Clinical fMRI

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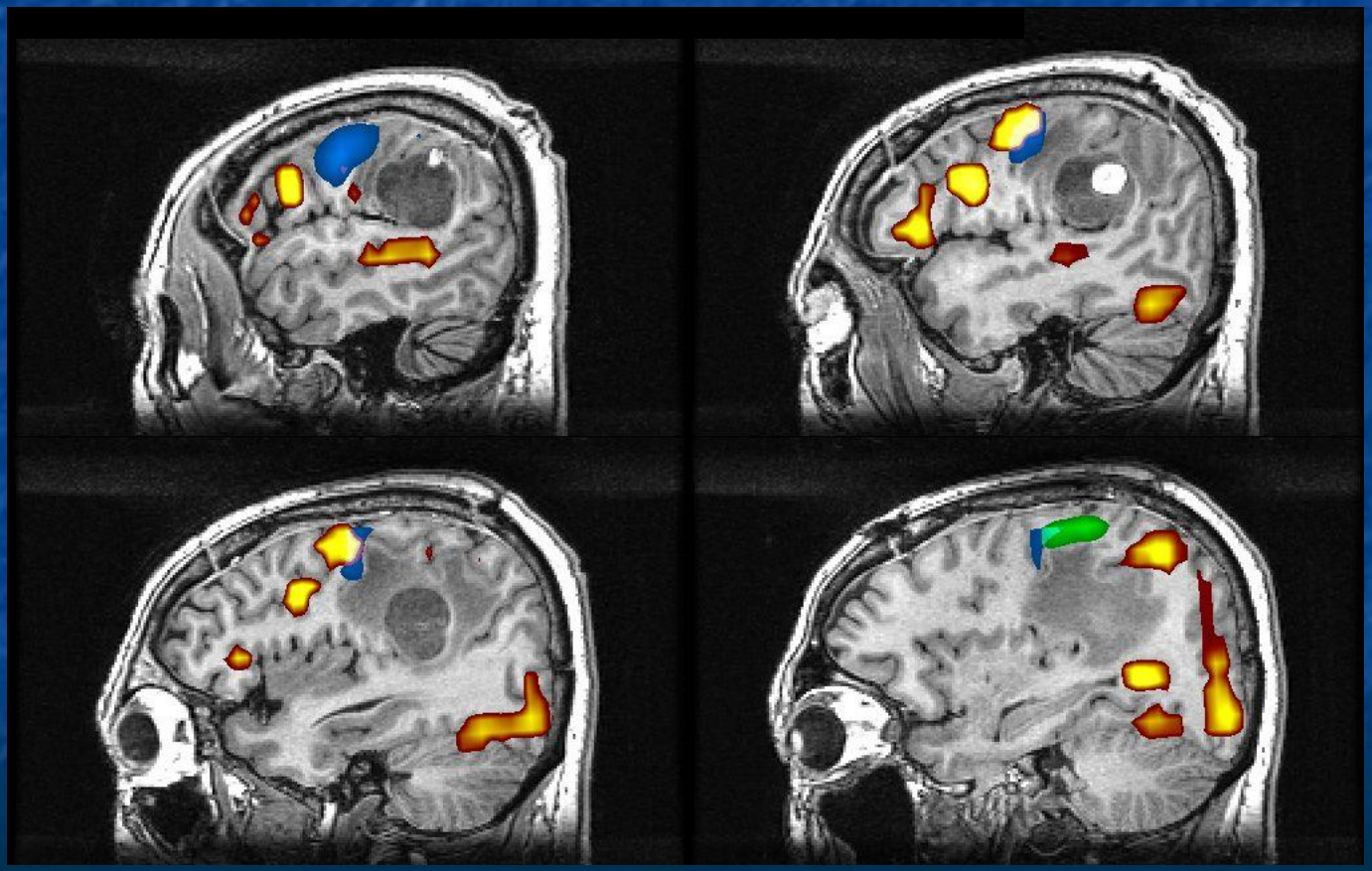
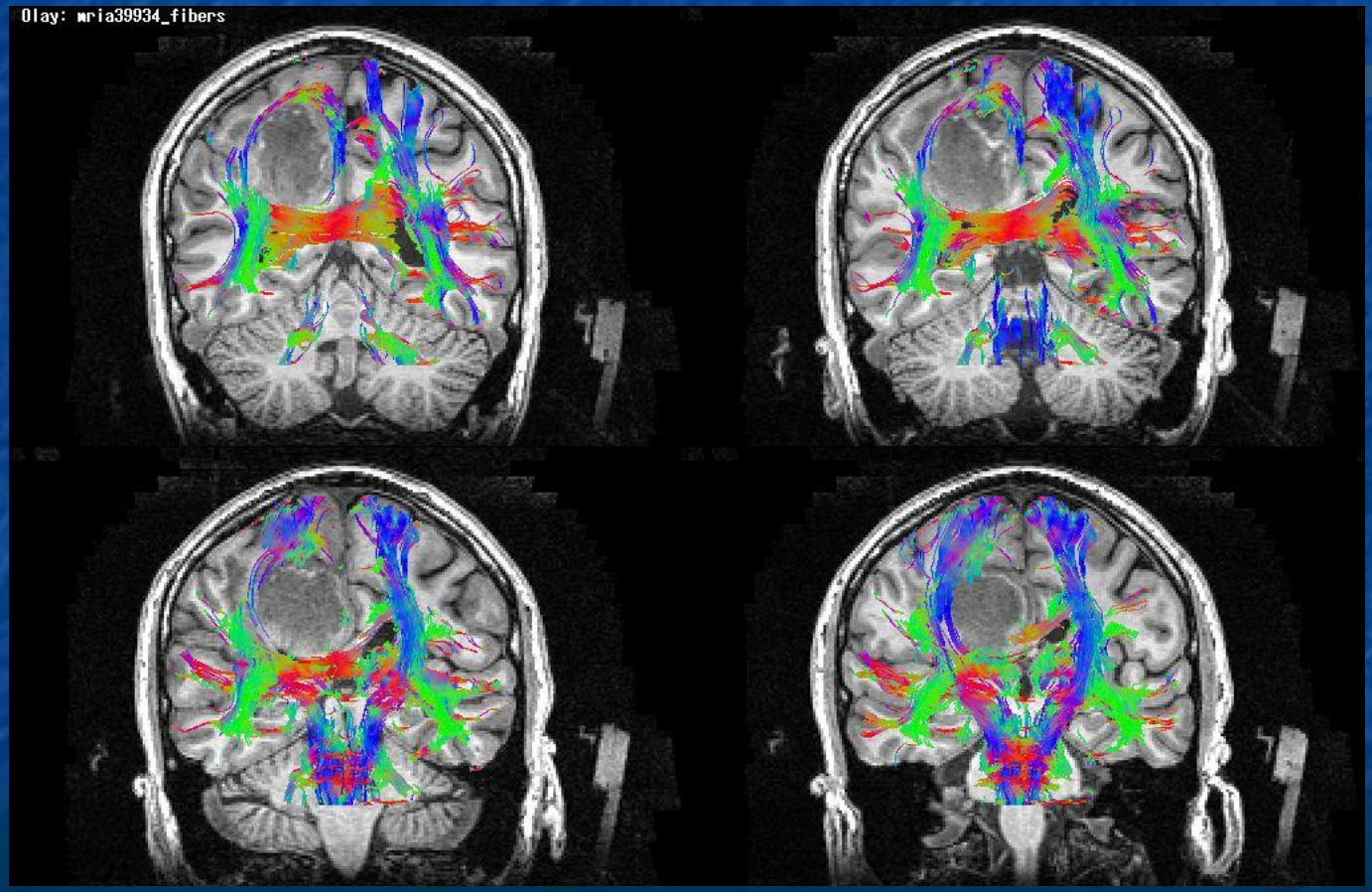
Outline

- Why is clinical fMRI done?
- How is clinical fMRI done?
- What sort of results does it provide?
- What can go wrong?
- How is scan quality assessed?
- Research on improving clinical fMRI

Functional MRI (fMRI) is primarily used clinically to map speech and motor function prior to brain surgery



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



fMRI & DTI
Clinical goals

- Determine location and borders of eloquent (essential) 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]
- Measure brain connectivity
- Measure brain function (or change in function)

fMRI – Patient performs tasks using simple visual cues and alternating block designs

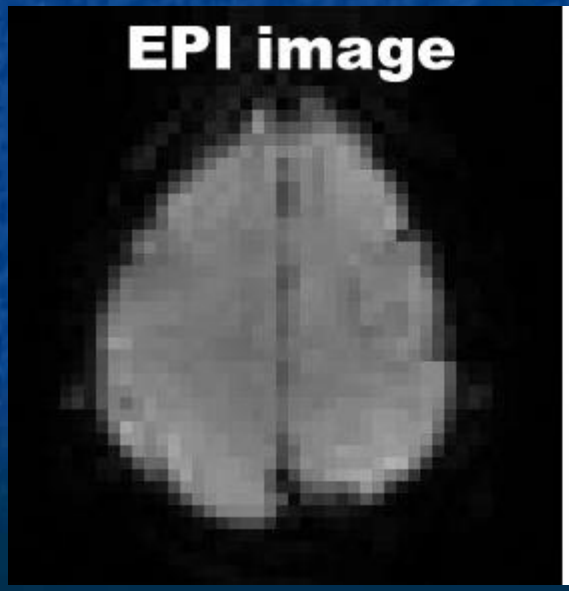
Bilateral hand motion task

Silent sentence-completion task

Old MacDonald had a _____ .	vs	Bnd MwjGhdchkj ckr n _____ .
15s		15s

Image acquisition

During a ~5-minute fMRI scan the patient performs many cycles of a simple task.
20-30 echo-planar images are acquired every TR (~1.5s),
This yields a time series of ~200 brain image volumes.
Image intensity varies with the task in some voxels.



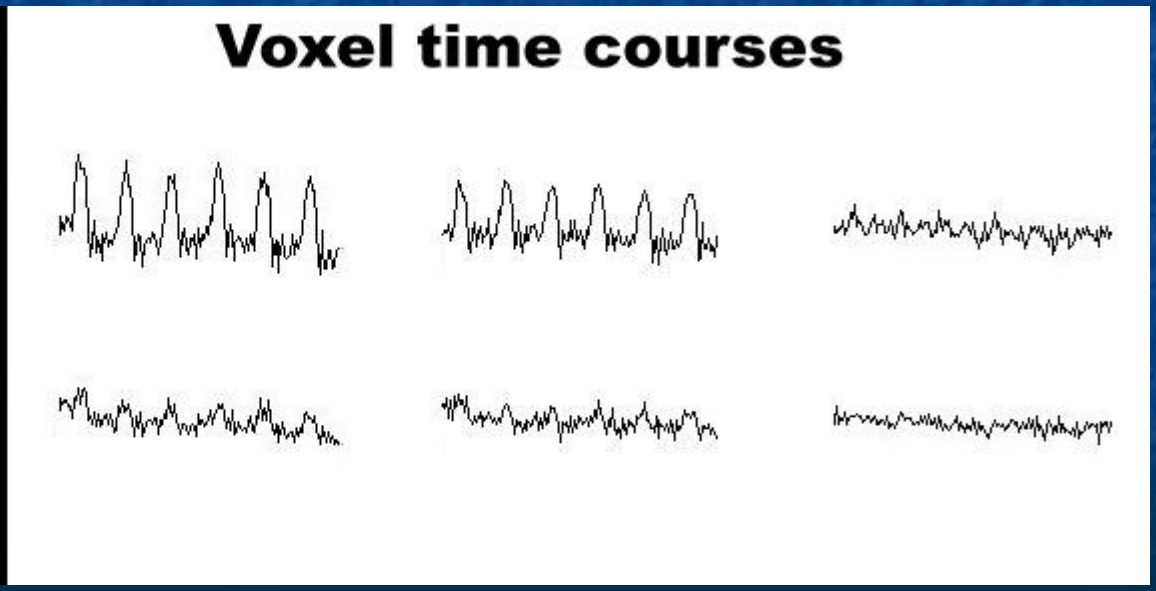


Image signal pre-processing

- Filter out known nuisance signals (sometimes)
  - Head motion (measure motion - realign images)
  - Regression filter (heartbeat, respiration, drift)
- Filter out high-frequency noise (always)
  - Spike filter
  - Spatial smoothing
  - Temporal smoothing

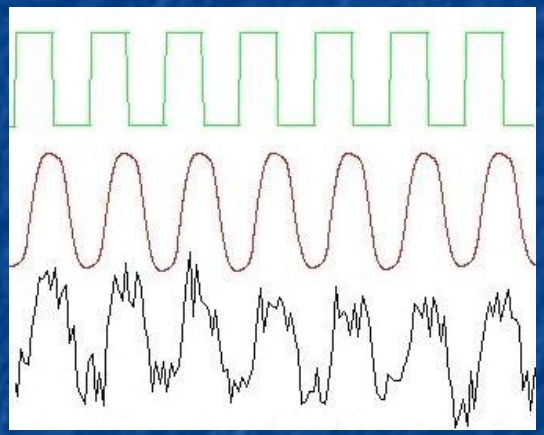
Statistical image processing

Compare the timing of the observed fluctuations in the fMRI images to the expected fluctuations of the BOLD response.

