What's Next for fMRI?

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http://fim.nimh.nih.gov

&

Functional MRI Facility

http://fmrif.nimh.nih.gov

Where are we now after 25 years?

Steady Improvements…

- **Technology is more sophisticated**
  (hardware, computers, software)
- **Images are better**
  (SNR, acquisition speed, resolution)
- **Easier to implement**
  (what was cutting edge is now routine)
- **Data are more interpretable**
  (we understand it better and trust it more)
- **More groups working with fMRI**
- **Wider applications**
  (growth $\propto$ utility)
- **Resting state has exploded.**
  (robust results being found, processing improving)
- **fMRI is more believable/established.**
  (multi-modal cross vali)

Technology

Magnet
RF Coils
Gradients
Pulse Sequences

Methodology

Paradigm Design
Pre and Post Processing
Subject Interface
Data Display and Comparison

Interpretation

Increases
Decreases
Dynamics
Locations
Fluctuations

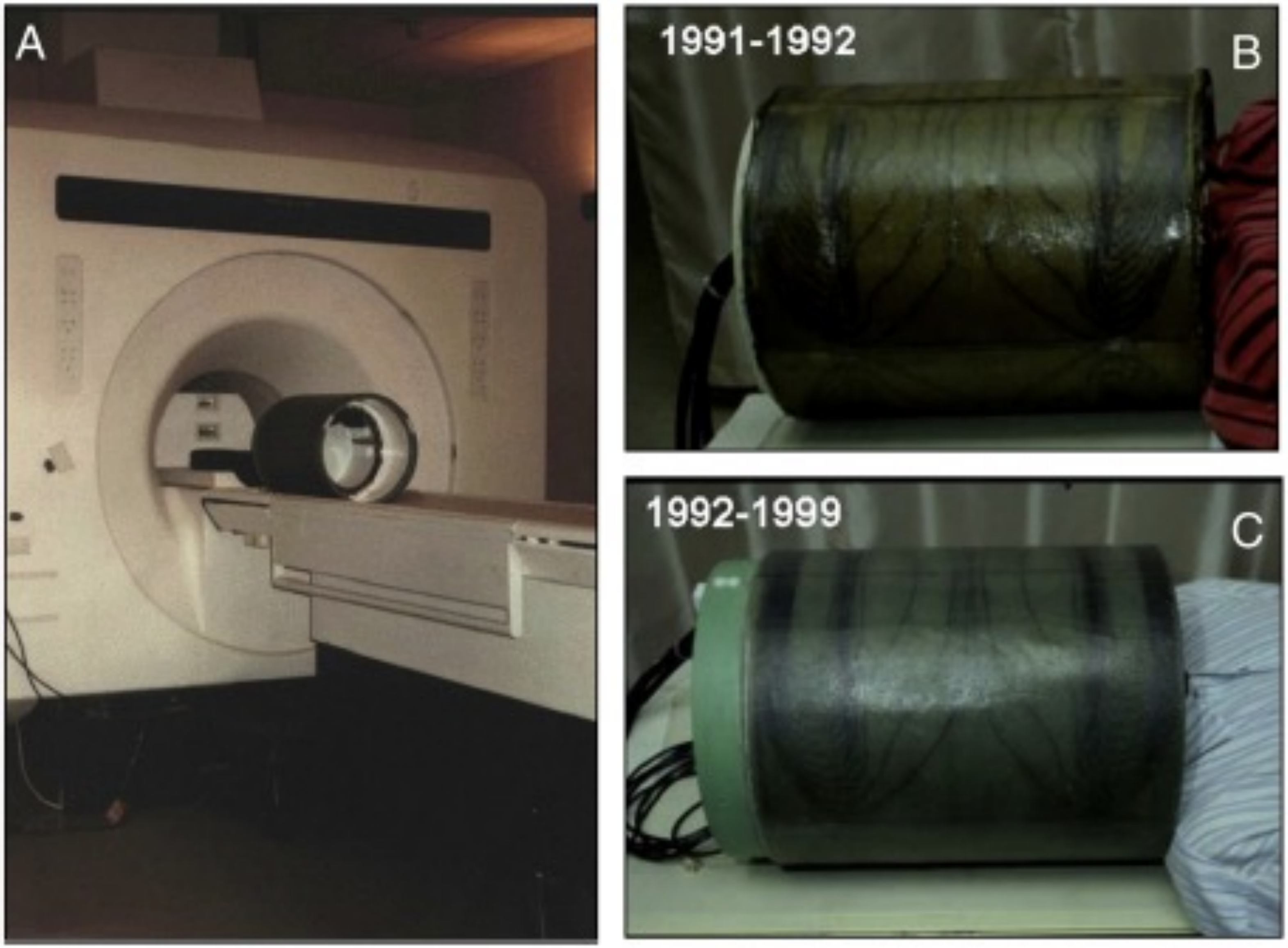
Applications

Neuroscience
Physiology
Genetics
Clinical
Law
Marketing
Entertainment

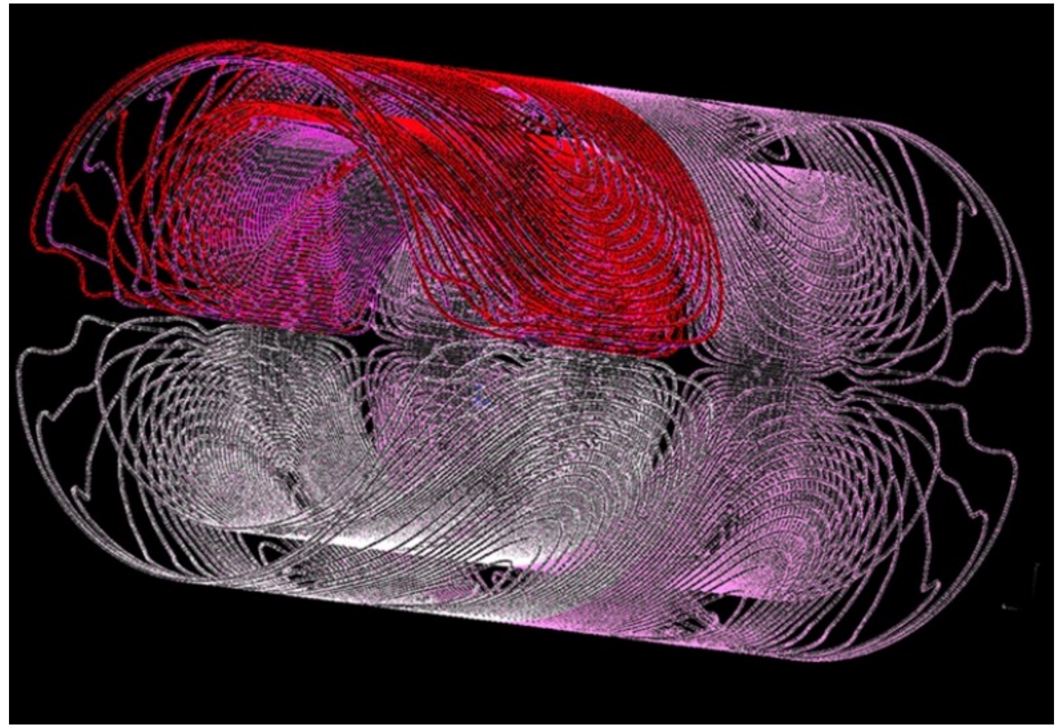
Technology is more sophisticated

Gradient coils / Amplifiers
