Ultra-high resolution Gradient Echo and Spin Echo BOLD fMRI in the human visual cortex at 7 Tesla

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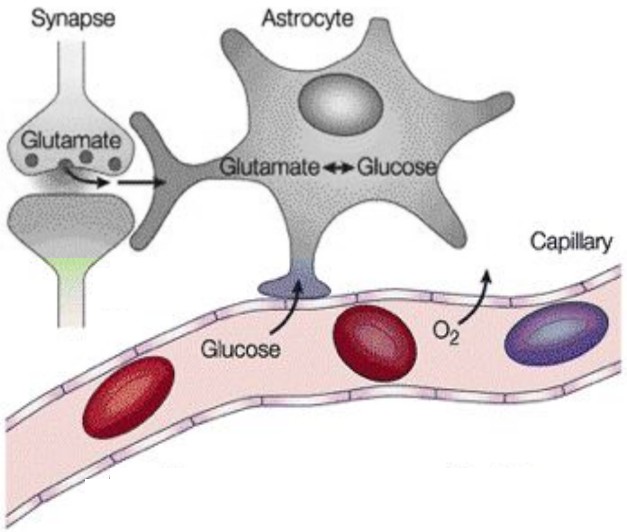
Pre-thesis Seminar (Pisa, 2015)

Outline

- Introduction
  - Functional Brain imaging
  - Spatial distribution of BOLD fMRI
  - Gradient Echo & Spin Echo BOLD
  - Ultra-high field fMRI
- Aim of the study
- Methods
  - Acquisition Protocol
  - Data analysis
- Results
- Discussion and Conclusions
- Future Work

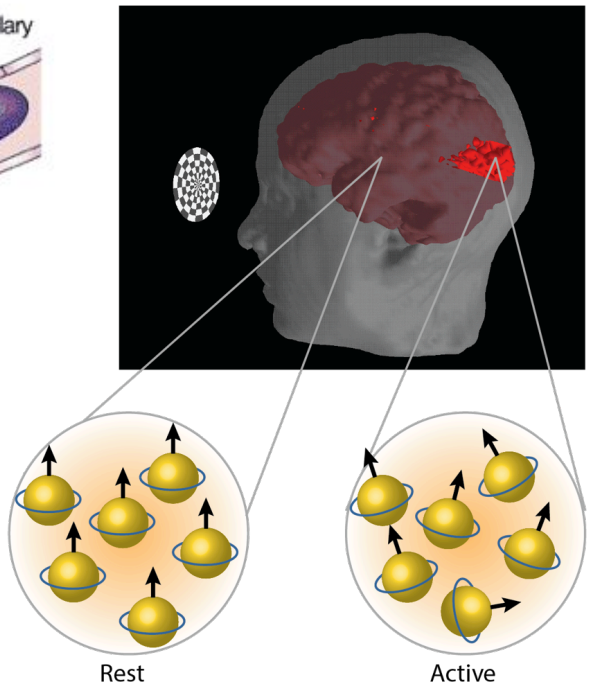
Functional MRI: the BOLD effect

Functional MRI is based on **secondary** metabolic and hemodynamic events that follow neuronal activity, and not on the electrical activity itself.

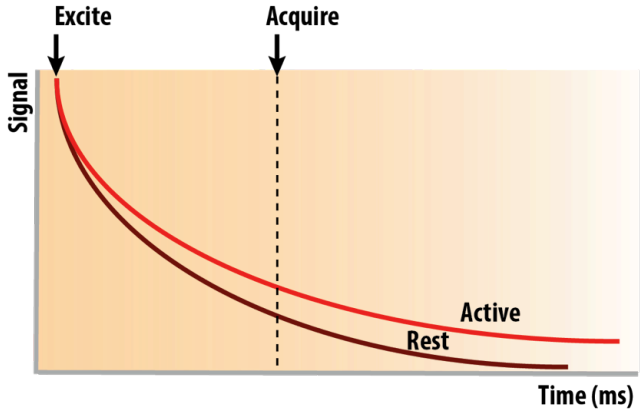


***BOLD**=Blood Oxygen Level Dependent*

Variations of the local magnetic field are induced by variations in deoxyhemoglobin (dHb) consumption across the brain tissue.



1. Precession behaviour of the water proton nuclei is altered
2. Local increase in T2* (and T2)
3. Local increase in Signal.



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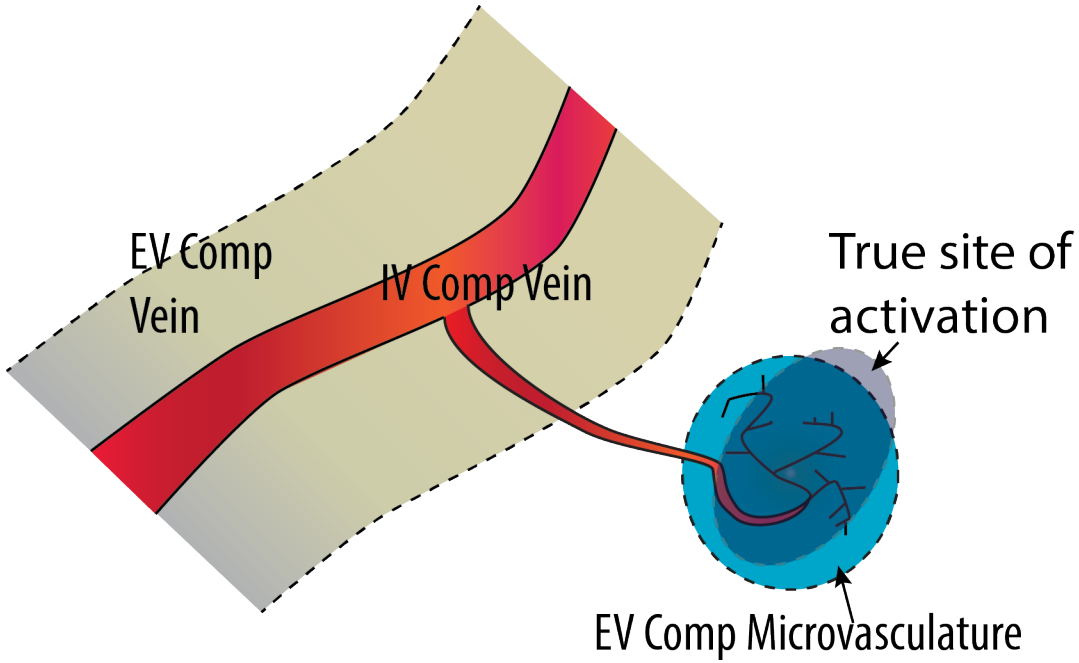
Spatial Resolution of BOLD fMRI

