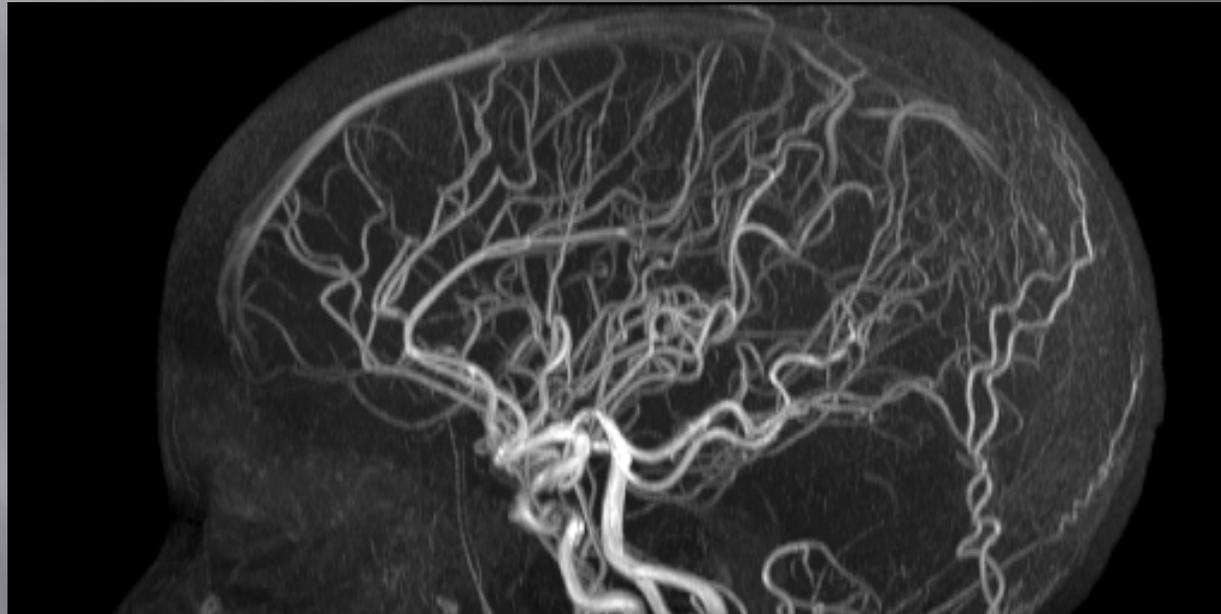


Gradient echo or T2 weighted
imaging: An introduction and
some clinical applications*



E. Mark Haacke, PhD, nmrimaging@aol.com
Director, MR Research Facility, Wayne State University
Detroit, Michigan

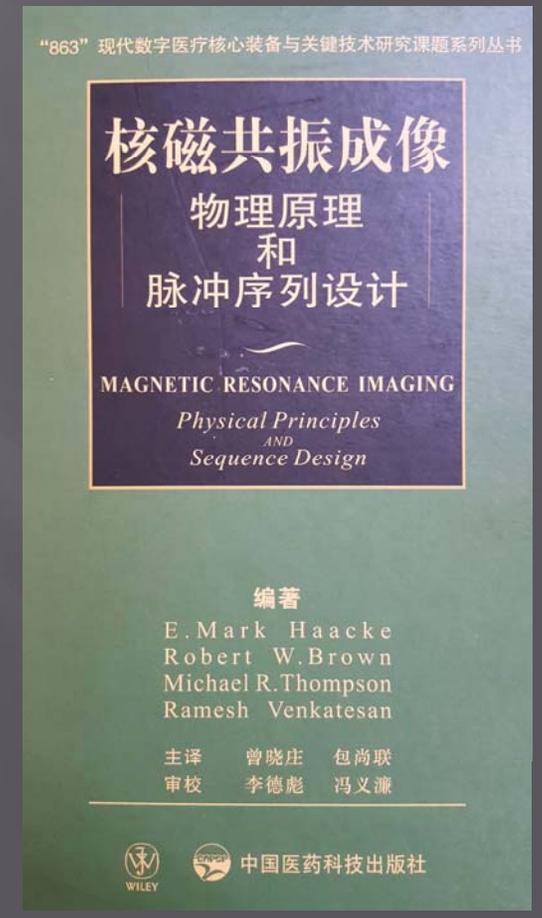
Honorary Faculty Positions

Visiting Professor (1999), *"The Roentgen Professor of Physics"*,
Wuerzburg, GERMANY

Visiting Foreign Professor (2012-2017),
Northeastern University, Shenyang, CHINA

Visiting Professor (2014),
"The Copernicus Professor of Physics",
University of Ferrara, Ferrara, ITALY

Visiting Professor, *"Zijiang Visiting Scholar"*
East China Normal University, Shanghai
CHINA (2014-2016) and (2014-2018).
"Top 1000 Talent Foreign Professors"



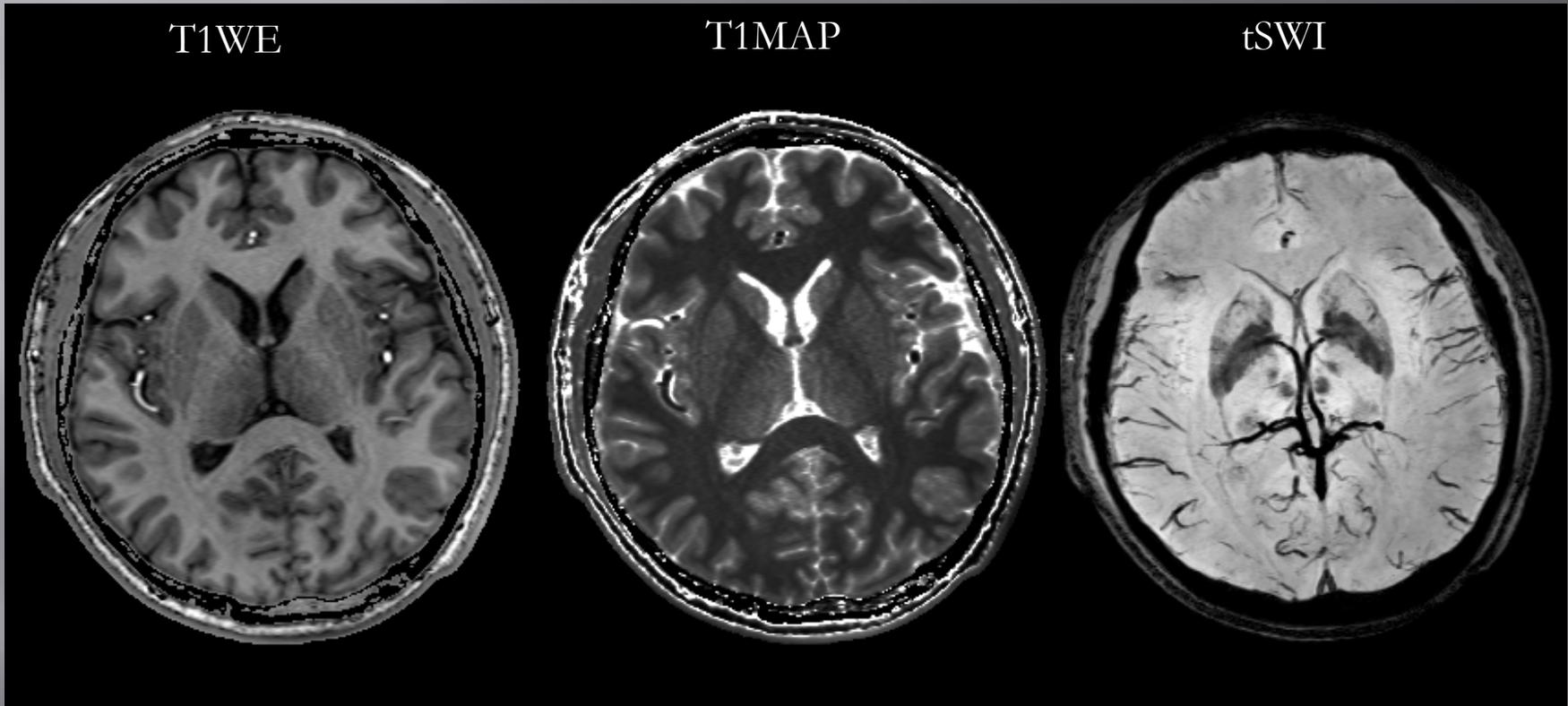
Ruminations

Bai Suzhen Ivory Carvings



Hangzhou, Westlake, *China*

Magnetic Resonance Imaging

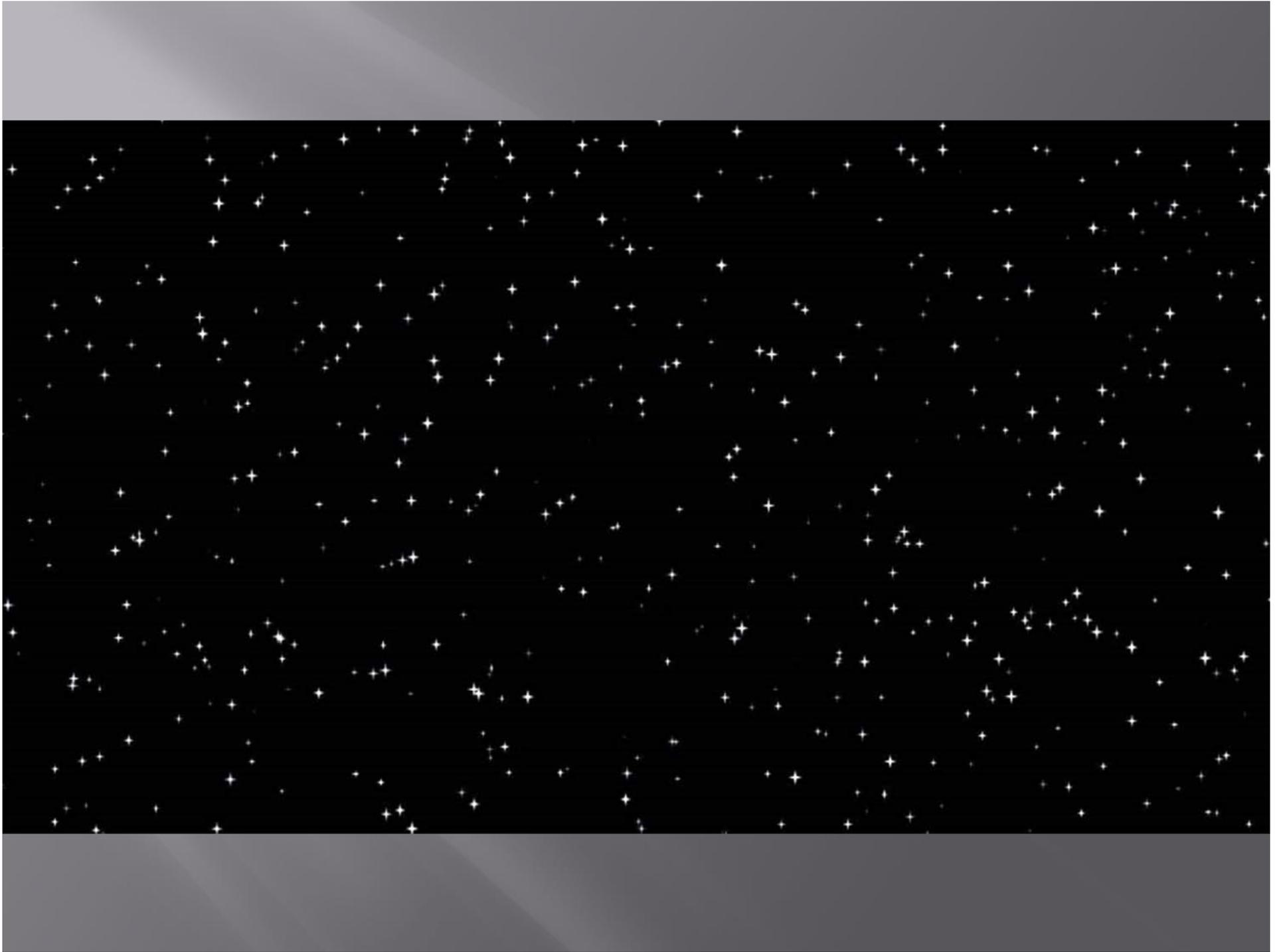


Visualizing Quantum Mechanics

Your mission, if you decide to accept it,



Is to boldly go where no man has gone before!



MAGNETIC RESONANCE PIONEERS

By 1946 Bloch and Purcell and co-workers captured the essence of the behavior of an atom with a non-zero magnetic moment situated in a magnetic field. Their contributions to the field from these first papers was precocious and even 70 years later their work carries modern significance.

Although quantum physics was needed to formulate the experimental and theoretical results, the final impact rests on the very simple relationship given by relating the frequency of rotation or precession frequency (ω) and the local magnetic field (B) via $\omega = \gamma B$, known as the Larmor equation.

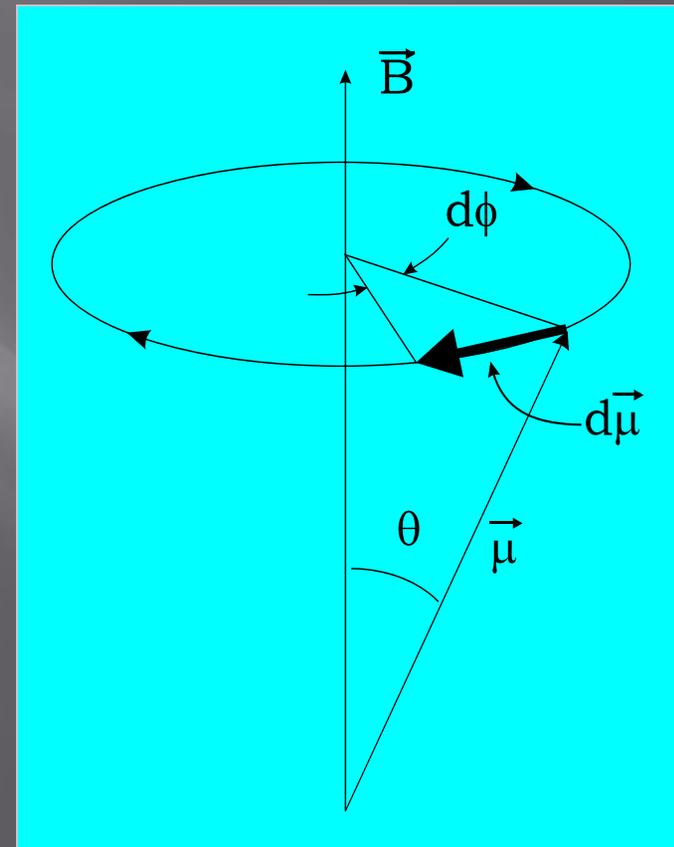
Basic MRI concepts: A precessing spin in a magnetic field

$$\omega = -\gamma * \mathbf{B}$$

\mathbf{B} the applied magnetic field

γ the gyromagnetic ratio
for the proton

ω the magnetic resonance
frequency

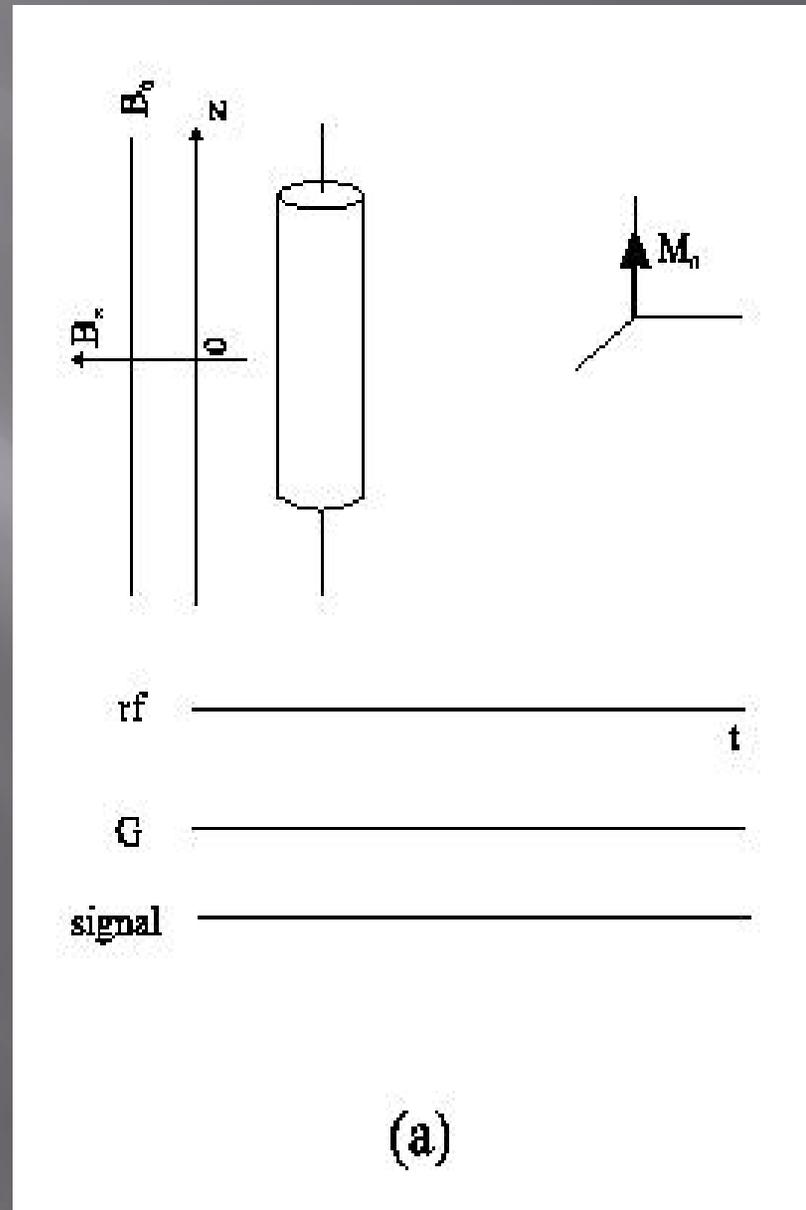


Magnetizing our body

A cylindrical object in a constant magnetic field.