RF coils
Processing Power

Local gradient coils needed to perform EPI



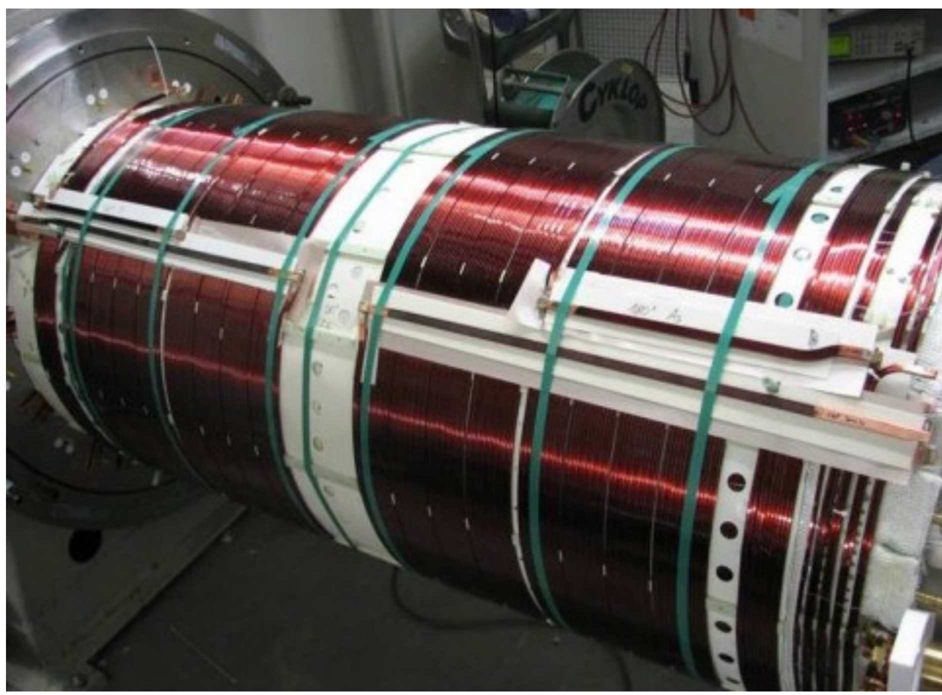
MGH Connectome Coil

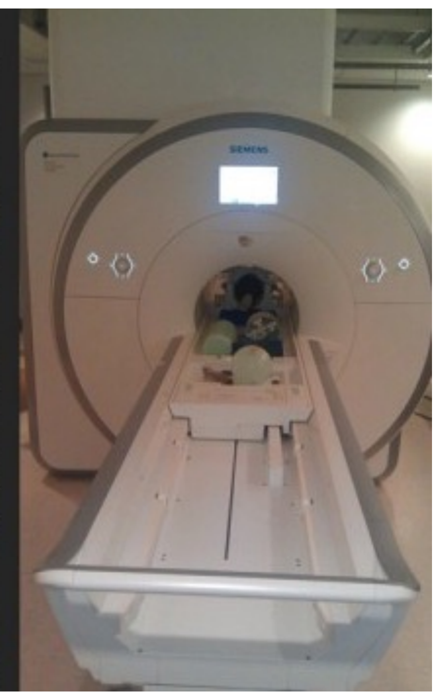


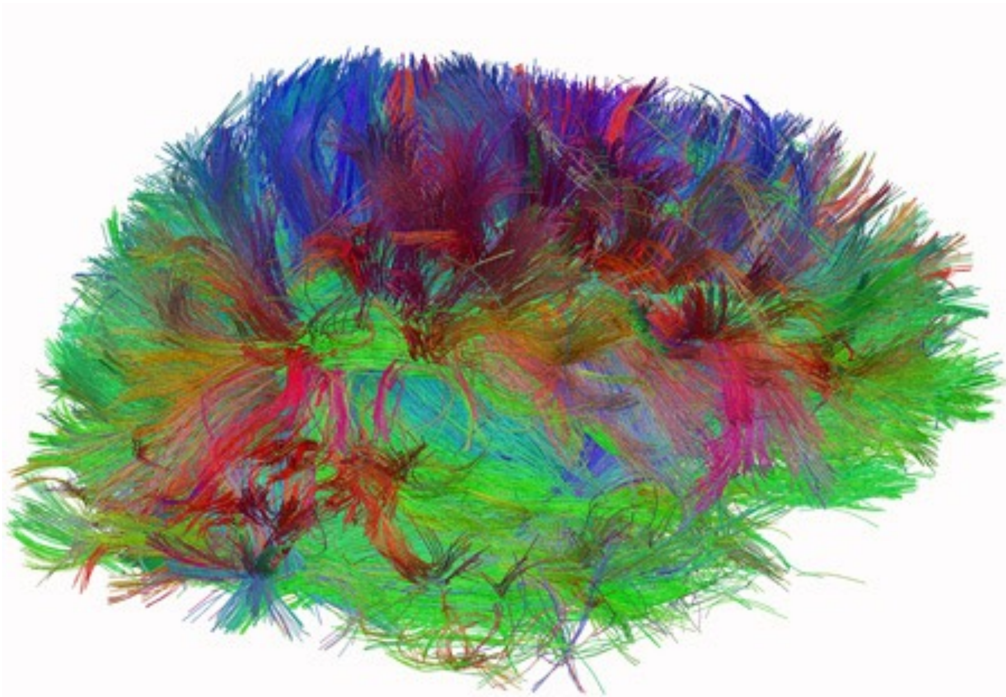
Gmax= 300 mT/m

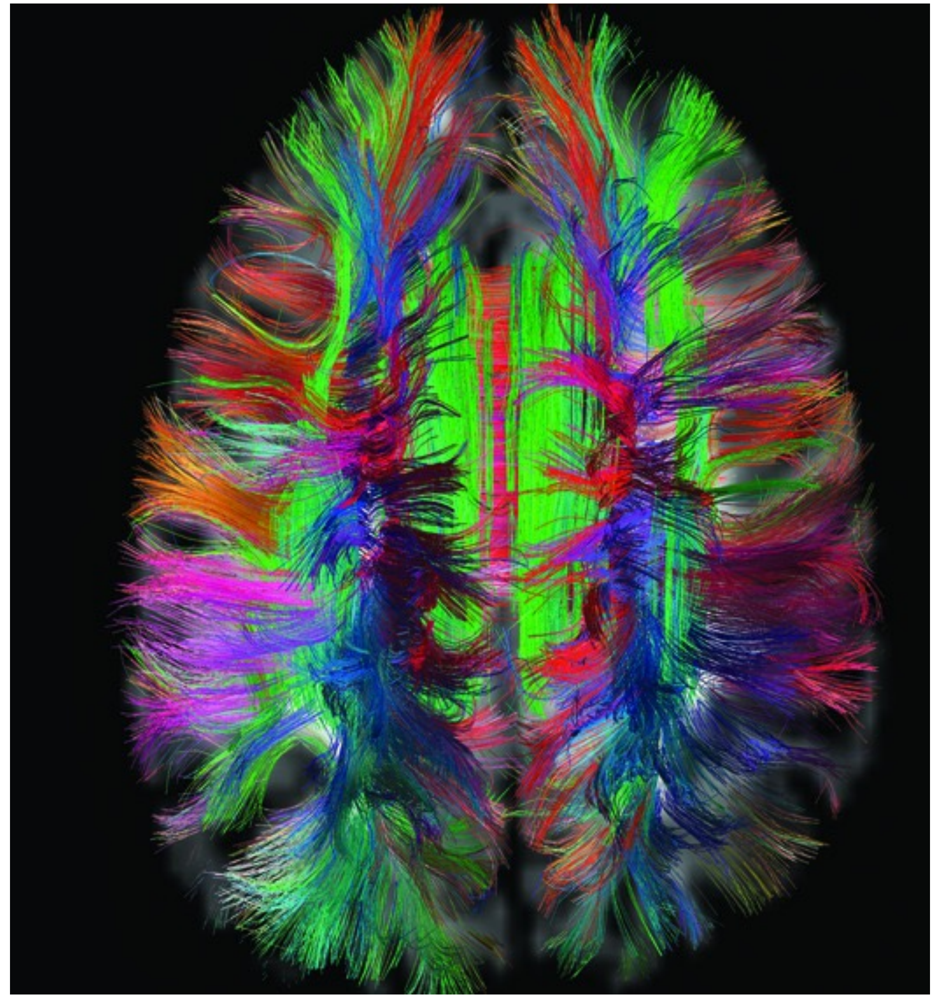
Slew rate 200 T/m/s

b - values up to 20,000 s/mm^2



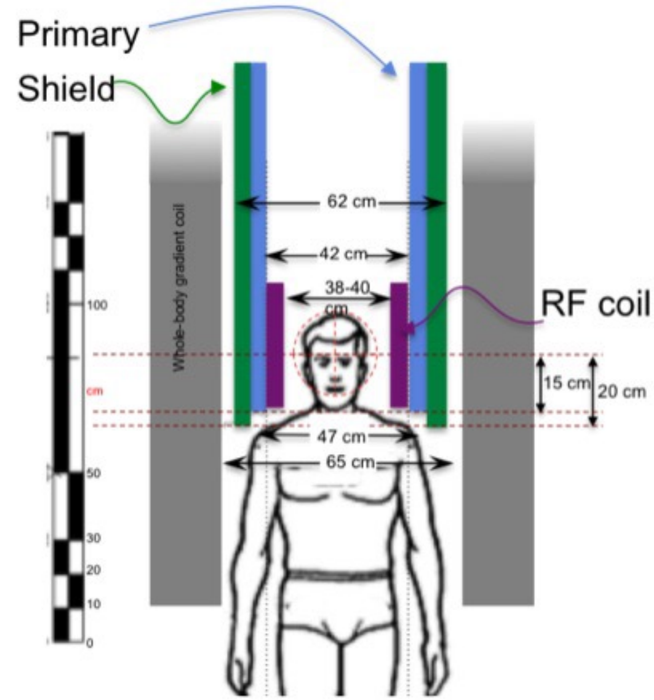


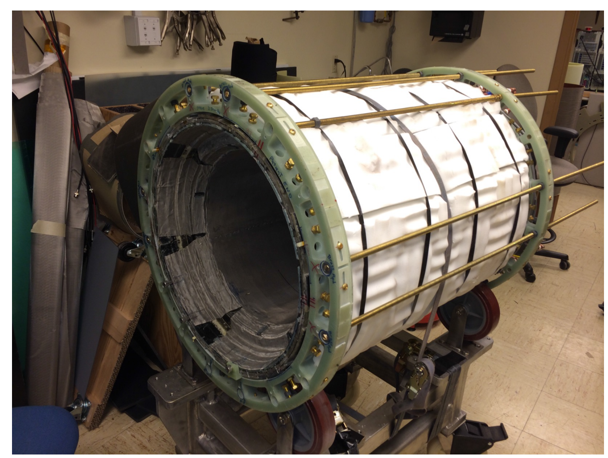




GE Prototype High performance gradient coil

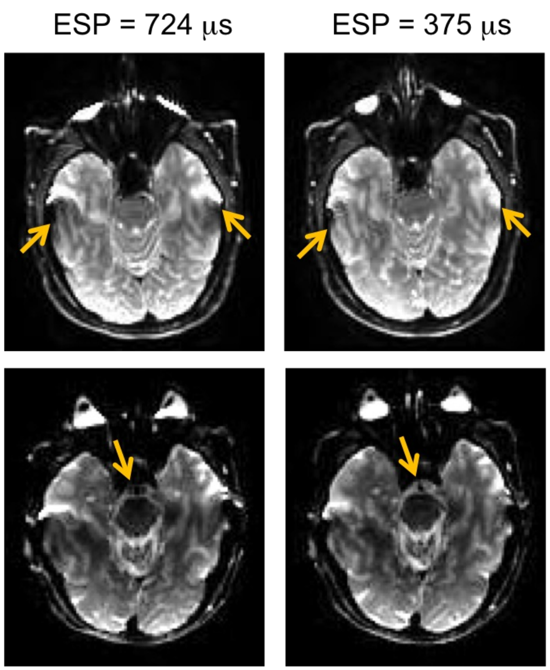
Feature	Specification
Dimensions	
Gradient outer diameter	60 cm
Gradient inner diameter	42 cm
Patient bore size (head)	37 cm
Patient bore size (shoulders and arms)	65 cm
[1]Distance from edge to FOV center @ 45-cm ID	14.5 cm
[1]Distance from edge to FOV center @ 55-cm ID	20.5 cm
[1]Distance from edge to FOV center @ 65-cm ID	28.5 cm
Performance	
Gradient maximum amplitude	85 mT/m
Gradient maximum slew rate	700 T/m/s
Imaging FOV	26 cm
Gradient non-linearity	
20-cm DSV	< 0.4% (post-gradwarp)
26-cm DSV	0.5% (post-gradwarp)
Gradient Duty Cycle	
Gradient amplitude at 100% duty cycle	56 mT/m
Gradient amplitude at 70% duty cycle	81 mT/m
Gradient amplitude at 30% duty cycle	85 mT/m



