Clinical fMRI & DTI: Mapping brain function and pathways for surgical planning

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- Department of Radiology
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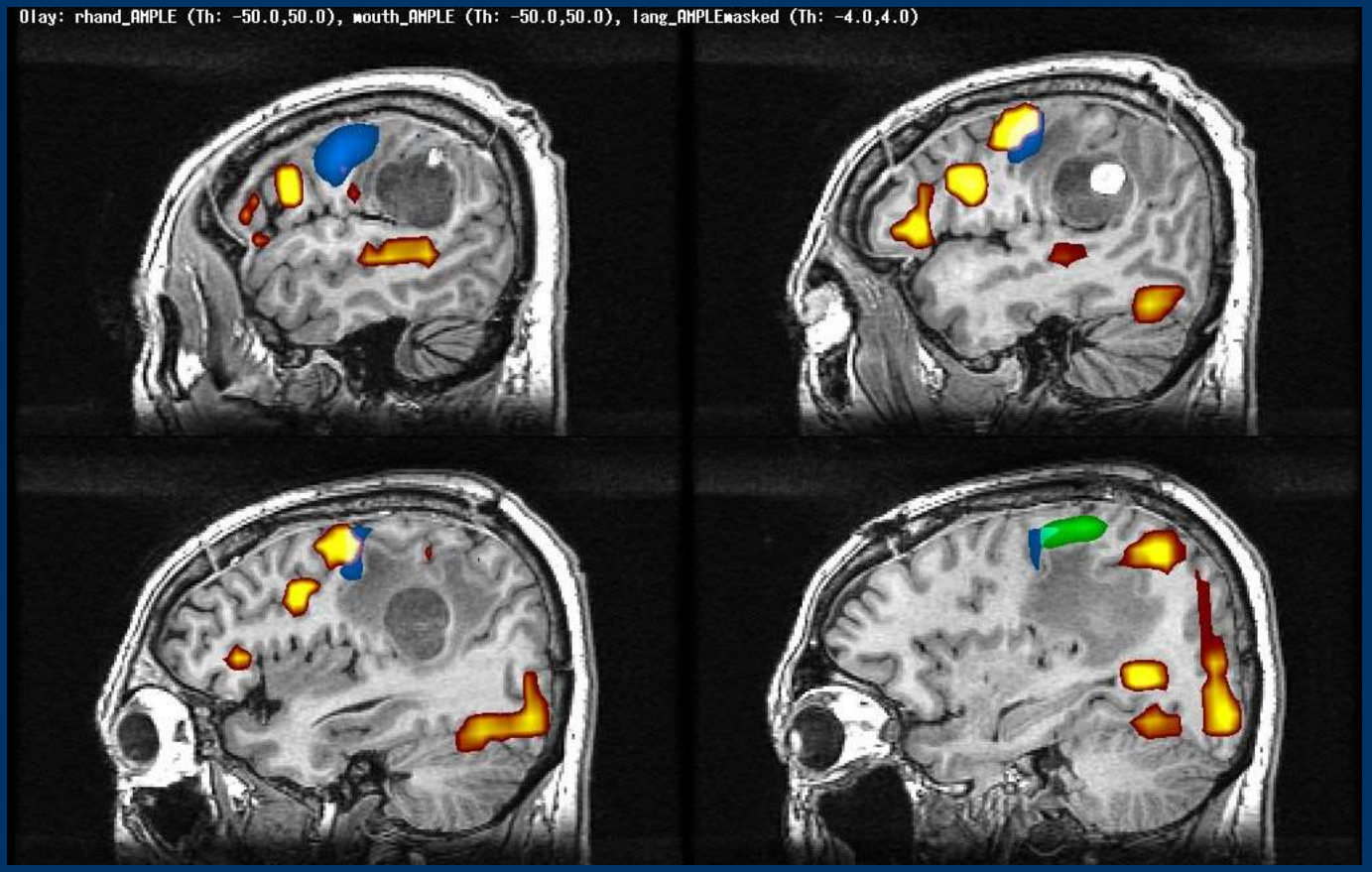
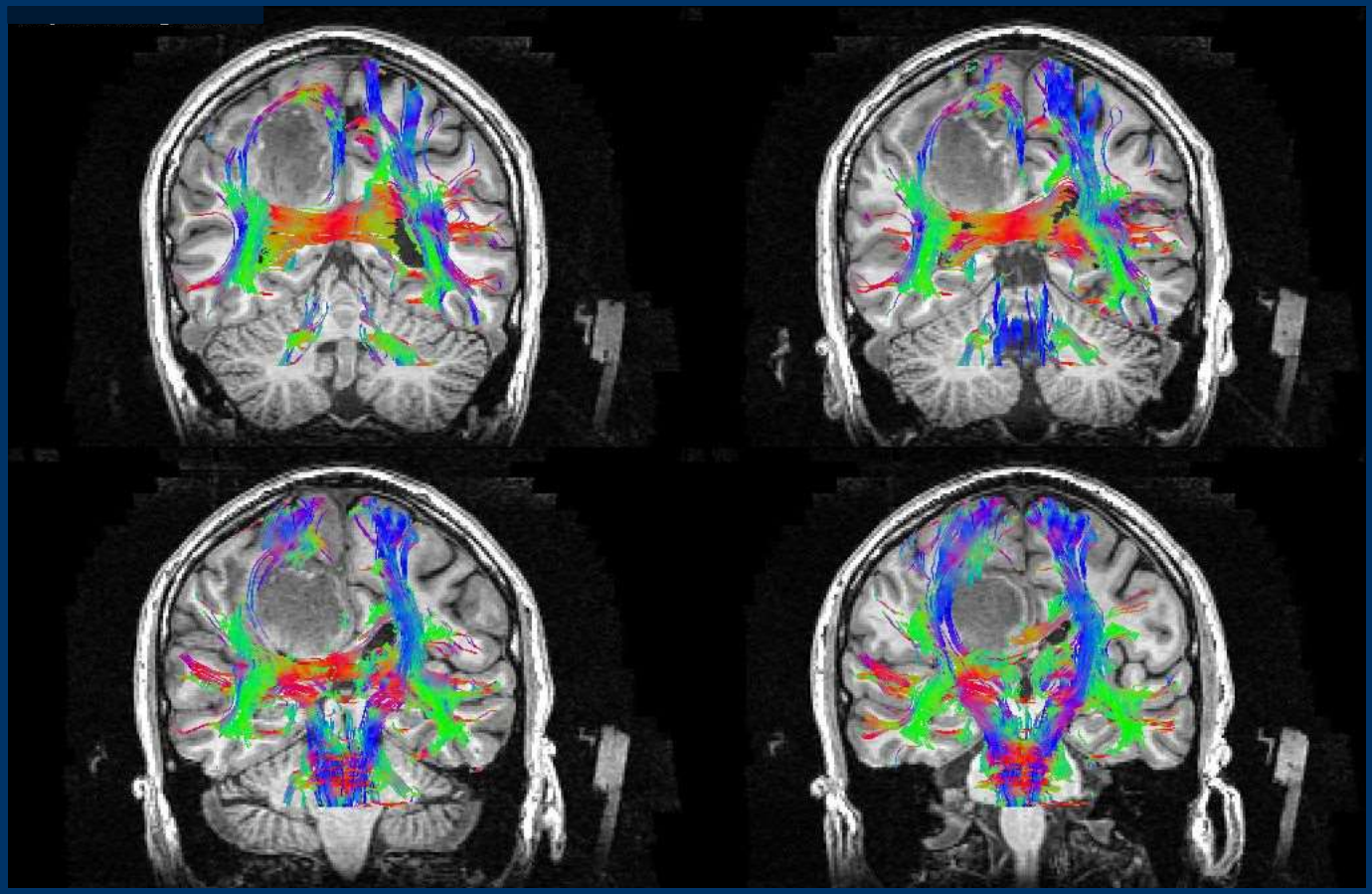
Functional MRI (fMRI) is primarily used clinically to map speech and motor function



Diffusion tensor imaging (DTI) is used to map major white matter tracts



fMRI & DTI
Clinical goals

- Determine location and borders of eloquent cortical areas relative to lesions
- Determine location of major white-matter tracts connecting eloquent areas
- Evaluate risk of post-surgical functional deficits
- Decide whether surgery is advisable
- Plan surgical approach and extent of resection
- Decide whether intraoperative mapping is necessary

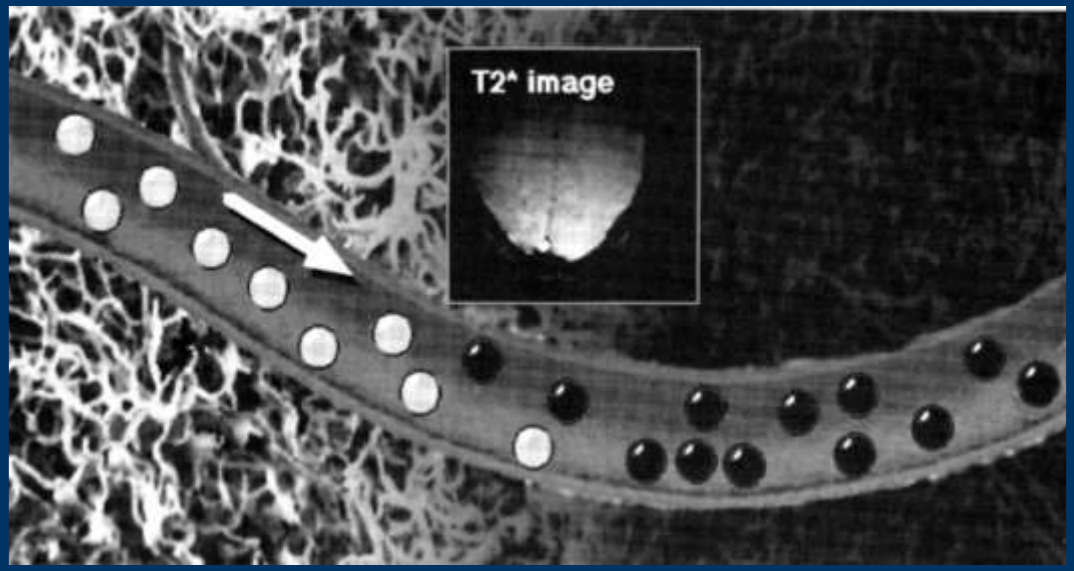
fMRI & DTI
Technical goals

- Identify eloquent brain areas
  [sensitivity & specificity]
- Map location relative to anatomy and pathology
  [image registration]
- Evaluate laterality of language dominance
  [relative activation]
- Map edges of areas and proximity to lesion
  [thresholding & quantitative reproducibility]

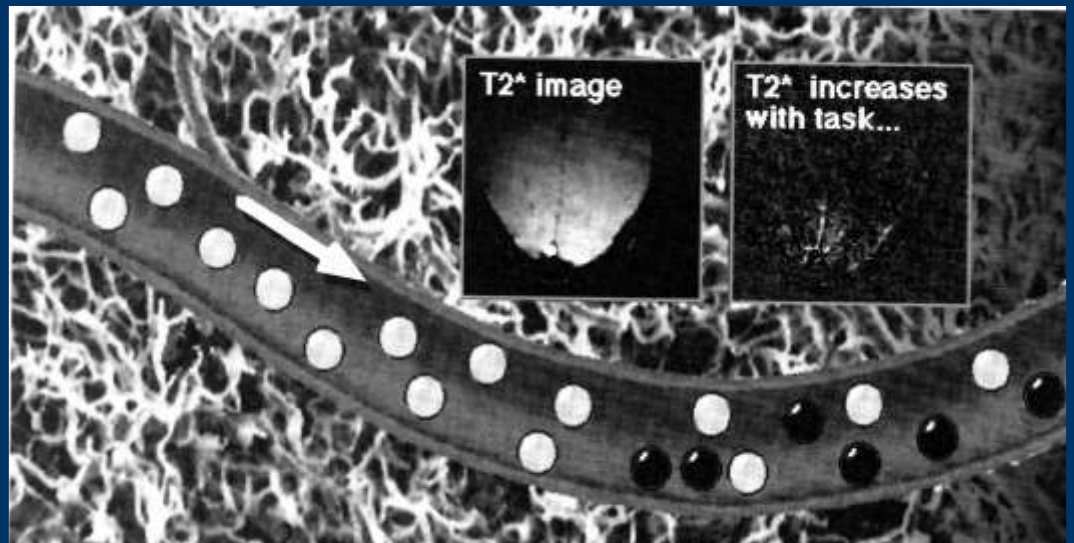
How does fMRI work?

Blood Oxygenation Level Dependent (BOLD) imaging is sensitive to local activity-dependent changes in blood flow.

"Baseline"



"Task"



from Mosley

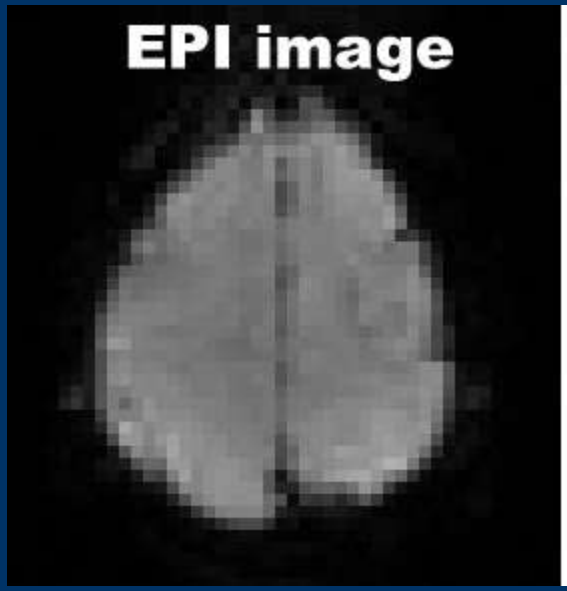
Simple visual cues are used for a variety of movement tasks.

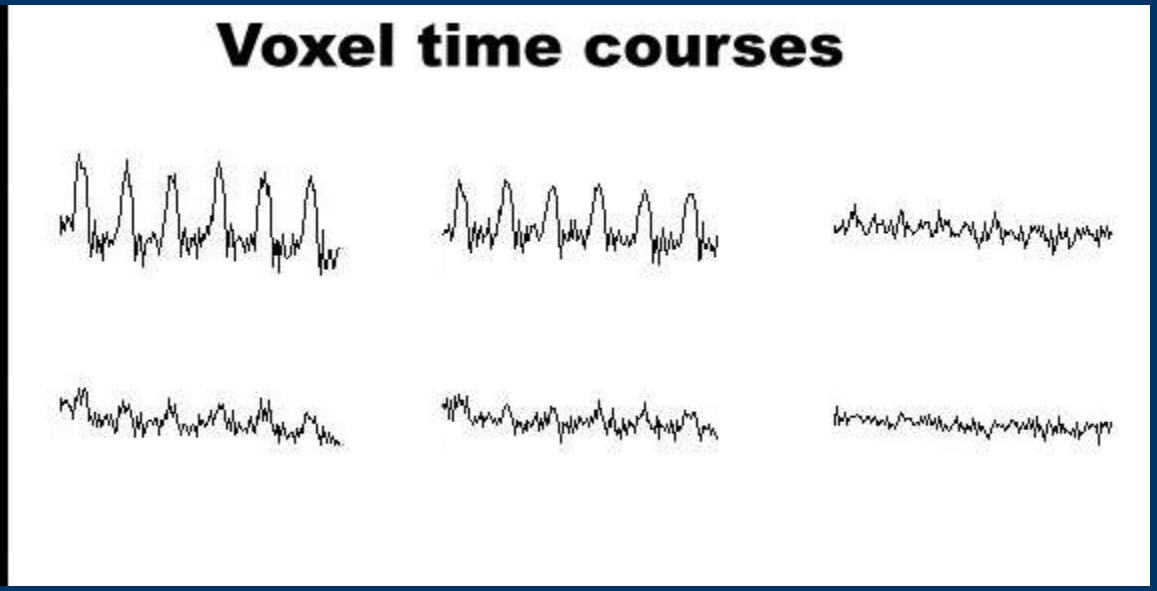
Alternating side motion

Bilateral motion

Image acquisition

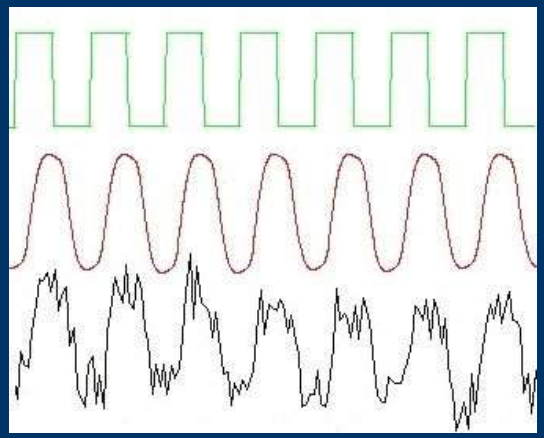
During a ~5-minute fMRI scan, 20-30 echo-planar images are acquired repeatedly (TR 1.5s) to obtain a time series of hundreds of image intensity measurements while the patient performs many cycles of a simple task.
Image intensity varies with the task in some image voxels.





Statistical image processing

An “activation map” is created by comparing the timing of the observed fluctuations in the fMRI images to the expected fluctuations of the BOLD response.
Statistical significance identifies “active” voxels.

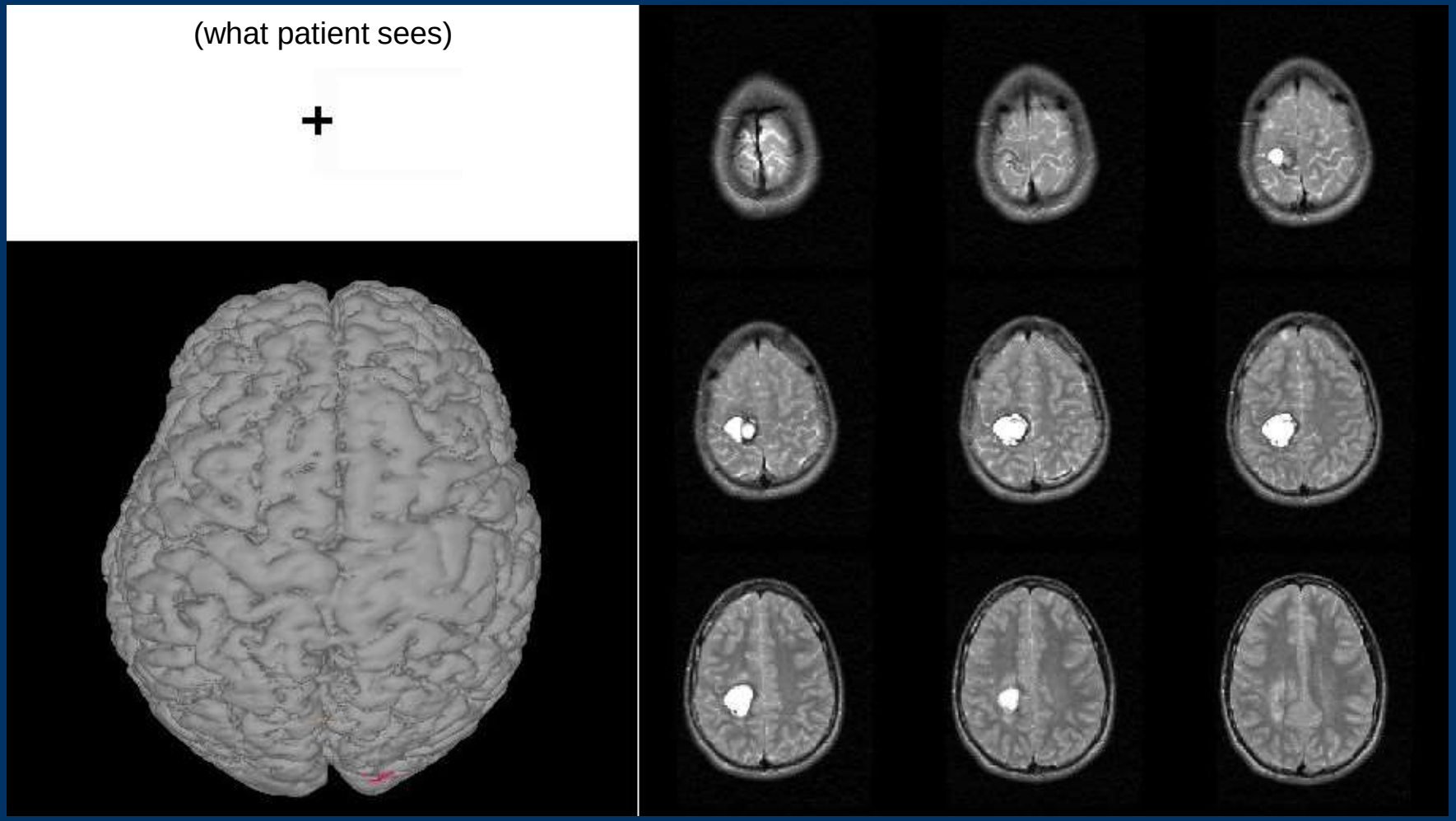


Active voxel “map” overlaid on other MR images

Many different ways to generate statistical maps:

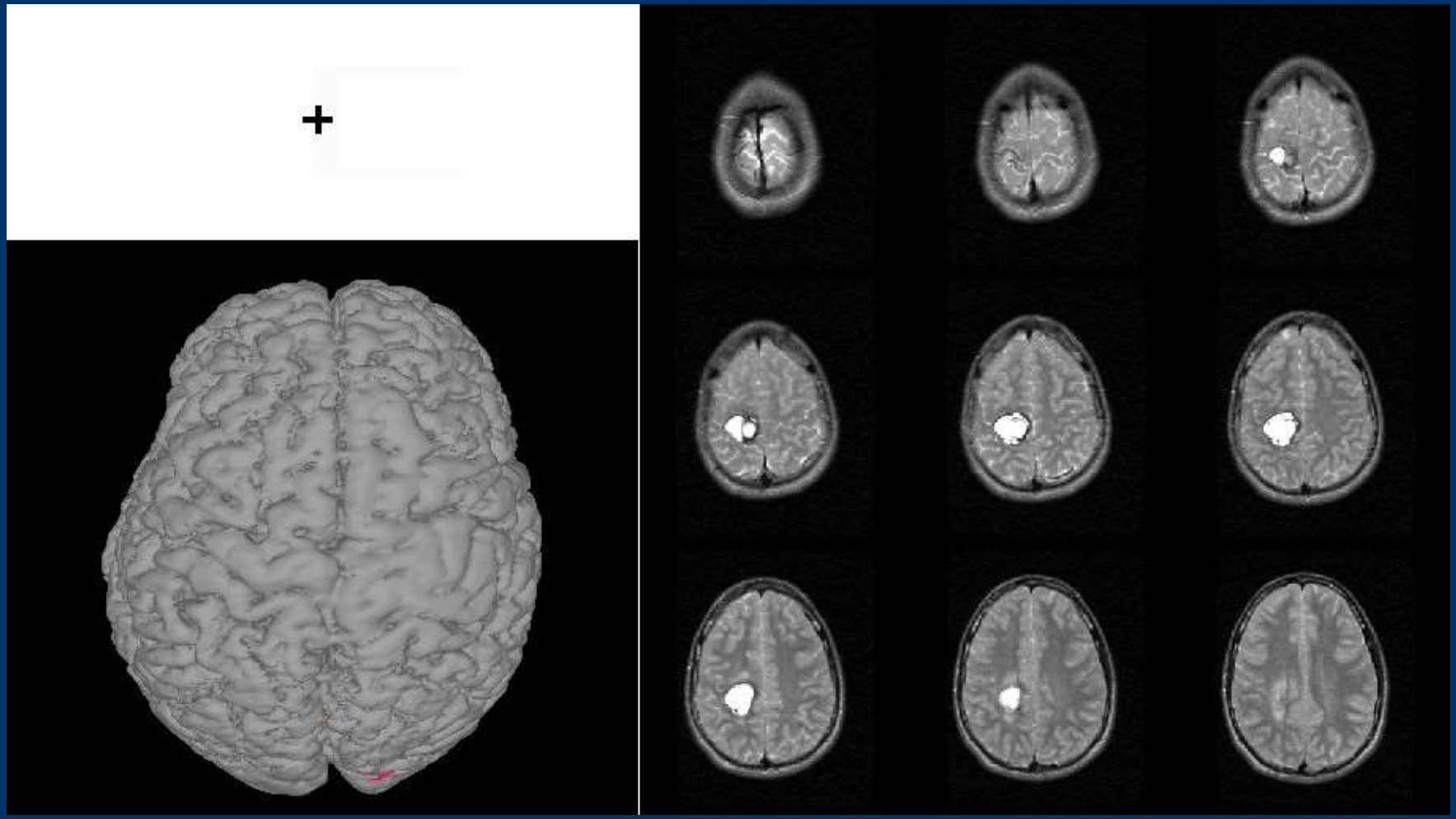
- image subtraction
- t-test differences
- temporal correlation
- General Linear Model (analysis of variance)