Its bulk magnetization lies parallel to the main field.

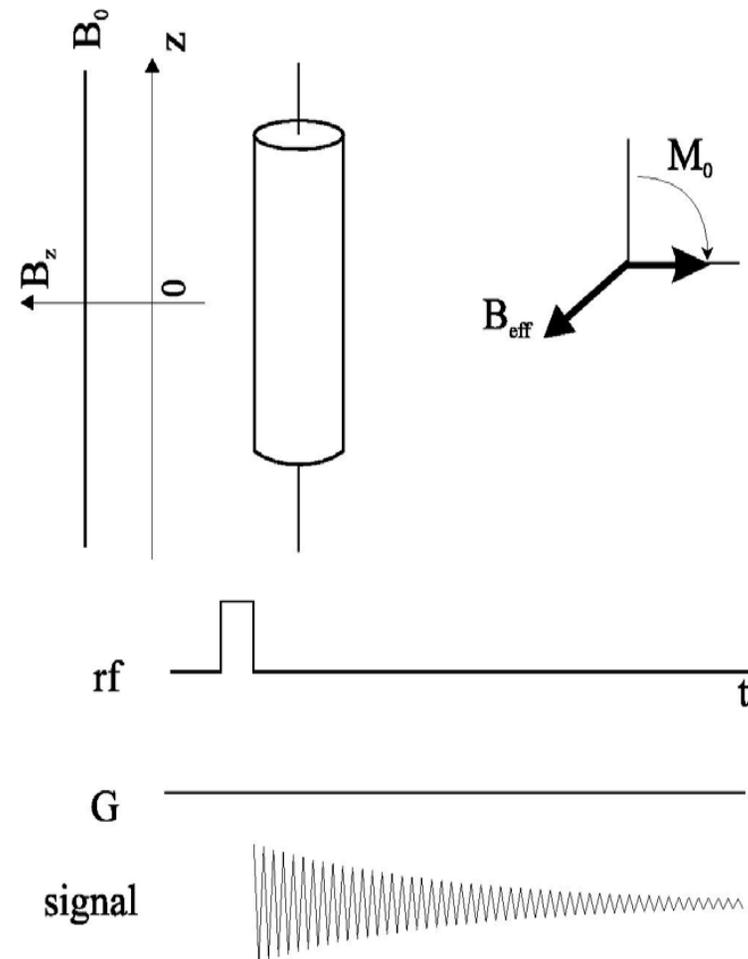
Present or not?



Creating a visible signal

Applying an oscillating rf field along the x-axis rotates M_0 from the z-axis into the transverse plane so that it lies along the y-axis.

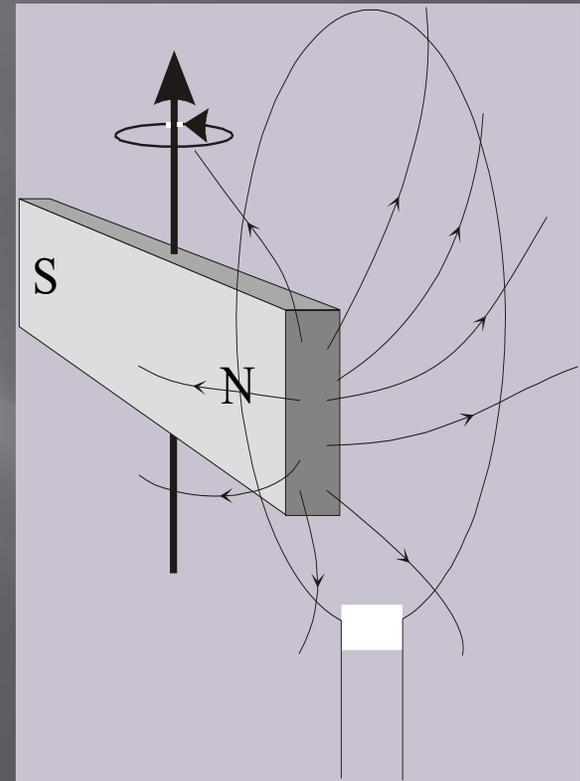
At this time, the rf field is turned off and the transverse magnetization precesses clockwise about the main field B_0 .



(b)

MR Signal Readout

The precessing transverse component induces a voltage in a coil which is placed so that it sees a changing magnetic flux. This generates a current that we can measure.



GRADIENT ECHOES AND 1D IMAGING



The Larmor equation

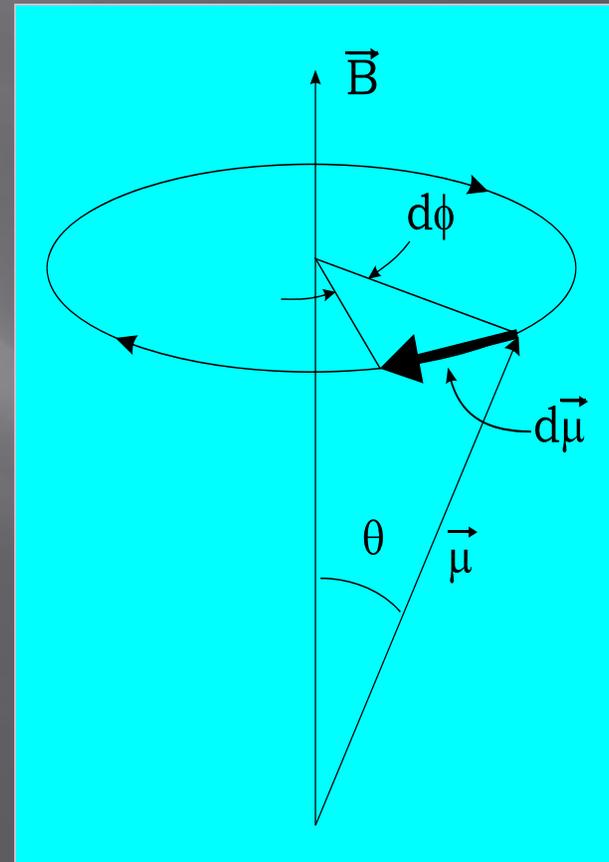
$$\omega = -\gamma^* \mathbf{B}$$

$$\phi = \omega t$$

$$\phi = -\gamma \mathbf{B}t$$

For hydrogen,

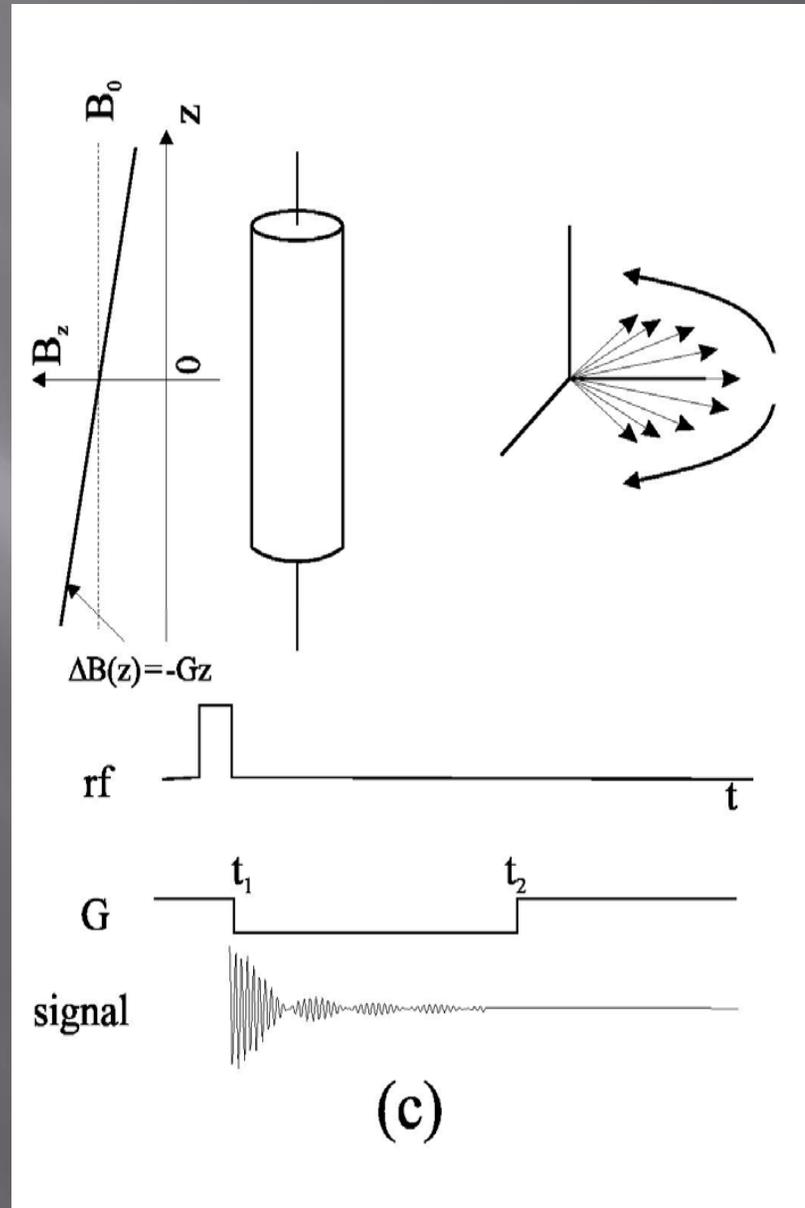
$$\dot{\gamma} = \gamma / 2\pi = 42.6 \text{ MHz/T.}$$



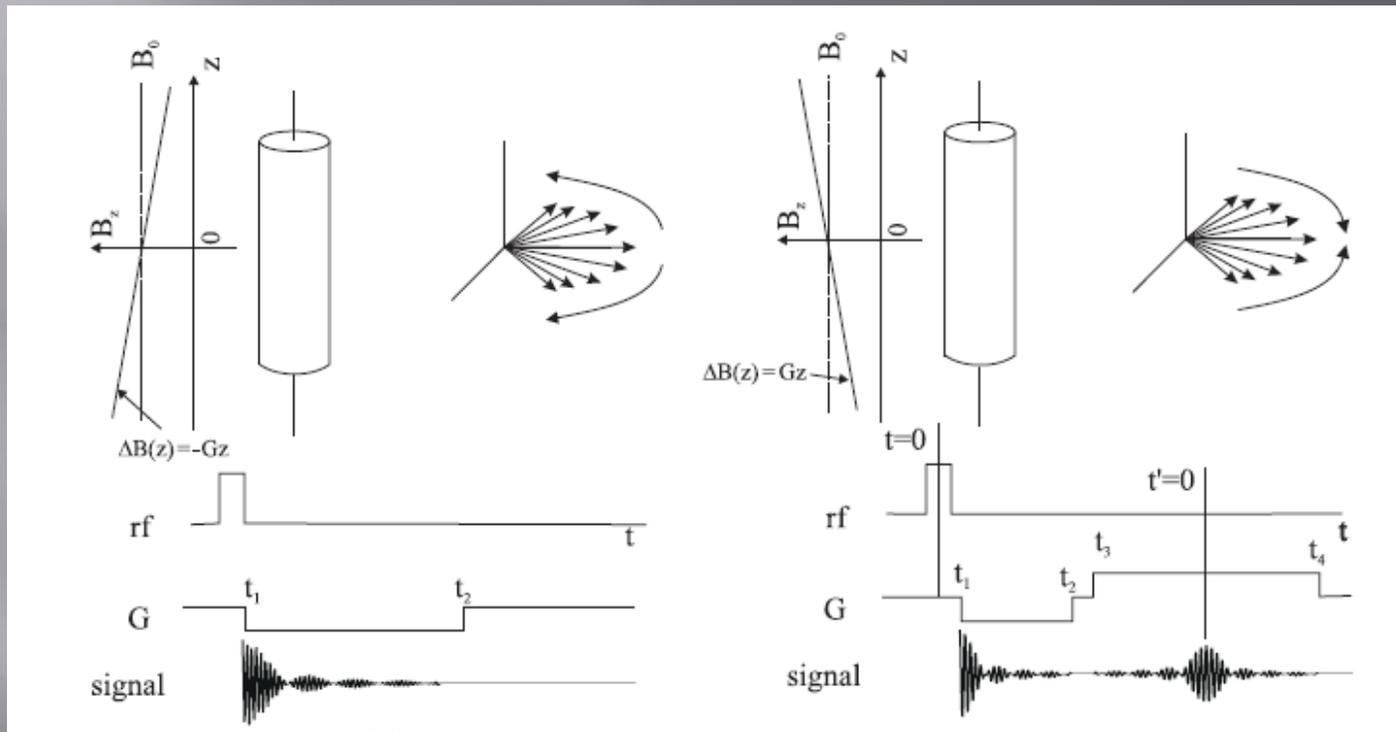
AHA a Nobel Prize Winning Idea

By purposely adding
a gradient field G ,
we can spatially
distinguish the spins
by their frequency
content since now

$$\omega(x) = \gamma (B_0 + Gx)$$



Creating an echo and going back in time



Applying a dephasing gradient followed by a rephasing gradient causes the spins to first run away from each other and then to turn around and run back creating a gradient echo.

