Foundations for Multi-site MRI

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Declaration of Conflict of Interest or Relationship

Speaker Name: Gary H. Glover

I have the following conflict of interest to disclose with regard to the subject matter of this presentation:

Company name: General Electric HealthCare Systems

Type of relationship: (Unpaid) Insultant

Outline

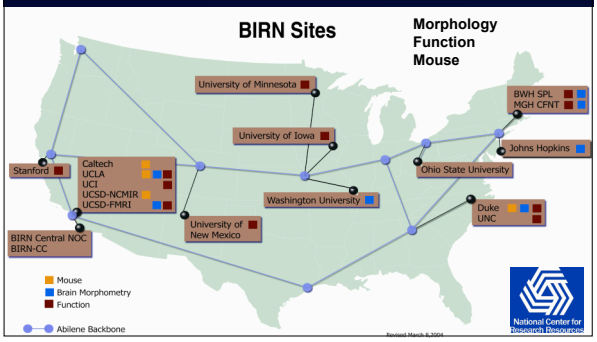
- Motivation for multicenter imaging studies
- Issues in multicenter MRI studies
- Standardization of protocols
- QA
- Site Equalization
- Calibration

Why do Multicenter Studies?

- Potential use of MRI as a biomarker
  - structural/functional differences may predict disease; large study numbers are necessary for biodiversity
  - ADNI study (VBM methods to study cortical thickness)
  - BJ Casey study (fMRI to examine ADHD)
- Generate large data sets rapidly
- Access wide or targeted demographic characteristics
- Populate image databases with controlled data for data mining

Alzheimer's Disease Neuroimaging Initiative

Biomedical Imaging Research Network



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Multicenter MRI

- Desire to pool results across sites equally requires standardization
- Different venders may have incompatible characteristics/ definitions- e.g.
  - pulse sequence contrast in FSPGR vs MPRAGE
  - meaning of BW/echo spacing in EPI imaging -> artifacts/SNR
  - k-space apodization filters -> smoothness/CNR
  - grad distortion correction
  - geometric calibration precision
  - temporal stability

Multicenter MRI

- Need to qualify sites for entry into study
  - develop characteristics for acceptance
    - geometric accuracy
    - contrast/resolution
    - SNR, CNR, tSNR (SFNR)
    - temporal stability
    - reliability/reproducibility
    - artifacts (ghosts/distortion/eddy current-related,…)
  - understand sensitivity of scanner characteristics relative to desired measurements
- Set criteria for acceptance
- Need to maintain minimum performance standards
  - develop a QA program

Multicenter MRI

- Decide policy for upgrades (chances virtually 100% for at least one site to upgrade)
  - minor: software only
  - major: hardware & software
- Develop procedures to control for/reduce site effects
- Develop procedures to reduce data acquisition confounds, e.g. hemodynamics in BOLD fMRI- test scientific question

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Standardization

- Study design
- Acquisition parameters
- Scanner characteristics
- Study procedures
- Analysis pipeline
- Database structures

Structural MRI Imaging Characteristics

Highest importance:

- Geometric accuracy
- Image contrast uniformity
  - grey/white/CSF; tumor delineation
- Both must be
  - adequate for tissue segmentation and volume/thickness quantification
  - stable over study duration -> QA

Low importance

- Eddy currents
- RMS stability

fMRI Imaging Characteristics

Modest importance:

- Geometric accuracy (since fMRI is low resolution- e.g. 3.4x3.4x4 mm^3)

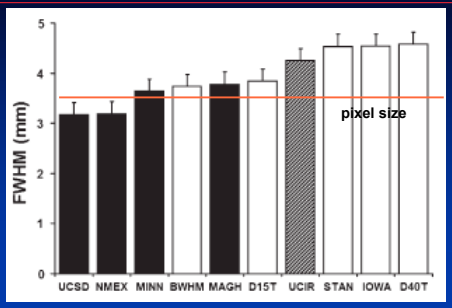
Highest importance:

- Stability (short/long term)
- BOLD CNR- B1 uniformity (coil choice)
- Susceptibility-induced distortion/dropout (seq. params)
- Ghost/spike noise/other artifacts