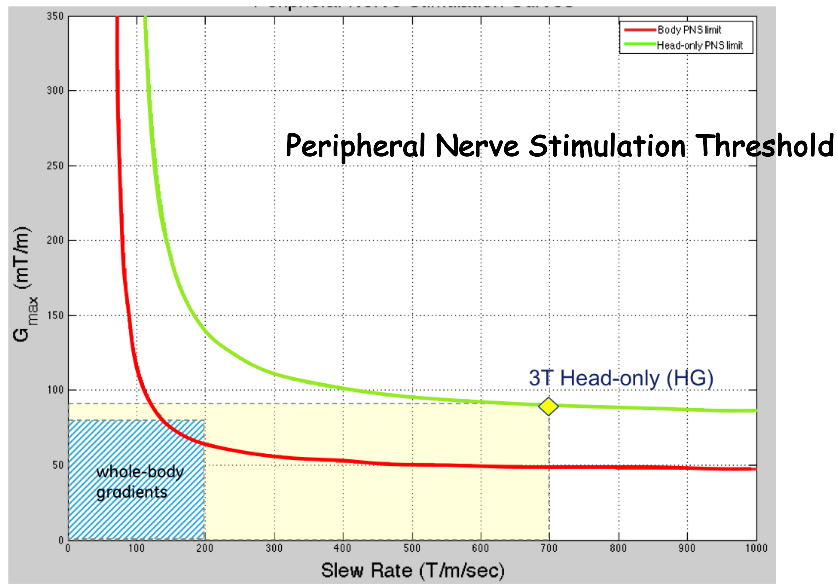


Local Gradient Coil Advantages

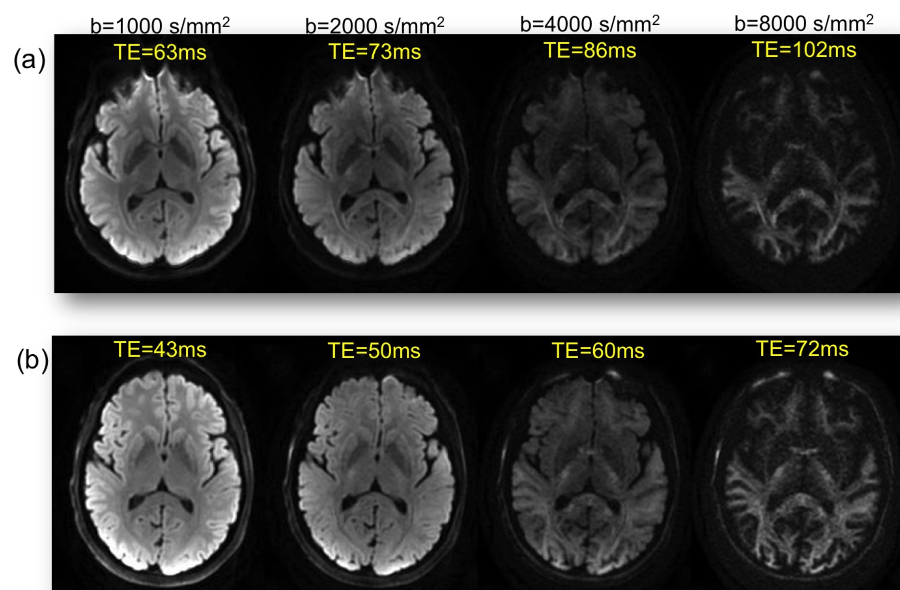
1. Shorter Readout Window Width



Examples of reduction of spatial distortion and signal pile-up in a 128 x 128, 24-cm FOV EPI acquisition
at slew rates achievable in a MR750 (130 T/m/s, echo-spacing (ESP) = 724 sec) and the HGI system (500 T/m/s,
ESP = 375 sec) at two different levels in the brain.

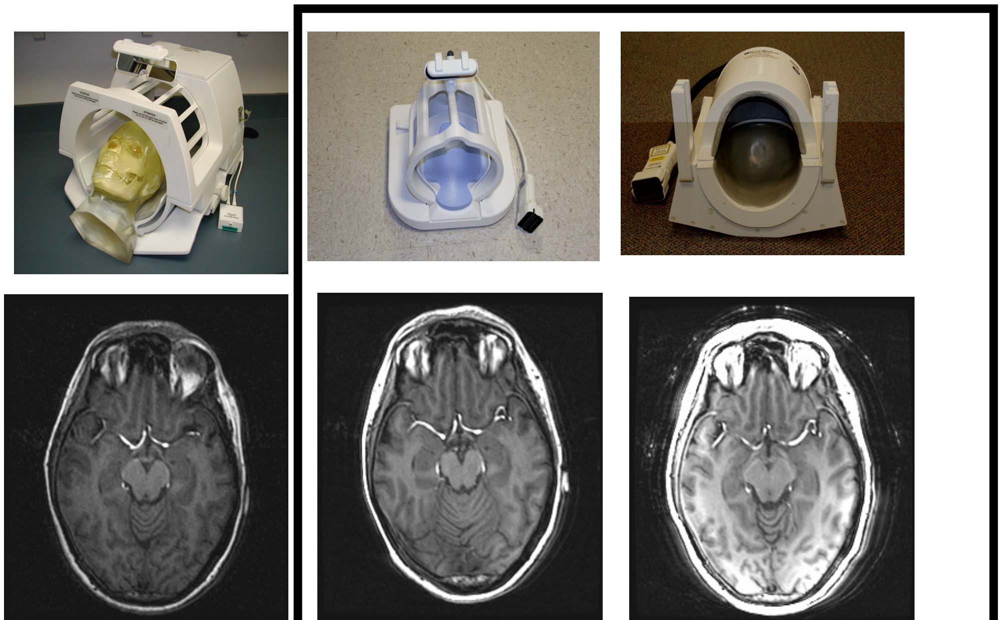


2. Shorter TE



Comparisons between diffusion-weighted EPI acquisitions for (a) whole-body MR750 system, and (b) HGI system at b-values of 1,000, 2,000, 4,000, and 8,000 s/mm2. Images were single-echo EPI acquisitions with: 24-cm FOV; 128 128 matrix; 3.2 mm sections; R=2 acceleration; 4 NEX; 30-directions; TR = 6000 ms. Echo spacing achieved was: (a) 712 s for the whole-body MR750, and (b) 376 s for the head-only HGI system. In this example, Gmax was 80 mT/m, while the slew rate was 500 T/m/s. The substantial improvement in spatial distortion with the HGI system is apparent, as well as the SNR improvement from the shorter TE times.