The MR signal as a Fourier transform

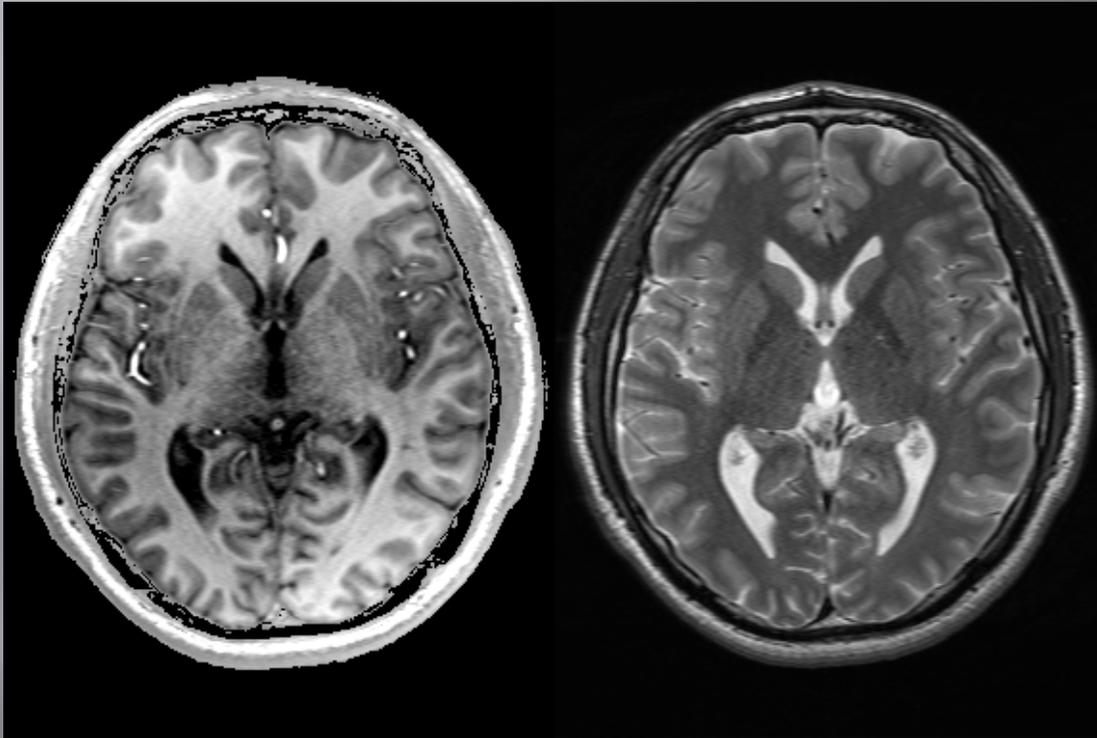
$$s(t) = \int dx \rho(x) \exp(-i\gamma Gxt)$$

where $\rho(x)$ is the spin density and
using $k = \gamma Gt$ as the spatial frequency we find

$$s(k) = \int dx \rho(x) \exp(-i2\pi kx)$$

$$\rho(x) = \int dk s(k) \exp(i2\pi kx)$$

Visualizing Quantum Mechanics



Lauterbur



born – May 6,
1929
died – March 27,
2007



Mansfield

born – 9 October,
1933
died – 8 February,
2017

Thin slice T1 and T2 weighted 3D STAGE images of the brain. Nobel prize in Medicine or Physiology 2003.

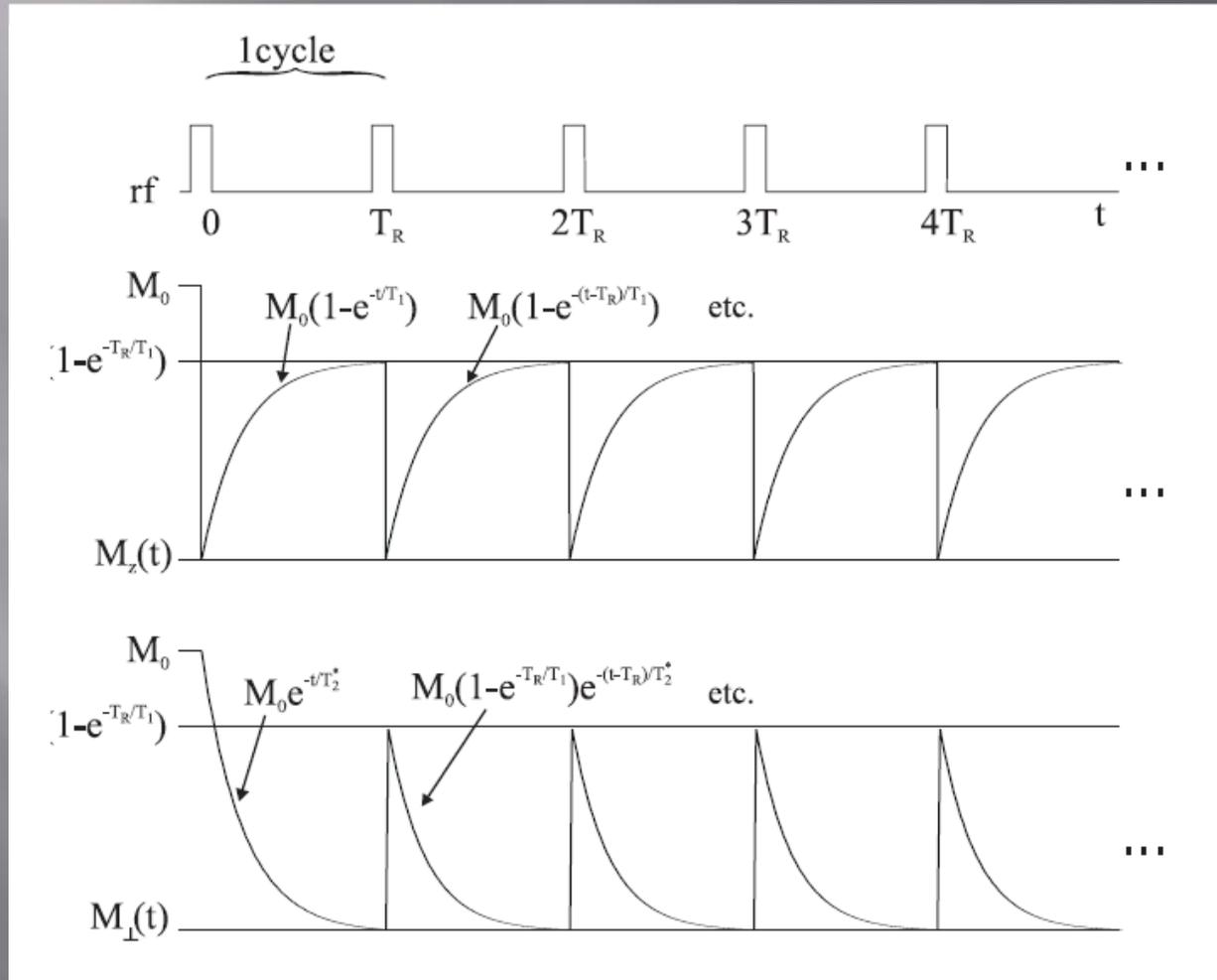
T1 relaxation

Describes recovery of magnetization toward the equilibrium state

$$M_z(t) = M_o(1 - e^{-t/T1})$$

where t is the time between the rf pulse (with $\theta = \pi/2$) and the readout interval.

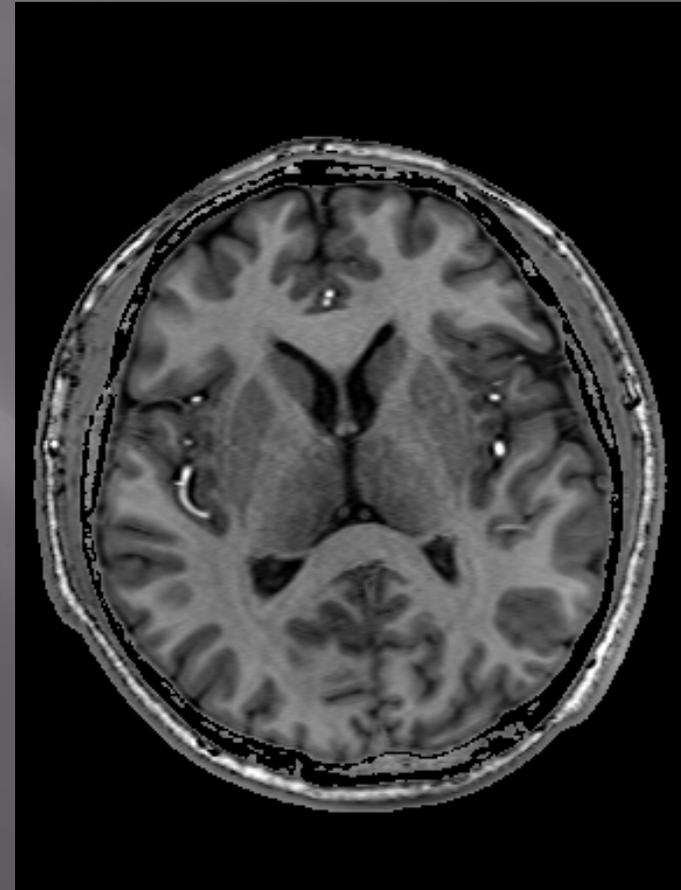
General signal behavior



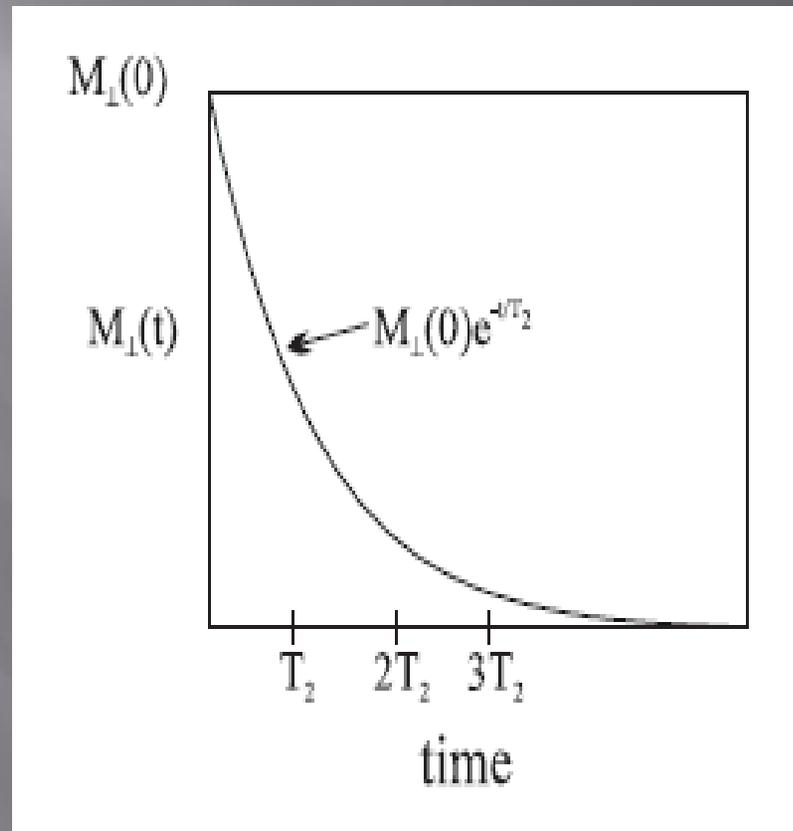
$\rho^*(1-E1)*E2^*$ where $E1 = \exp(-TR/T1)$ and $E2 = \exp(-TE/T2^*)$

Longitudinal or T1 relaxation time

Tissue	T_1 (ms)	T_2 (ms)
gray matter (GM)	950	100
white matter (WM)	600	80
muscle	900	50
cerebrospinal fluid (CSF)	4500	2200
fat	250	60
blood ³	1200	100-200 ⁴



T2 relaxation



$$M_{xy}(t) = M_{xy}(0)e^{-t/T_2}$$

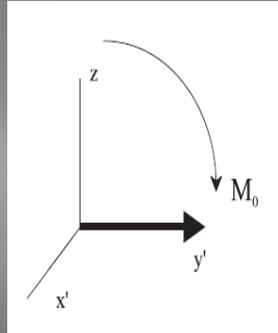
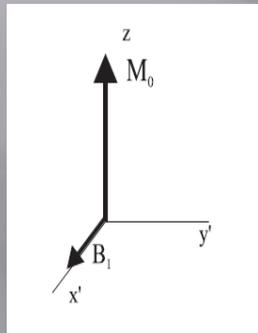
T2 relaxation

- Spin-Spin interaction
- Describes decaying rate of M_{xy}
- Practically, T_2^* decay, rather than T_2 decay, is observed in FID due to field inhomogeneity

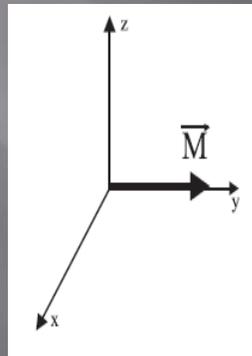
Tissue	T_1 (ms)	T_2 (ms)
gray matter (GM)	950	100
white matter (WM)	600	80
muscle	900	50
cerebrospinal fluid (CSF)	4500	2200
fat	250	60
blood ³	1200	100-200 ⁴



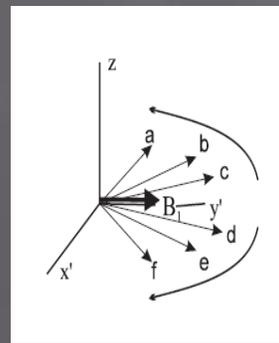
T2* relaxation



$$M_{xy}(t) = M_{xy}(0)e^{-t/T2^*}$$



T2 decay (ideal)



T2* decay (actual)

Why choose 90° flip angle?

It limits the total T1 recovery and for small TR the signal only recovers to TR/T1.

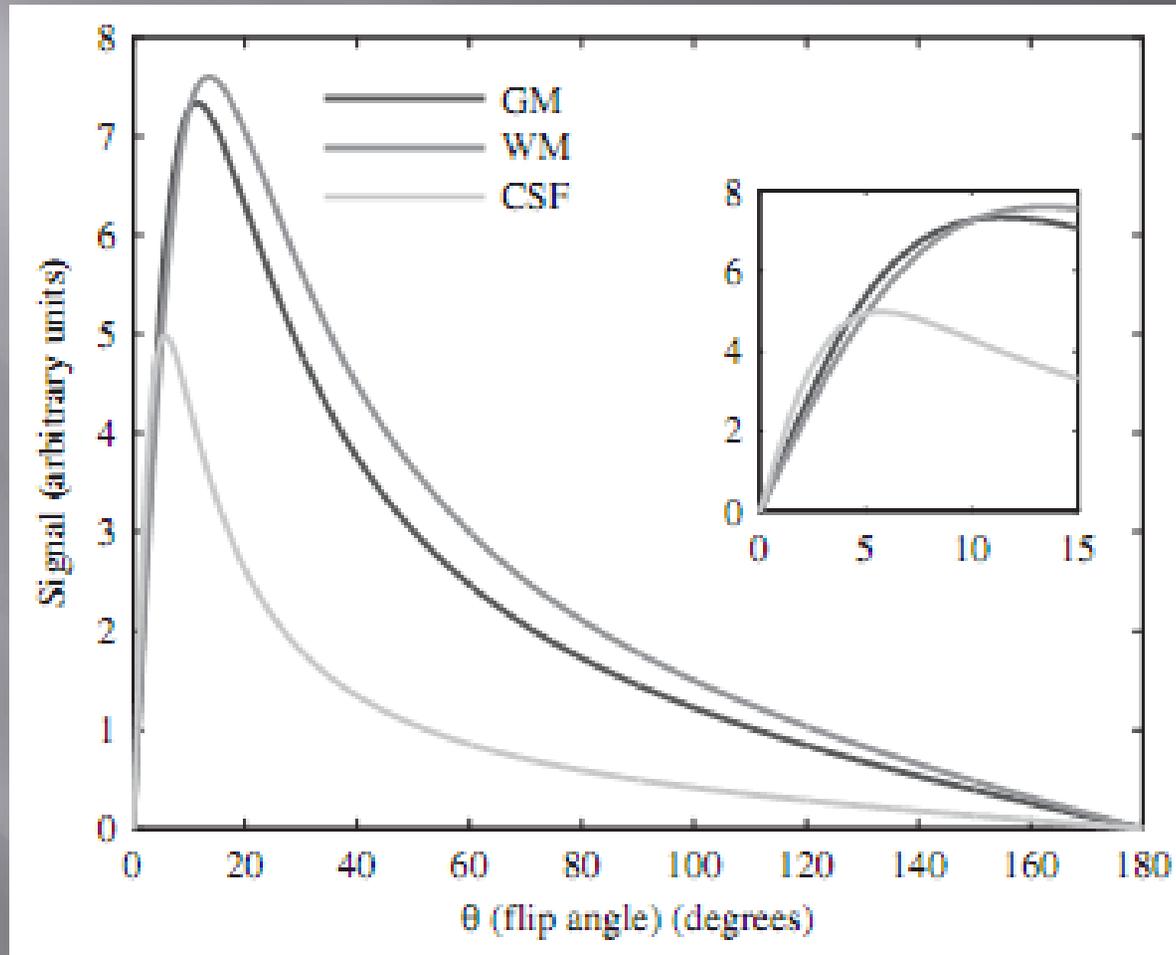
If TR = 10ms and T1 = 2000ms, the signal is only 0.5% of its maximum value.