Task timing

Predicted response

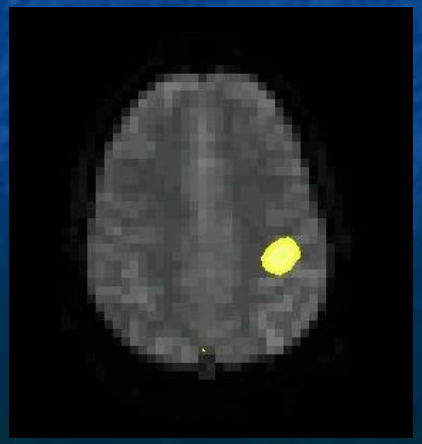
Actual response



Comparison methods:
- image subtraction
- t-test differences
- frequency analysis (FFT)
- temporal correlation
- General Linear Model (analysis of variance)

Statistical significance identifies "active" voxels (statistical value above some minimum threshold)

Thresholded "map" of active voxels is overlaid on MR images



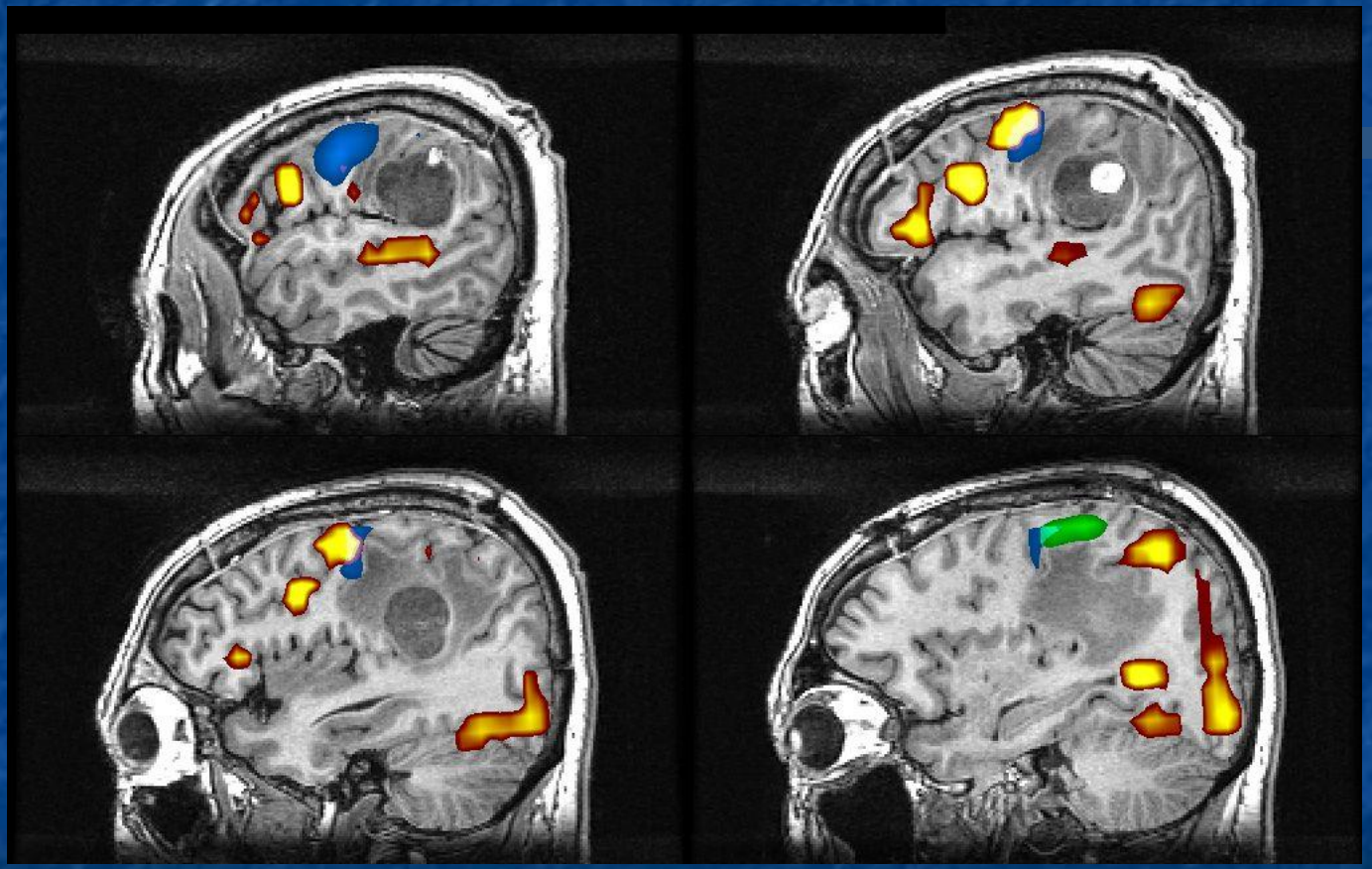
Patient compliance is a bigger issue for fMRI than other scans

- Training
  - Patients must actively participate in fMRI
  - Tasks must be appropriate and understood
  - Task fMRI is 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

Clinical fMRI exam

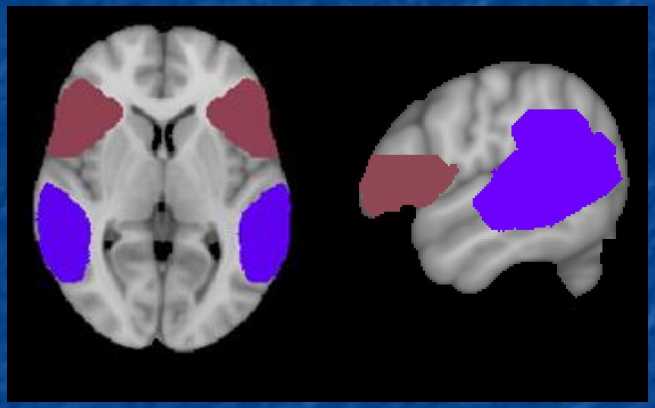
- 10 min pre-scan assessment and training
- 45 min MRI session
  - 10 min anatomical scans (T1 & FLAIR)
  - 15-20 min fMRI – 3-4 tasks (4 min each)
  - 5 min 30-direction DTI scan
- 30-60 min post-scan image analysis
  - Registration of fMRI and DTI with T1 images
  - Definition and statistical analysis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

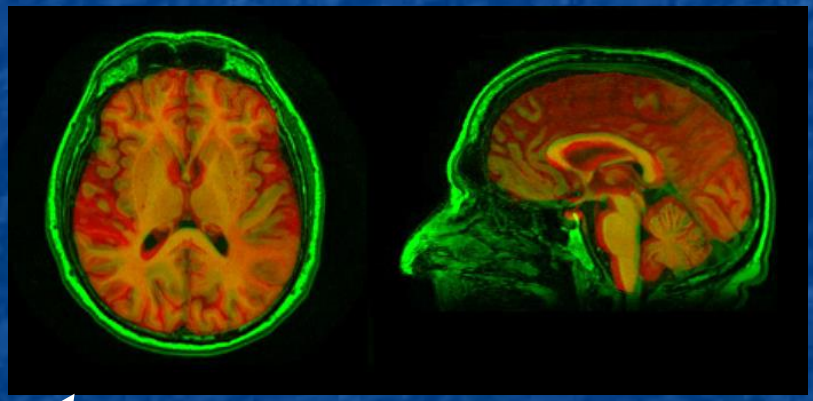
Summary fMRI maps can combine multiple task areas and pathology



This fMRI map was made from 3 tasks and ~14,000 images.

