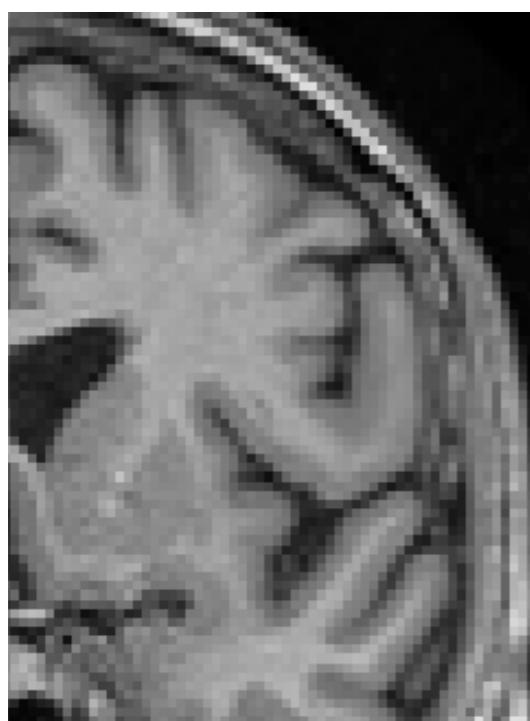
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# Cortical thickness

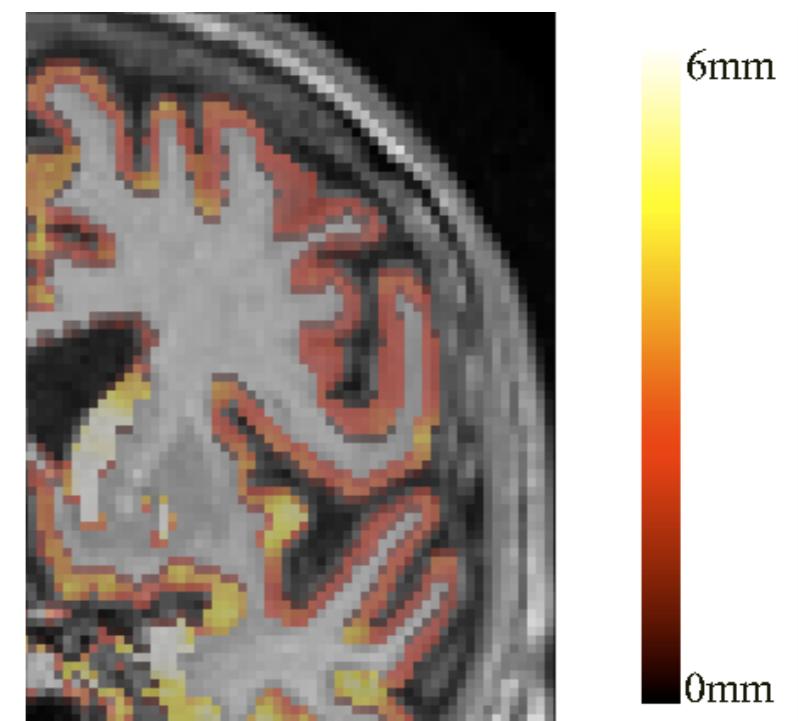
- Segmentation of the cortex
  - Very convoluted surfaces
  - Differentiate at least three kinds of tissues (GM, WM, CSF)
  - Inhomogeneities in intensity (bias field correction)
- Estimation of the cortex thickness



Original MRI

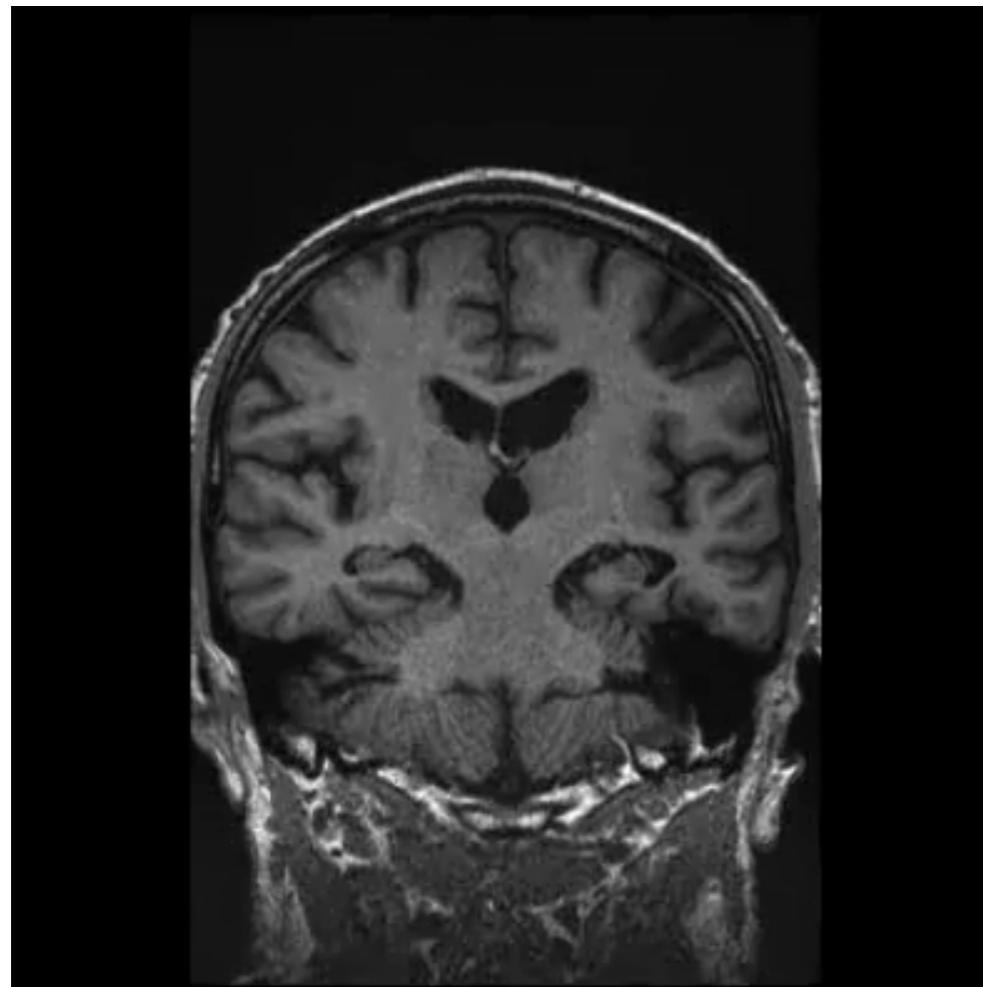


Segmentation

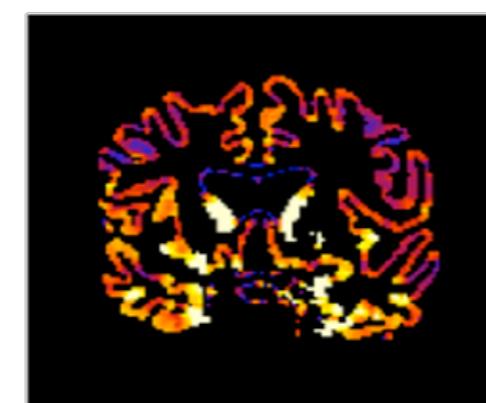
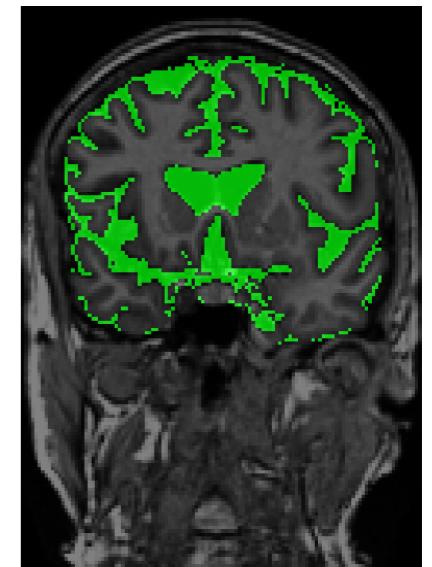
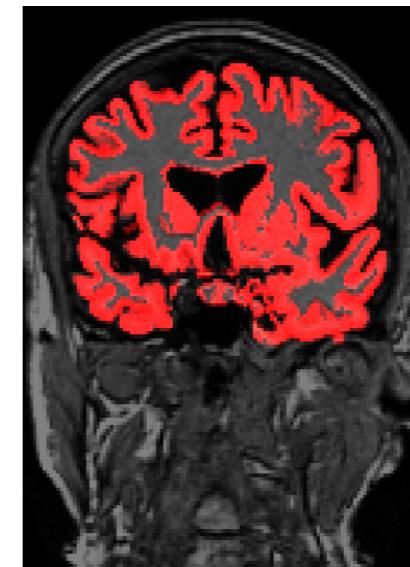
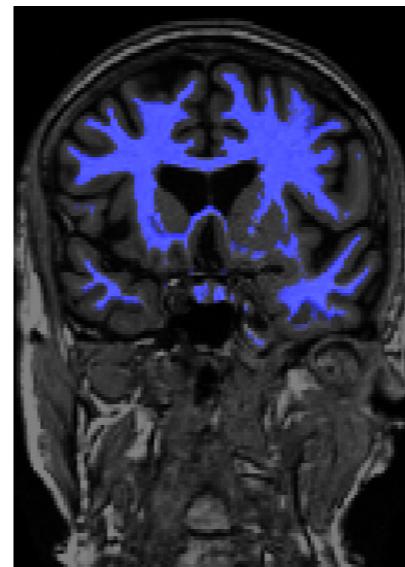


Cortical thickness  
estimation

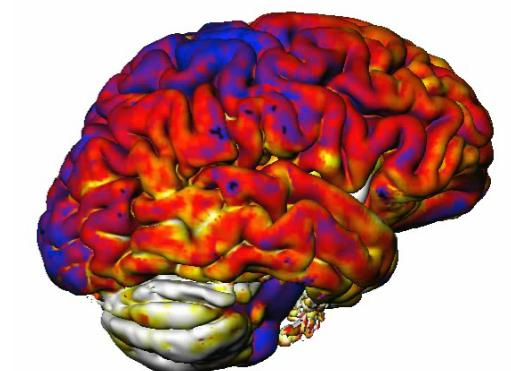
# Brain tissue segmentation



Evolution/convergence of  
an Expectation  
Maximisation (EM)  
algorithm for brain tissue  
segmentation



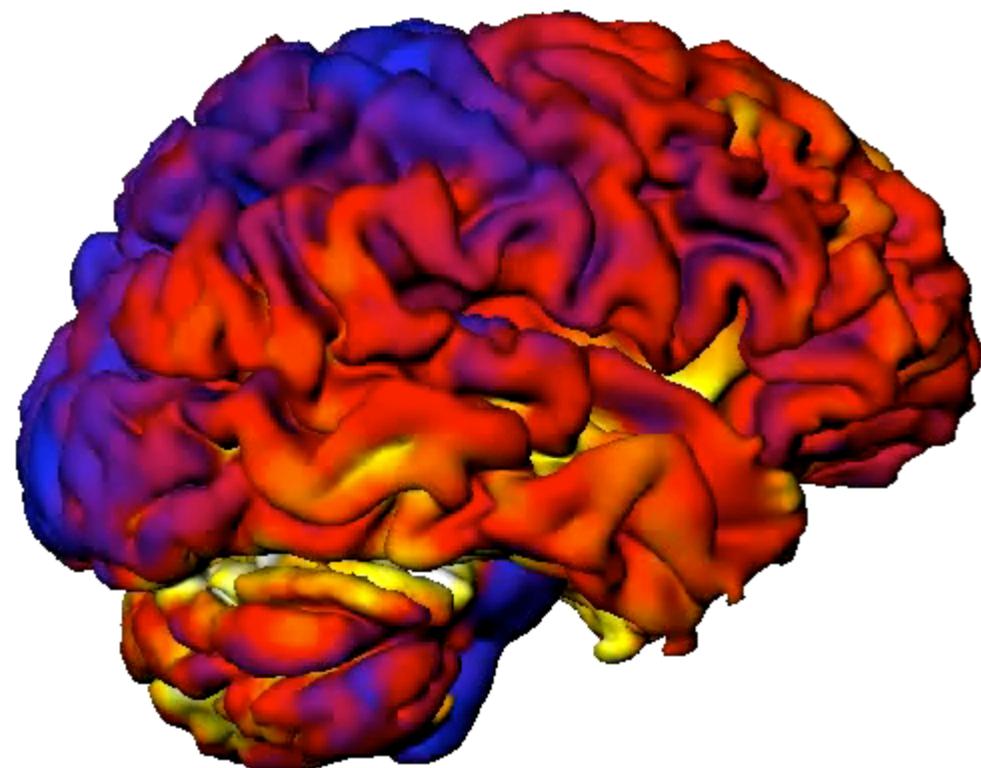
GM thickness map



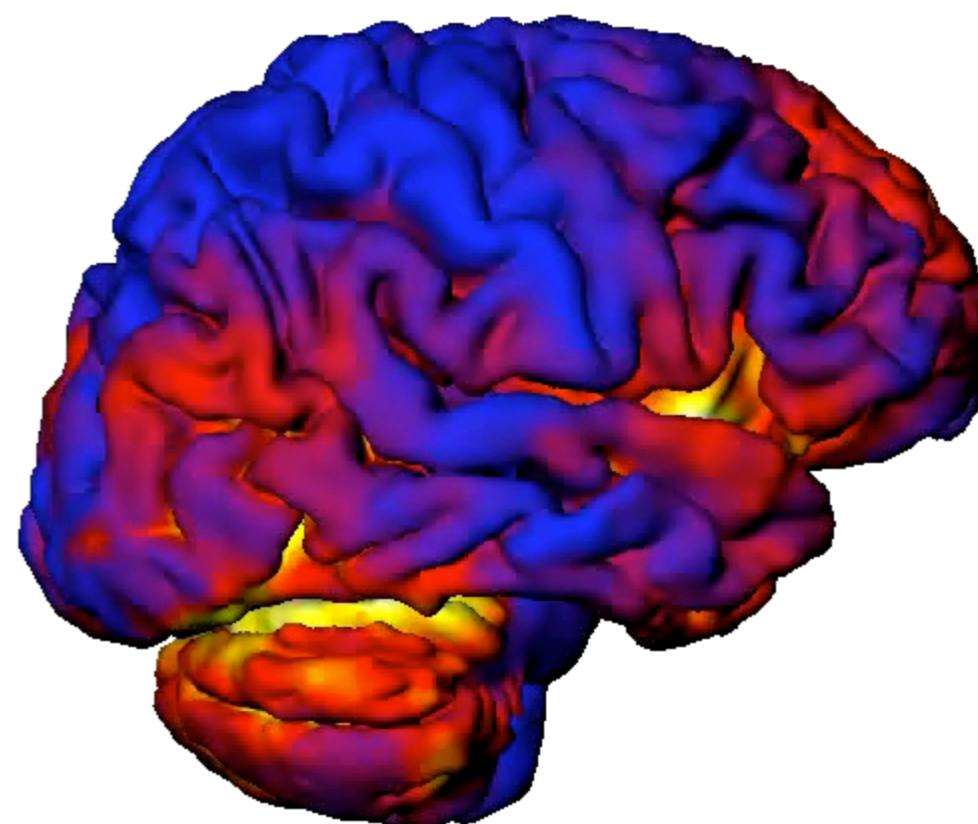
3D representation

# Brain tissue segmentation

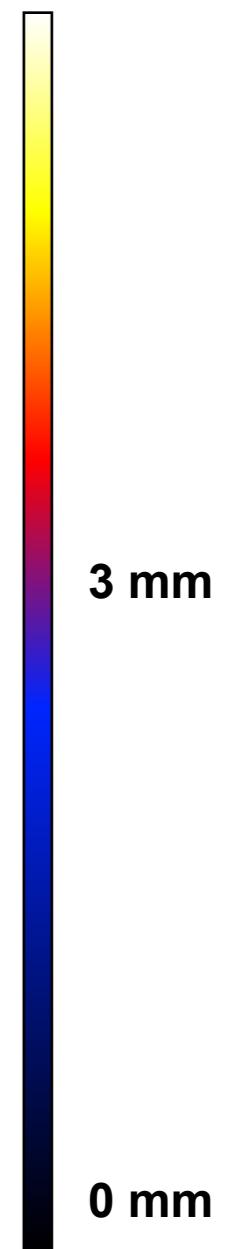
- Significant differences between AD and NC in the temporal, parietal and occipital