Important fMRI Characteristics

- fMRI acquisition contrast/smoothness
  - control parameters:
    resolution (FOV & matrix size), but…
    actual resolution may not = pixel size

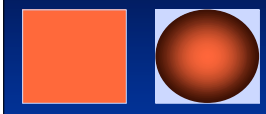
Intersite smoothness differences



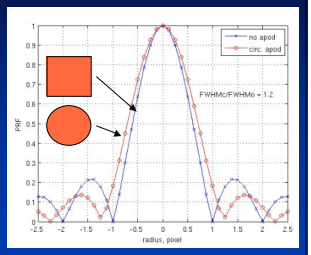
Friedman et al. NI (2006)

Why smoothness differences?

- k-space reconstruction kernel



Vender "S" Vender "G"

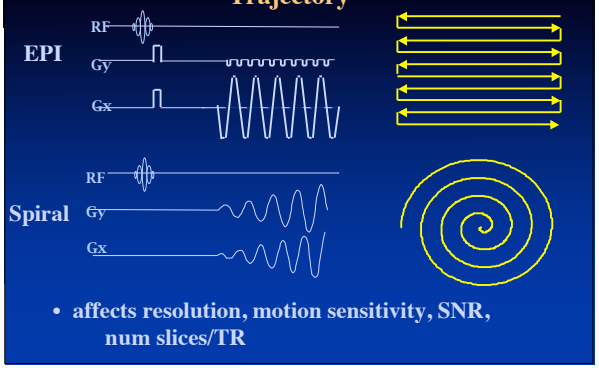


- Apodization- lower resolution, higher SNR

Important fMRI Characteristics

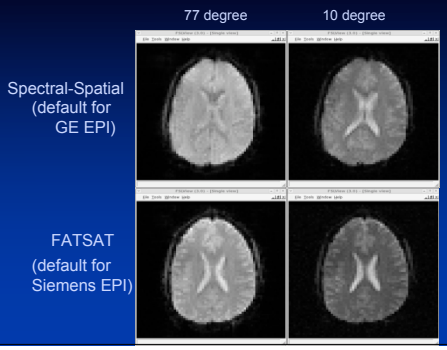
- fMRI acquisition contrast/smoothness
  - control parameters:
    resolution/smoothness (resel != FOV/matrix_size)
    BW: keep ESP constant across venders
    slice spacing/skip/orientation
    fat saturation vs. water excitation
    readout trajectory (EPI vs. spiral), affects smoothness, artifacts
    field strength (affects SNR, CNR, vessels vs. tissue, artifacts)

Trajectory



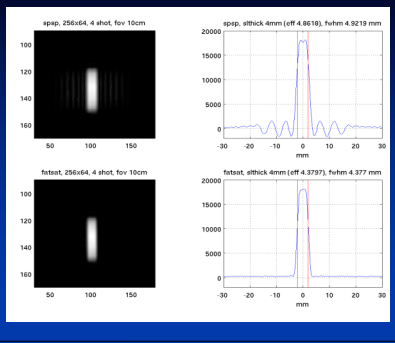
- affects resolution, motion sensitivity, SNR, num slices/TR

RF Excitation/Slice Select



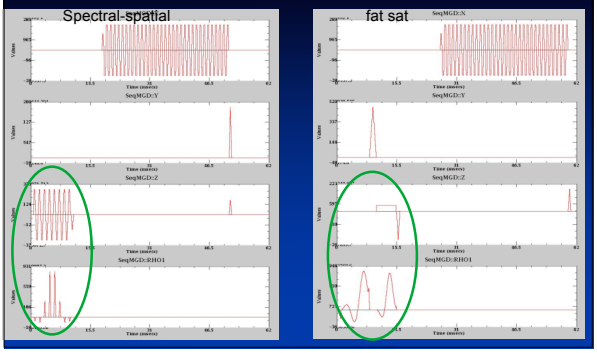
Bryon Mueller (UMinn)

Measured Slice Profile



Kun Lu, Tom Liu (UCSD)