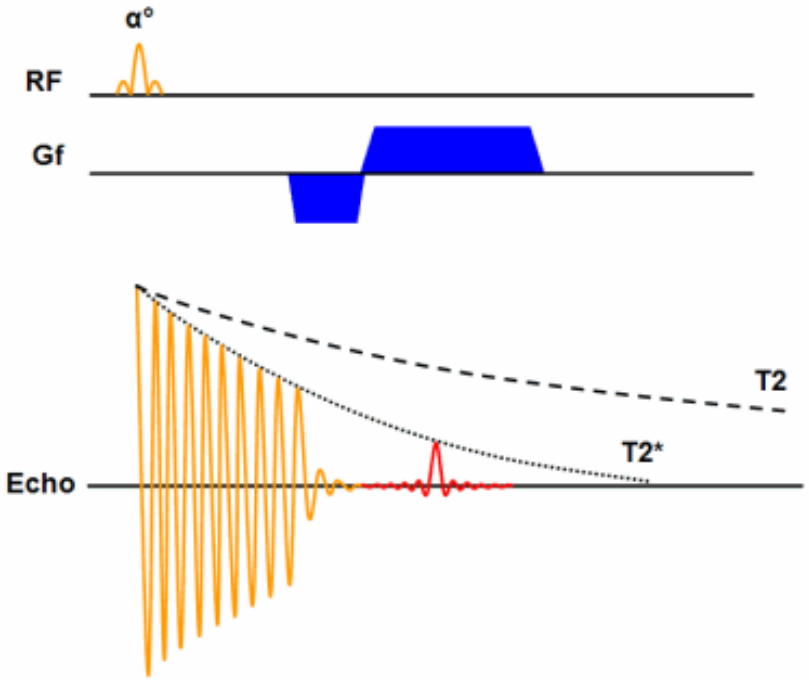
- Anatomical source of the MR signal: combination of dephasing effects
  - happening inside the vessel (intravascular, IV) -> from blood T2* (and T2)
  - and in extravascular (EV) surroundings -> grey matter tissue T2* (and T2)

(Ogawa et al. 1993).

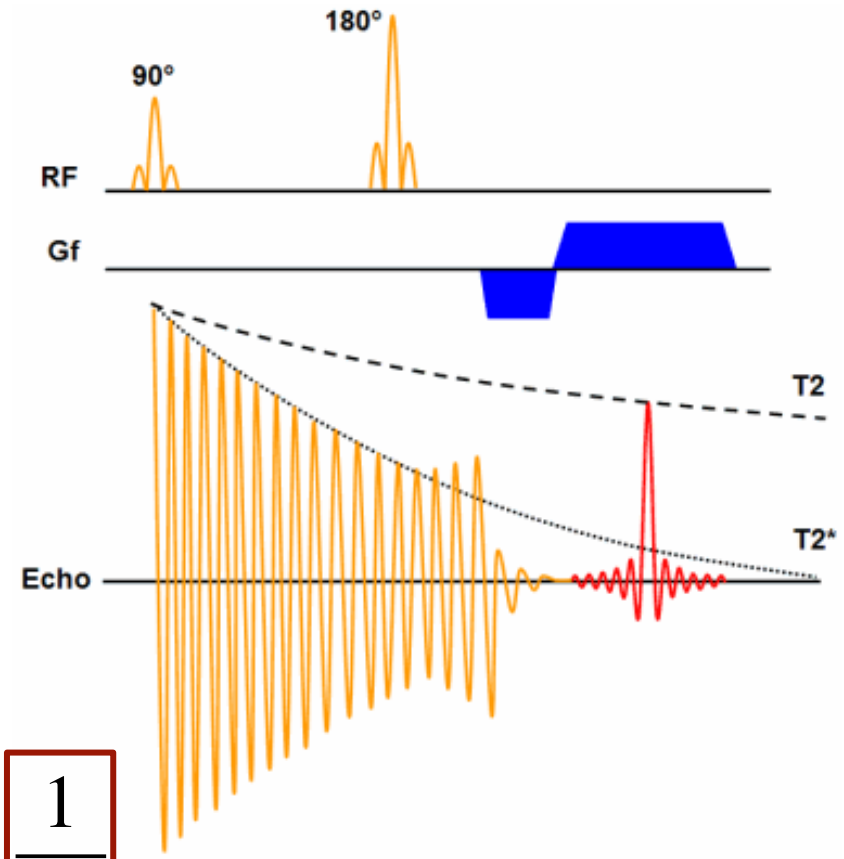


fMRI Sequences

Gradient Echo



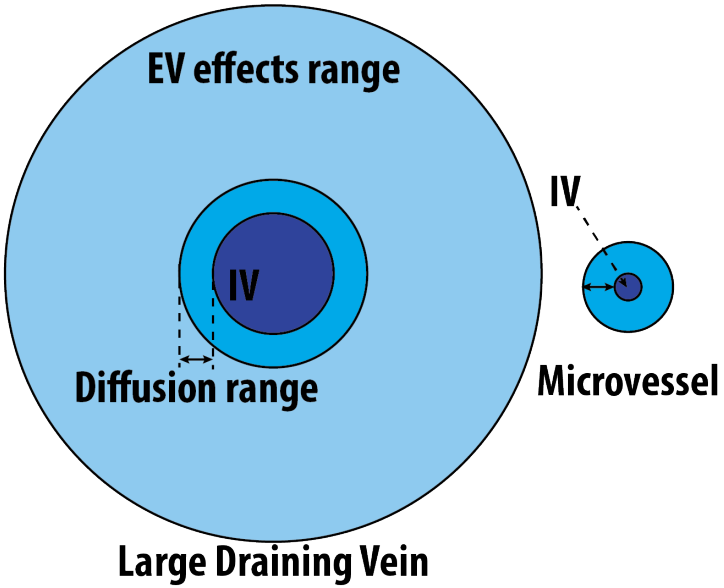
Spin Echo



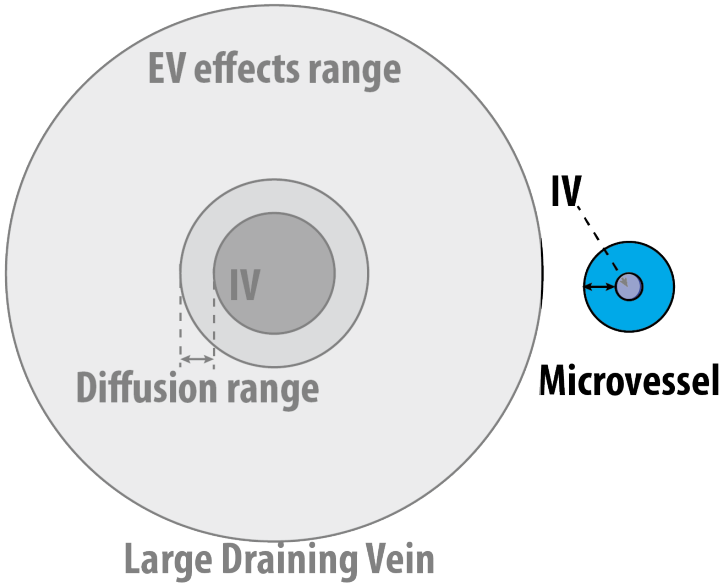
$$\frac{1}{T_2^*} = \frac{1}{T_2} + \boxed{\frac{1}{T_2'}}$$