Motor cortex mapping prior to neurosurgery

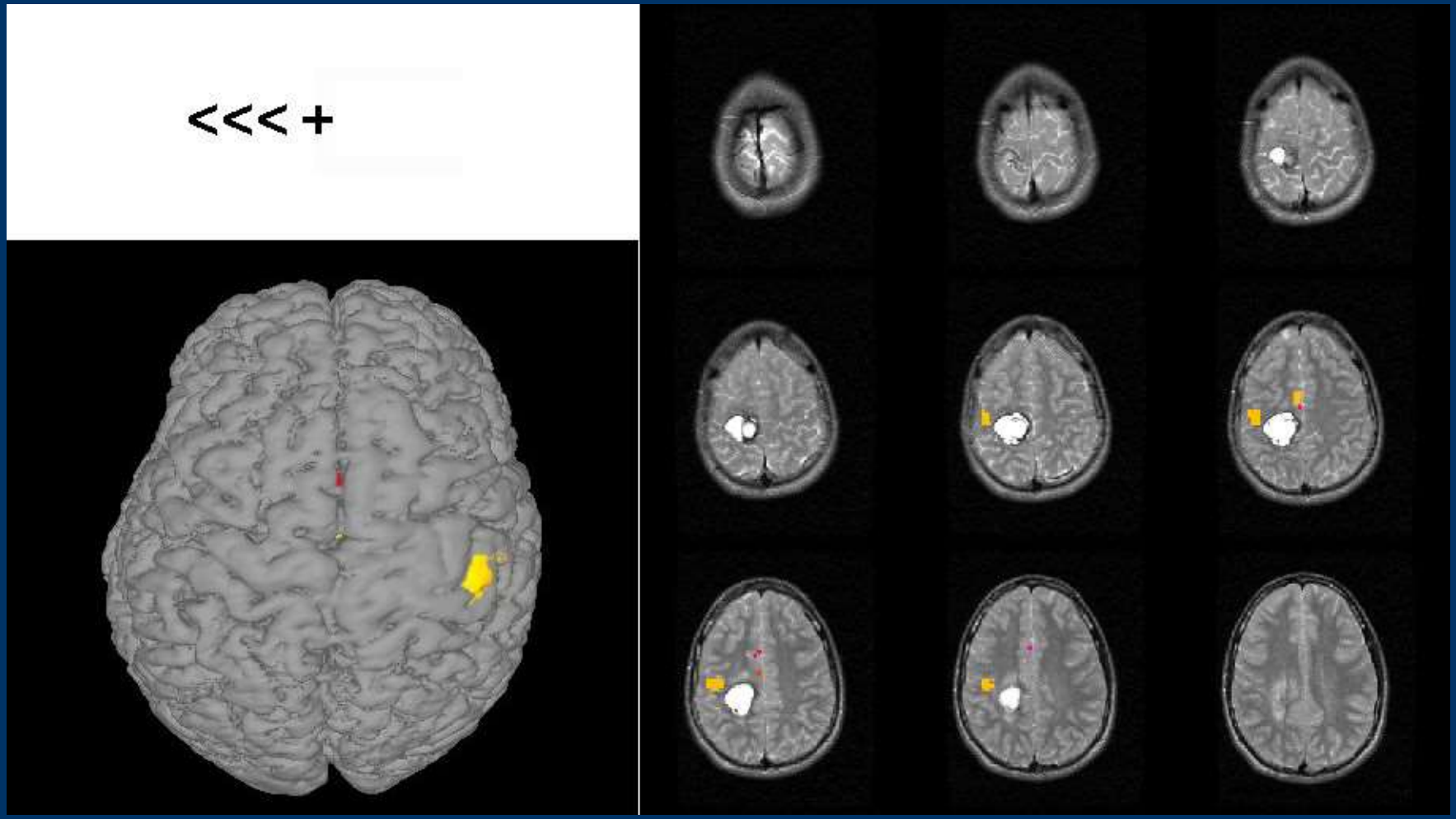


Average brain activation across 1 task cycle

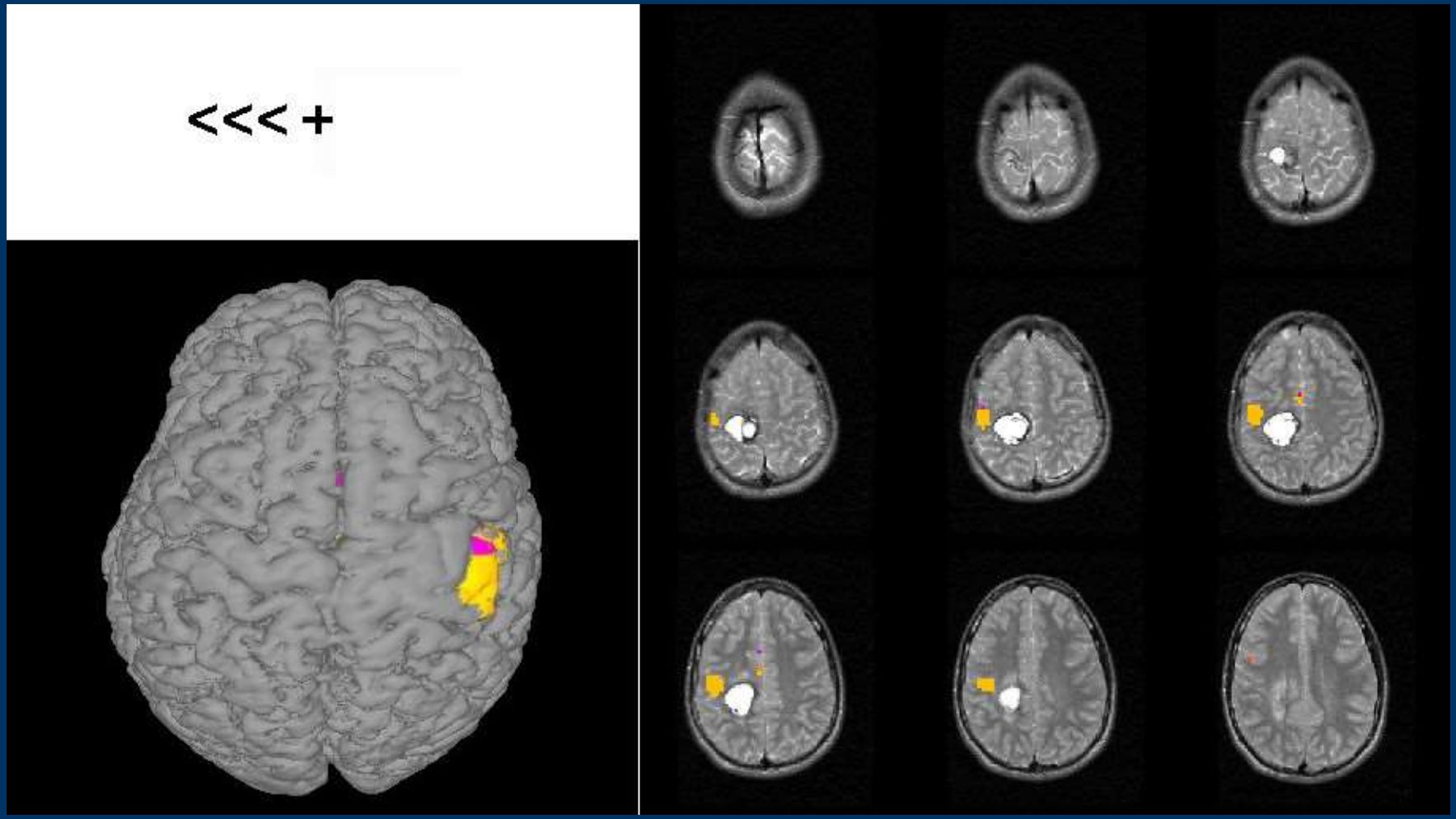
T = 0 s



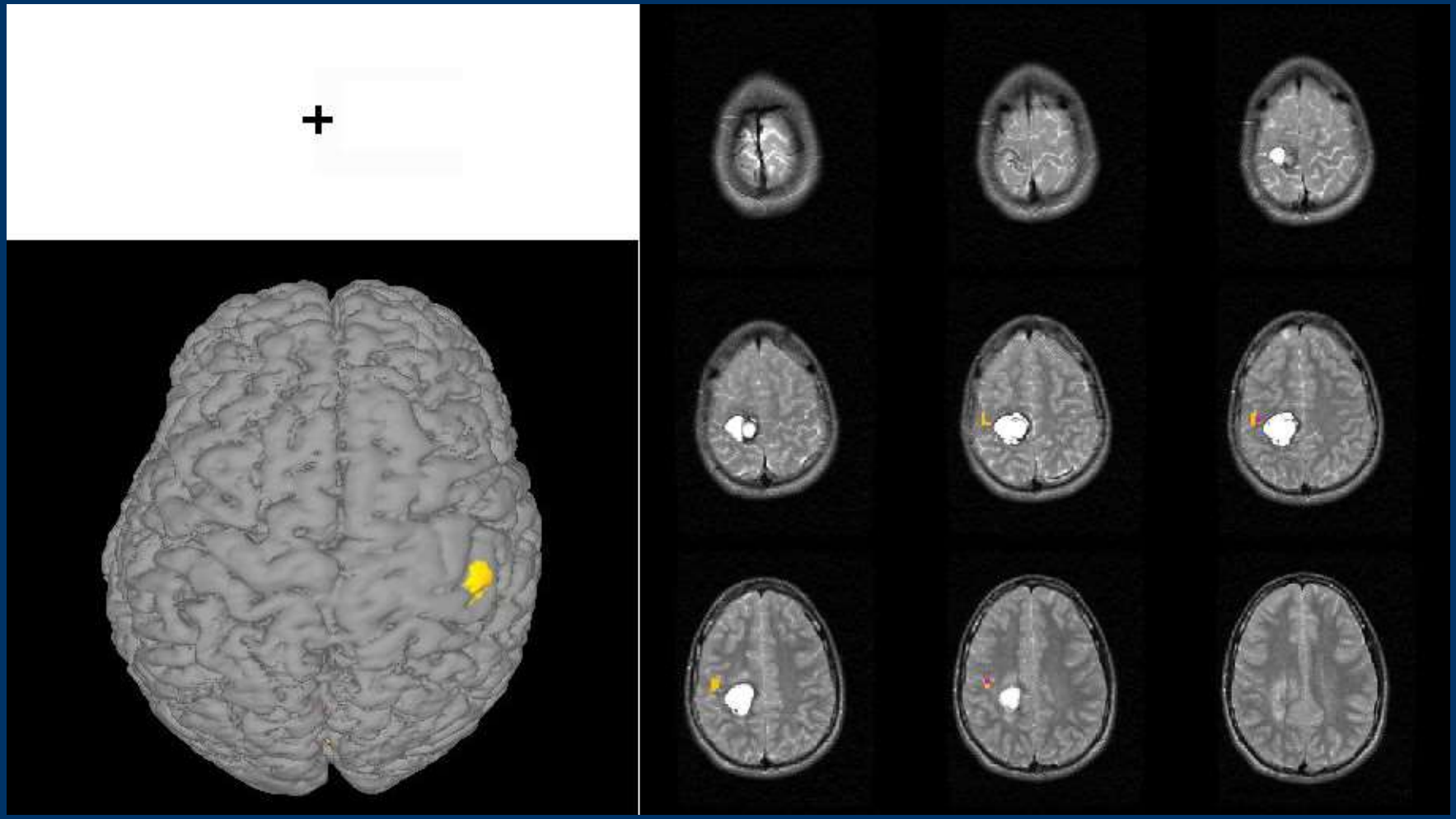
T = 4.5 s



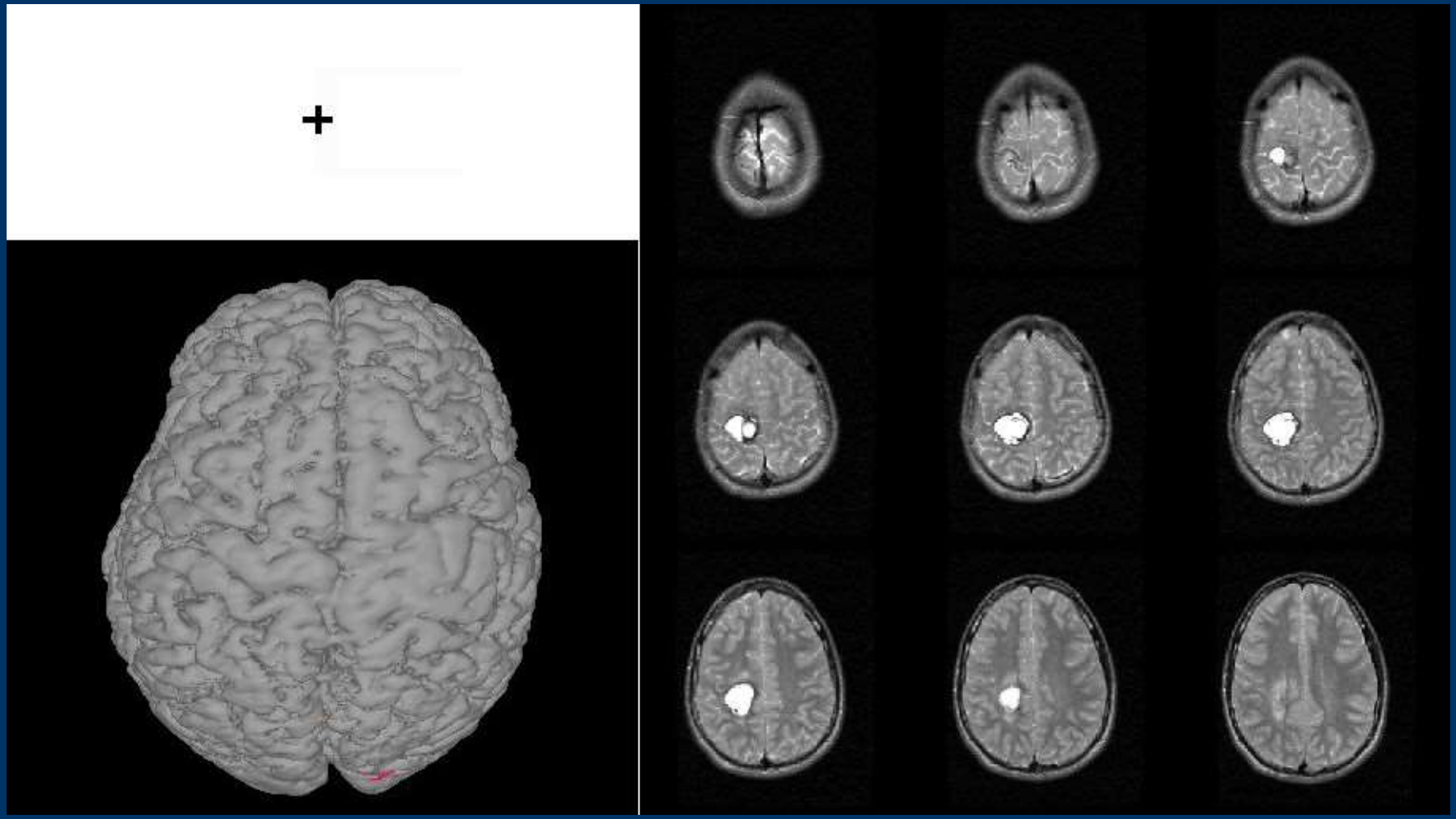
T = 9.0 s



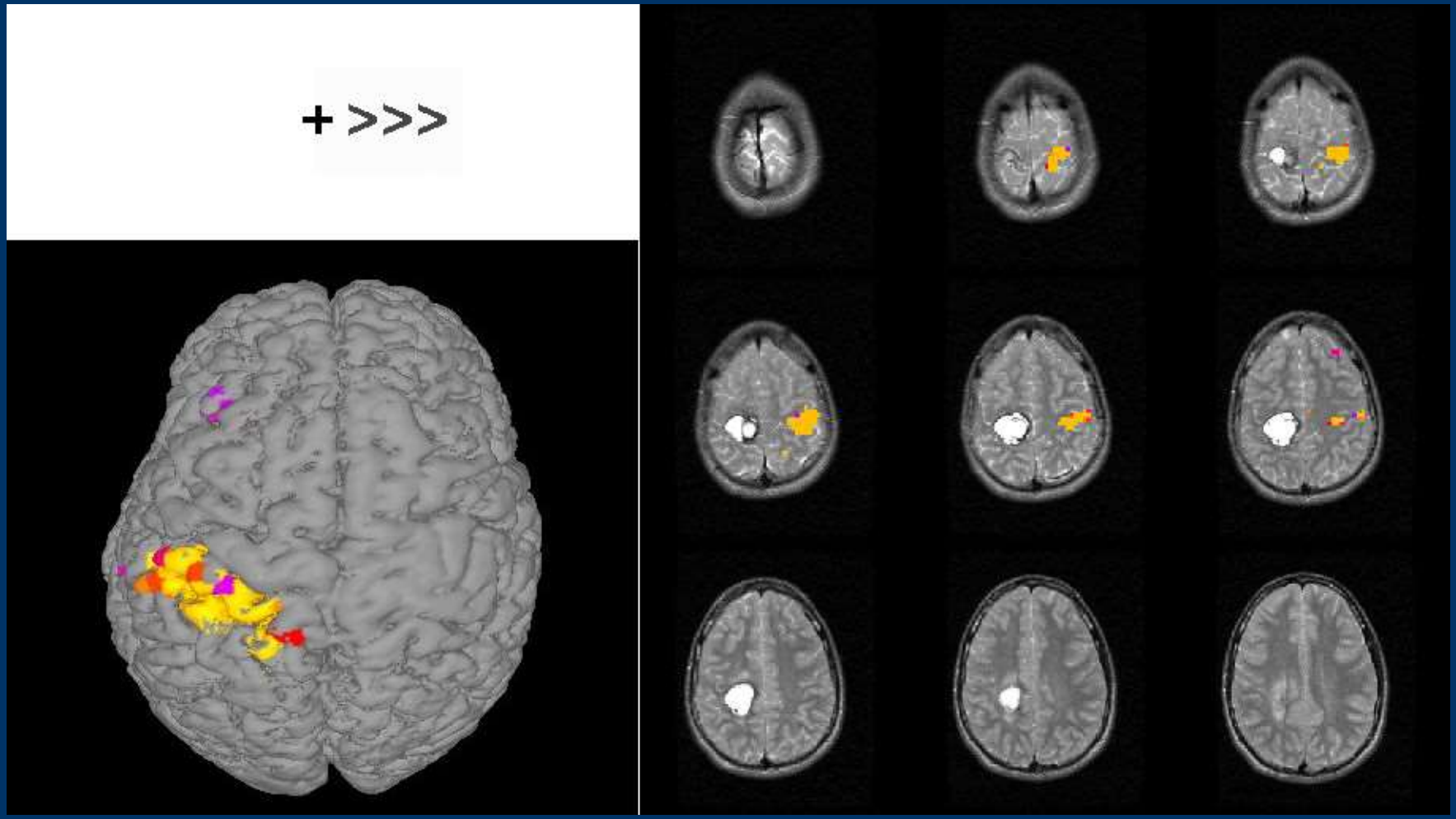
T = 13.5 s



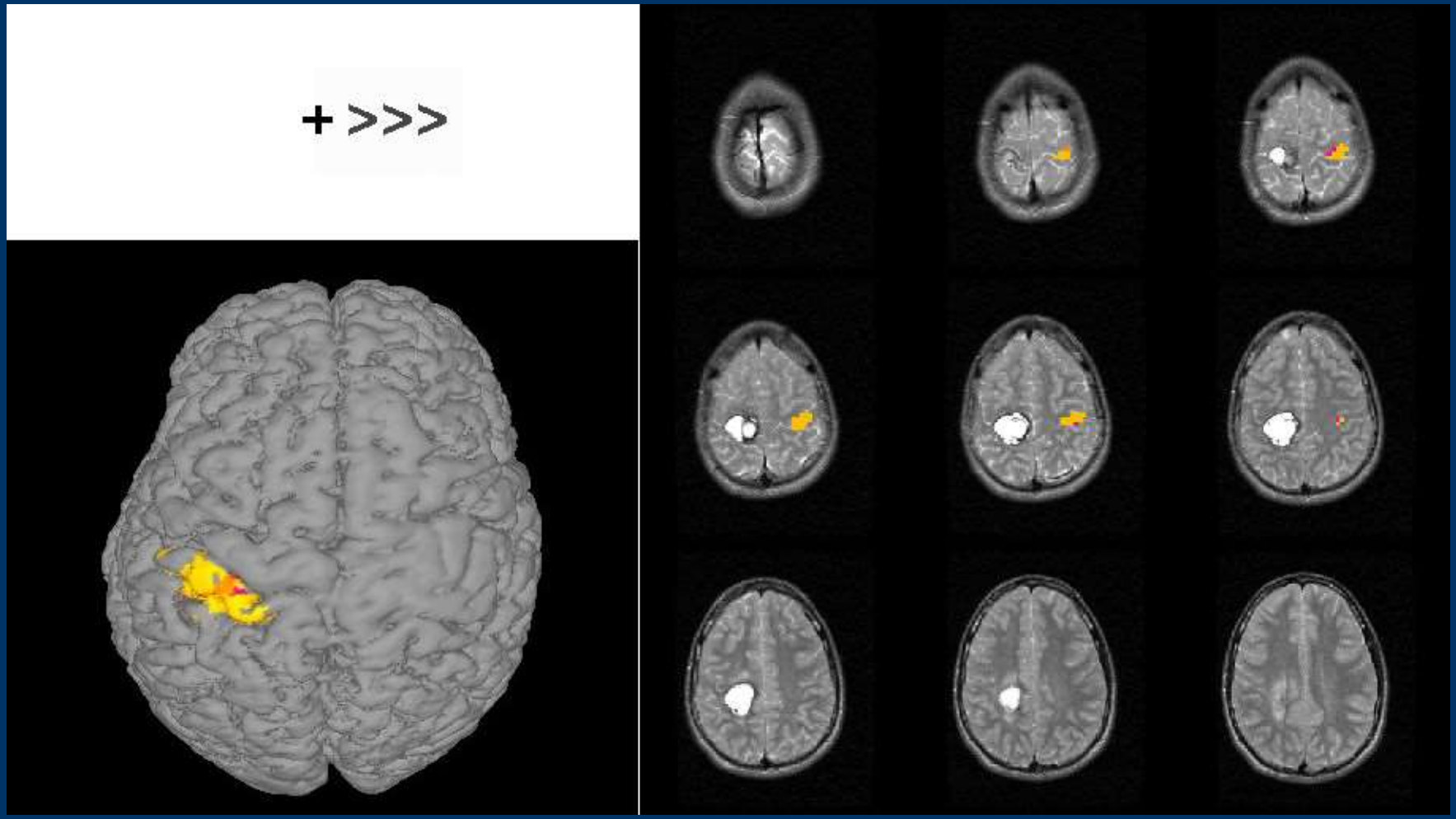
T = 18.0 s



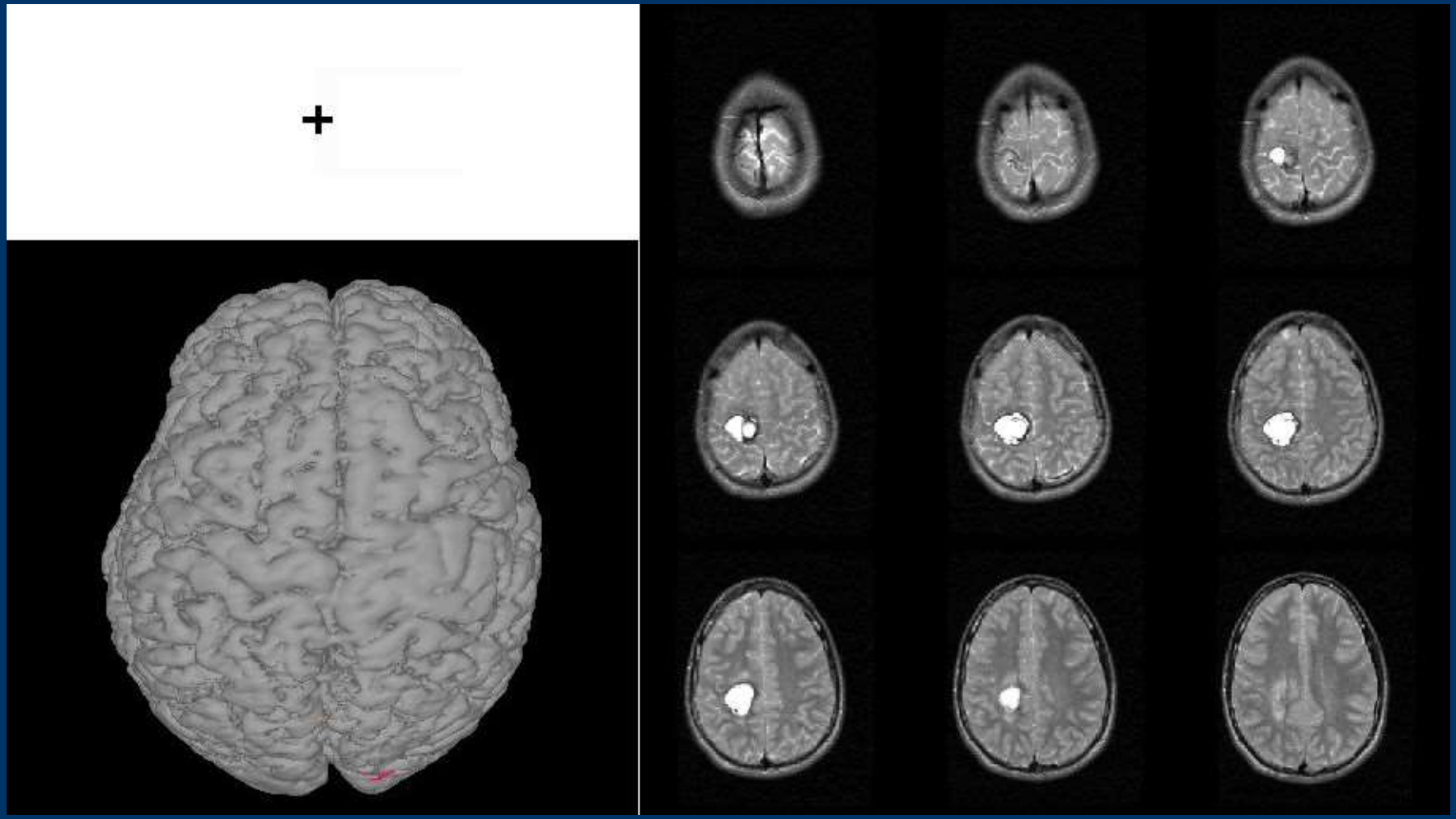
T = 22.5 s



T = 27.0 s



T = 31.5 s



T = 38.0 s

Limitations of fMRI mapping

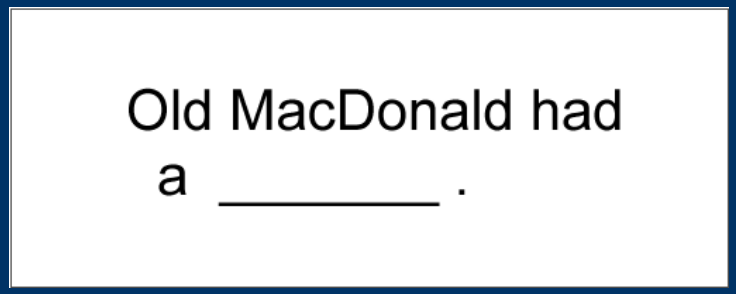
- BOLD fMRI is an indirect measure of neuronal function
- BOLD signal arises from nearby capillaries and remote veins
- Vascular BOLD response is slow (~4s delay to peak)
- Tissue pathology may interfere with normal BOLD signal
- fMRI shows any area active with task, not just essential areas
- Ultrafast functional images are sensitive to B0 inhomogeneity
- Functional & anatomical images need to be properly aligned
- Task performance is critical (i.e., attention, accuracy, anxiety)
- Head must remain still (motion is most common problem)
- Cardiac and respiratory fluctuations can also affect results

Many fMRI tasks are available

- Language
  - Reading sentence completion
  - Word generation (opposites, verbs, etc)
  - Picture naming
  - Auditory sentence completion
  - English, Spanish, Japanese, Hebrew, German, etc.
  - Passive video viewing
- Motor
  - Hand motion
  - Foot motion
  - Mouth motion
  - Imagined motion
- Somatosensory
  - External tactile stimulation
- Vision
  - Visual field mapping
- Memory (not yet)

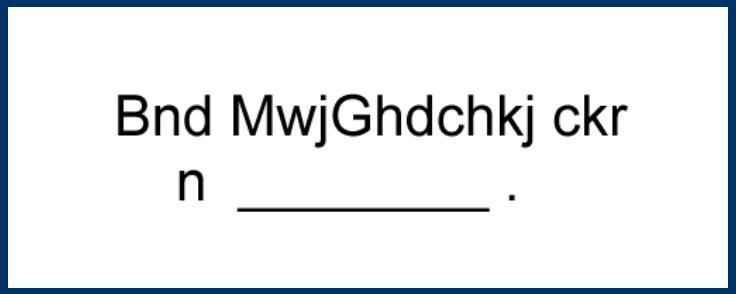
Language mapping – fMRI for locating brain areas involved in speech

Patients perform a silent sentence-completion task



15s

vs



15s

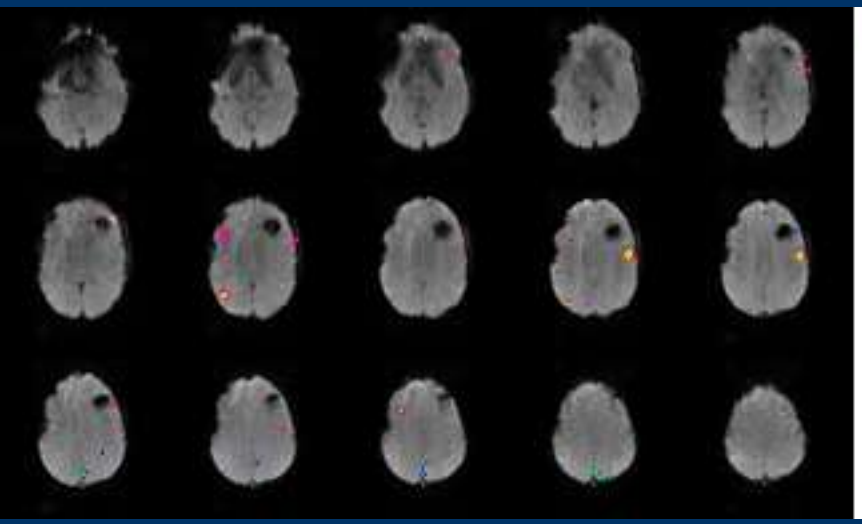
The “task” condition makes the patient use “comprehension”, “word finding”, and “expressive” speech areas. It also involves vision and eye movement.

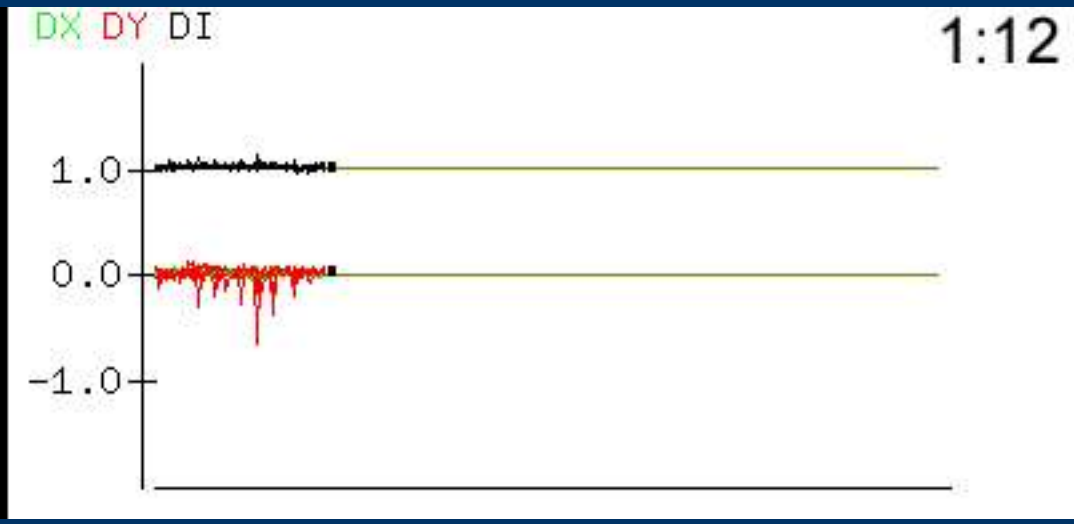
The “control” condition attempts to match vision function and eye movement, but with no language components.

Patient compliance

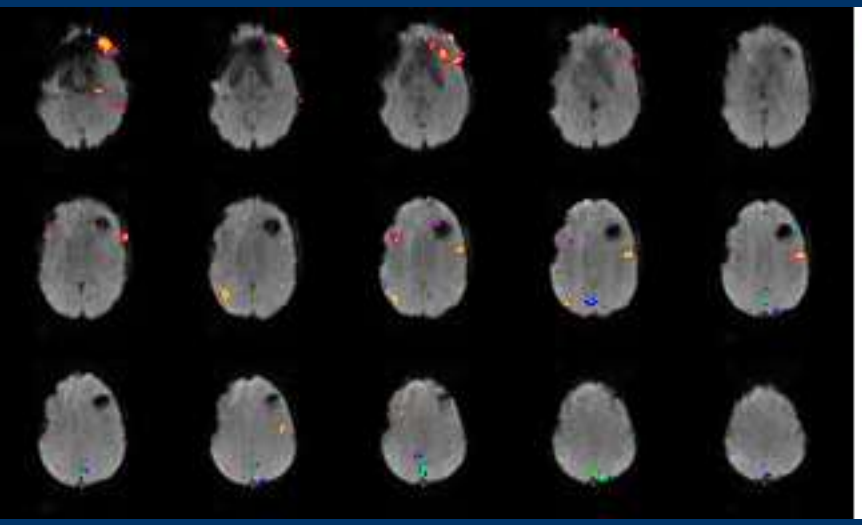
- Training
  - Patients must actively participate in fMRI
  - Tasks must be appropriate and understood
  - Task fMRI done on patients 5yo to >80yo
- Task performance
  - Anxiety affects fMRI results
    - Getting patients relaxed is important
  - Head motion is most common problem
  - Important to assess performance in real-time

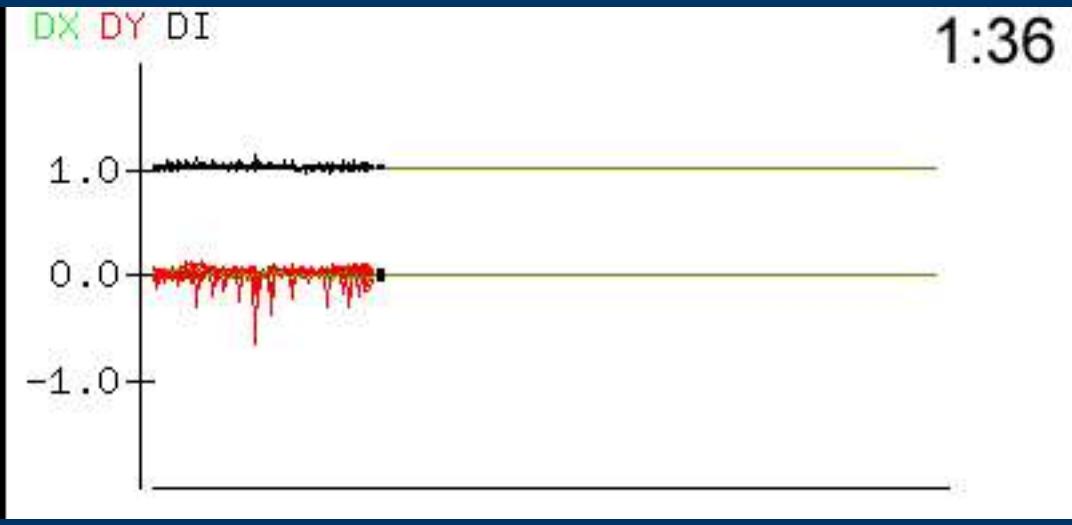
Silent sentence-completion reading task





Real-time fMRI mapping and head-motion plots

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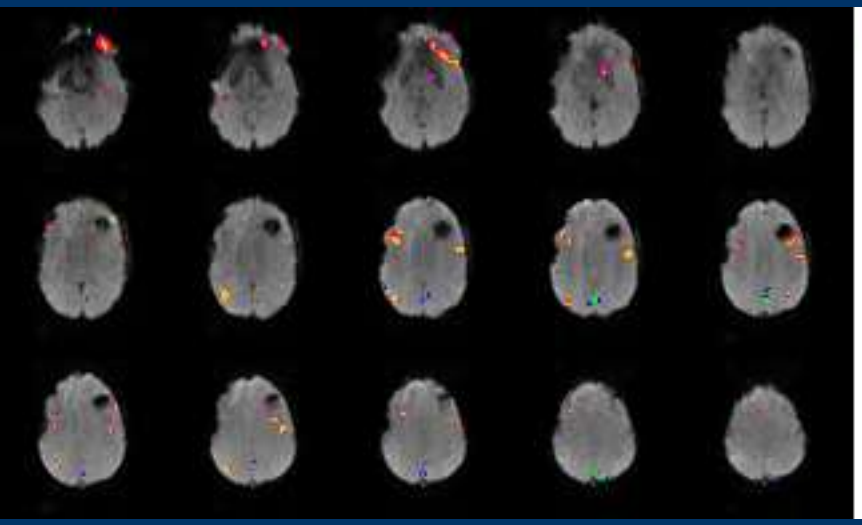

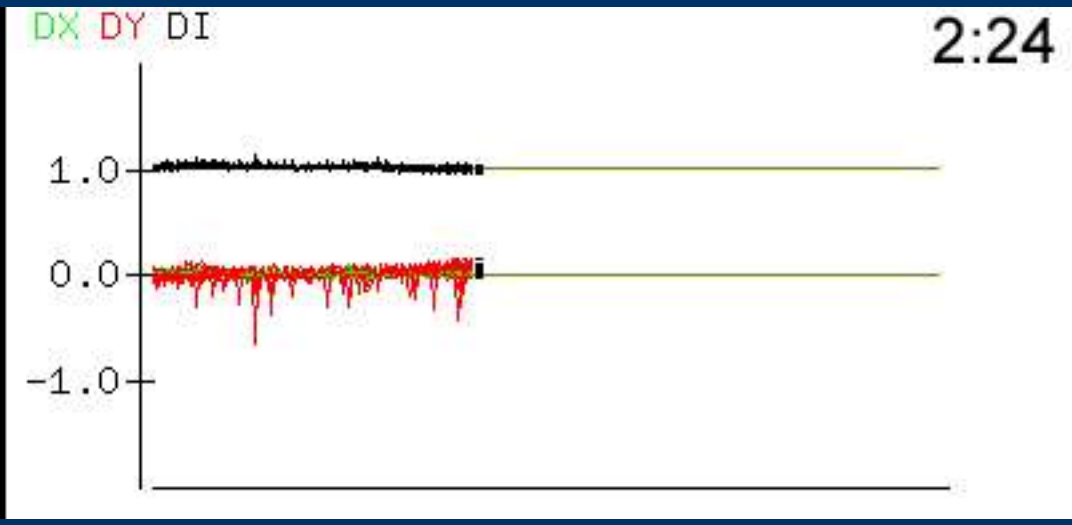
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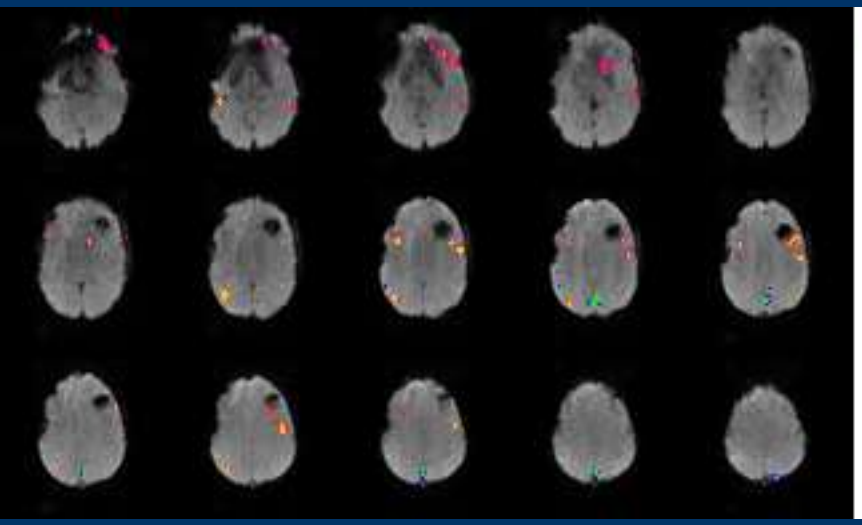