Using a smaller flip angle, we find:

$$\hat{\rho}(\theta, T_E) = \rho_0 \sin \theta \frac{(1 - E_1)}{(1 - E_1 \cos \theta)} e^{-T_E/T_2^*}$$

At the optimal flip angle (also known as the Ernst angle), given by $\cos \theta = E_1$, we find the peak signal is roughly $0.5\sqrt{2TR/T_1}$ or 5% of the total (that is 10 times bigger).

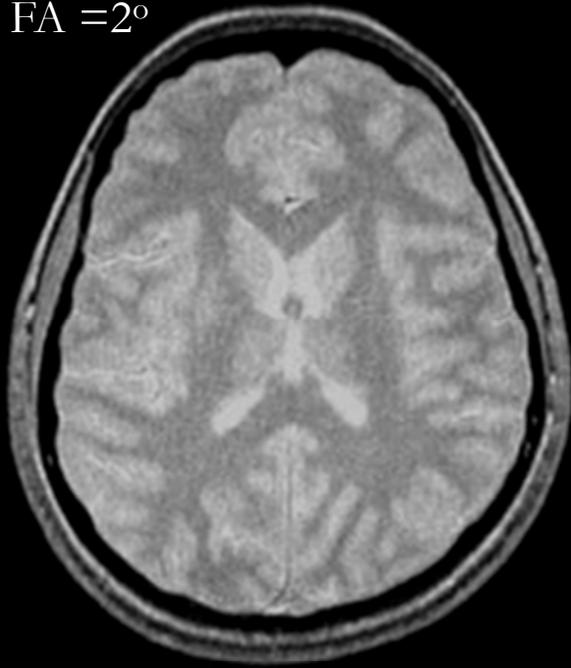
Signal behavior at 1.5T for a TR of 20msec



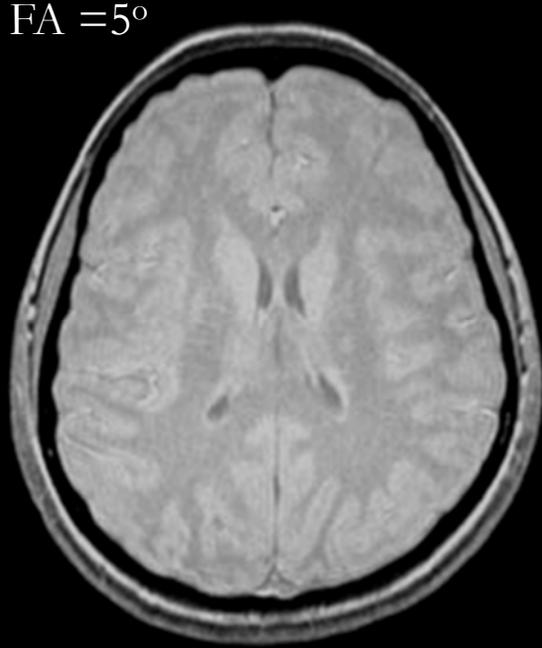
$$\hat{\rho}(\theta, T_E) = \rho_0 \sin \theta \frac{(1 - E_1)}{(1 - E_1 \cos \theta)} e^{-T_E/T_2^*}$$

$$E_1 \equiv e^{-T_R/T_1}$$

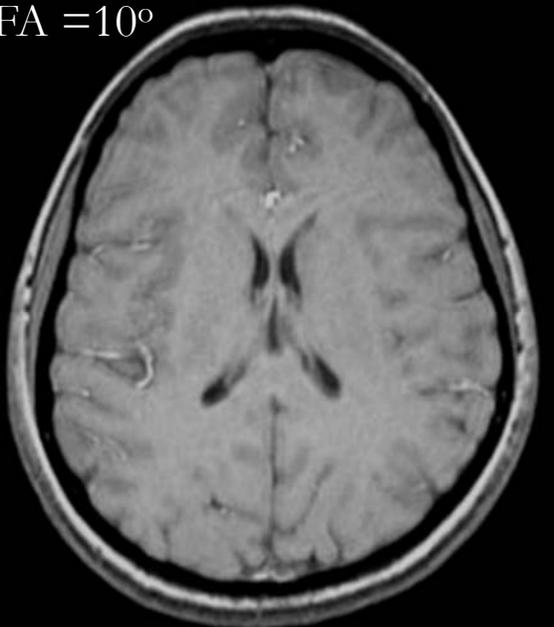
FA = 2°



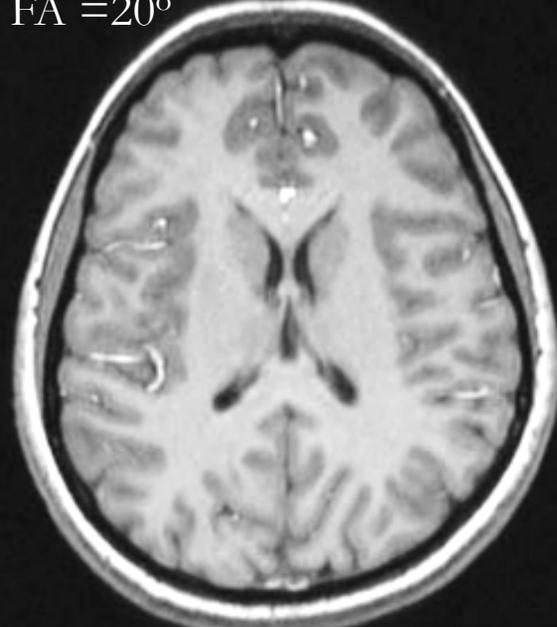
FA = 5°



FA = 10°



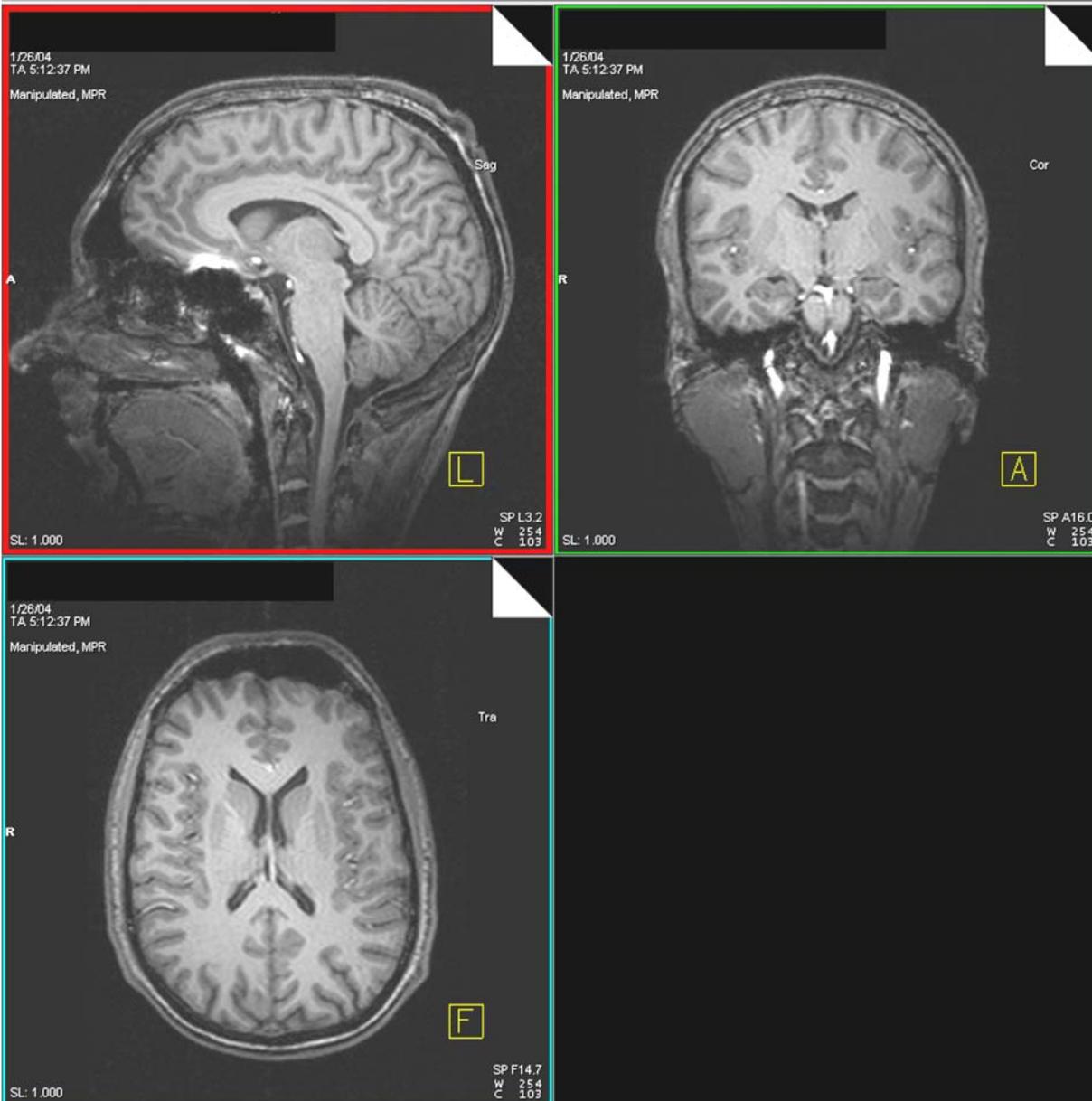
FA = 20°



Example data from a 3D gradient echo sequence with short TE and short TR = 20ms at 1.5T.

Small flip angles generate a spin density weighted image while large flip angles generate a T1 weighted image.

3D MP-RAGE



Structural Imaging:

- T1 3D MPRAGE
- $1.0 \times 1.0 \text{ mm}^2$ in plane resolution
- 1 mm slice thickness
- 176 slices
- TE 5 ms
- TR(total) 2500 ms
- Flip angle: 12°
- Bandwidth 200 Hz/Px
- Scan time: 10:32 min

Part 1: Questions

- 1) What is the Larmor equation?
- 2) How is a gradient used to help create an image?
- 3) What are T1 and T2*?
- 4) How do they affect contrast in the image?

Strategically Acquired Gradient Echo (STAGE)

Correcting for RF Inhomogeneities in Estimating T1 and Proton Density



Wang Yu
Shanghai Key Laboratory of Magnetic
Resonance
East China Normal University

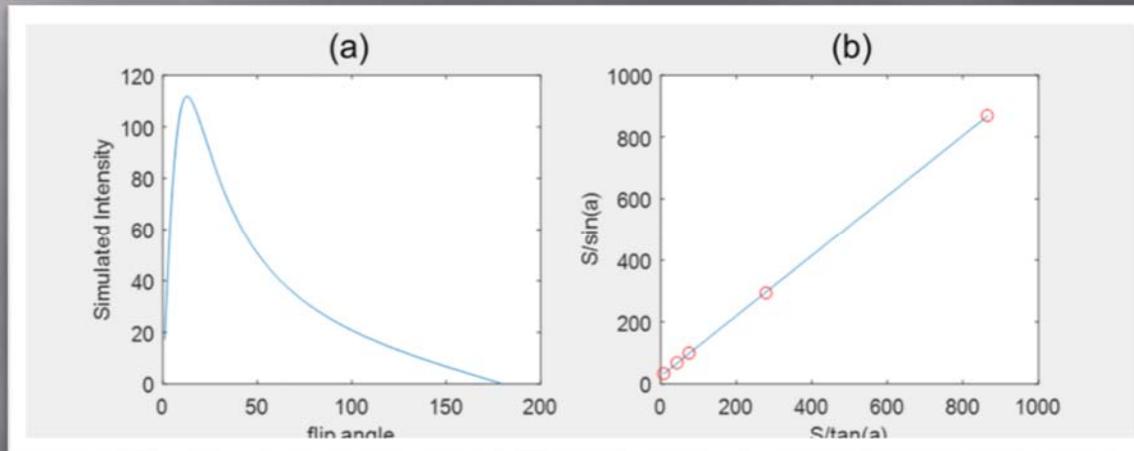
Basic Theory of VFA

- Signal formula:

$$S = PD \cdot bias \cdot \sin(k \cdot \theta) \frac{1 - \exp(-TR/T1)}{1 - \cos(k \cdot \theta) \cdot \exp(-TR/T1)} \cdot e^{-TE/T2}$$

- Rewrite the formula:

$$\frac{S}{\sin(k \cdot \theta)} = E1 \cdot \frac{S}{\tan(k \cdot \theta)} + PD_{eff} \cdot (1 - E1)$$



Extracting T1 is an ill-posed problem for low flip angles

- Two flip angles can provide **an apparent T1 map** with satisfying SNR when one angle is below the Ernst angle and the other is above it.

$$T1_{app} = T1 * k^2, PD_{app} = PD * k * bias$$

- Ill-posed problem:

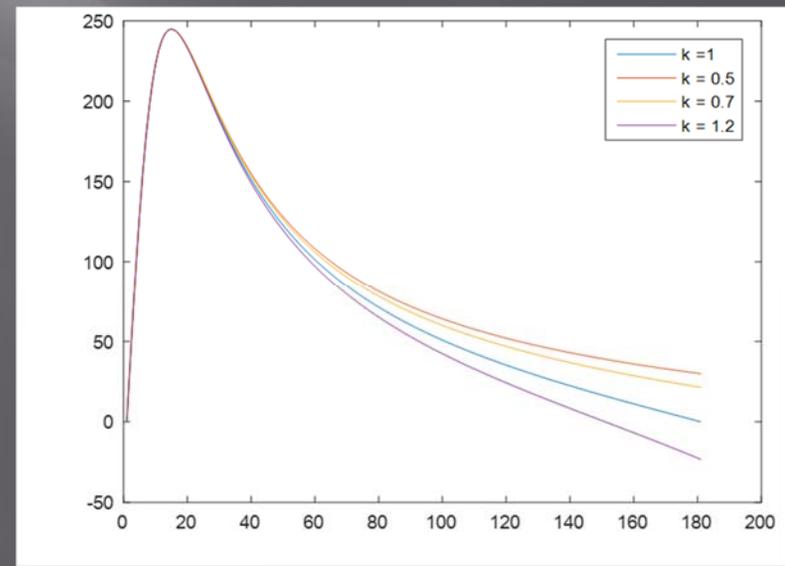
$$S(\theta) = \theta / (1 + \theta^2 / \theta_E^2)$$

where $\theta_E = \text{sqrt}(2TR/T1)$

If θ goes to $k \theta$

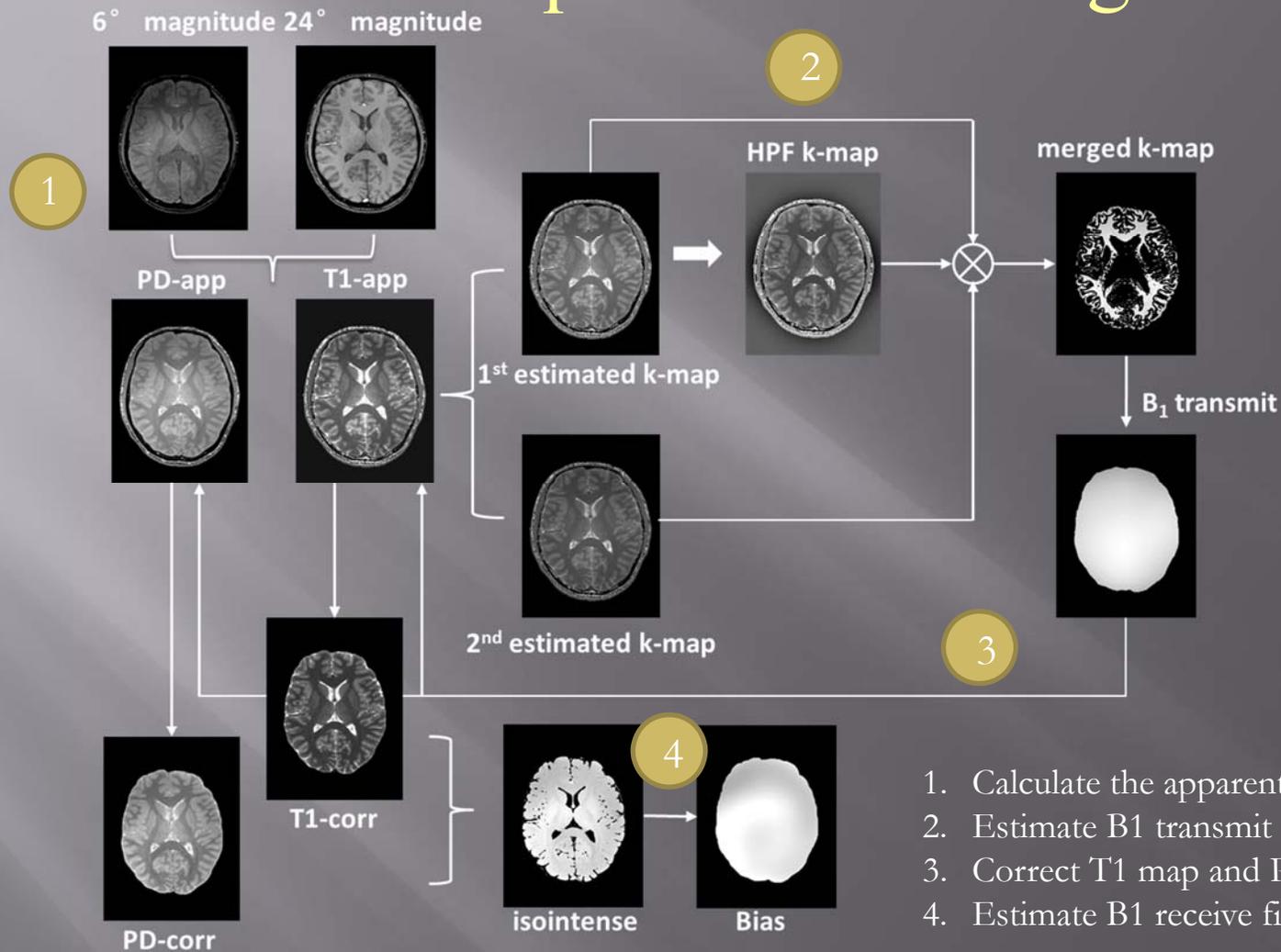
then $T1_{app} = T1 * k^2$

Intensity simulation



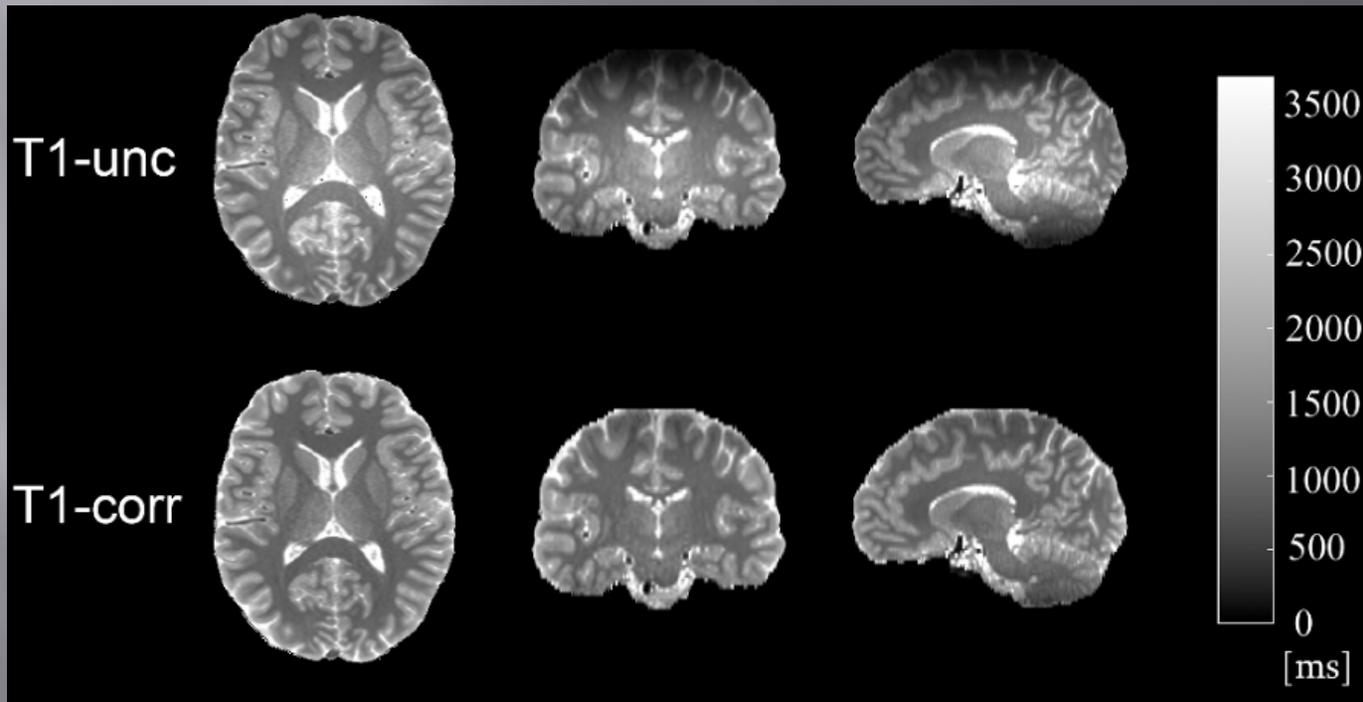
flip angle

Flow chart to create homogenous and quantitative images

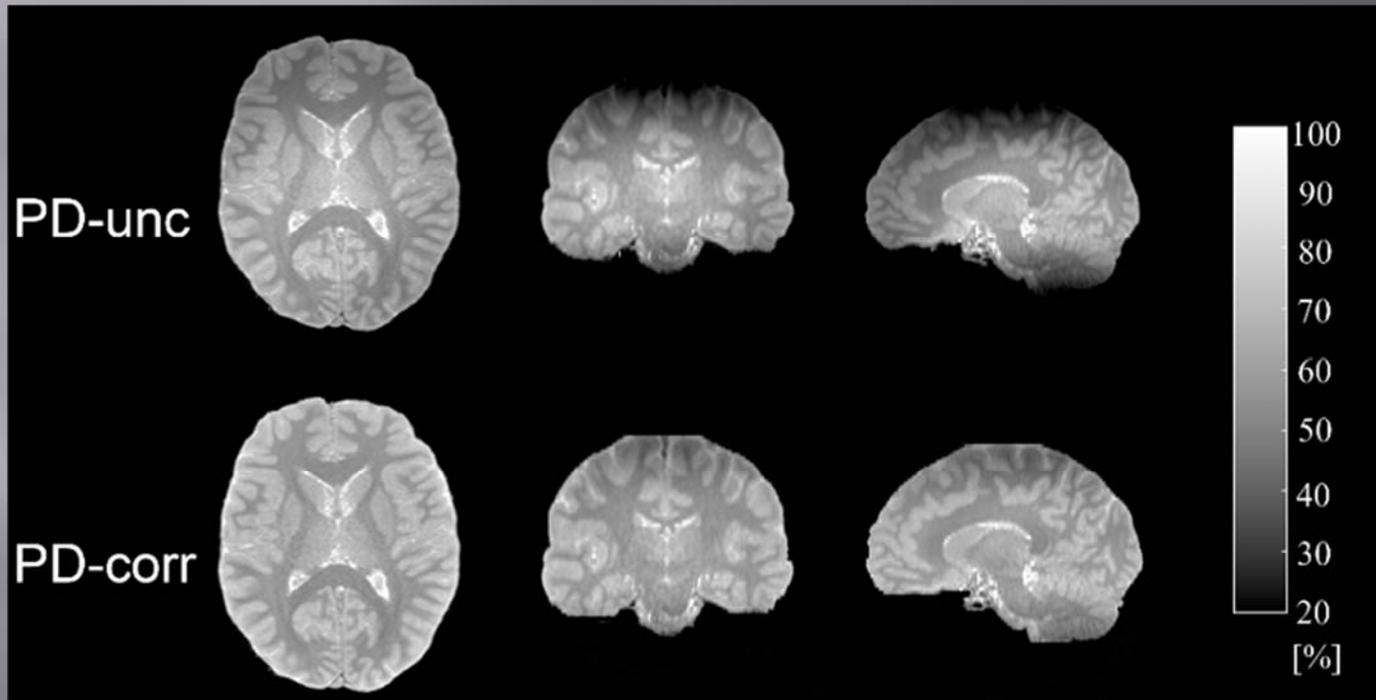


1. Calculate the apparent T1 map and PD map
2. Estimate B1 transmit field
3. Correct T1 map and PD map
4. Estimate B1 receive field

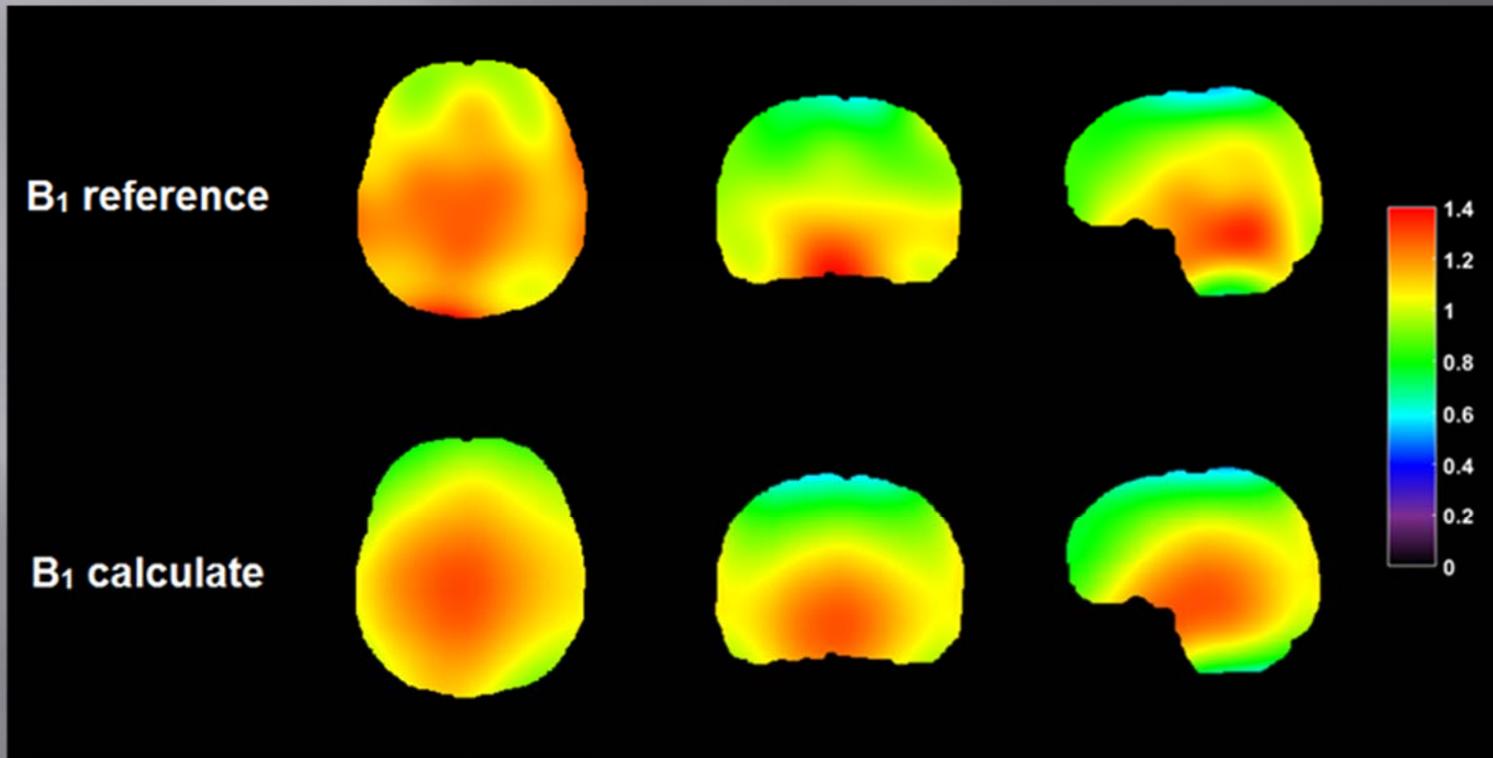
Corrected T1 map



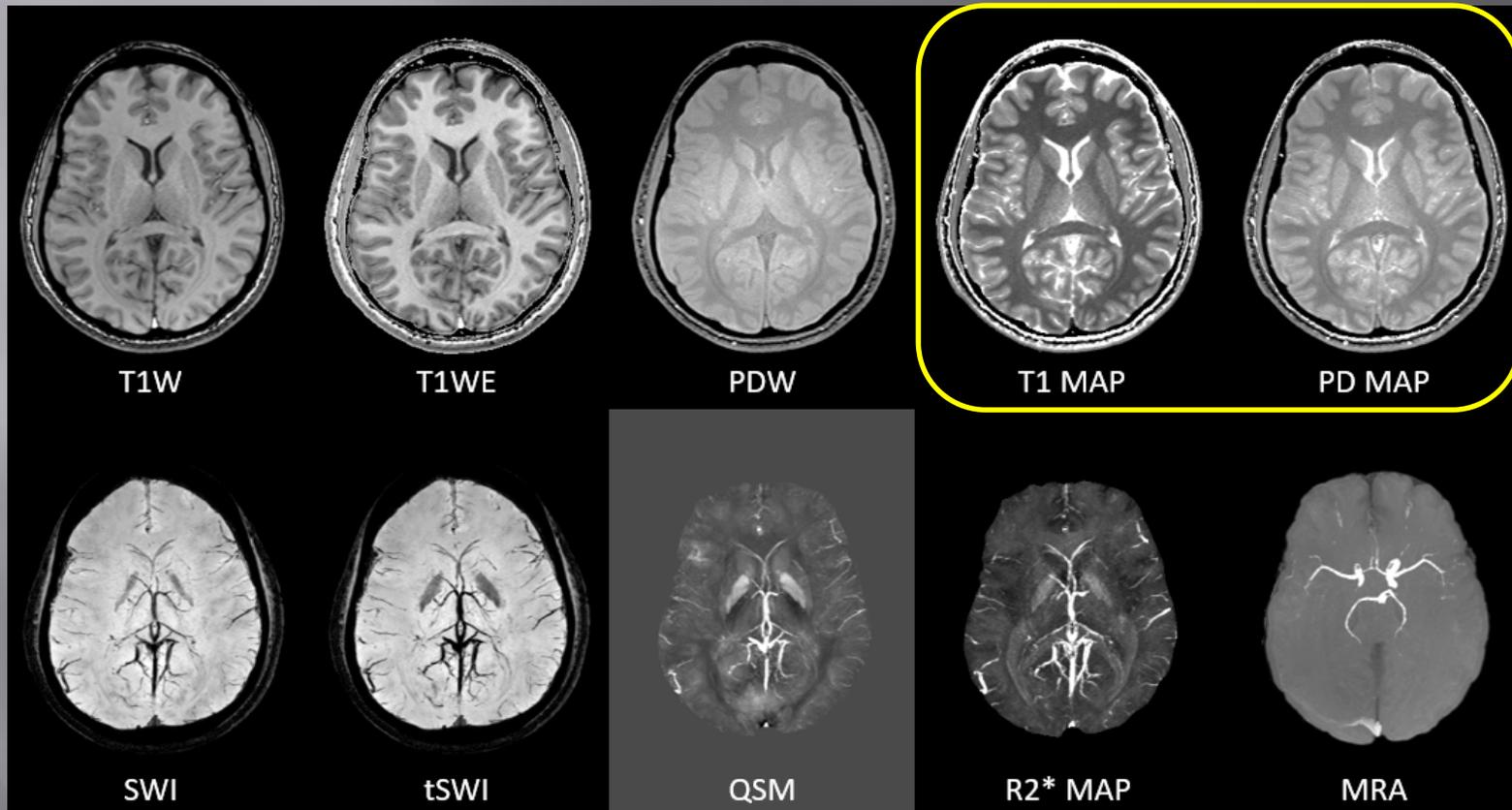
Corrected PD map



Comparison to another algorithm



STAGE imaging provides 10+ images four of them quantitative in just 5 minutes



*Chen Yongsheng,
Wang Yu*

Part 2: Questions

- 1) Why are two low FAs not enough to find T1 and PD?
- 2) How does correcting the B1 field help improve the images?

