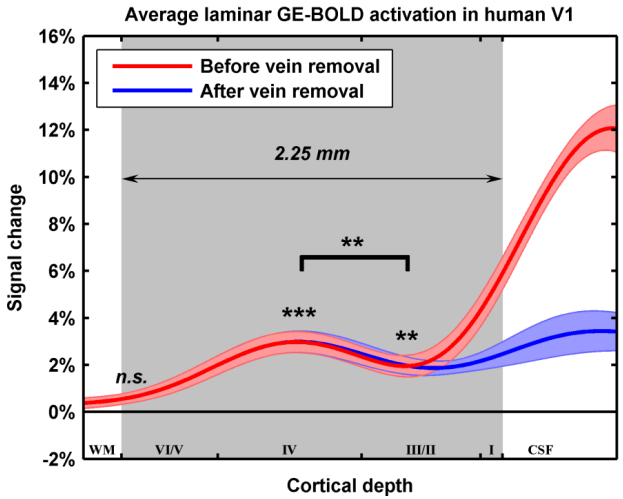
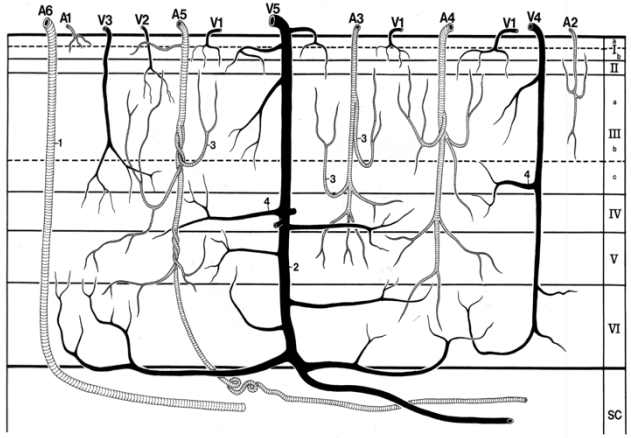
# The possibility to image functional changes in cortical laminae using fMRI




A/Prof. Dr. Markus Barth

Centre for Advanced Imaging,

The University of Queensland

# Probing laminar circuitry

- The laminar level is a relevant level to address important neuroscience questions (next talks and references below)
- This scale of spatial resolution is difficult to obtain in humans but was reliably obtained in animal experiments
- First studies show that non-invasive experiments can be performed in vivo using BOLD fMRI in the human brain

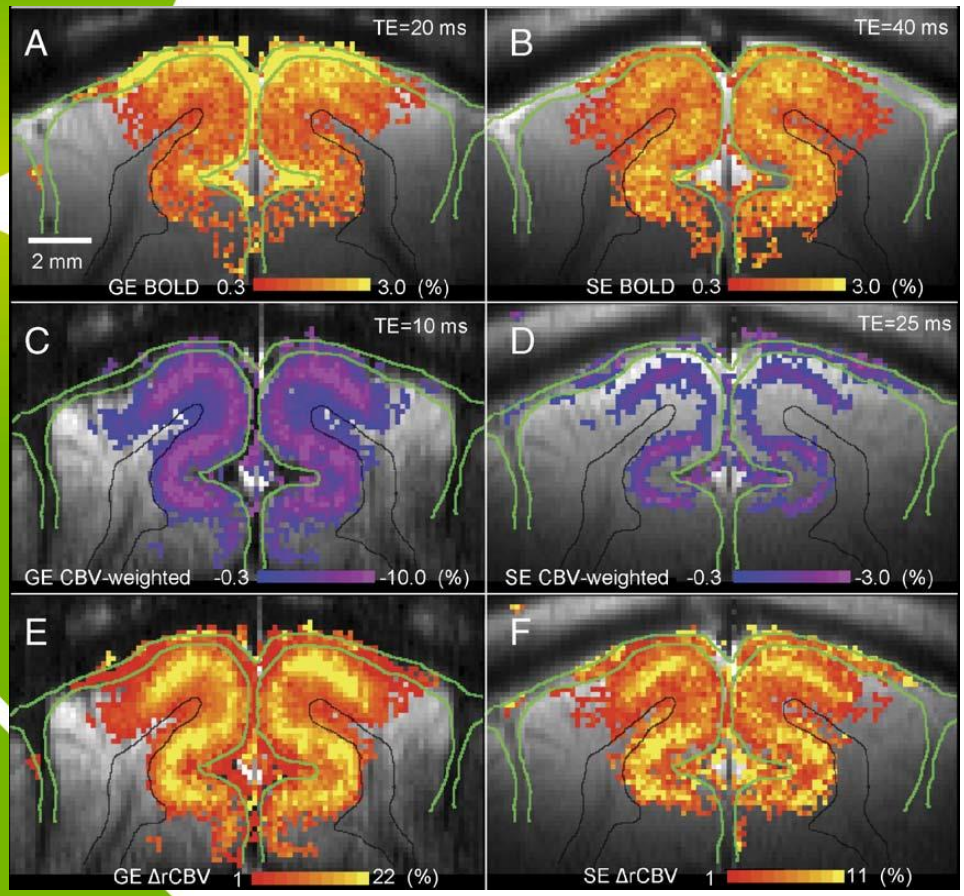
Self, M. W., van Kerkoerle, T., Supèr, H., & Roelfsema, P. R. (2013). Distinct Roles of the Cortical Layers of Area V1 in Figure-Ground Segregation. *Current Biology*

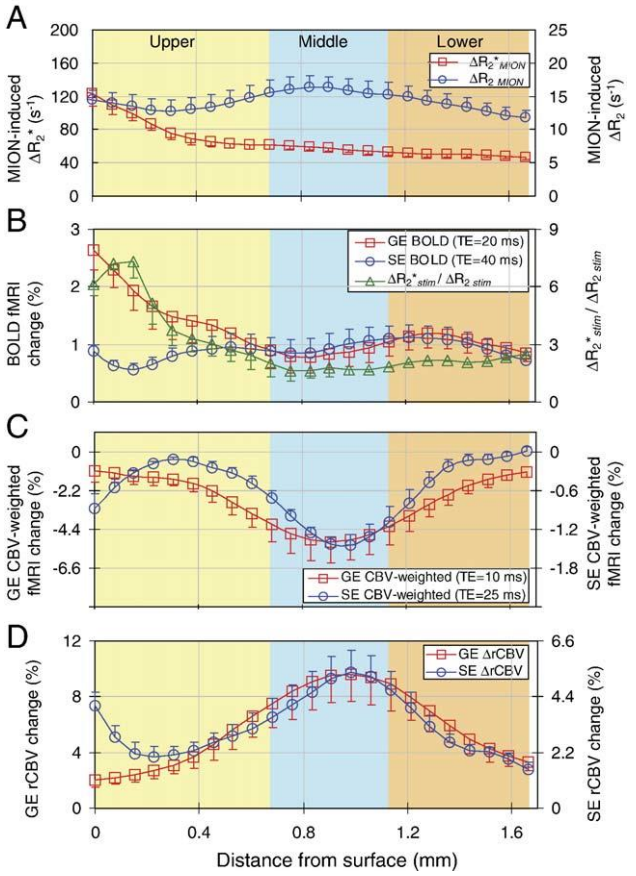
Constantinople, C. M., & Bruno, R. M. (2013). Deep cortical layers are activated directly by thalamus. *Science*

# Animal Studies

Laminar fMRI has been successfully performed in animal studies using various methods, such as blood volume (CBV), perfusion, SE and GE BOLD fMRI:

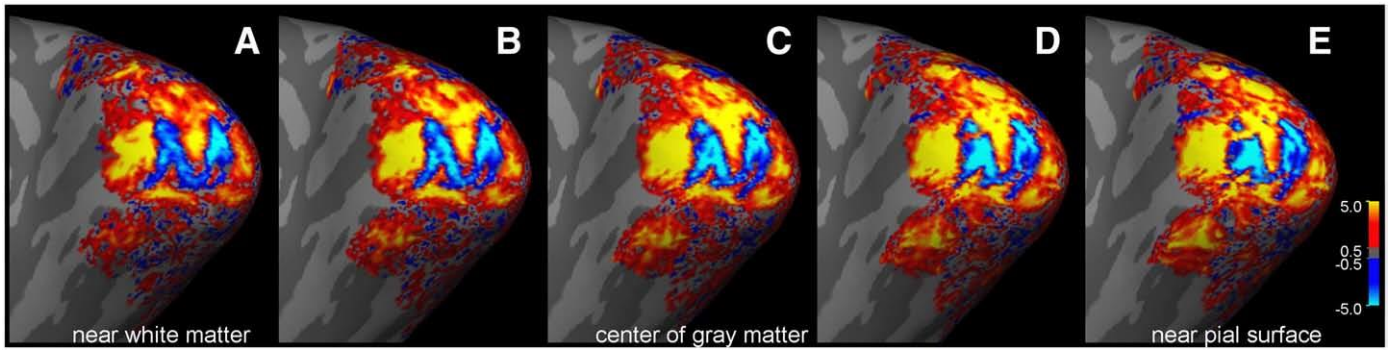
Bissig and Berkowitz, 2009; Chen et al, NI 2013; Goense and Logothetis, MRI 2006; Harel et al, NI 2006; Lu et al, 2004; Silva and Koretsky, 2002; Shih et al, NI 2013; Smirnakis et al, JCBFM 2007; Zappe et al, JCBFM 2008; Zhao et al, NI 2006