70 Years old normal control

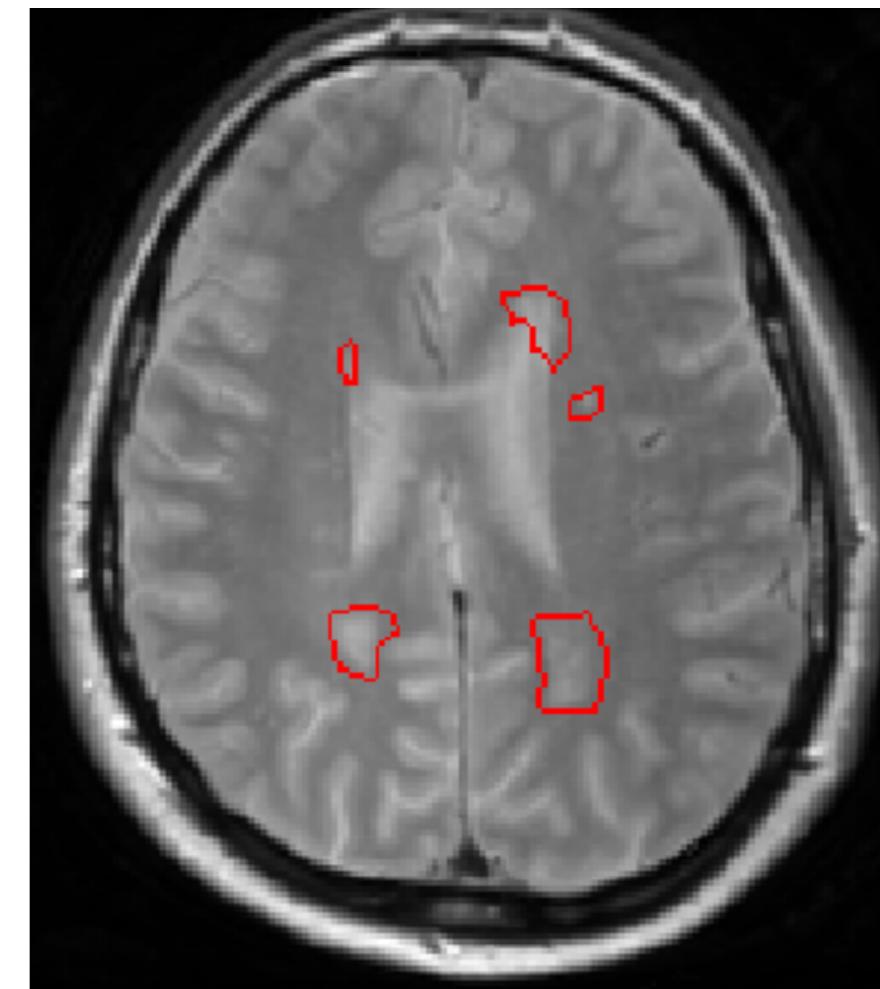
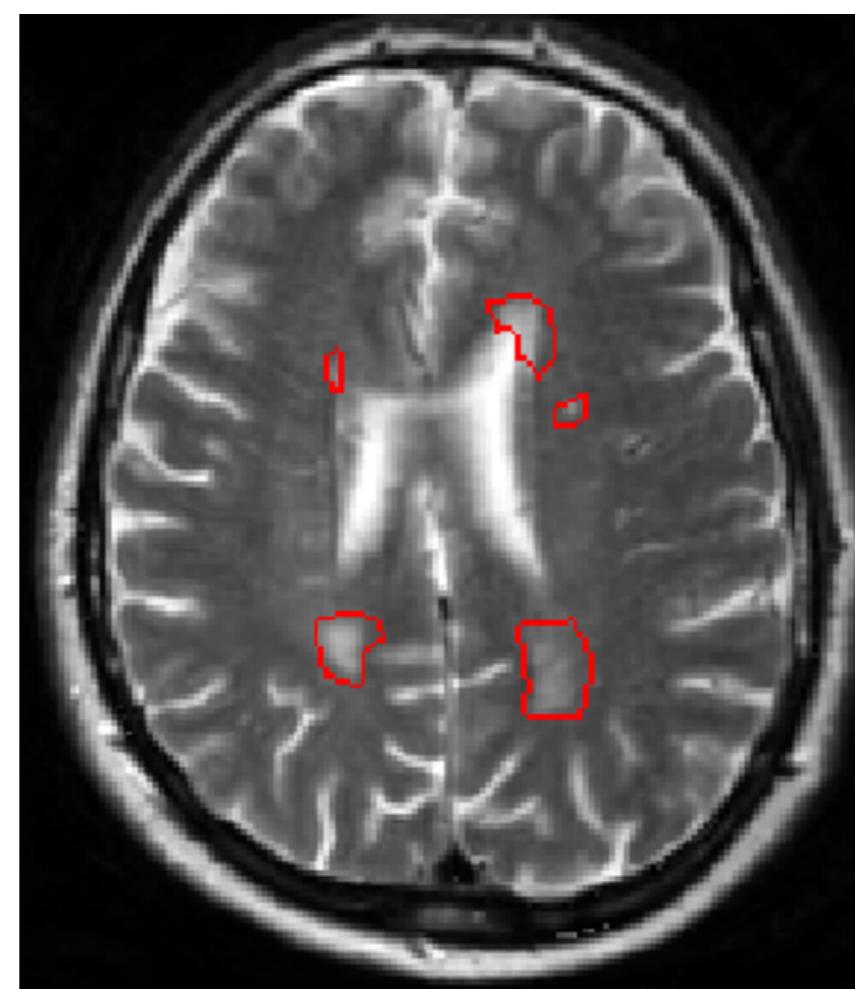
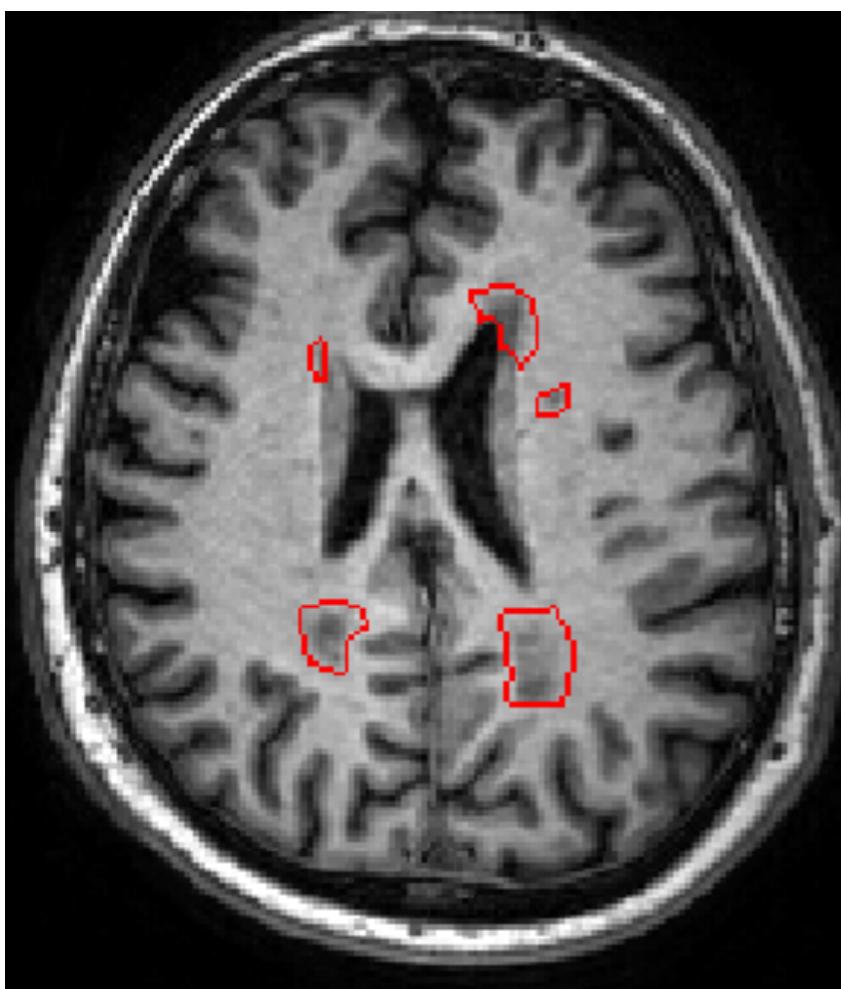


70 Years old Alzheimer's disease subject

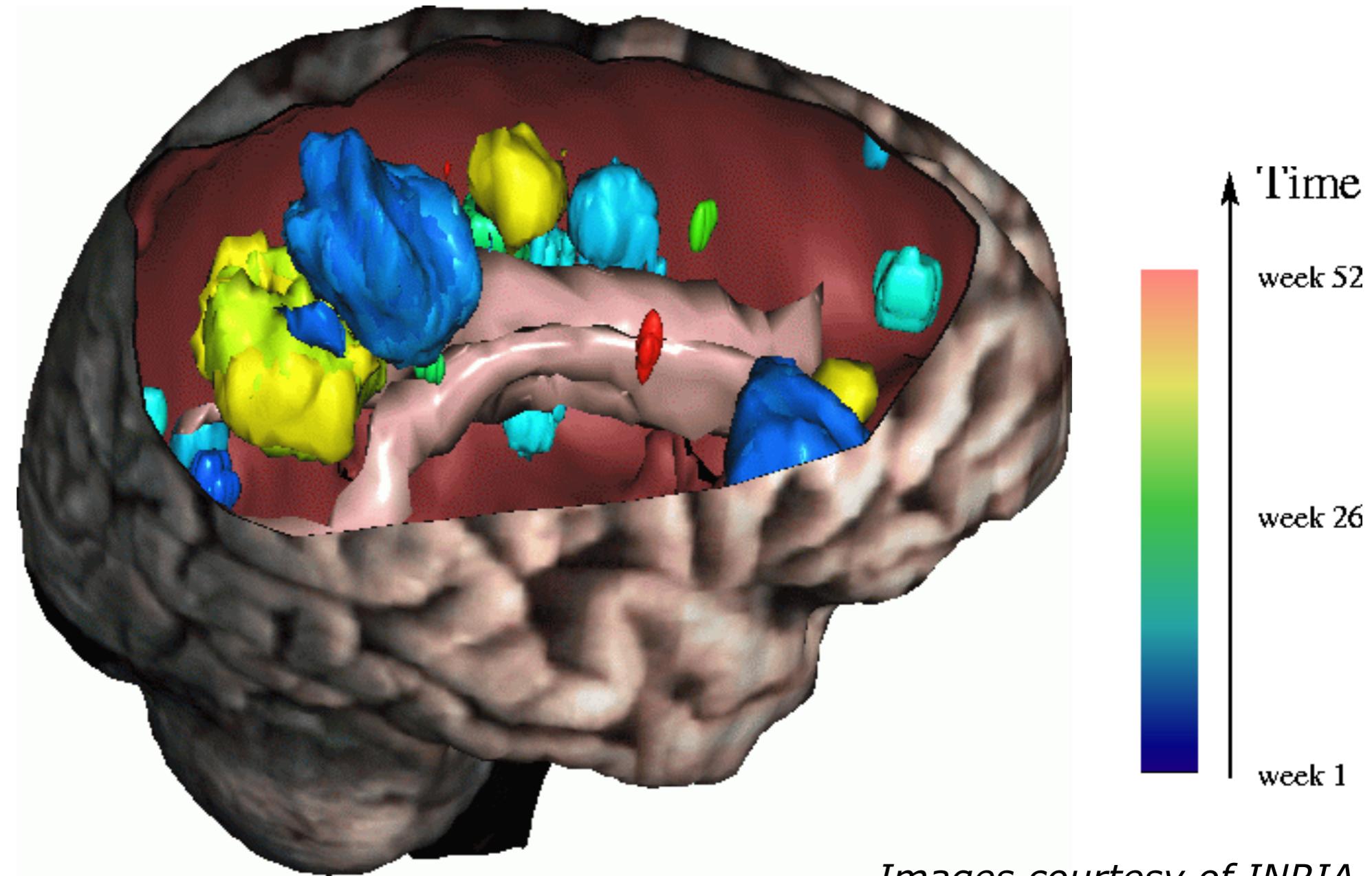
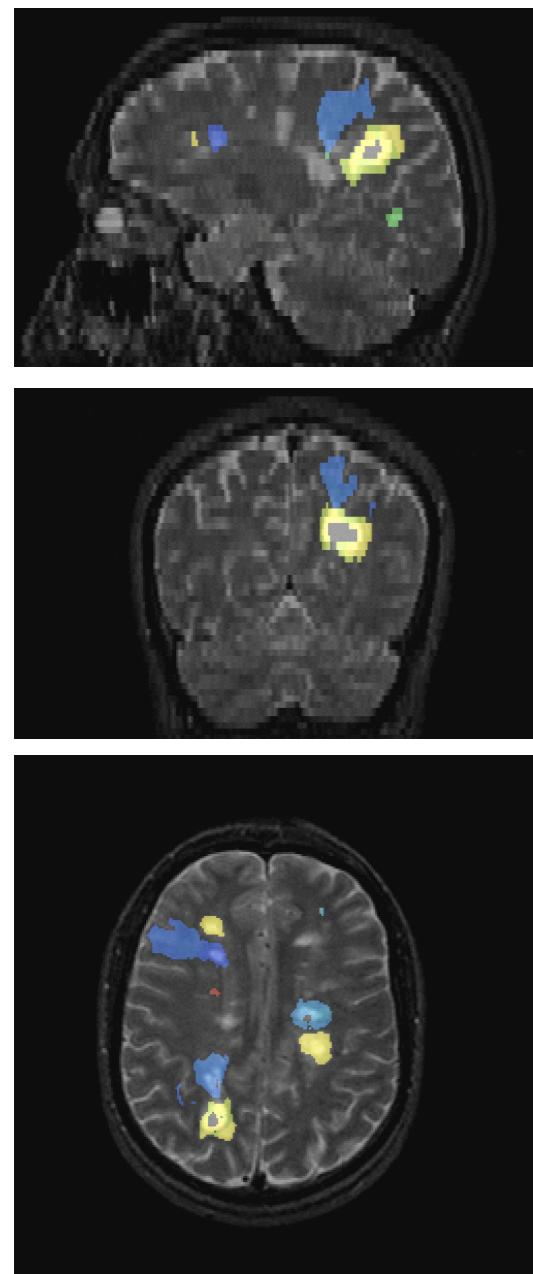


# Multiple Sclerosis

- Examples of white matter lesions visible on MRI



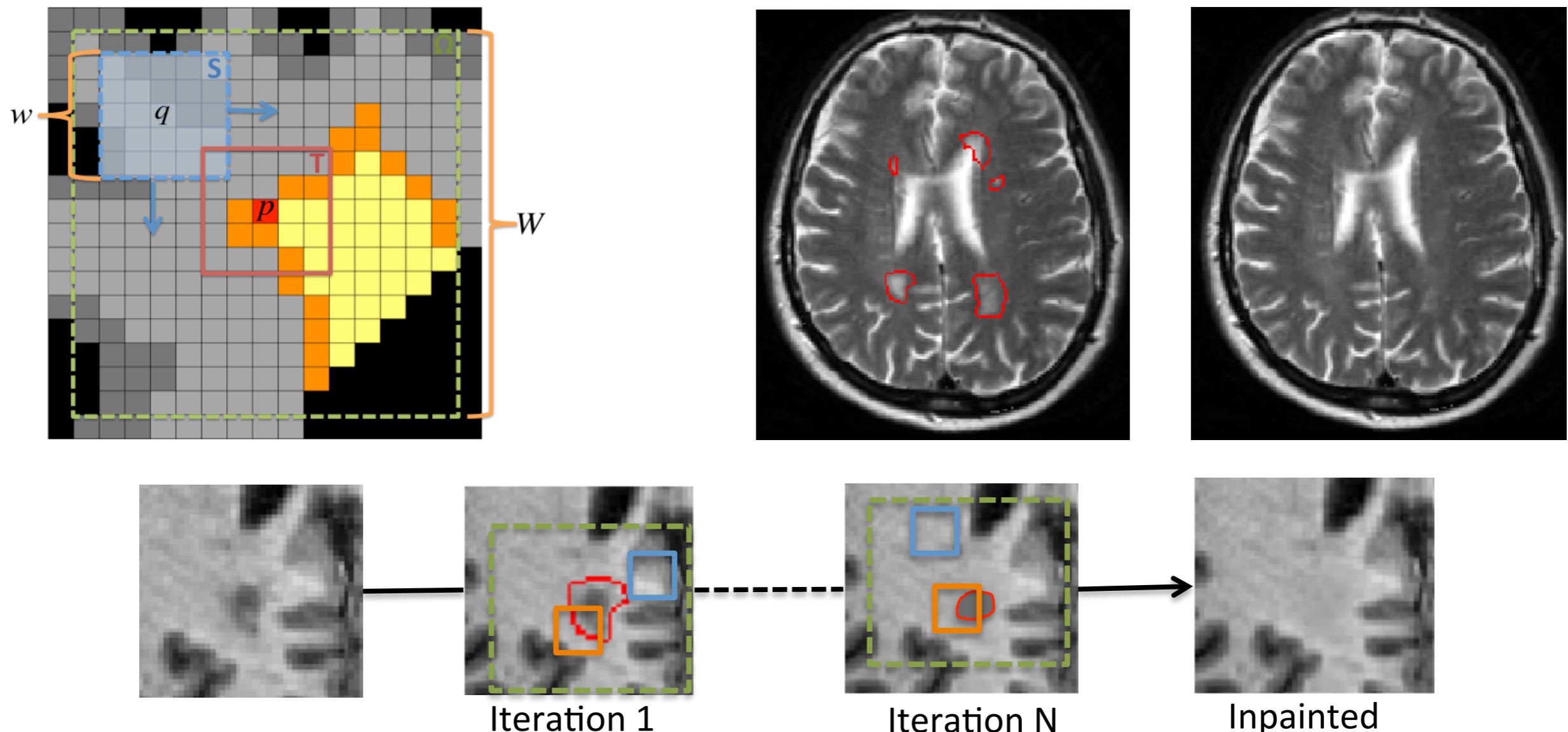
# Temporal evolution of multiple Sclerosis



