

Advanced MRI in the Clinic : Functional MRI (fMRI)

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AAPM 2022



Declaration of Financial Interests or Relationships

I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.

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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

BOLD Signal Curve: Initial dip → Stimulation → Positive BOLD (Overshoot) → Post-stimulus undershoot

Brain Scans: Inhalation of pure O₂ (top), Inhalation of normal air (bottom)

CMRO₂ and BV Changes:

Parameter	Resting	Stimulated	Change
CMRO ₂	0.8	2.4	1.6
BV	38.7 ± 3.3 μm	51.6 ± 5.0 μm	12.9 ± 1.7 μm
CMV	8.7%	16.3%	7.6%

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

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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

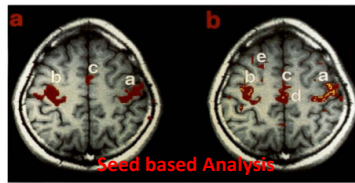
Letter fluency
Category naming
Sentence completion

t scale: 3 to >10

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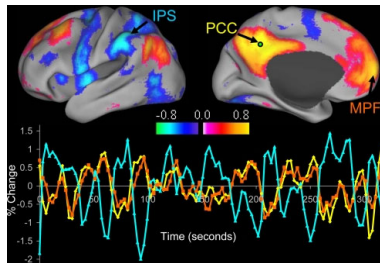
Resting-state fMRI: Detecting Functional Connectivity from the inter-region correlations of BOLD signal fluctuation

Motor
Network

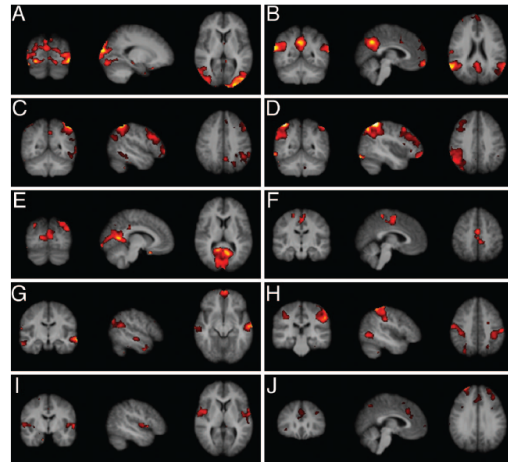


Biswal, MRM, 1995

Default Mode
Network



Fox, PNAS, 2005



Independent
Component
Analysis
(ICA)

Damoiseaux, PNAS, 2006

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fMRI in the Clinic

- **Current Procedural Terminology (CPT) Codes**
 - 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

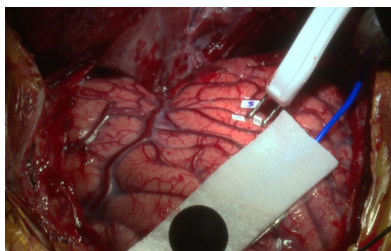
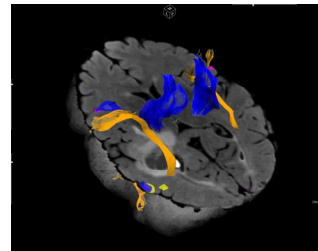
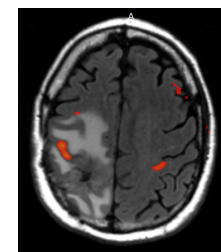