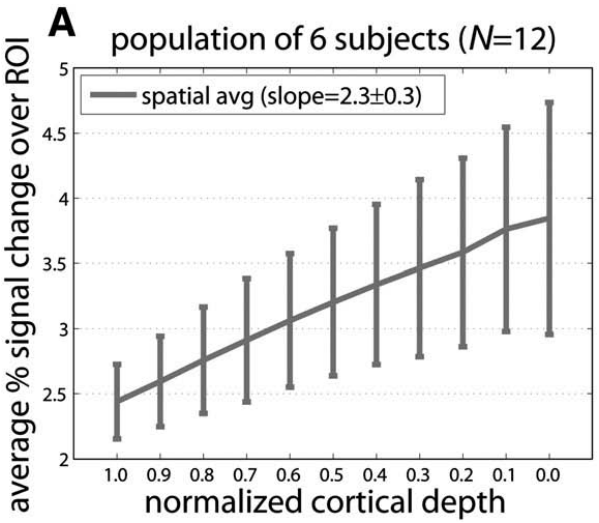


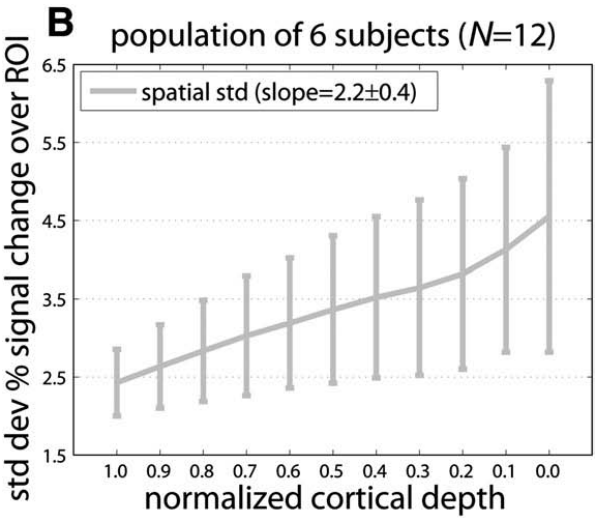



# Human studies

De Martino et al, PloS One 2014; Koopmans et al, HBM 2010 and NI 2011; Olman PloS One 2012; Polimeni et al, NI 2010; Ress et al, 2007; Siero et al, JCBFM 2011 and MRM 2014

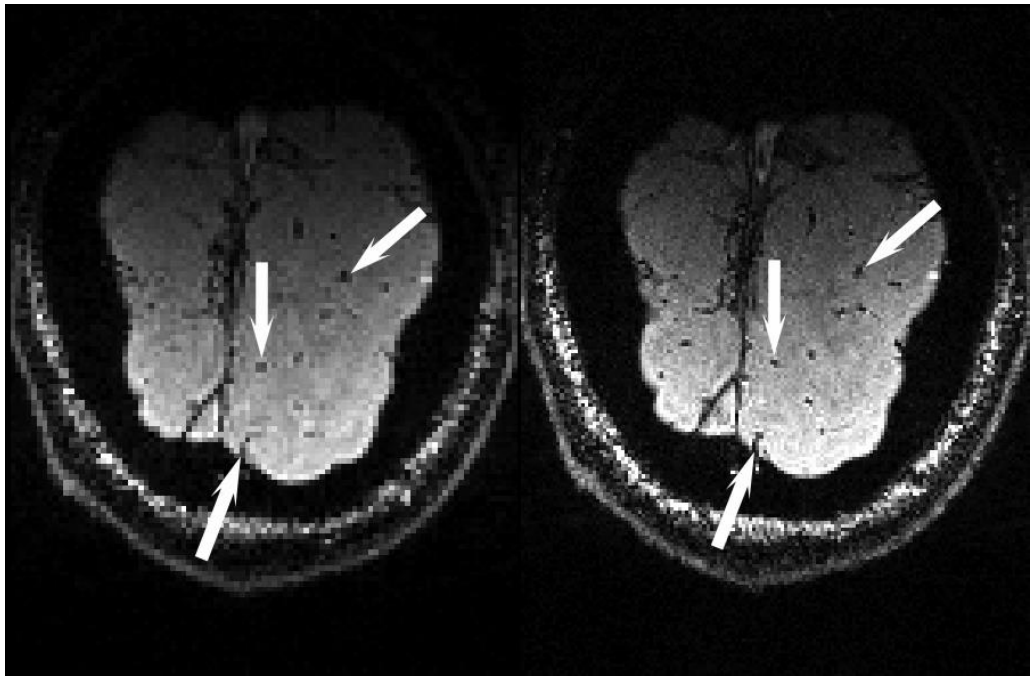


# Proof of principle:
# High resolution "*functional* MR venography"

- Large veins cause degradation of the spatial localisation of activation in fMRI
- We aimed to identify the veins directly in the functional scans and remove them from analysis (manually or automatically) to increase specificity of BOLD signal
- We used parallel imaging to obtain a temporal resolution compatible with a functional block design

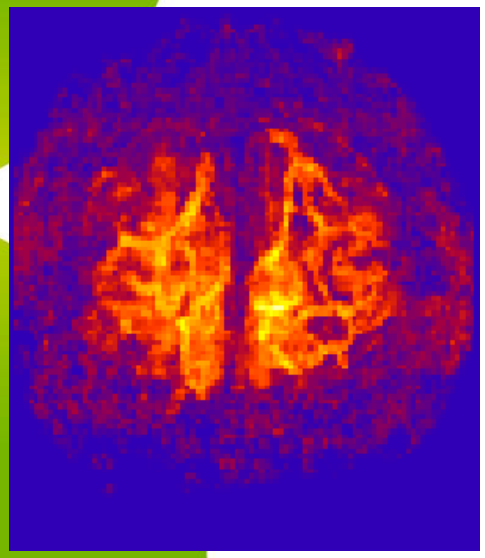


Single slice @ 1 mm resolution (left) and 0.75 mm resolution (right); white arrows depict veins

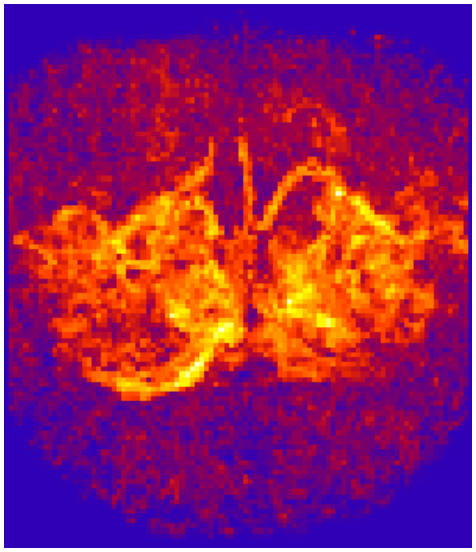
*Barth & Norris, NBM 2007*

# Before elimination of veins

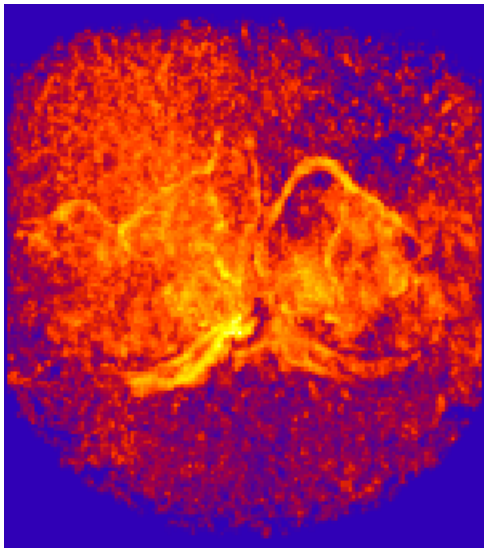
Subject 1: 1 mm



Subject 2: 1 mm



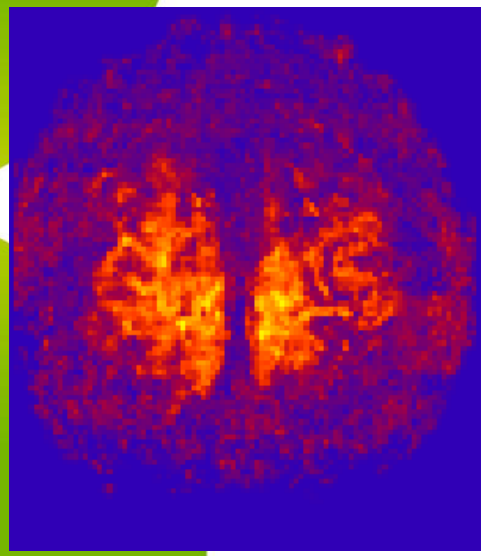
Subject 2: 0.75 mm



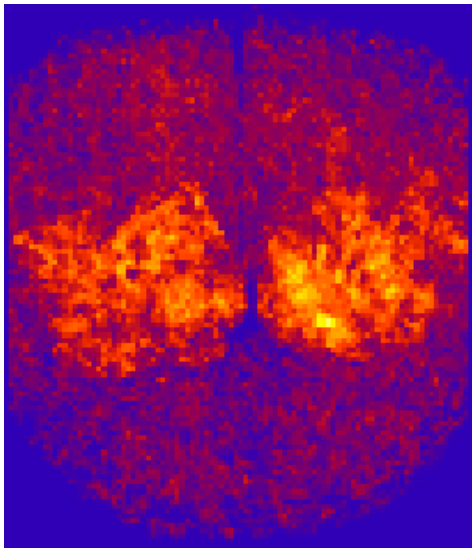
*Barth & Norris, NMR in Biomedicine 2007*