fMRI Sequences: signal distribution

Gradient Echo



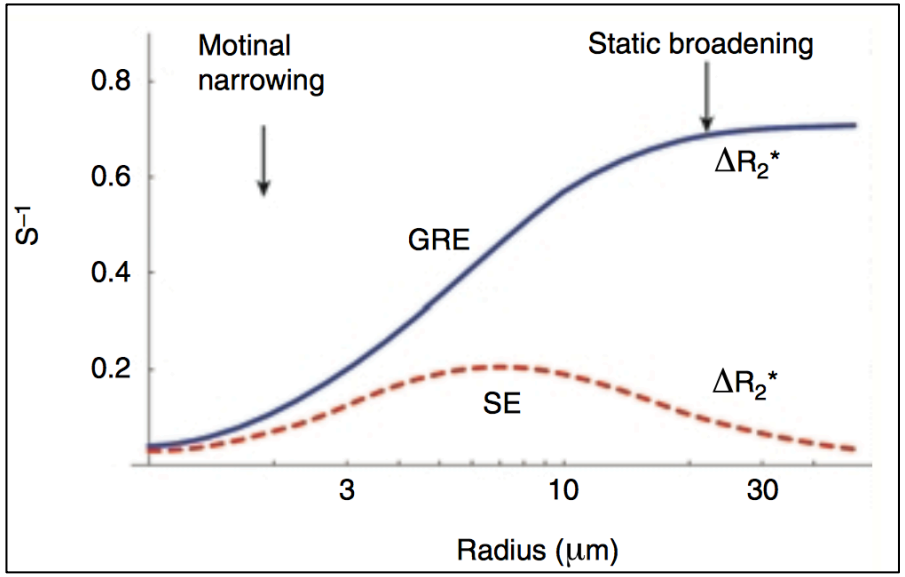
Spin Echo

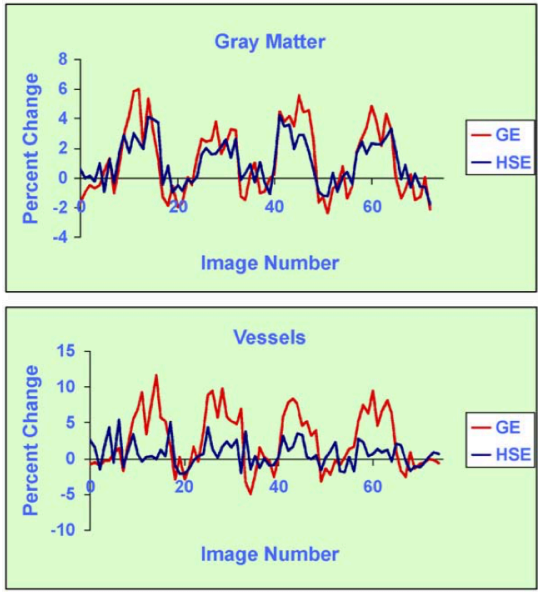


The T2* and T2 contrasts will reflect the signal's spatial selectivity patterns.

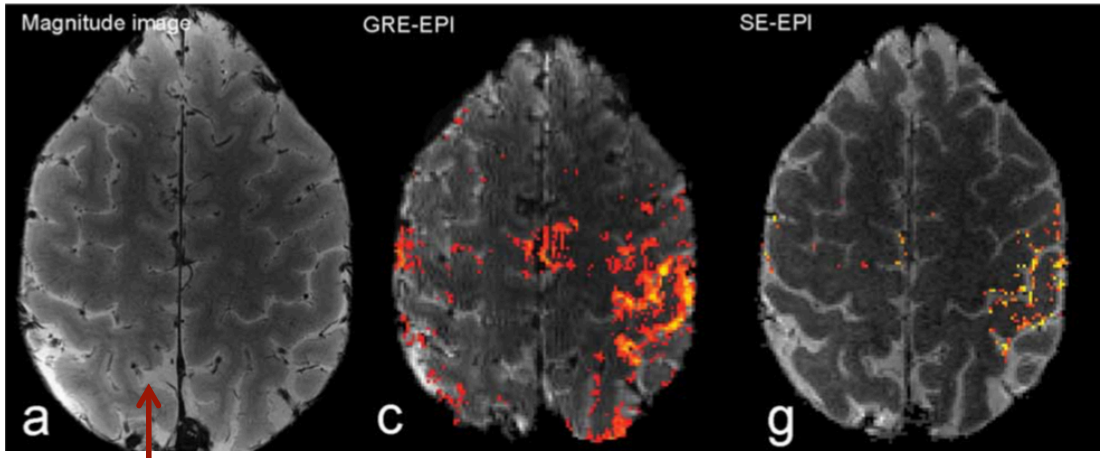
$$\frac{1}{T_2^*} = \frac{1}{T_2} + \boxed{\frac{1}{T_2'}}$$

fMRI Sequences: signal distribution





(Yacoub et al. NeuroImage (2005))



(Budde et al. MRM (20014))

Example of SE vs GRE comparison in motor cortex at 9.4T.

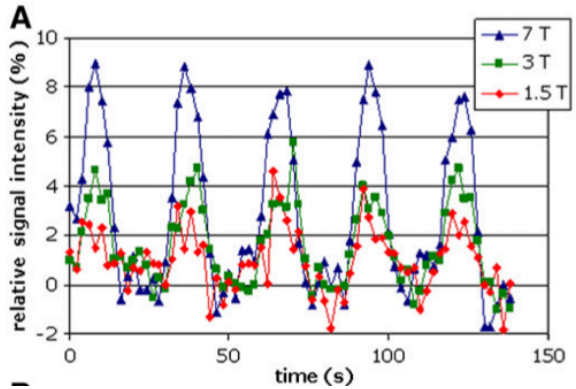
Ultra-High field fMRI

A. BOLD contrast increases with increasing static magnetic fields

B. IV component of the BOLD signal is substantially smaller.

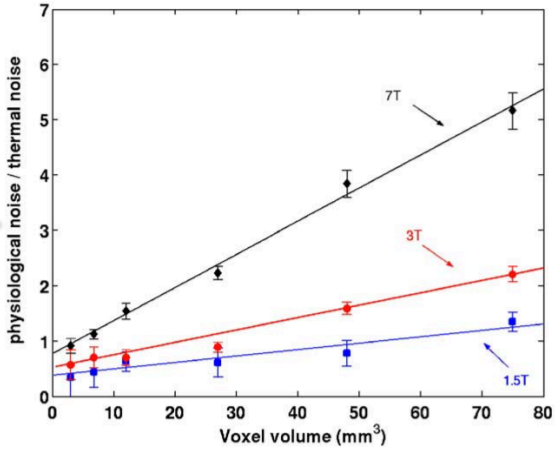
C. Field inhomogeneities will increase, producing more severe geometrical distortions.

D. Physiological noise to increase proportionally.



(Van der Zwaag et al. *NeuroImage* (2009))

	1.5Tesla	7Tesla
T2(blood)	127 ms	12-15 ms
T2(GM)	90 ms	55 ms



(Triantafyllou et al. *NeuroImage* (2005))

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Ultra-High field fMRI: Spin Echo vs Gradient Echo

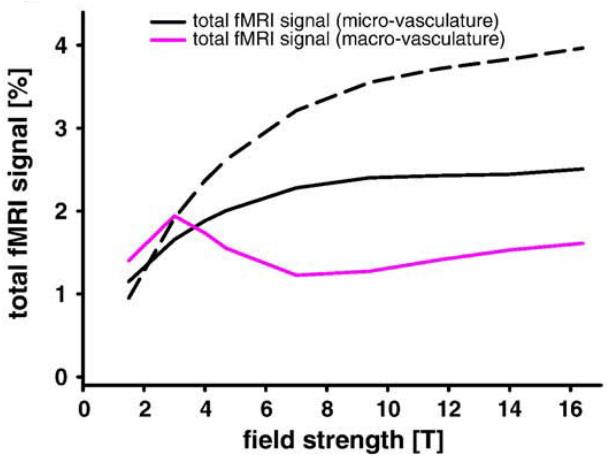
Recently studies attempted a performance evaluation in different set-up designs

- Occipital cortex (Yacoub et al, Neuroimage, 2005; Siero et al, PLOS One, 2013; Chiacchiaretta et al, Neuroimage, 2013; Kemper et al, frontiers Neurosci, 2015), Retinotopy (Panchuelo et al, Brain Topogr, 2015), Motor cortex (Harmer et al, NMR Biomedicine, 2011; Budde et al, MRM, 2014), Orbito-frontal (Boyacioğlu et al, Neuroimage, 2014), BOLD simulations (Uludağ et al, Neuroimage, 2009; Pflugfelder et al, MRI, 2011).

