

Advanced MRI in the Clinic : Functional MRI (fMRI)

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AAPM 2020

Declaration of Financial Interests or Relationships

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

Outline

- Introduction of fMRI and clinical fMRI
- Implementation of fMRI in the clinic
- Challenges and opportunities

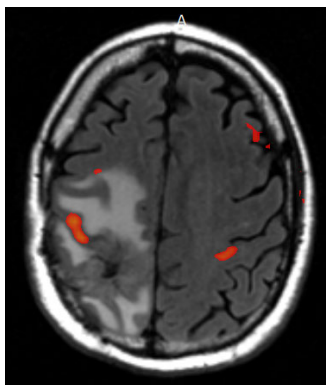
fMRI: Functional Brain Mapping using MRI

Perfusion-based fMRI

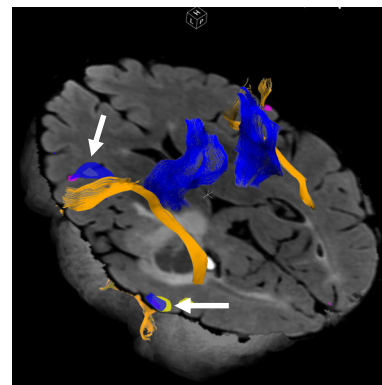


Belliveau, *Science*, 1991

BOLD-based fMRI



Motor fMRI



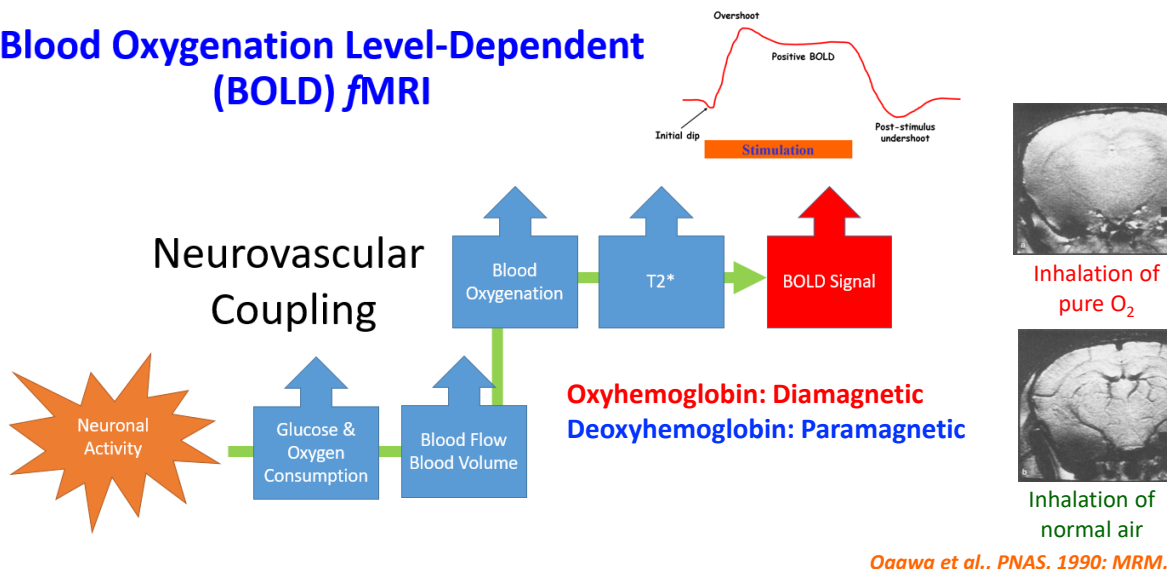
Language fMRI with DTI fiber tracking

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Blood Oxygenation Level-Dependent (BOLD) fMRI



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BOLD fMRI w/ T2*-weighted GRE-EPI