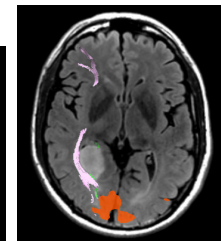
Photo from Sujit Prabhu, MD



Language fMRI



**Motor
(Hand)
fMRI**

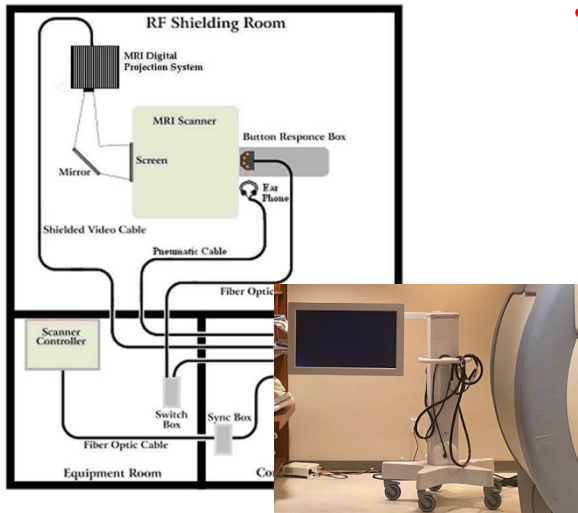


**Visual
fMRI**

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fMRI Hardware and Software

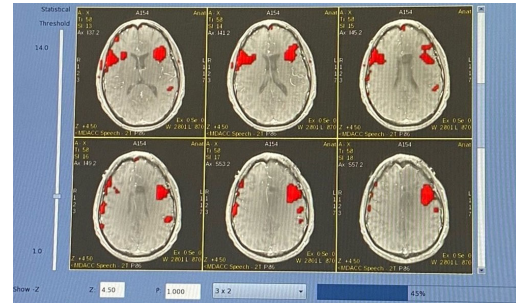
- **fMRI stimulation systems**



- **Real-time fMRI software**

- **Post-processing software**

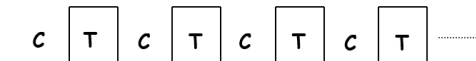
- Vendor software
- FDA-cleared 3rd party software
- Research software (AFNI, FSL, SPM etc.)



Real-time fMRI

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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 ...

Sentence Completion

- Rest but keep your eyes open when you see a series of nonsense letters.

Example: Fkoniwe kasd iepaw akd ___dfe.

- If you see an English sentence, read it to yourself and think of a word that fits into the blank.

Example: Young cats are called _____.

- Don't speak out loud, don't move your mouth or lips.

Try to keep still.

- **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



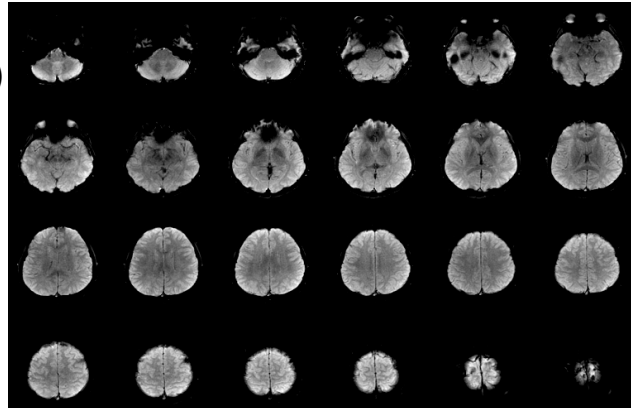
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Image Acquisition

- **Typical clinical fMRI protocol:**

- Single-shot GRE-EPI
- TR = 2-3 s (≤ 2 s 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 EPI images



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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**

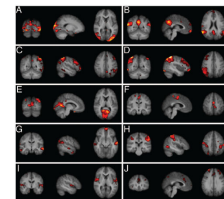
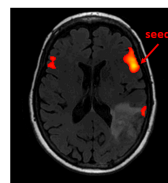
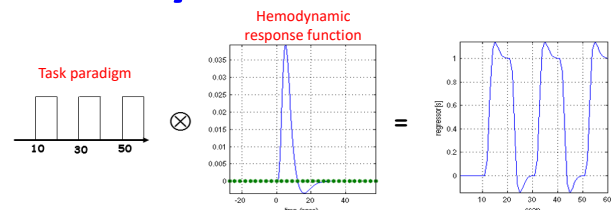
- Correlation/General Linear Model (GLM)