Phase is the foundation for understanding MR imaging

The Larmor equation $\omega = -\gamma * \mathbf{B}$

Phase $\varphi = \omega t = -\gamma Bt$

Phase at the echo time $\varphi = -\gamma \Delta\chi B_0 TE$

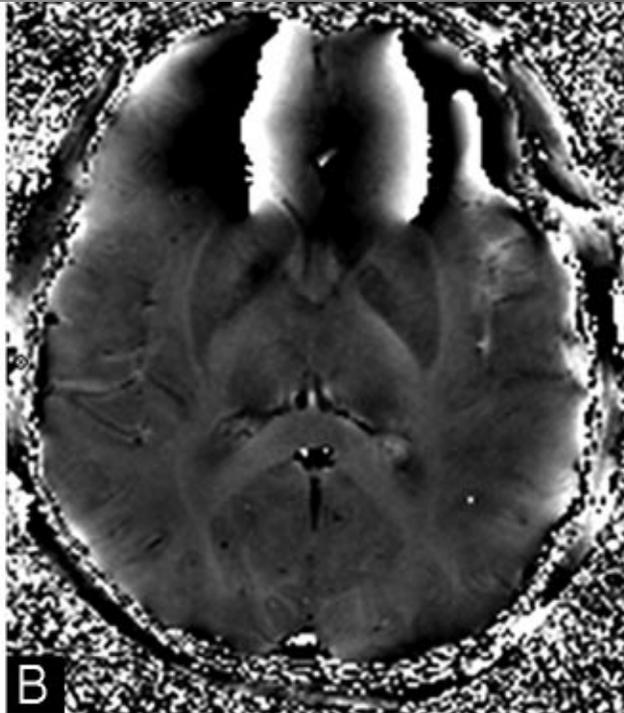
where $\Delta\chi$ is the susceptibility change from one tissue to another.

Basics of SWI



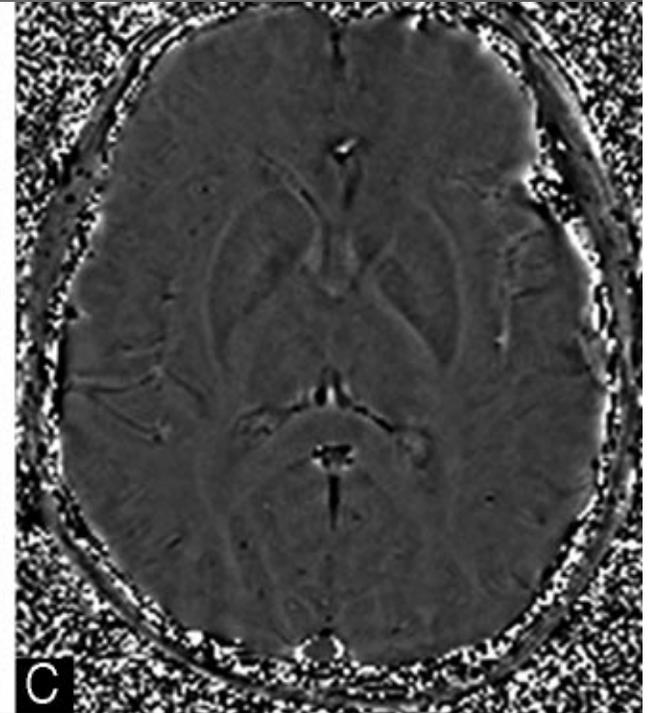
A

Original phase



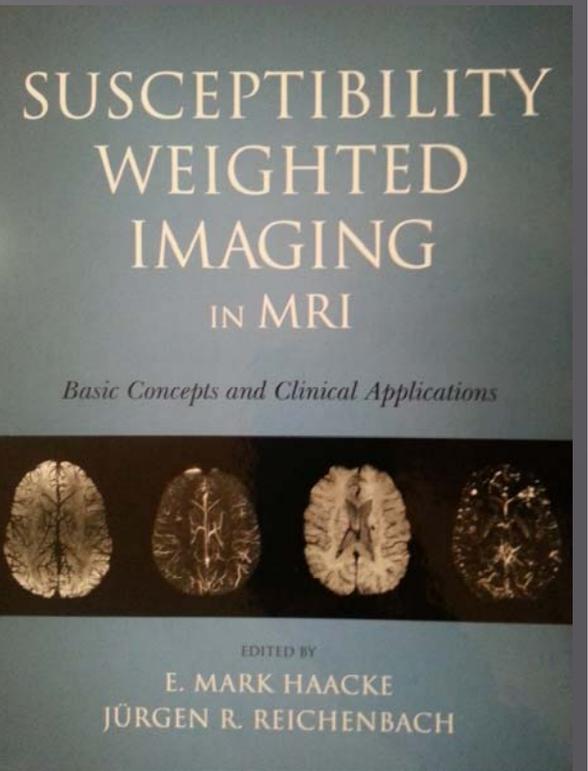
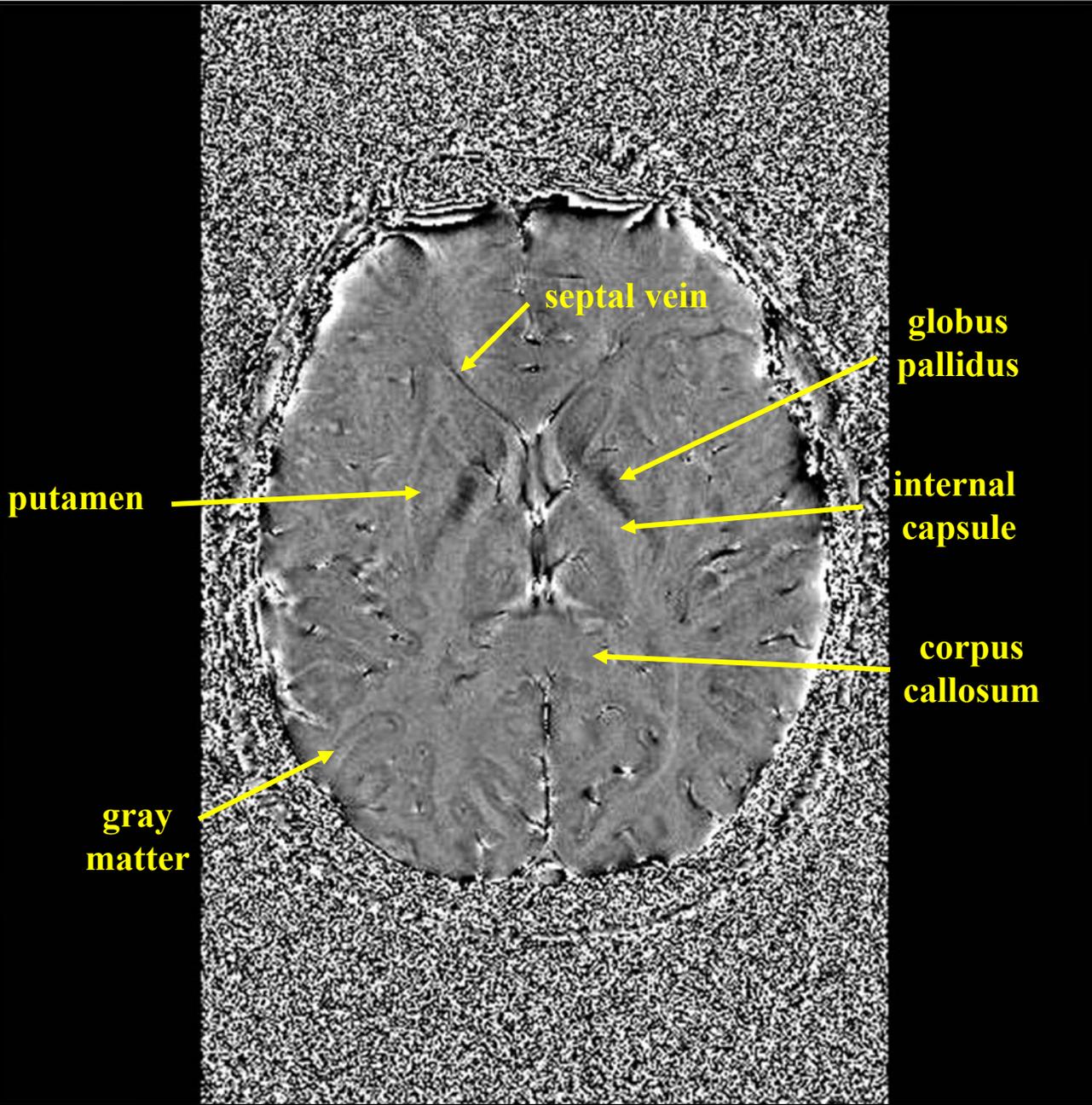
B

Processed with a
32x32 high-pass filter

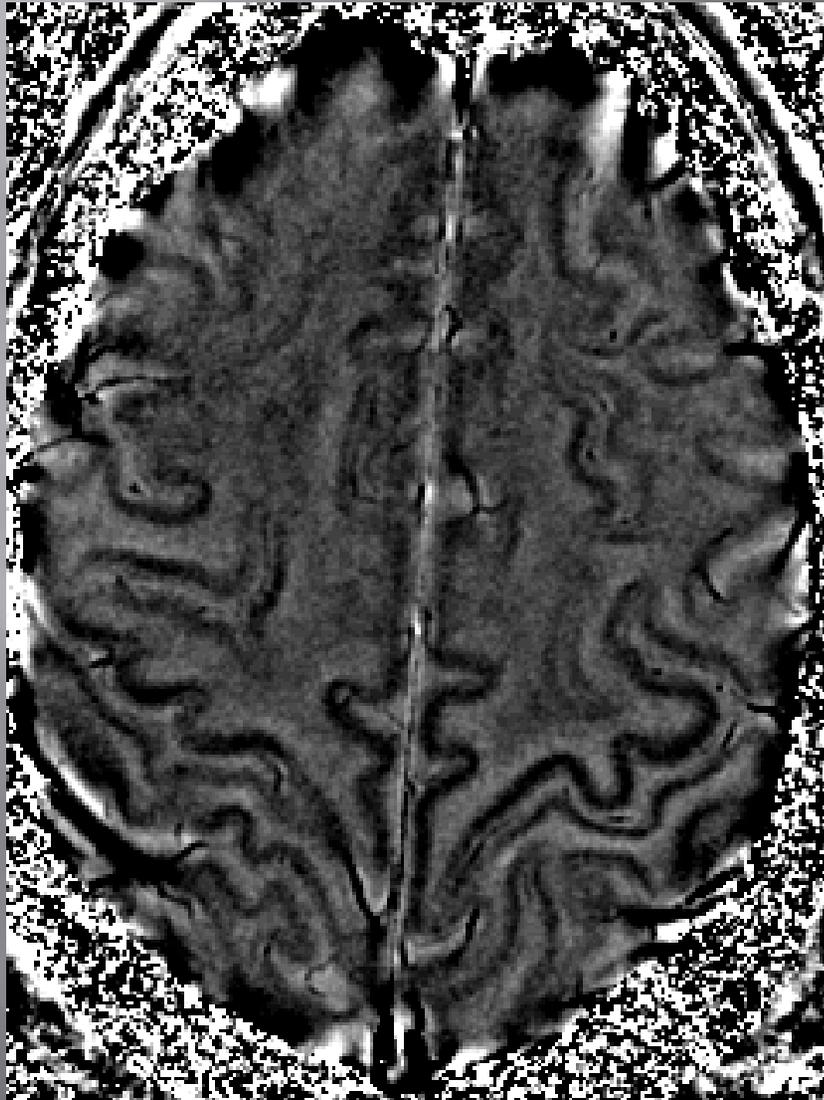


C

Processed with a
64x64 High-pass filter



Filtered Phase Image at 3.0T



In this left handed example of a high pass filtered phase image, we can see the high iron content (dark structures) of the central sulcus.

From this perspective the phase represents a frequency shift and a phase image is like a high resolution spectroscopic image for bulk water.