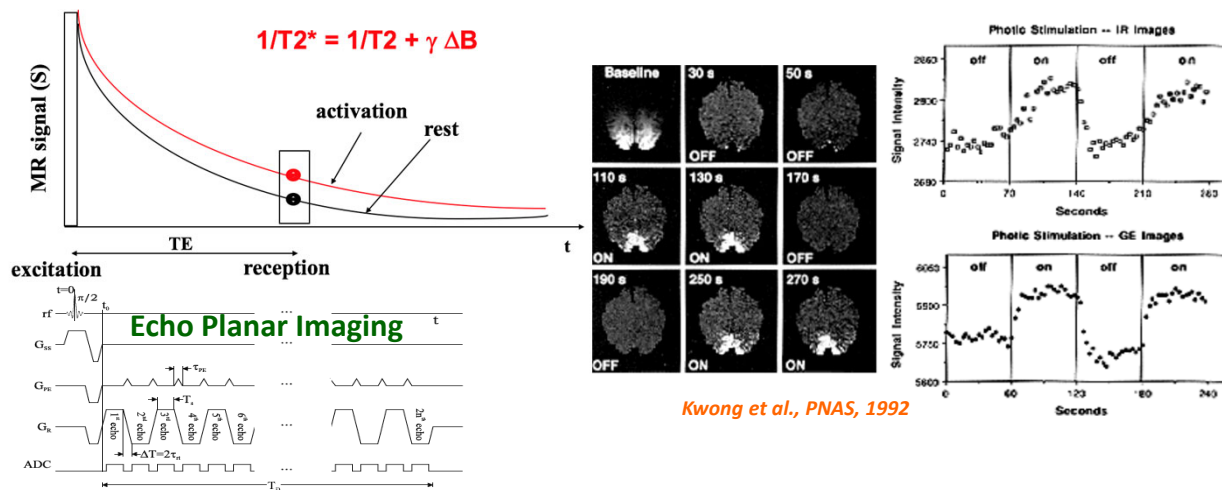


Figure adopted from Haacke et al., 1st Ed, 1999

Kwong et al., PNAS, 1992

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fMRI in the Clinic

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

- **70554:** ...functional MRI; including ...repetitive body part movement and/or visual stimulation, not requiring physician or psychologist administration
- **70555:** ...functional MRI; requiring physician or psychologist administration of entire neurofunctional testing
- **96020:** Neurofunctional testing selection and administration during ...functional brain mapping, with test administered entirely by a physician or psychologist, with

- **ACR-ASNR-SPR Practice Parameter (rev. 2017)**

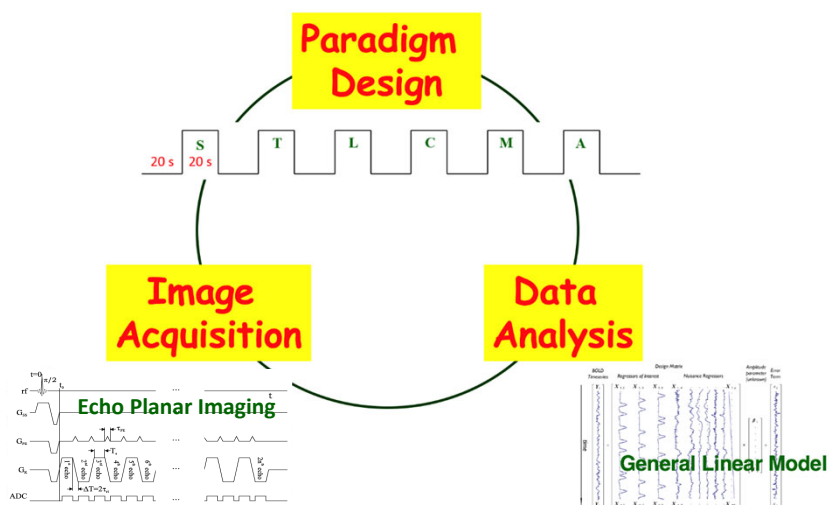
Primary indications for fMRI include, but are not limited to, the following:

1. Assessment of intracranial neoplasm and other targeted lesions
 - a. Presurgical planning and operative risk assessment
 - b. Assessment of eloquent cortex (eg, language, sensory, motor, visual centers) in relation to a tumor or another focal lesion
 - c. Surgical planning (biopsy or resection)
 - d. Therapeutic follow-up
2. Evaluation of preserved eloquent cortex
3. Assessment of eloquent cortex for epilepsy surgery
4. Assessment of radiation treatment planning and post-treatment evaluation of eloquent cortex