Measuring activation in task-relevant areas

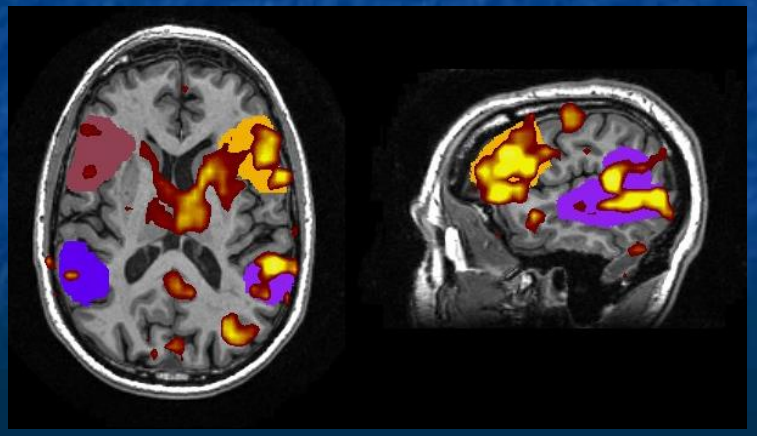




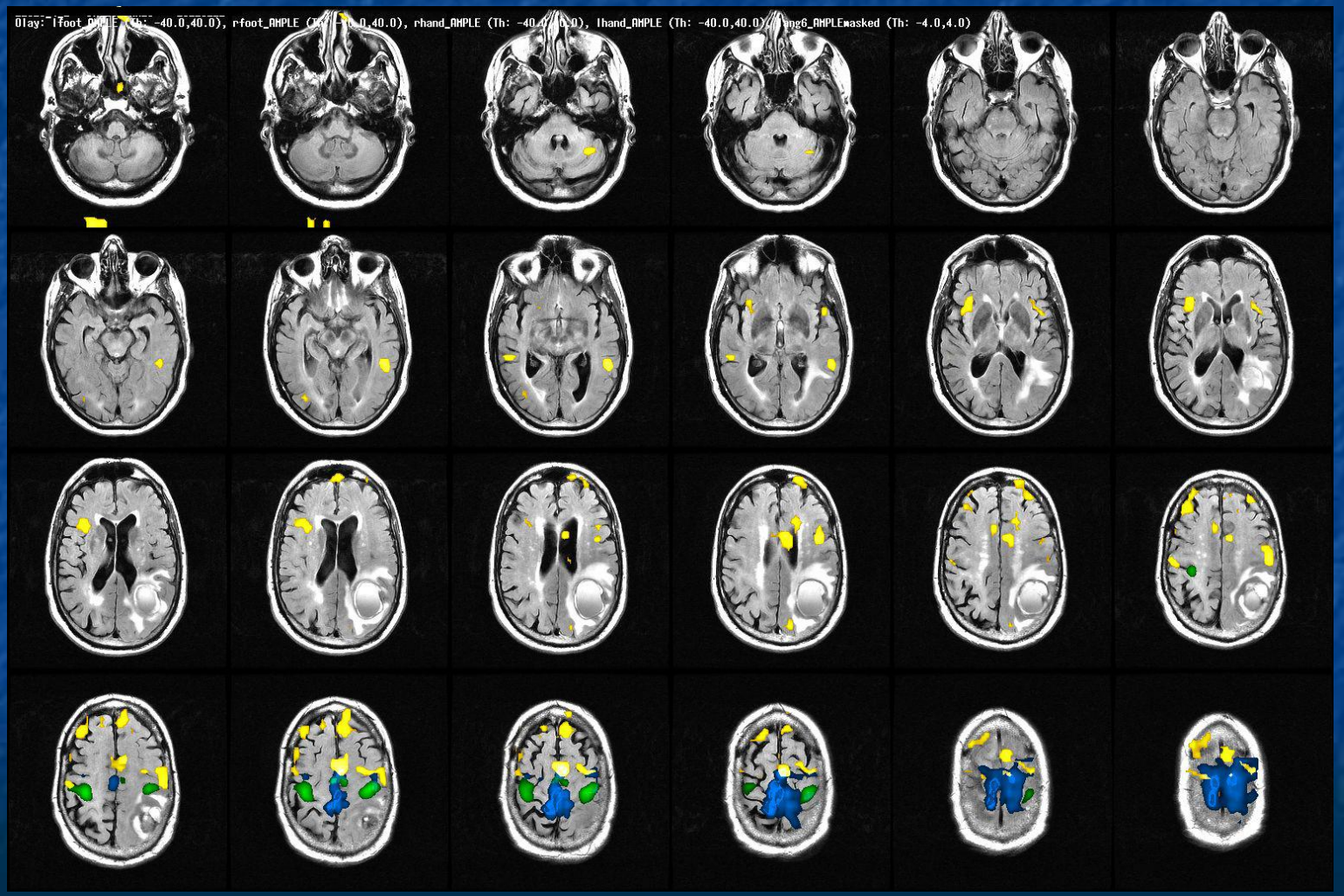
Use atlas of language areas

Align atlas brain to patient brain

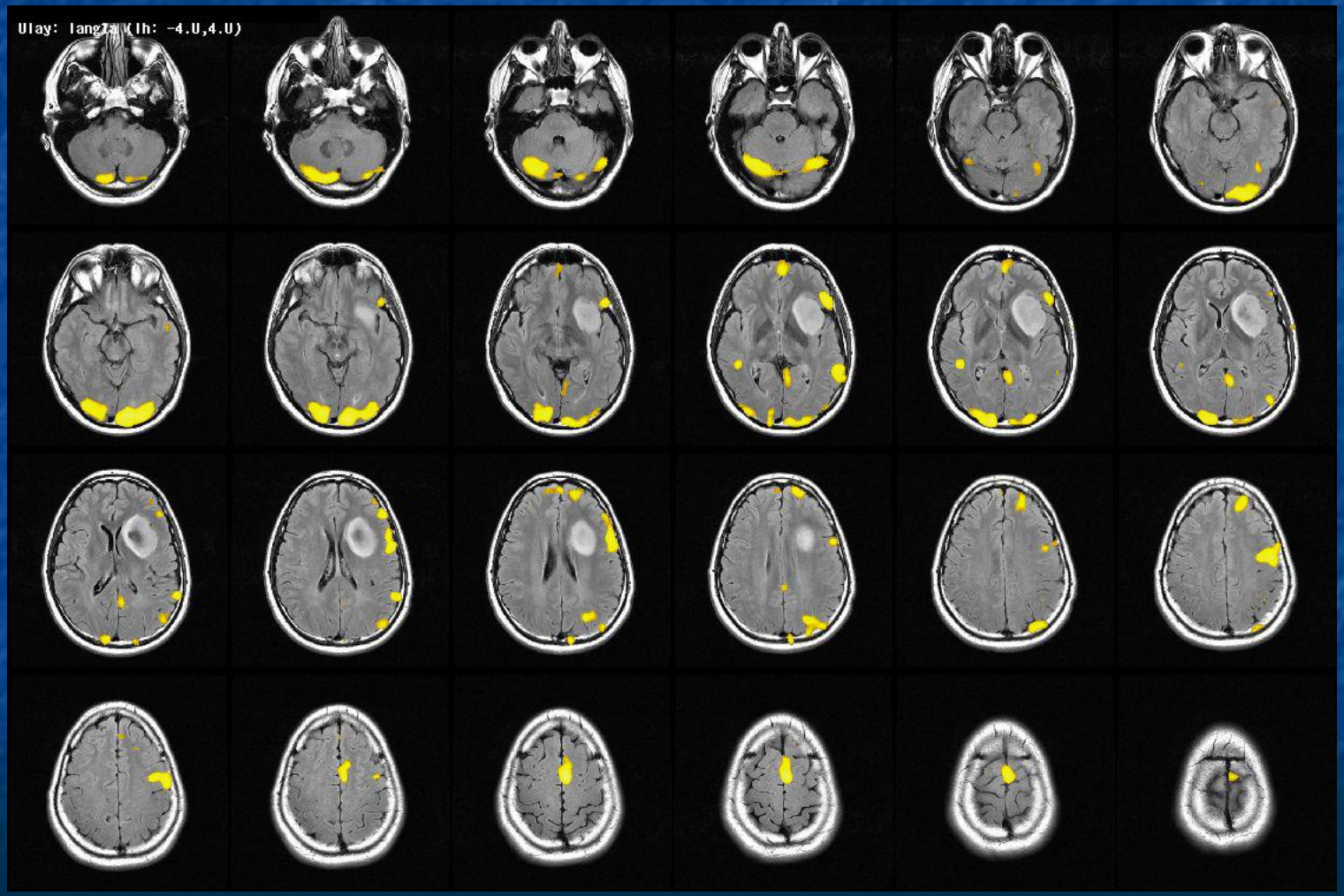
Measure activation in language areas
(e.g. LPeak and Laterality Index)



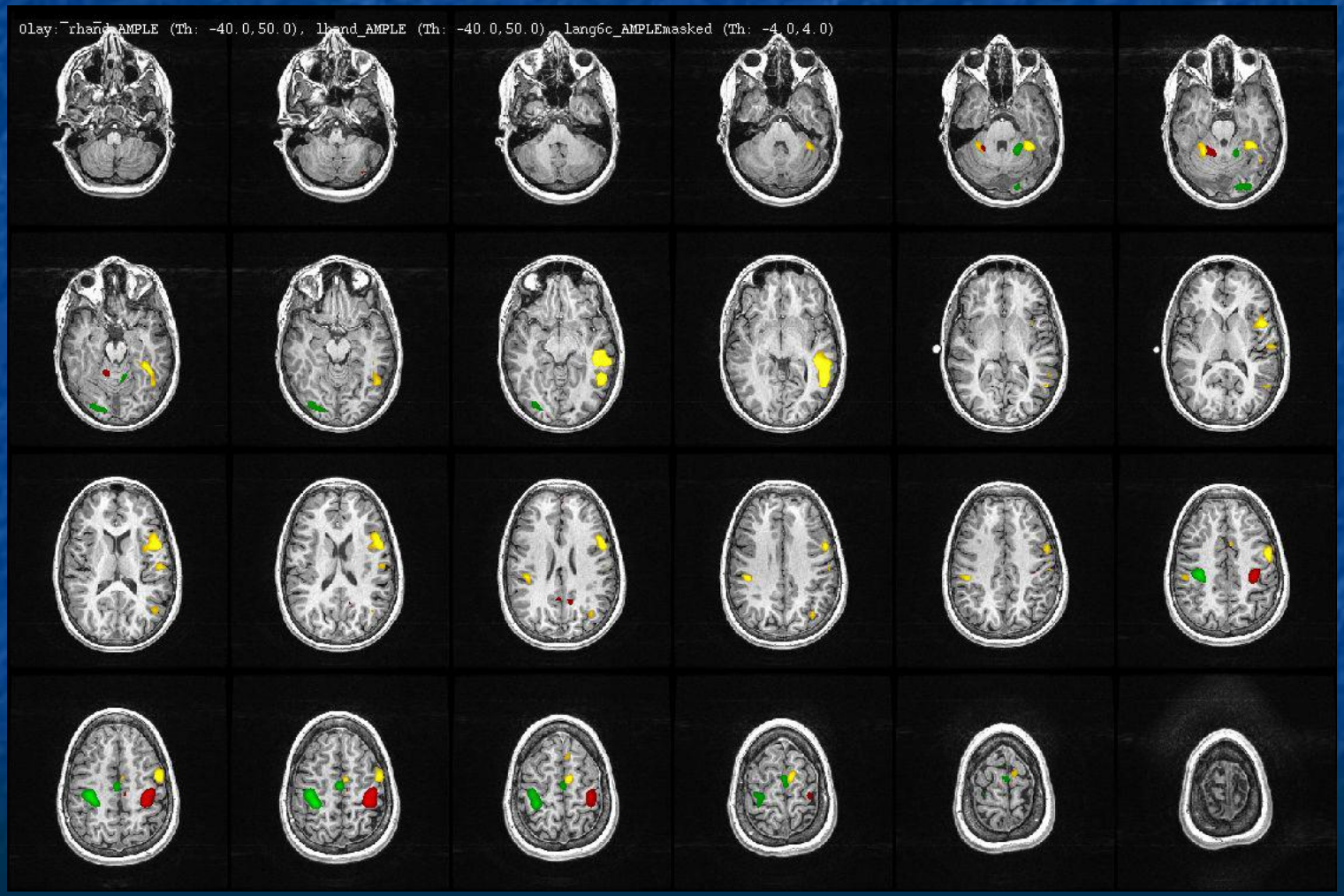
Language & motor – RH 82 yo parietal tumor



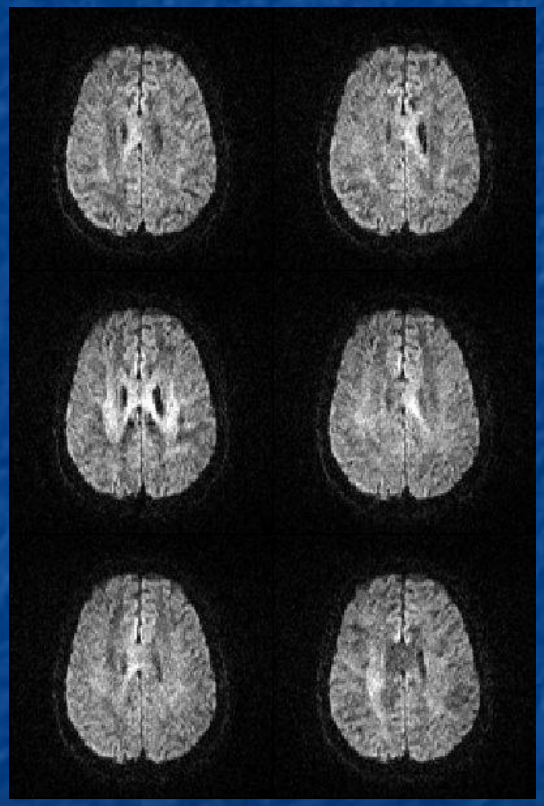
Examples
Language – LH 34 yo with insular tumor



Language & motor – RH 12 yo with epilepsy

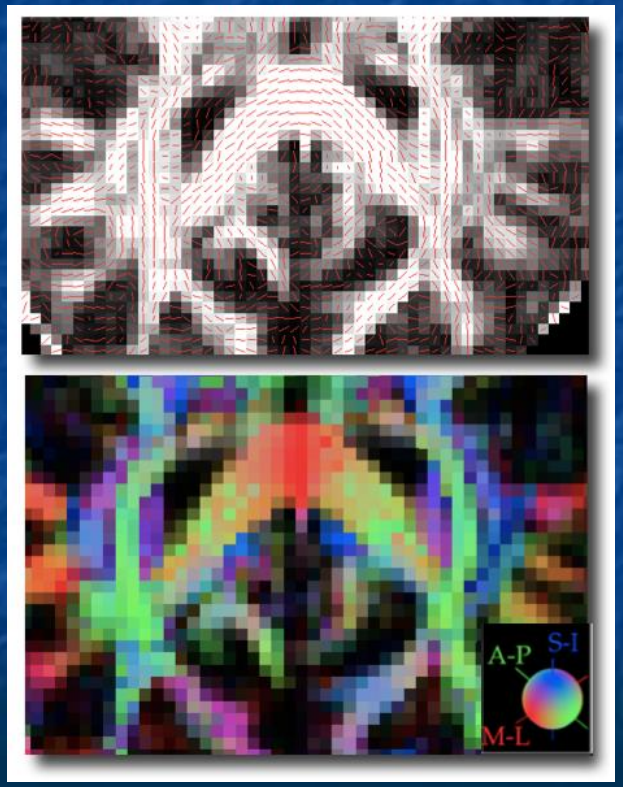


Diffusion tensor imaging (DTI)