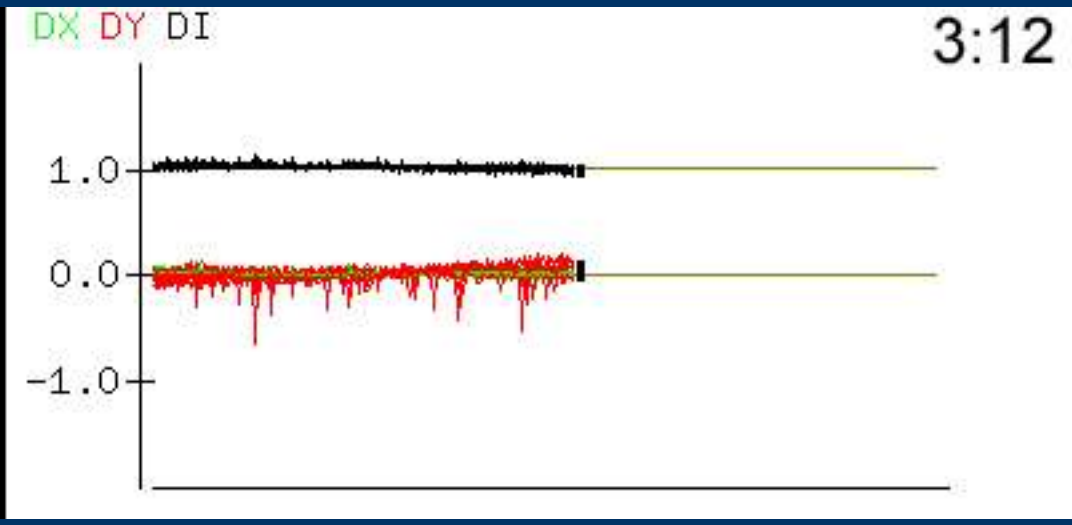
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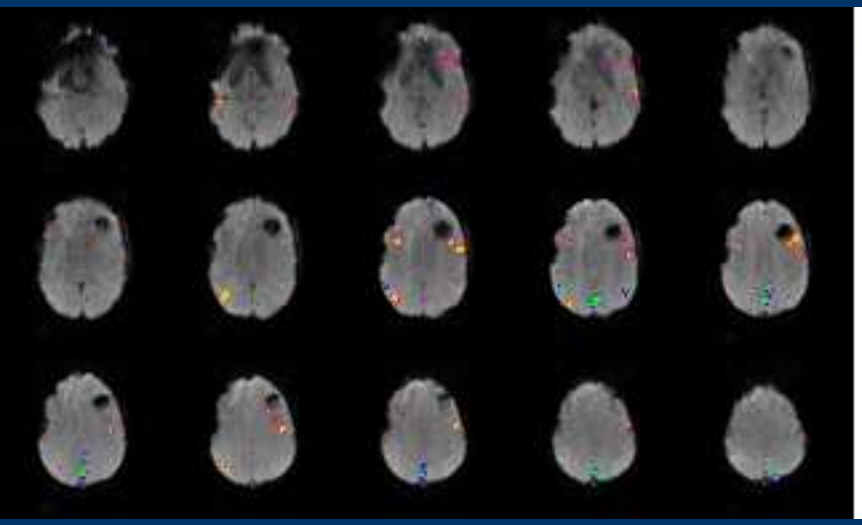

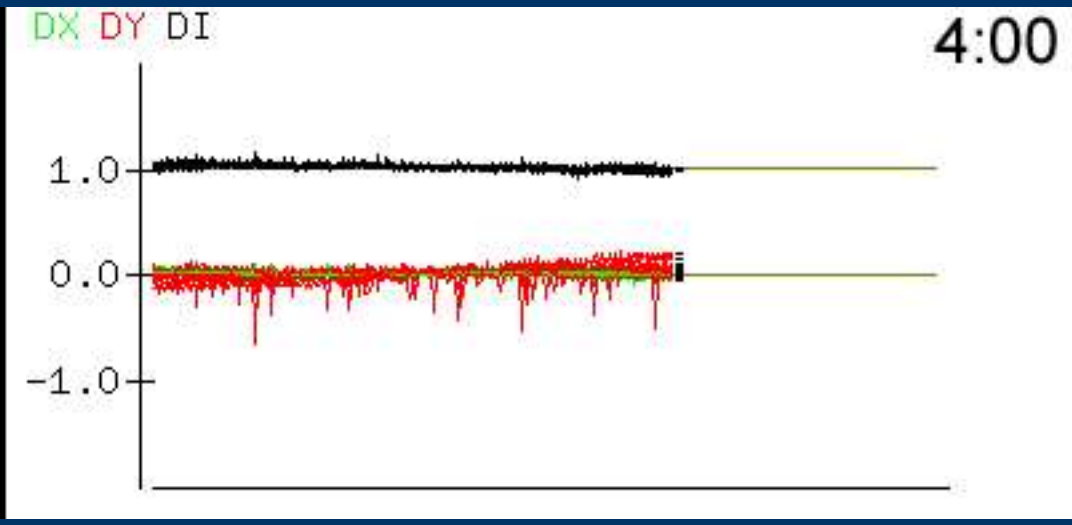
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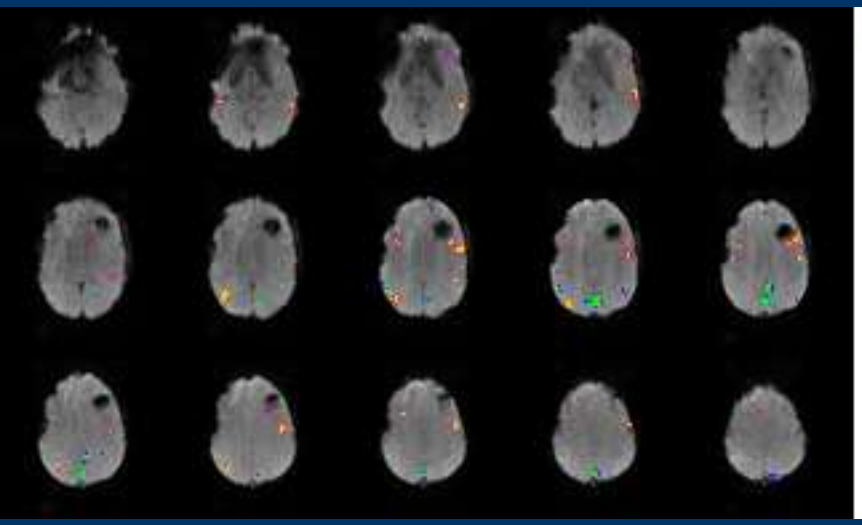

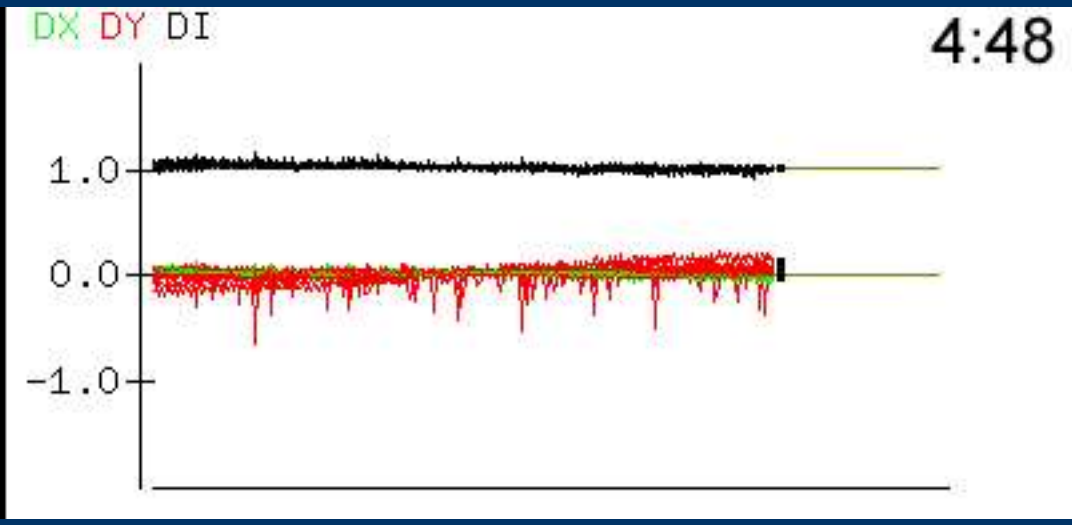
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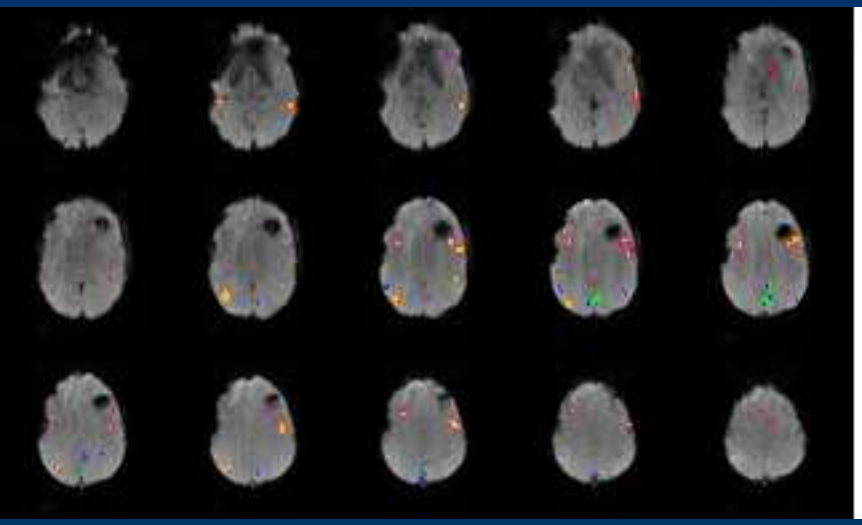

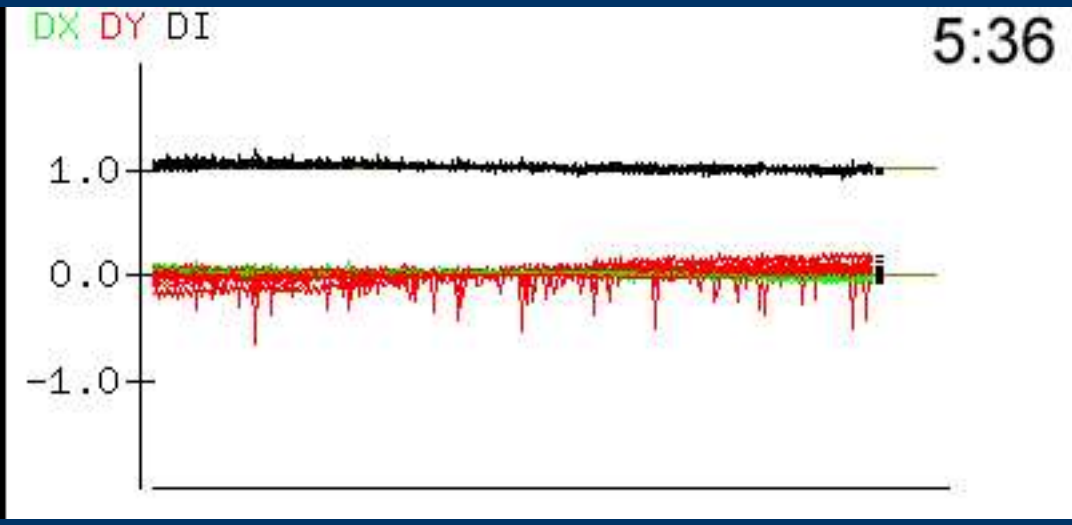
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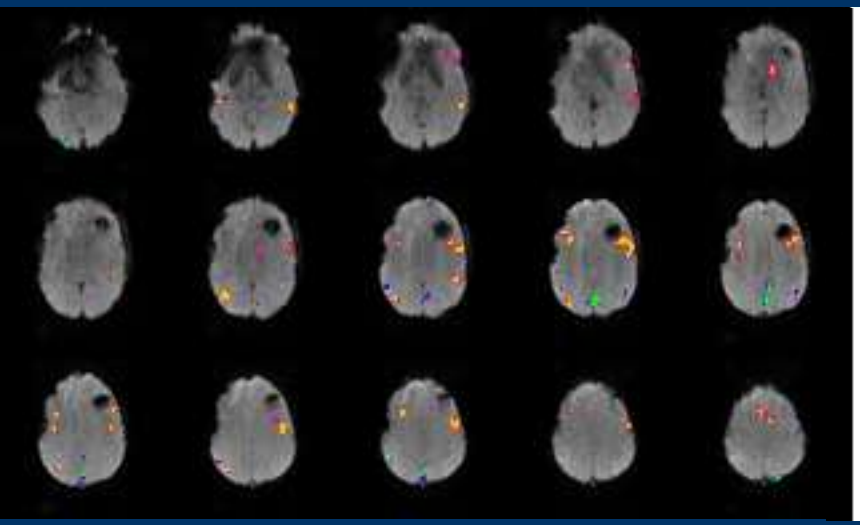

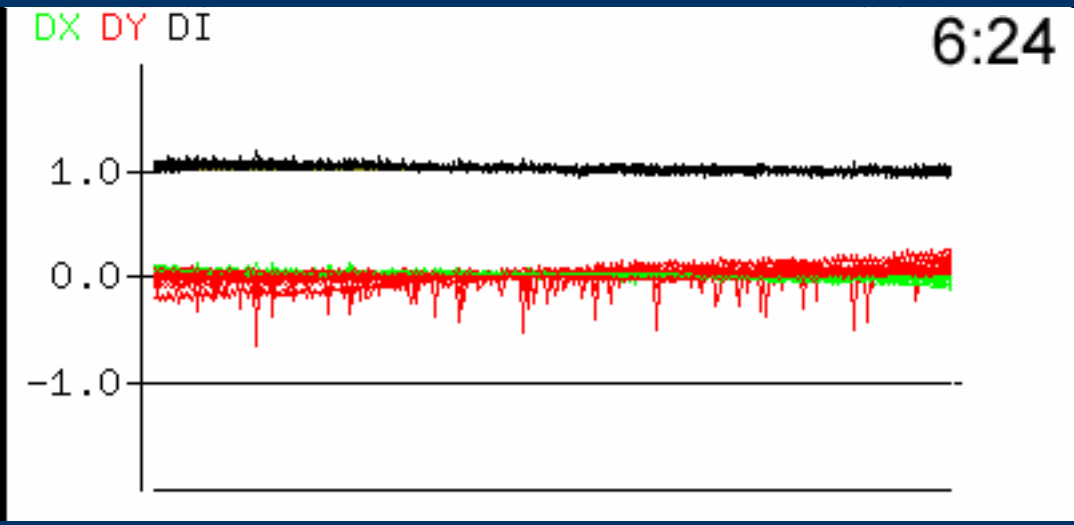
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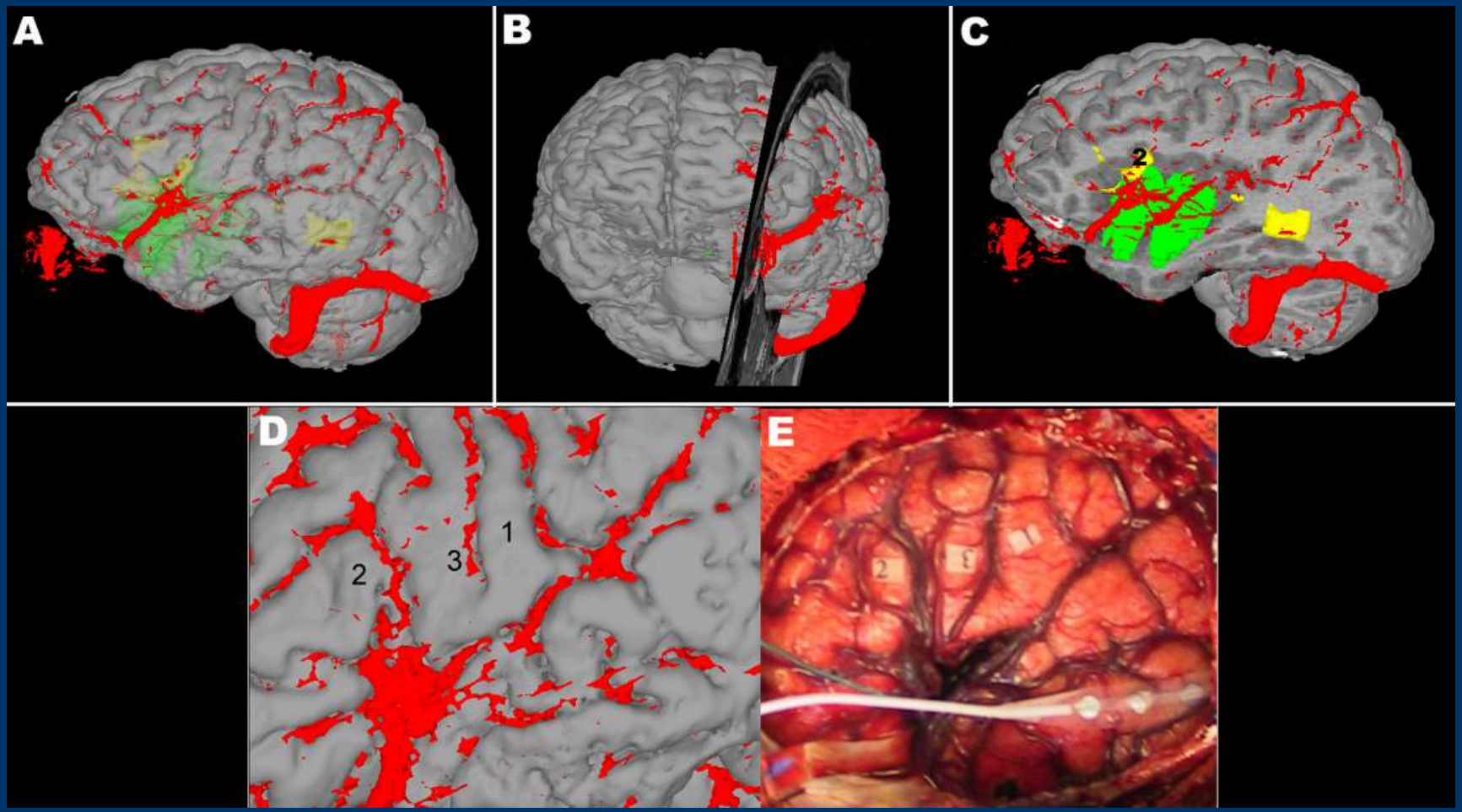
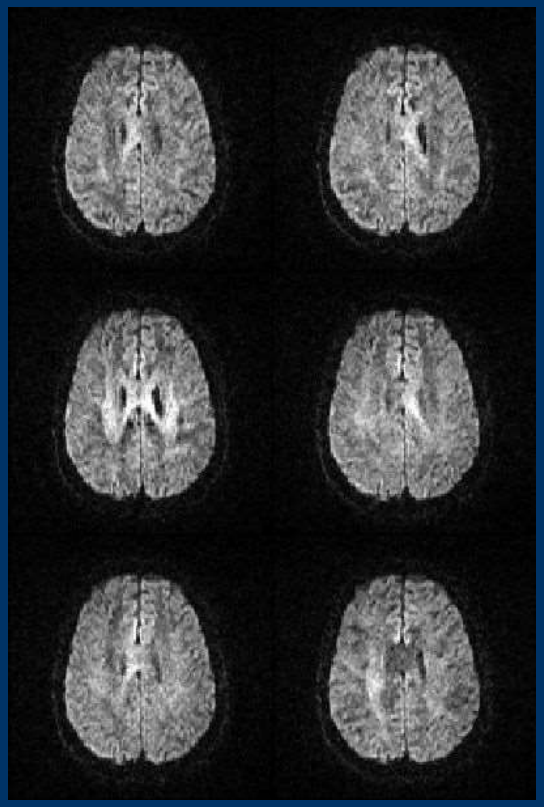
fMRI has been validated by direct comparison with intraoperative mapping

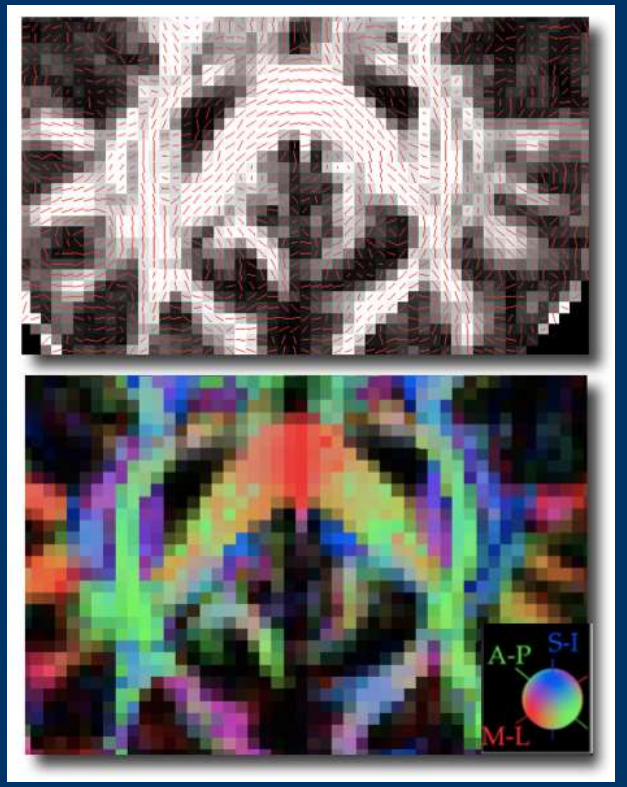


How does DTI work?