Commercial 8 channel parallel receiver coils

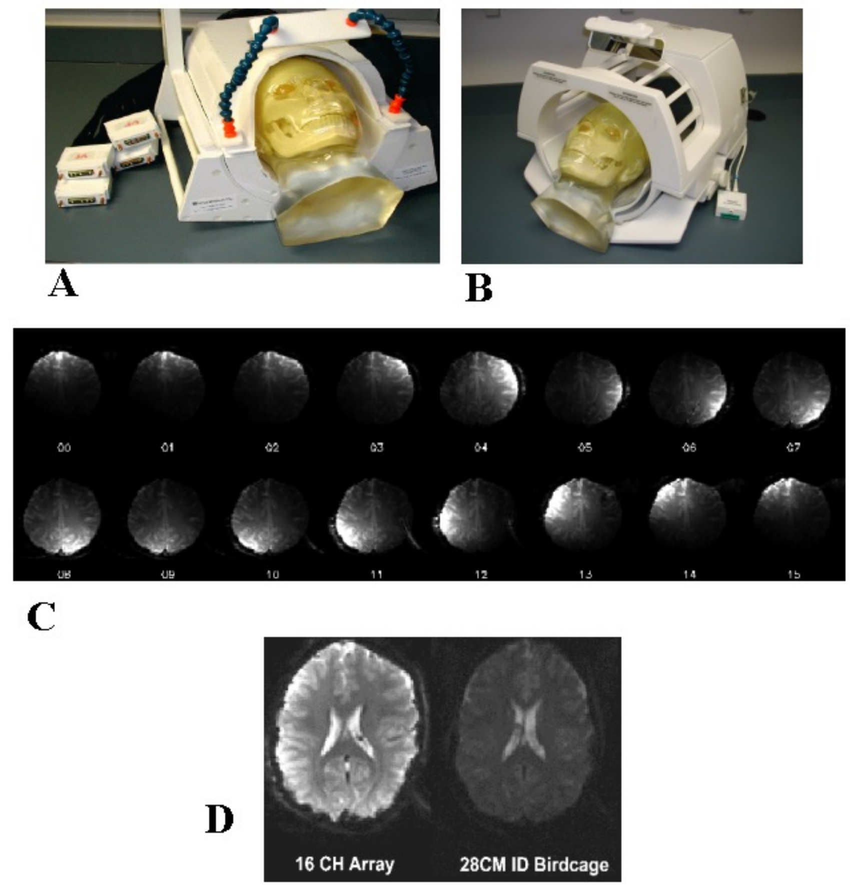


GE birdcage

GE 8 channel coil

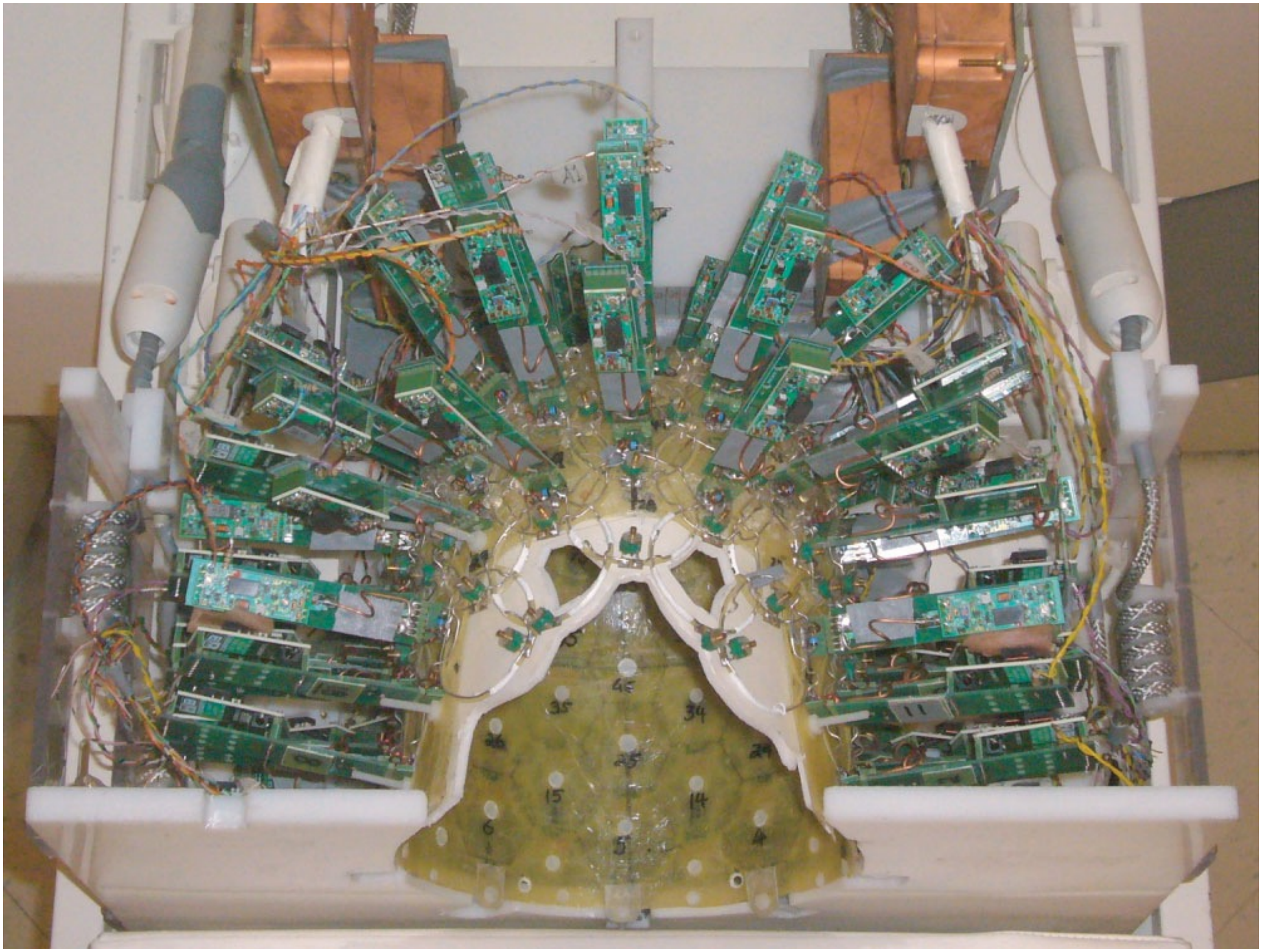
Nova 8 channel coil

Home-built16 channel parallel receiver coil



J. Bodurka, et al, Magnetic Resonance in Medicine 51 (2004) 165-171.

96 Channel Head RF Coil



G. C. Wiggins, J. R. Polimeni, A. Potthast, M. Scmitt, V. Alagappan, L. L. Wald, 96-channel receive-only head coil for 3 Tesla, MRM, 62, 754-762 (2009)

Images are better

Resolution

Contrast

Signal to Noise

Acquisition speed

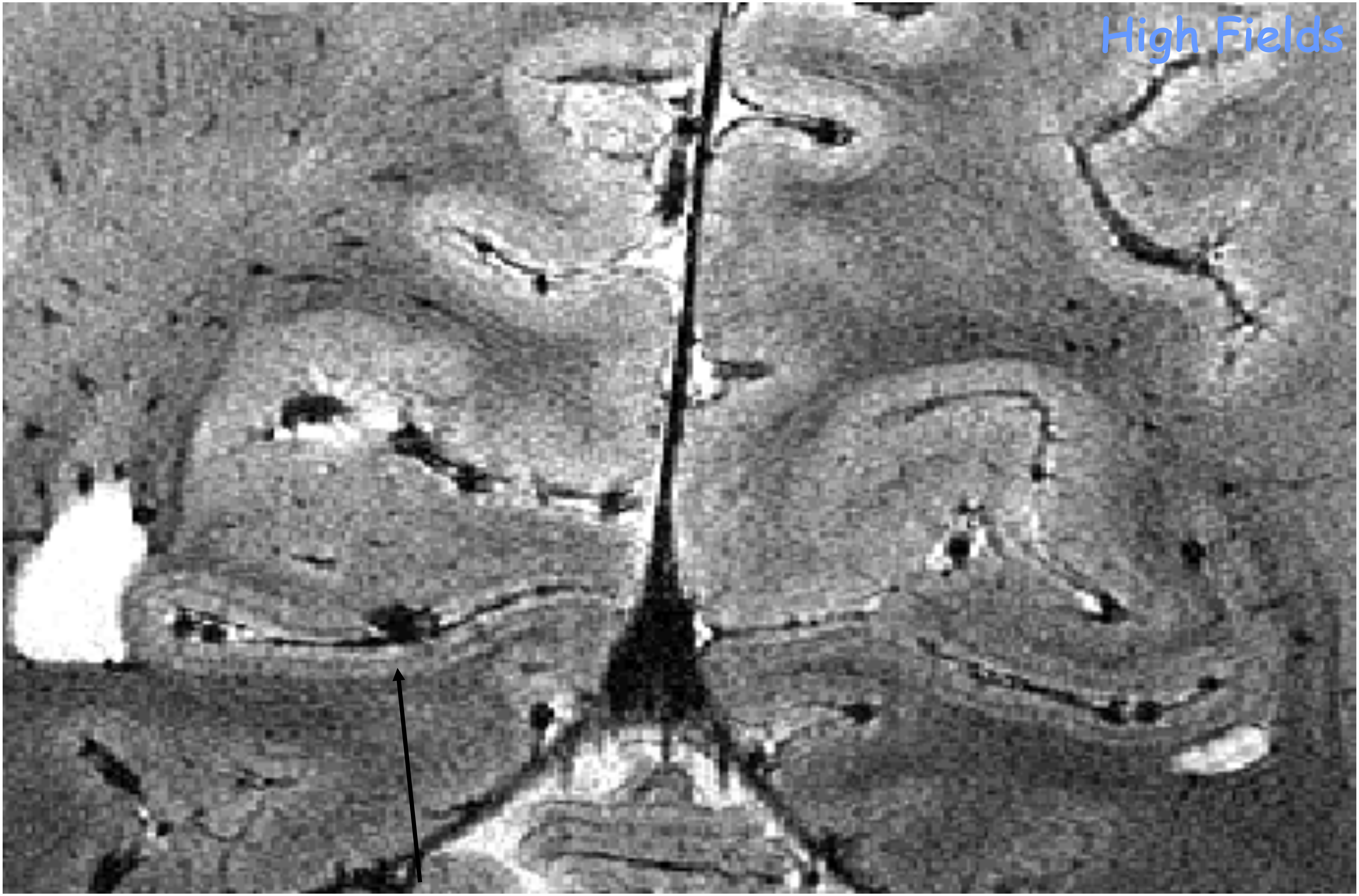
7 Tesla

GRE
TE 31ms
TR 700ms

1024x1024

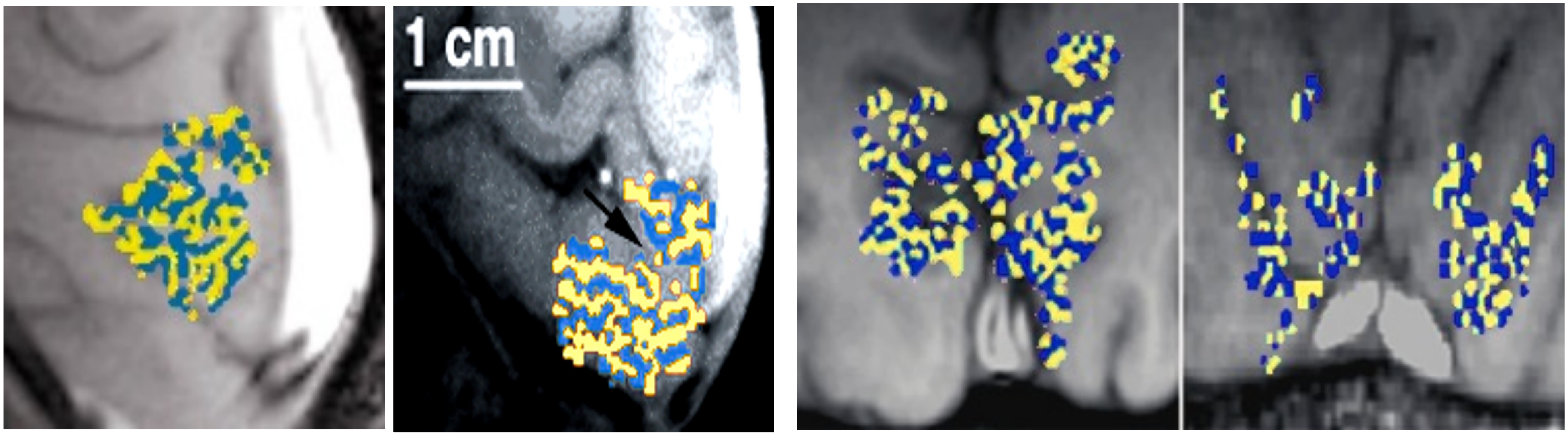
Resolution
236μm
0.5mm slice

Courtesy :
P. Van Gelderen
and J. Duyn



Layered structure in the visual cortex

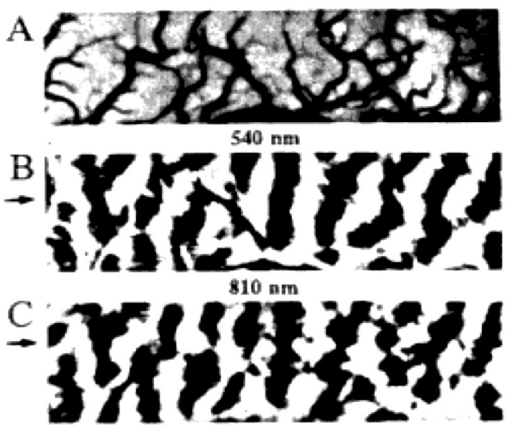
Ocular Dominance Column Mapping



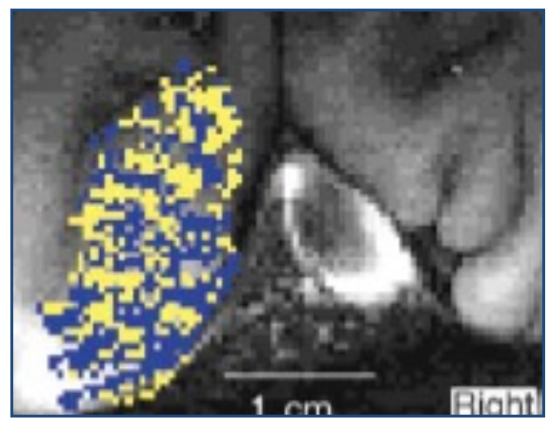
Menon, R. S., S. Ogawa, et al. (1997). J Neurophysiol 77(5): 2780-7.