# After elimination of veins

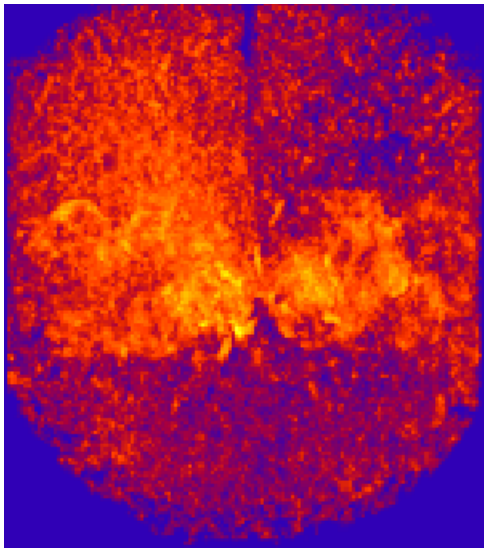
Subject 1: 1 mm



Subject 2: 1 mm



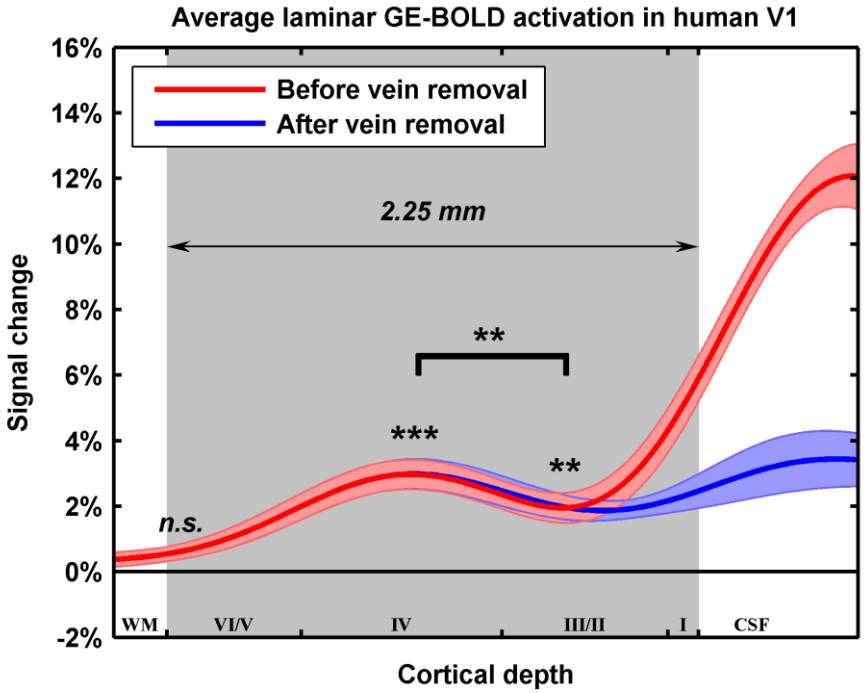
Subject 2: 0.75 mm



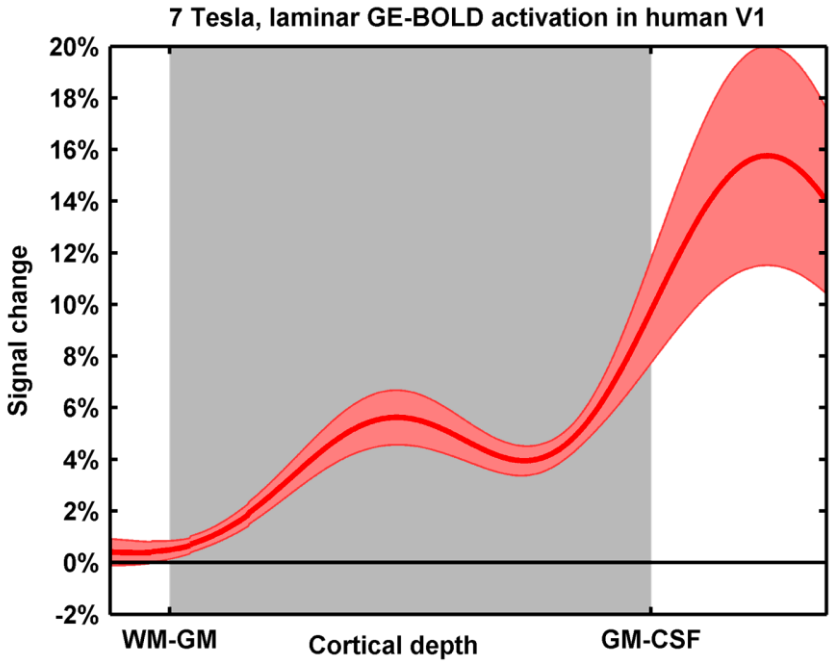
*Barth & Norris, NMR in Biomedicine 2007*

# fMRI with laminar resolution

## 3 Tesla




## 7 Tesla



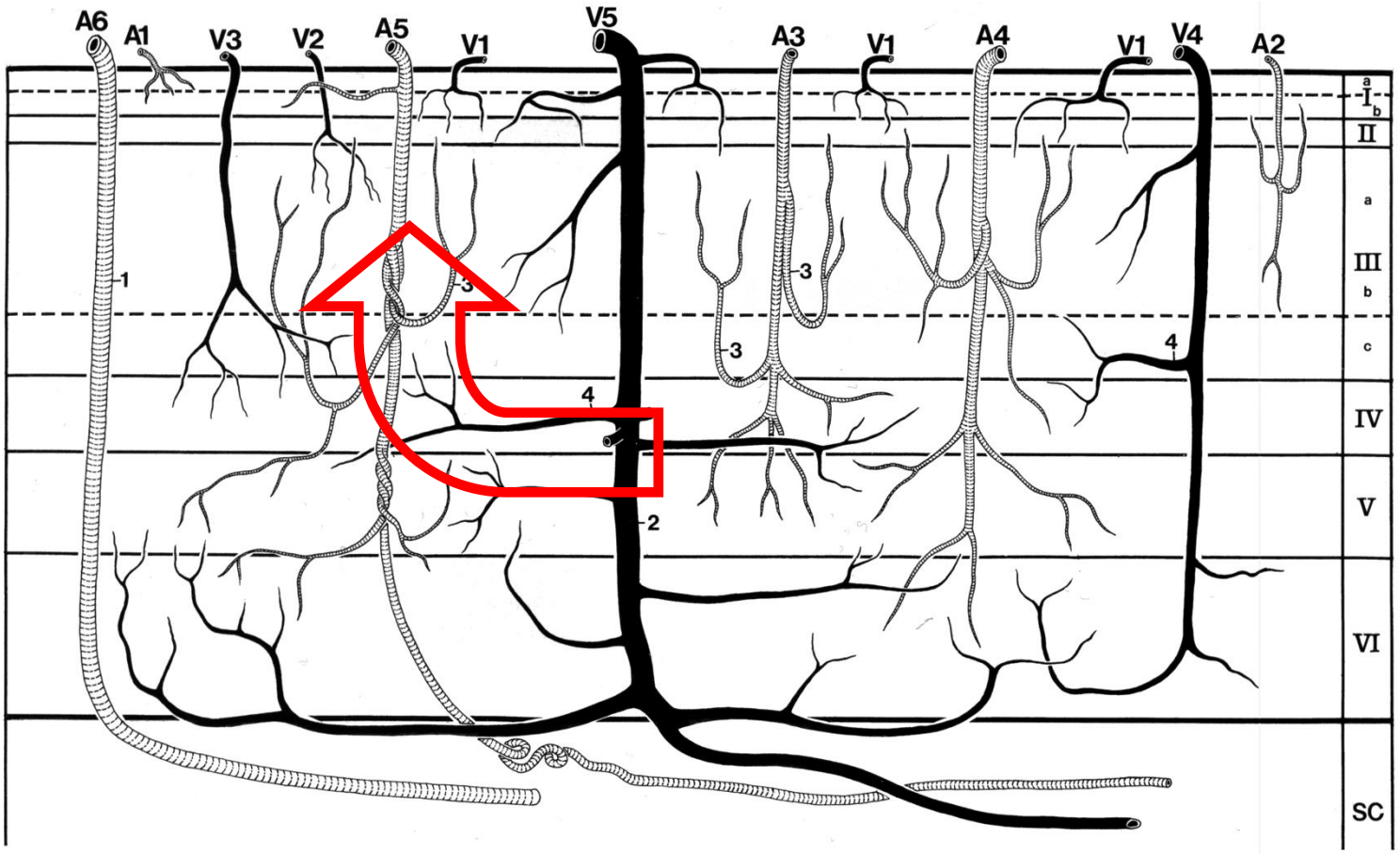

Signal change versus cortical depth. The gray shading depicts the approximate cortical thickness. The red shading depicts standard error of the mean.

*Koopmans et al, HBM 2010*

*Koopmans et al, NI 2011*

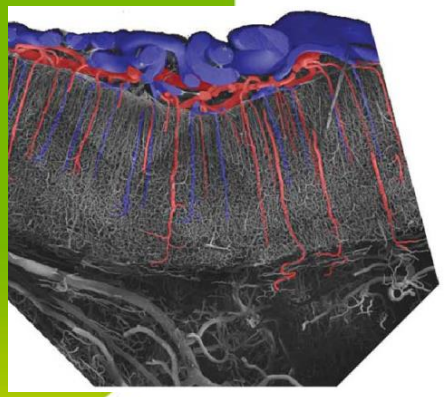
# Why should laminar BOLD fMRI be possible?