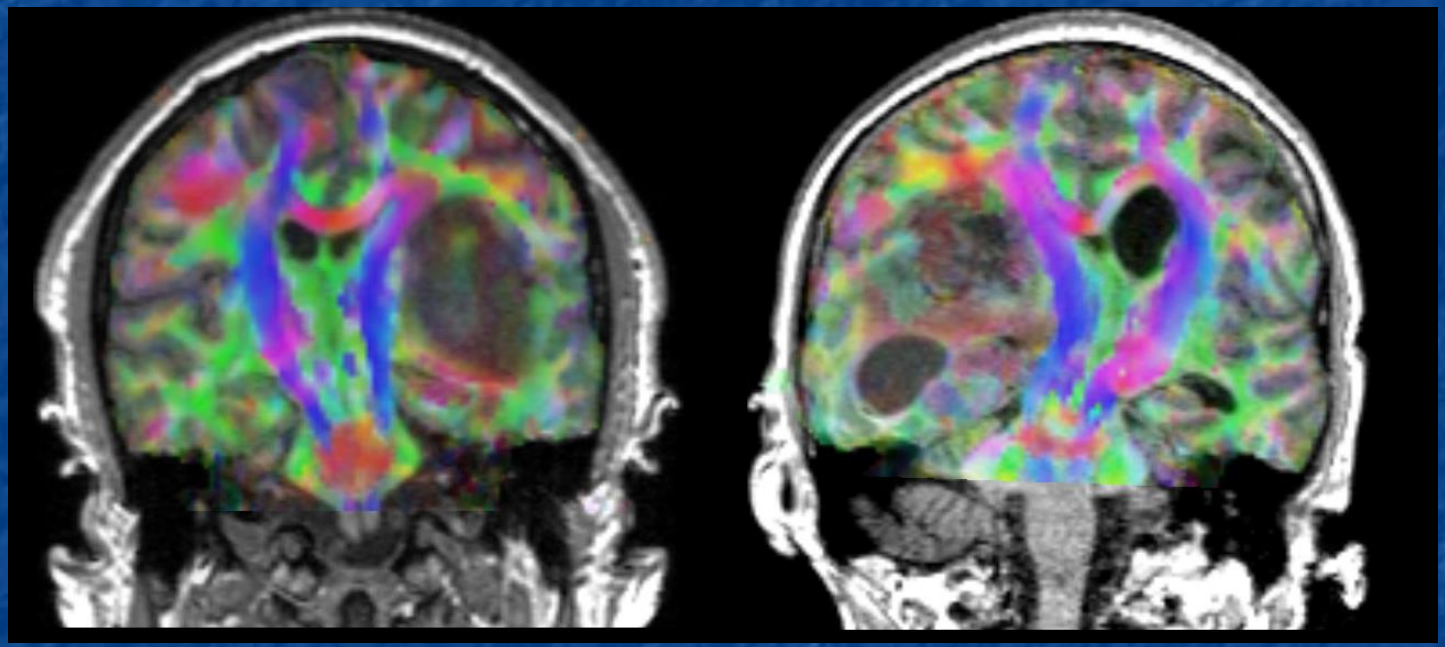
Acquire diffusion-weighted images at multiple diffusion orientations (6-60)

Calculate diffusivity and orientation at each voxel



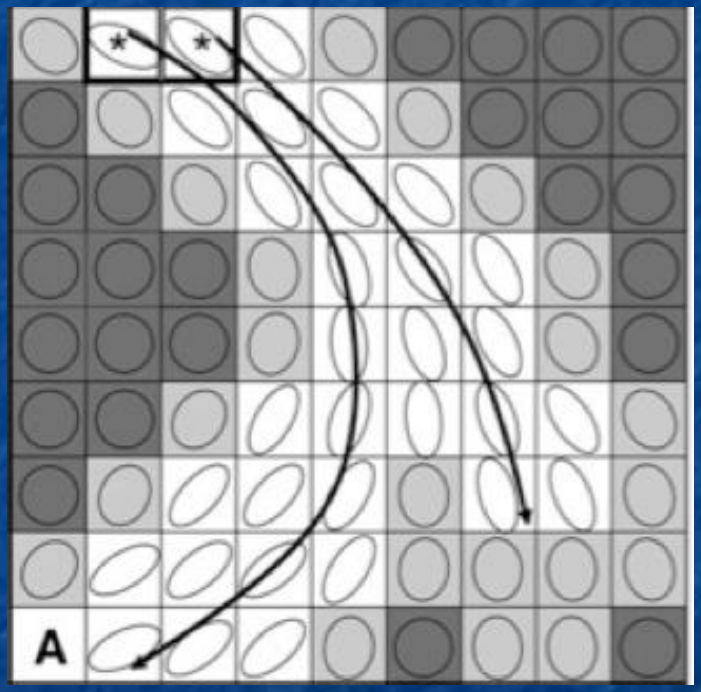
Color-code orientations

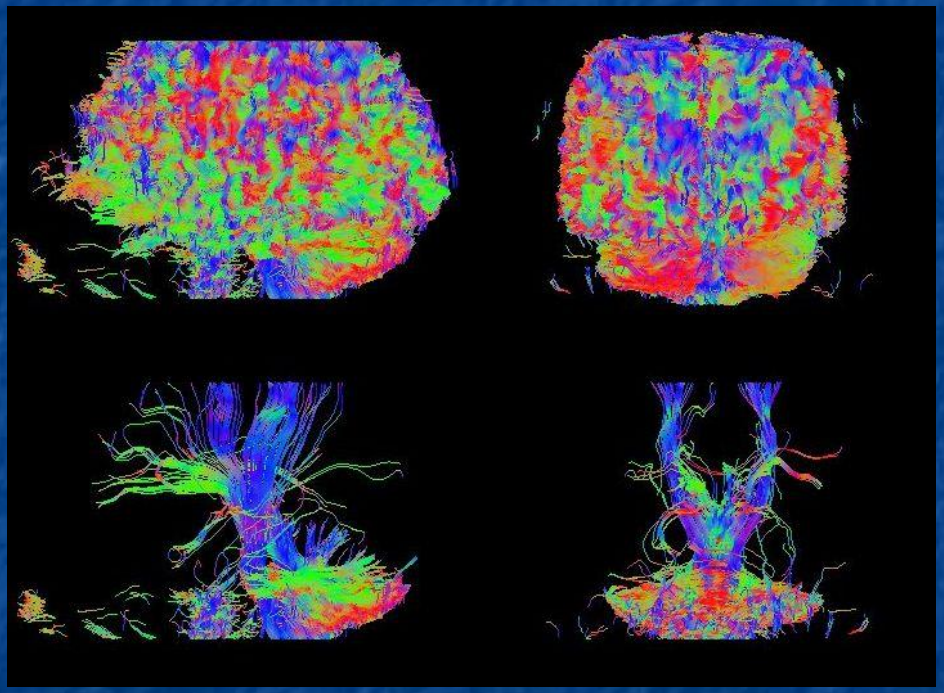
Can overlay color-coded FA map on anatomy



DTI – fiber tracking

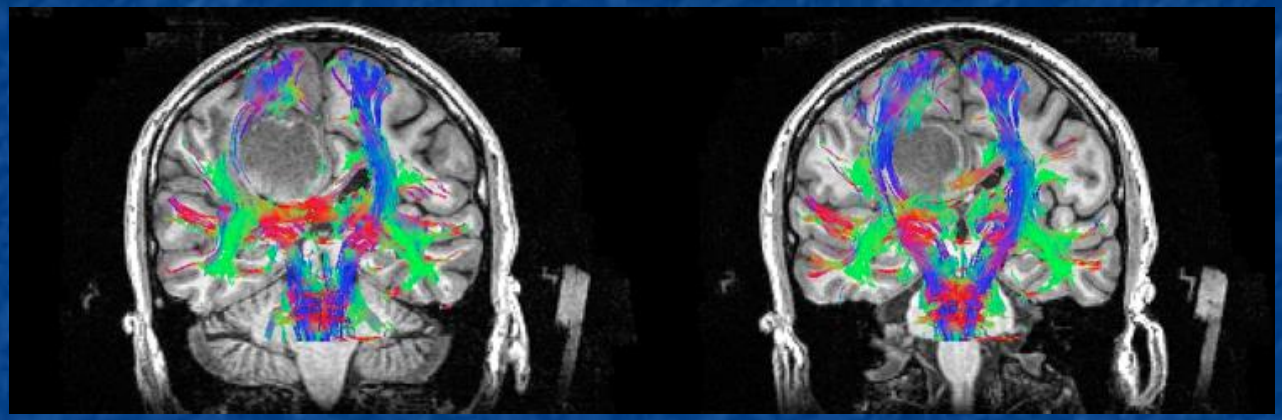
Start at any ‘seed’ and connect voxels with similar orientations

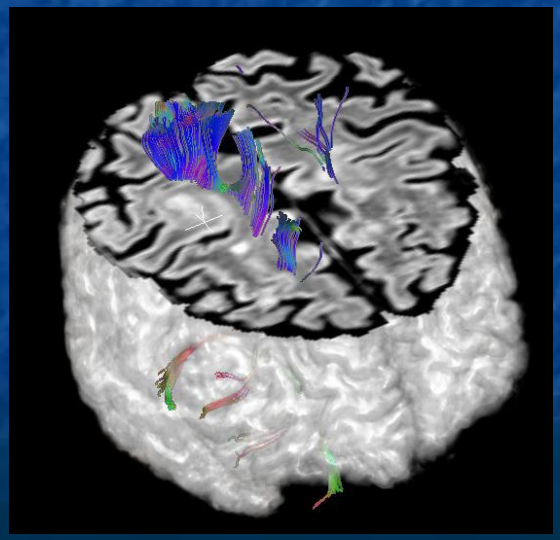




Basser et al., Magn Reson Med, 2000

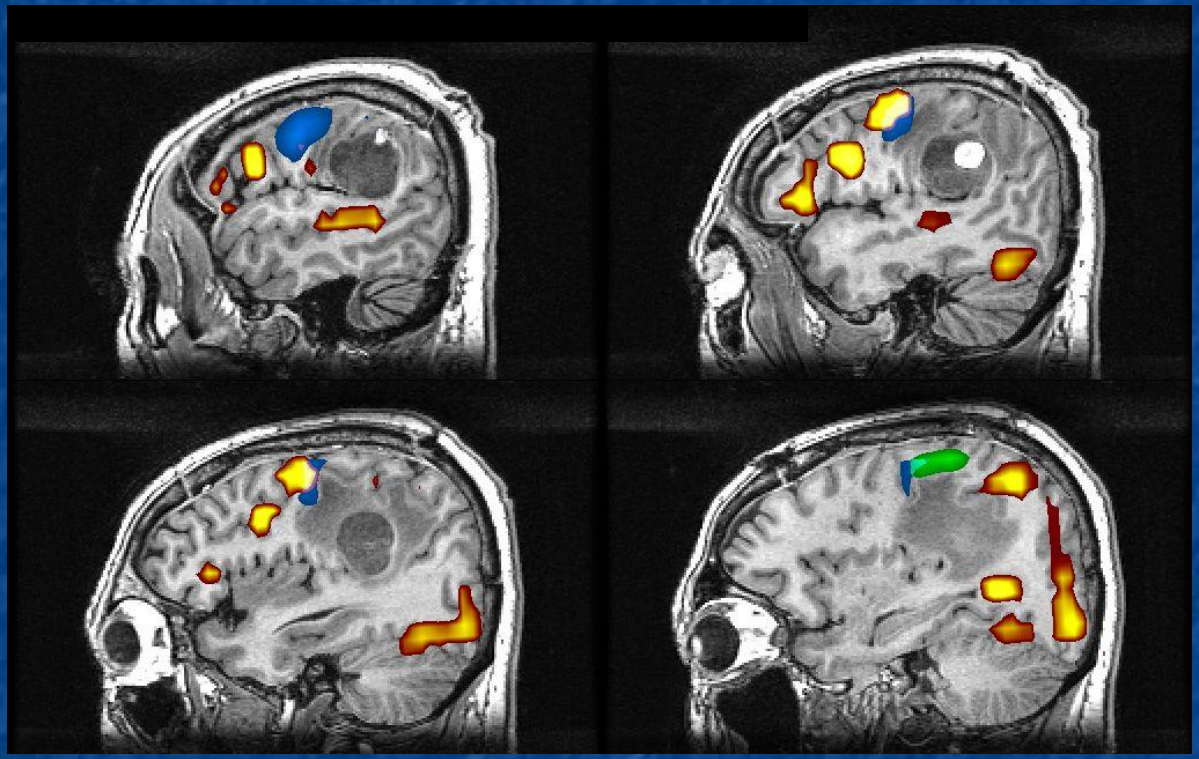
Overlay fiber tracks on anatomy





When all goes well fMRI is easy

Statistical significance provides map of brain activity



Clinically, how do we assess whether all went well?