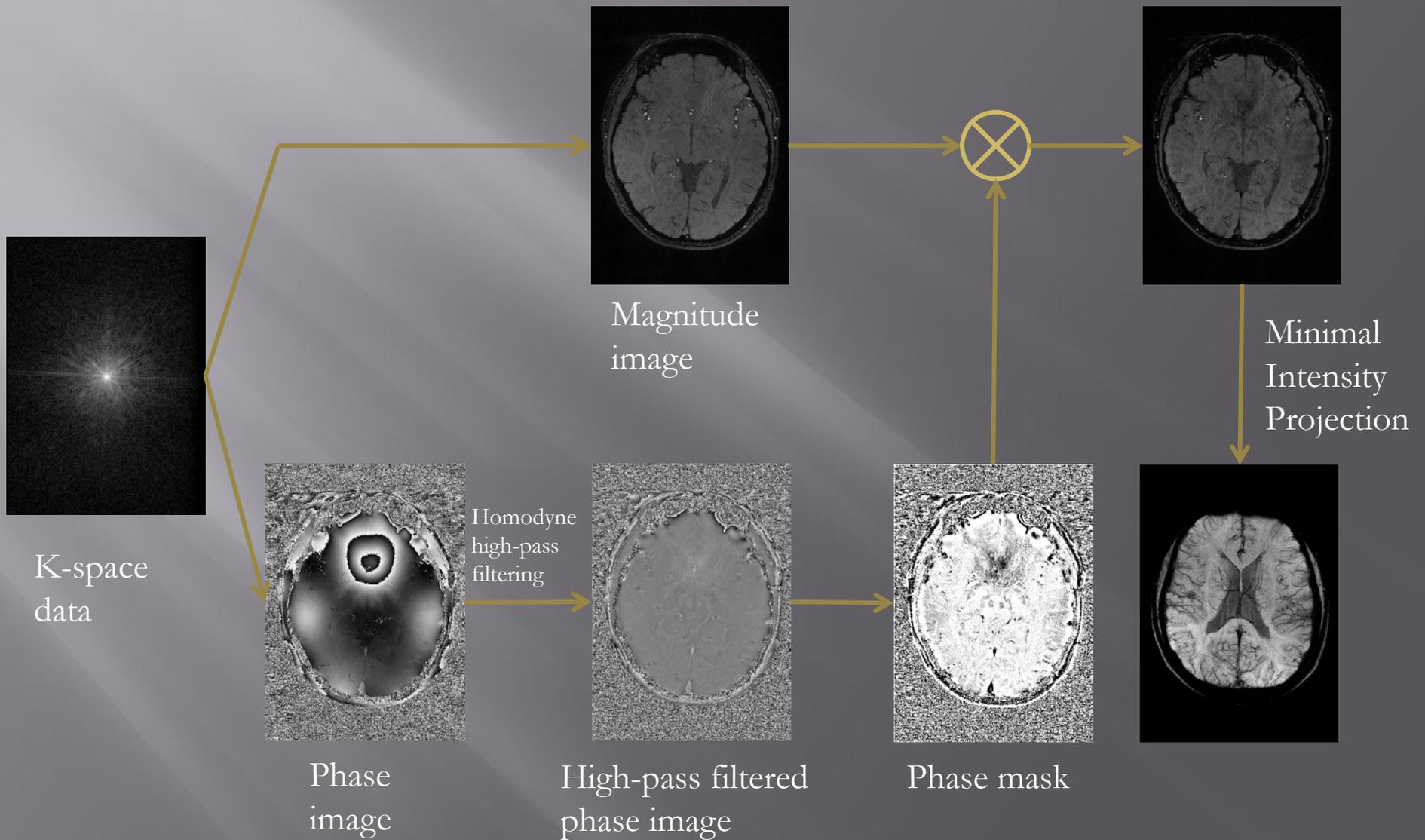
Basics of SWI

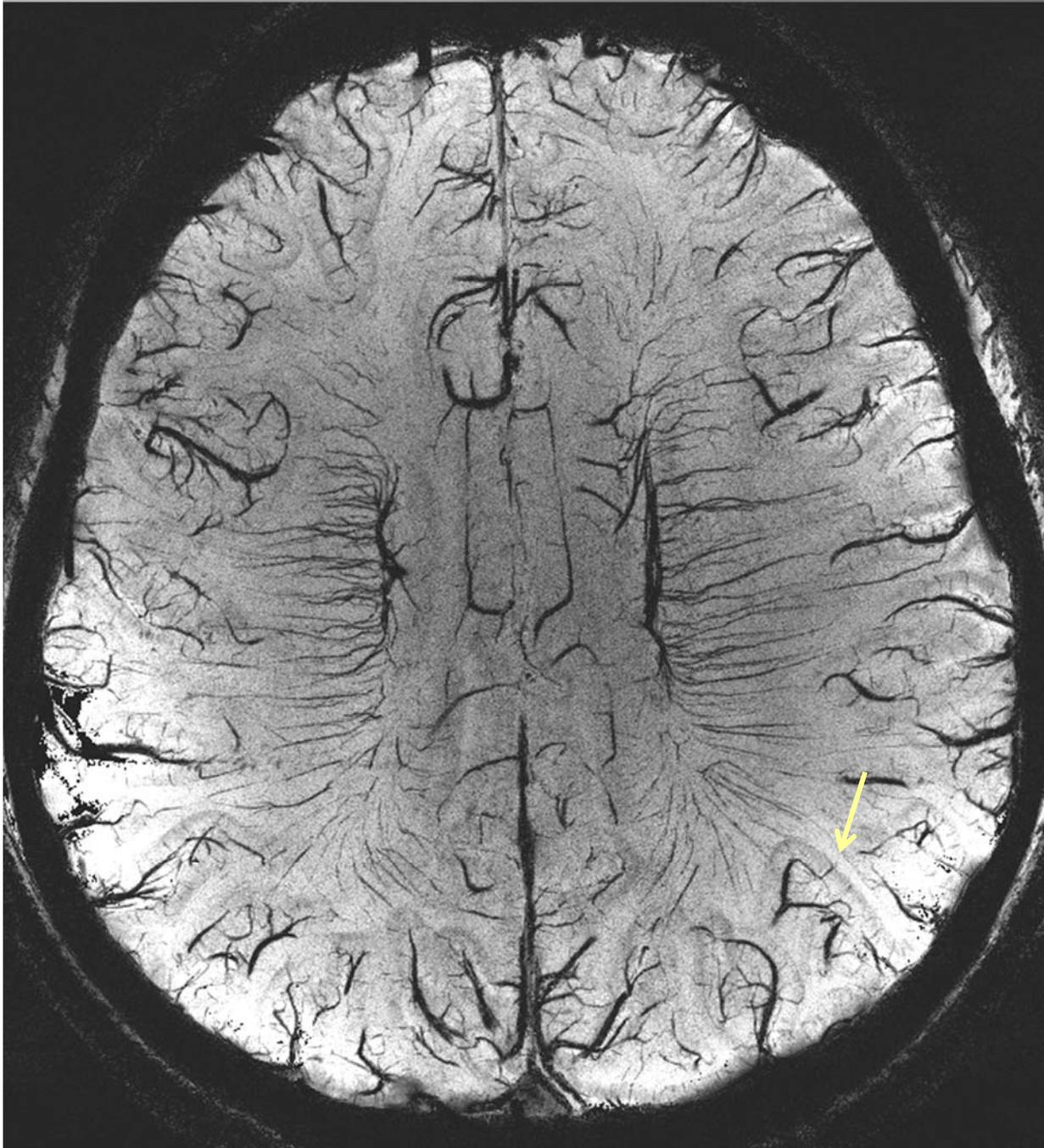
- Phase mask generation:

$$f(x) = \begin{cases} \frac{[\pi + \varphi(x)]}{\pi}, & \text{for } -\pi < \varphi(x) < 0 \\ 1, & \text{otherwise} \end{cases}$$

- Applying the masks to the original images:
- $\rho''(x) = f^m(x)\rho(x)$, m is usually chosen to be 4.

Basics of SWI





7T SWI

$215\mu \times 215\mu \times 1000\mu$

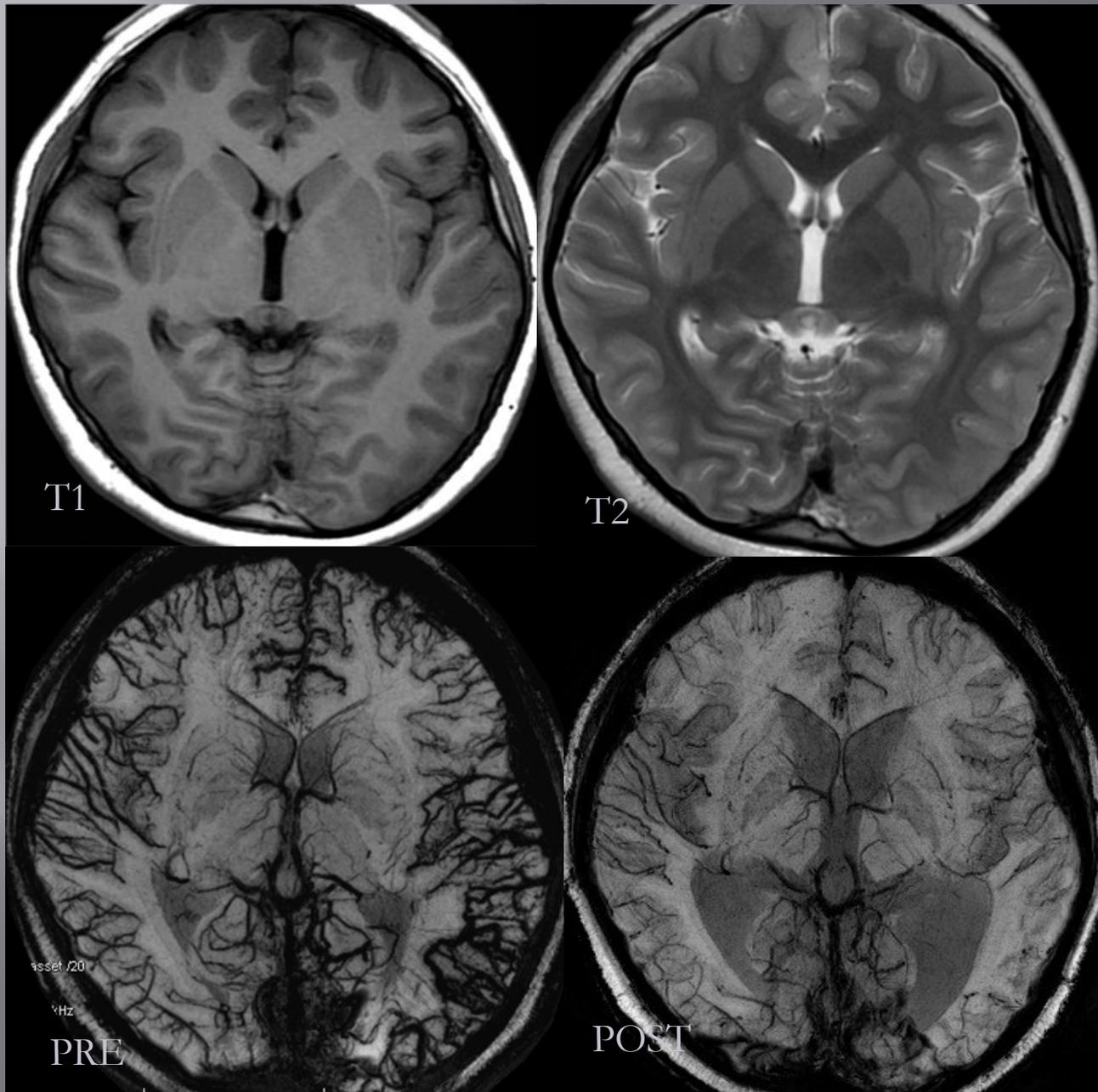
TE = 16ms

TR = 45ms

FA = 25°

8 slice mIP

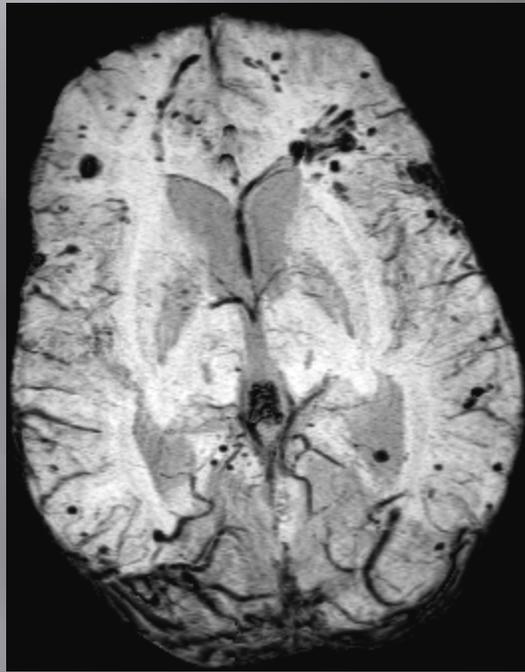
Image courtesy of Yulin Ge, NYU



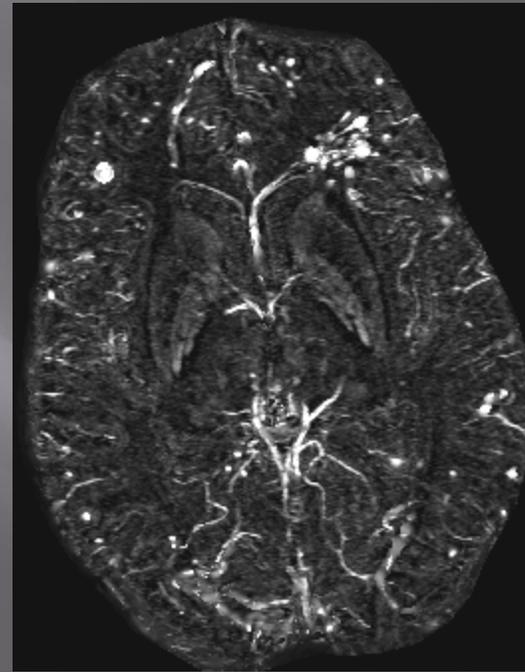
Venous Thrombosis: before treatment and after thrombolysis

Guangbin Wang M.D.
Shandong Medical
Imaging Research
Institute

Clinical Applications of SWIM in Traumatic Brain Injury (TBI)