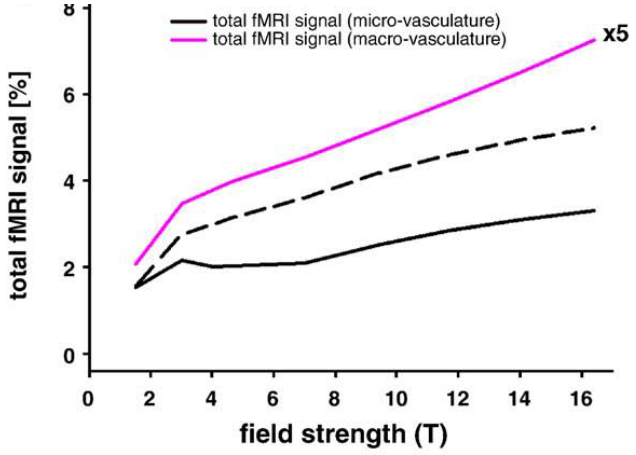
A. Simulations show ratio between micro and macrovasculature signal at 7T in SE is still higher than that in GRE

B. Inconsistent conclusions are obtained since there is a heavy influence on the type of study conducted:
   1. Sequence design and protocol set-up
   2. Region of the brain analysed
   3. Functional Paradigm choice

SE data



GRE data



(Uludağ et al Neuroimage (2009))

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Ultra-High field fMRI: Spin Echo vs Gradient Echo at sub-millimeter acquisitions

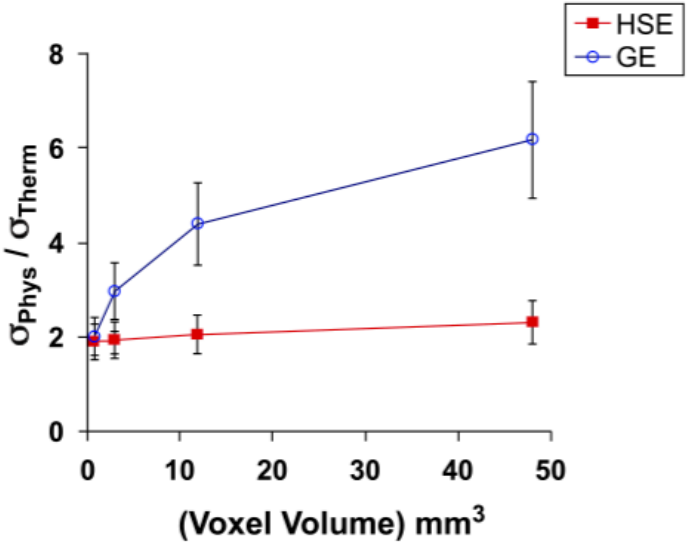
What happens at very high resolution fMRI:

A. Decrease in SNR_0 and tSNR;

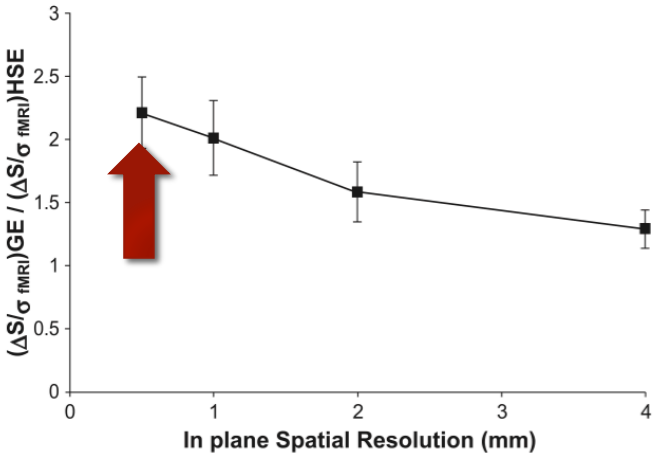
B. It was observed that in a high field regime the image SNR is not anymore dominated by physiological noise;
(observed in GRE data; a spin-echo sequence should not be effected).

C. Partial Volume Effects will decrease -> intrinsic increase in spatial specificity;

D. Percentage signal change is still higher in GRE data -> amount of ***meaningful*** active voxels can be distinguished?



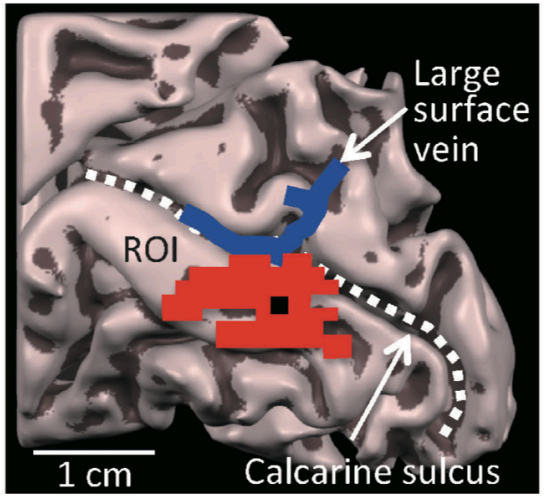
(Yacoub et al. Neuroimage (2005))

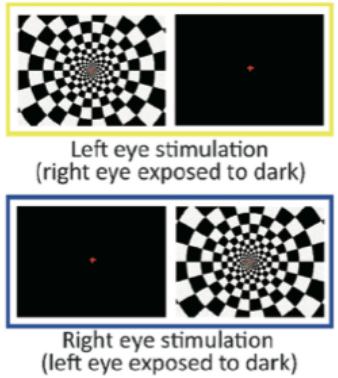


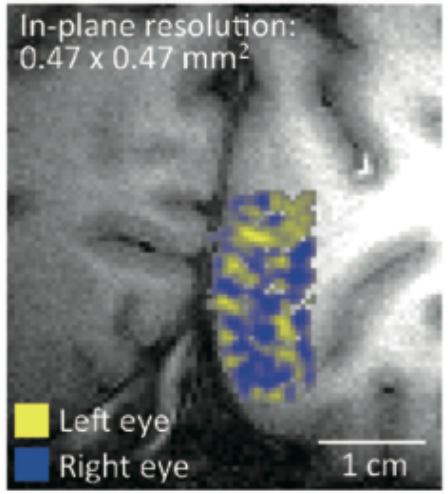
Aims of the project

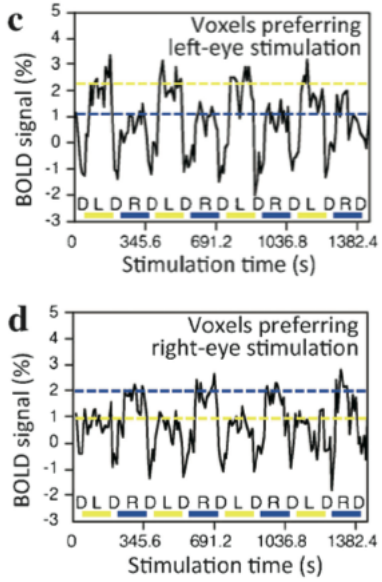
Complete characterization of the BOLD response in high field GRE and SE-EPI fMRI at different spatial resolutions.