Acquire diffusion-weighted images at multiple diffusion orientations (6-60)

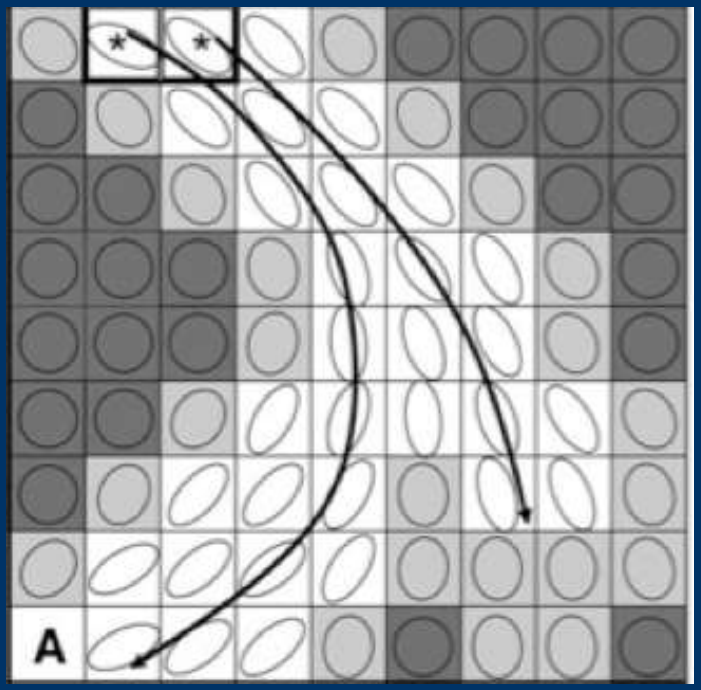
Calculate diffusivity and orientation at each voxel

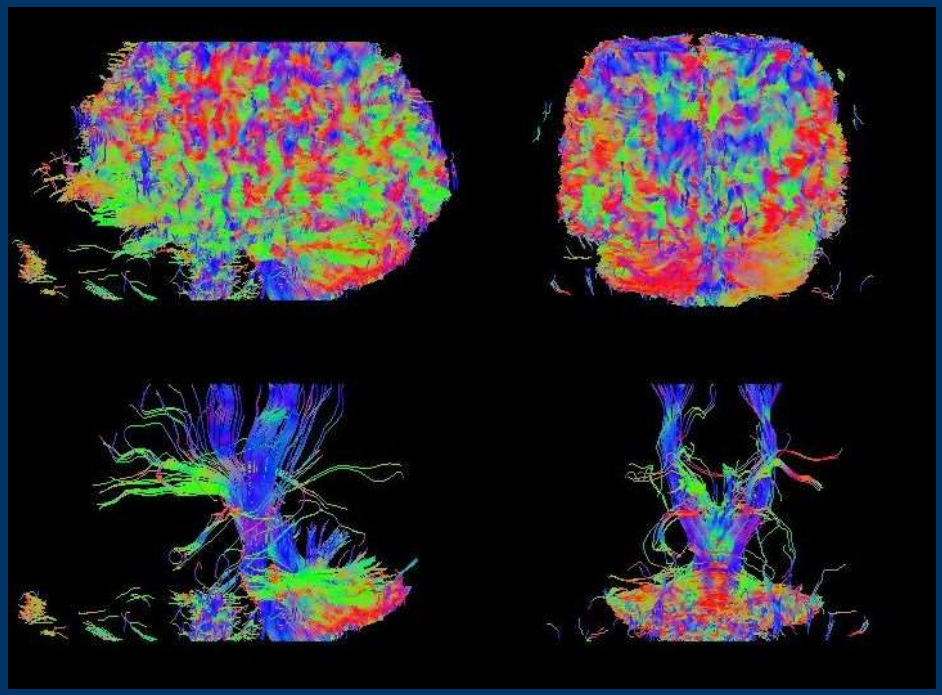


Color-code orientations

DTI – fiber tracking

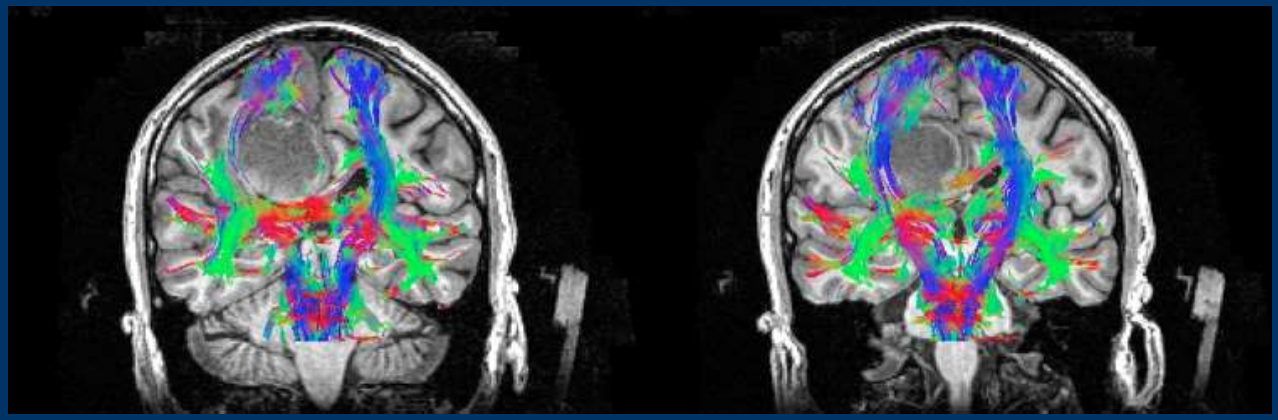
Start at any ‘seed’ and connect voxels with similar orientations

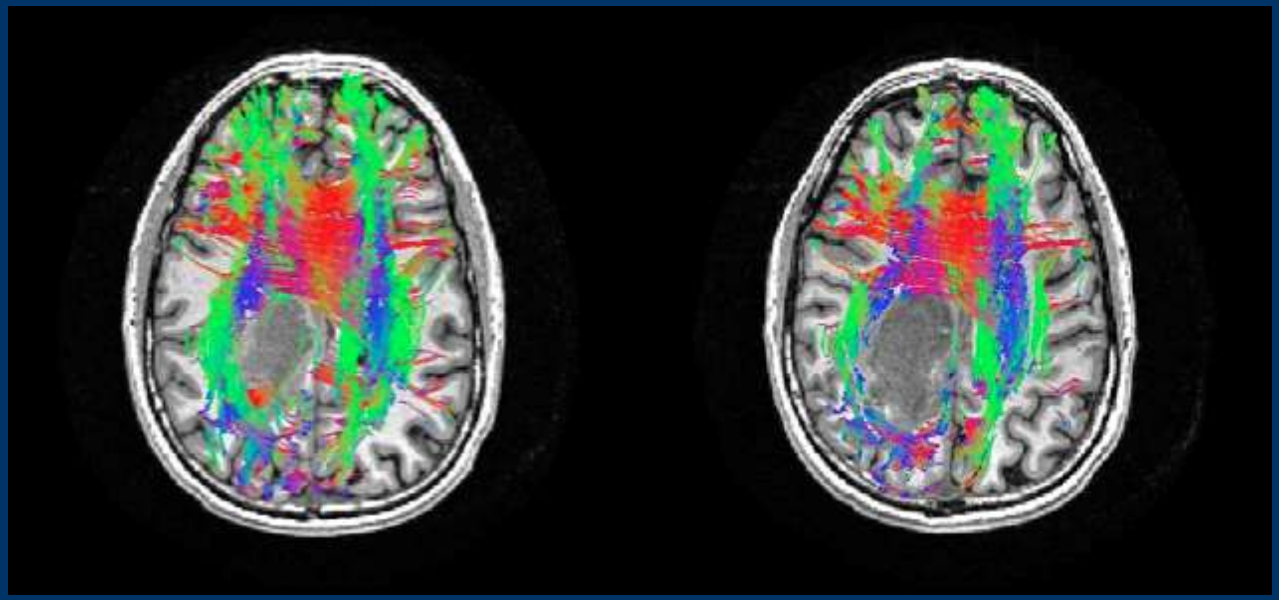




Basser et al., Magn Reson Med, 2000

Overlay fiber tracks on anatomy





fMRI/DTI exam

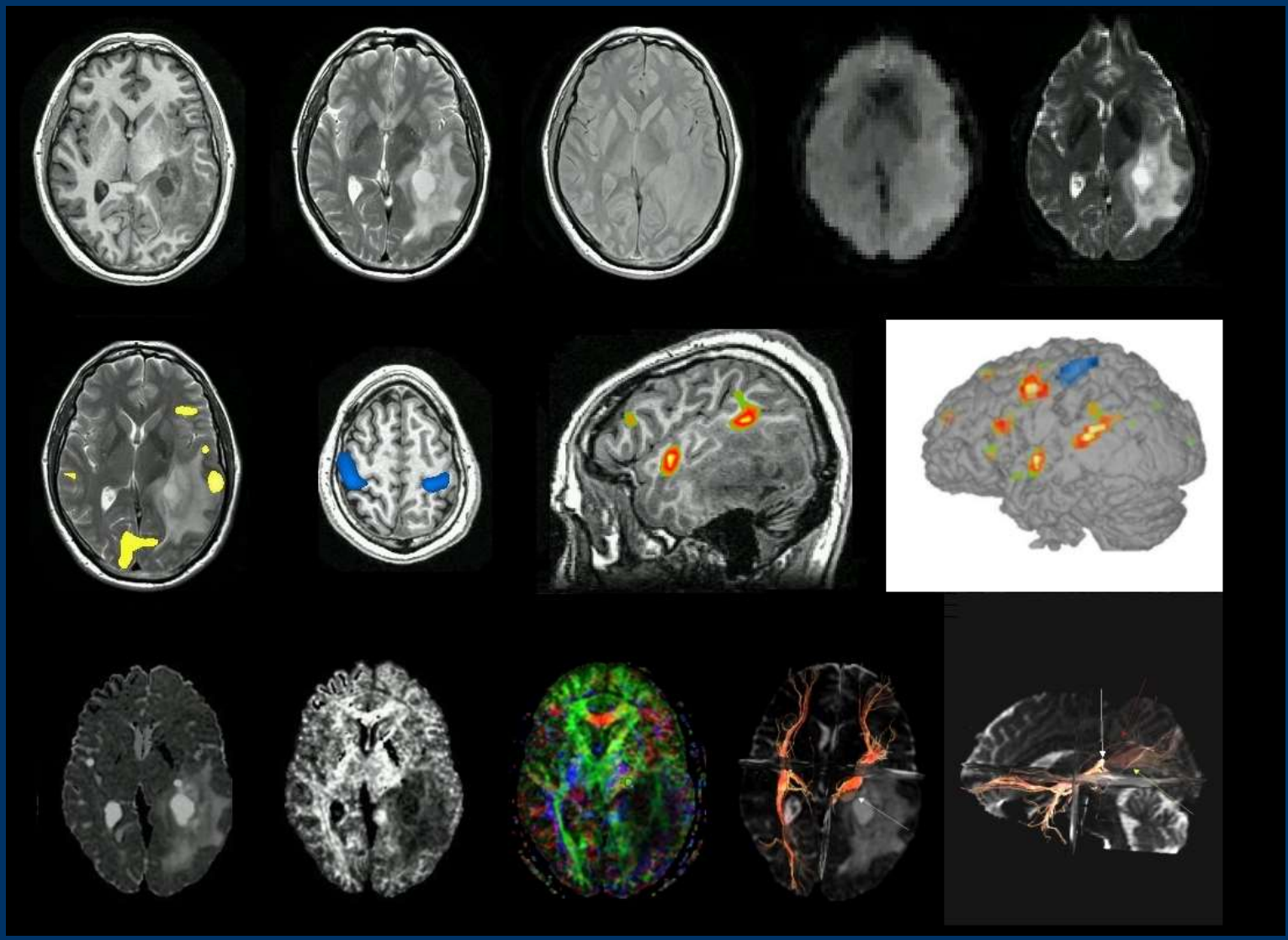
- 10 min pre-scan assessment and training
- 45-60 min MRI session
  - 10 min anatomical scans (T1 & FLAIR)
  - 15-20 min fMRI – 3-4 tasks (4 min each)
  - 5 min 30-direction DTI scan
- 30-60 min post-scan image analysis
  - Registration of fMRI and DTI with T1 images
  - fMRI statistical analysis of “active” voxels
  - Overlay of fMRI and DTI on anatomical images
- Neuroradiological interpretation

fMRI and DTI maps involve post-processing

Anatomical Images

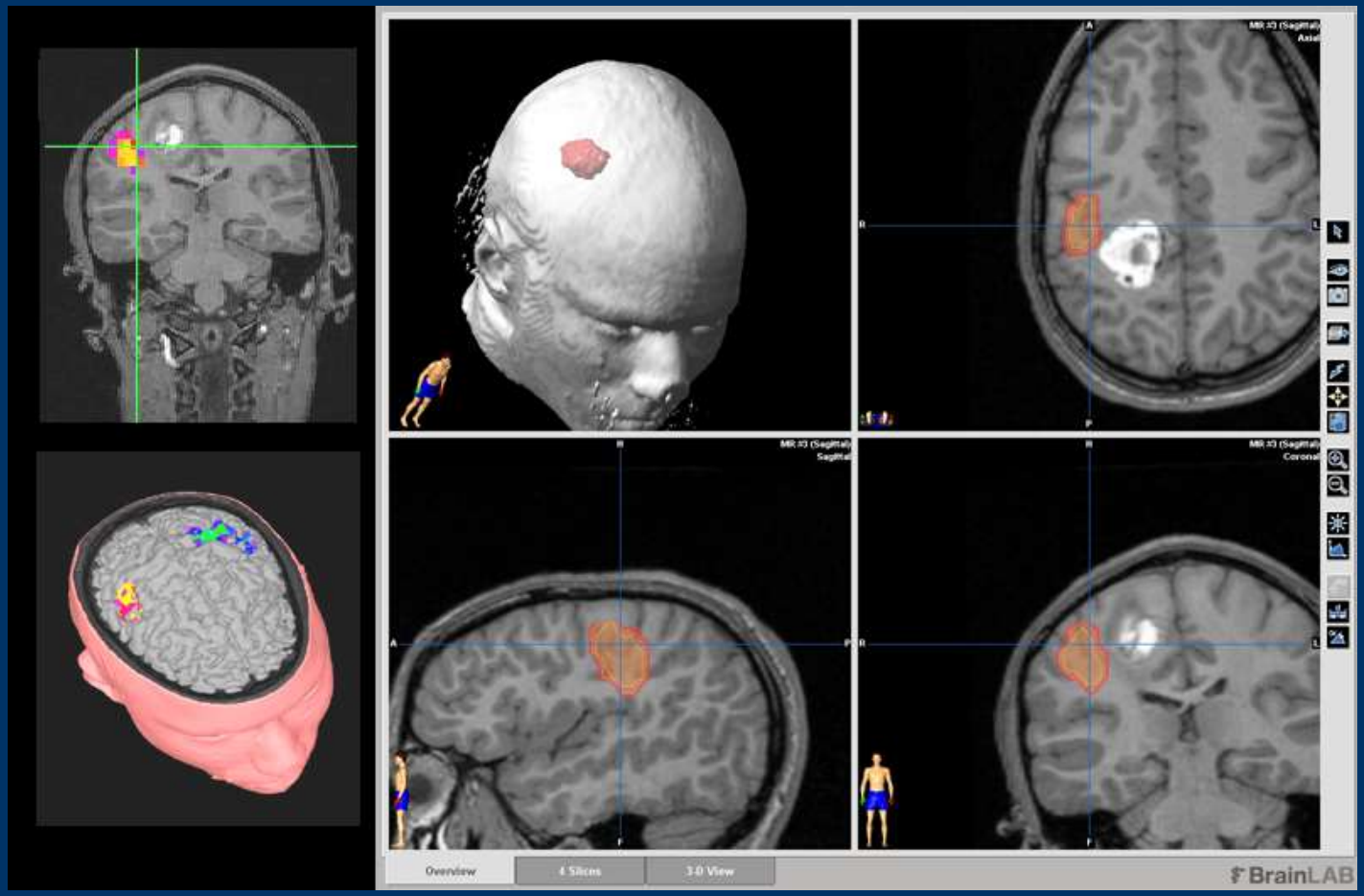
fMRI statistical maps, overlaid on anatomy or brain surface

Diffusion maps and white-matter tracts from DTI



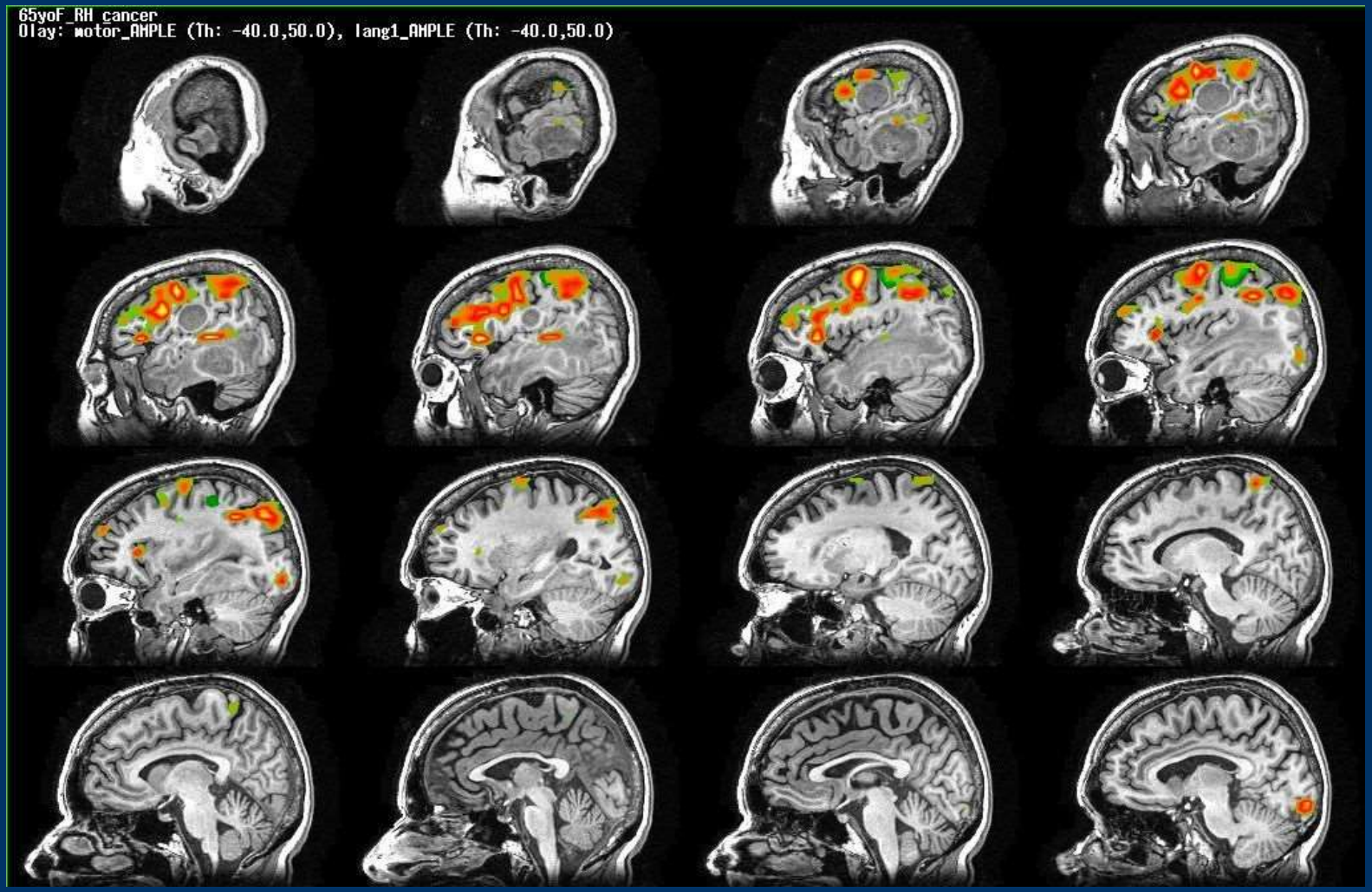
Visualization image processing

Merge functional activation maps with anatomical images
Reconstruct MRI images and maps for 3-D viewing