0.54 x 0.54 in plane resolution

Optical Imaging

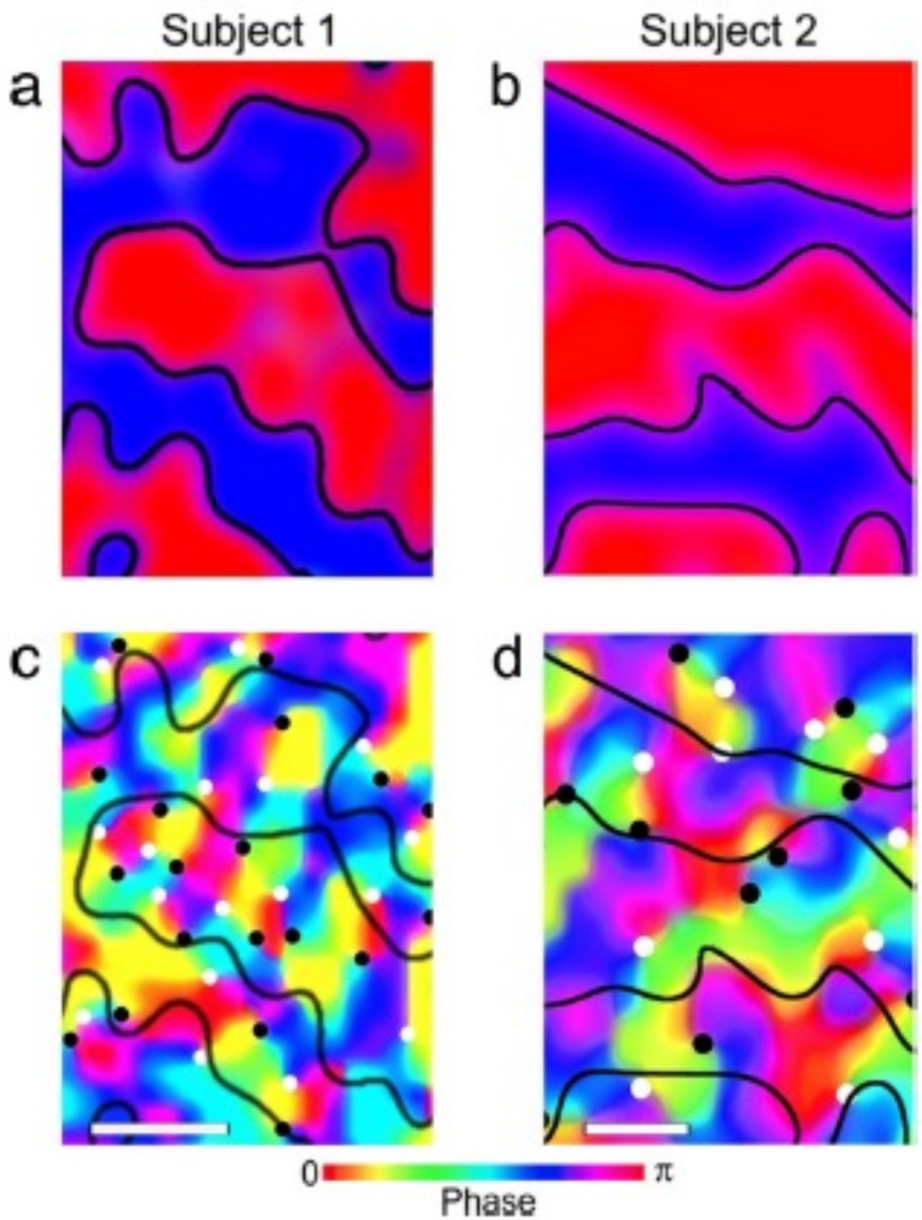


R. D. Frostig et. al, PNAS 87: 6082-6086, (1990).



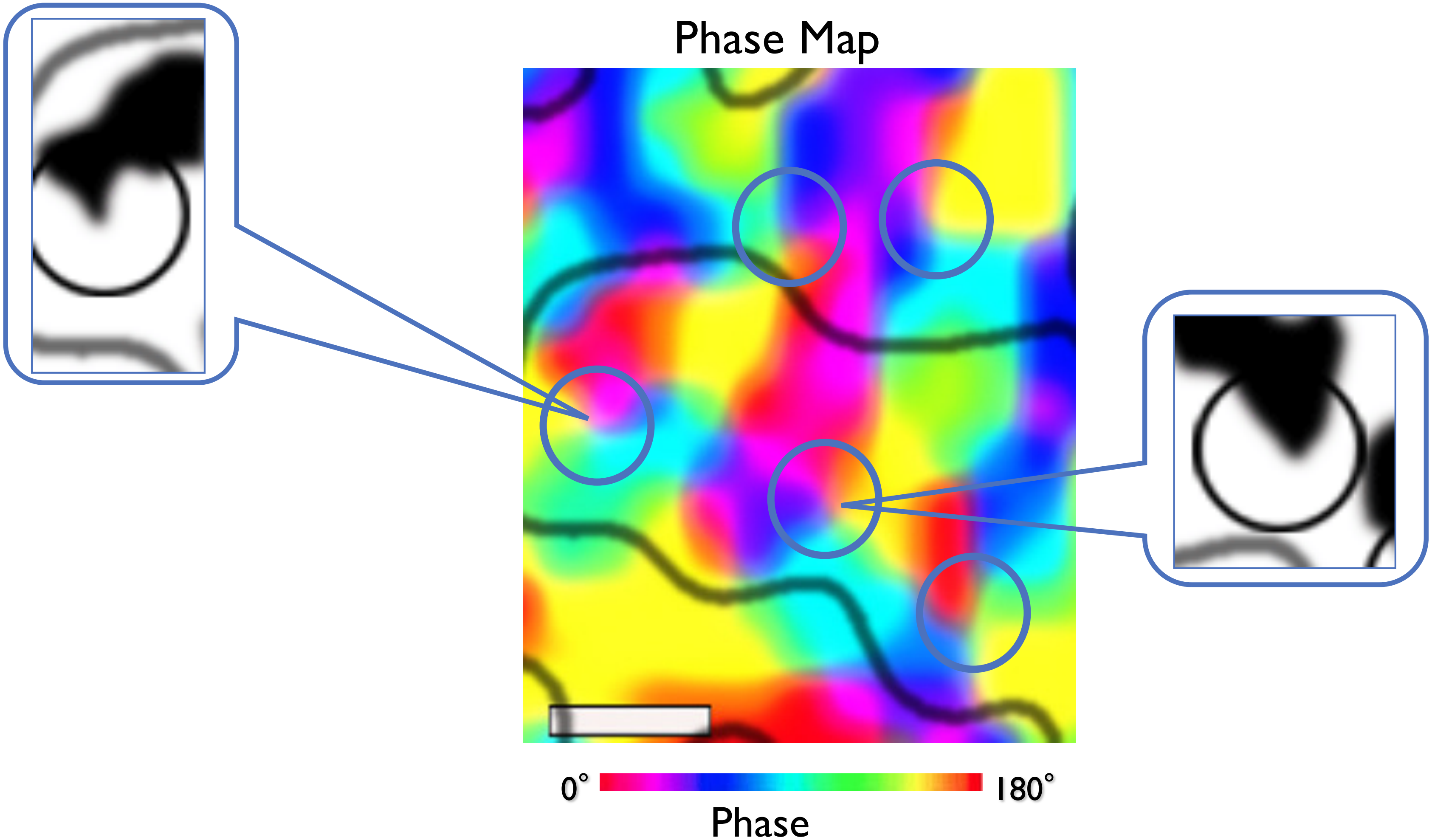
Cheng, et al. (2001) Neuron,32:359-374

0.47 x 0.47 in plane resolution



Yacoub et al. PNAS 2008

Orientation Columns in Human V1 as Revealed by fMRI at 7T



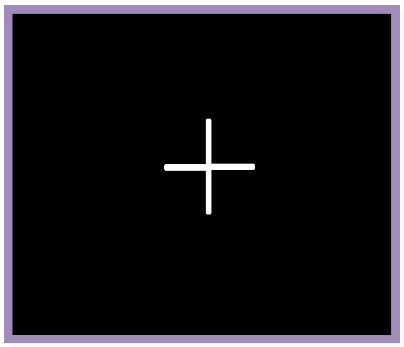
Scalebar = 0.5 mm

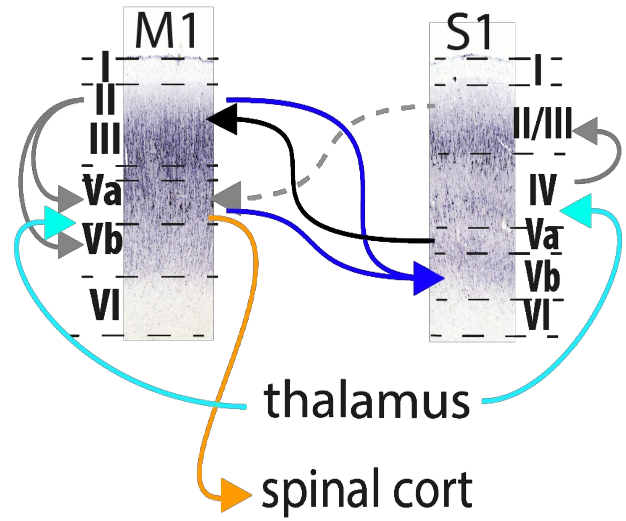
Yacoub et al. PNAS 2008

fMRI tasks to probe directional connectivity

Resting-state (12 min)

[Polimeni et al., ISMRM, 2010]



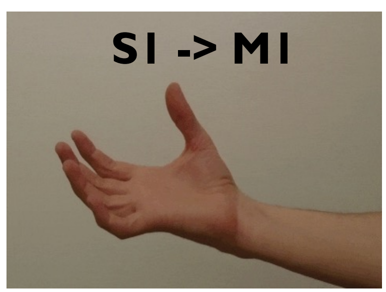


Tapping:

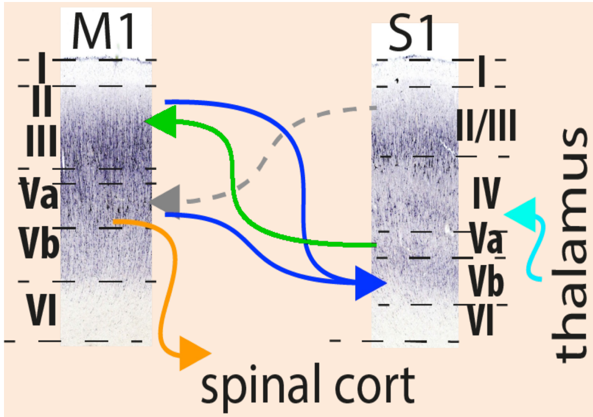
12 minutes (30 sec act vs. 30 sec rest)

fast right tapping

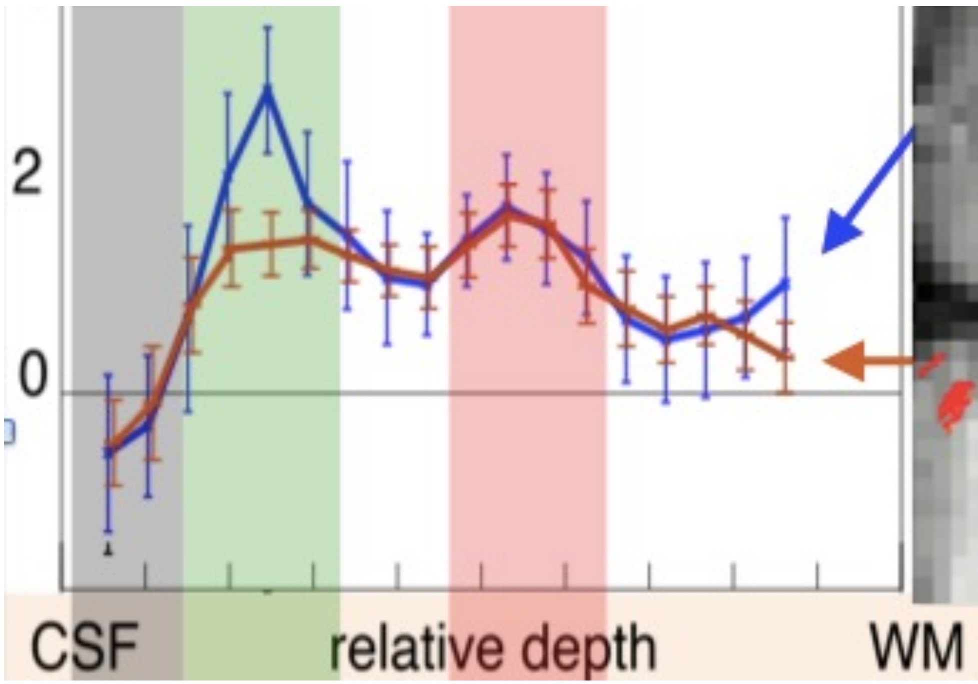
no touch

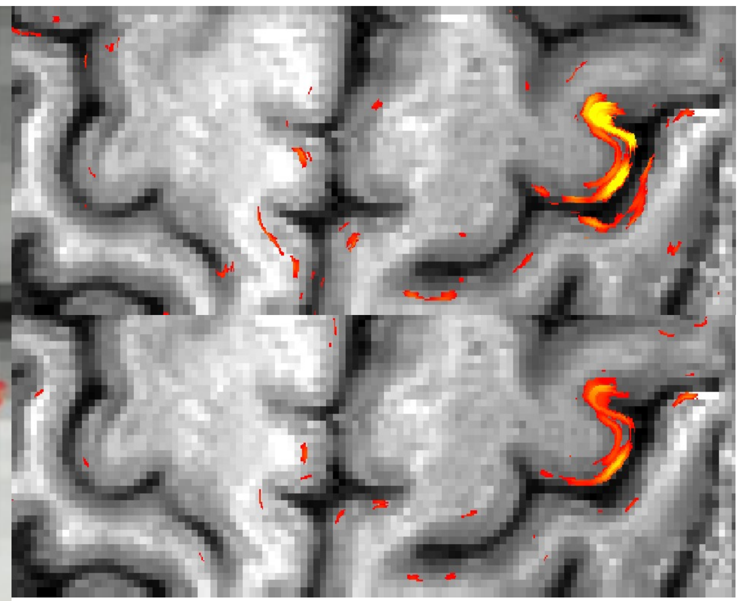


Validation with task data



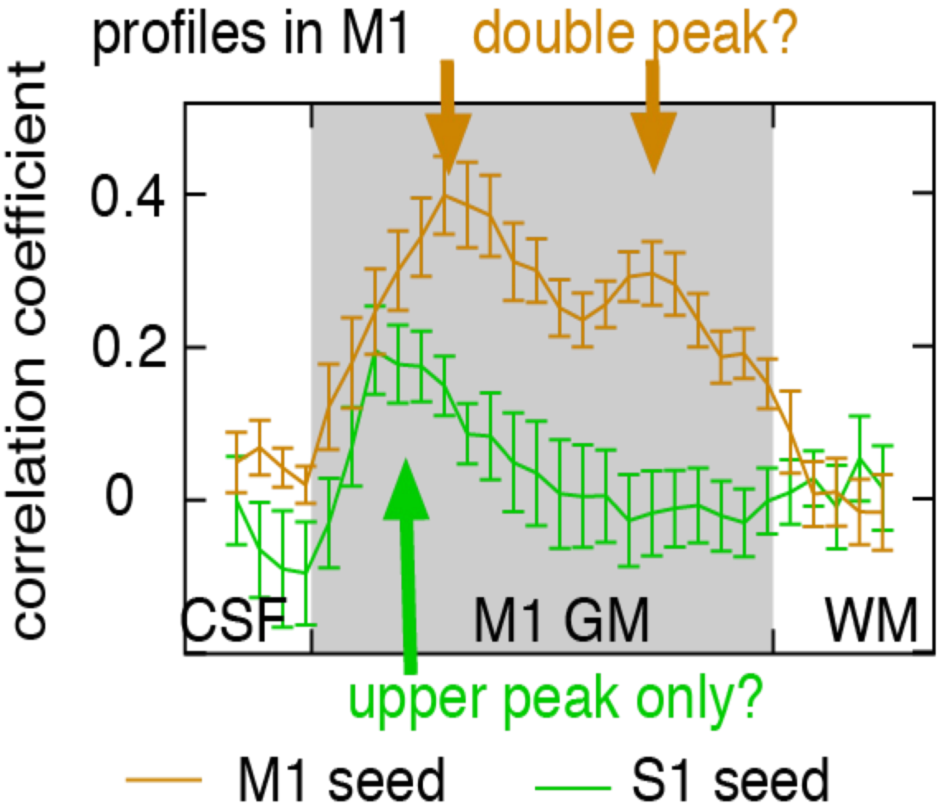
with touch

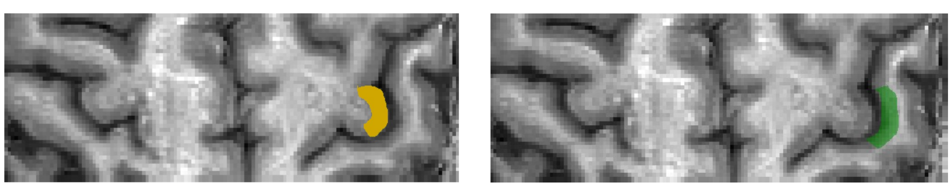


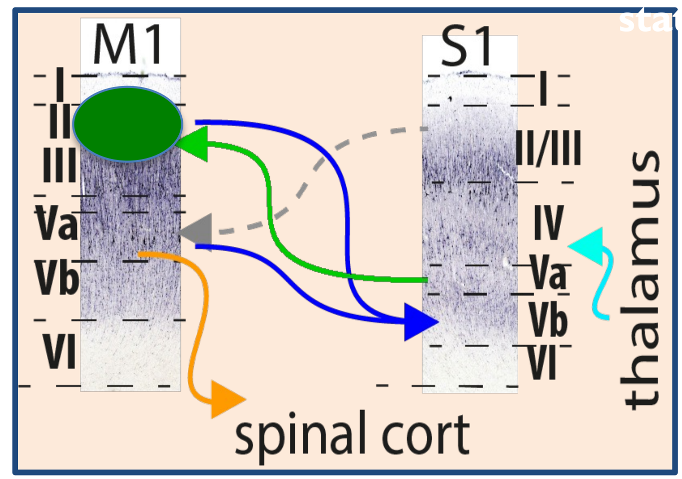


without touch

Resting state Connectivity from S1 to M1

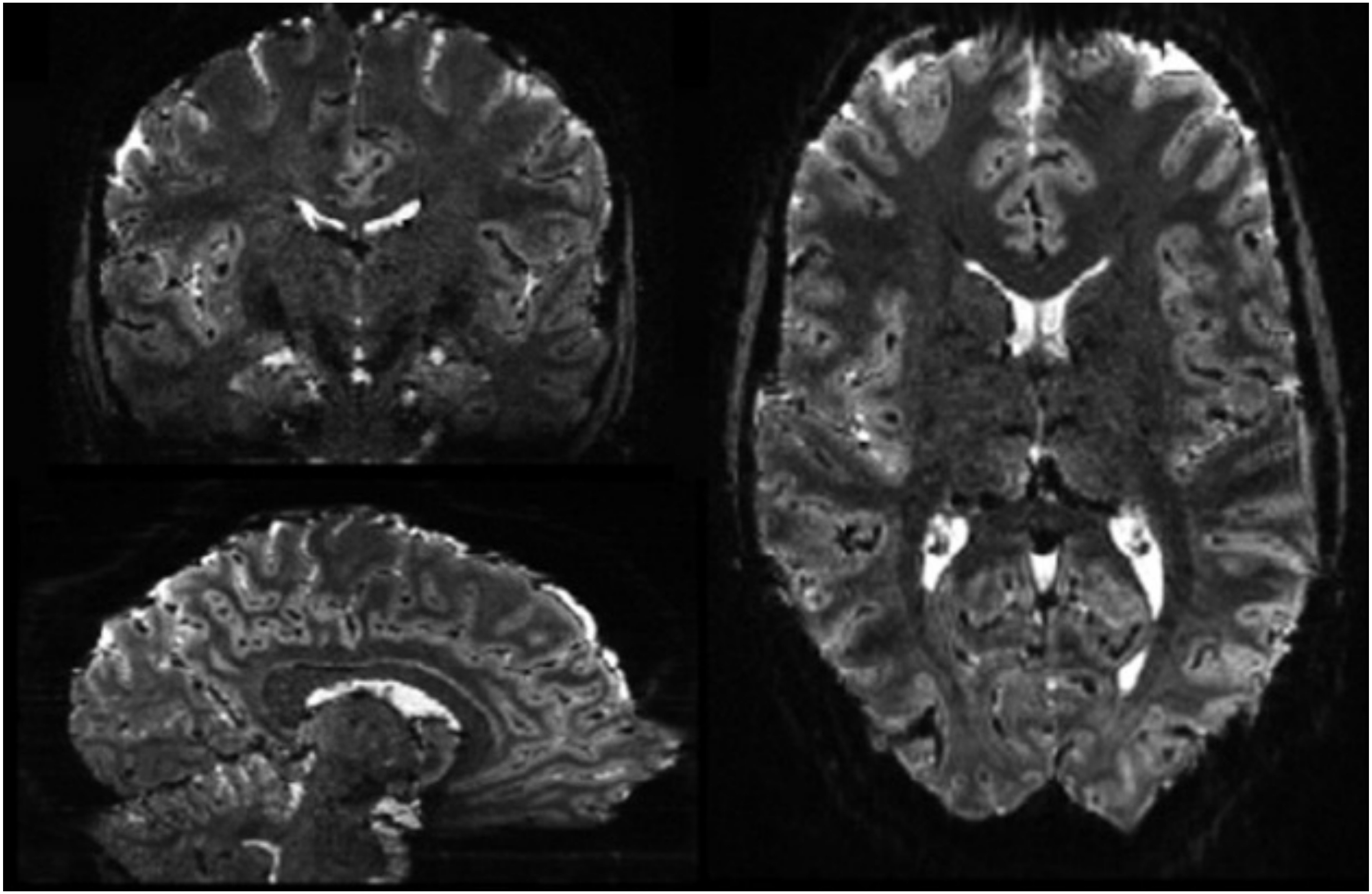






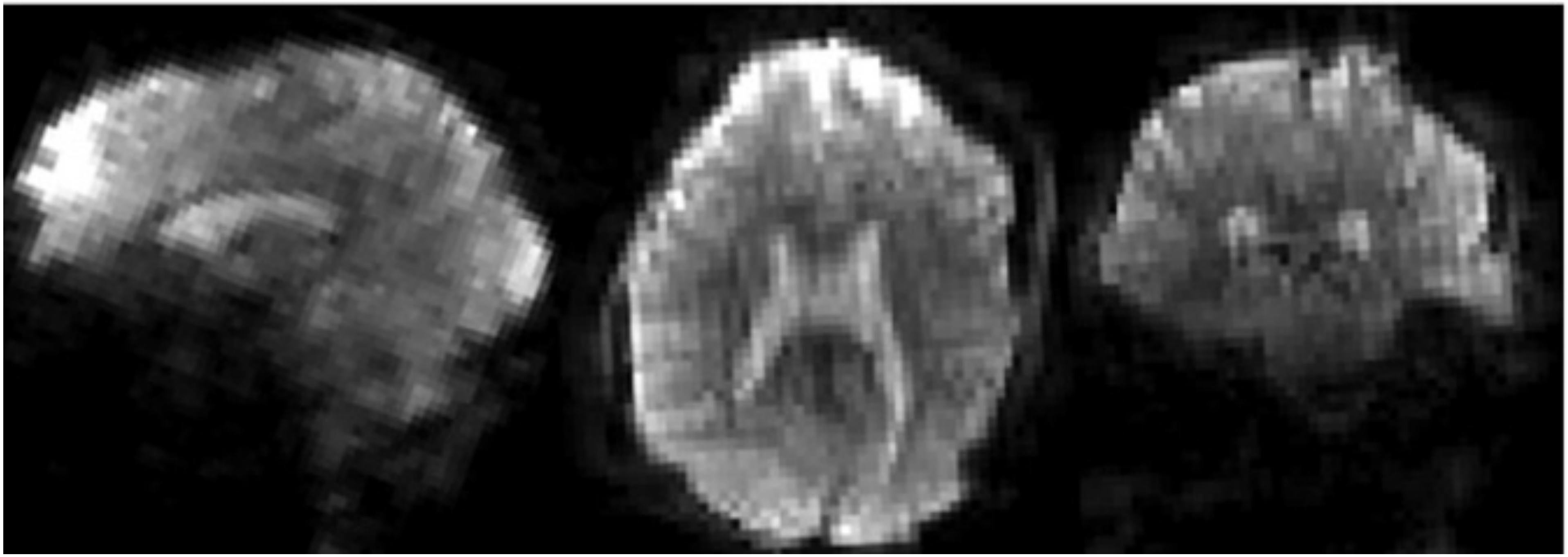
Approximate EPI Timeline

1976 P. Mansfield conceives of EPI
1989 EPI of humans emerges on a handful of scanners
$3 \times 3 \times 3\text{-}10\ mm^3$