- Determine an adequate acquisition strategy for targeted high-resolution fMRI in human visual areas.









(Kang Cheng MRM (2015))

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Methods: Acquisition Protocol

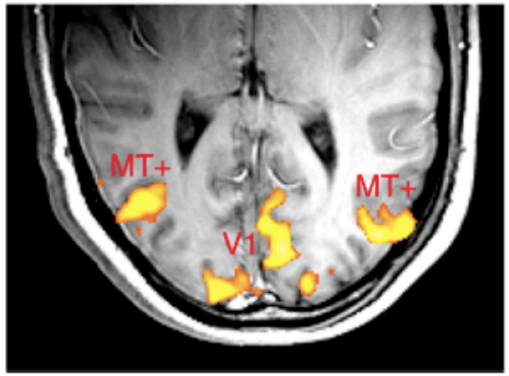
- Scanned 4 subjects at 7T
- fMRI acquisitions: **Optic Flow Paradigm** with both SE and GRE at different in-plane resolutions (slice thickness=1.4mm, 0.1mm gap)
  - 1.5x1.5mm^2;
  - 1.00x1.00mm^2;
  - 0.75x0.75mm^2.

Sequence Parameters: 2-shot EPI (shot-TR=1.5s), Fat Sat, TE_{GRE}=23ms, TE_{SE}=45ms, Flip $angle_{GRE}$=60º, ASSET fact=2, Phase Encoding=A->P; slice thickness=1.4mm, slice spacing 0.1mm, nº slices=14 oblique covering V1 and MT.

Paradigm: 3'00" acquisition

Visual stimuli evoke strong activity in the primary visual cortex (V1);

Coherent motion will also involve activation in visual motion perception (MT/V5).



(Born et al. Reviews in Neuroscience (2005))

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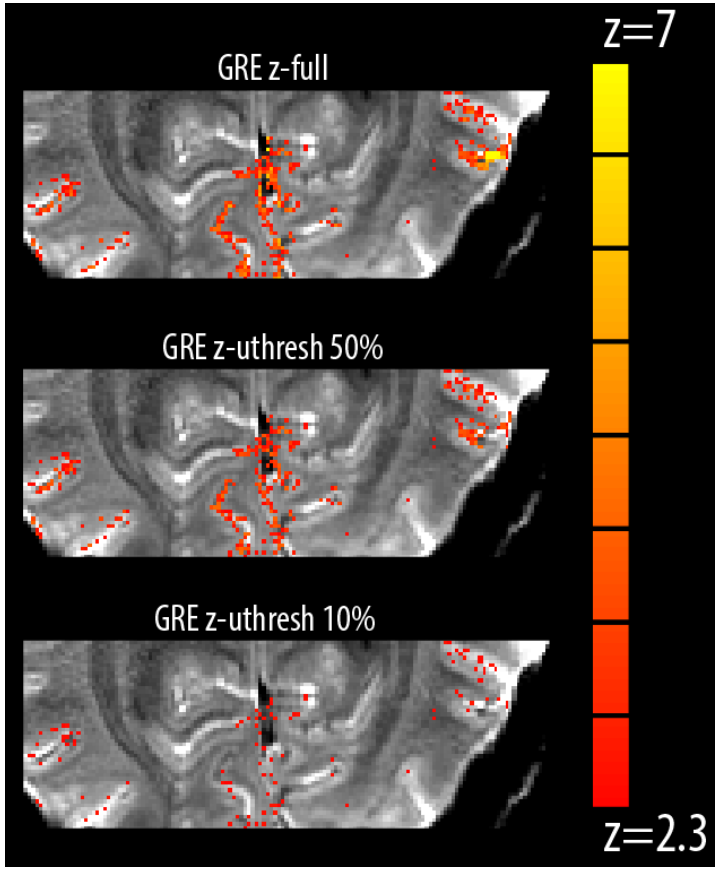
Methods: fMRI data processing

1. Motion correction with AFNI;
2. High-pass temporal filtering (filter cut-off=60s);
3. Pre-whitening;
4. General Linear Model (GLM) analysis: standard gamma variate HRF convolved with block design;
5. z-score maps: response of SPIRAL vs BLANK stimuli; cluster-wise thresholded at z>2.3. (**"z-full"**);
6. further upper-thresholds at 5 different percentages of robust range of non-zero voxels (z-uthresh 10%, 30%, 50%, 70%, and 90%).



Methods: data analysis

Noise Characteristics:

- Calculation of tSNR and $\sigma_{Phys}/\sigma_{Therm}$

$$\left(\frac{\sigma_p}{\sigma_T}\right)^2 = \frac{1}{k^2}\left(\frac{tSNR_{Phantom}}{tSNR_{Human}}\right)^2 - 1$$

Signal Characteristics:

- Percentage of BOLD signal change (ΔS/S);

Activation site:

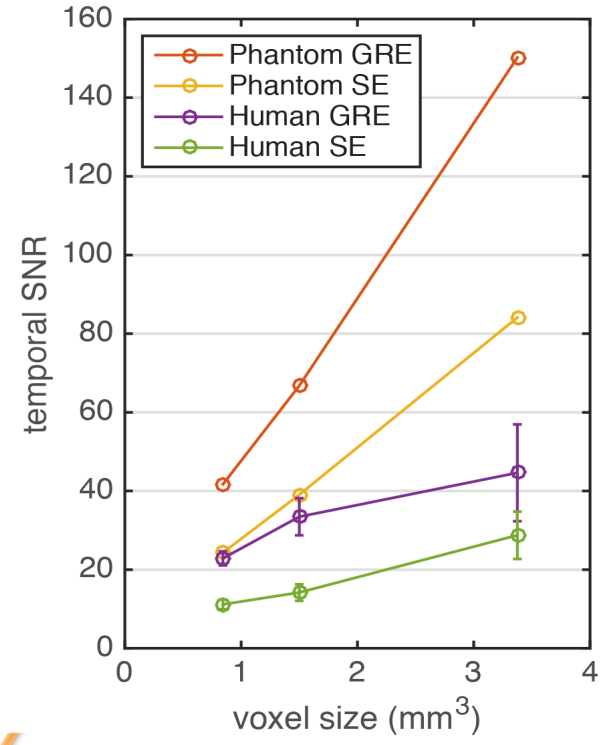
- Active volume (#significant active * voxel size);
- *Specificity* (weighted ratio of true negatives (tn) to the sum of tn and false positives(fp));
- *Precision* (weighted ratio of true positives (tp) to the sum of tp and false positives(fp));