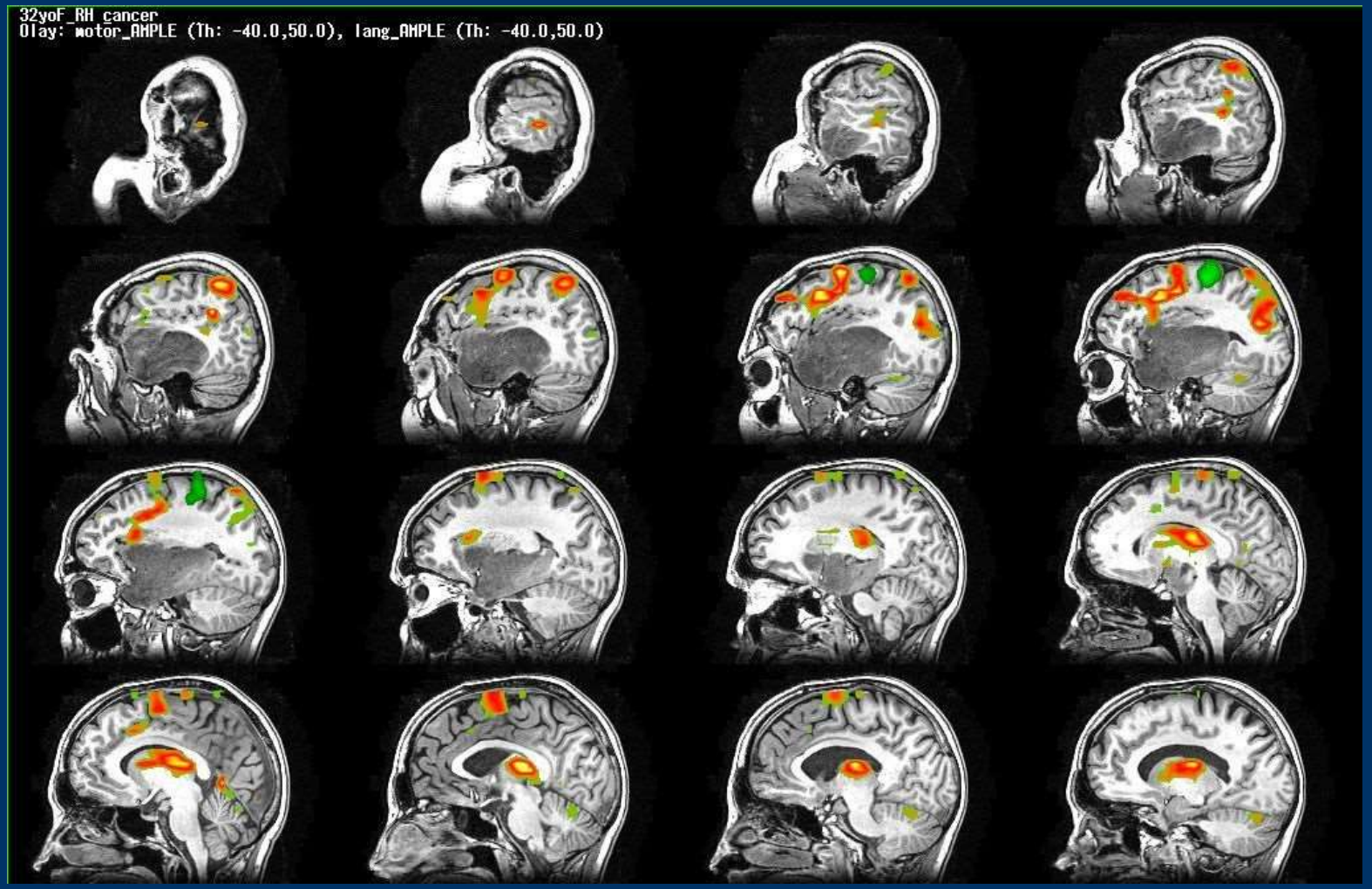
Case examples

RH 65yo F with cancer



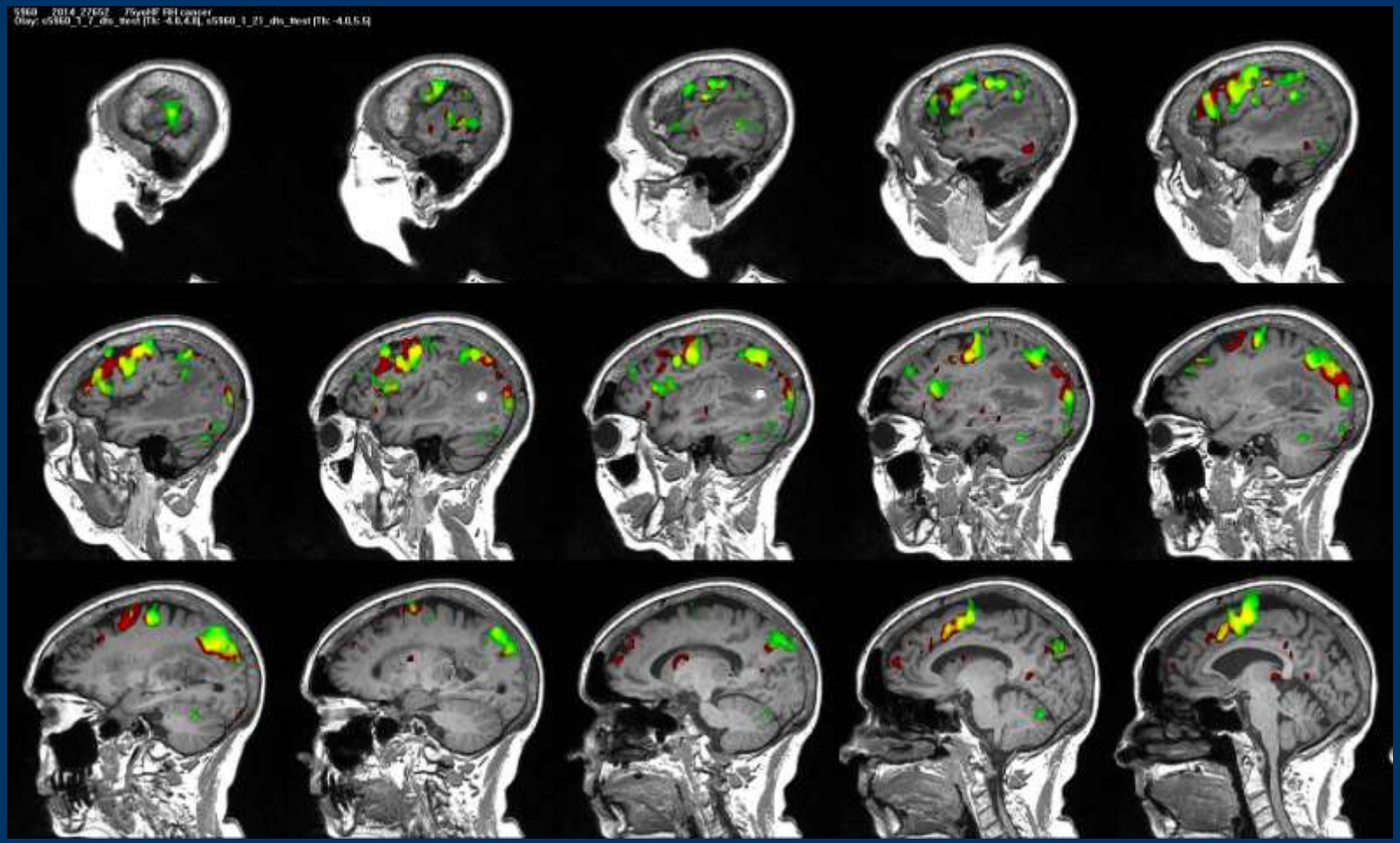
Orange – sentence-completion map
Green – hand movement map

RH 32yo F with cancer



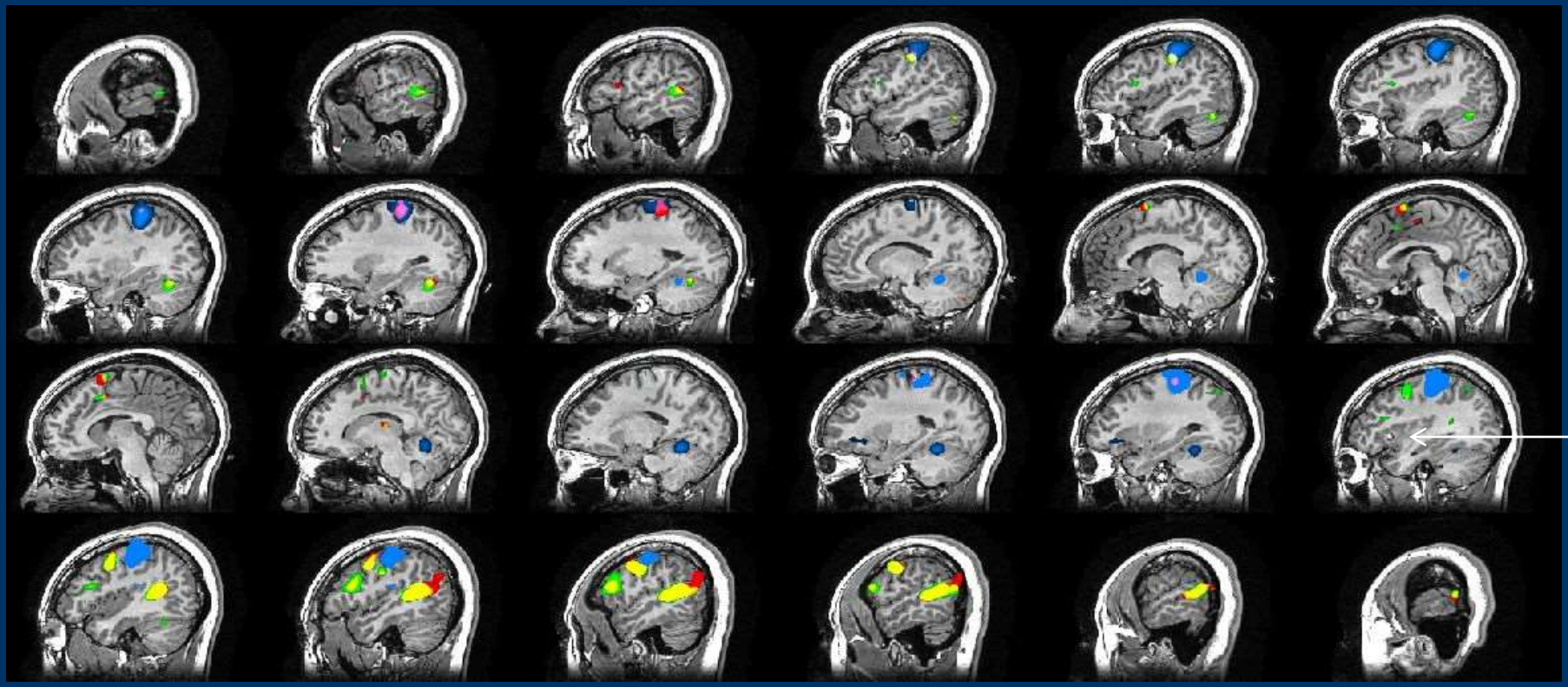
Orange – sentence-completion map
Green – hand movement map

RH 75 yo F, English+Spanish



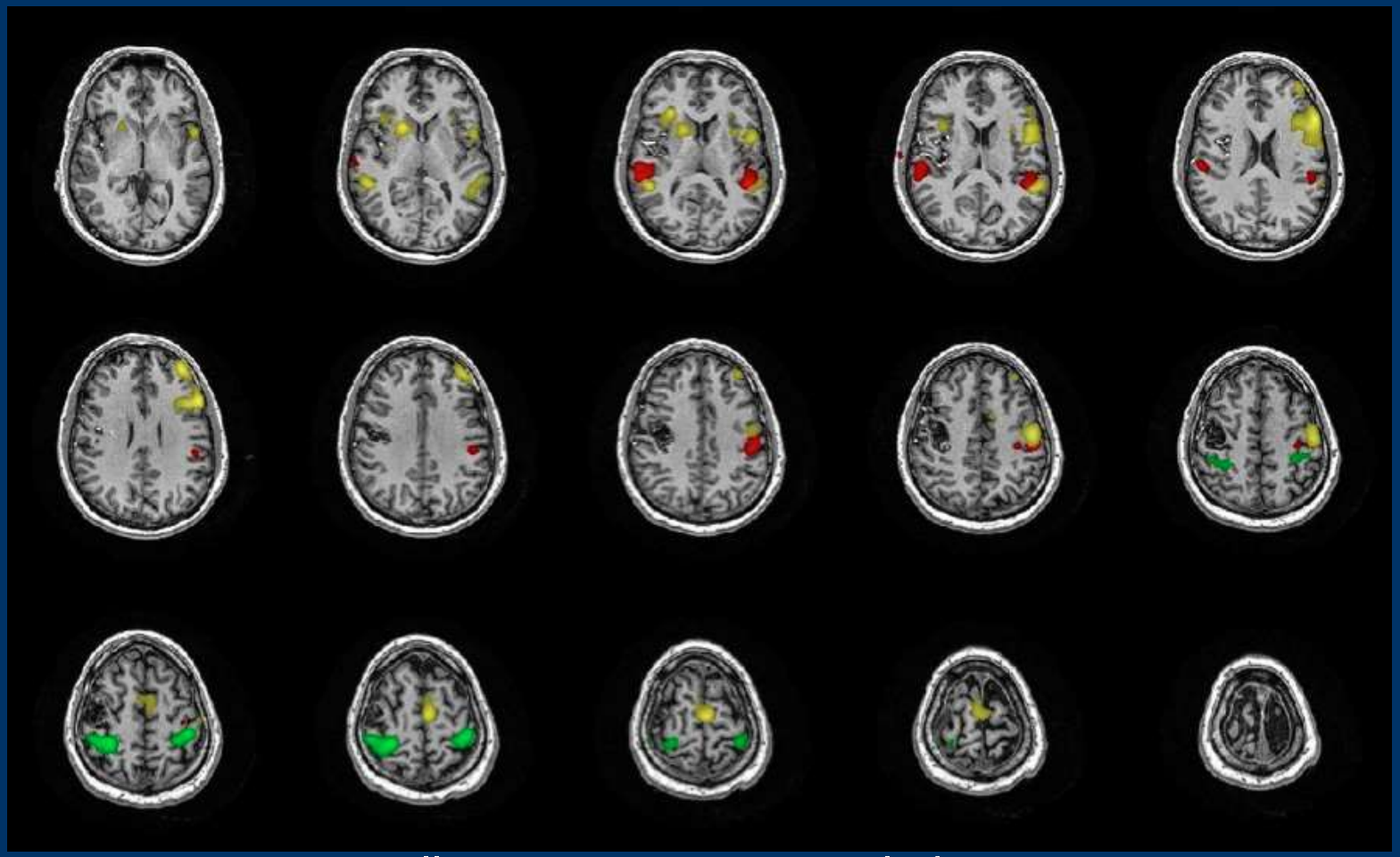
Red – English sentence-completion map
Green – Spanish senctence-completion map

LH 23yo F with cancer



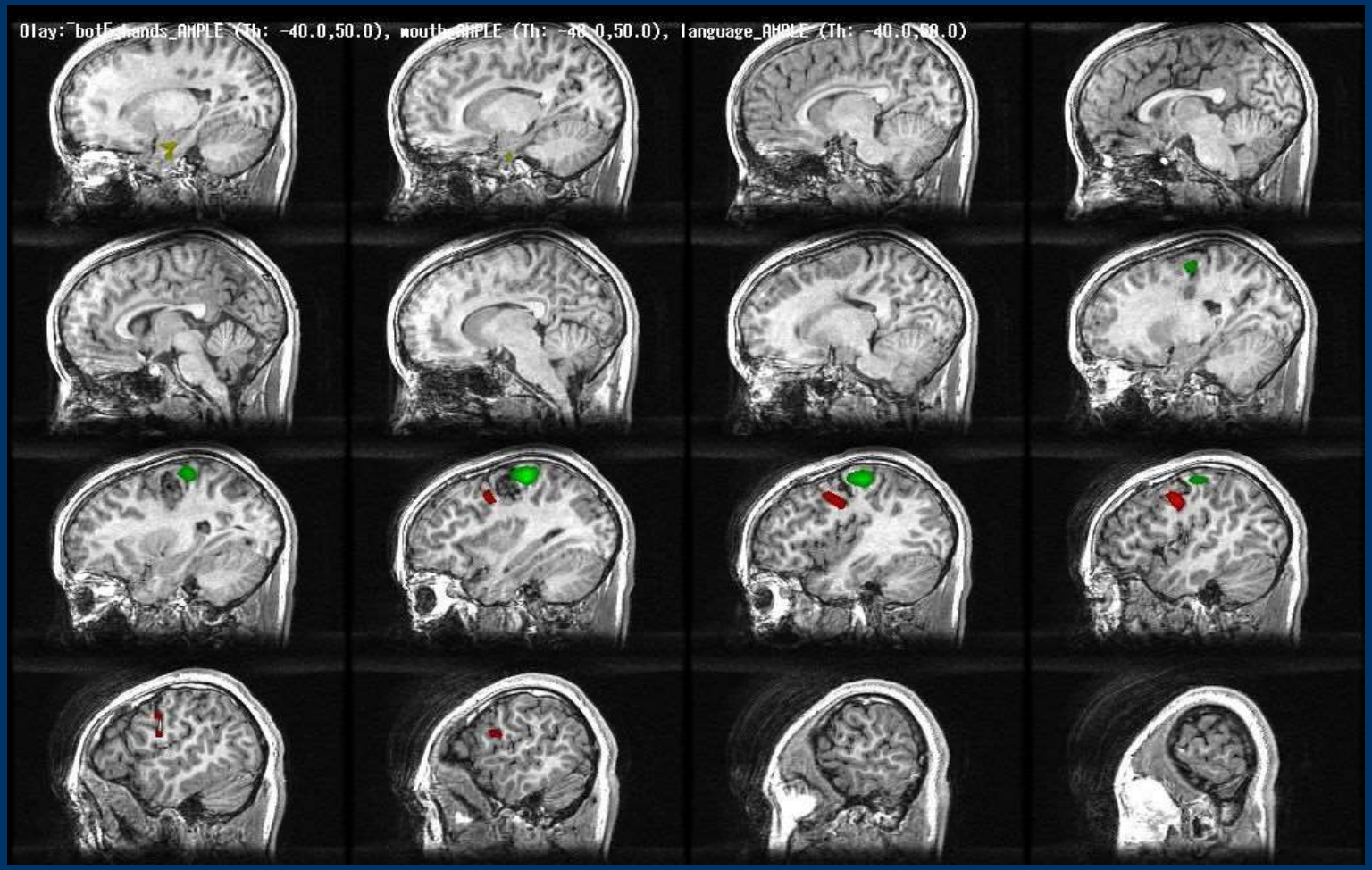
Yellow – 1st sentence-completion map
Green – 2nd sentence-completion map
Blue – hand movement map

RH 33yo M with AVM



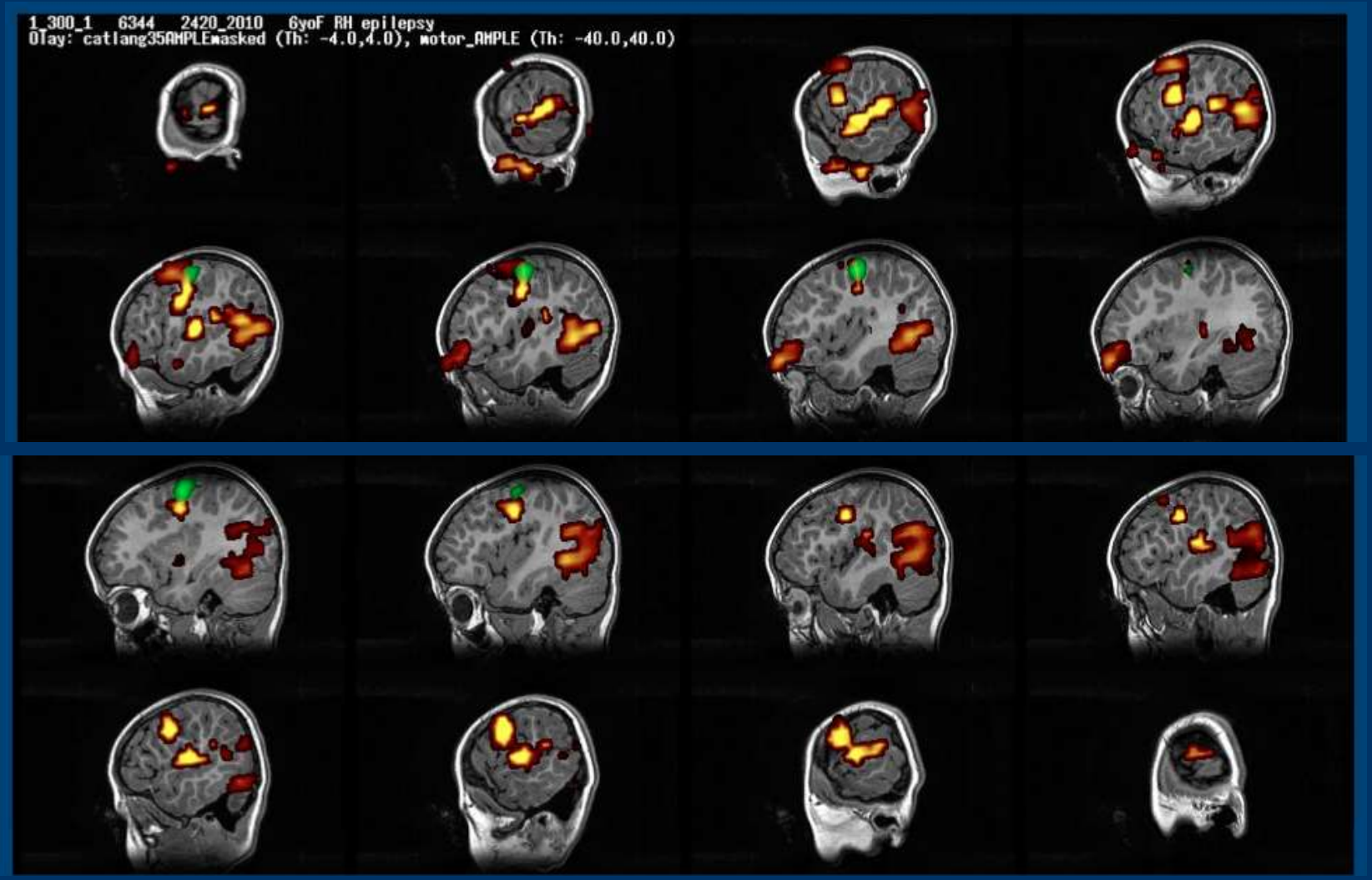
Yellow – sentence-completion map
Green – hand movement map
Red – mouth movement map