1989 ANMR retrofitted with GE scanners for EPI
1991 Home built head gradient coils perform EPI
1996 EPI is standard on clinical scanners
2000 Gradient performance continues to increase
2002 Parallel imaging allows for higher resolution EPI
2006 $1.5 \times 1.5 \times 1.5\ mm^3$ single shot EPI possible
2009 At 7T sub – mm single shot EPI for fMRI is possible
2010 60 slices / sec multi-band EPI for fMRI is possible
2014 Multi-band EPI widely distributed on research scanners



1 mm isotropic at 7T, 120 slices acquired with a TR = 2.88 sec.
(Non-GRAPPA and CAIPIRINHA would take 8.64 sec.)

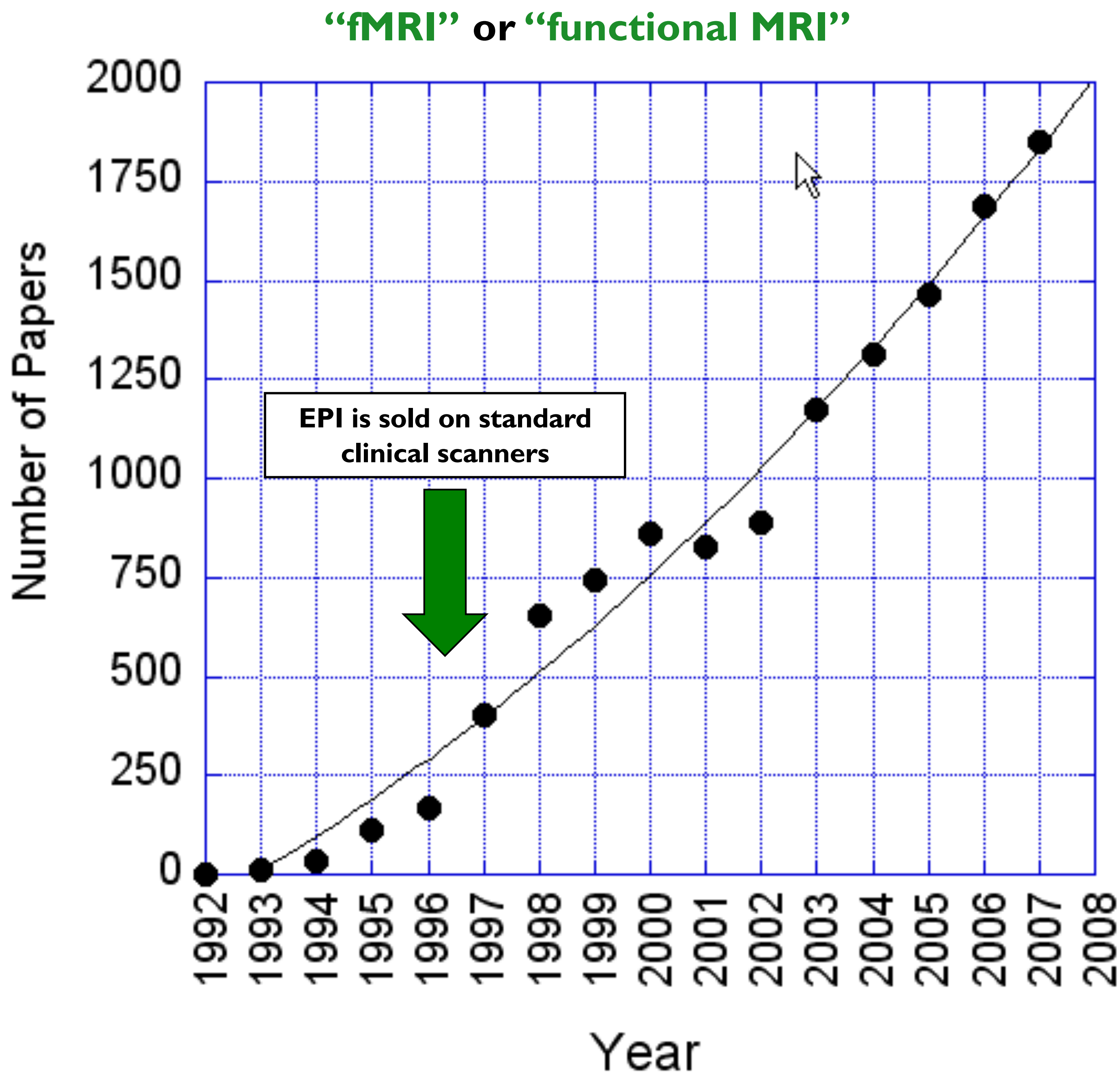
L.L. Wald, NeuroImage pp. 1221-1229, 62 (2012)