Results: physiological-to-thermal noise ratio

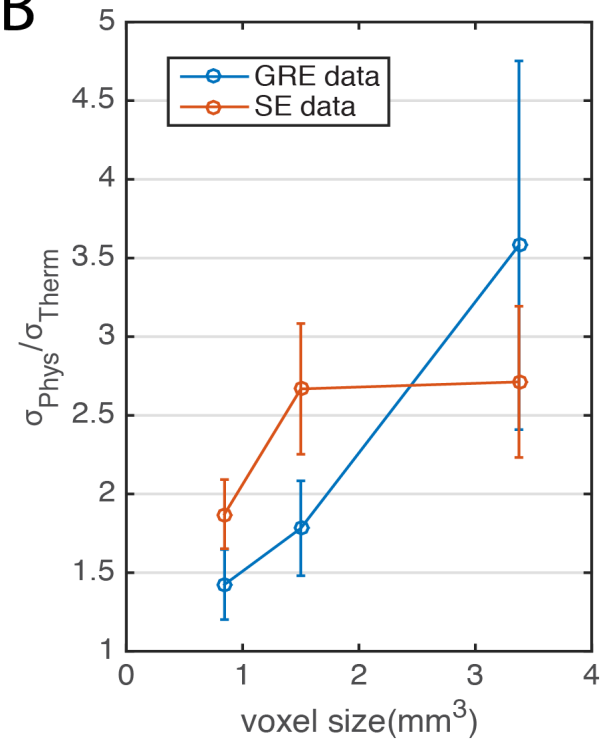
- **Temporal SNR** was significantly **lower in humans than in phantom data** due to the presence of additional noise sources, but significantly **higher in GRE than in SE**.

- **Variations of physiological-to-thermal noise**: GRE decreases with increased resolution; SE stable but suffers significant drop at sub-millimetre acquisitions.

A

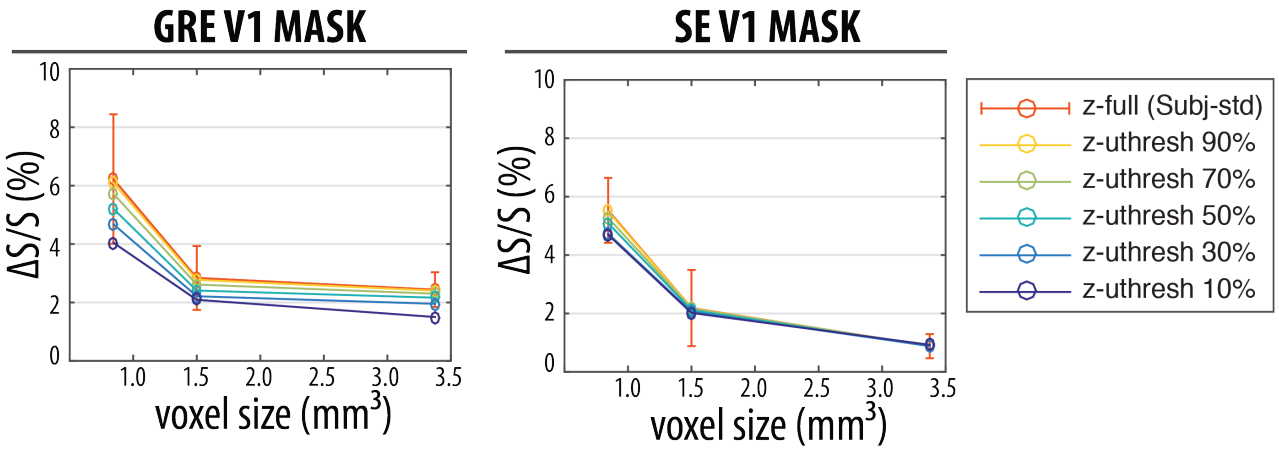


B

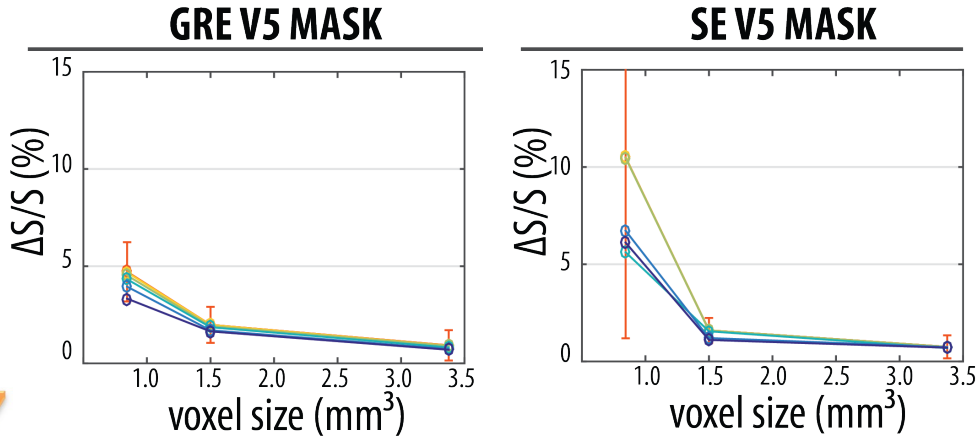


Results: variations in BOLD signal change

1. Percent BOLD signal change **did not vary** significantly **between SE and GRE**; **increased** in a non-linear way **with increasing resolution**.



2. Dispersion between different z-score masks **diminished in V5 for GRE**.

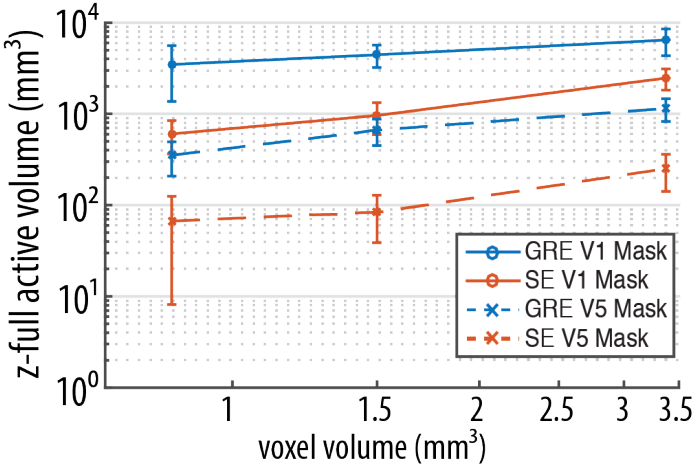


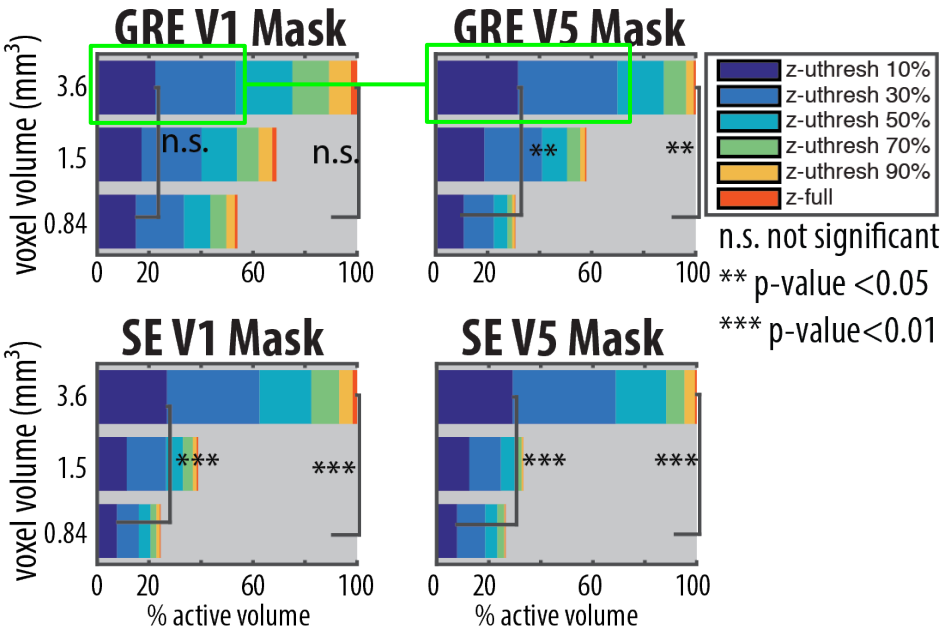
Results: Volume of activation

1. **GRE** acquisitions **present larger cluster sizes** at all resolutions compared to SE.