*Images courtesy of INRIA*

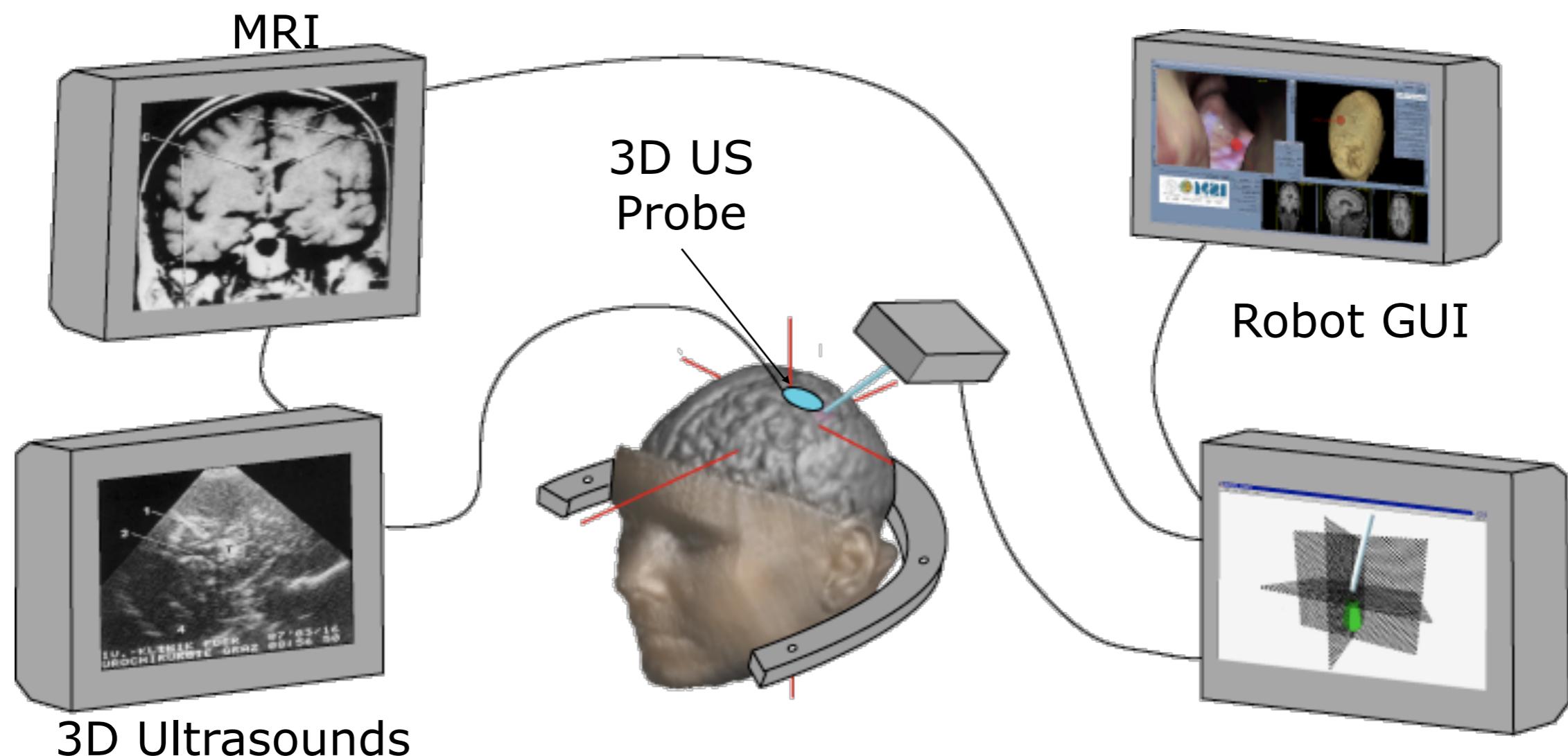
# Multiple Sclerosis

- Lesions can have an impact on processing pipeline using for example registration or segmentation



# Image guided neurosurgery - MRI/US

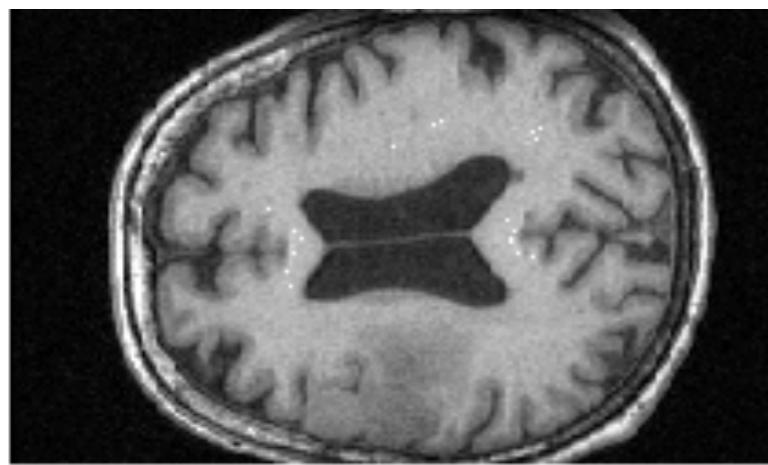
- Endoscopic Neurosurgery assisted by robotics and images



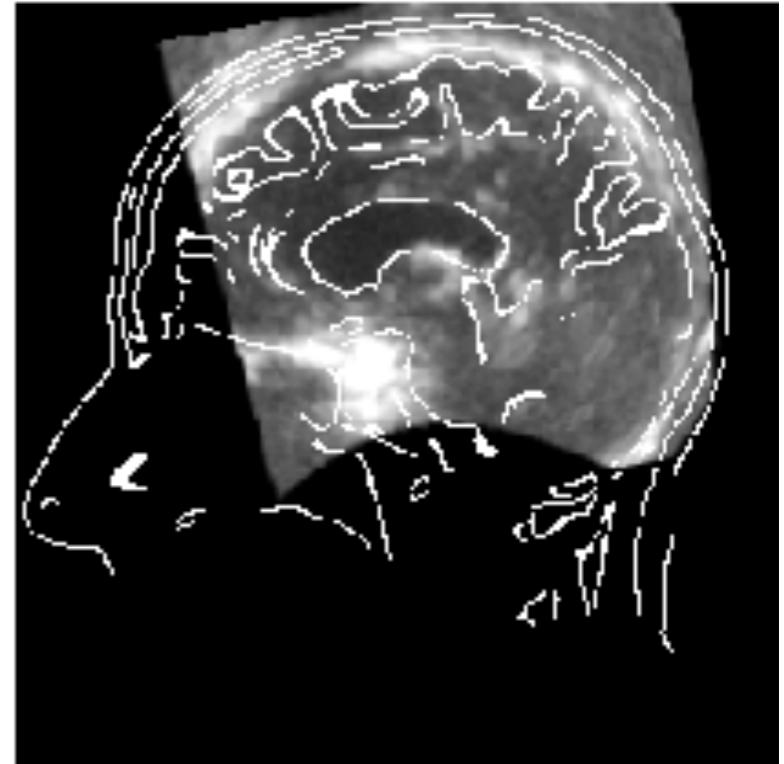
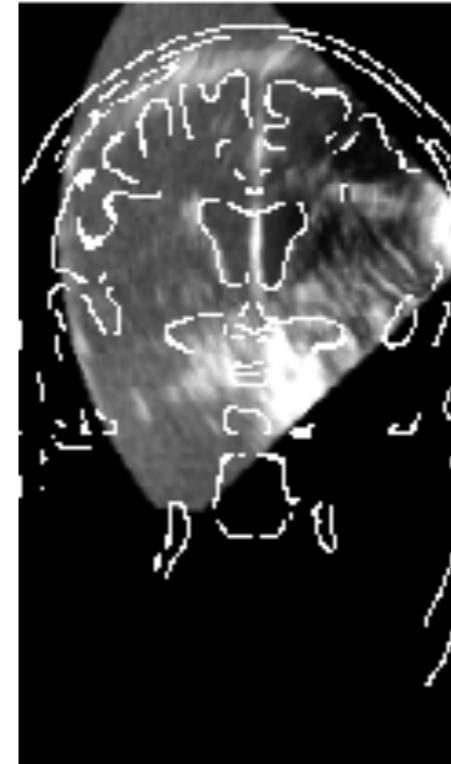
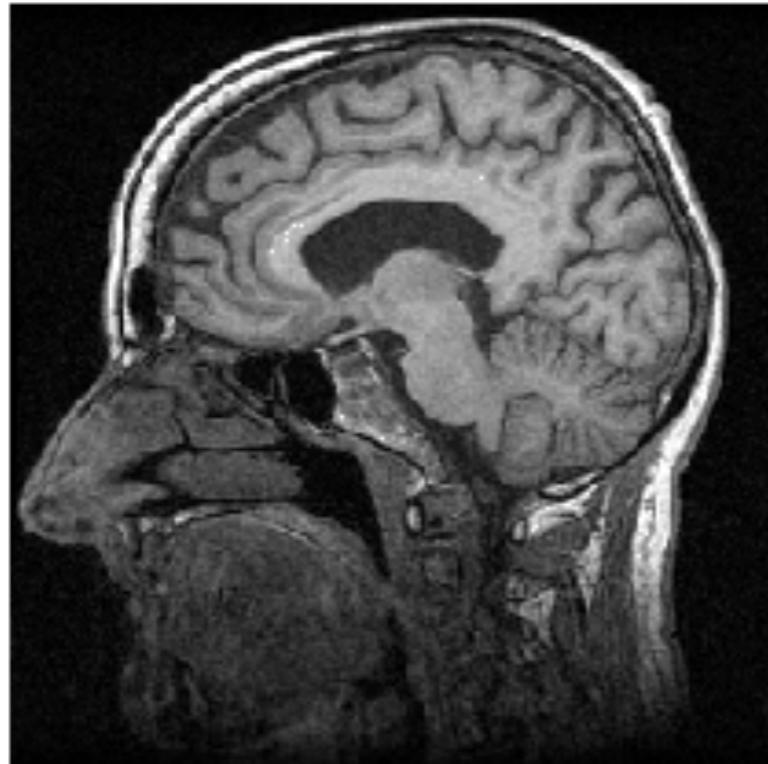
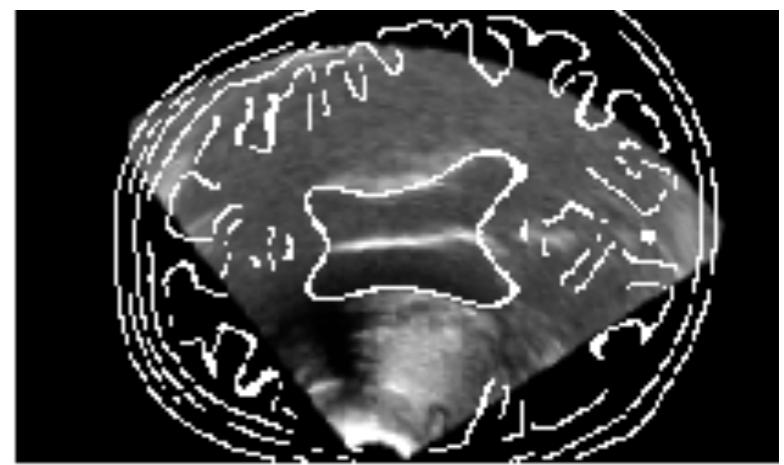
Courtesy Brian Davies

# Image guided neurosurgery - MRI/US

Pre-operative  
MRI

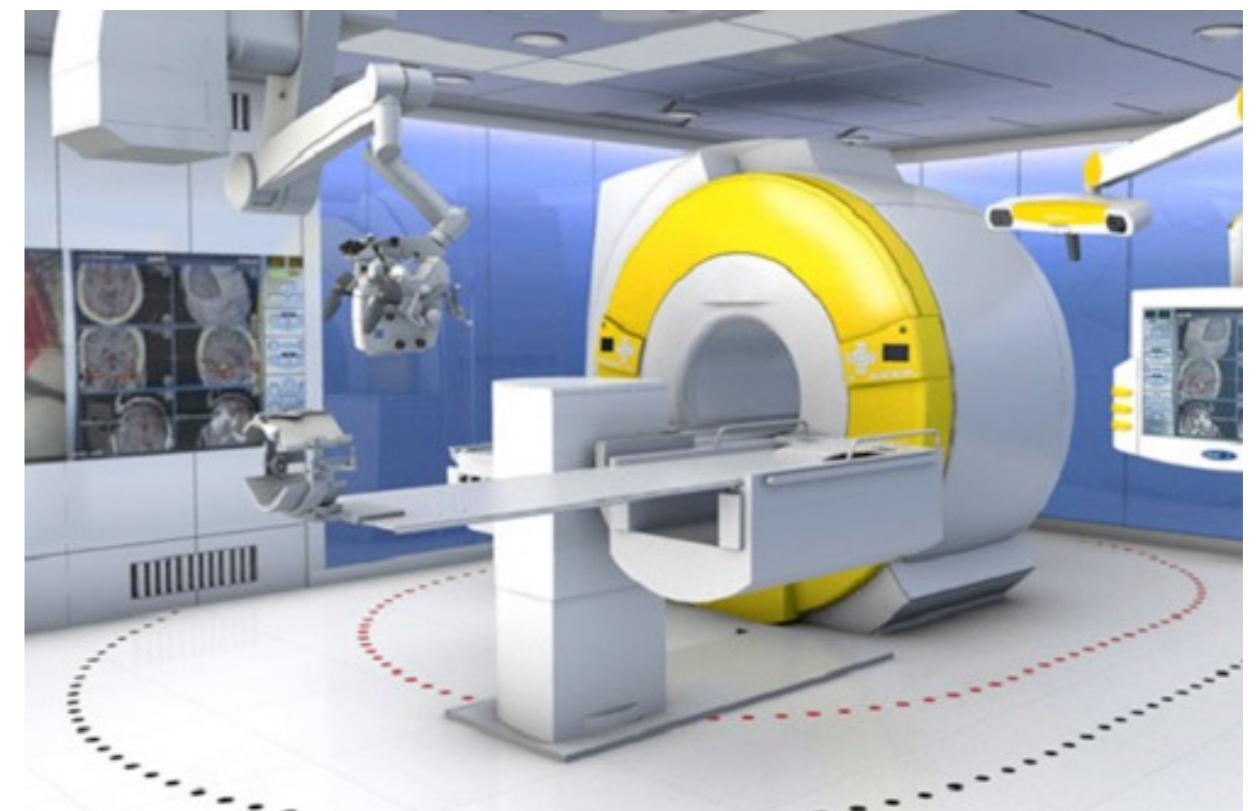


Registered  
MRI-US



# Interventional MRI facility at Queen's Square, IoN, UCL

- Standard 1.5T MRI scanner with 8-element array coil capable of full diagnostic imaging.
- BrainLAB VectorVision Sky with Cranial navigation