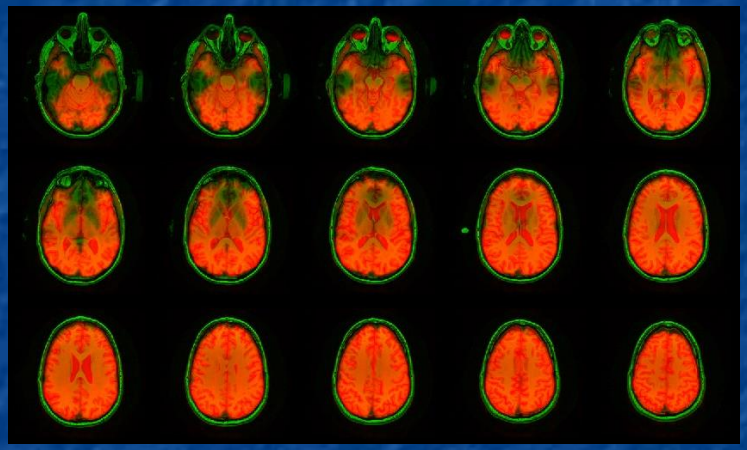
If we repeat the scan, do we get the same result?

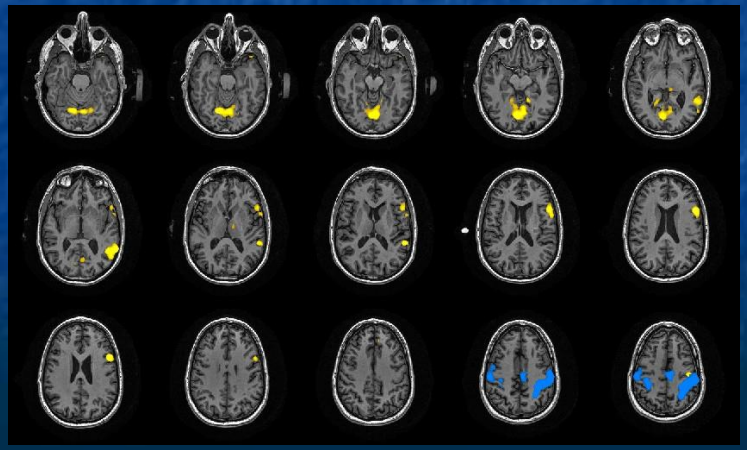
What can go wrong?

- Head motion
- Poor task performance
  - Can't read
  - Can't move
  - Inattentive or falls asleep
  - Confused
- Poor hemodynamic regulation
- Susceptibility artifacts