- **Rs-fMRI network detection**

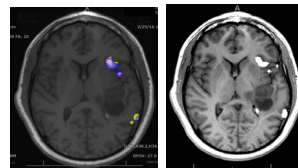
- Seed-based analysis
- Independent component analysis (ICA)

- **Data reporting and visualization**

- Compatible for planning/ navigation systems



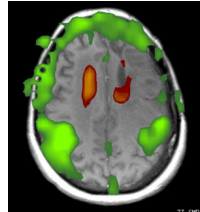
Damoiseaux,
PNAS, 2006



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fMRI Quality Management

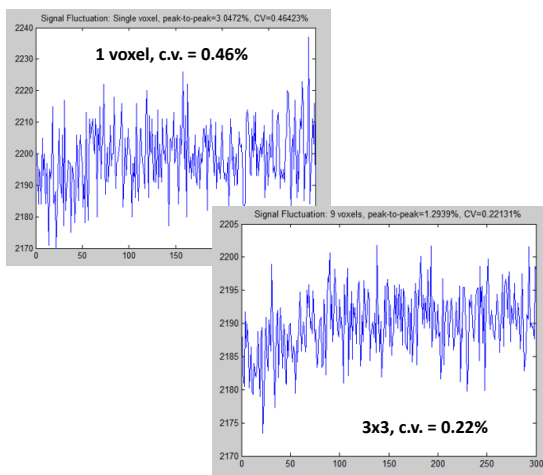
- **Periodic QC testing**
 - EPI stability and artifact
- **Before fMRI**
 - Patient compliance verification
 - Patient training
- **During/After fMRI:**
 - Performance confirmation
 - Real-time fMRI monitoring
- **During post-processing**
 - EPI to T1 registration
 - Susceptibility artifact
 - Head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



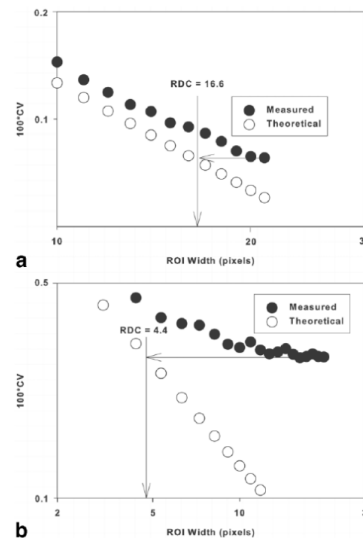
Real-time fMRI
showing task-
correlated motion

fMRI QC Testing: System Stability

Scan a uniform phantom for ~ 10 mins



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

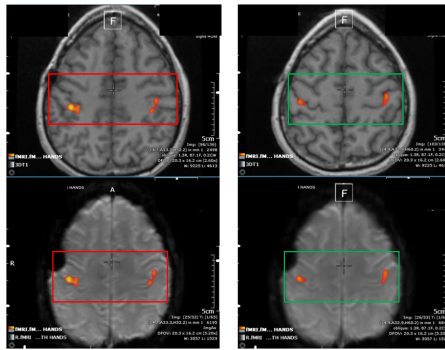


Radius of
decorrelation (RDC)
= $CV(1)/CV(N_{max})$

Weisskoff, MRM, 1996;
Friedman & Glover, JMRI, 2006

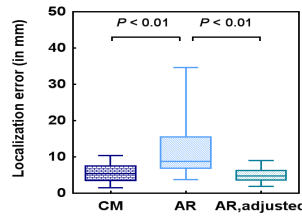
Functional vs. structural image registration

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



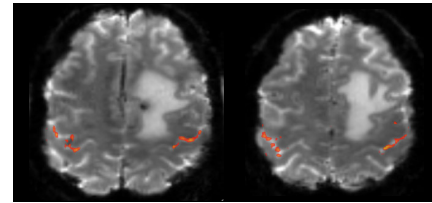
Automated registration

After adjustment



CM: Coordinate matching
 AR: Automated registration
 AR_{adj}: AR with manual adjustment