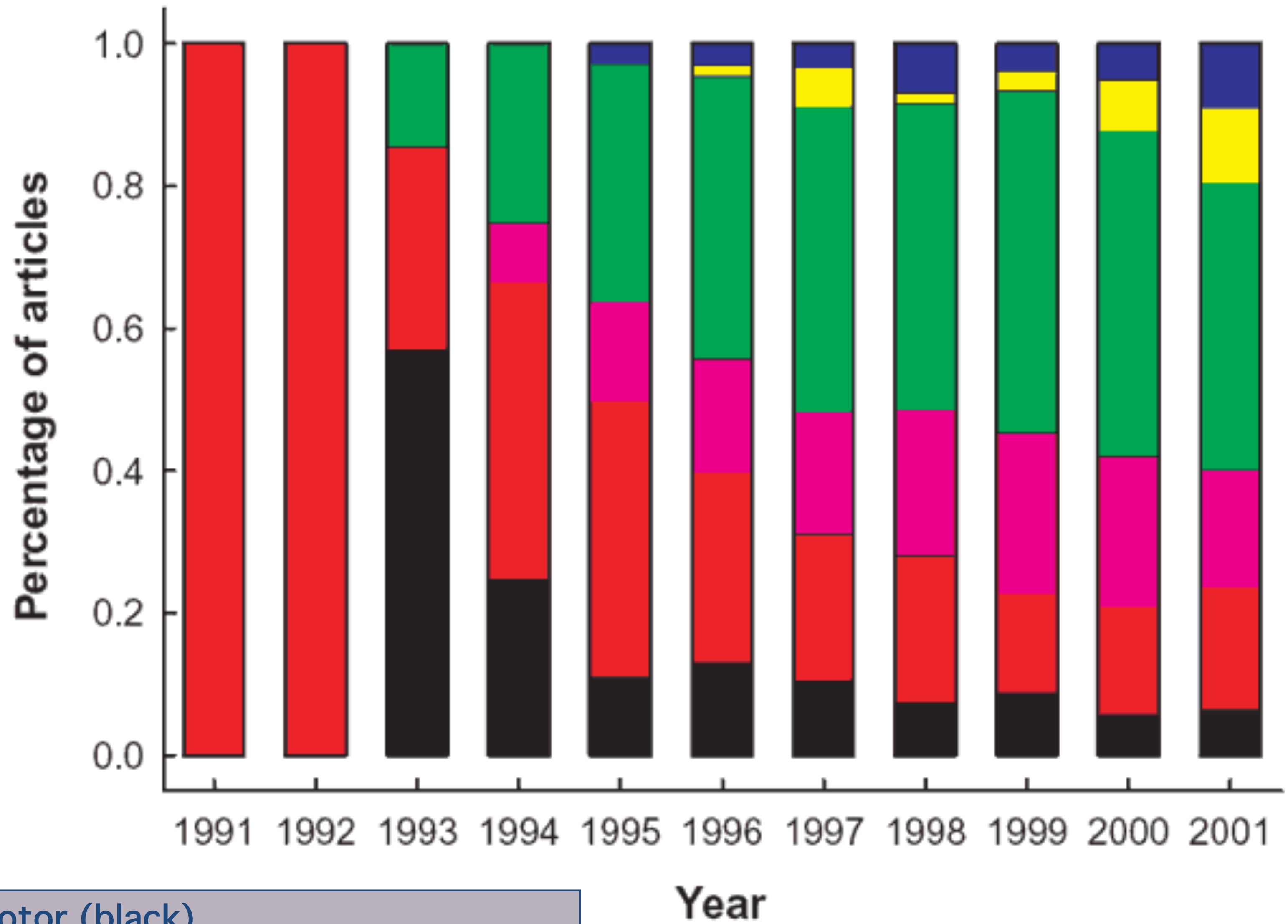
Single shot, whole brain 3T Echo Volume Imaging (EVI) in 120 ms.
64 x 64 x 56 resulting in 3.4 mm voxel size.

L.L. Wald, NeuroImage pp. 1221-1229, 62 (2012)

Scopus: Articles or Reviews Published per Year



Data are more interpretable



Motor (black)
Primary Sensory (red)
Integrative Sensory (violet)
Basic Cognition (green)
High-Order Cognition (yellow)
Emotion (blue)

J. Illes, M. P. Kirschen, J. D. E. Gabrielli,
Nature Neuroscience, 6 (3)m p.205

Technology

- Magnet
- RF Coils
- Gradients
- Pulse Sequences

Methodology

- Paradigm Design
- Pre and Post Processing
- Subject Interface
- Data Display and Comparison

Interpretation

- Increases
- Decreases
- Dynamics
- Locations
- Fluctuations

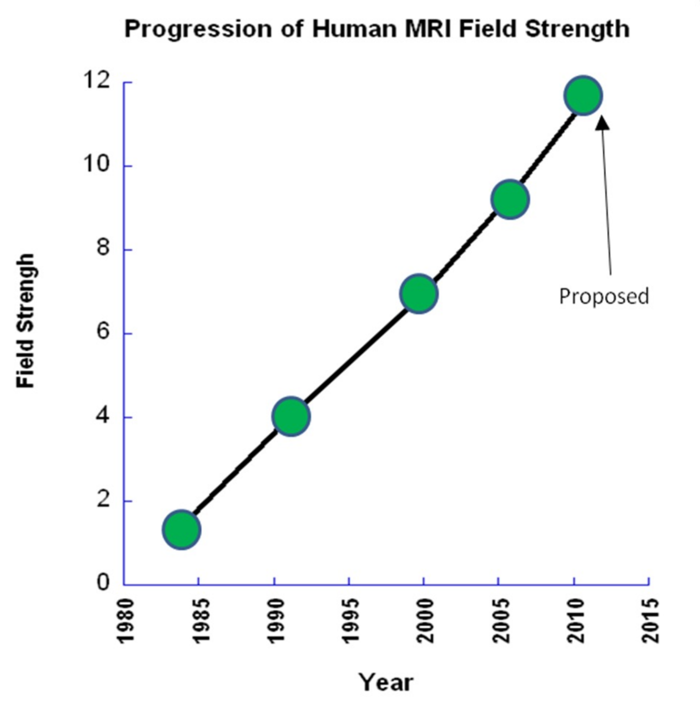
Applications

- Neuroscience
- Physiology
- Genetics
- Clinical
- Law
- Marketing
- Entertainment

Magnet

Currently:

- **We have about 50 7T scanners and almost one 11.7T scanner**



In 5 years:

- **Two 11.7T scanners**

In 10 years:

- **High field plateaus as we improve other aspects. Perhaps one scanner at higher than 11.7T.**

RF Coils

Currently:

- **Most use 32 channel receive only.**

5 Years:

- **Most will use 32 to 64 channel receive only & 8 channel excite.**
- **Cutting edge will be 128 channel receive and 8 channel excite.**

10 Years:

- **Most will use 32 to 64 channel receive only & 8 channel excite.**
- **Cutting edge will be 512 channel receive and 64 channel excite.**

Gradients & shims

Currently:

- **Most use 6 Gauss/cm & 3'rd order shims**
- **Rise time determined by biologic limits**
- **Cutting edge: 30 Gauss/cm for Diffusion Imaging (DSI).**

5 Years:

- **Most will use 6 to 12 Gauss/cm. No change in rise time.**
- **More local gradient coils (30 Gauss/cm) for head-only imaging.** **(Rise time can be a bit faster as it bypasses bio-limits)**
- **Non-orthogonal shims implemented.**
- **Field Camera based feedback in more common use.**
- **Separation into gradient strength optimized vs speed optimized. Easily switchable head modules.**

10 Years:

- **Most will use 6 to 20 Gauss/cm. No change in rise time.**
- **Cutting edge will be 512 channel receive and 64 channel excite.**
- **Shim will be subject specific and essentially solved by a combination of higher order shims, local non-orthogonal shims and passive shims.**

Pulse Sequences

Currently:

- **2 mm isotropic EPI is common. Many still use 3 mm isotropic.**
- **Cutting edge: 128 slices in 2 sec, 1 mm isotropic, single shot EPI**

5 Years:

- **1.5 mm isotropic, 128 slices in 2 sec, will be commonly used.**
- **Multi-echo will be more commonly used.**
- **Cutting edge will be compressed sensing strategies for fMRI.**
- **Cutting edge will also be 100 um single shot EPI.**
- **Integration of acquisition and goal directed analysis (real time calibration, multi-contrast fusion, etc..)**

10 Years:

- **1.5 mm isotropic, 128 slices in 2 sec, will be commonly used.**
- **Embedded contrast (i.e. multi-echo, simultaneous flow/BOLD/volume) will be more common as this will be critical for specific information extraction and time series cleanup.**

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Most exciting trends in Applications

•From Populations to Individuals

•Longitudinal fMRI / MRI studies over multiple time scales

•Clinical Use:

Current: **pre-surgical mapping, "locked-in" patients.**

Future: **psychiatric assessment, behavioral prediction, drug effect prediction, neurologic assessment, genetic correlation, differential diagnosis of PTSD vs TBI, recovery/plasticity assessment, therapy with real-time feedback, neuroinflammation.**

For the Individual:

- psychiatric assessment behavioral prediction
- drug effects
- neurologic assessment using resting state
- differential diagnosis of PTSD vs. TBI
- recovery/plasticity assessment
- therapy with real-time feedback
- Machine Learning will augment all clinicians reading scans as the information is highly multivariate and very subtle.

The challenge:

- Effect size / variability > 10
- Classification and modeling can improve this ratio…depending on the question being asked.
- Needs large databases and well curated data to generate biomarkers.

What Areas Seem Promising?

- **High Resolution fMRI for *activation and fluctuations* – layers, columns, and causal connections everywhere. Connectivity vs Magnitude.**
- **Non-canonical responses everywhere.**
- **Resting & Activation hybrid paradigms to draw out differences in individuals.**
- **Resting and activation-related multimodal decoding.**
- **Dynamic Correlation Analysis – brain "state" classification.**
- **Steady improvement in simultaneous neuromodulation.**
- **Data and Code Sharing explosion.**
- **Biomarker & Individual Assessment Explosion.**
- **Machine learning to augment all analysis.**
- **Synthetic Anatomic Contrast (combination of multiple contrasts)**

What could change everything?

- **Room temperature superconductors – *wearable scanners?***
- **Noninvasive nano probes - *electrical & hemodynamic & metabolic contrast.***
- **One critically useful biomarker or clinical application – *inroad to clinical propagation – leading to more rapid growth overall.***
- **Reliable layer dependent fMRI – *to tease about network causality and perhaps inhibition/excitation.***

In 20 years

Technology

Field Strength -7T most common,
-19 T human scanner in place
-wearable 1.5T scanner helmet
-ultra low (Larmor = brain frequencies)
RF Coils -128+ arrays common, flexible, highly configurable, micro-coils
Gradients – Flexible, wearable, up to 100 G/cm
Shim – Solved.
Pulse Sequences -automated optimization based on menu of what's desired
-multiple simultaneous contrast and synthetic contrasts the norm
Image resolution -50 um common, 10 um doable

Methodology

Real time
Fully automated real time scanning, analysis, and assessment
Wireless, comprehensive subject interface
-eeg, nano-electrode implants
-nerve transmission
-temperature
-muscle tension
-eye position
-respiration, CO2, heart, blood pressure
-hormone level
-GSR
Optogenetics
Focused acoustic activation
3D coordinate system in decline, new network-based system

Interpretation

We will be using every aspect of signal:
-magnitude
-undershoot
-fluctuations at each frequency and phase
-transients
-rise time
-fall time
-refractivity
-slow trends
-NMR phase
We will have full calibration and likely new contrast agents
-metabolism will be routine
All non-neuronal noise will be completely removed

Applications

Neuroscience
Physiology
Genetics
Psychotherapy
Physical therapy
Education (track activation, myelin and grey matter changes)
Lie detection (motivation, sincerity & bias detection)
Biofeedback for self improvement
Job testing and screening
Entertainment (reality shows, amusement parks…)
Brain-Interfaced Video games
Communication enhancement
Brain Computer interface guidance
(where to put the nano-electrodes and nano-stimulators)
MRI scan part of routine checkup

Most studies will be resting state/activationhybrids with machine learning to do all the heavy lifting to interpret

Thank you!

- **Attendees**
- **Speakers**
- **Roark Maccado & Dorian Van Tassell**

The End