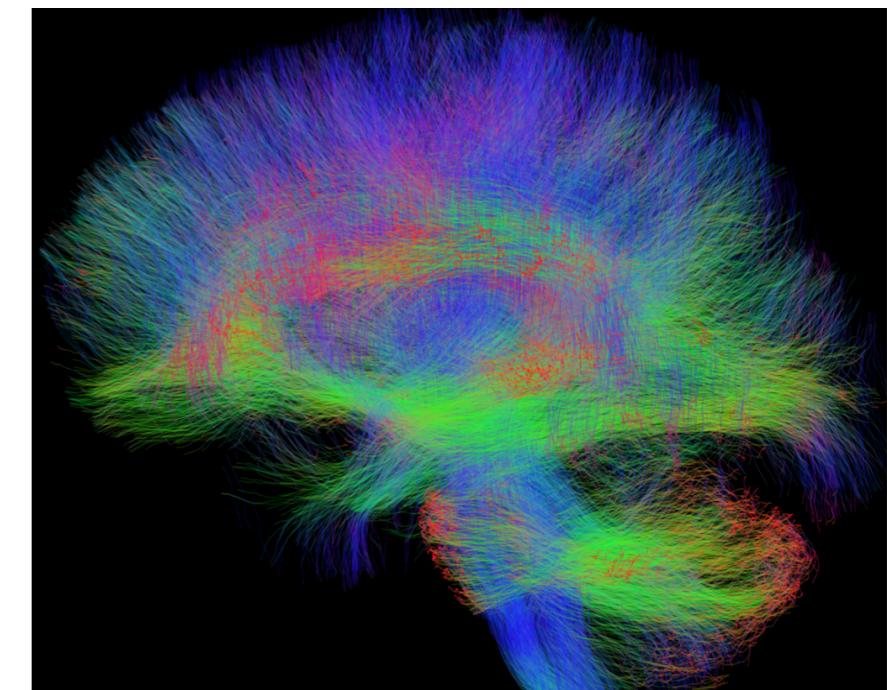
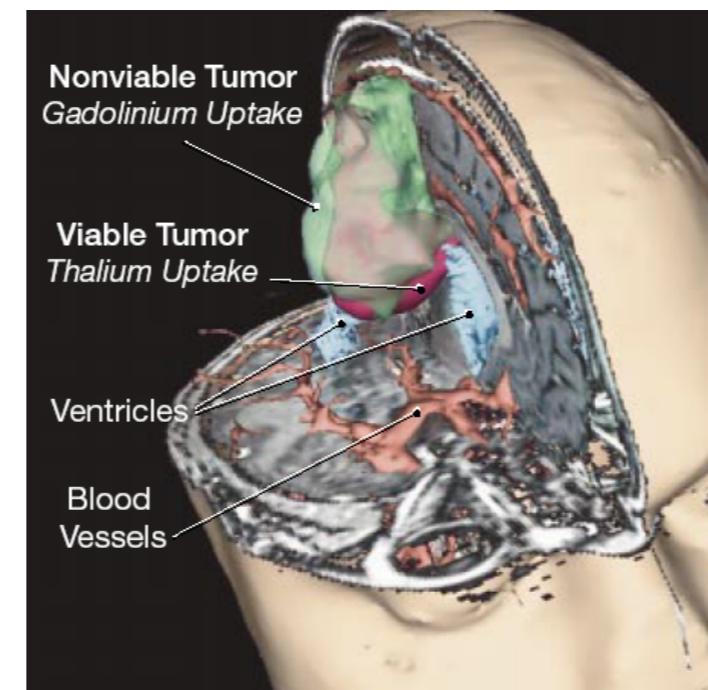
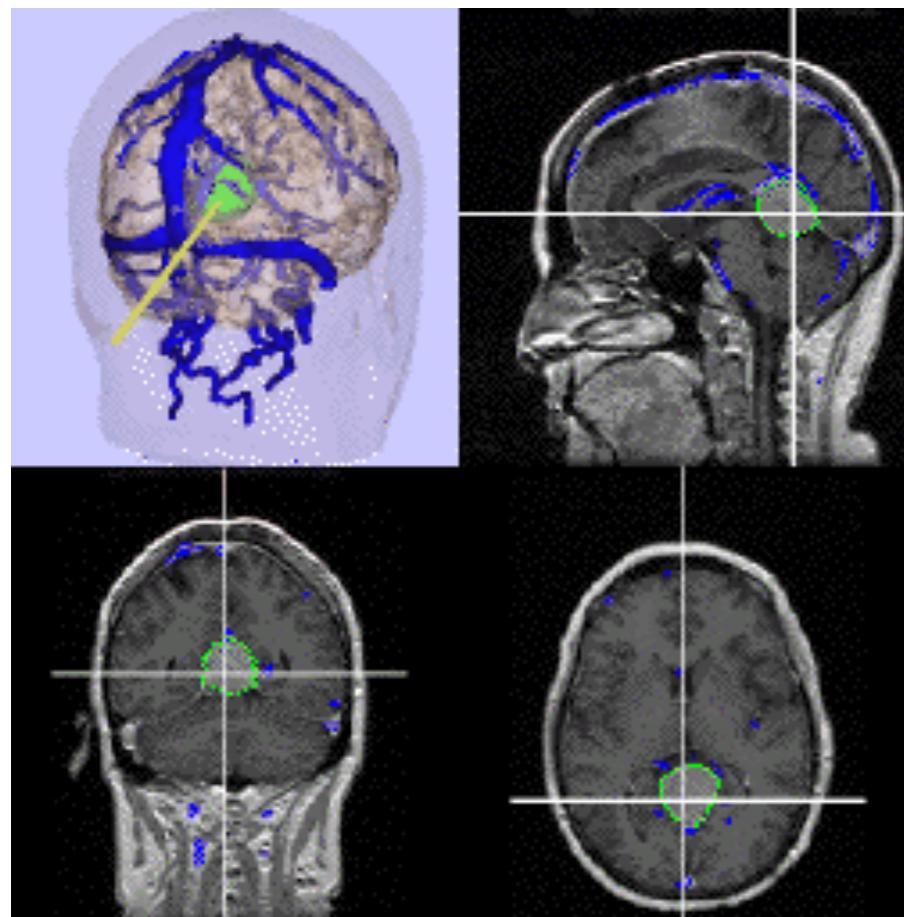
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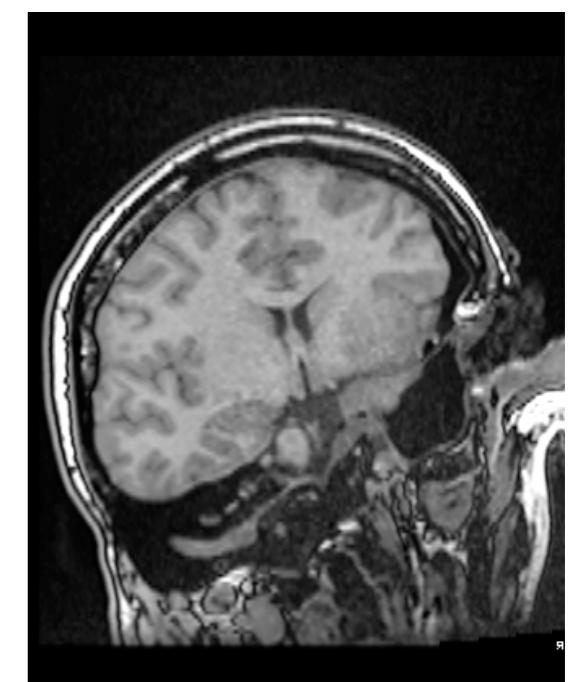
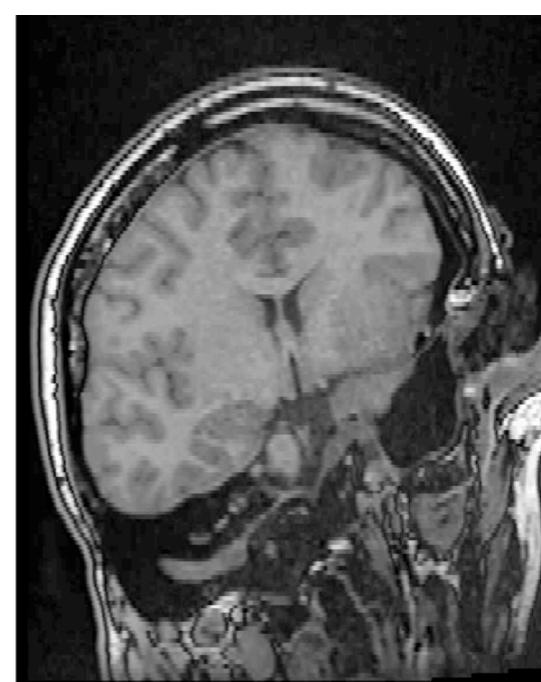
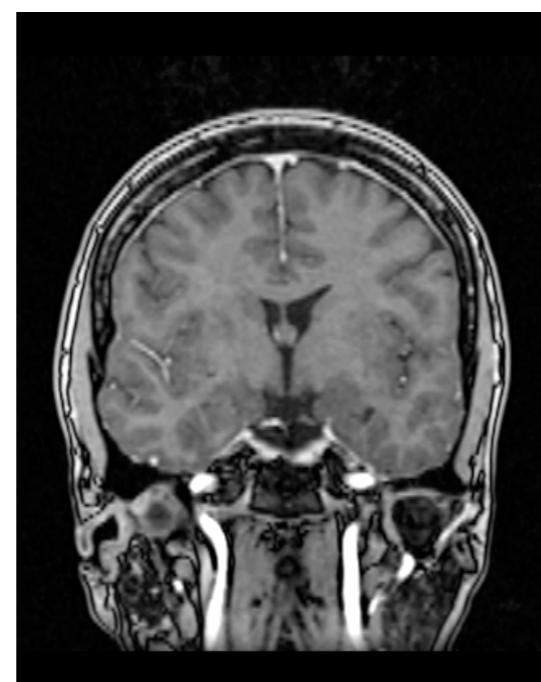
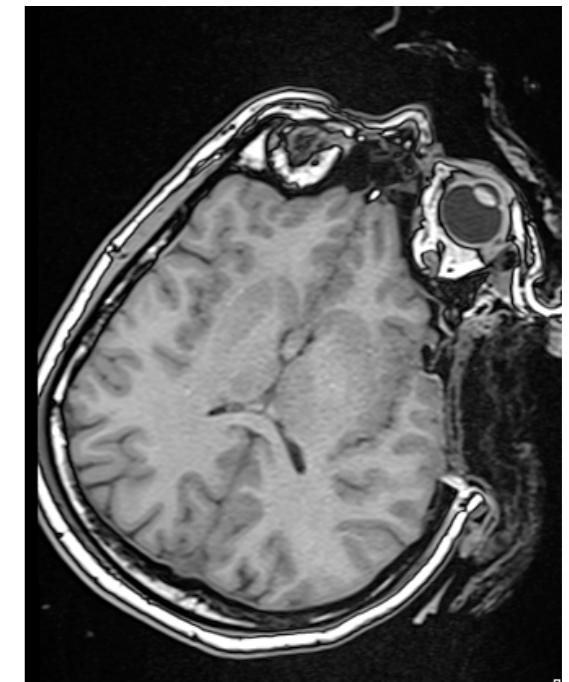
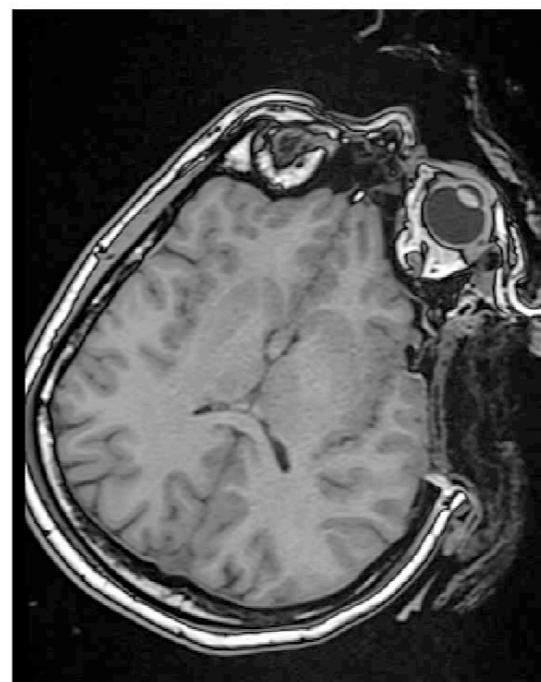
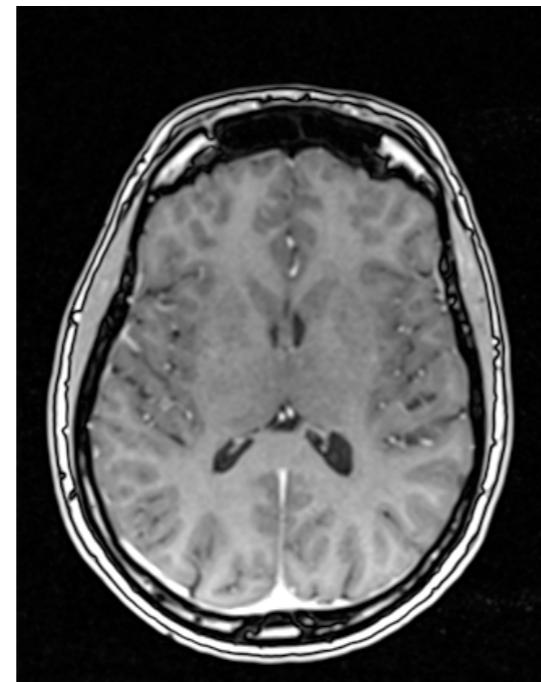
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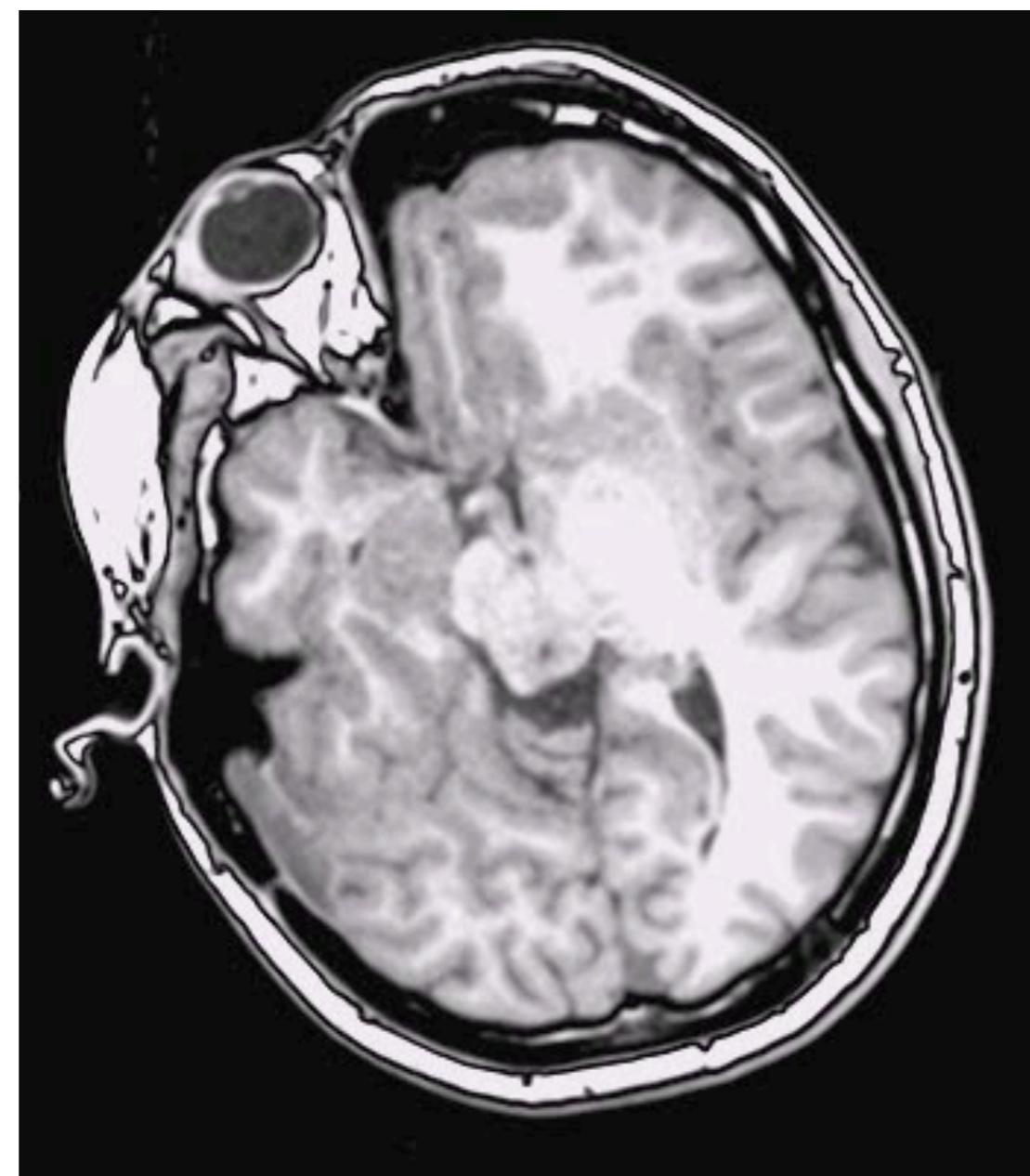
# Updating Surgical Planning during the intervention