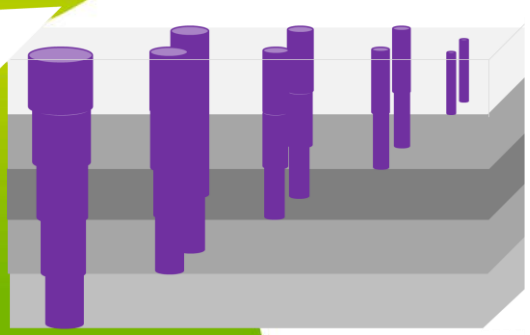
Due to venous architecture: Blood drains within a layer first

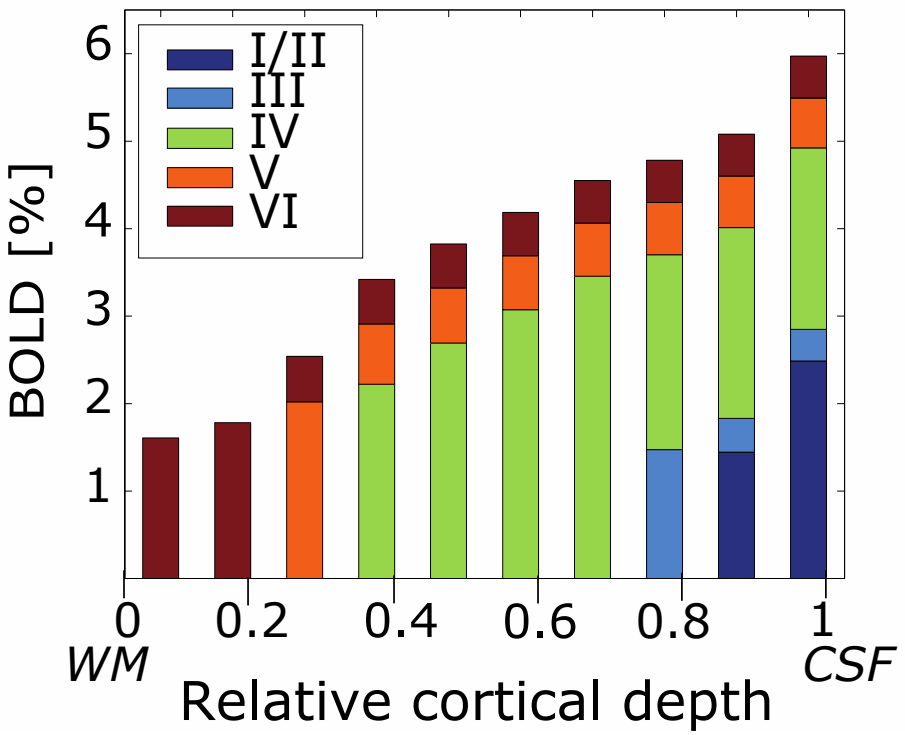



*Duvernoy HM, The Human Brain. 2nd Edition, 1999*

# Laminar BOLD model








*Origin of BOLD signal across the cortex from a vascular layer for GE*

*Markuerkiaga et al, ISMRM 2014*

# Limitations of 2D EPI

- 2D EPI has been the workhorse of BOLD fMRI since twenty years using a ‘typical’ resolution ~3.5 $mm^3$ and typical $B_0$
- Standard 2D EPI was slow for high resolution with many slices, this is now solved by Multiband (MB) EPI

Issues that remain even with MB 2D EPI:

- Thin slices result in low SNR
- Imperfect slice profile
- Increased motion-sensitivity (spin-history effects)
- High power deposition with MB EPI

# 3D sequence vs. 2D sequence

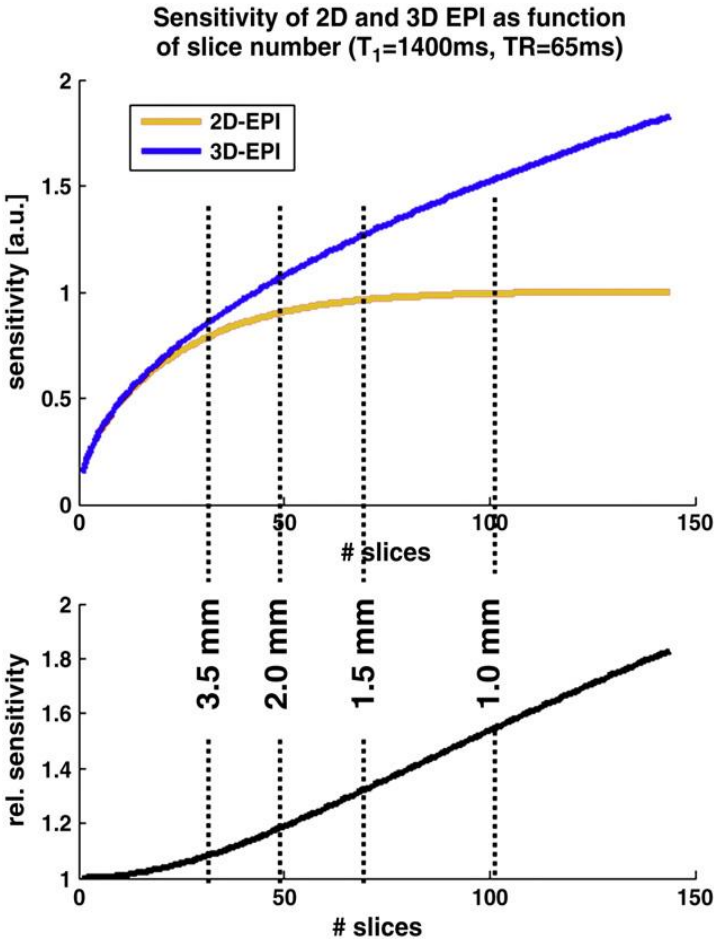
3D excites the whole volume

→ $M_z$ is lower

→ sample signal from factor $N_{slices}$ larger volume

→ $\sqrt{N_{slices}}$ efficiency and SNR increase

more slices → larger gain




Poser et al, NI 2010

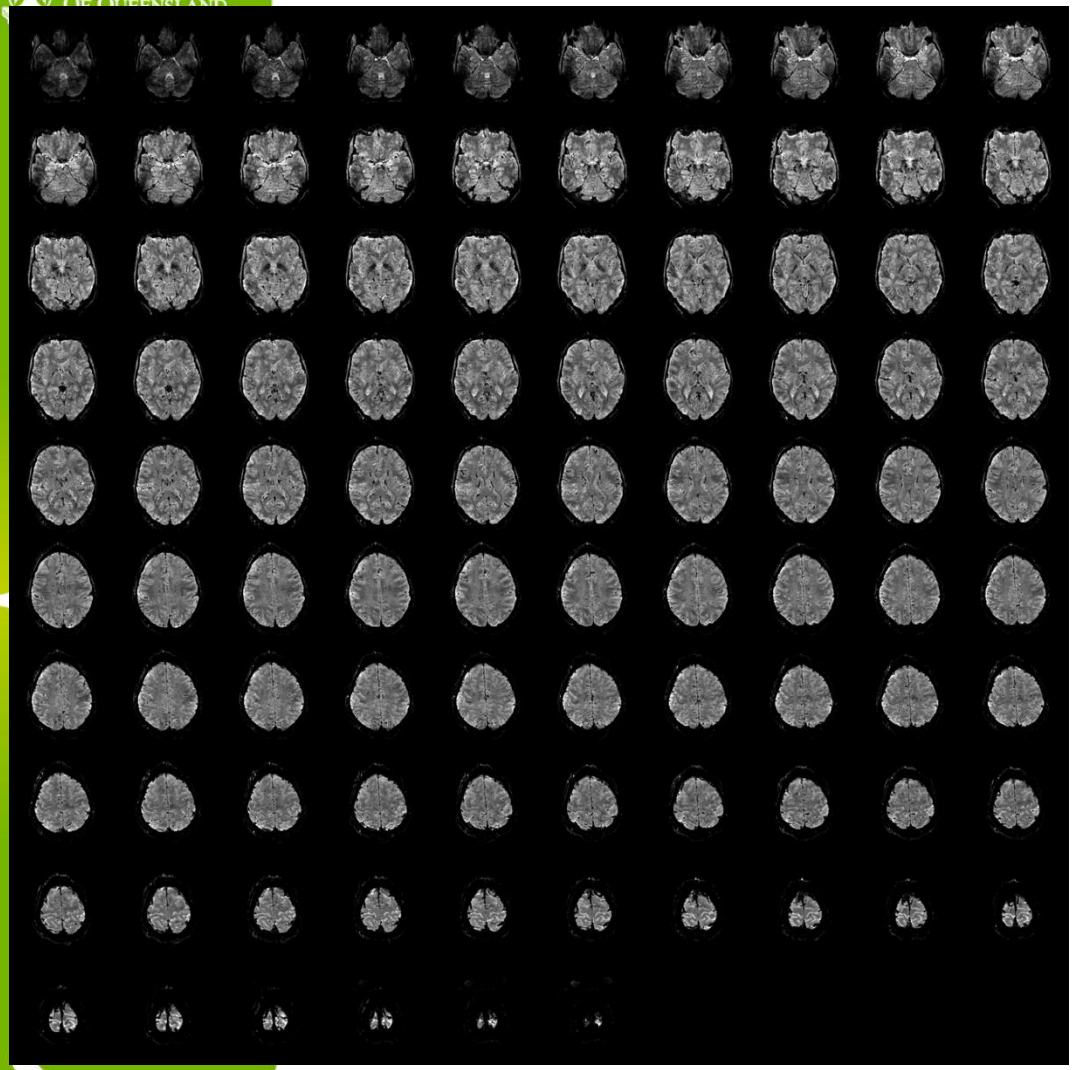
MR acquisition with 3D EPI:

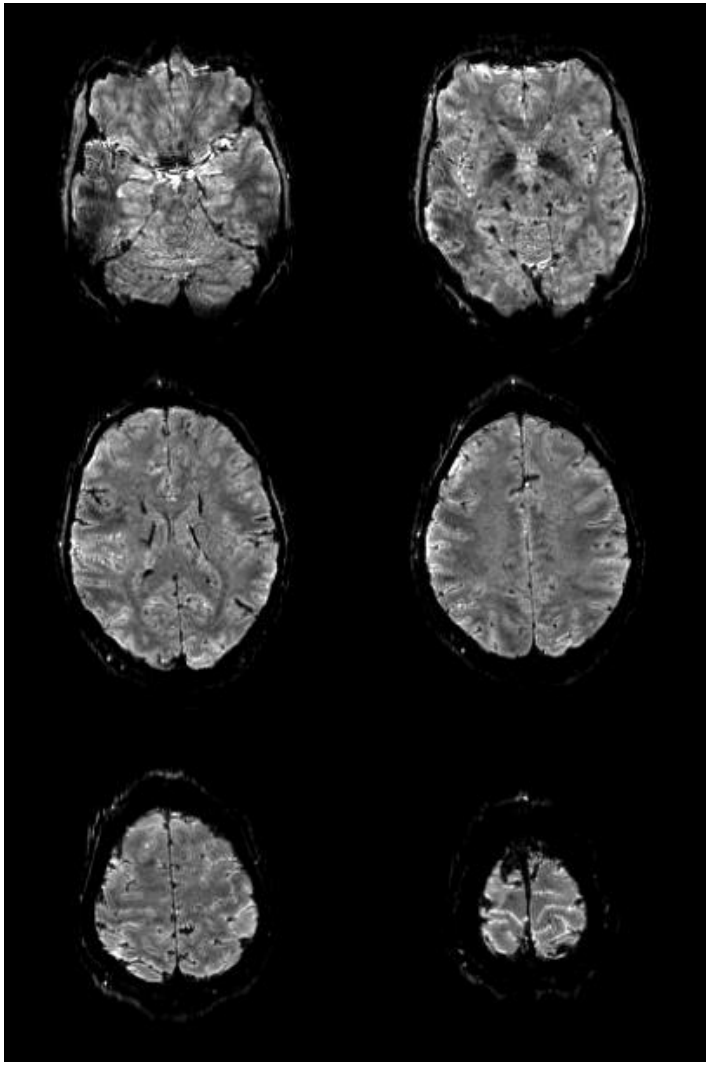
- 3 T or 7 Tesla MR scanner (Magnetom, Siemens Healthcare)
- 32 channel head coil