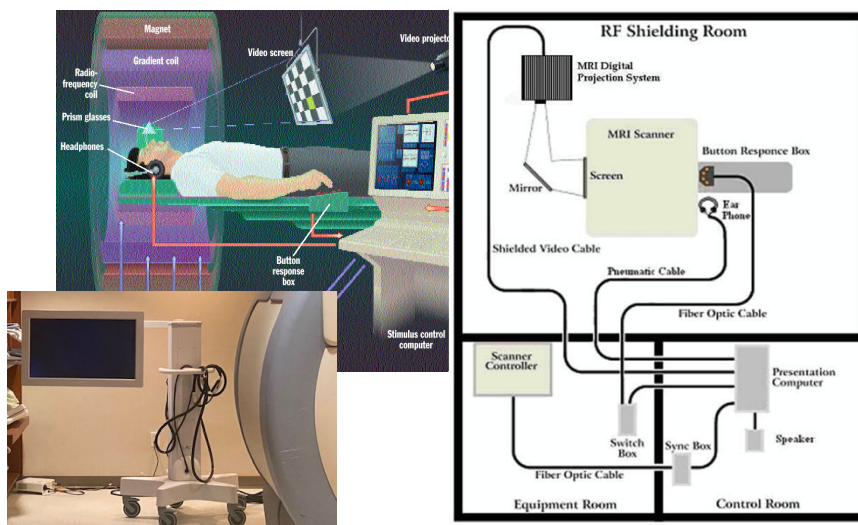
Implement a clinical fMRI program

It's a Team work:

- Neurosurgeon
- Neuroradiologist
- Neuropsychologist
- Specialized Technologist
- Physicist



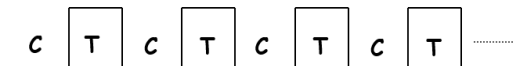
Need special hardware/software



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

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Clinical fMRI Paradigms



- **Blocked design is more common for clinical fMRI**
- **Need to provide patient w/ proper instruction and training**
- **Block duration: 10 - 30 s**
- **Number of cycles: 3 - 6**
- **Task block:**
 - Motor: hand, toe, tongue ...
 - Visual: checkerboard stimulation ...
 - Speech: word generation, letter fluency, sentence completion ...
- **Control block:**
 - fixation, visual, motor ...

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Paradigm Examples: Motor

Motor Task – Hand Movement

We are now going to begin the 'motor task'. You will first see a hand image with a red cross on the screen. Just keep still and you don't need to do anything during this time.

After 15 seconds, you will see the hand image without the red cross. When you see this, start closing and opening both of your hands. Try to close and open your hand to the full extent, in a fast pace, while keep your head very still.

After 15 seconds, the red cross will return. Stop moving your hands and just keep them in a comfortable position. You will continue alternating between rest and hand movement for approximately 3 and a half minutes.

Remember to remain very still during this scan. Do not change the positions of your head and arms between the rest and hand movement periods.


Hand Motion


When you see:  Rest

When you see:  Open & close your hands

Keep your eyes open the whole time.
Keep the rest of your body still.

Tongue Movement

When you see:  Rest

When you see:  Move your tongue side-to-side

Keep your eyes open the whole time.
Keep the rest of your body still.

15 s 15 s

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Paradigm Examples: Language

Silent Word Generation

When you see a single letter on the screen, try to think of as many words as you can that begin with that letter. Only think of the words, do not say them out loud.

Try to keep very still.

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.

