Clinical fMRI

Jim Voyvodic, Ph.D.
Brain Imaging and Analysis Center
Radiology Dept.
Duke University Medical Center
Functional MRI (fMRI) is primarily used clinically to map speech and motor function prior to brain surgery.
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 ________.

15s

vs

Bnd MwjGhdchkj ckr n ________.

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.

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
Clinical fMRI exam

Anatomy & pathology

fMRI maps & 3D reconstructions

DTI Maps & Fiber tracks
Summary fMRI maps can combine multiple task areas and pathology

This fMRI map was computed from ~14,000 images.
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
Start at any ‘seed’ and connect voxels with similar orientations

Overlay fiber tracks on anatomy
fMRI validation by direct comparison with intraoperative mapping
Examples
Language – LH 34 yo with insular tumor
Language & motor – RH 82 yo parietal tumor
Language & motor – RH 12 yo with epilepsy
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?
Traditionally, fMRI is not quantitatively reproducible

Liu et al., “Reproducing fMRI at 1.5T in a Strictly Controlled Motor Task”, MRM 2004
Same data analyzed at 8 clinical fMRI sites

Bilateral hand motion scan data sent to 8 clinical sites.

Clinical sites differ in software packages, algorithms used, and statistical thresholding methods.
Identical sentence language task data

Silent sentence-completion language scan data sent to 8 clinical sites.
Hand task data analyzed at 8 clinical sites

“Standard” threshold

AMPLE 50% threshold
Language data analyzed at 8 sites

"Standard" threshold

AMPLE 50% threshold
Another sentence task analyzed at 8 sites

“Standard” threshold

AMPLE 50% threshold
Sources of variance affecting fMRI

- Scanner*
- Stimulus presentation system*
- Training procedures*
- Task design*
- Analysis procedures*
- Physiology
- Pathology, hemodynamic response
- Patient movement
- Task performance

Variance reduced by standardization
Need for method improvement and standardization
Within patient Disease related
Major sources of variance Within and between scans

* Emphasis is on standardization
Task design

Almost all clinical fMRU uses block-design tasks

- Sensitivity: Strongest signal obtained from on-off block-designed tasks (steady state)
- Specificity: Ideally, active and rest blocks differ only in function of interest

There is increasing interest in passive task designs

- Resting-state (task-free) fMRI for clinical mapping can work but is controversial
- Designs involving passive tasks may be a compromise
Currently, clinical fMRI can locate eloquent cortex.

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.