- Brain Shift correction



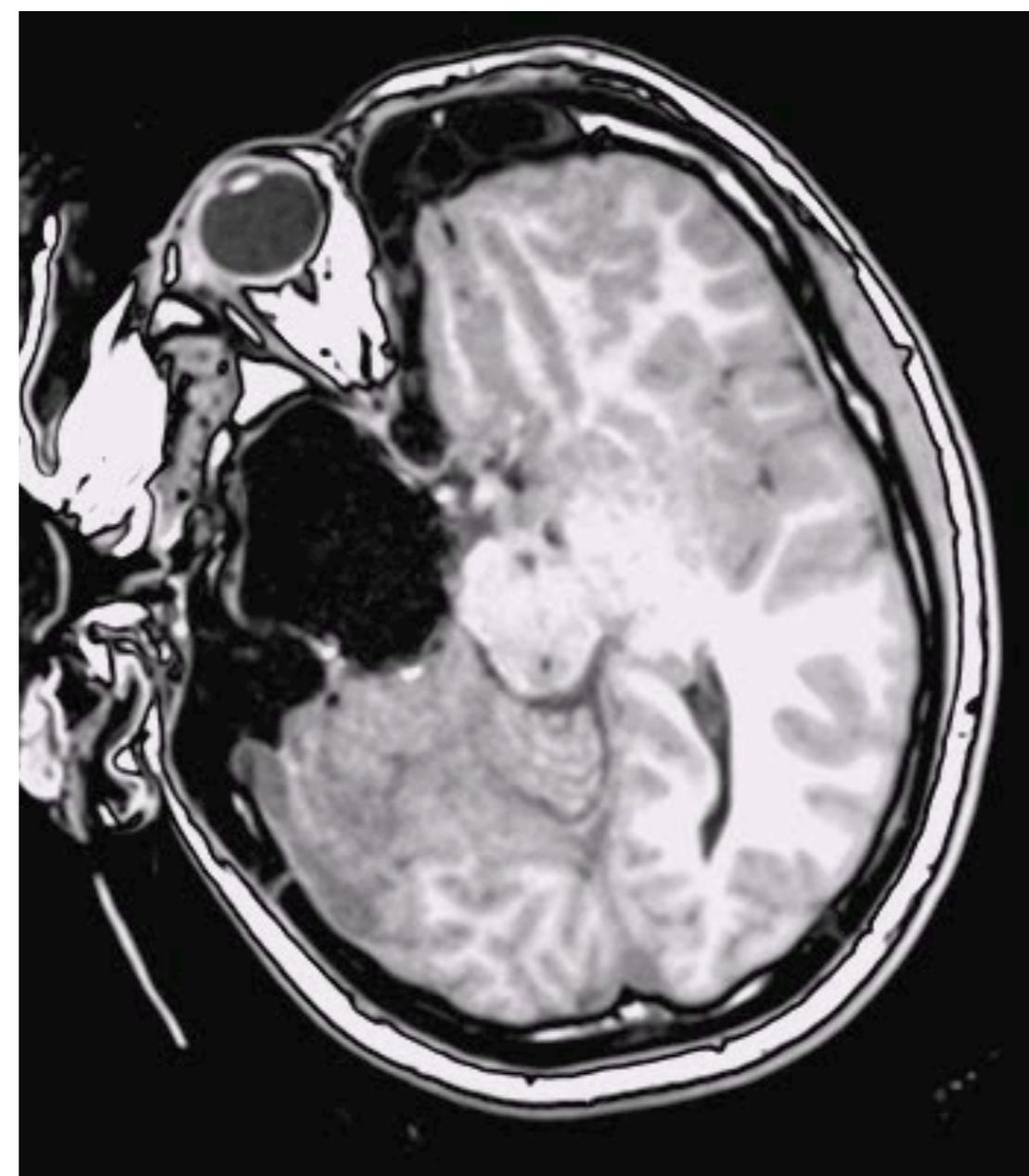
# Updating Surgical Planning during the intervention

- Optic Radiation tracking (first intra-op scan)

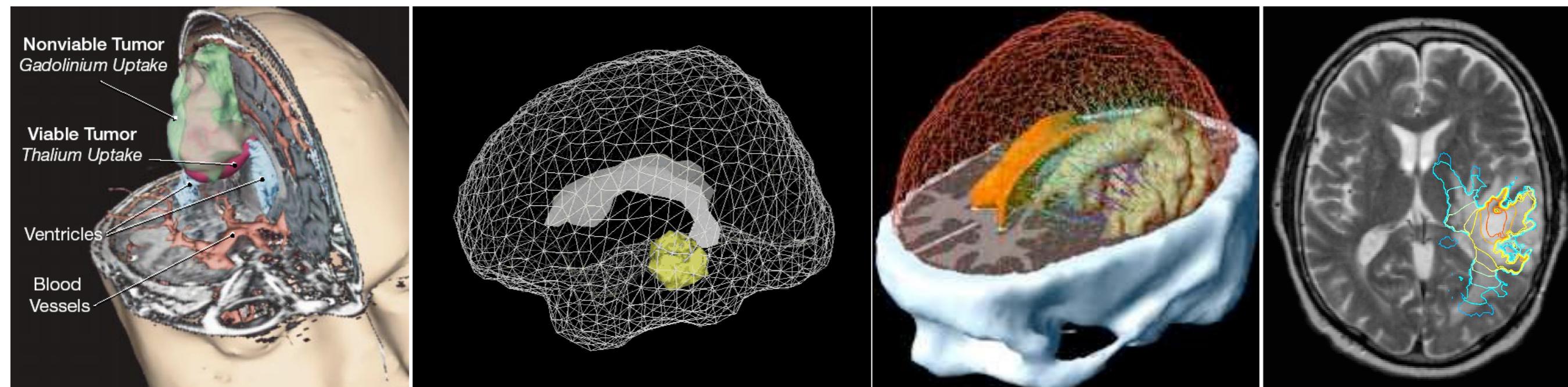


# Updating Surgical Planning during the intervention

- Optic Radiation tracking (first intra-op scan)



# Creation of Body Double Patient Specific Biomechanical Model and Growth evolution



Patient specific modelling

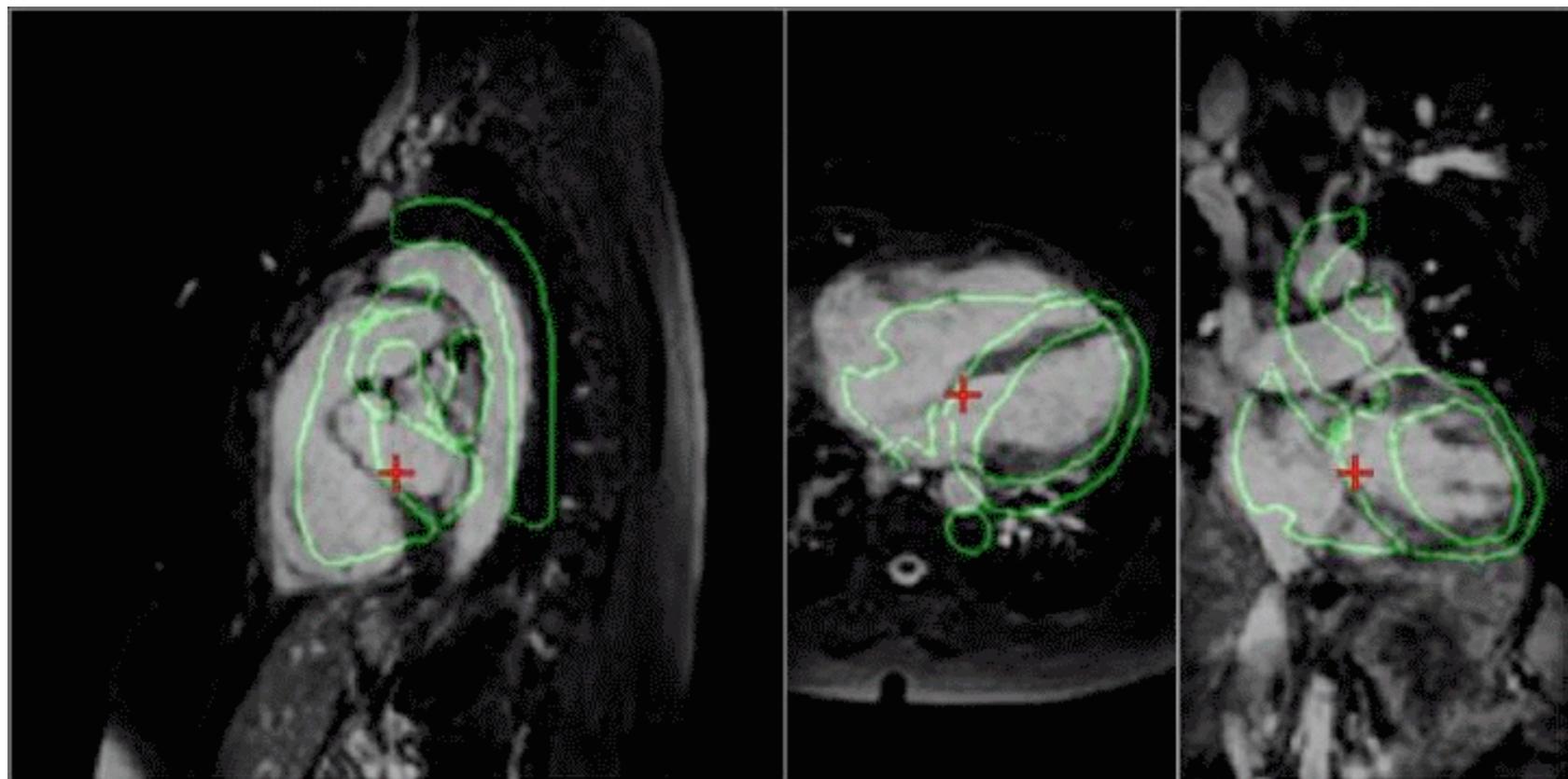
*Courtesy of INRIA and Brigham & Women's Hospital*

# Cardiovascular application

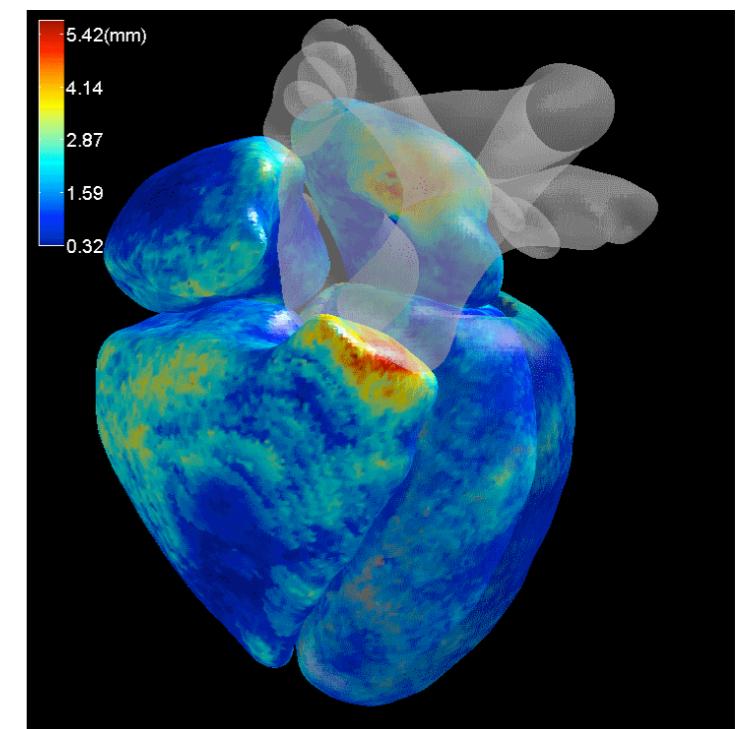
- Measuring cardiac ejection fraction, wall motion
  - segmentation of ventricles and myocardium.
- Catheter-based Interventions
  - align x-ray images with pre-op images.
- Measuring blood flow & Quantifying fat
  - segmenting relevant tissue,
  - quantifying images.
- Atherosclerosis
  - segmenting vessel walls, quantifying stenosis, characterising plaque.

# Cardiovascular application

- Example of heart ventricle segmentation using registration



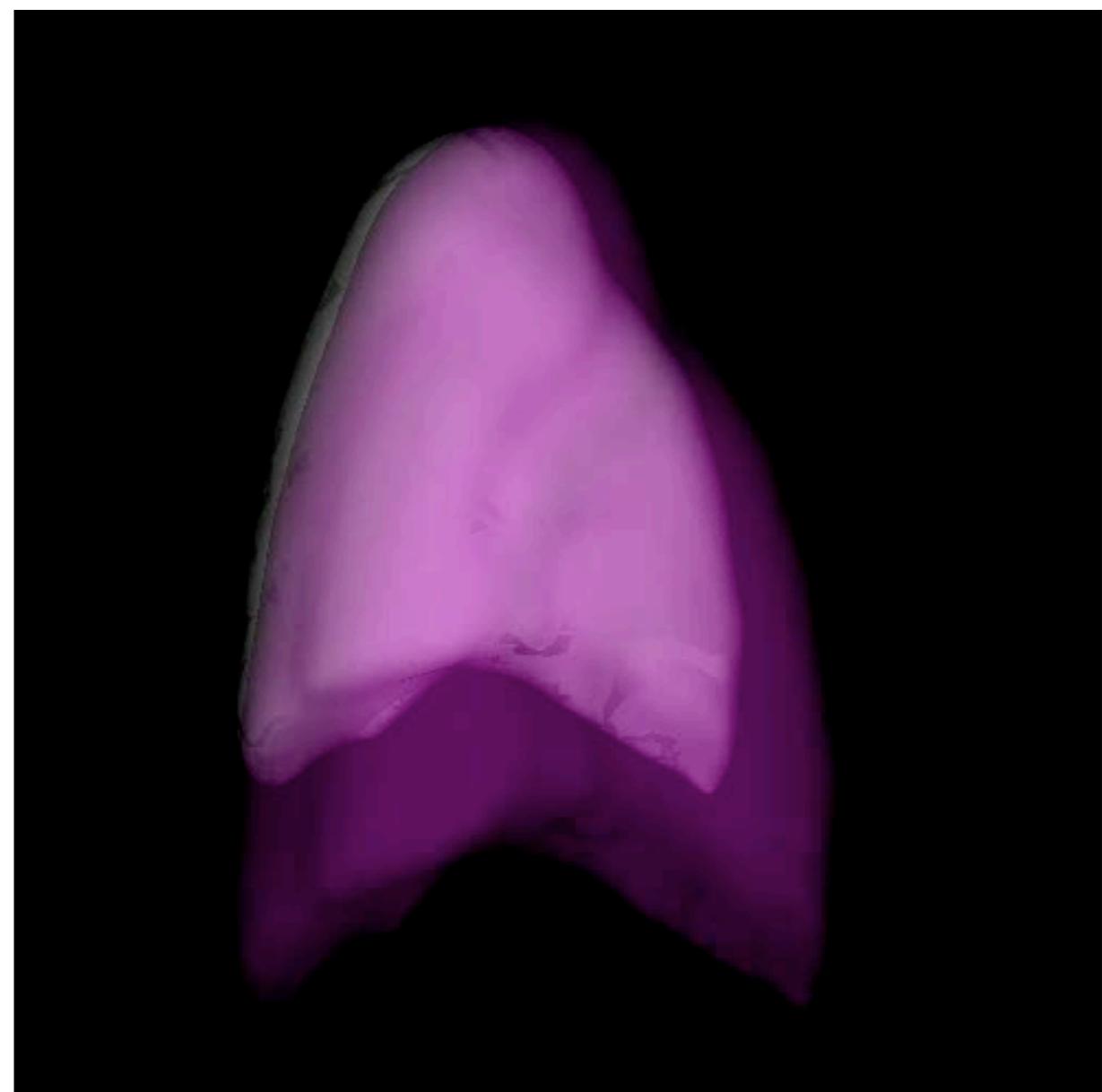
Whole heart segmentation using segmentation propagation