Typical sequence parameters for 3D EPI:

- 1 mm isotropic resolution, TR/TE/alpha = 45ms/17ms/15deg, **TR(volume) = 2.3 – 3.2 s**, MA = up to **200x200**, up to **112 slices**, **2D acceleration = 4x2** or **3x3**

# High resolution EPI at 7 Tesla

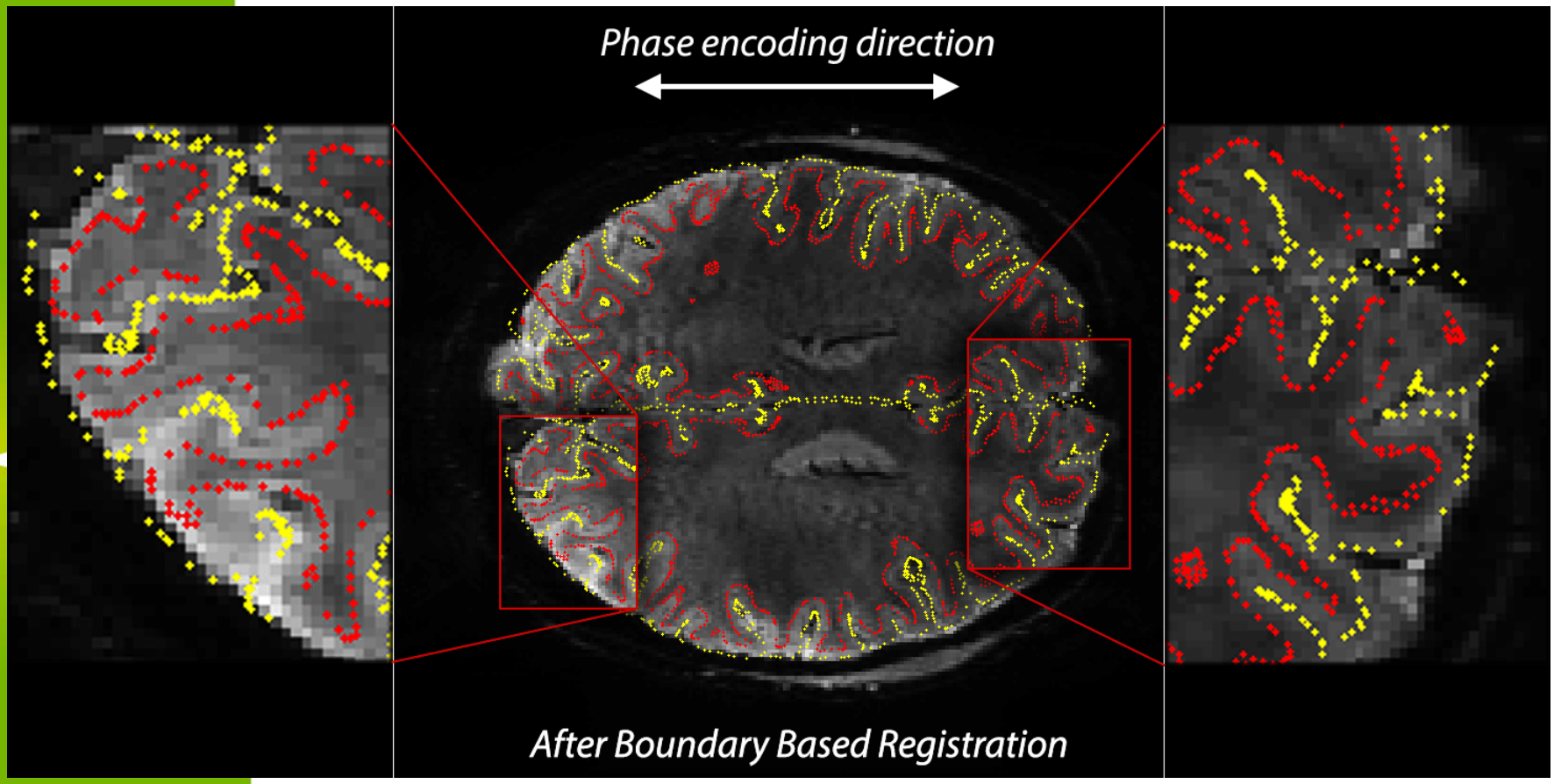




Example of a single 3D EPI volume with 96 slices acquired in 2.3 seconds at a resolution of 1 mm (left) and several enlarged slices (right)