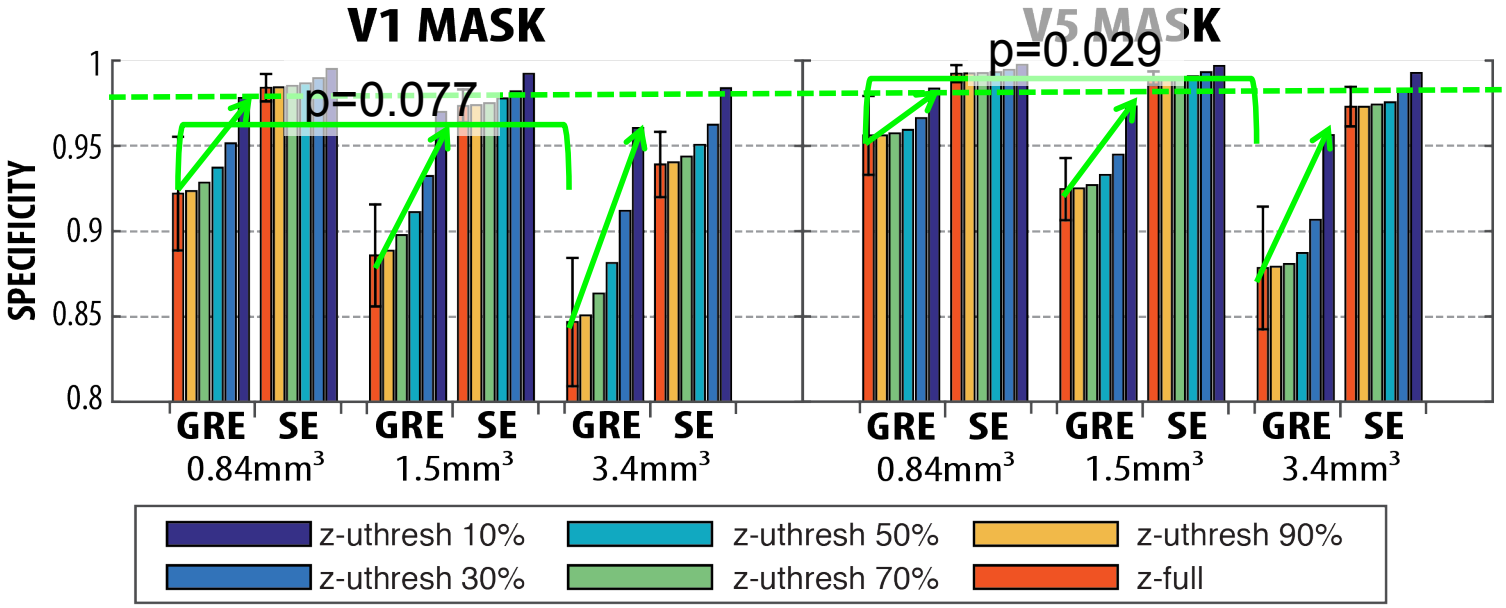
2. **The volume of active regions** in **SE markedly decreases** with **increasing resolution**. For GRE data this decrease is not statistically significant in V1.

3. **V5**: **GRE data presents a larger contribution of low-z scored voxels** to the active region compared to V1.





Results: Specificity



1. **Specificity in SE acquisitions** was largely invariant across different acquisition resolutions (Spec=0.97±0.02), and it **was higher than in GRE data** (Spec=0.88±0.08).

2. **In GRE the specificity increases nearly significantly** with increasing **resolution** + **increased specificity** with **decreasing z-score.**

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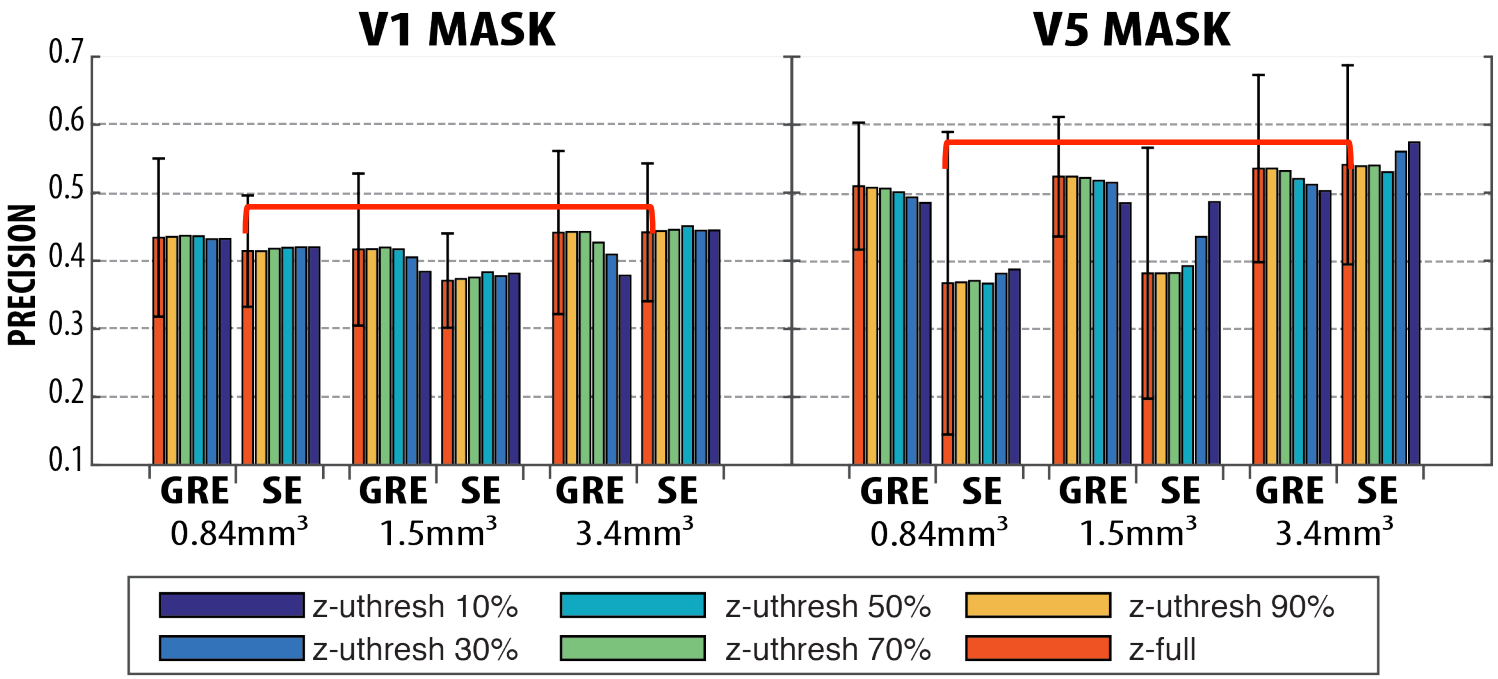
Results: Precision



1. **Large inter-subject variability** affecting the statistical significance;

2. Compared to GRE, in **SE data** it was observed a **general decrease in precision**, particularly evident in V5.

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Discussion and Conclusions

Many factors contribute for the successful acquisition in a BOLD-based fMRI experiment, and they differ with the acquired spatial resolution.