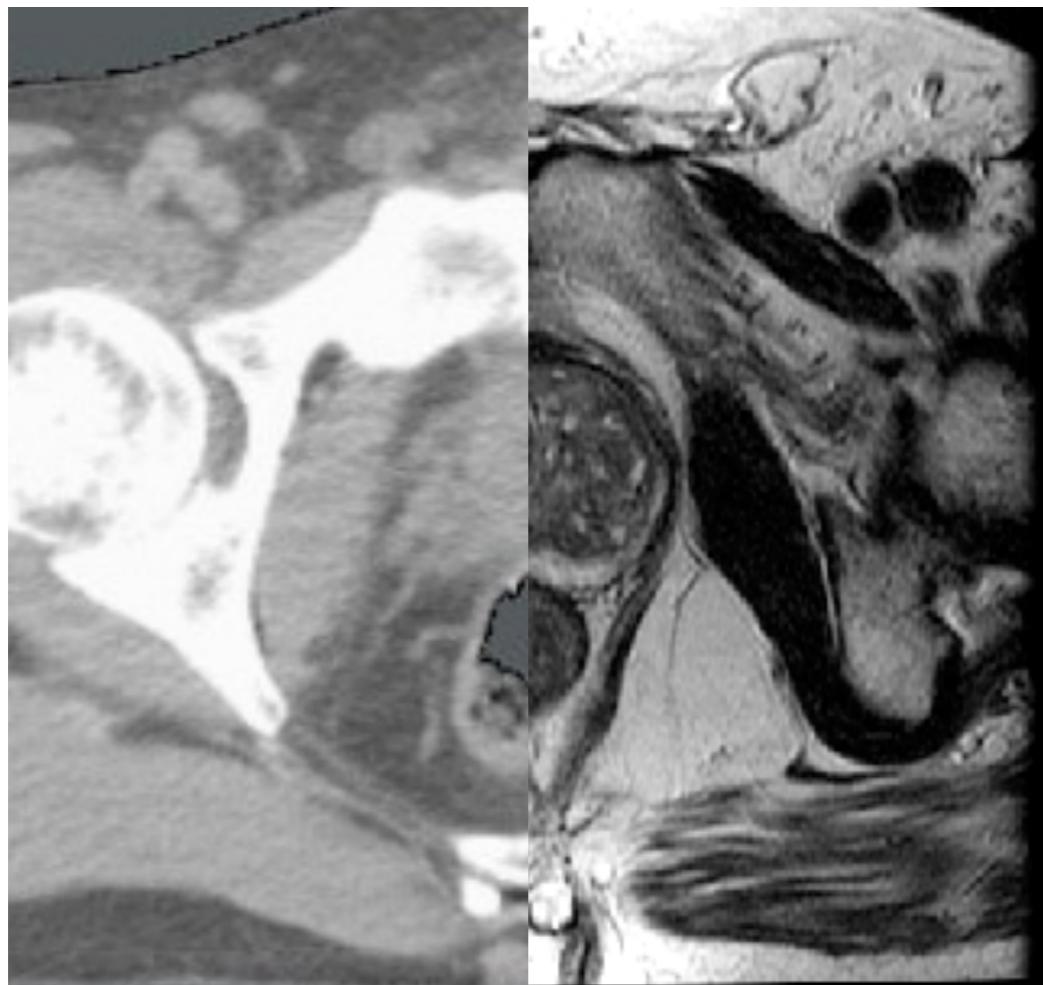
Error distribution

# Image Targeted Radiotherapy in the lung

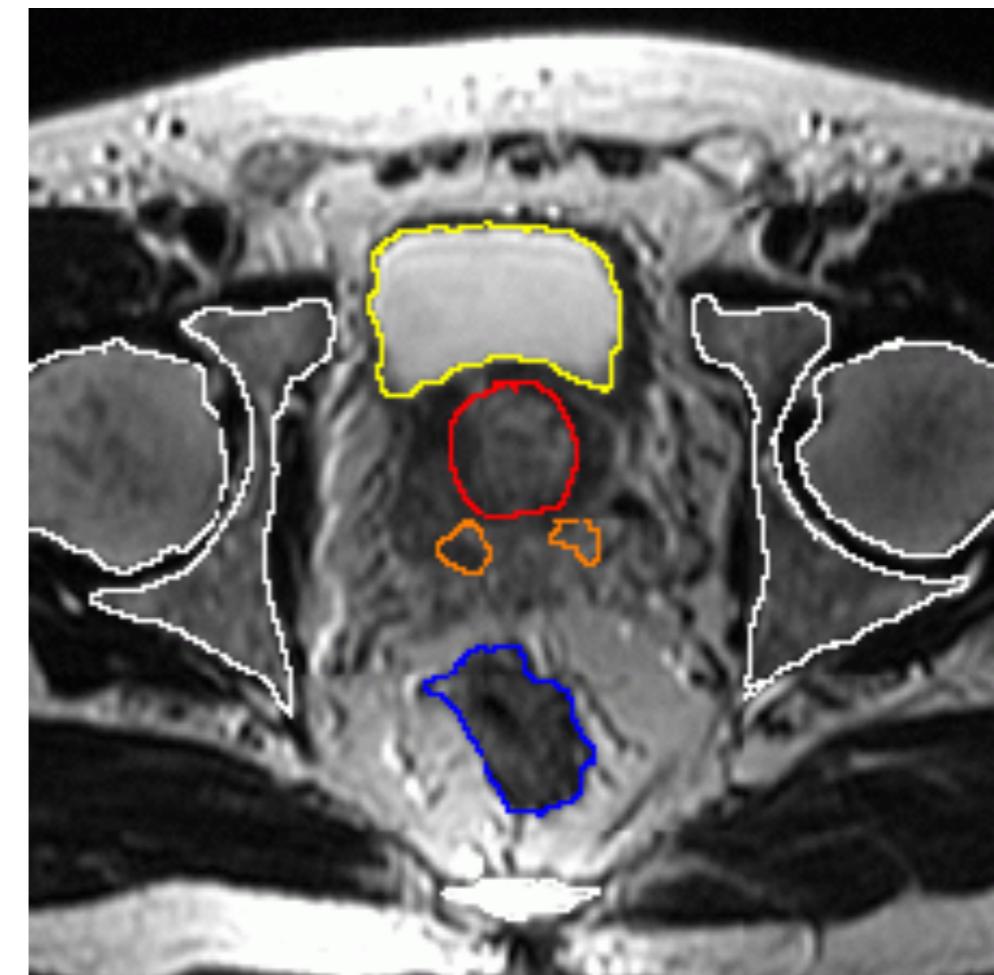
- Non-rigid registrations can be used to construct models of the respiratory motion.
- These can provide a better estimate of the true motion than 4DCT, and have many uses for the planning and delivery of RT.



# CT/MR fusion for radiotherapy

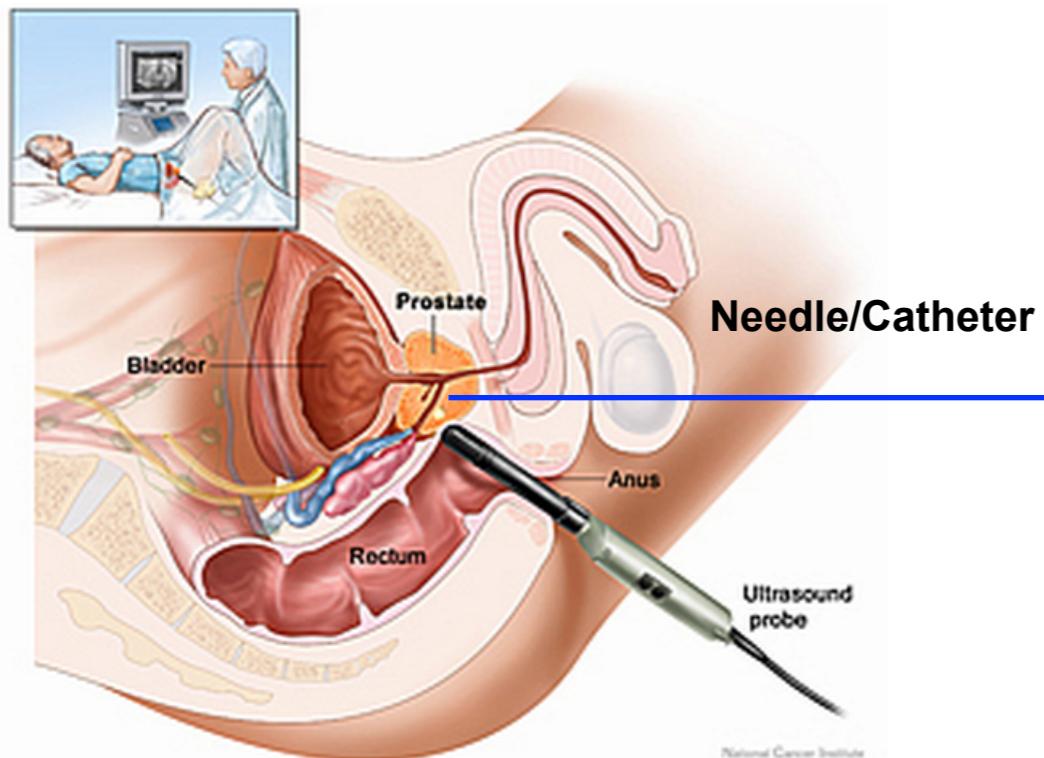


Tissular differentiation  
between MR and CT.  
Visualisation of the intra and  
peri prostatic structures

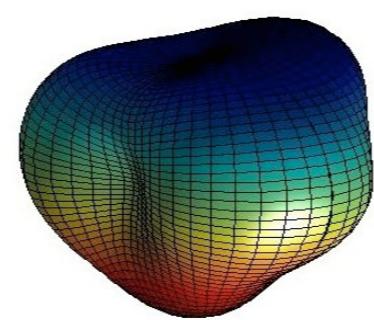
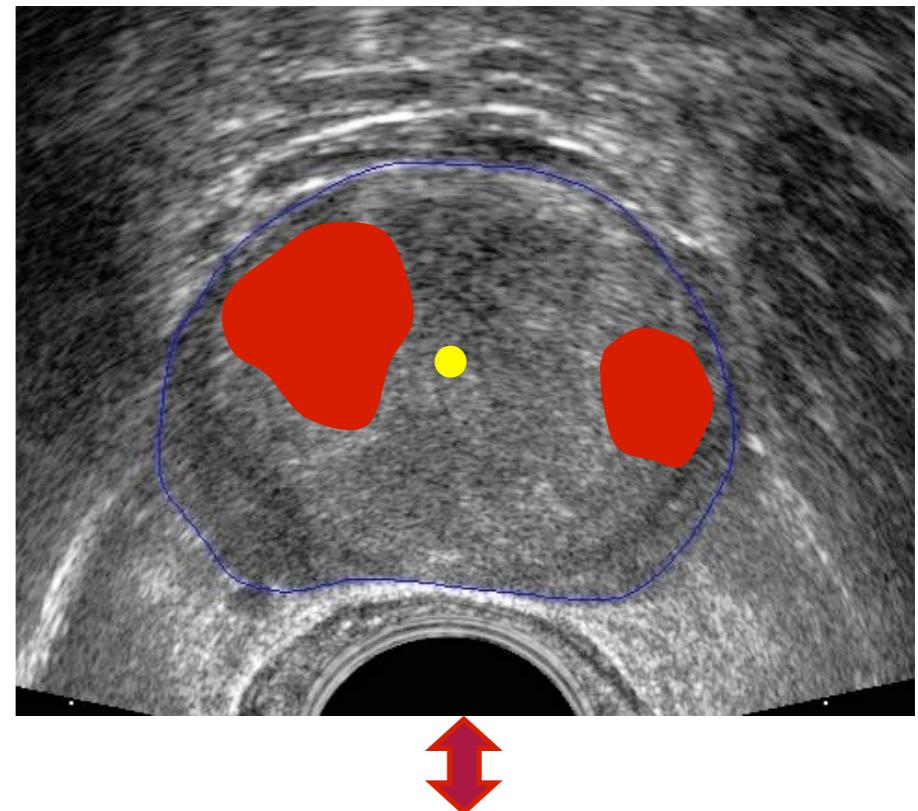


Fusion CT / MR  
(dosimetry / delineation)

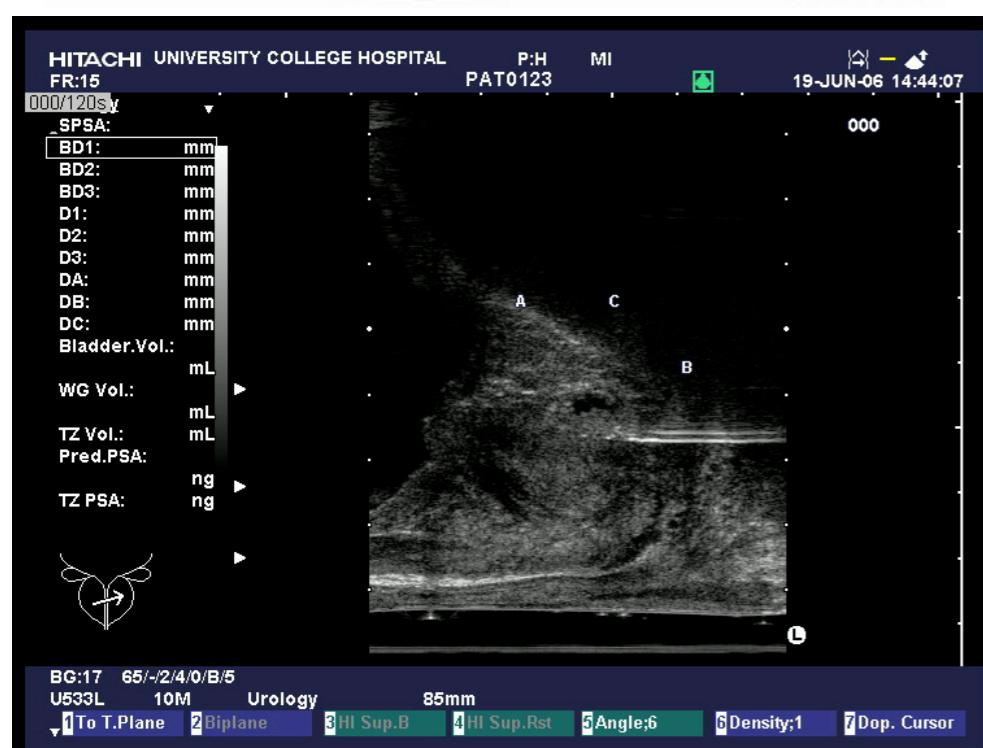
# Transrectal ultrasound (TRUS) guidance