20 s 20 s

S

T

L

C

M

A

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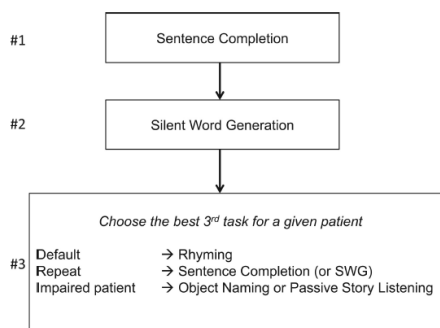
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American Society of Functional Neuroradiology–Recommended fMRI Paradigm Algorithms for Presurgical Language Assessment

D.F. Black, B. Vachha, A. Mian, S.H. Faro, M. Maheshwari, H.I. Sair, J.R. Petrella, J.J. Pillai, and K. Welker



Summary of individual task usefulness

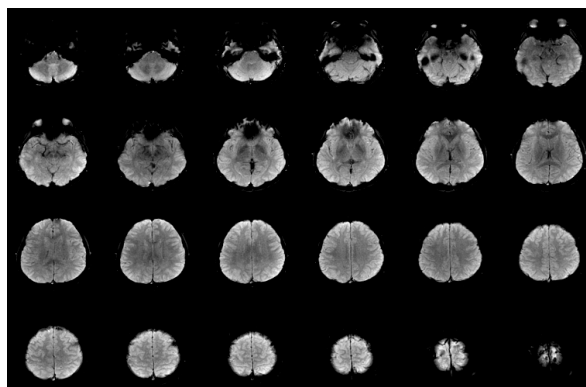
Paradigm	Areas Activated	Pertinent Notes
Sentence Completion	Temporal > frontal Ventral language stream	Robust overall May repeat
Silent Word Generation	Frontal > temporal Middle frontal gyrus	More lateralizing than SC No patient performance metric
Rhyming	Frontal > temporal Middle frontal gyrus	More lateralizing than SC
Object Naming	Frontal > temporal	Most patients can perform
Antonym Generation	Frontal > temporal Middle frontal gyrus Geschwind	Good for pediatric patients No patient performance metric
Passive Story Listening	Temporal > frontal	Easy task for pediatrics or impaired adults

FIG 4. Adult algorithm for presurgical language fMRI.

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Image Acquisition

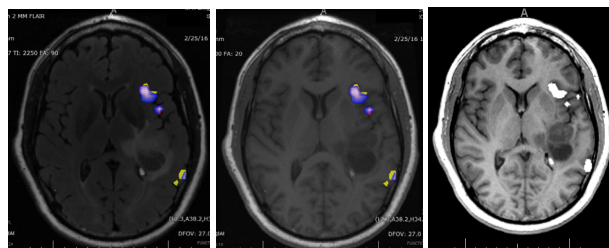
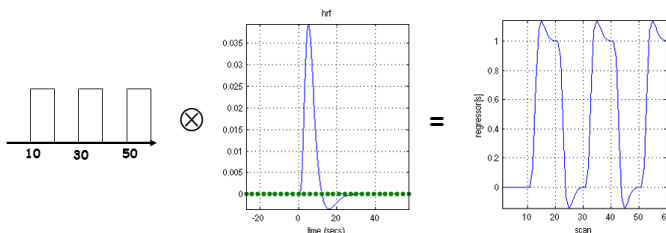
- **Typical fMRI protocol at 3T:**
 - Single-shot GRE-EPI
 - TR = 2-3 s (<=2s for er- and rs-)
 - TE = 25-35 ms
 - FA = 70-90°
 - matrix size = 64-128 (w/ PI)
 - in-plane resolution = 2-4 mm
 - slice thickness = 3-5 mm
 - 25-45 slices
 - dynamics = 60-150
 - scan time = 3-5 min



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fMRI data analysis

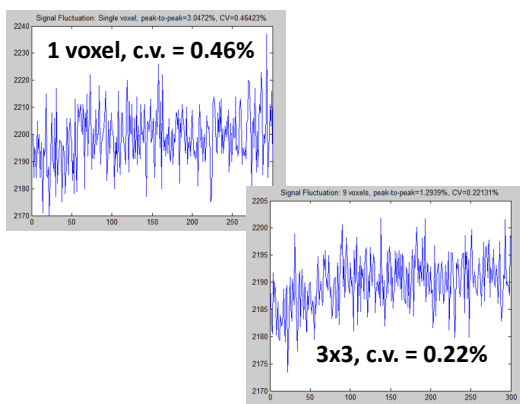
- **Data pre-processing**
 - **Motion correction**
 - **(Slice timing correction)**
 - **(Spatial normalization)**
 - **Spatial smoothing**
 - **(Temporal filtering)**
- **Activation maps: statistical analysis I**
 - **Correlation/GLM analysis**
 - **Thresholding (intensity / cluster size)**
- **Group analysis: statistical analysis II**
 - **Voxel-based analysis**
 - **ROI analysis**
- **Data reporting and visualization**