*Poser et al, NI 2010*

# Co-registration of EPI and structural MRI data

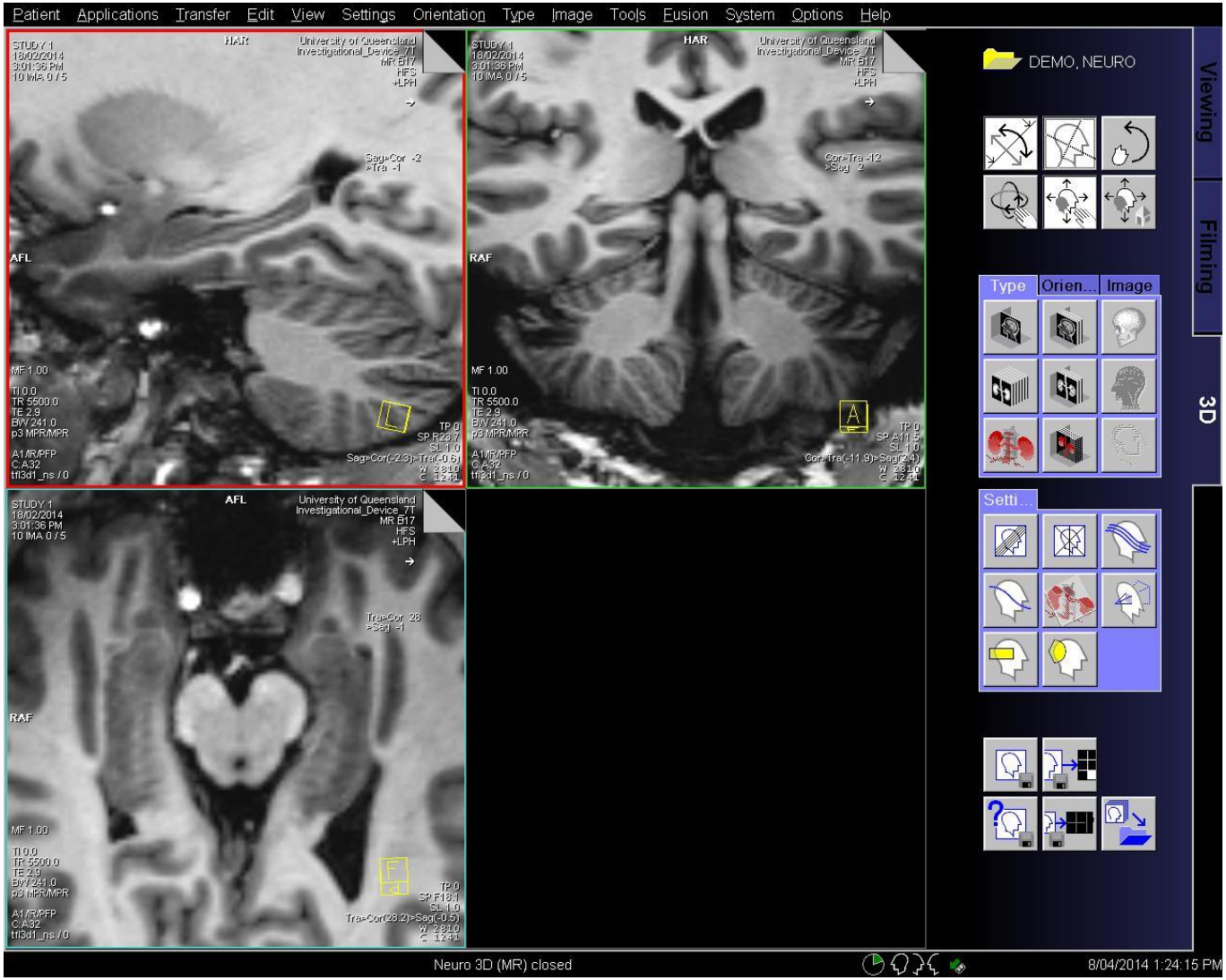



van Mourik et al, ISMRM 2014

# 7T MP2RAGE at different resolutions

Resolution: 1 mm isotropic

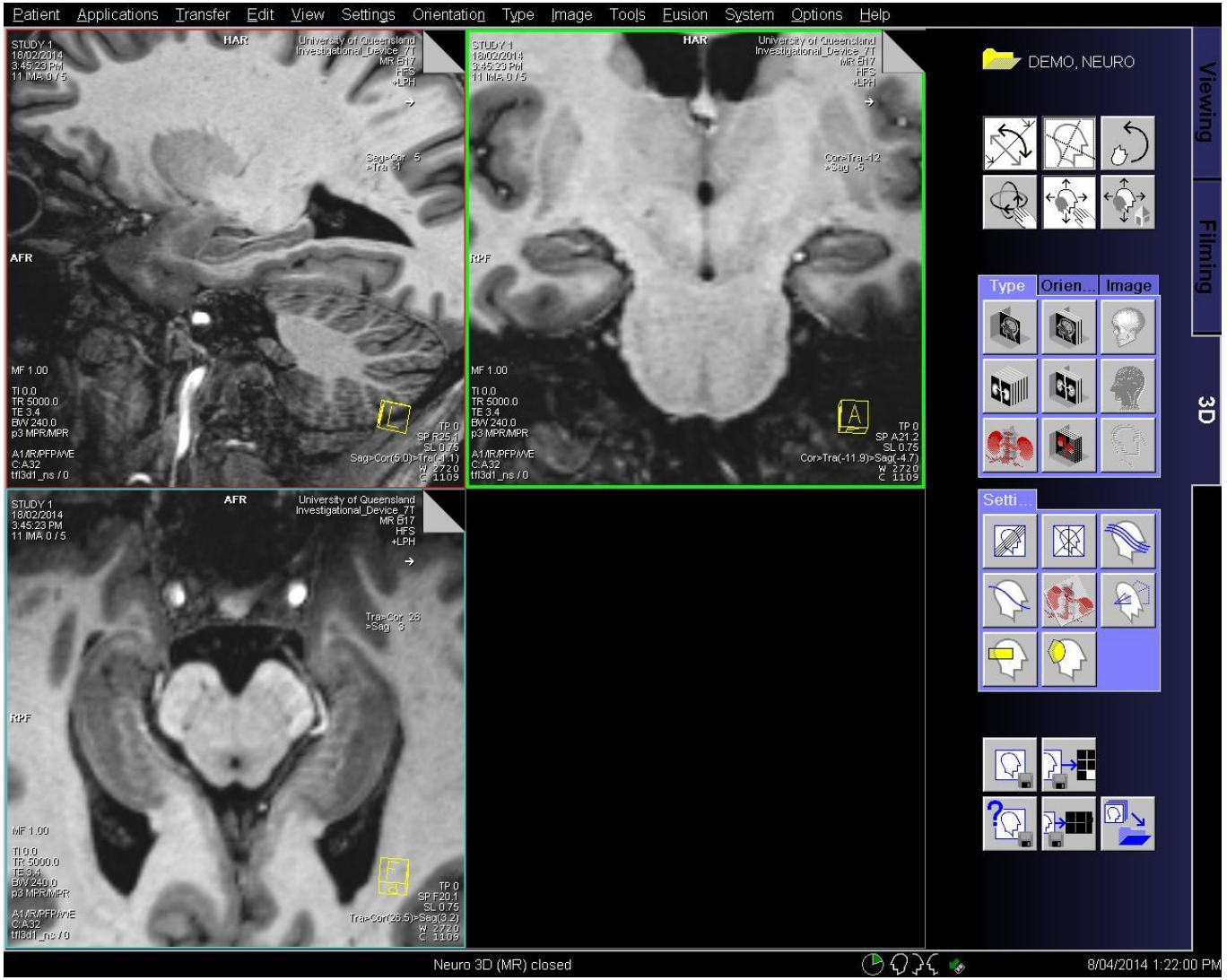
TA: 6min



# 7T MP2RAGE at different resolutions

Resolution: 0.75 mm isotropic

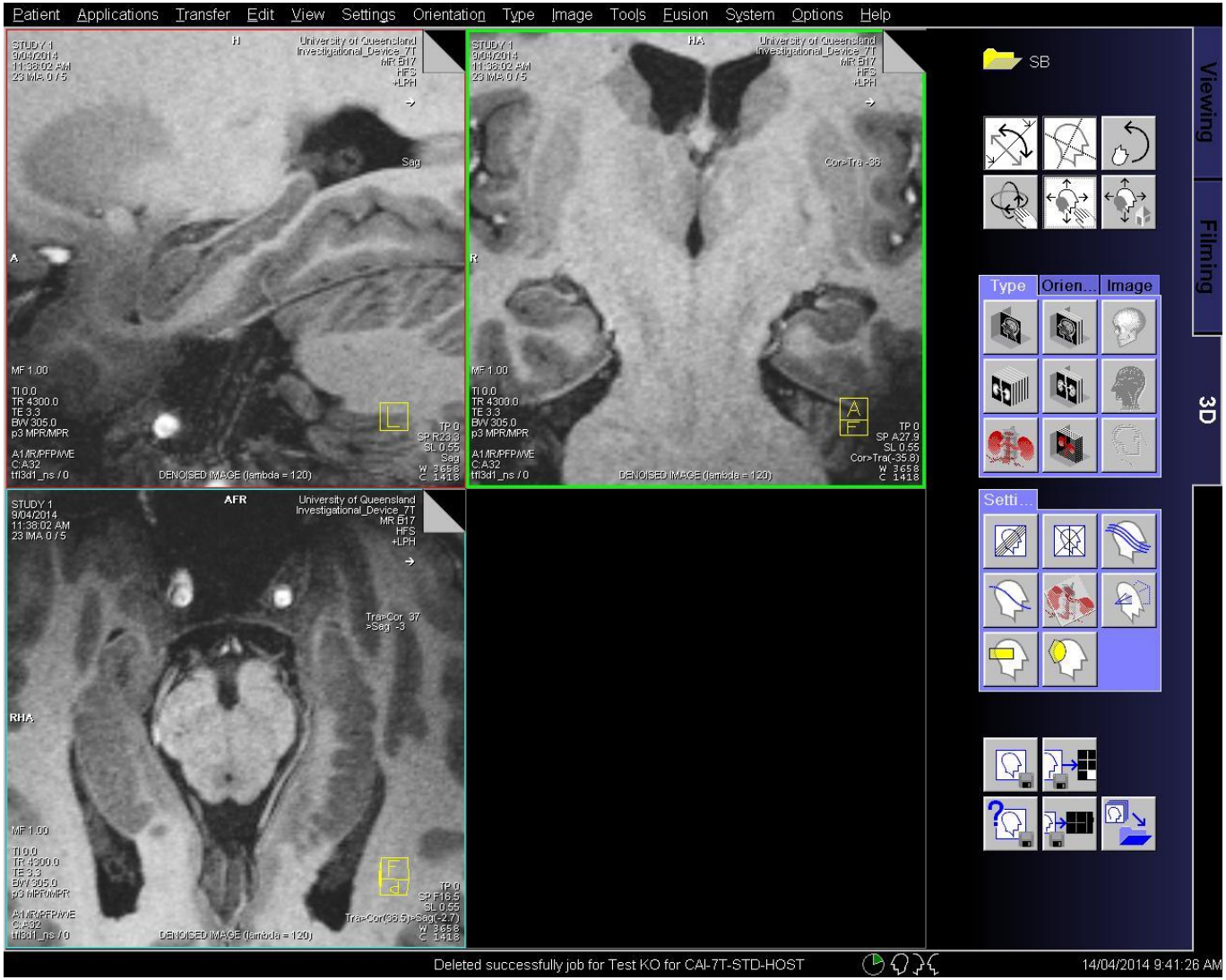
TA: 7.5 minutes



# 7T MP2RAGE at different resolutions

Resolution: 0.5 mm isotropic

TA: 9.5 minutes