Slice select

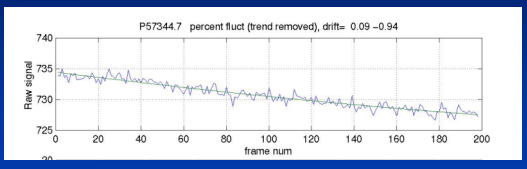


Important MRI Characteristics

- Dynamic image stability

  fMRI & ASL depend on subtraction to compare conditions

  scanner stability must be << brain noise



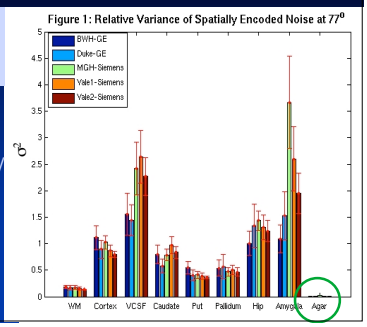
Brain noise relative to thermal noise: to set acceptance criteria

$$\sigma^2 = \sigma_0^2 + \sigma_s^2 + \sigma_p^2$$
$$= \sigma_0^2 + (\lambda_s + \lambda_p)S^2(\alpha)$$

G. Krueger (MRM 2000)

- Acquire data at 10°, 77°
- Calc fraction of scanner/ brain noise vs. thermal noise, using human & phantom scans

D. Greve (MGH, ISMRM 2008)



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QA: What to measure?

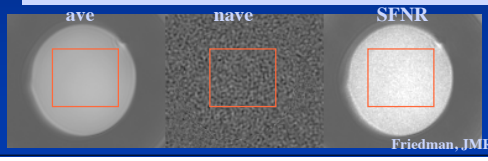
- Time series image stability
- Signal to noise ratio
- Signal intensity
- Xmtr/Rcvr Gains
- MRS characteristics
- Eddy currents
- Geometric accuracy

SNR, SFNR

$$I_{even} = \frac{2}{N}\sum_{even} I_i - I_{trend}(i) \qquad I_{odd} = \frac{2}{N}\sum_{odd} I_i - I_{trend}(i)$$

$$I_{ave} = \frac{1}{2}(I_{even} + I_{odd}) \qquad I_{nave} = \frac{1}{2}(I_{even} - I_{odd})$$

$$\sigma^2 = \frac{1}{N-1}\sum [I_i - I_{trend}(i)]^2 \qquad SFNR = I_{ave}/\sigma$$