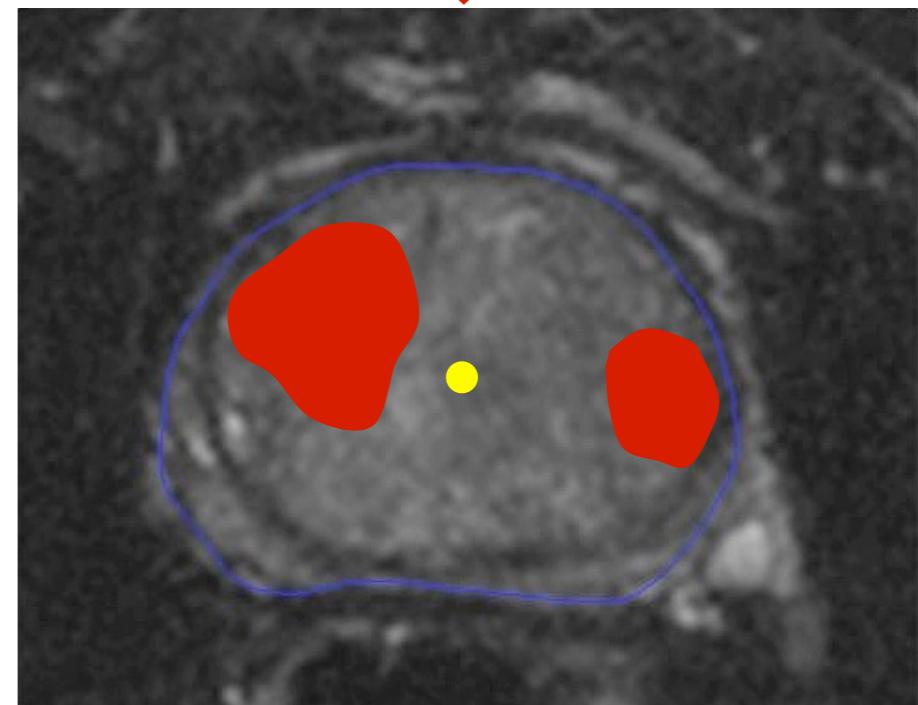
TRUS



3D prostate  
model from  
MRI

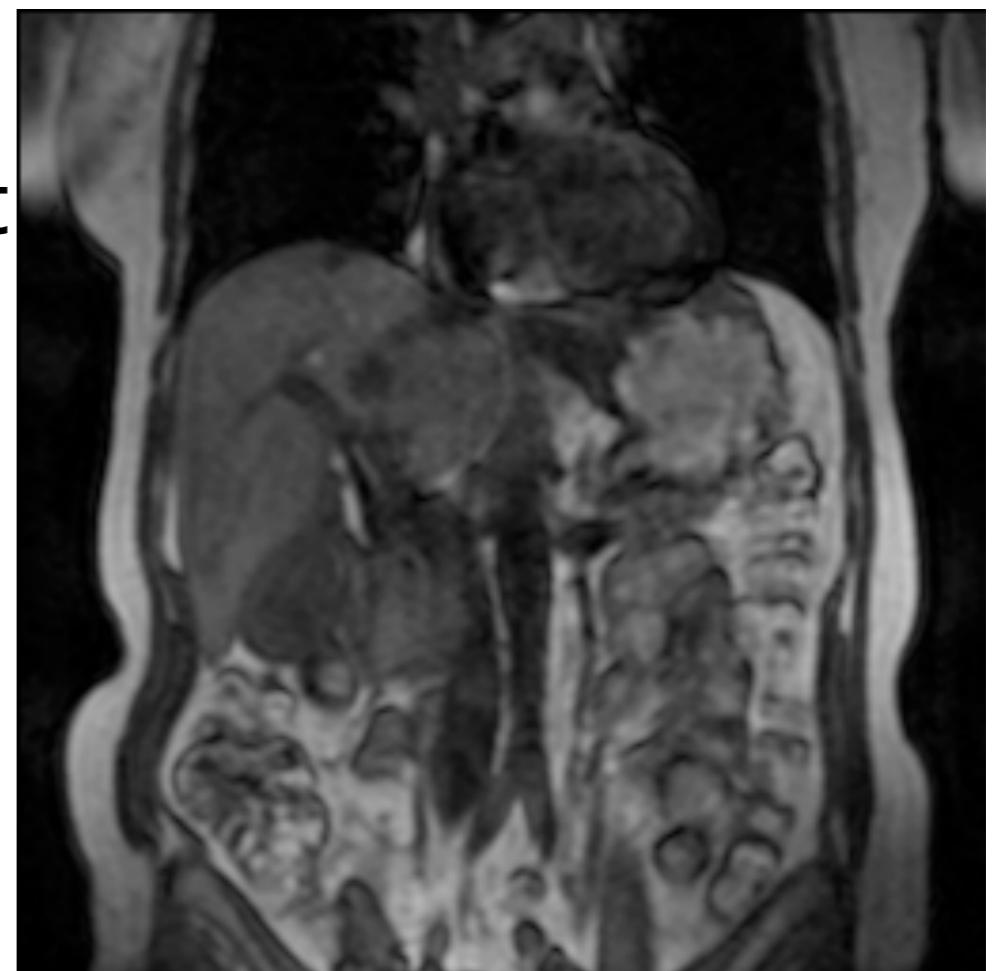


Preop. MR



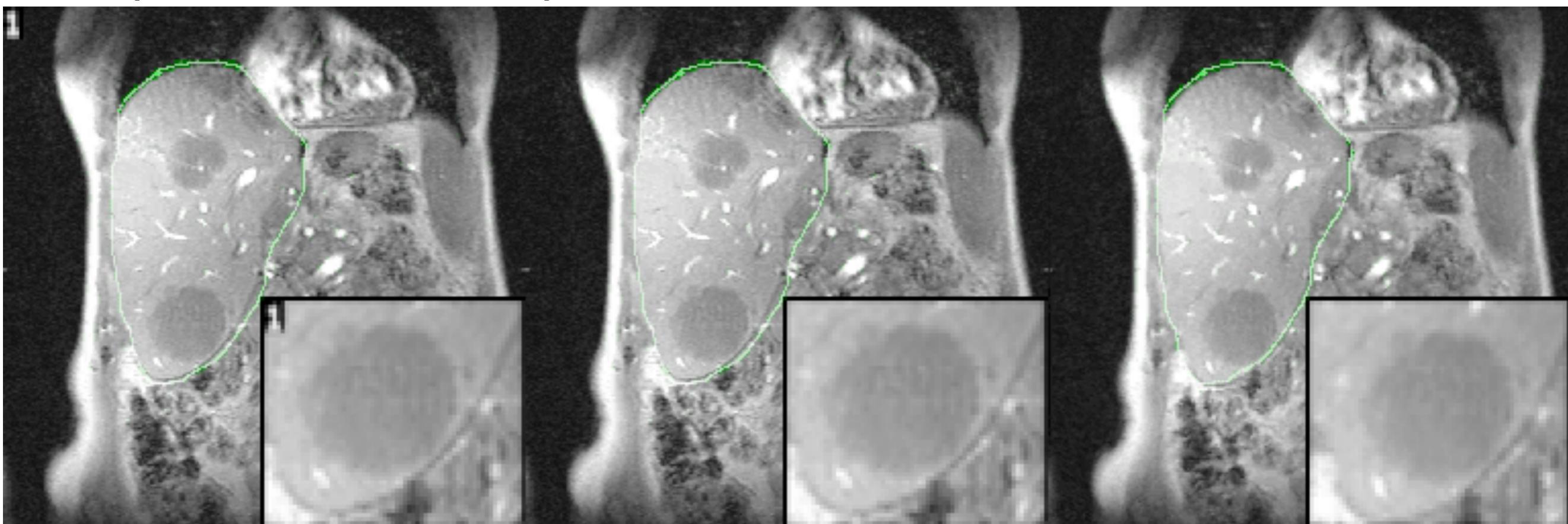
# Motion correction for DCE-MRI

- Observing the passage and distribution (the pharmacokinetics) of contrast agent through organs allows analysis of the vascular status of organs or features.
- Dynamic Contrast-Enhanced MRI (DCE-MRI) monitors enhancement this can be used to provide extra information not possible in conventional MRI or X-ray CT



# Motion correction for DCE-MRI

- Application to liver
  - Motion correction allows improved model-fitting and pharmacokinetic parameter estimation



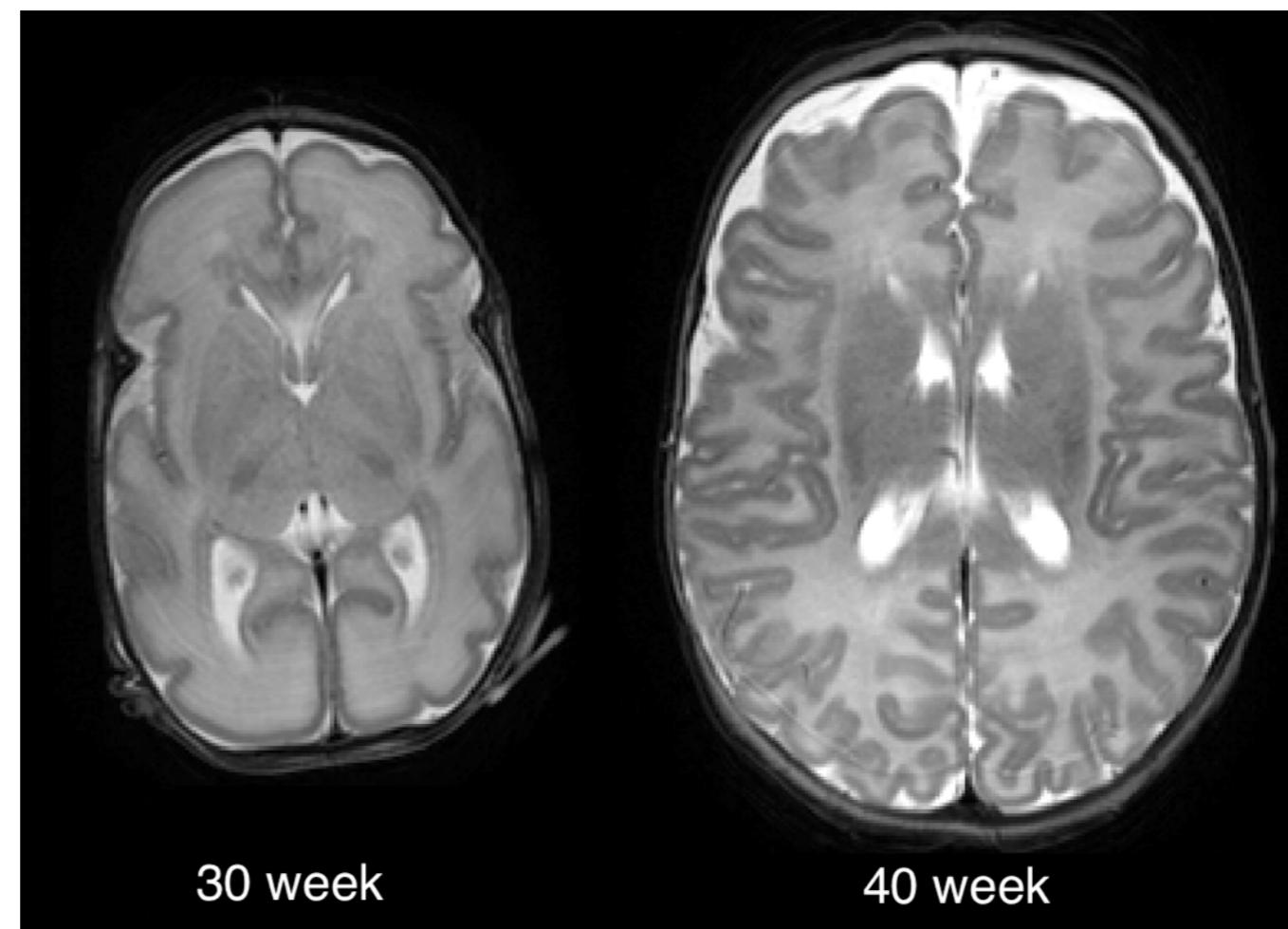
Unregistered data

Non-specific registration  
algorithm

DCE-MRI specific  
registration algorithm

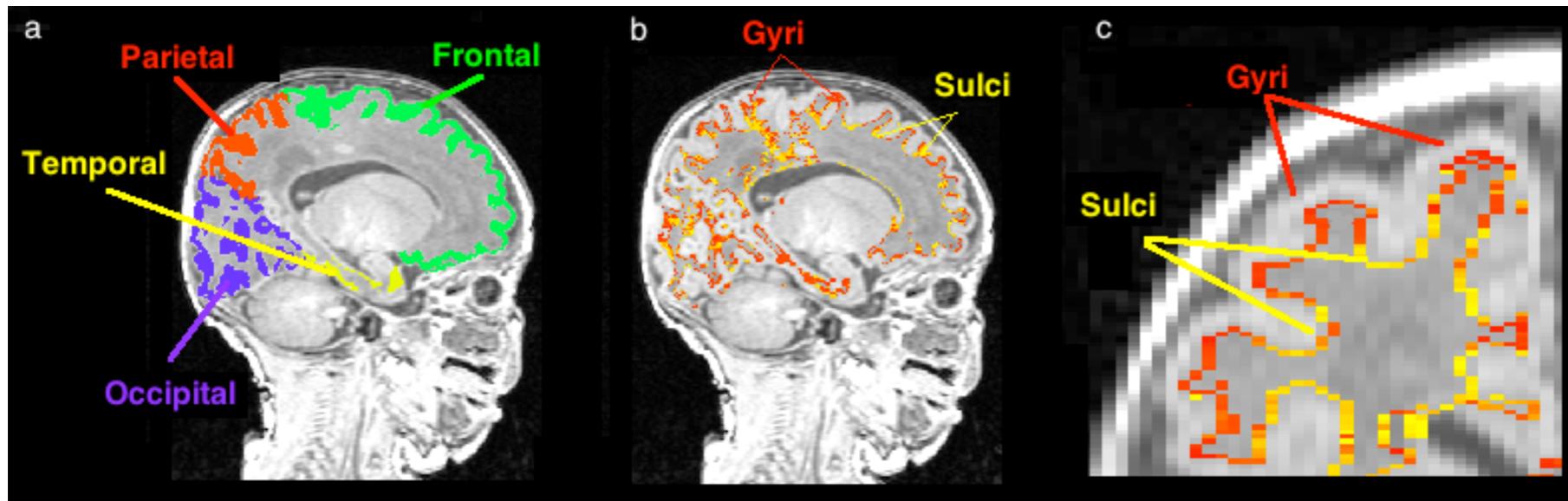
# Pre-term imaging

- Birth at <32 weeks gestation is associated with increased risk of later developmental problems.
- MRI is used to investigate the neuro-developmental precursors to allow improved understanding or early intervention



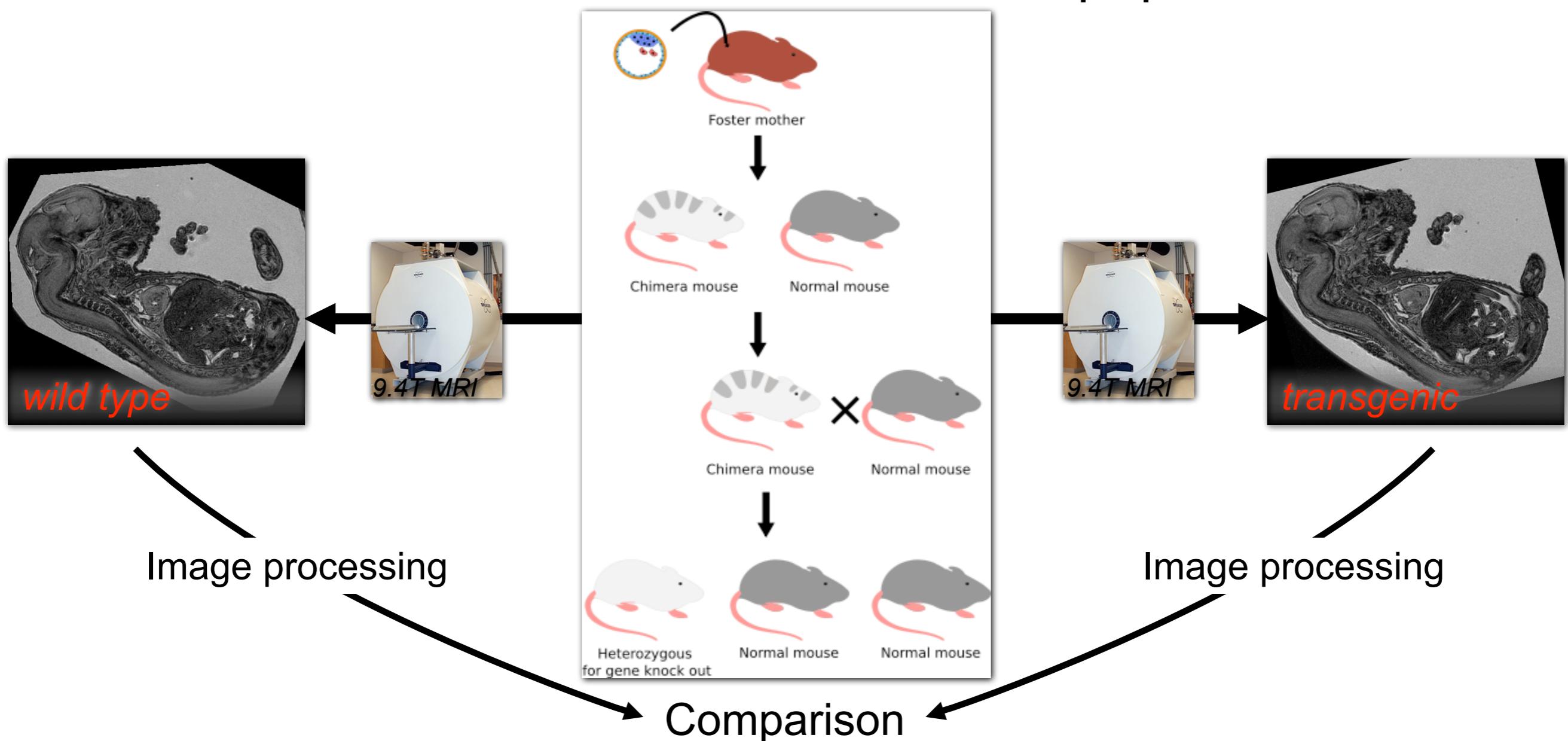
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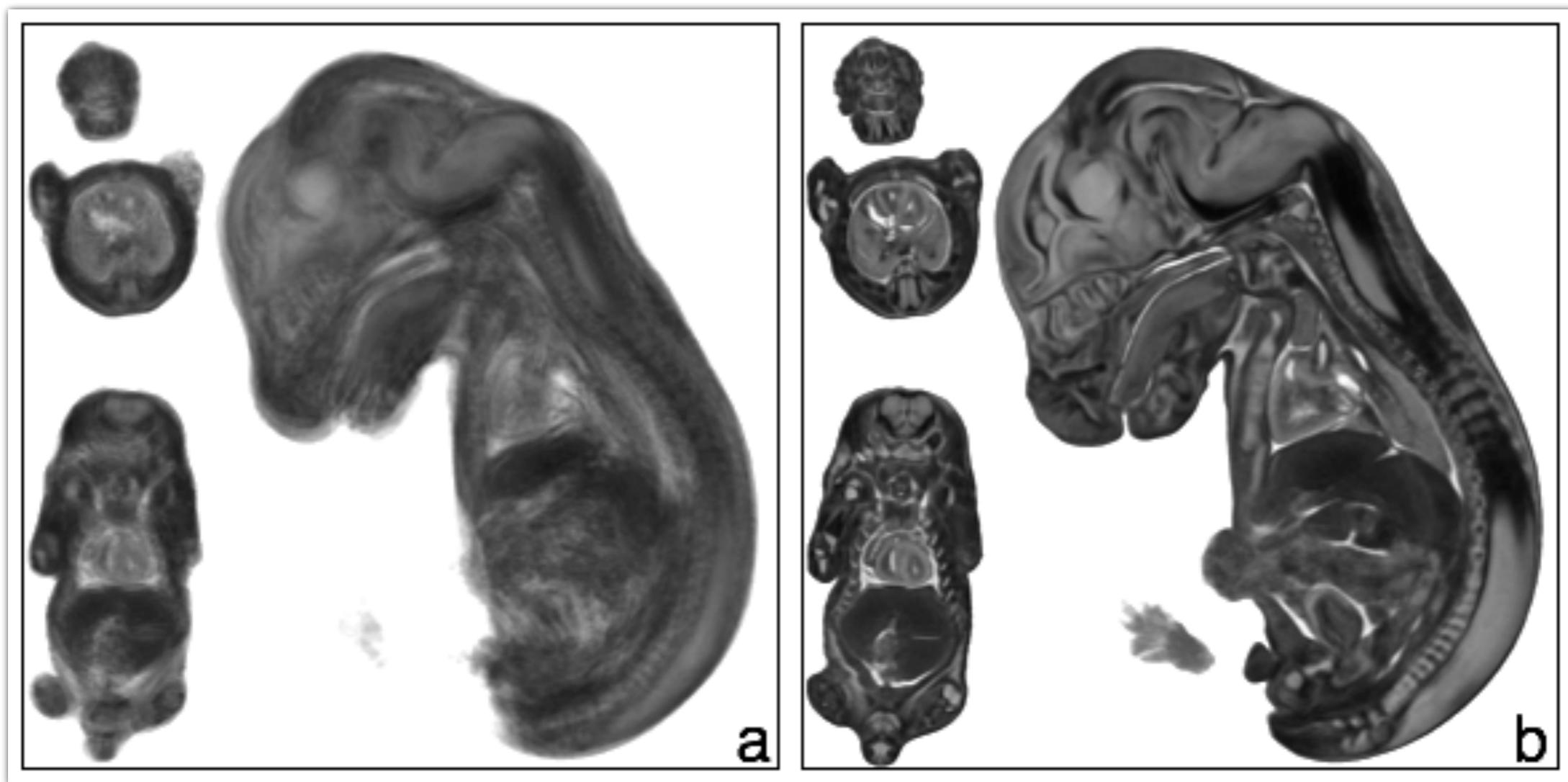
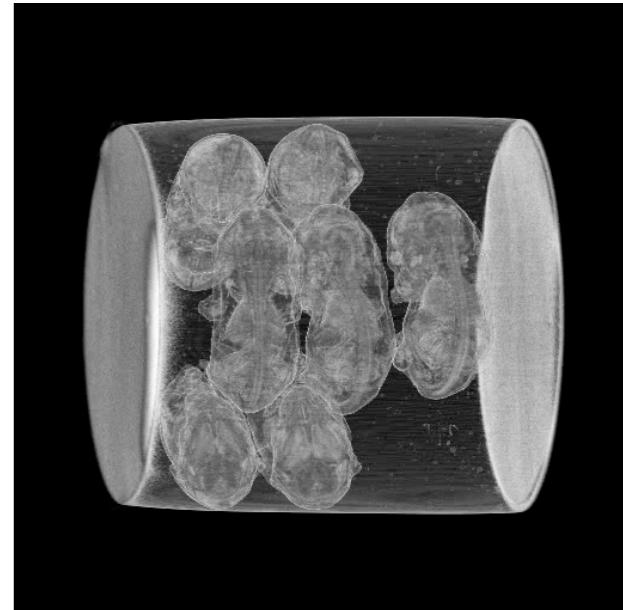
# Mouse phenotyping

- Can we link a genotype to a phenotype?
- Can we detect difference between two populations?