The University Of Queensland
AUSTRALIA

# 350 µm

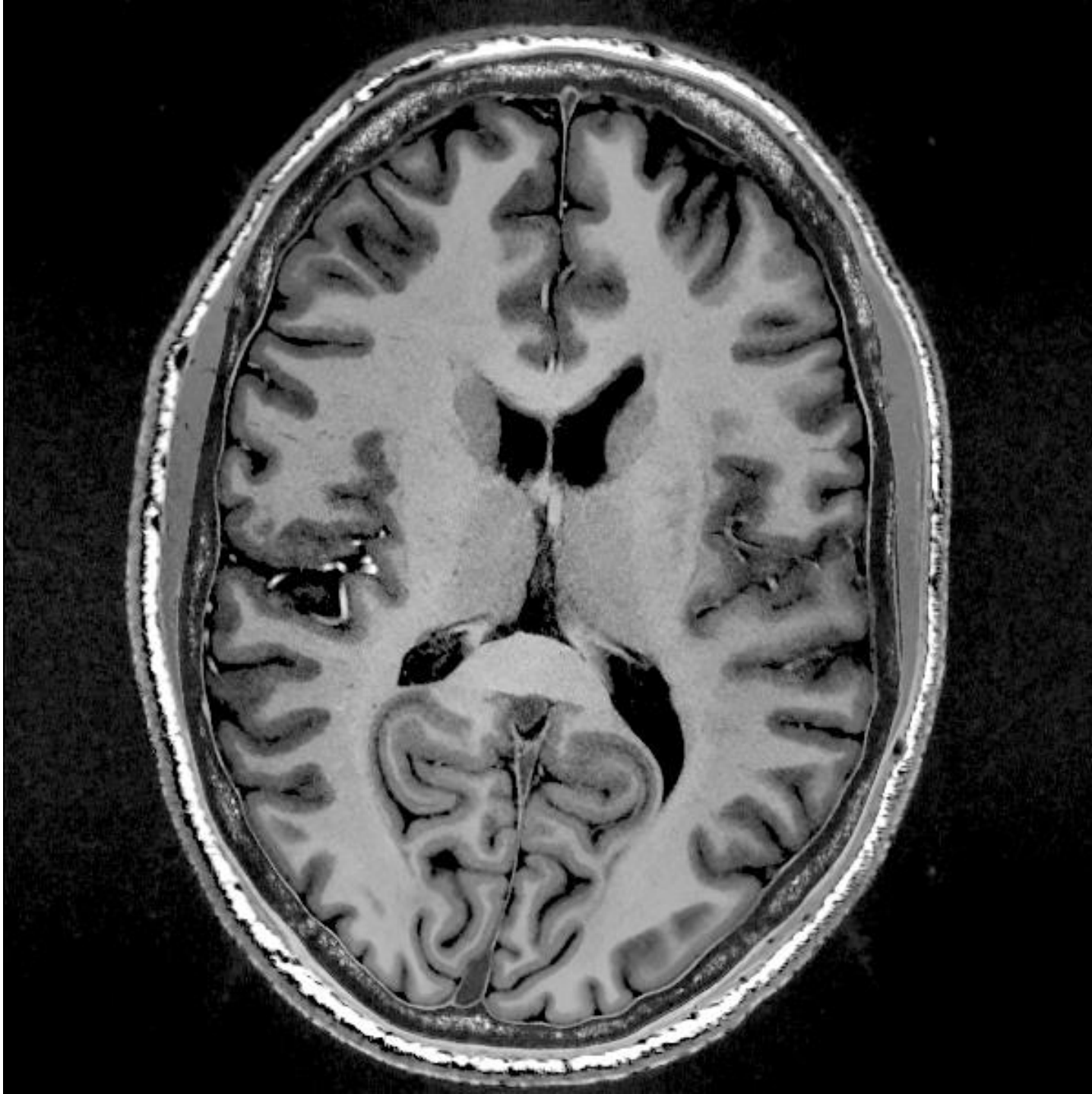
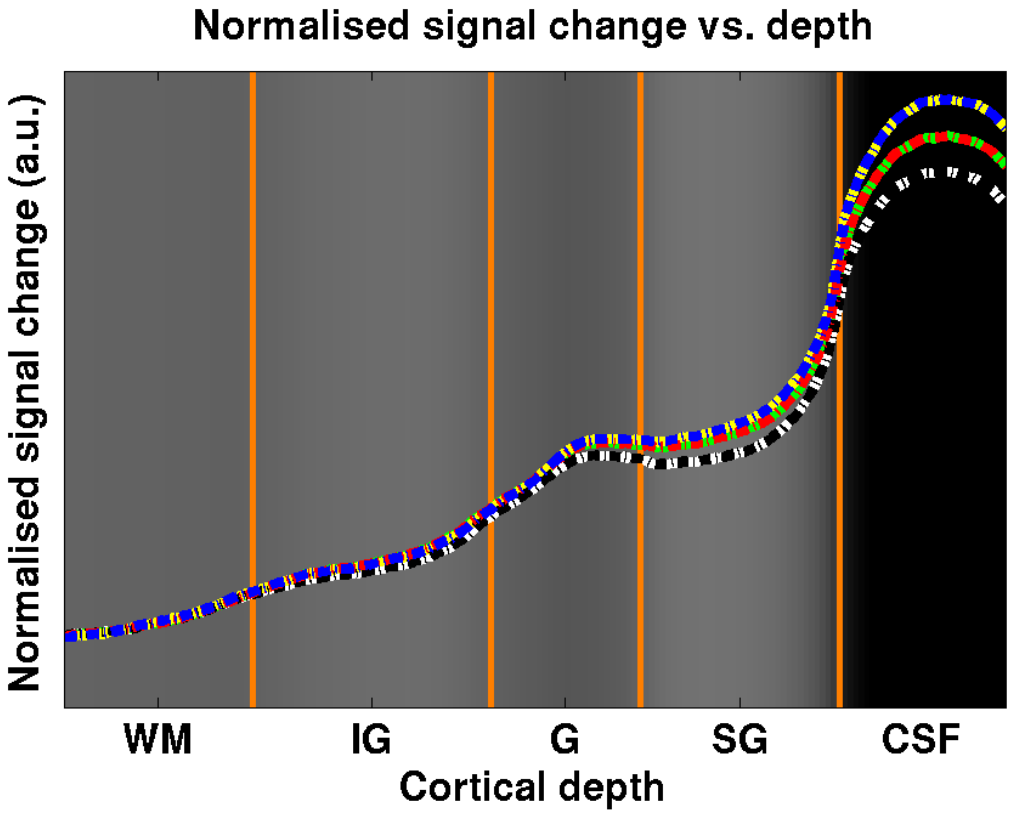


Image processing:
A. Jancke

# Layer specific fMRI using 3D EPI at 3 Tesla using chromatic vs. achromatic stimuli

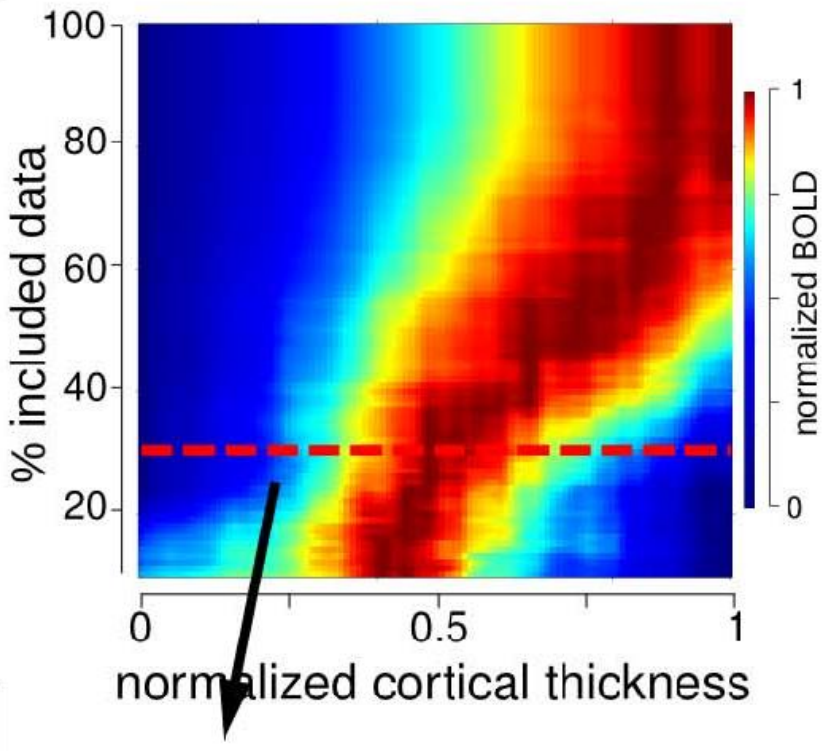



Normalised signal change versus cortical depth

*Koopmans et al, abstract HBM 2010*

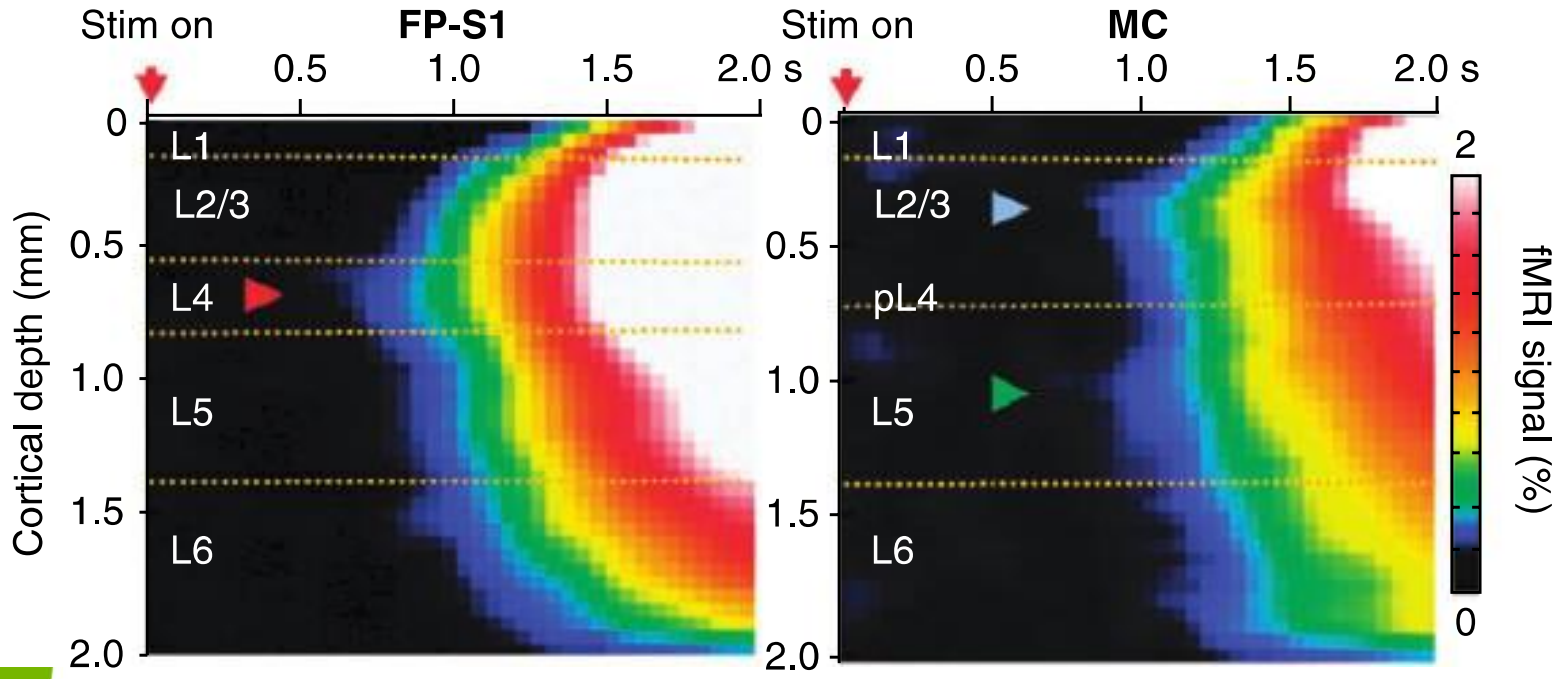
# Replication of the BOLD increase around the middle layers