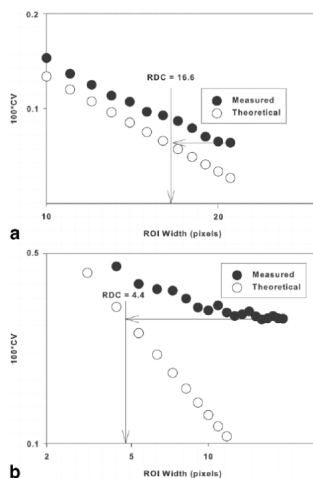
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fMRI QC Testing: System Stability

Scan a uniform phantom for ~ 10 mins



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



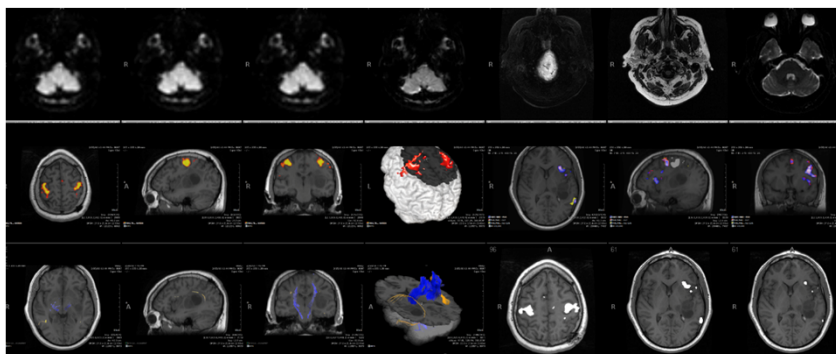
Radius of decorrelation
(RDC) = CV(1)/CV(Nmax)

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

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Presurgical fMRI has been proven helpful to the clinic:

- Reducing post-operative deficits
- Maximizing tumor resection
- Guiding intra-operative functional mapping



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Agreement with intraoperative stimulation /Specification to eloquent areas is task-dependent

- Task-fMRI performs well for motor mapping
- For speech-fMRI, agreement with direct cortical stimulation is moderate.
- Task in general will activate more areas than eloquent cortices.

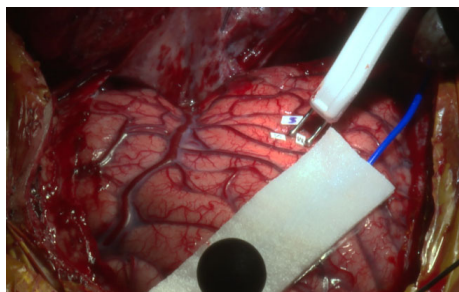
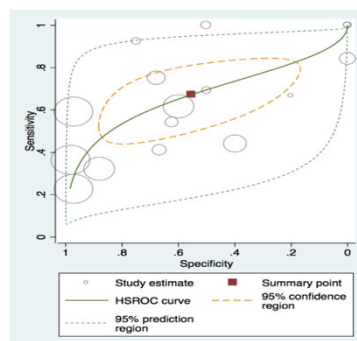


Image courtesy of Sujit Prabhu, M.D.