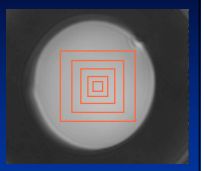
Friedman, JMRI 2006

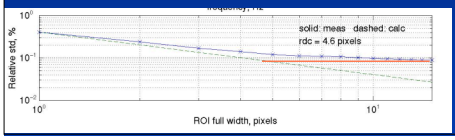
Weisskoff Analysis

$$\bar{I}_i(w) = mean_{(wx\,w)}[I_i - I_{trend}(i)]$$

$$\sigma(w) = stdev[\bar{I}_i(w)]$$

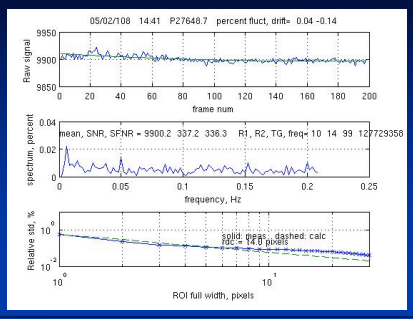
$$\sigma_{theory}(w) = \sigma(1)/w$$





R. M. Weisskoff, *MRM* **36,** 643-645 (1996).

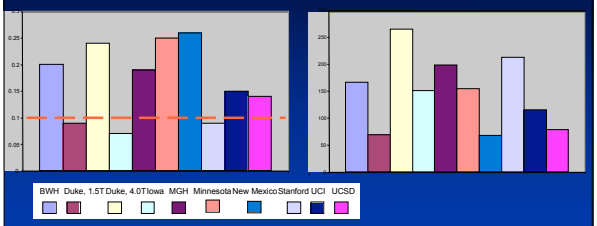
Stability



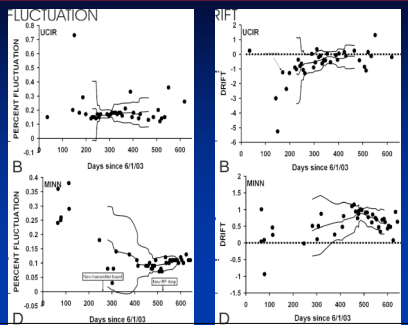
Site differences

RMS instability, %

SFNR



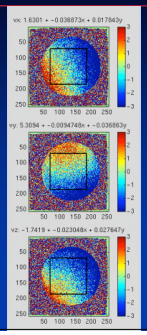
QA helped to bring scanners into spec



Friedman, JMRI 2006

Eddy Current Maps

- 3-directions phase contrast scan on agar phantom
- Analyze velocity maps for error
- Useful as on-going QA



R/L

A/P

S/I

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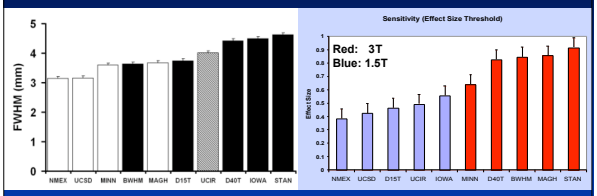
Equalization across sites: fMRI

- Compensation for smoothness
- Compensation by SFNR

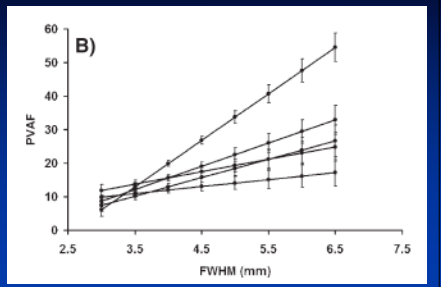
Smoothness/BOLD Differences



Friedman, et al. 2006

Sensitivity vs. Smoothness

5 traveling subjects at 10 sites performing sensorimotor task



Friedman, et al. 2006

Smoothness equalization

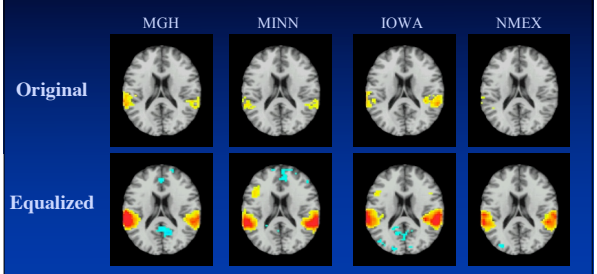
- In first-level analysis: Use "smooth to" instead of "smooth by"
- Smooth each site to largest FWHM using Gaussian filter

$$FWHM_{out}^{-2} = FWHM_{meas}^{-2} + FWHM_{filter}^{-2}$$

e.g., AFNI program (thanks to R. Cox)

Friedman, et al. 2006

BOLD Sensitivity: Oddball Task

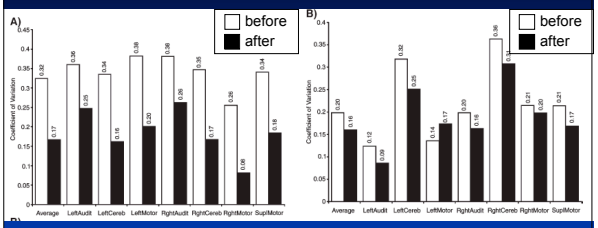


Novel Tones - Effect Size

Friedman, et al.