Laminar profiles exhibit strong or weak linear trends




Fracasso et al, ISMRM 2014

# Single line-scanning BOLD fMRI in rat somatosensory and motor cortex: 50 um resolution with 50ms temporal resolution




Yu et al, Nature Methods, 2014

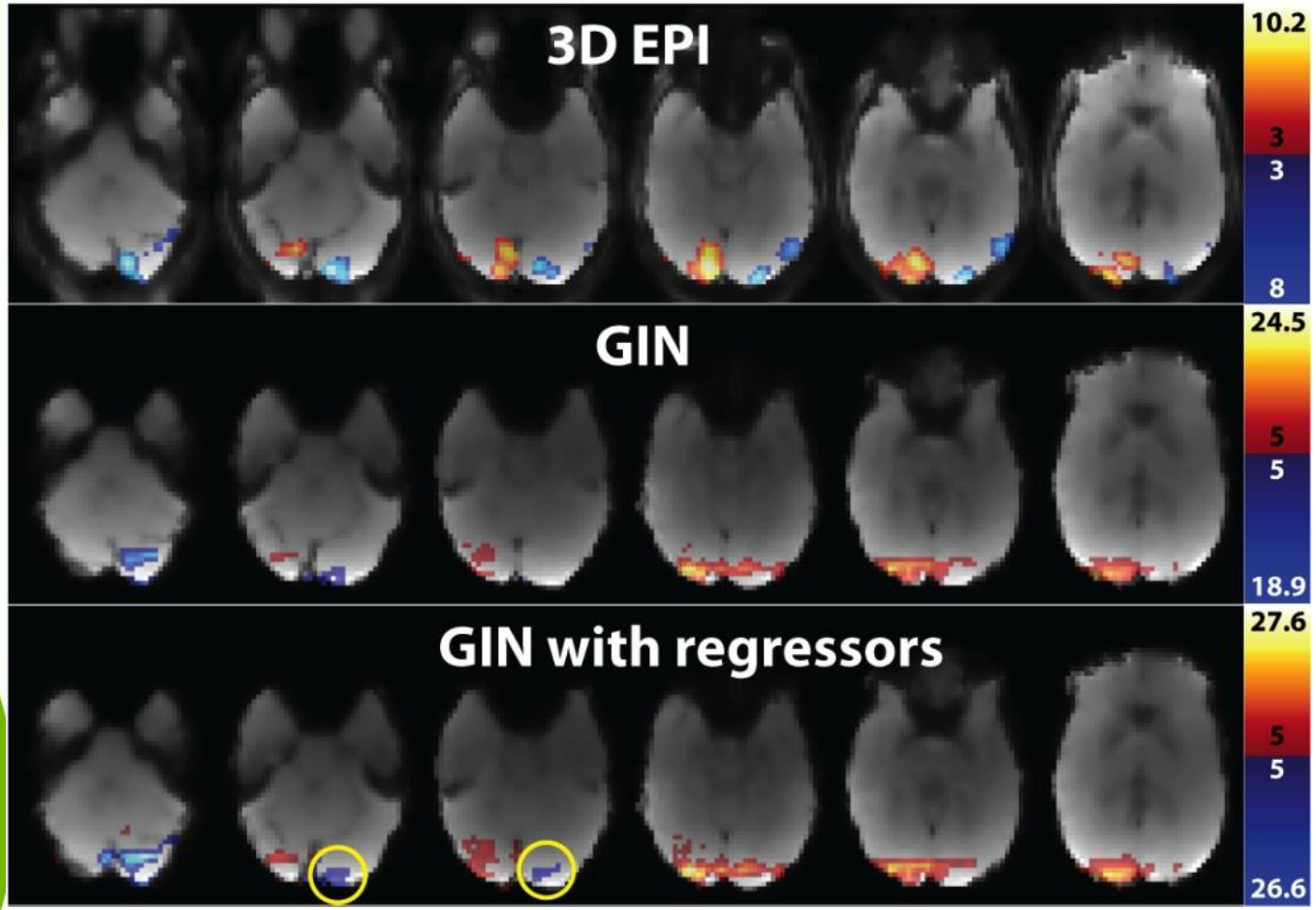
# Inverse Imaging (InI) or MR-encephalography (MREG)

- Extreme case of parallel imaging where one dimension of gradient encoding is completely replaced by using only coil sensitivities, i.e. a 3D volume is collapsed into only one thick 2D slice
- regularization using prior knowledge (e.g. reference data, pre-scan) is needed
- ultra-fast acquisition times are achievable (TR~100ms)
- but this results in reduced spatial resolution in the aliased dimension

Lin et al, MRM 2005

Hennig et al, NI 2007

# Generalized INverse (GIN) imaging: functional results



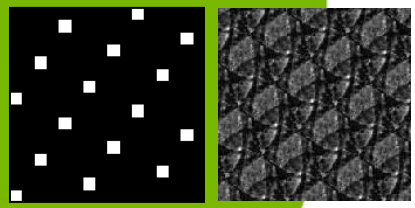

Addition of the confound regressors into the GLM improves localization (yellow circles) and increases z-statistics.

Boyacioglu and Barth, MRM 2013

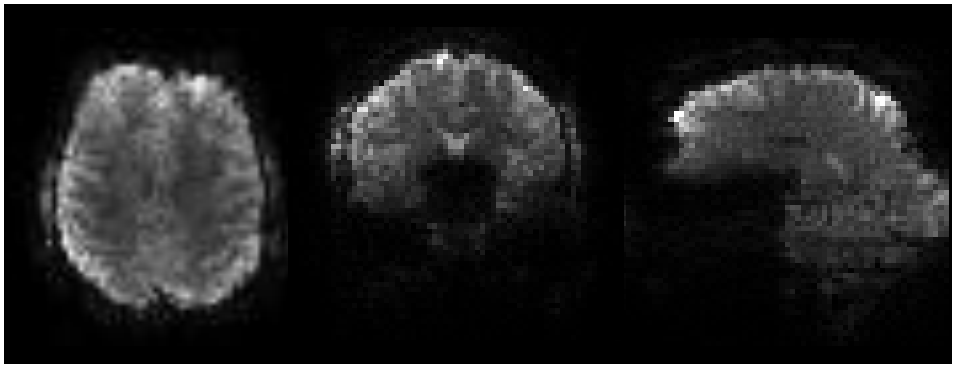
# 3D EPI with CAIPIRINHA
# 7T examples @16x acceleration

The University Of Queensland
AUSTRALIA

## 1x16



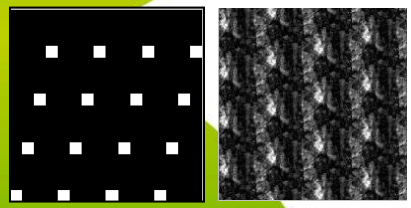
1x16_z6



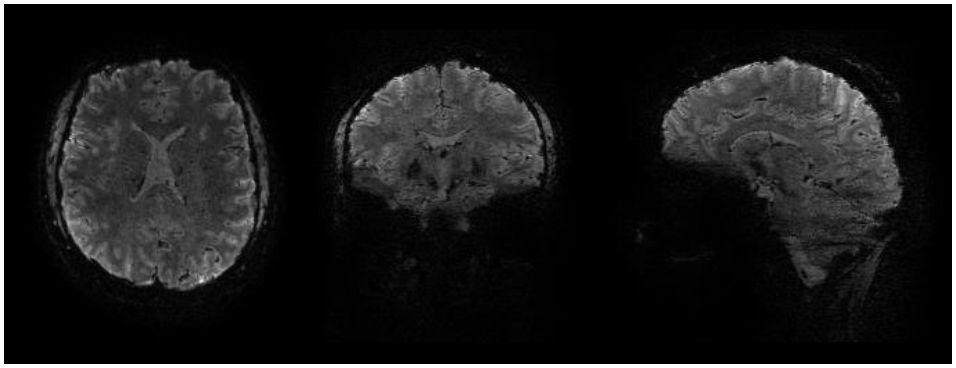
3.0mm, 64x64x64
TE=19ms

***TR=148ms***

## 16x1



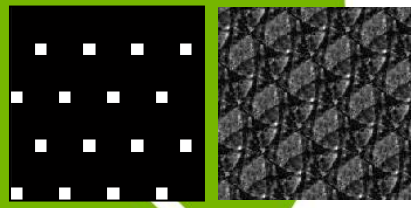
4x4_z1



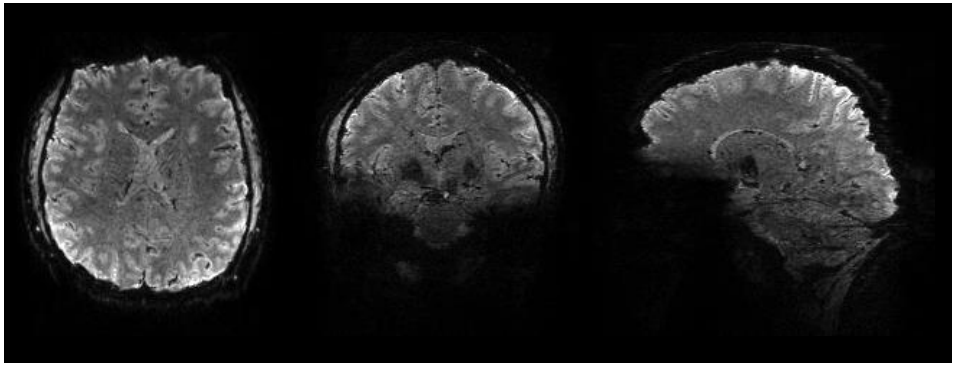
**0.8mm**, 240x240x208
multi-TE=9/**22**/35ms

***TR=7.3s***

## 4x4



4x4_z2



**0.8mm**, 240x240x208
TE=19ms

***TR=1.99s***

# Discussion and Conclusions

- fMRI on a laminar scale is possible in humans, but is challenging regarding acquisition and analysis
- potentially useful to investigate brain function on a mesoscopic scale

Open questions:

- How does BOLD relate to neural activity?

- Will it possible to distinguish timing/onset differences in humans on a laminar scale?

# Acknowledgements

Nijmegen: Tim van Mourik, Irati Makuerkiaga, David Norris and the MR techniques group

Maastricht: Benedikt Poser

Oxford: Peter Koopmans