Accuracy of Presurgical
Functional MR Imaging for
Language Mapping of Brain
Tumors: A Systematic Review and
Meta-Analysis¹

Sensitivity = 67%
Specificity = 55%

Weng, Radiology, 2018



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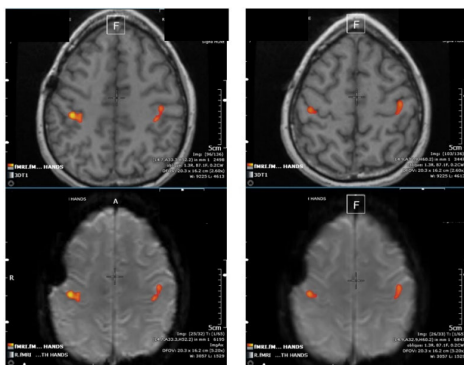
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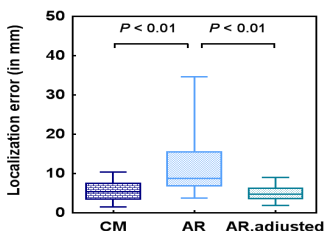
Functional/structural image registration

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



Automated registration

After adjustment

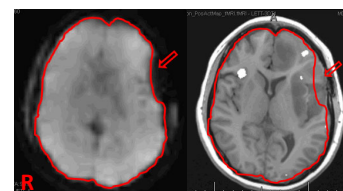


CM: Coordinate matching
 AR: Automated registration
 AR_{adj}: AR with manual adjustment

Jen, Med Phys, 2018

Susceptibility artifact:

- Image distortion
- Signal loss



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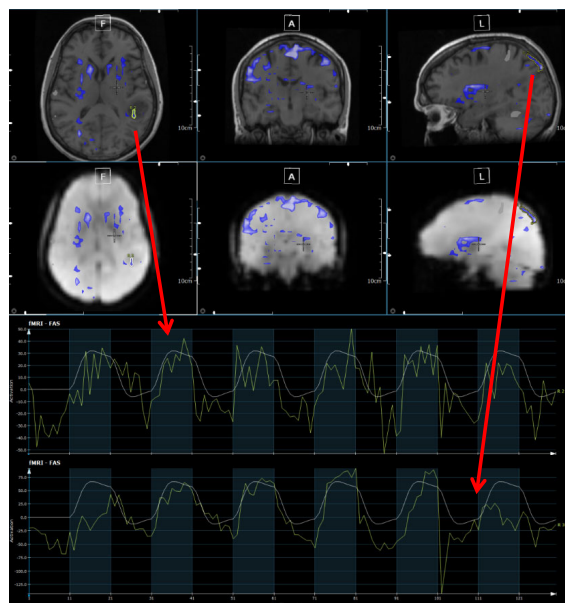
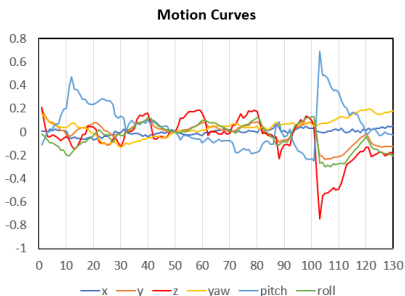
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Head Motion: A common source of fMRI failure

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



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Statistical Threshold: A challenge for individual fMRI

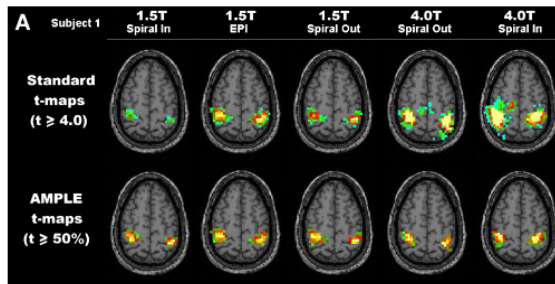


Available online at www.sciencedirect.com
 ScienceDirect
 Magnetic Resonance Imaging 24 (2006) 1249–1261

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

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



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Neurovascular Uncoupling can cause False Negative fMRI results