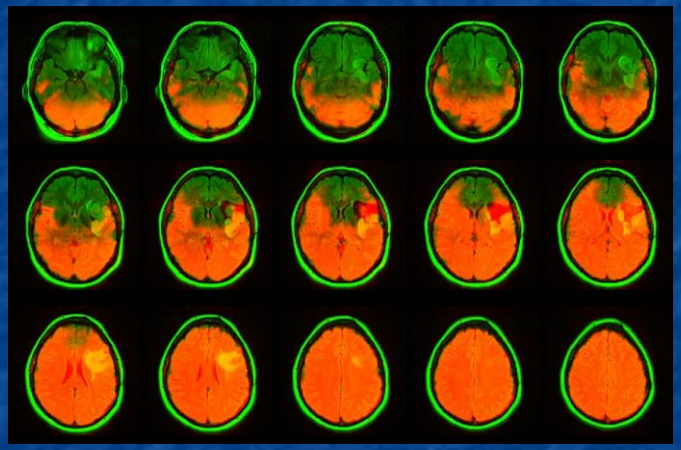
Susceptibility artifacts

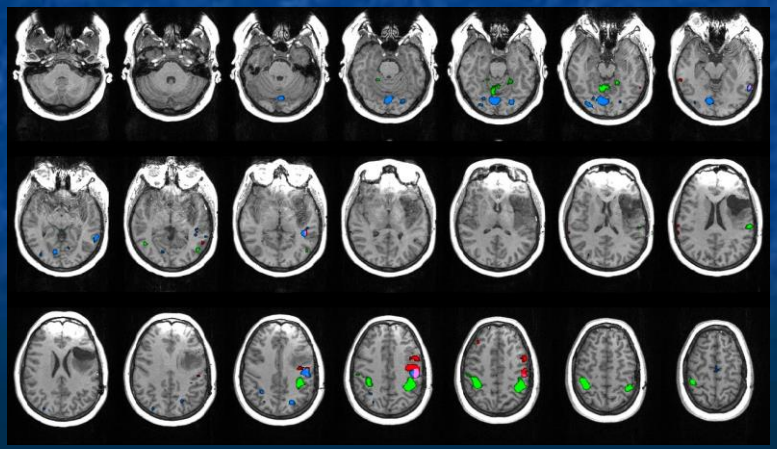
Normal





With dental braces



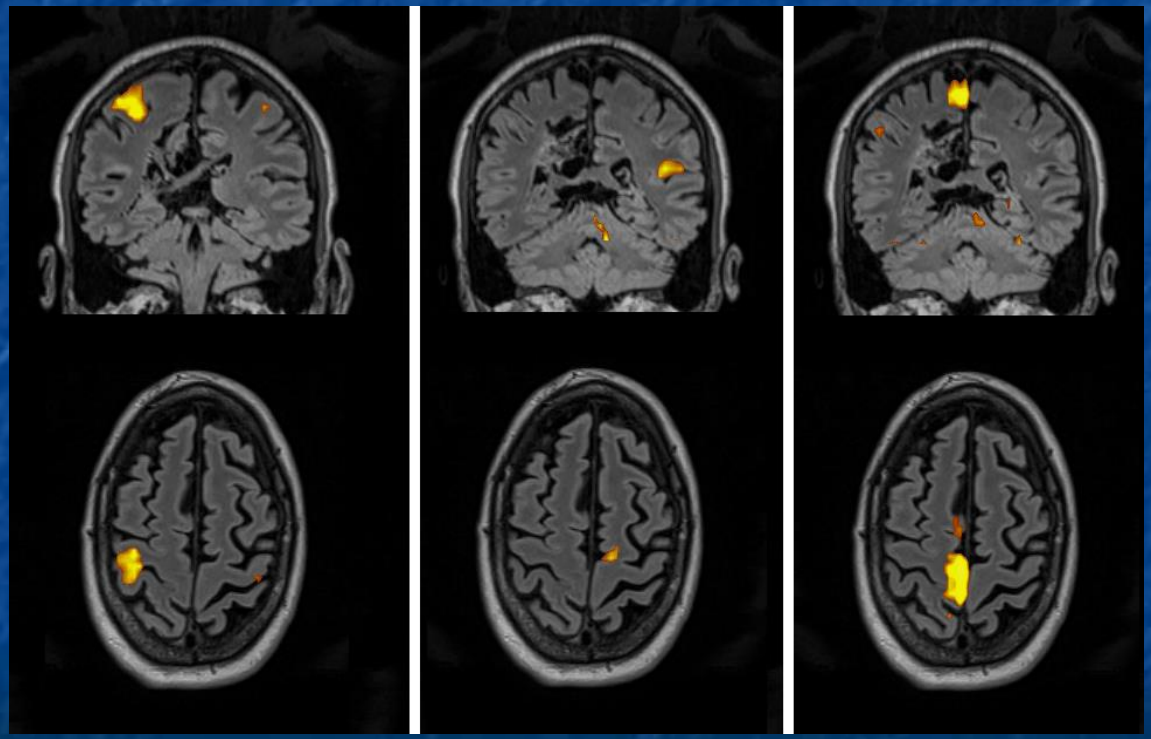


Pathology can disrupt fMRI response timing

AVM slows neurovascular coupling

Hand task

Left foot task

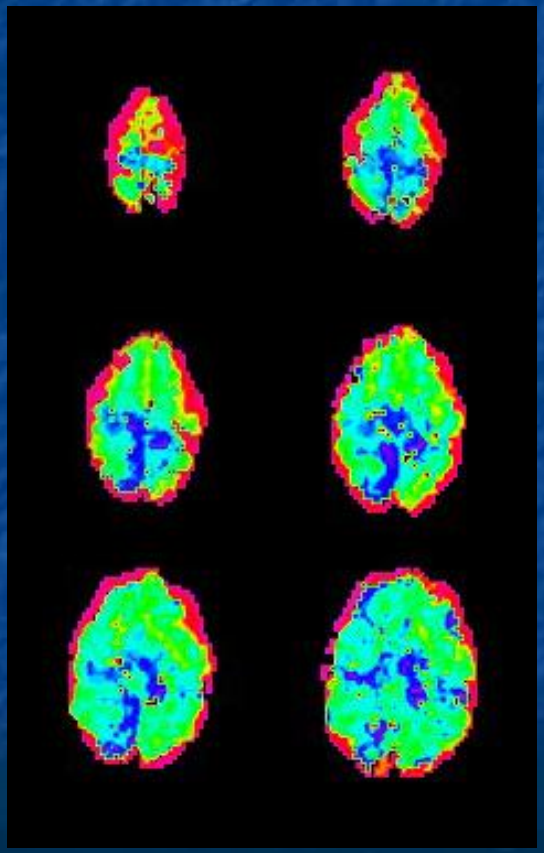


5s delay

5s delay

11s delay

Latency map

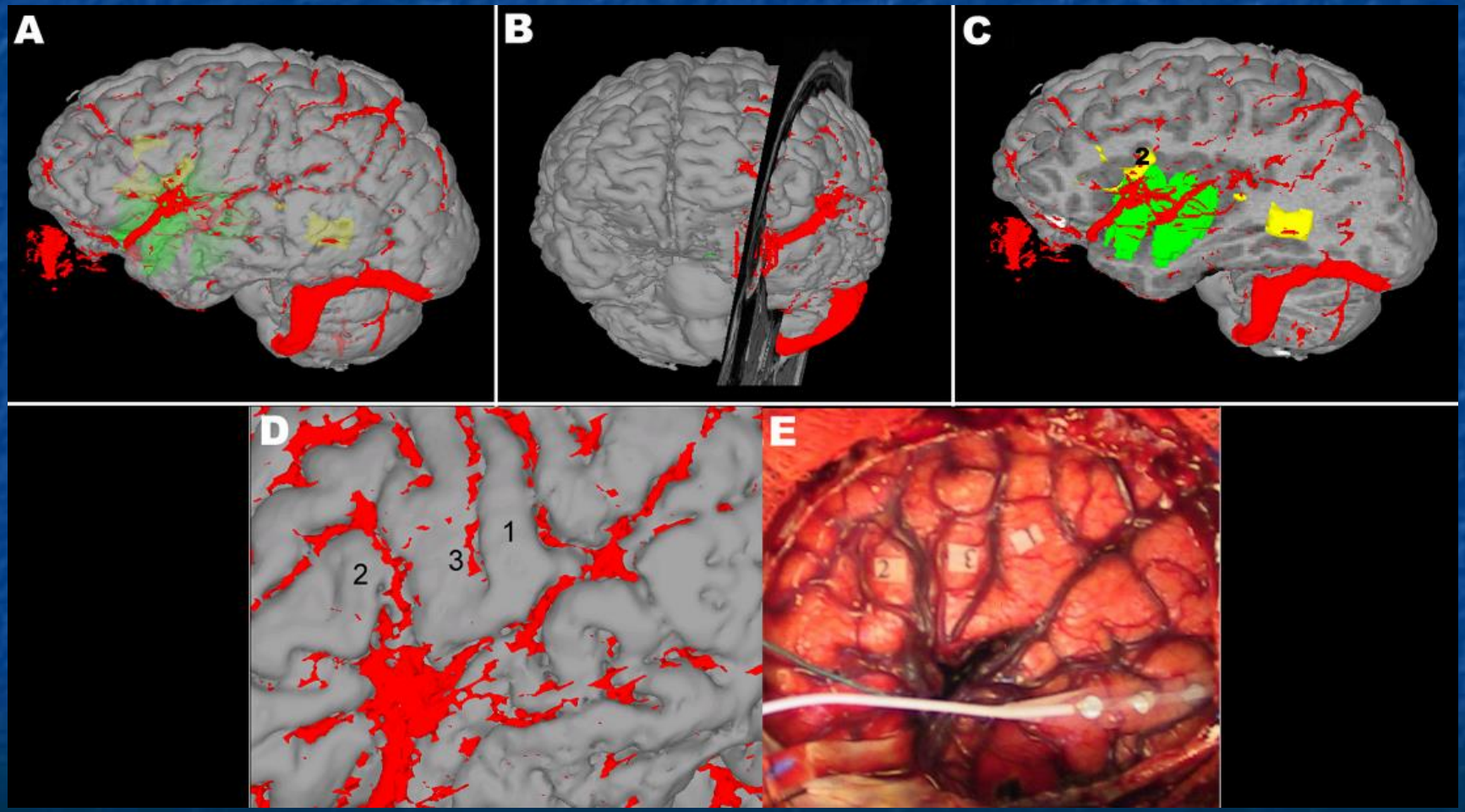


Time-to-peak

How to assess fMRI scan quality

- Comparison with intraoperative mapping
- Real-time analysis
- Reproducibility
- Simulation studies (where truth is known)
- Quantitative QA metrics
- Expert interpretation

fMRI validation by direct comparison with intraoperative mapping

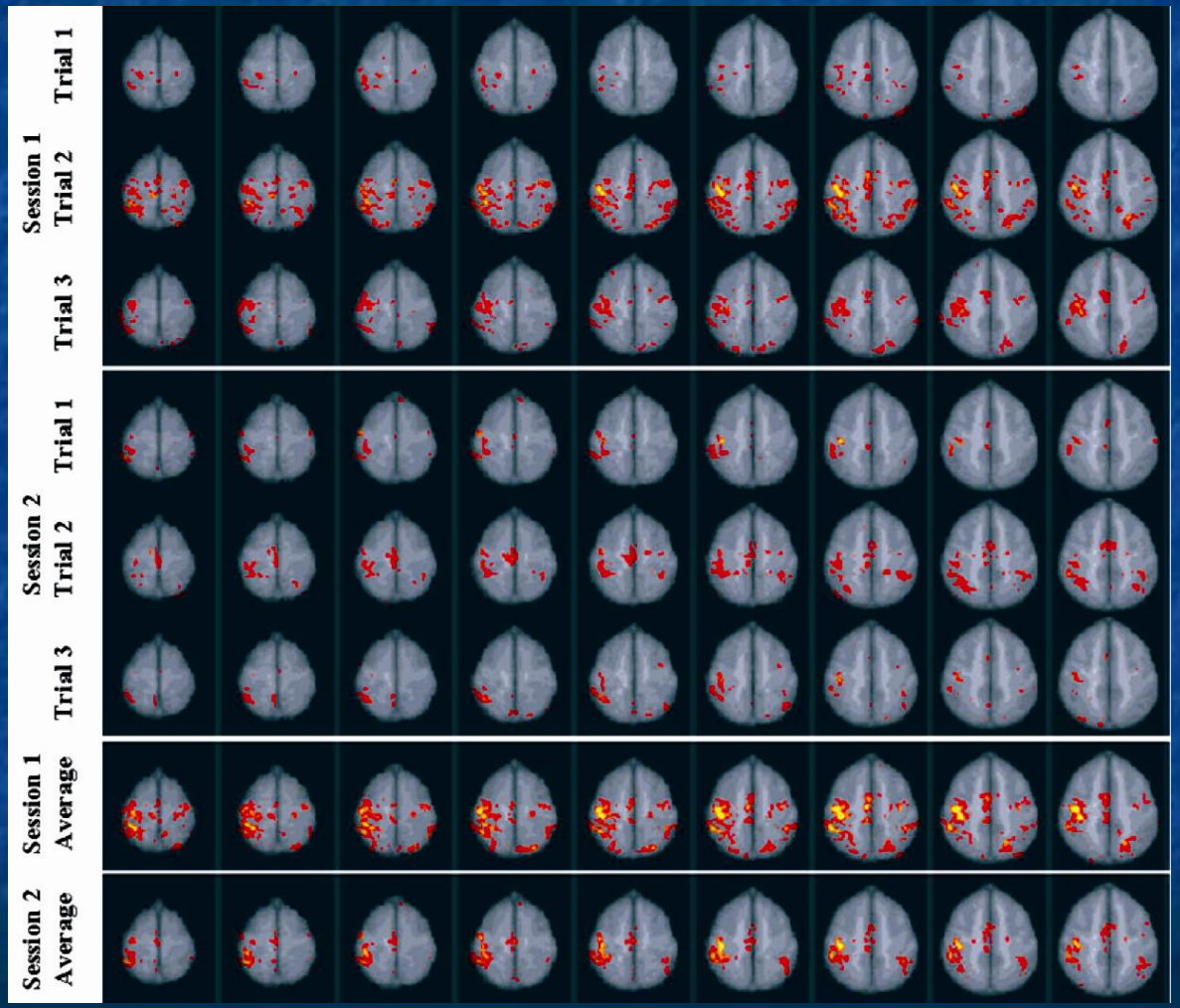


fMRI near-real-time quality control (QC)

Goal: make it easier to assess scan quality quickly

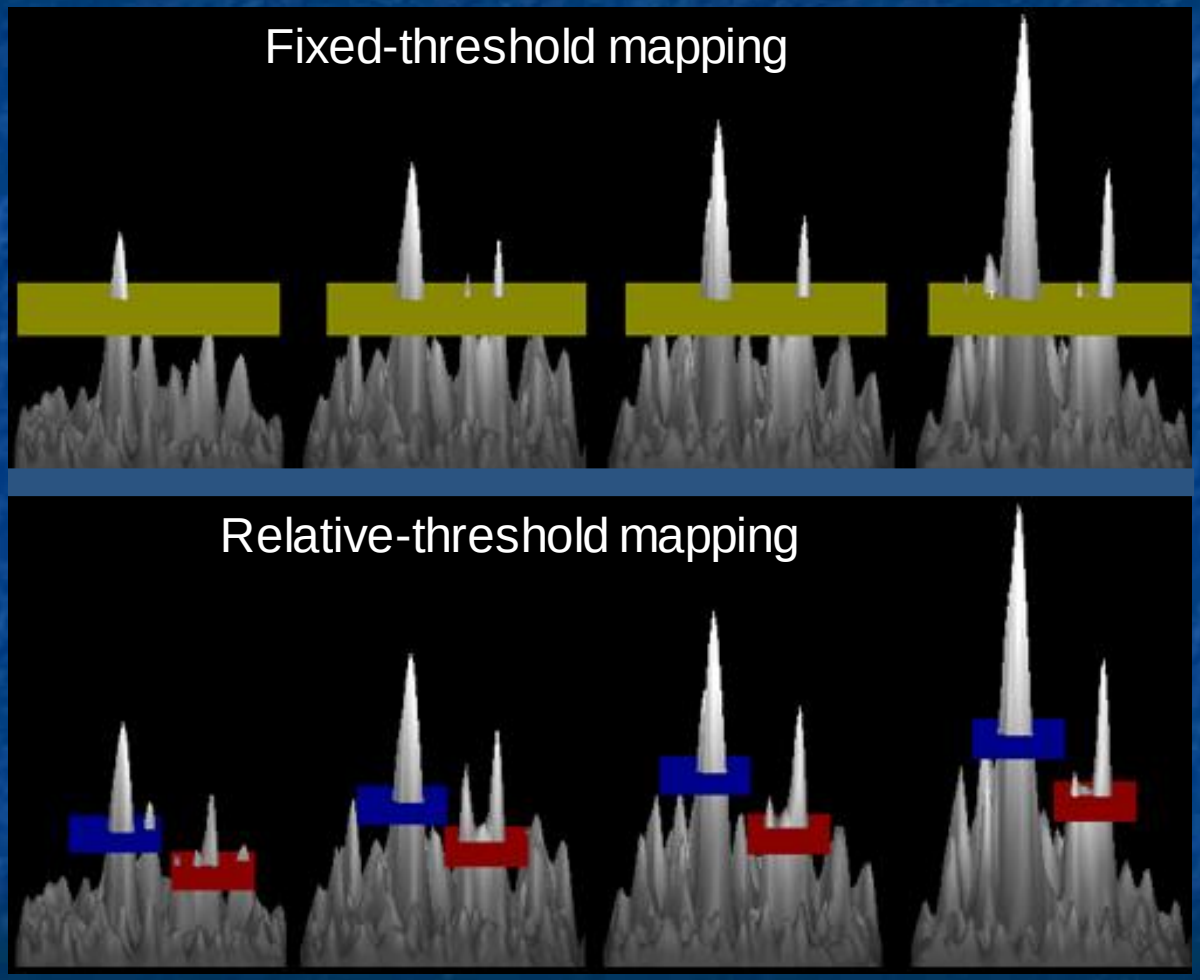
New Duke website lets us see fMRI results during session