RH 10yo F with AVM



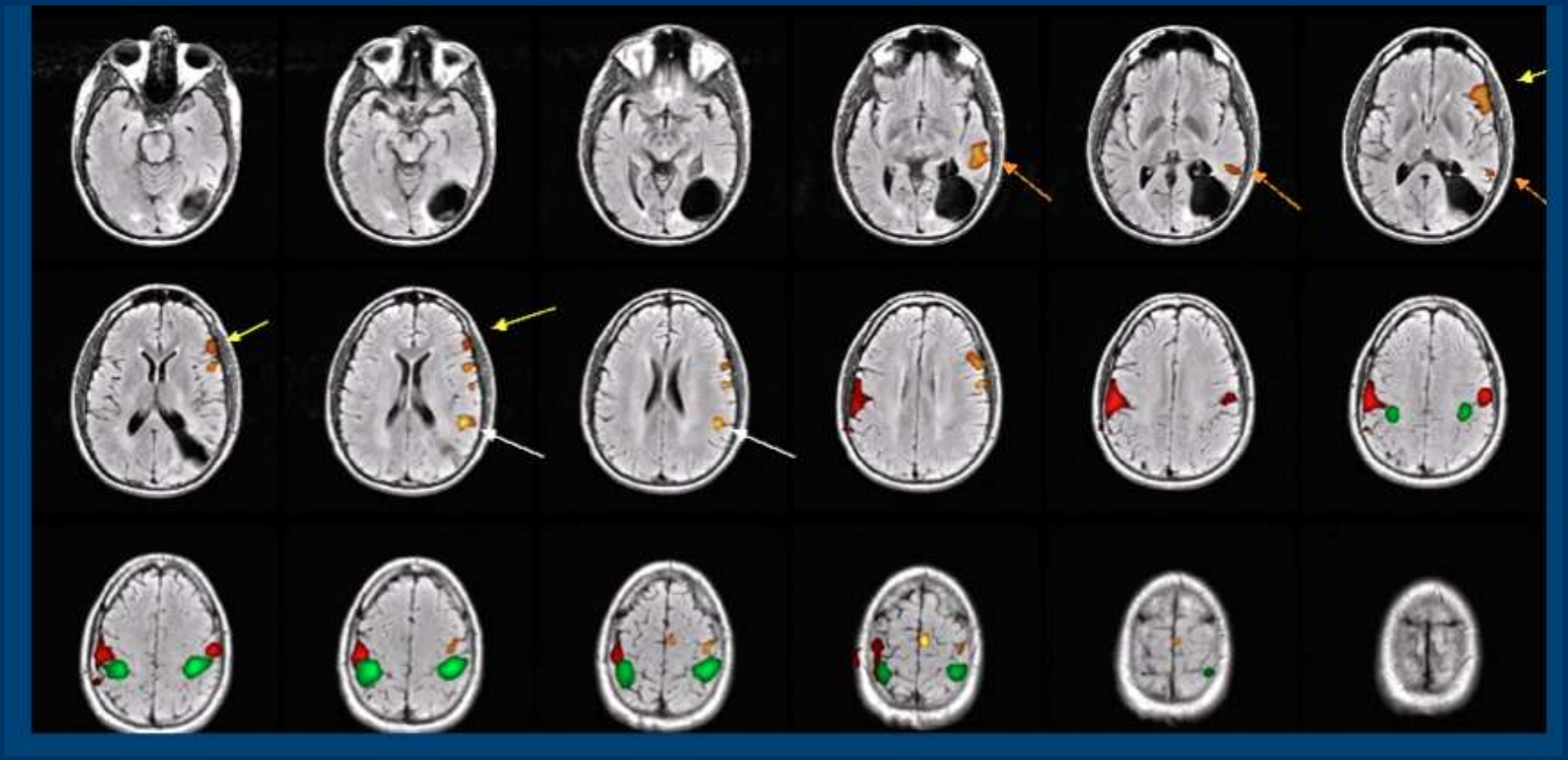
Green – hand movement map
Red – mouth movement map

RH 6yo F with Epilepsy



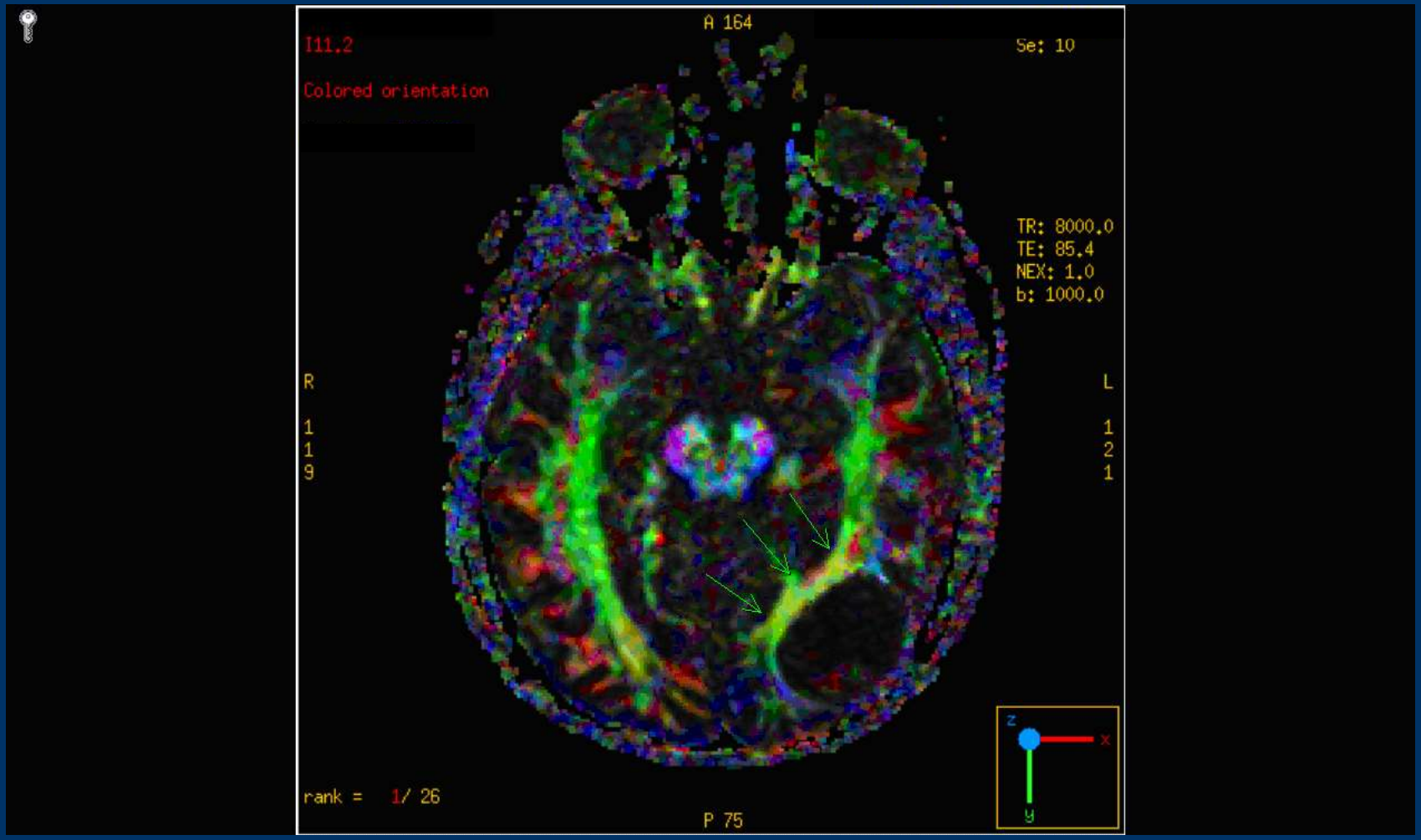
Yellow/Red – storybook language map
Green – hand movement map

LH 20yo M with cancer



Yellow – sentence-completion map
Green – hand movement map
Red – mouth movement map

20yo M – DTI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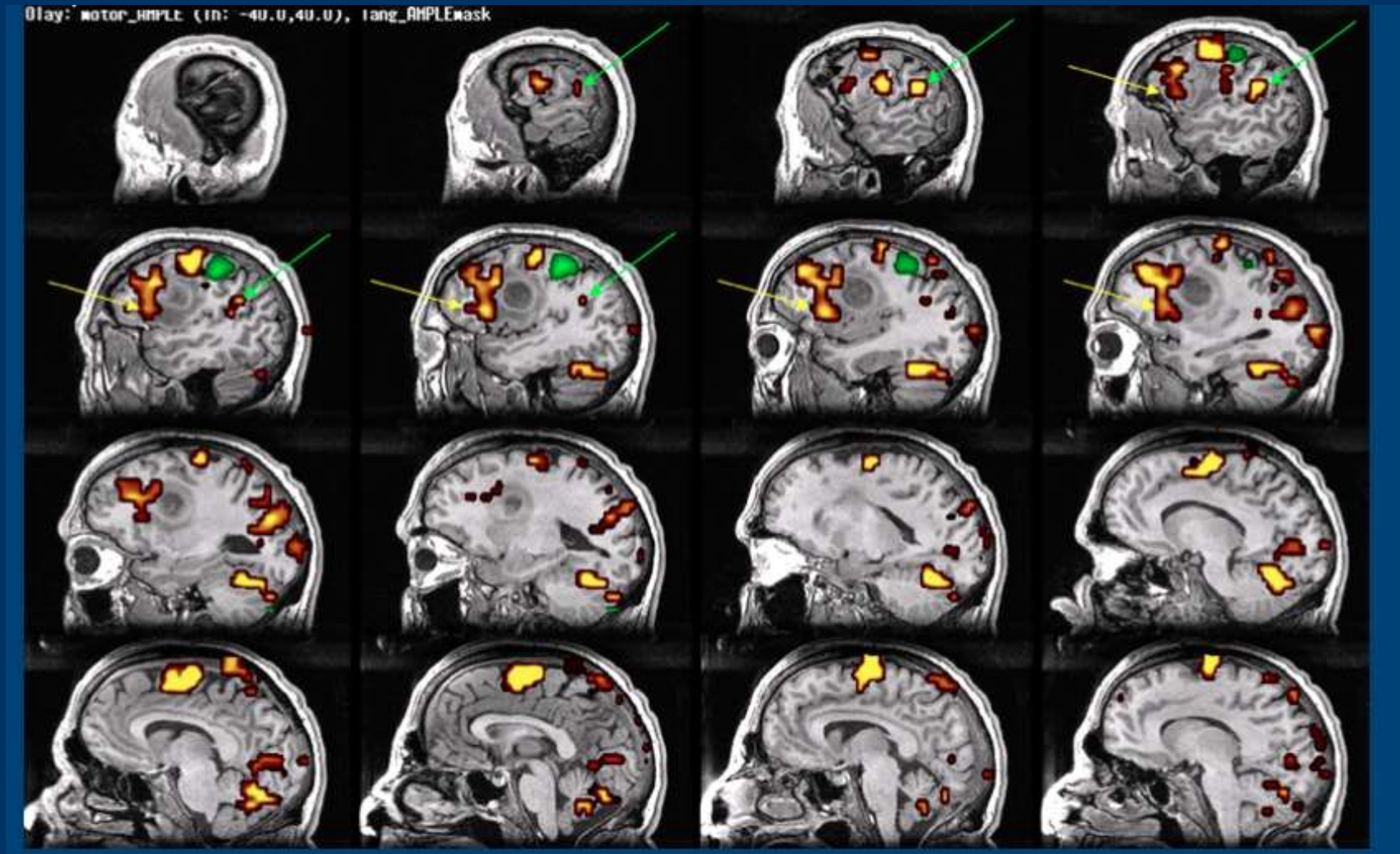
RH 55yo M with cancer



Yellow – sentence-completion map
Green – hand movement map

Does fMRI help?

- Improve outcome?
- Save time?
- Reduce costs?

Post fMRI Intervention

Pre fMRI Plan		No Surgery	Biopsy	Awake Craniotomy	Asleep Craniotomy
	No Surgery	2	2	5	0
	Biopsy	0	0	7	1
	Awake Craniotomy	0	1	13	3
	Asleep Craniotomy	0	0	0	5
	Total # of patients= 39				

Petrella et al., Radiology 2006

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Petrella et al., Radiology 2006

Post-surgery questionnaire

fMRI usefulness (N=69)

- 48% Very helpful
- 42% Helpful
- 6% Lateralization only
- 4% Not helpful
- 0% Counterproductive

Accuracy (N=45)

- 64% Within 1 cm
- 33% Within 2 cm
- 4% More than 2 cm

6/69 tumor resected despite uncooperative pt

Does fMRI help?

- Improve outcome?
  - Enables more aggressive resection
  - Can enable resection when pt uncooperative
- Save time?
  - Avoids or speeds up intraoperative mapping
- Reduce costs?
  - Shorter surgery

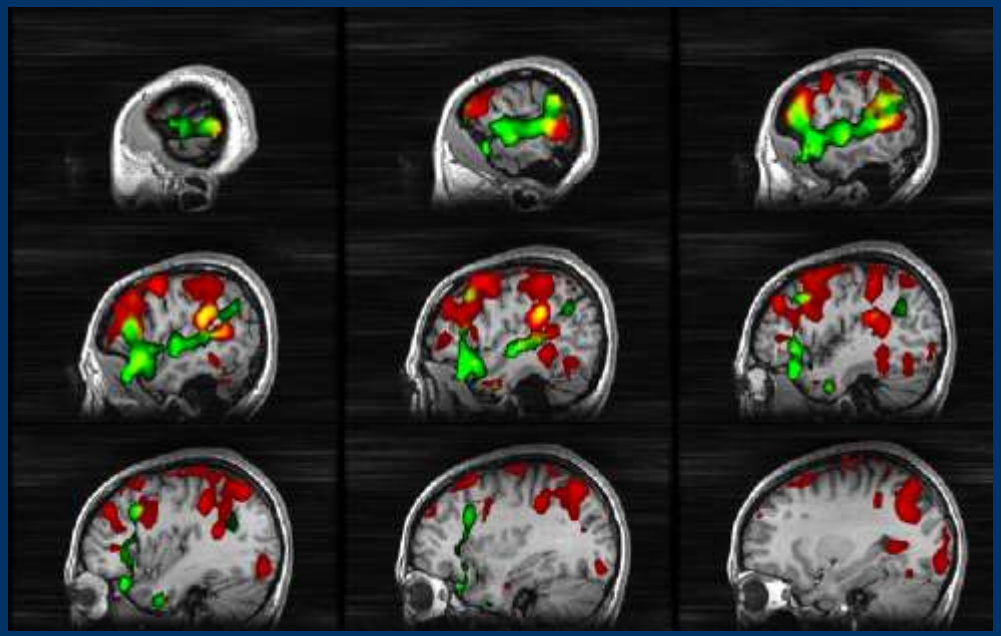
Improving functional imaging

- New pulse sequences
- New tasks
- Improved analysis methods

Passive language tasks

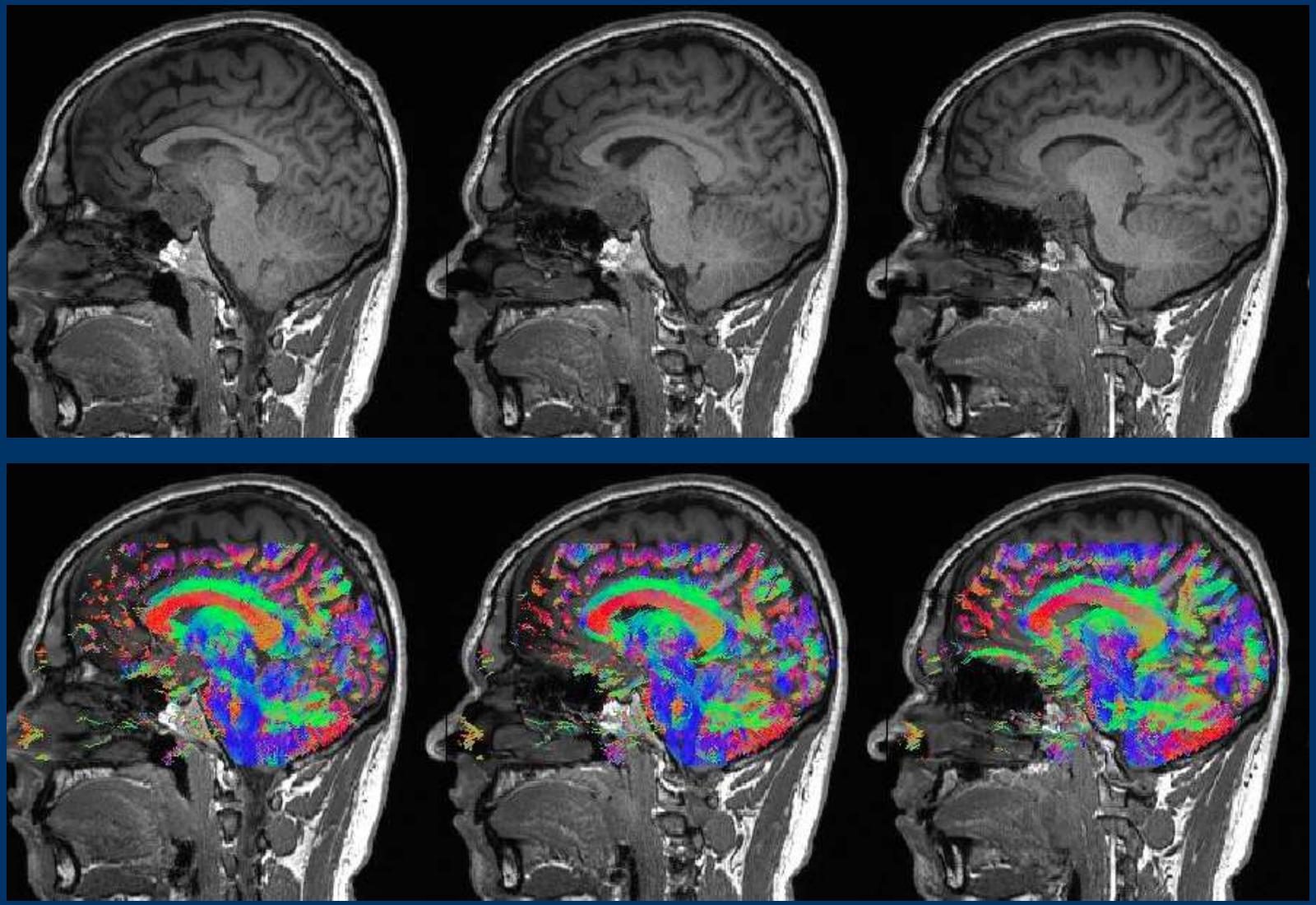
Receptive and expressive language areas can also be activated using passive tasks such as listening to a story or watching a video.

4 min video with narration
In alternate15s blocks



Red – sentence-completion task
Green – video narration

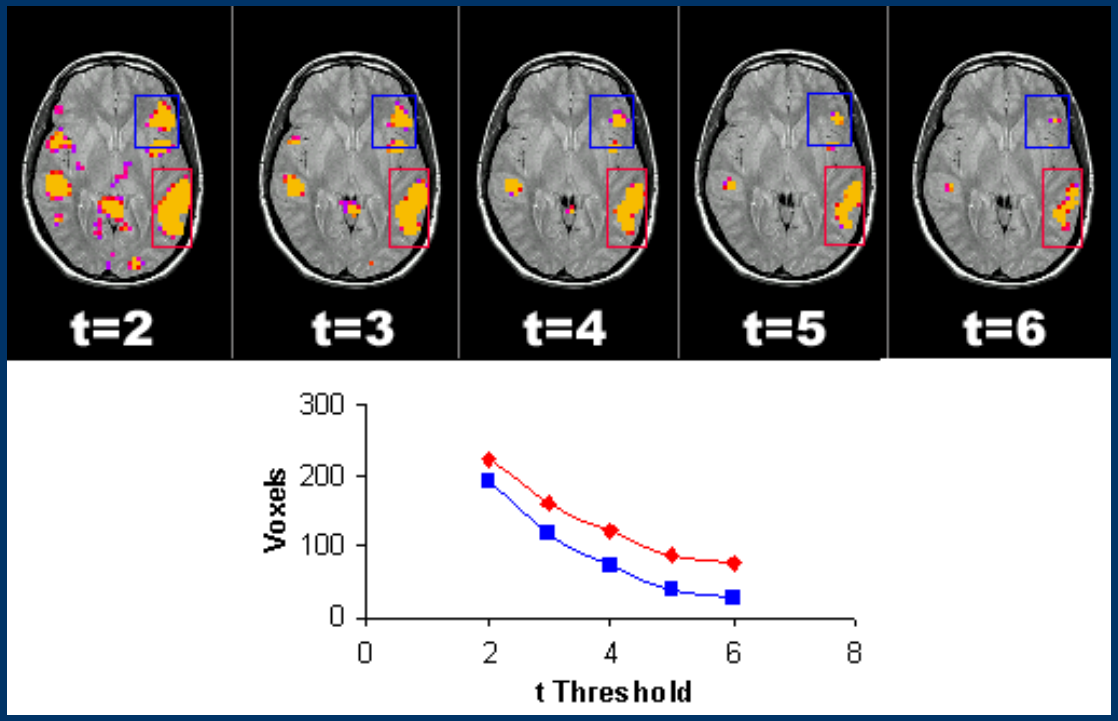
DTI through optic chiasm tumor



Reproducibility of fMRI mapping

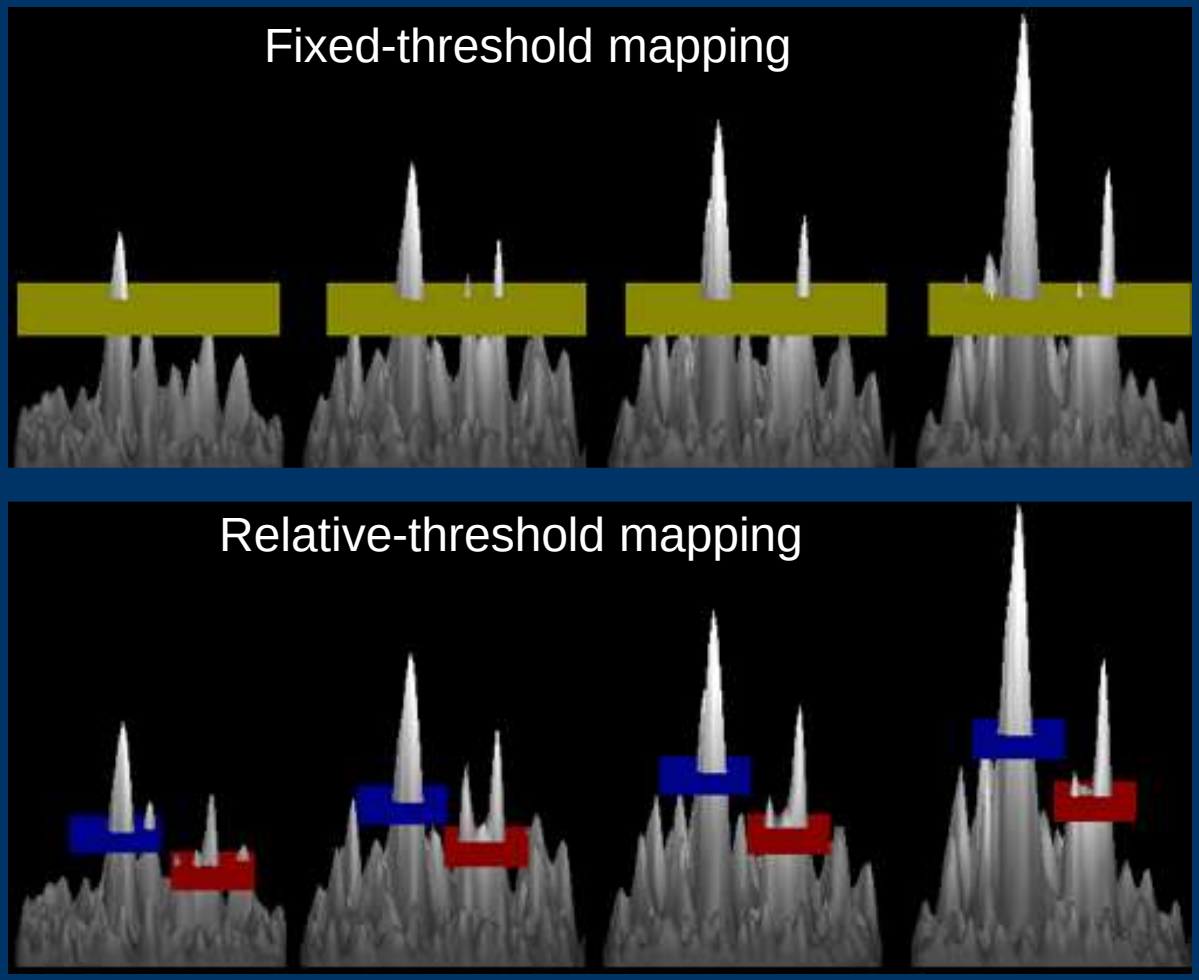
- Task performance variability
  - Accuracy, attention, anxiety can change over time
- Magnetic field strength and pulse sequence dependence
- Physiological/metabolic variability
  - E.g. caffeine, tobacco affect vascular hemodynamic response
- Biological variability
- Statistical threshold definition of ‘activity’