Intersite CV

1.5T 3T



Friedman, et al. 2006

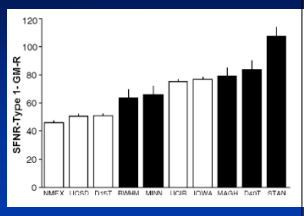
fMRI equalization across sites

- Compensation for smoothness
- Compensation by SFNR

fMRI equalization by SFNR

- Measure SFNR using
  - GM - Rest
  - WM - Rest
  - GM - SMresid
  - WM - SMresid
- Covary for SFNR

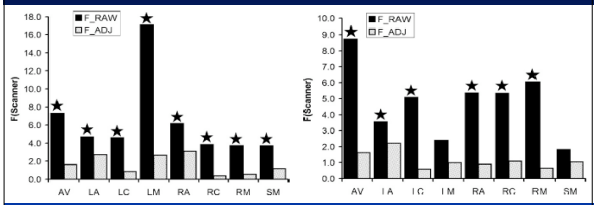
Original SFNR



Friedman, et al. 2006

Site equalization by SFNR

1.5T 3T



Friedman, et al. 2006

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Calibration Goals

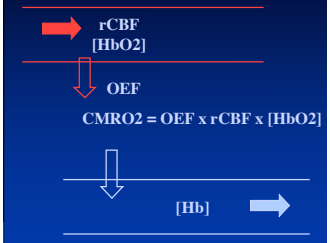
Remove variance not related to effect of interest

- Scanner differences (site effects)
- Confounds of the experiment (subject effects)

e.g., subject effects in fMRI:

- HRF differences
- Physiological noise

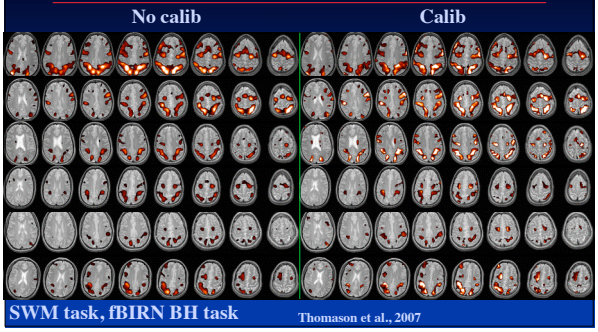
Calibration of BOLD Signal



Davis, 1998
Buxton, 2003
Thomason, 2007

$$\Delta R2^* \propto rCBV_a[Hb]_a^\beta - rCBV_0[Hb]_0^\beta$$
$$BOLD \propto -TE \cdot \Delta R2^*$$
$$rCBV \propto rCBF^\alpha$$
$$BOLD_a = M[f^\alpha(\frac{m}{f})^\beta - 1]$$
$$m = CMRO2_a / CMRO2_0$$
$$f = rCBF_a / rCBF_0$$
$$BOLD_{BH} = M[f_{BH}^{\alpha-\beta} - 1]$$
$$BOLD_a = BOLD_{BH}\frac{[f_a^\alpha(\frac{m}{f_a})^\beta - 1]}{[f_{BH}^{\alpha-\beta} - 1]}$$

BH Calibration: WM Task



SWM task, fBIRN BH task

Thomason et al., 2007

BH Calibration: Group Activation

SWM task, fBIRN BH task, N = 7

Thomason et al., 2007

Conclusions: Standardize

- Standardize scanners, imaging params, coil type
- Standardize ancillary equipment
- Standardize scan procedure- order of scans, scan script, subject preparation, slice prescription QA scans
- Use cross site visiting coordinator
- Use automated upload scripts, processing pipeline
- Single data analysis center

Conclusions

- Develop good QA and <u>frequently</u> use it
  - requires established criteria; keep database
  - fix scanners when broken
- Compensate inter-site differences in SFNR, etc.
- Compensate for experimental confounds

Acknowledgements

fBIRN Calibration Working Group

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Moriah Thomason
Catie Chang

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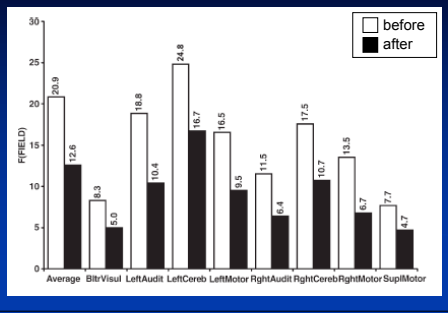
P41 - RR009784
M01 - RR00827
F31 - AG032168
F31 - MH71996

Spiral-in/out in Firenza

Intersite Effect of Field



Friedman, et al. 2006