Traditionally, fMRI is not quantitatively reproducible



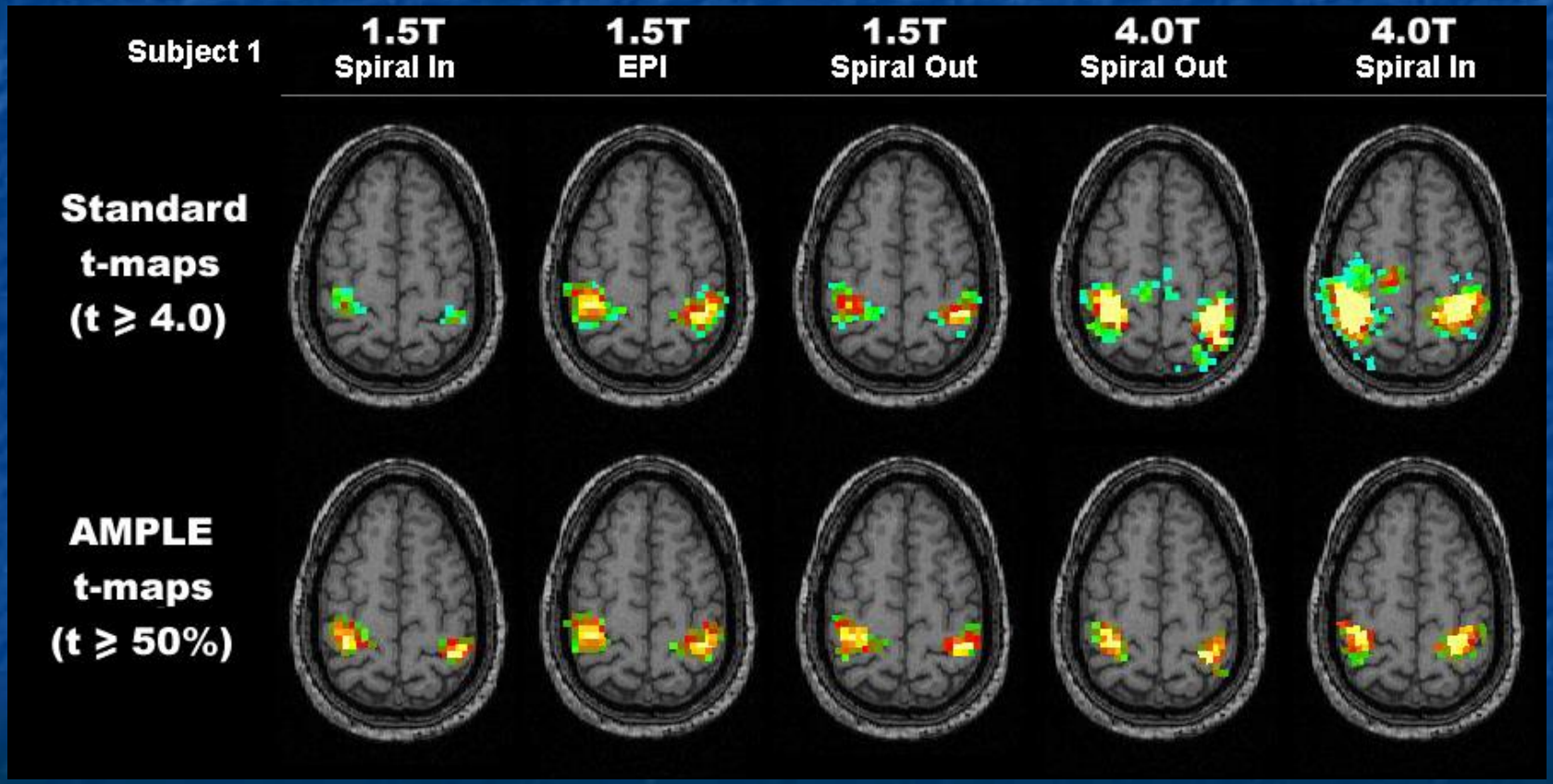
Liu et al., "Reproducibility of fMRI at 1.5T in a Strictly Controlled Motor Task", MRM 2004

Statistical significance of activation changes as a function of scan time

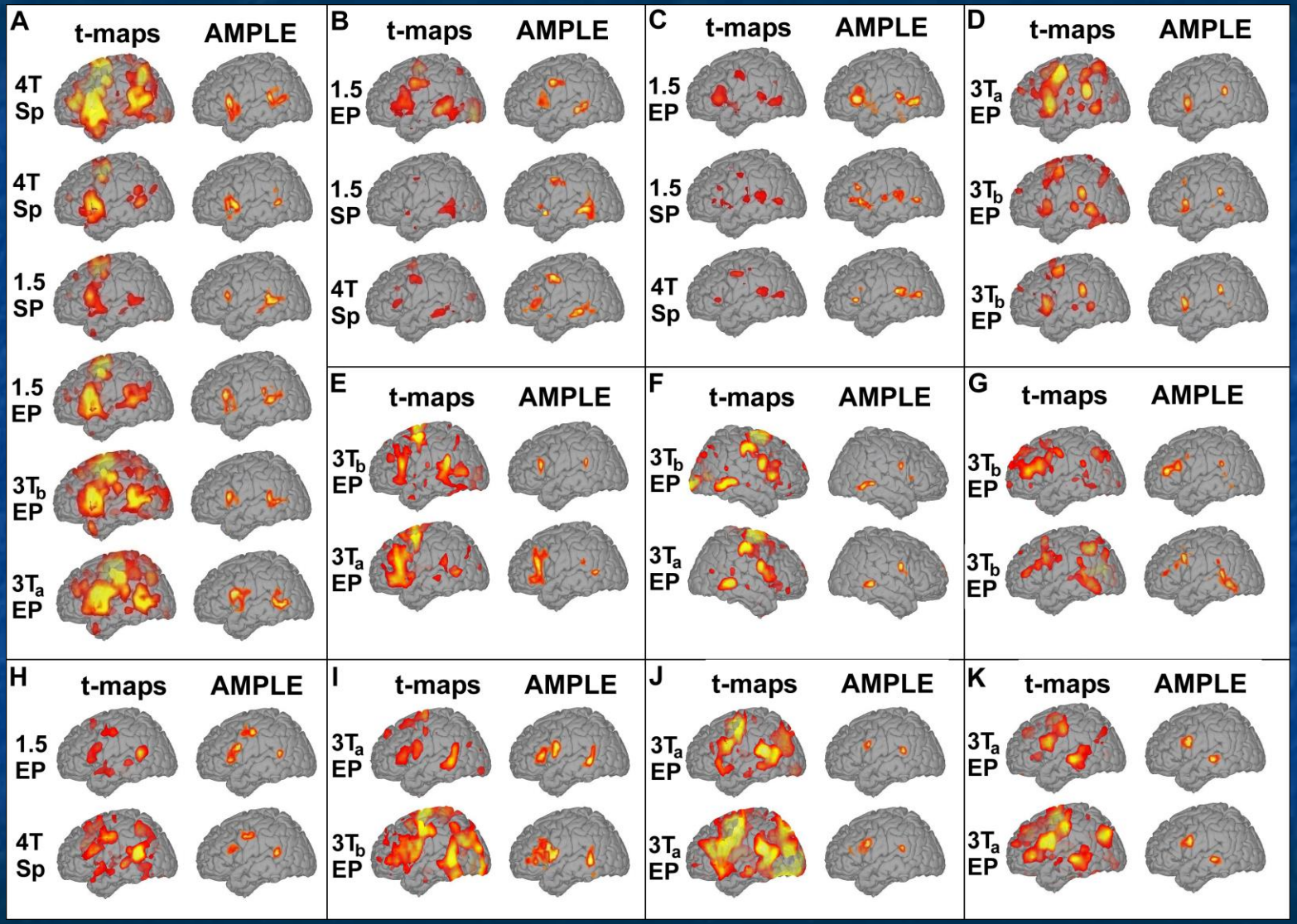


Activation mapping as percentage of local excitation (AMPLE)