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

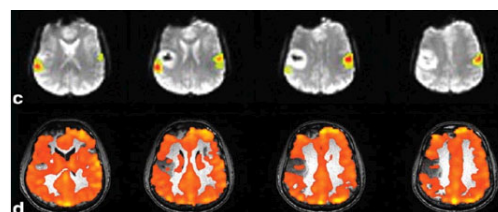
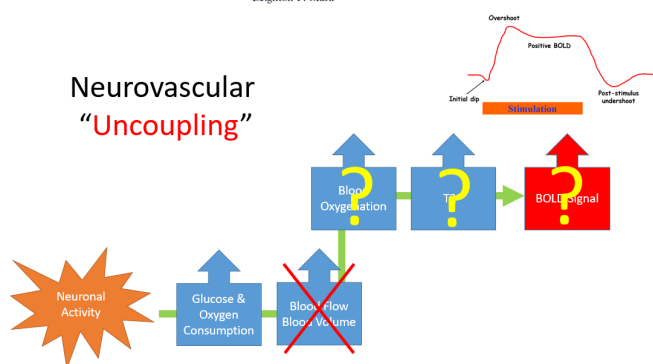
John L. Ulmer MD, Hendrikus G. Krouwer, Wade M. Mueller, M. Sahin Ugurel, Mehmet Kocak, and Leighton P. Mark

REVIEW ARTICLE

Cerebrovascular Reactivity Mapping: An Evolving Standard for Clinical Functional Imaging

JJ. Pillai and DJ. Mikulis

Pillai & Mikulis, AJNR, 2015



Zaca, JMIRI, 2014

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Patient's Ability and Performance

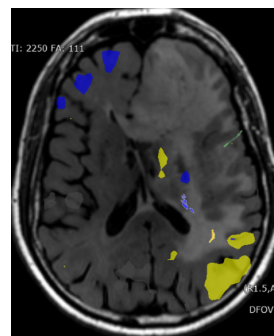
- Task-based fMRI fails in 30-40% of patients indicated for presurgical functional mapping.

Patient X has moderate to severe aphasia ... While receptive language is better than expressive, his comprehension breaks down for more complex tasks...verbal fluency was very poor (1-3 words per 1 minute trials), ... so his fMRI may be impacted...

Table 2. Comparison of performance between task-fMRI and resting state fMRI.

A. Cause Of Failure	rs-fMRI (n = 232)	task-based fMRI (n = 83)
Patient Motion	14 (6.0%)	0 (0%)
Susceptibility artifact	6 (2.6%)	0 (0%)
Unable to follow commands	0 (0%)	10 (12%)
No activation	2 (.9%)	20 (24%)
Technical failure NOS / did not pass QA	3 (1.2%)	2 (2.5%)
Anatomic misregistration to atlas	3 (1.2%)	0 (0%)
Total	28 (13%)	32 (38.5%)

Leuthardt et al., 2018



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Opportunity: Standardization



QIBA Profile: **(Stage 1: Public Comment Profiles)**

Mapping of **Sensorimotor** Brain Regions using Blood Oxygenation Level Dependent (BOLD) Functional MRI as a Pretreatment Assessment Tool.

Claim 1: If X,Y,Z is the measured **location** of the weighted center-of-mass of a single focus of fMRI hand motor activation (wCMA), then the **95% confidence interval** for the X,Y,Z of the true wCMA is **+/-5mm** in any direction (Euclidean distance, assuming no systematic bias).

http://qibawiki.rsna.org/images/b/b8/QIBA_fMRI_Profile_1_PC-rev1.pdf

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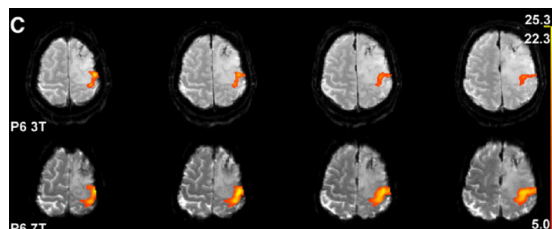
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Opportunity: Clinical fMRI at Ultrahigh Field (e.g. 7T)

- Increased SNR and BOLD contrast
 - For high spatial resolution & accuracy
 - For partial neurovascular uncoupling
 - For compromised performance



ELSEVIER journal homepage: www.elsevier.com/locate/ynimg

Clinical fMRI: Evidence for a 7 T benefit over 3 T

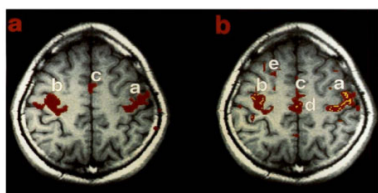
R. Beisteiner ^{a,c,*}, S. Robinson ^{b,c}, M. Wurnig ^{a,c}, M. Hilbert ^{a,c}, K. Merksa ^{a,c}, J. Rath ^{a,c}, I. Höllinger ^{a,c}, N. Klingner ^{a,c}, Ch. Marosi ^d, S. Trattnig ^{b,c}, A. Geißler ^{a,c}