# Mouse phenotyping

- Average atlas creation using registration

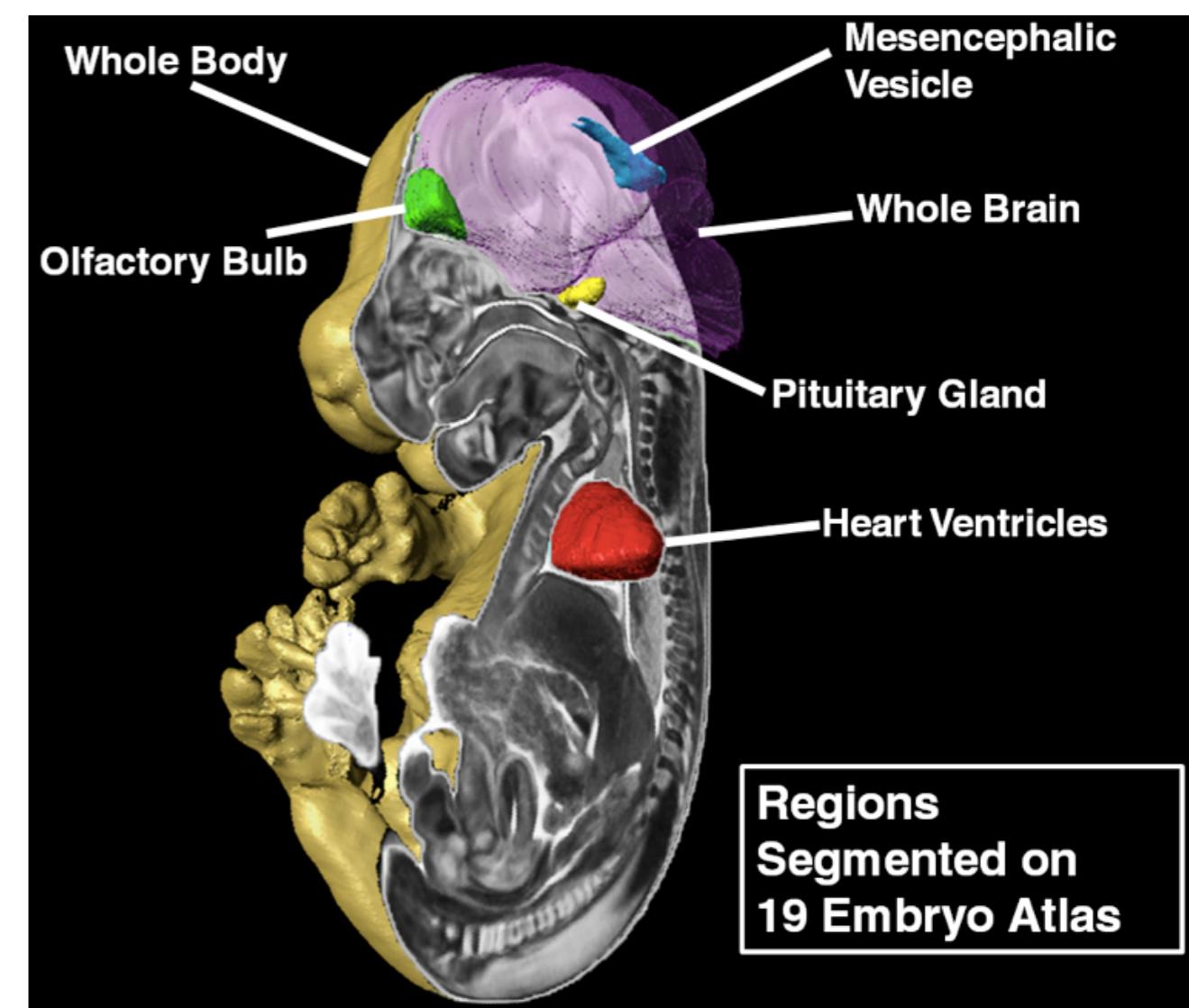
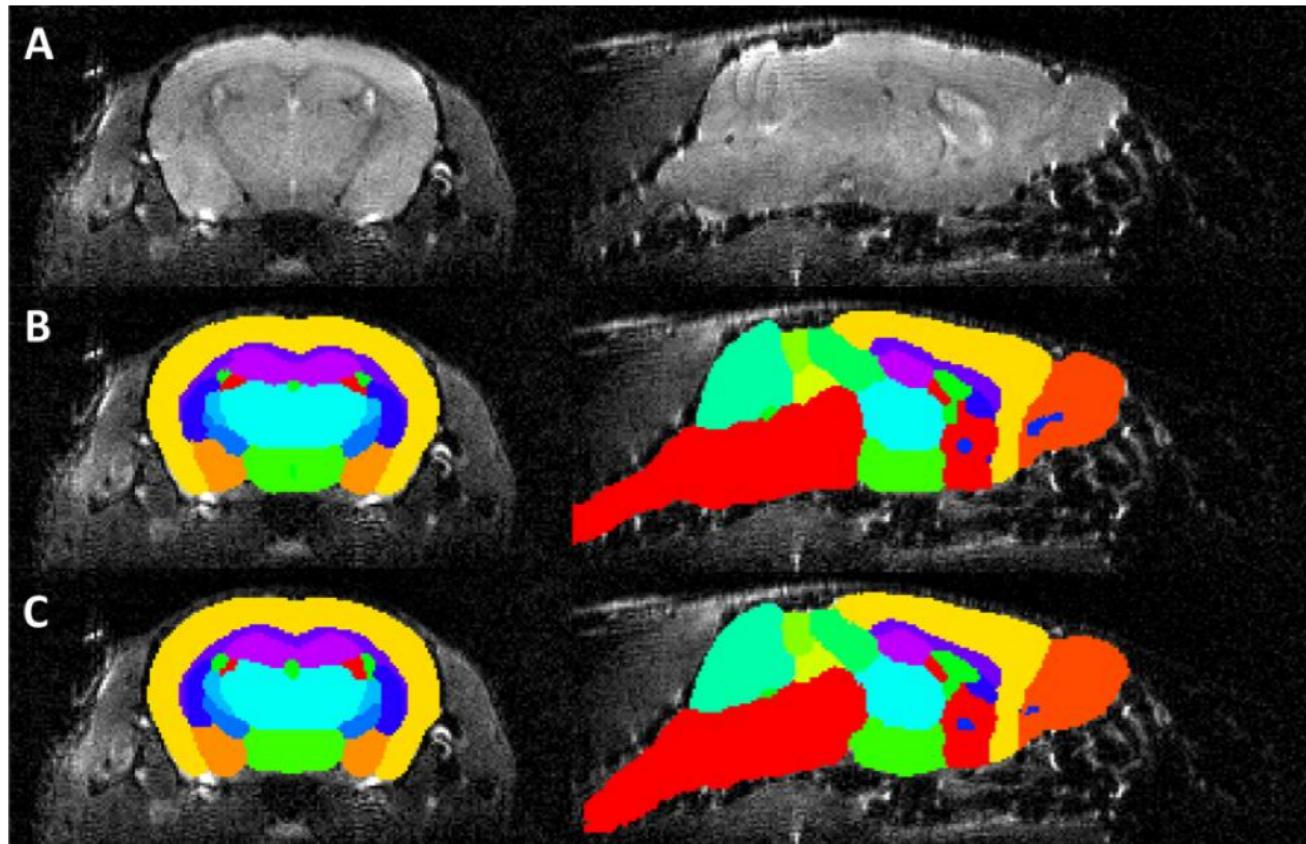


Global registration result

Local registration result

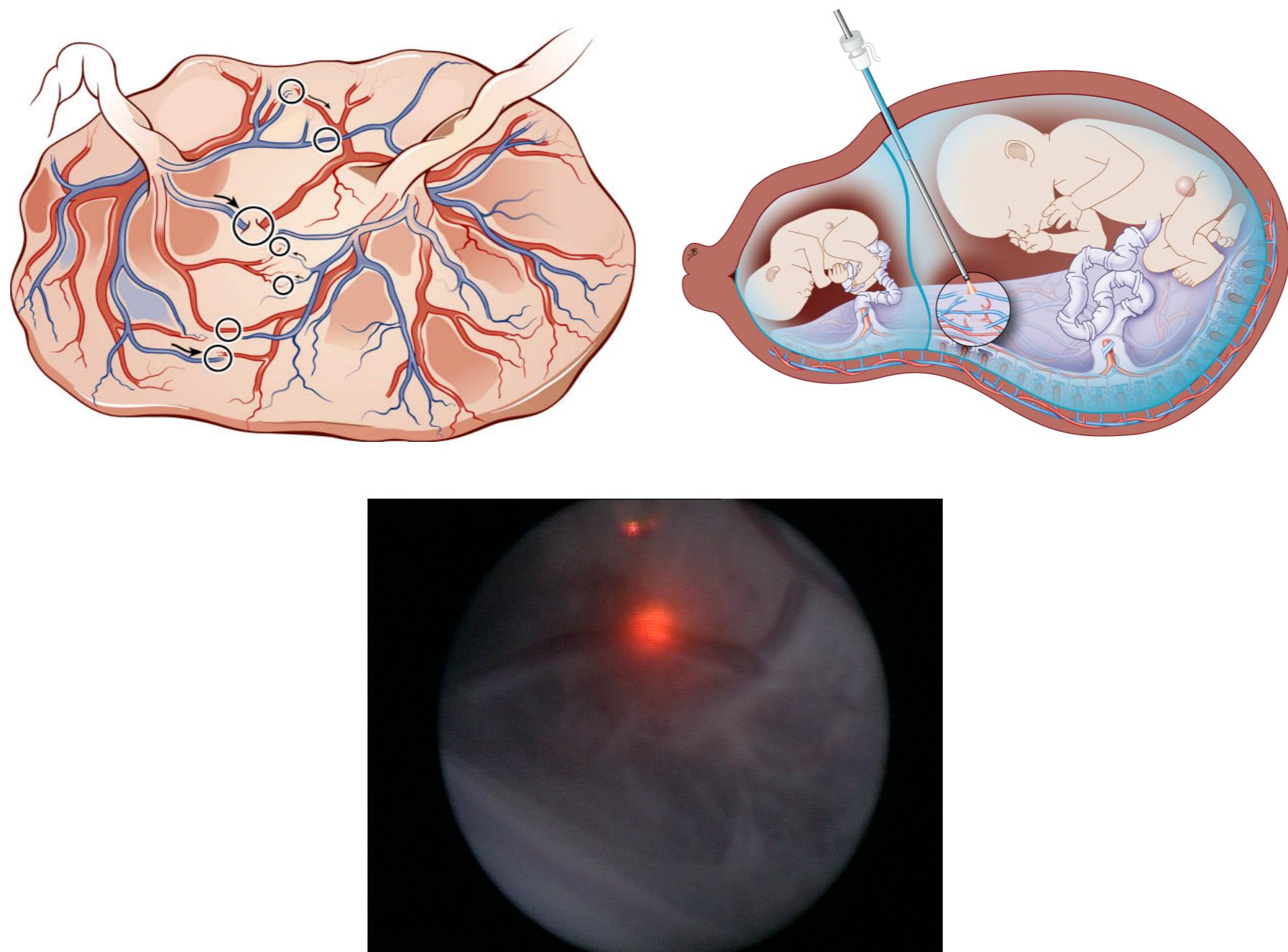
# Mouse phenotyping

- Parcelation



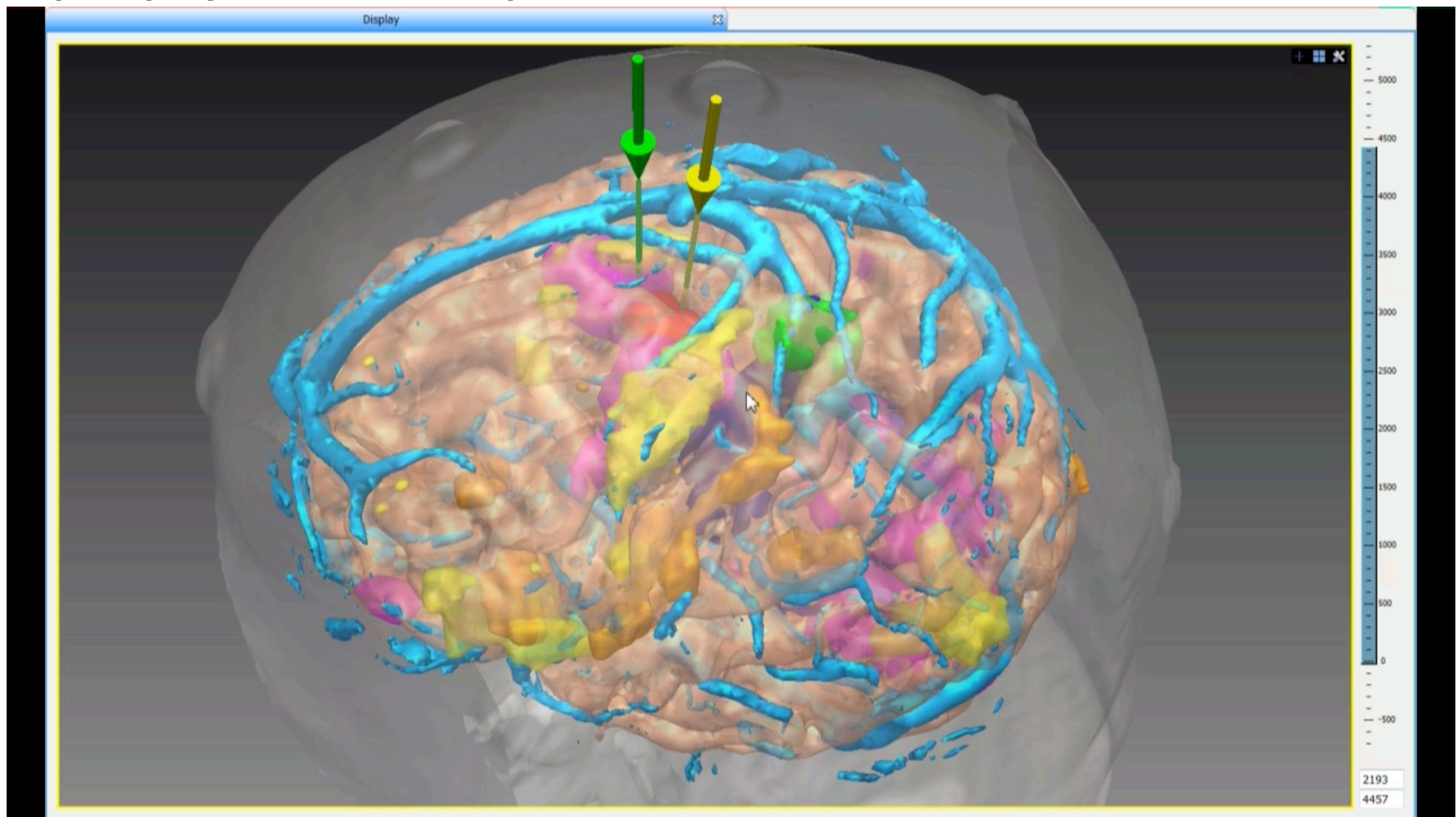
# Image guided intervention

- Twin-to-Twin transfusion syndrome (TTTS)



# Image guided surgery

- Epilepsy electrode placement



# Questions?