Statistical thresholding can be subjective



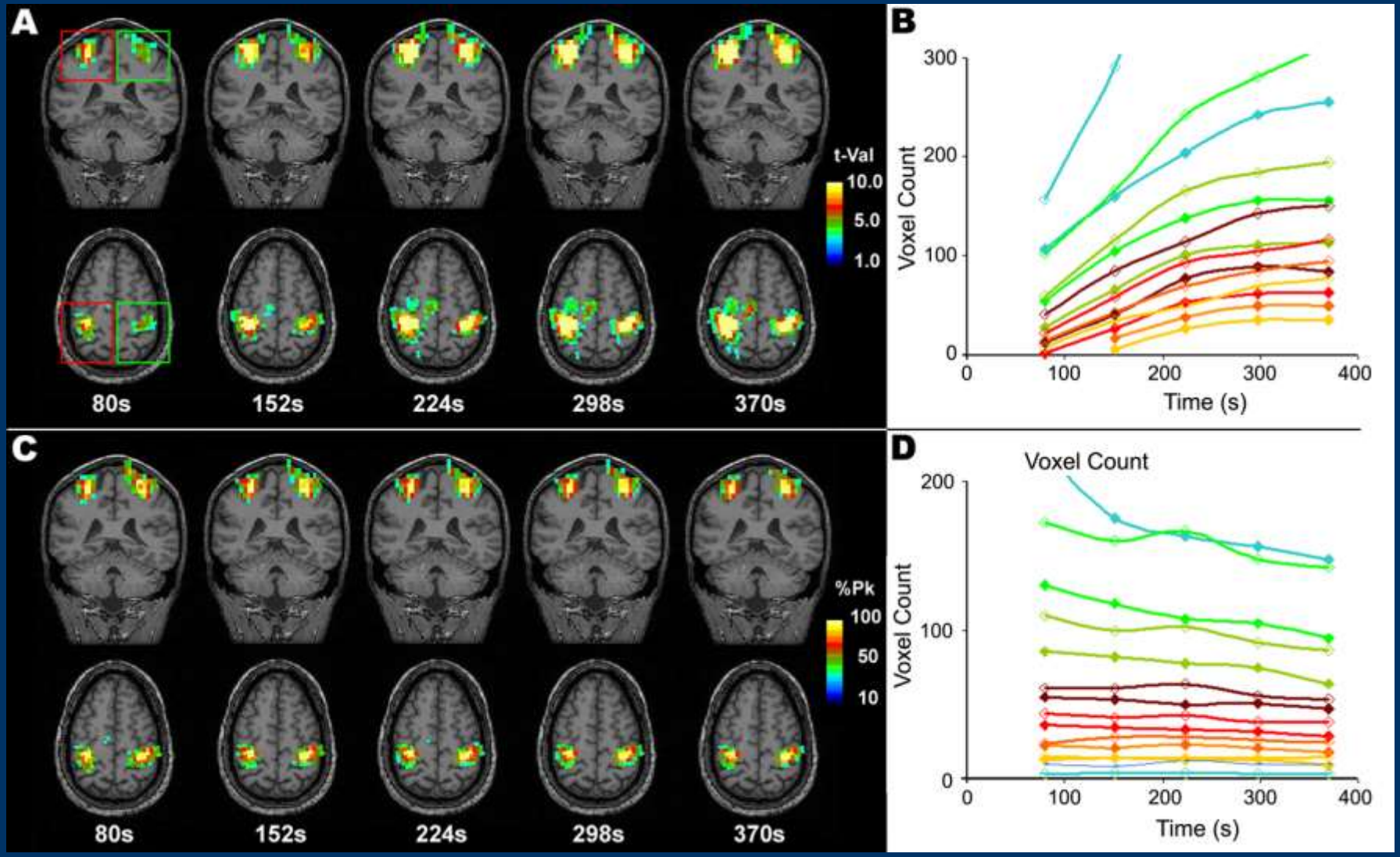
A constant pattern of brain activity can result in very different activation maps, depending on statistical threshold

Statistical significance of activation changes as a function of scan time

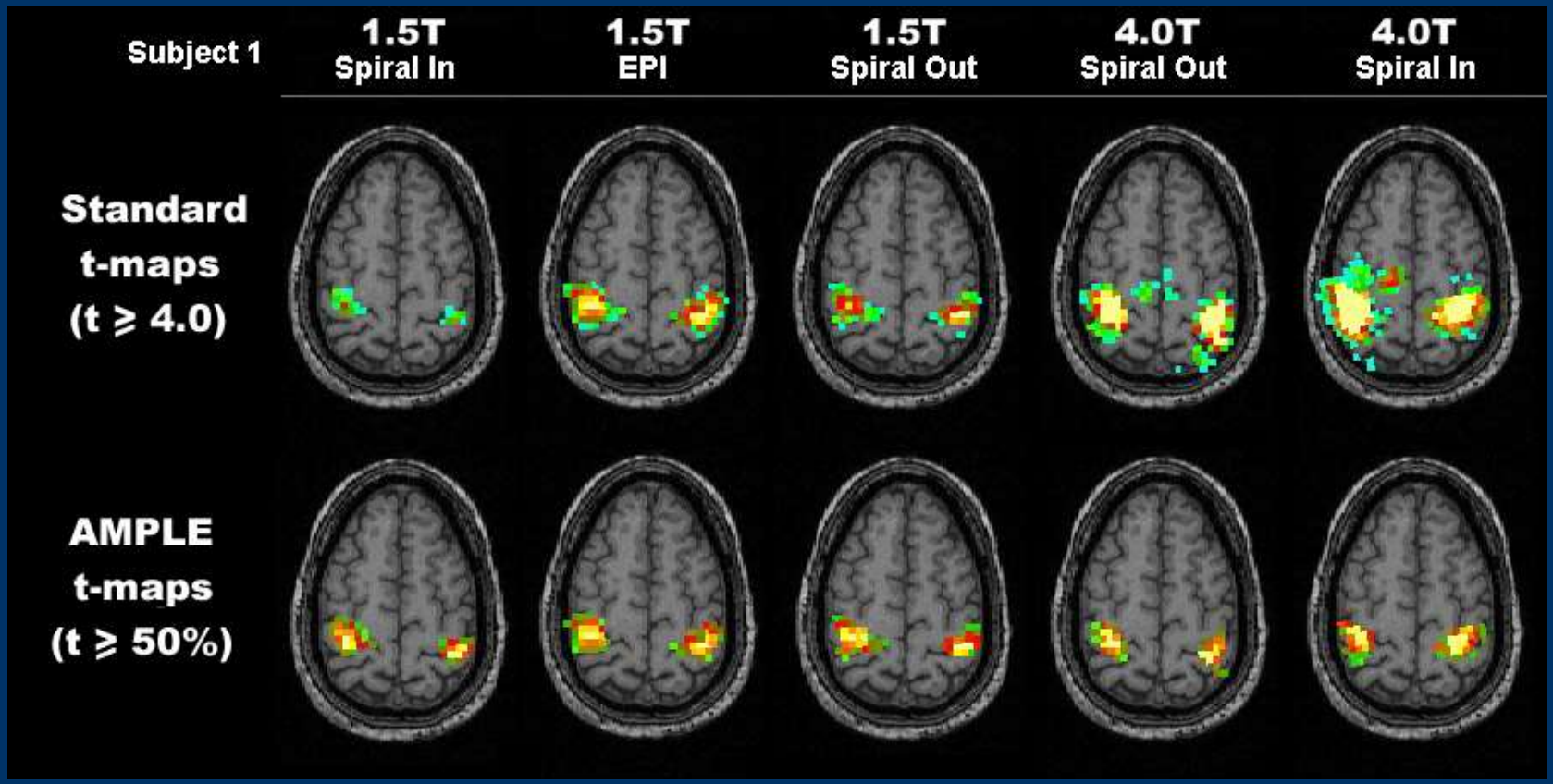


Activation mapping as percentage of local excitation (AMPLE)

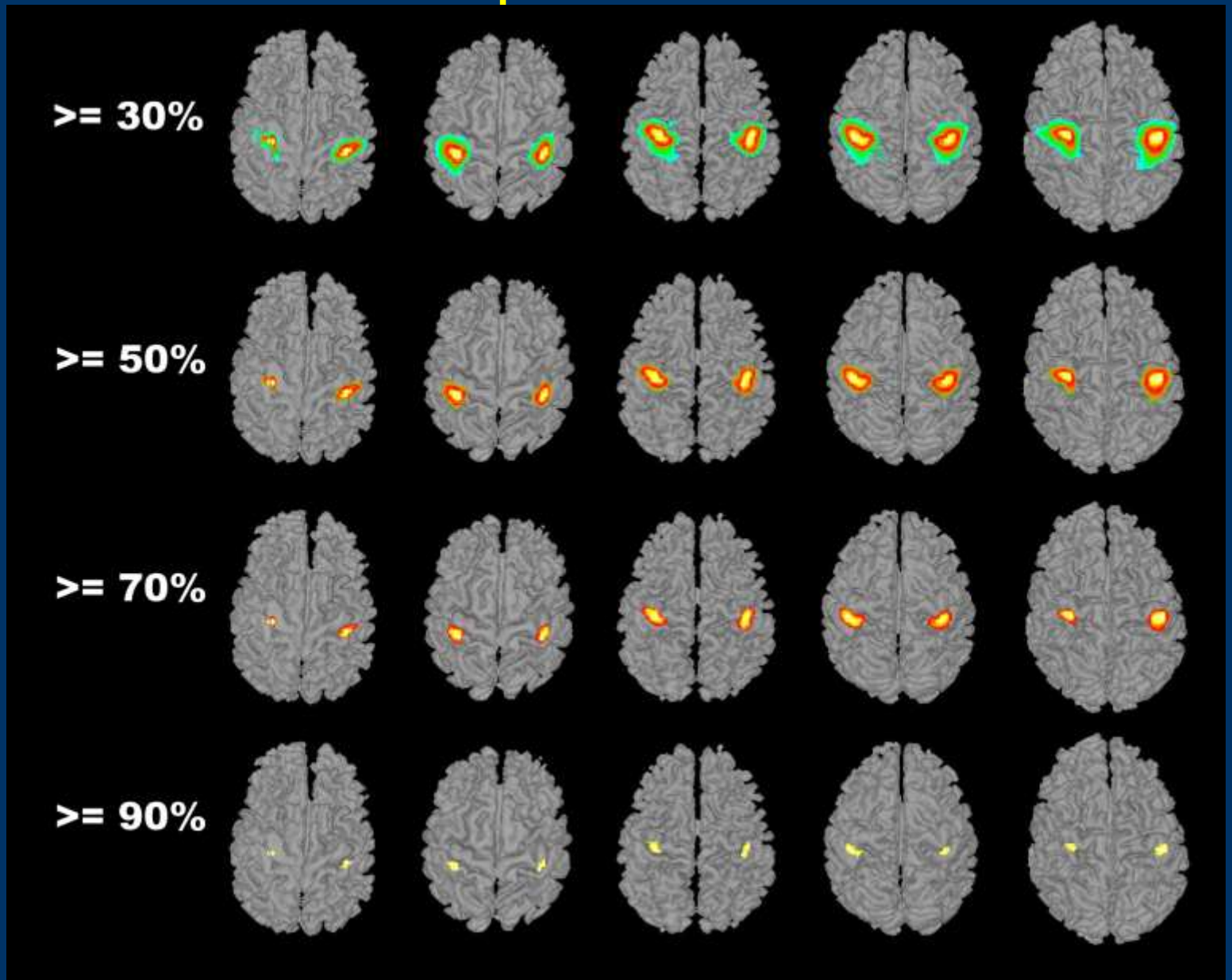
Activation mapping as percentage of local excitation (AMPLE)



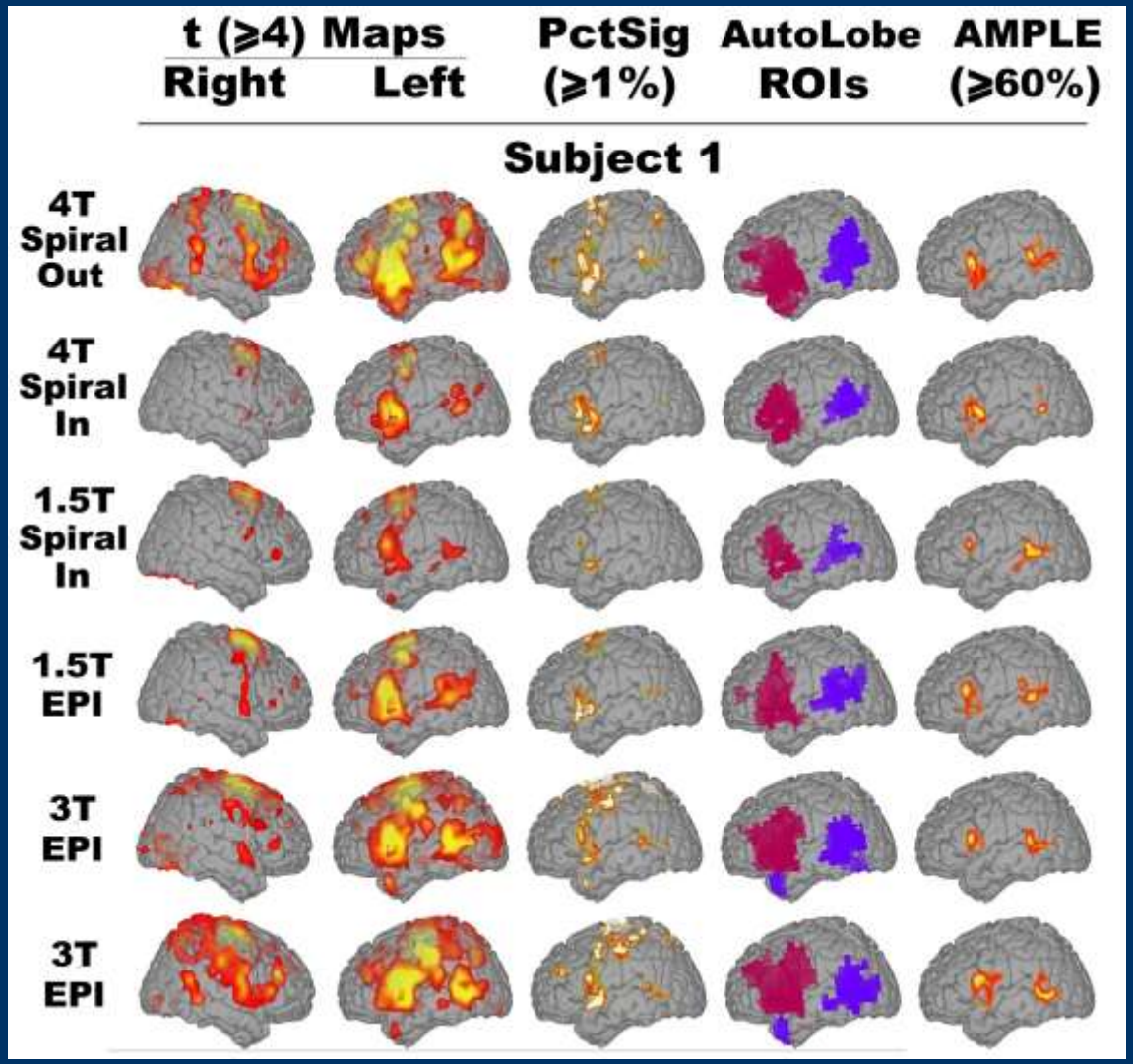
AMPLE maps are consistent across scans or scanners



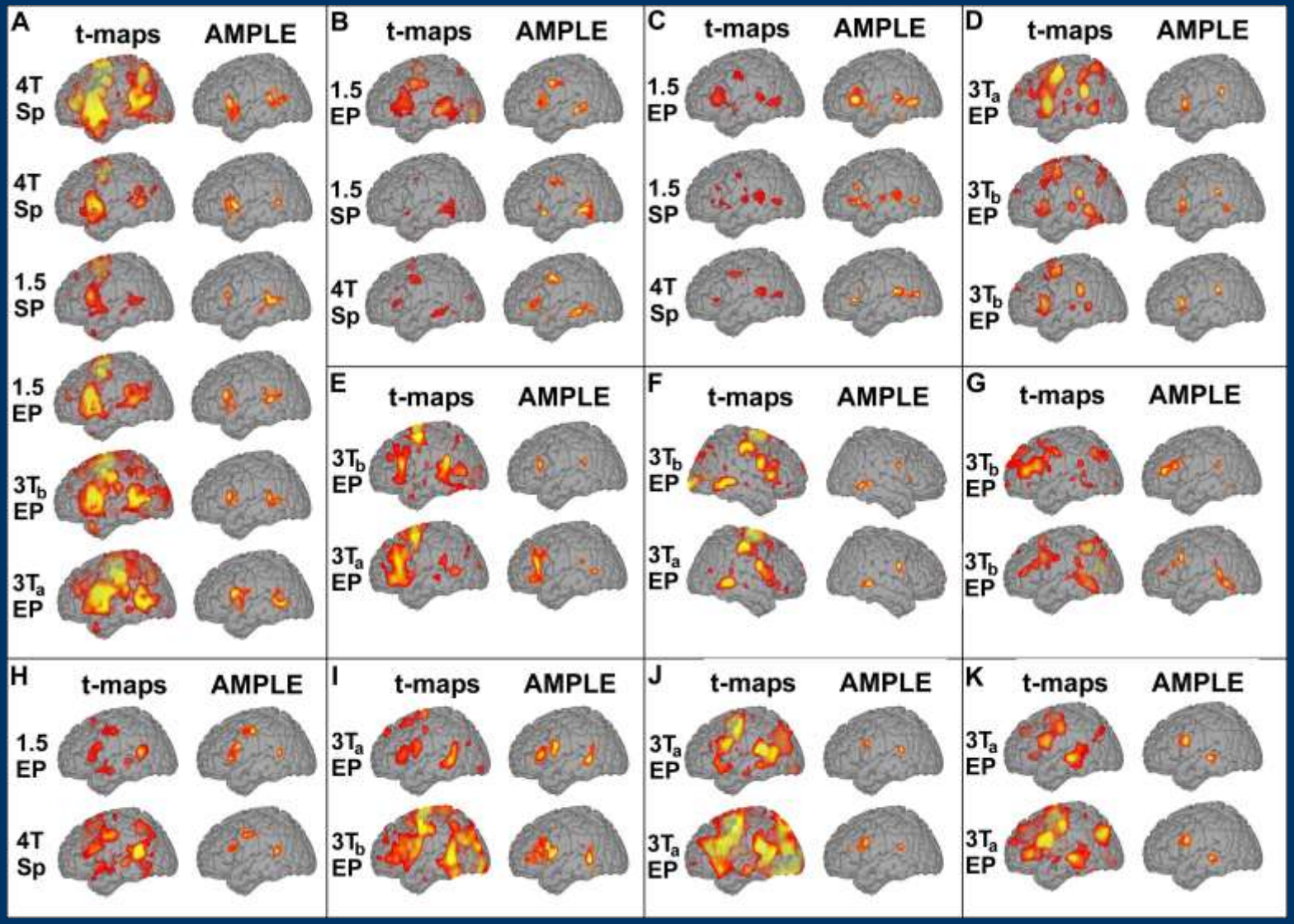
Anatomical spread of active voxels



AMPLE maps improve language reproducibility



Language AMPLE maps improve reproducibility



Upper 40% of AMPLE peaks are most reproducible

Conclusions

- fMRI for language laterality and location
- fMRI for motor cortex mapping
- DTI for mapping WM pathways
- Help assess risks of post-op deficits
- Help plan surgical approach
- Speeds up intra-op mapping
- Can be used when intra-op mapping fails
- Technology continues to improve