Jen, Med Phys, 2018



1.4 mm isotropic @ 7T

Spatial localization accuracy (n=12)

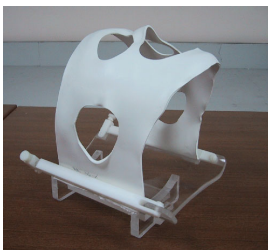
	< 2 mm	2-4 mm	5-10 mm
7T (1.4x1.4x1.4 mm ³)	100%	0	0
3T (1.9x1.9x4 mm ³)	33%	50%	17%

MDACC unpublished data

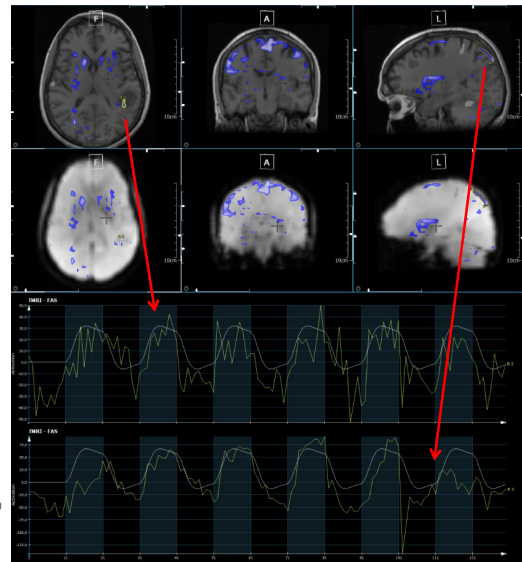
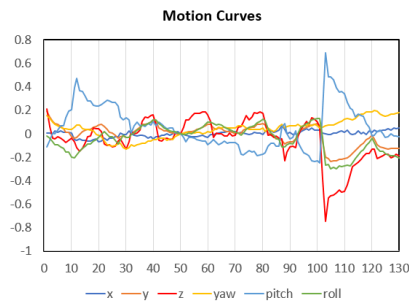


Head Motion: A common source of fMRI failure

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



(Photo taken in 1998)



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Statistical Threshold: A challenge for individual fMRI

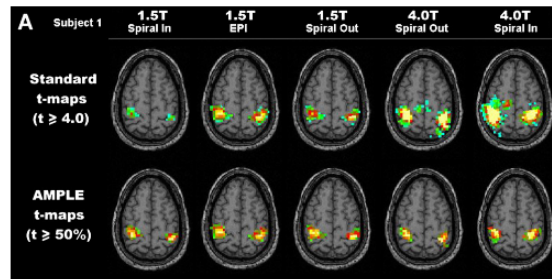
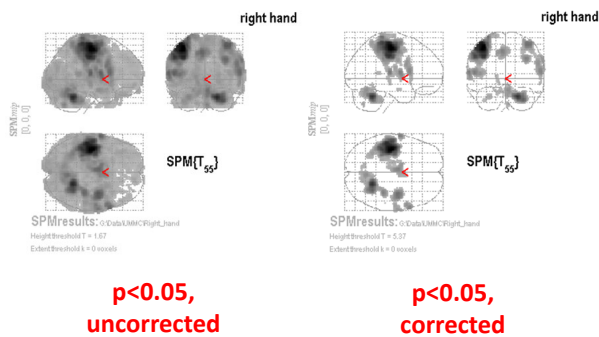
- Statistical threshold is about confidence.
 - Sensitivity vs. Specificity
- Correction for multiple comparison adds another layer of complexity.