NeuroImage, 2011

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Opportunity: Resting-state fMRI in the Clinic



Biswal, MRM, 1995

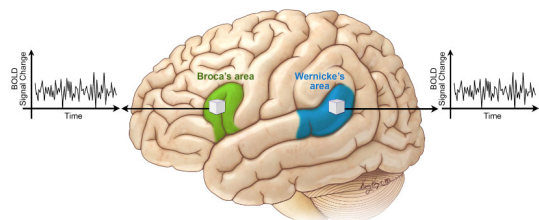
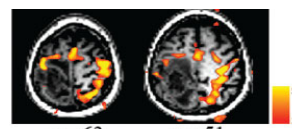
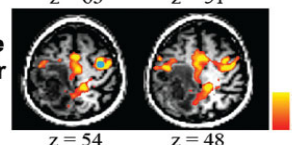


Image courtesy of Vince Kumar, M.D.

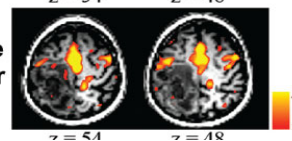
Task evoked activity



C Resting state sensorimotor network



D Resting state sensorimotor IC

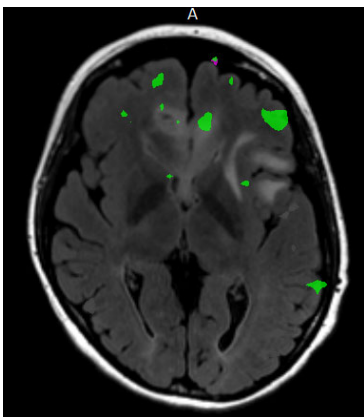


Zhang, Neurosurgery, 2009

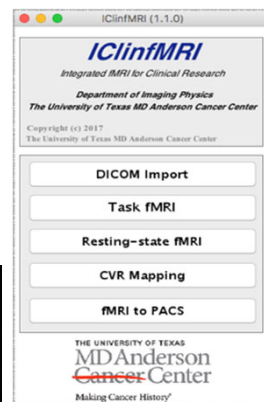
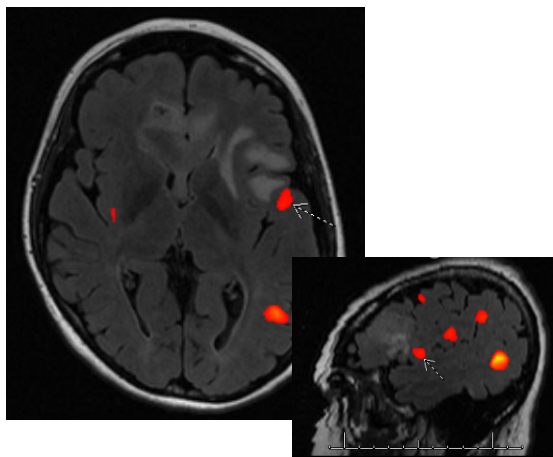
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Language fMRI with limited patient performance



Resting-state fMRI validated w/ intra-op stimulation



Hsu, *Front Neuroinform*, 2018
Hsu, *MRM*, 2020

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Summary

- BOLD-fMRI using T2*-weighted GRE-EPI can reliably detect brain activations.
- fMRI has become a clinical routine, especially for presurgical evaluation.
- Requirements for fMRI in the clinic:
 - **Interdisciplinary clinical care**
 - Neurosurgeon, Neuroradiologist, Neuropsychologist, Specialized Technologist, Physicist
 - **Patient centered**
 - Paradigm, lesion location, performance, fMRI statistics
 - **Accurate**
 - Detection and spatial localization
 - **Reasonable times**
 - Scan time and post-processing
 - **Compatible output**
 - Radiology PACS, surgical navigation system

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