AMPLE scaling makes maps consistent across scans or scanners



Language AMPLE maps improve reproducibility

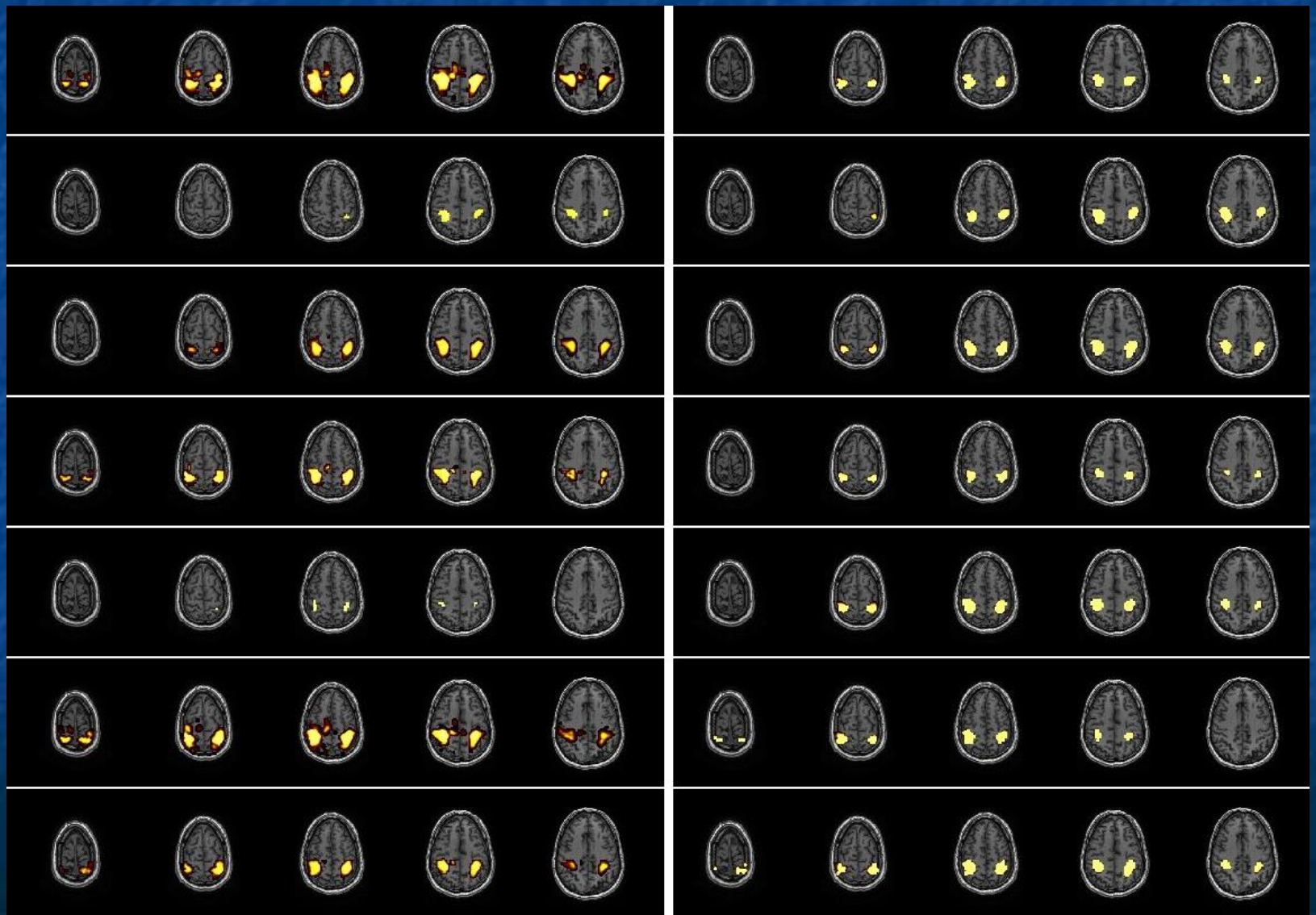


Upper ~half of AMPLE peaks are most reproducible

Hand task data analyzed at 8 clinica sites

"Standard" threshold

AMPLE 50% threshold



DRO1

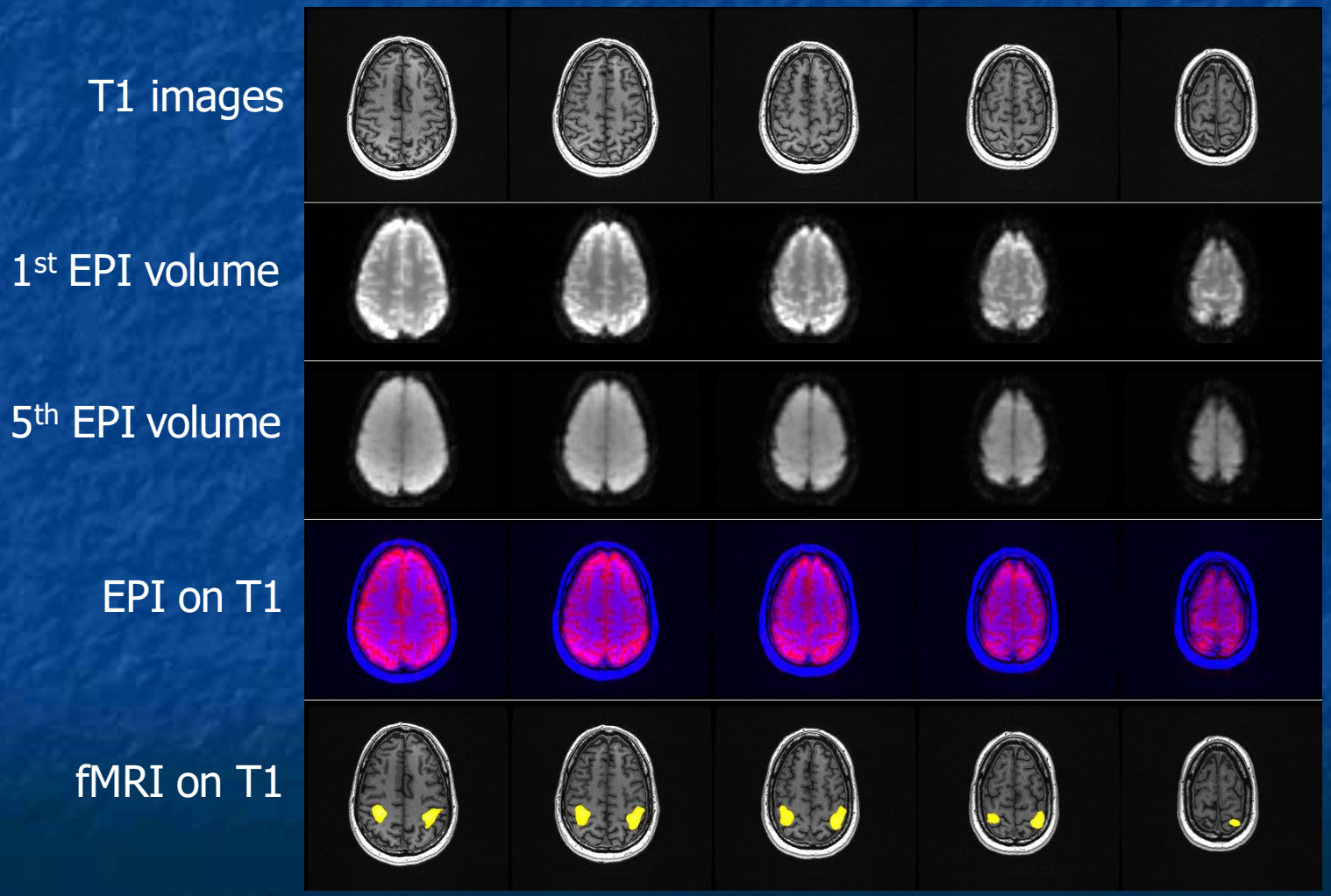
Language data analyzed at 8 sites

"Standard" threshold

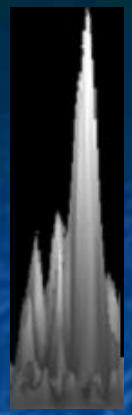
AMPLE 50% threshold

DRO1

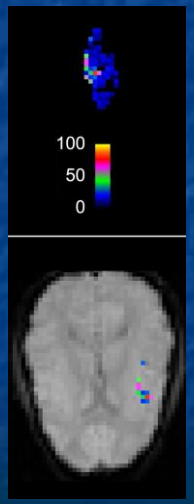
Aligning EPI and anatomical images

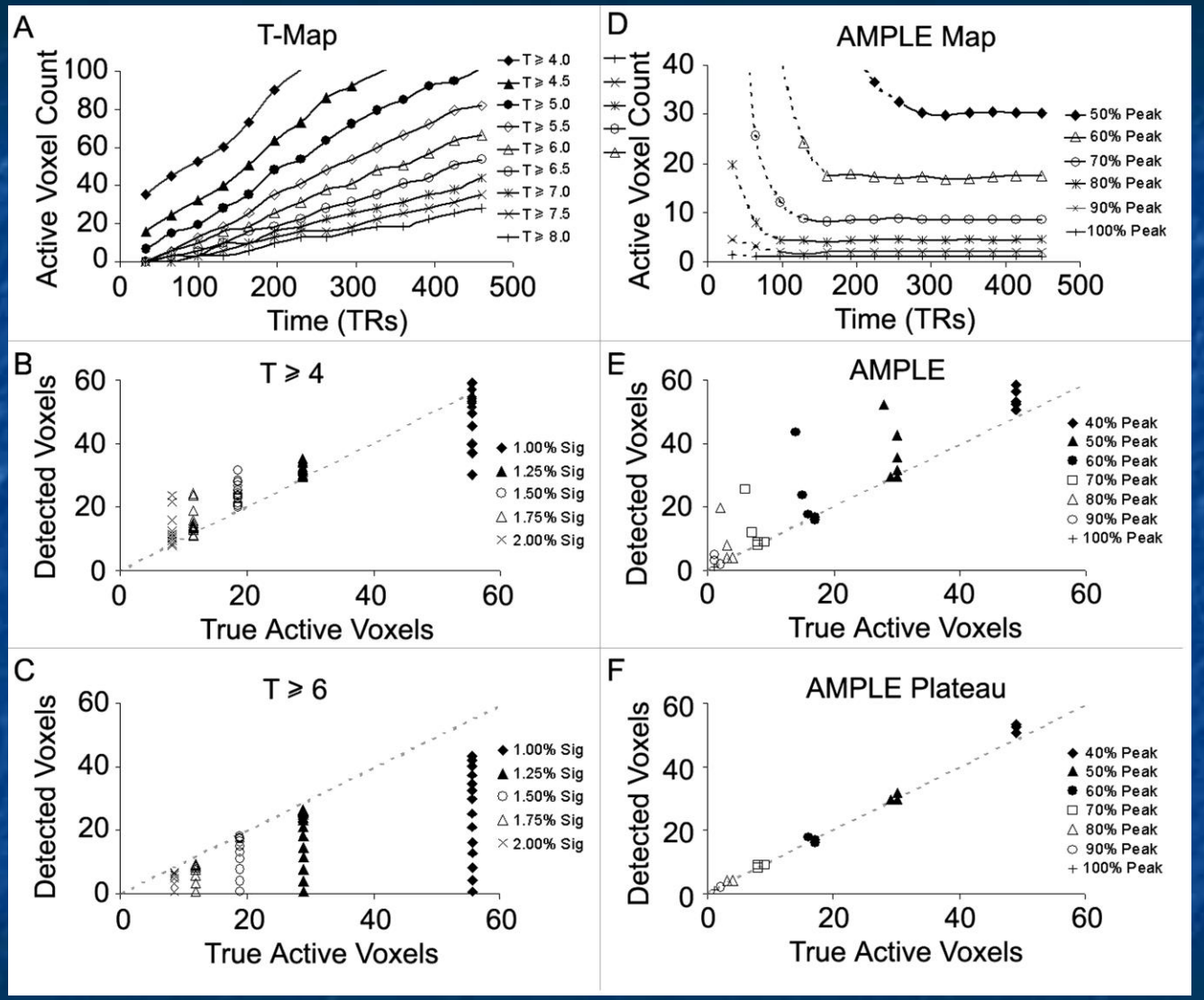


Threshold Reproducibility DROs



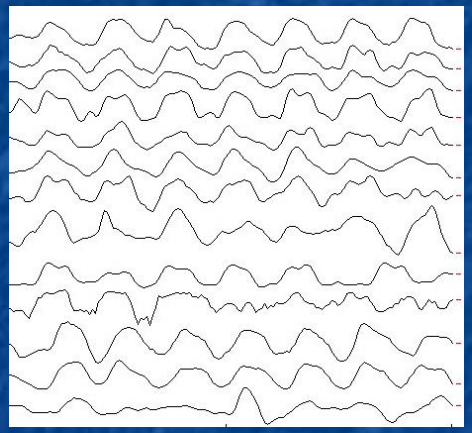
Generate simulated fMRI data with known activity levels

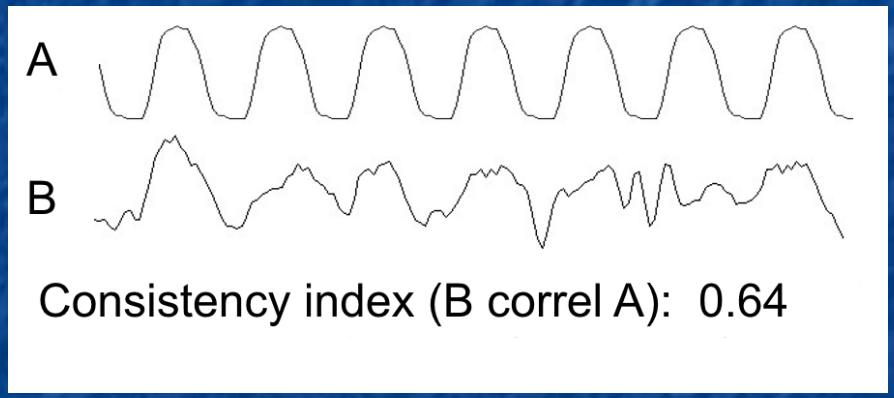


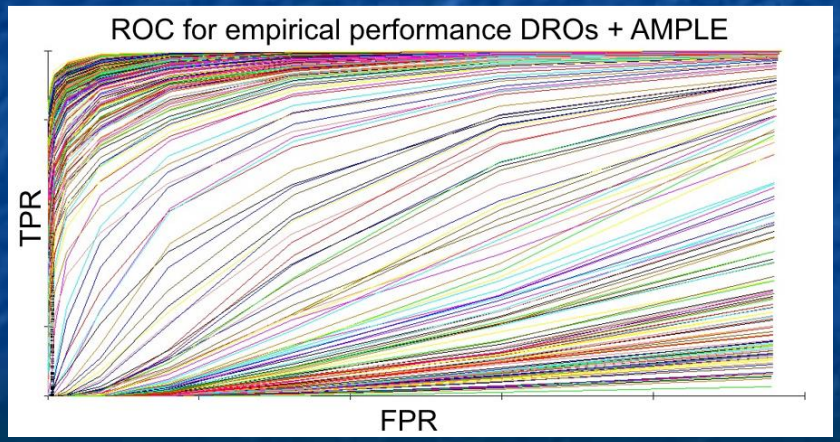


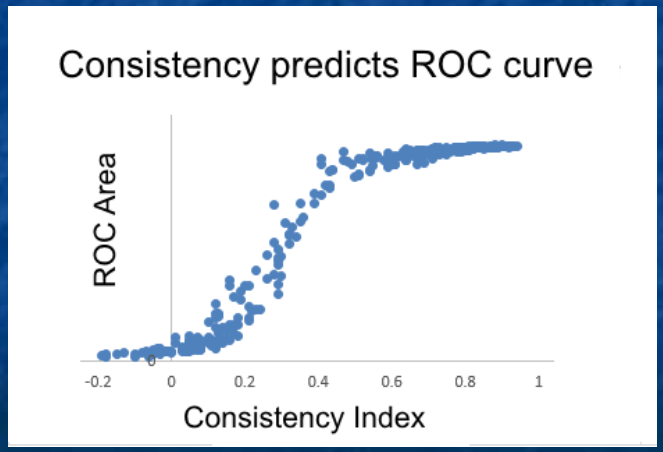
Conclusion: Once AMPLE time plots stabilize activation is reliable.

Simulations using task performance from 400 different patients









Conclusion: Consistency index > 0.5 is "good" task perfomance

Current research interests

Task design

- Standard tasks use active on-off block-designs
  - Can tailor stimuli to accommodate different patients
- Can also use passive tasks
  - Passive listening to spoken sentences
  - Passive viewing of video (block-design or stimulus coded)
  - Passive external manipulation of sensorymotor function

Resting-state fMRI

- Rs-fMRI can show networks (but hard to verify)
- There are many different ways to analyze rs-fmri signals

Sleeping fMRI (under general anesthesia)

- BOLD signal responses under propofol anesthesia
- For otherwise unscannable (pediatric) patients

Conclusion

- Currently, clinical fMRI can locate eloquent cortex, which is a critical concern in any brain surgery
- In the future, clinical fMRI will be used to measure changing levels of brain activity
- Doing so will require improved reproducibility, improved tasks, and improved analysis methods (improved acquisition methods will also help)
- Data quality criteria are critical for interpreting results
- Once able to measure brain activity, fMRI could be used clinically to assess neurological or psychiatric disorders, disease progression, and patient response to therapies