Available online at www.sciencedirect.com
 ScienceDirect
 Magnetic Resonance Imaging 24 (2006) 1249–1261

MAGNETIC
 RESONANCE
 IMAGING

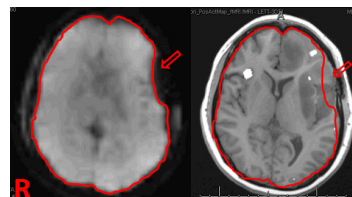
Activation mapping as a percentage of local excitation: fMRI stability within scans, between scans and across field strengths
 James T. Voyvodic*



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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**



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Cerebrovascular Reactivity (CVR) Mapping: To indicate areas with potential False Negative fMRI

AJNR Am J Neuroradiol 24:213–217, February 2003

Case Report

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

John L. Ulmer MD, Hendrikus G. Krouwer, Wade M. Mueller, M. Sahin Ugurel, Mehmet Kocak, and Leighton P. Mark

BOLD/perfusion MRI for CVR Mapping:

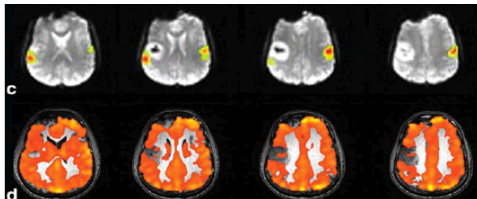
- Acetazolamide injection
- CO₂ inhalation
- **Breath hold**
- Resting state

Cerebrovascular Reactivity Mapping: An Evolving Standard for Clinical Functional Imaging

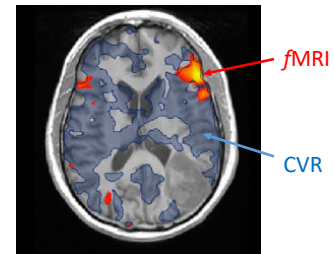
Pillai & Mikulis, AJNR, 2015

REVIEW ARTICLE

J.J. Pillai and D.J. Mikulis



Zoca, JMIR, 2014



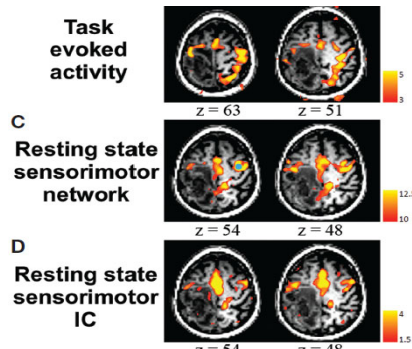
Hsu, Front Neuroinform, 2018

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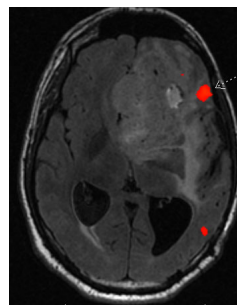
Resting-state fMRI: For patients who cannot comply with tb-fMRI

- 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.

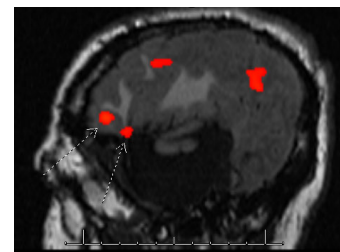
Kumar, Cancer Imaging, 2020



Zhang, Neurosurgery, 2009



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



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The screenshot displays the IClinfMRI (1.1.0) software interface. On the left, a menu lists options: DICOM Import, Task fMRI, Resting-state fMRI (highlighted with a red box), CVR Mapping, and fMRI to PACS. The main window is titled 'Seed-based rs-fMRI analysis with guidance' and contains several panels: 'Preprocessing' (with options like Slice Timing, Motion Correction, and Bandpass), 'Imaging Data Input' (listing files like P1_Resting.nii), 'Preprocessed Data' (listing P1_Resting_TMD1N880108S4mm.nii.gz), and 'FC Mapping' (with Threshold and Wind.(Max) settings). Below the settings are two axial brain MRI slices. The left slice is labeled 'High-Res T1 + Guidance Map' and shows a brain slice with red and yellow activation regions. The right slice is labeled 'High-Res T1 + FC Map seeding @ X 178, Y 092, Z 068' and shows a similar slice with red and yellow activation regions. The MD Anderson Cancer Center logo is visible in the bottom right corner of the software window.

Hsu, *Front Neuroinform*, 2018

Task-based fMRI

Resting-state fMRI

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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).