1. At coarse resolutions the “conservative approach” of a SE sequence overcomes the sparse GRE spatial distribution of the signal.

2. The decreasing temporal signal-to-noise at high spatial resolutions affects the extension of the activated volume in a SE acquisition.

3. At sub-millimeter resolutions in a GRE approach:
   1. **Reduction of partial volume effects**
   2. **Reduction of physiological noise**

Differentiate between very high BOLD signal that co-localizes mostly in non-GM regions, **from small but still statistically significant** active voxels predominantly in the true site of activation.

We conclude that a GRE-based functional map at a sub-cluster level excluding the highest z-scores, could potentially increase the performance of UHF high resolution fMRI in the primary visual cortex.

Future Work

Secondment at the BMMR, Magdeburg, Germany (6 months):

A. New acquisitions comparing SE/GRE at different resolutions including PSF geometrical distortion correction method for better GM/non-GM segmentation and analysis.

B. Add 3D-GRASE acquisition to the protocol: inner-volume 3D sequence combines EPI-readouts with fast spin- echo acquisition schemes (RARE/TSE) by acquiring multiple EPI readouts separated by refocusing pules .

(Kemper et al. frontiers of Neuroscience (2015))

C. Apply high resolution GRE/SE protocol in the investigation of ocular dominance columns in controls and possibly in patients with abnormal visual systems (Project led by Prof. M Hoffmann)

Acknowledgements

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HiMR
IMAGO7
BMMR

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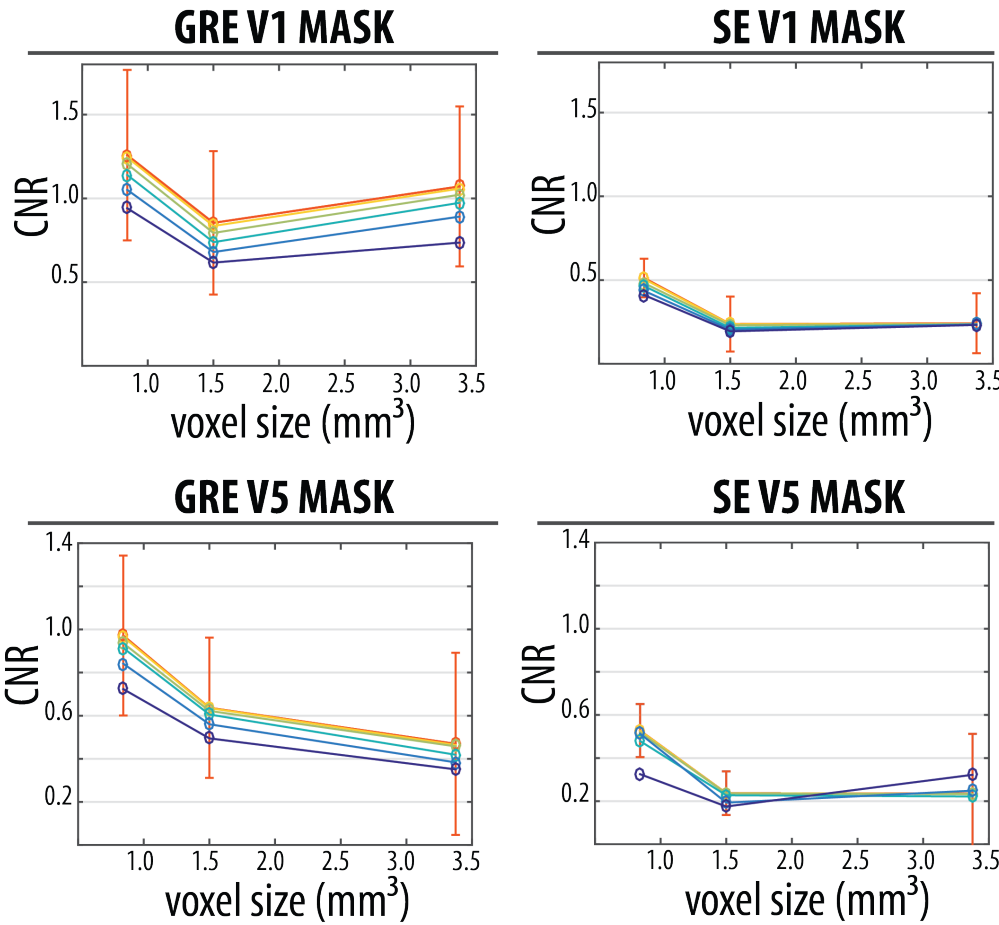
Results: Contrast-to-noise Ratio

1. Largely **invariant CNR** across resolutions in **SE**.

2. strong **statistical difference between GRE and SE** in CNR with resolution change (Kruskal-Wallis chi-squared=14.08; p-value=0.00017).

3. CNR in GRE and SE **increased with increasing resolution in V5**; but **GRE has still higher CNR** than SE (Kruskal-Wallis chi-squared=4.32; p-value=0.037).



Proposed Outline of Thesis

1. Introduction
2. NMR Theory
3. BOLD Imaging Theory
4. Characterization of BOLD spatial distribution at high spatial resolution in the visual cortex at 7T
5. Off-Resonance Field Effects in Echo Planar Imaging
    1. Demonstration of recovery of signal loss 7T in Gradient Echo EPI using Tailored-RF pulses
    2. Dynamic off-resonance field corrections with a reversed phase encoding blips approach
3. High resolution visual fMRI for the investigation of ocular dominance
4. Conclusions

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Marie Curie Fellow / PhD student University of Pisa Project: 'fMRI Applications'

Major Milestones:

0th month

- Testing the quality of the MRI system in order to undertake high-resolution fMRI studies.
- Develop experimental designs and imaging protocols for brain mapping.
- Attend university courses on physics and applied physics.

12th month

- Acquire knowledge on sequence programming (EPIC cource, Rotterdam, NE).

- Develop and apply new protocols to visual studies in pilot experiments on healthy human volunteers.
- Attend training courses of:
  - Spectroscopy and imaging at high field (Milan, IT)
  - RF coil design and simulation; RF Safety for UHF MR (Heidelberg, GE)
  - Acquisition and analysis for fMRI at UHF (Leipzig, GE)
  - Medical Imaging Industry (Elba, IT)
- Secondment at General Electric Global Research Centre (Munich, GE): understand the structure of the echo planar sequence and design optimized acquisition methods.

24th month

- Secondment to BMMR-OVGU(Magdeburg, GE)
  - Replication of designed fMRI studies on a Siemens system.
  - Application of fMRI methods for the comprehension of neuronal mechanisms underlying normal brain function or neuro-physiopathologies;
- Analyze the potential correlation between function and cytoarchitecture.

36th month

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