Advanced MRI in the Clinic: Functional MRI (fMRI)

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Declaration of Financial Interests or Relationships

I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.
**Functional MRI (fMRI) with Blood Oxygenation Level-Dependent (BOLD) Signal**

- **Neurovascular Coupling**
  - Neuronal Activity
  - Glucose & Oxygen Consumption
  - Blood Flow
  - Blood Volume
  - Blood Oxygenation
  - T2*

- **BOLD Signal**
  - Oxyhemoglobin: Diamagnetic
  - Deoxyhemoglobin: Paramagnetic

- **Inhalation of pure O₂**
- **Inhalation of normal air**

- Huettel, Song and McCarthy, Functional MRI, 2nd Ed.
- Fox, Science, 1988
- Ogawa et al., PNAS, 1990; MRM, 1990

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**Task-based fMRI:**
Detecting Task-induced Activation from the BOLD signal increase

- **Left Hand Movement**
- **Right Hand Movement**
- **Language fMRI + DTI fiber tracking**

- Letter fluency
- Category naming
- Sentence completion
Resting-state fMRI:
Detecting Functional Connectivity from the inter-region correlations of BOLD signal fluctuation

Motor Network

Motor (Hand) fMRI

Visual fMRI

Default Mode Network

Motor Network

Default Mode Network

fMRI in the Clinic

  - 70554: motor, visual; not requiring physician
  - 70555, 96020: language and others; requiring physician

• Indications: see ACR-ASNR-SPR Practice Parameter

• The most common use is presurgical fMRI:
  - Map eloquent brain areas
  - Minimize post-operative deficits and maximize tumor resection
  - Guide intra-operative functional mapping

Photo from Sujit Prabhu, MD

Language fMRI

Photo from Sujit Prabhu, MD

Biswal, MRM, 1995

Fox, PNAS, 2005

Damoiseaux, PNAS, 2006

Independent Component Analysis (ICA)
fMRI Hardware and Software

- **fMRI stimulation systems**
- **Real-time fMRI software**
- **Post-processing software**
  - Vendor software
  - FDA-cleared 3rd party software
  - Research software (AFNI, FSL, SPM etc.)

Clinical fMRI Paradigms

- **Task-based fMRI (tb-fMRI):**
  - Blocked design is commonly used in the clinic
  - Paradigm timing: (10 - 30 s) x (3-6 cycles)
  - Common clinical task paradigms:
    - Motor: hand, toe, tongue ...
    - Visual: checkerboard stimulation ...
    - Speech: word generation, sentence completion, object naming ...

- **Resting-state fMRI (rs-fMRI):**
  - Better before tb-fMRI
  - Resting state scan (~ 6-10 mins)
    - Eyes open (fixated) or closed
    - Don’t fall asleep
    - Not to think about anything in particular
Image Acquisition

• Typical clinical fMRI protocol:
  - Single-shot GRE-EPI
  - TR = 2-3 s (<=2s for rs-fMRI)
  - TE = 25-35 ms (3T)/45-55 ms (1.5T)
  - FA = 70-90°
  - matrix size = 64-128 (w/ PI)
  - in-plane resolution = 2-4 mm
  - slice thickness = 3-5 mm
  - 25-45 slices
  - dynamics = 60-150
  - scan time = 3-5 min

\[ T2^*-weighted \text{ EPI images} \]

fMRI Data Analysis

• Data pre-processing
  - Motion correction
  - (Slice timing correction)
  - Spatial normalization (not for clinical)
  - Spatial smoothing
  - (Temporal filtering): required for rs-fMRI

• Tb-fMRI activation detection
  - Correlation/General Linear Model (GLM)

• Rs-fMRI network detection
  - Seed-based analysis
  - Independent component analysis (ICA)

• Data reporting and visualization
  - Compatible for planning/navigation systems
**fMRI Quality Management**

- **Periodic QC testing**
  - EPI stability and artifact
- **Before fMRI**
  - Patient compliance verification
  - Patient training
- **During/After fMRI:**
  - Performance confirmation
  - Real-time fMRI monitoring
- **During post-processing**
  - EPI to T1 registration
  - Susceptibility artifact
  - Head motion
  - Statistical thresholding
  - Dealing with potential false positives
  - Dealing with potential false negatives

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**fMRI QC Testing: System Stability**

Scan a uniform phantom for ~ 10 mins

1 voxel, c.v. = 0.46%

3x3, c.v. = 0.22%

AAPM Report #100 suggests c.v. < 0.25%

Radius of decorrelation (RDC) = CV(1)/CV(Nmax)

Weisskoff, MRM, 1996;
Friedman & Glover, JMRI, 2006
Functional vs. structural image registration

- Limited by Spatial resolution and distortion of the echo planar image

Automated registration  After adjustment

CM: Coordinate matching
AR: Automated registration
ARadj: AR with manual adjustment

Jen, Med Phys, 2018

1.4 mm isotropic@ 7T

Spatial localization accuracy (n=12)

<table>
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<th></th>
<th>&lt; 2 mm</th>
<th>2-4 mm</th>
<th>5-10 mm</th>
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<tr>
<td>7T</td>
<td>100%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3T</td>
<td>33%</td>
<td>50%</td>
<td>17%</td>
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MDACC unpublished data

Head Motion: A common source of fMRI failure

- Random motion: False negative
- Task-correlated motion: False positive

(Photo taken in 1998)
Statistical Threshold: A challenge for individual fMRI

- Statistical threshold is about confidence.
  - Sensitivity vs. Specificity
- Correction for multiple comparison adds another layer of complexity.

\[ p<0.05, \text{ uncorrected} \quad p<0.05, \text{ corrected} \]

Causes of False Results

- **False Positives**
  - Head motion (task correlated)
  - System instability (task correlated)
  - Physiological noise (task correlated)
  - Statistical threshold (too low)
- **False Negatives**
  - Head motion (not correlated)
  - System instability (not correlated)
  - Physiological noise (not correlated)
  - Statistical threshold (too high)
  - **Susceptibility artifact** (previous surgery)
  - Neurovascular uncoupling
  - Patient performance
**Cerebrovascular Reactivity (CVR) Mapping:**
To indicate areas with potential False **Negative fMRI**

**Case Report**

**Pseudo-Reorganization of Language Cortical Function at fMR Imaging: A Consequence of Tumor-Induced Neurovascular Uncoupling**


**BOLD/perfusion MRI for CVR Mapping:**
- Acetazolamide injection
- CO₂ inhalation
- Breath hold
- Resting state

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**Zaca, JMRI, 2014**

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**Resting-state fMRI:**
For patients who cannot comply with tb-fMRI

- In a retrospective analysis of 134 patients, 49 cases (36%) had limited language fMRI and rs-fMRI was post-processed.
  - Radiologists found rs-fMRI beneficial in 84-88% of the cases.
  - Neurosurgeons found rs-fMRI “definitely” useful in 60% and “somewhat” useful in 30% of the cases.

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rs-fMRI in a patient with glioblastoma who could not perform language fMRI.
**Summary**

- **Functional MRI (fMRI)** can robustly detect brain activations using the BOLD contrast.

- **Clinical fMRI procedures** include:
  - Task paradigms (visual, motor, language etc.)
  - Dynamic T2*-weighted EPI scan
  - Image pre-processing, activation detection, and spatial registration

- **Presurgical fMRI** is a clinical routine, with limitations in localization and detection.
  - Functional to anatomy registration error should and can be controlled to ~ 5 mm.
  - Language mapping remains challenging with overall accuracy ~ 60%.

- **Ultrahigh field, CVR mapping, and rs-fMRI** are increasingly used for clinical fMRI.
  - Rs-fMRI helps ~30% of the patients who are limited for task-based fMRI.
  - CVR mapping helps indicating areas with potential neurovascular uncoupling (i.e. FN fMRI).