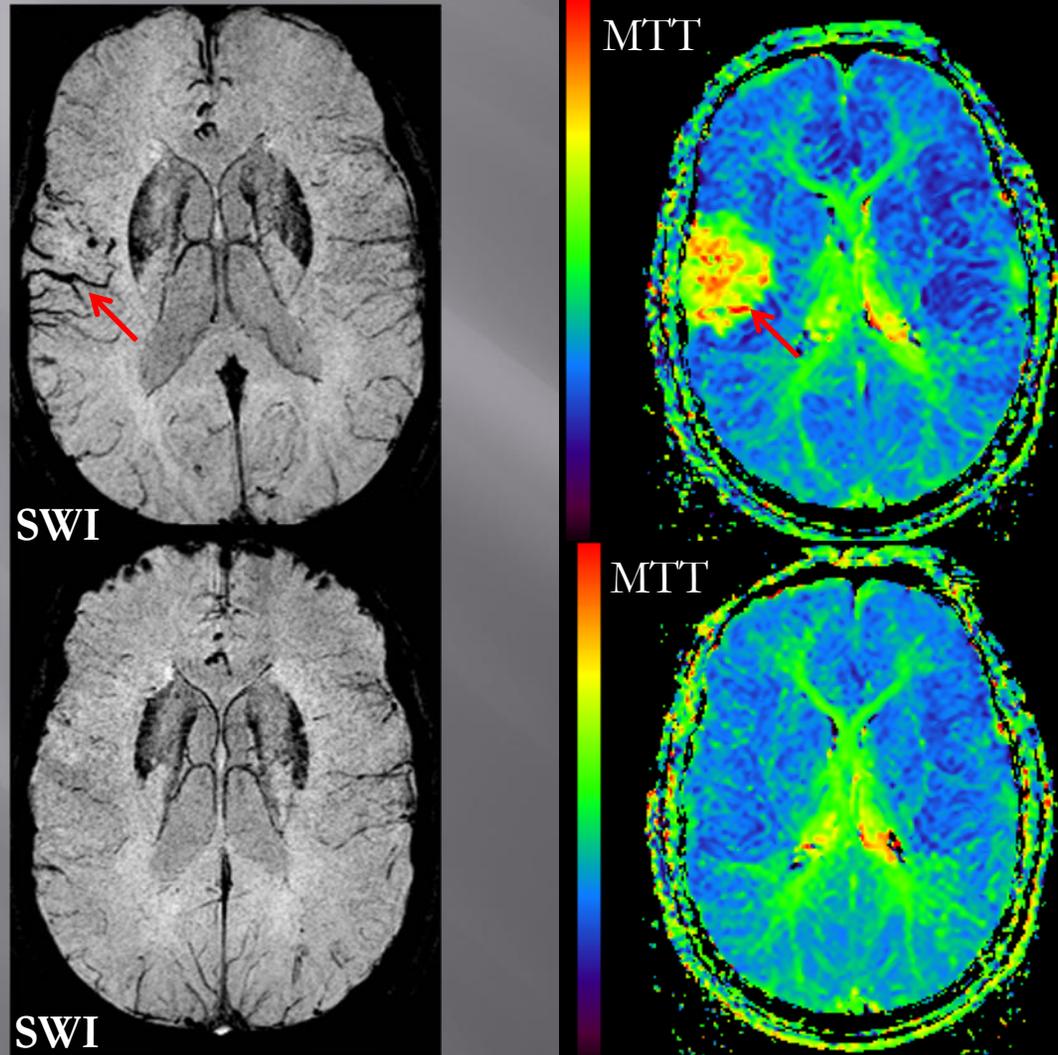
SWI minIP image projected
over 16mm



Corresponding MaxIP
susceptibility map image
projected over 16mm

Two scans from same stroke patient

MRI scan date: 2013.01.04

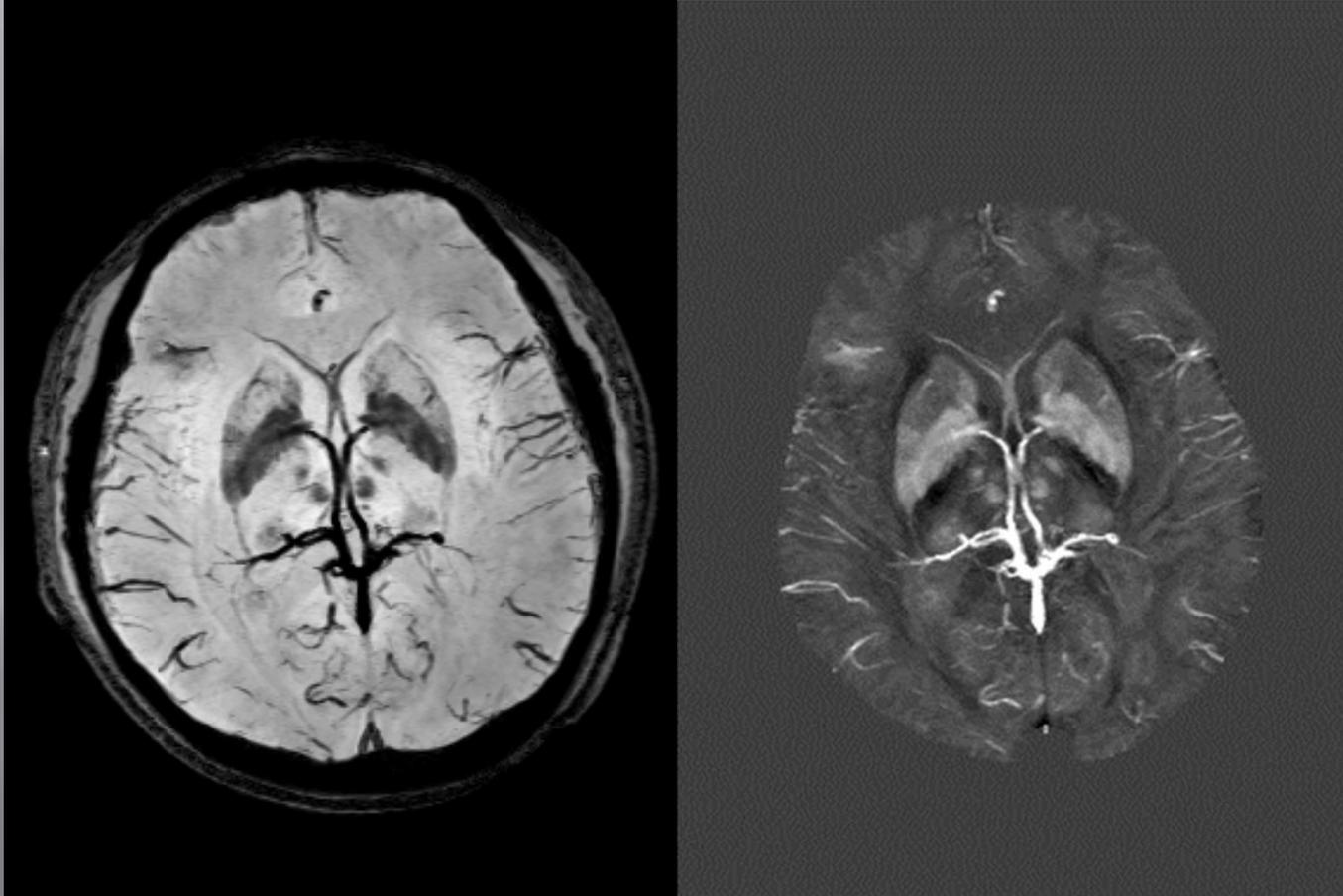


MRI scan date: 2013.01.11

Part 3: Questions

- 1) What does SWI stand for?
- 2) Why does reduced blood flow lead to darker veins?
- 3) Can SWI reveal structures smaller than a voxel, explain?
- 4) Why does gray matter show darker phase than other tissues?

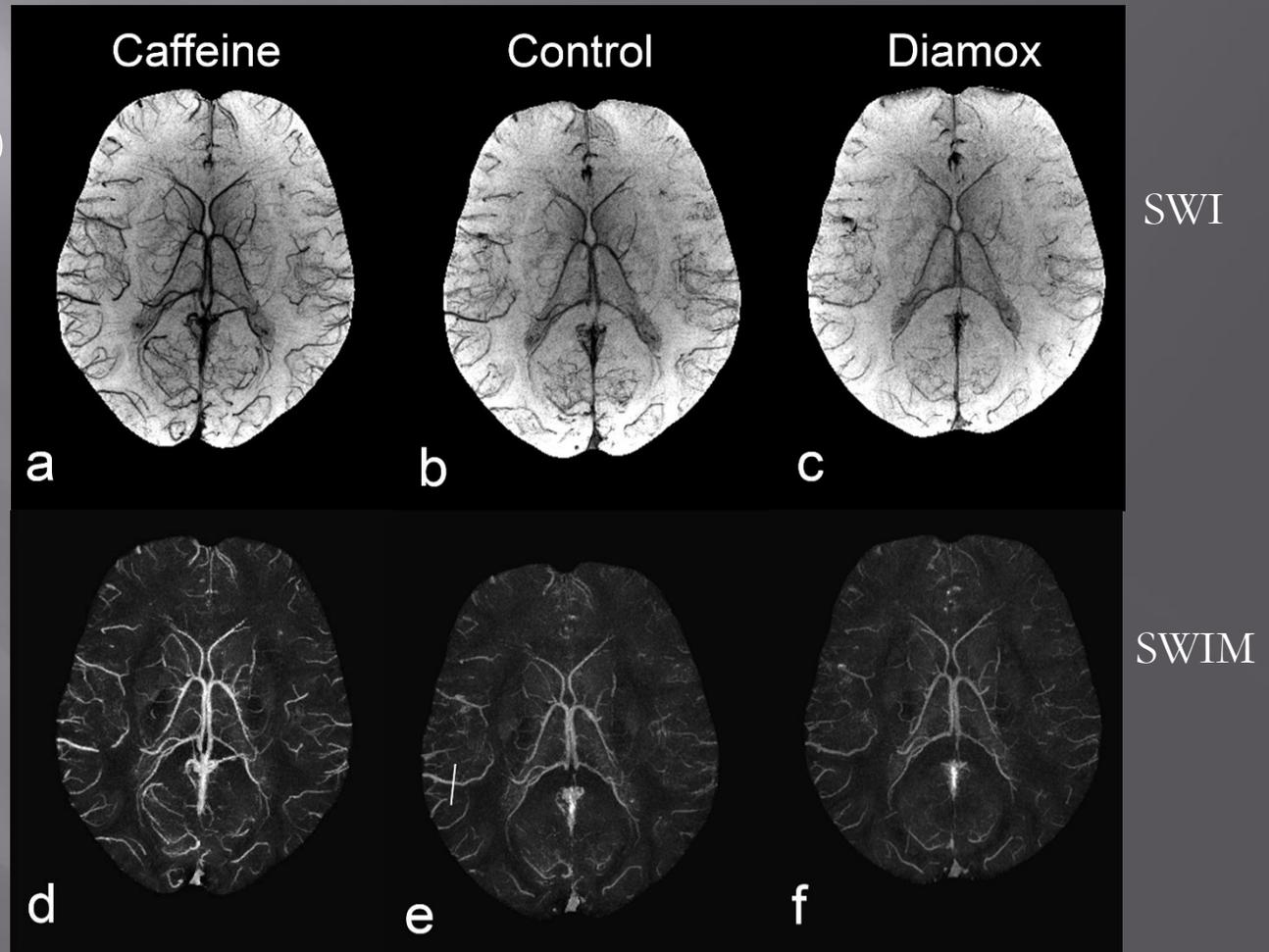
SWI versus SWIM comparison



IMAGING VEINS AND BLOOD PRODUCTS USING SWI AND SWIM: CHALLENGING THE NEUROVASCULAR SYSTEM

200mg caffeine pills (a, d)
or 1000mg diamox IV
injection (c, f).

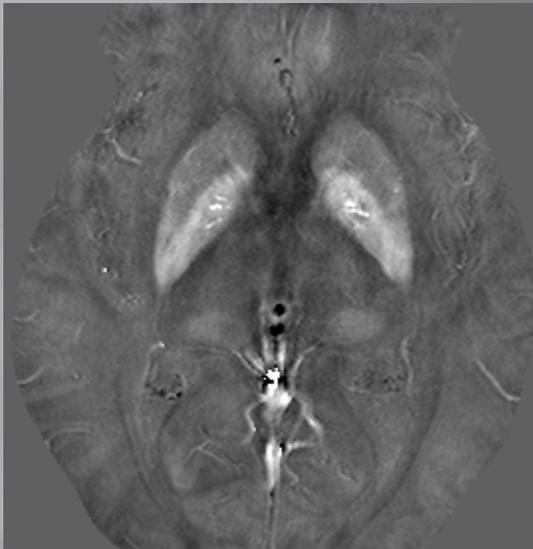
Compared to the control
condition (b,e),
significant oxygen
saturation changes are
observed post-challenge
on veins throughout the
brain.



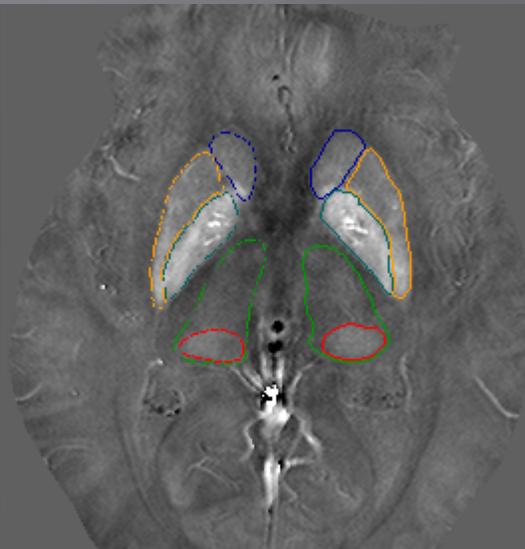
Caffeine: flow change = $-27\% \pm 9\%$ and $\Delta Y = -0.09 \pm 0.02$

Diamox: flow change = $+40\% \pm 7\%$ and $\Delta Y = +0.10 \pm 0.01$

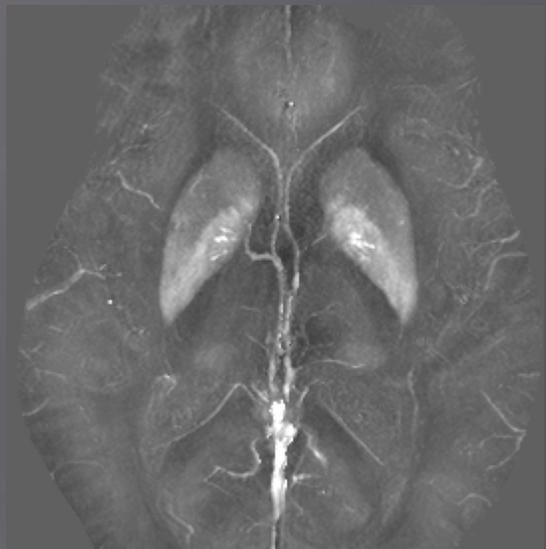
Normal volunteer



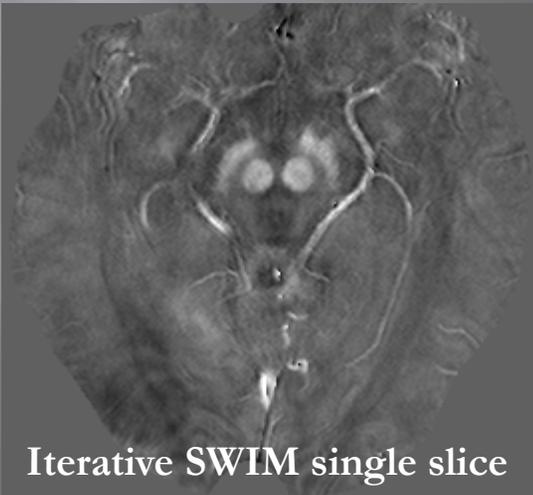
Iterative SWIM single slice



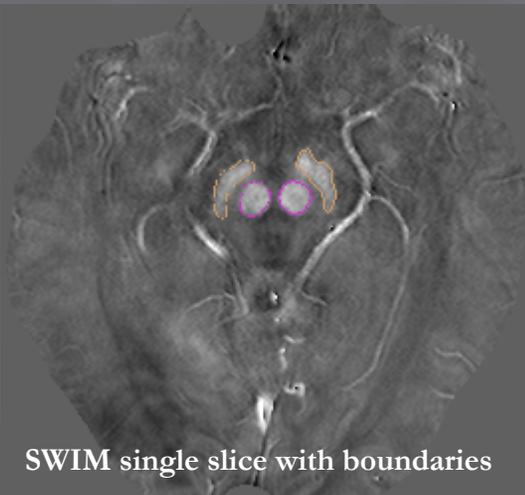
SWIM single slice with boundaries



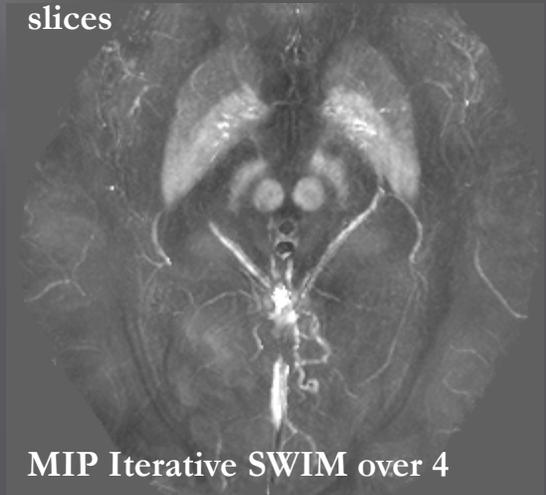
MIP Iterative SWIM over 4 slices



Iterative SWIM single slice

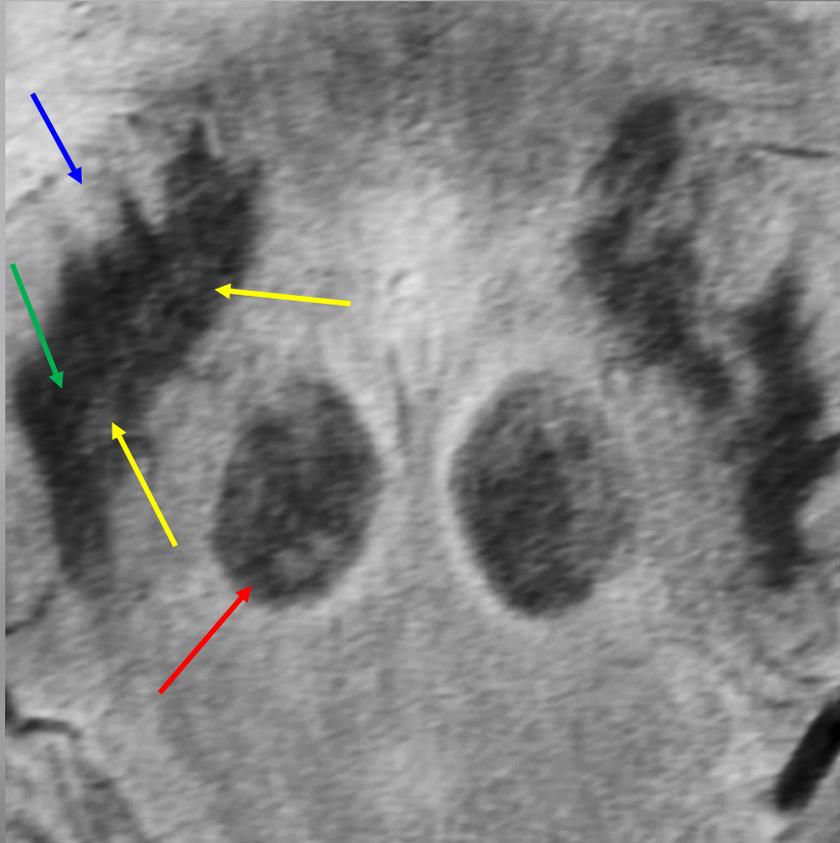


SWIM single slice with boundaries

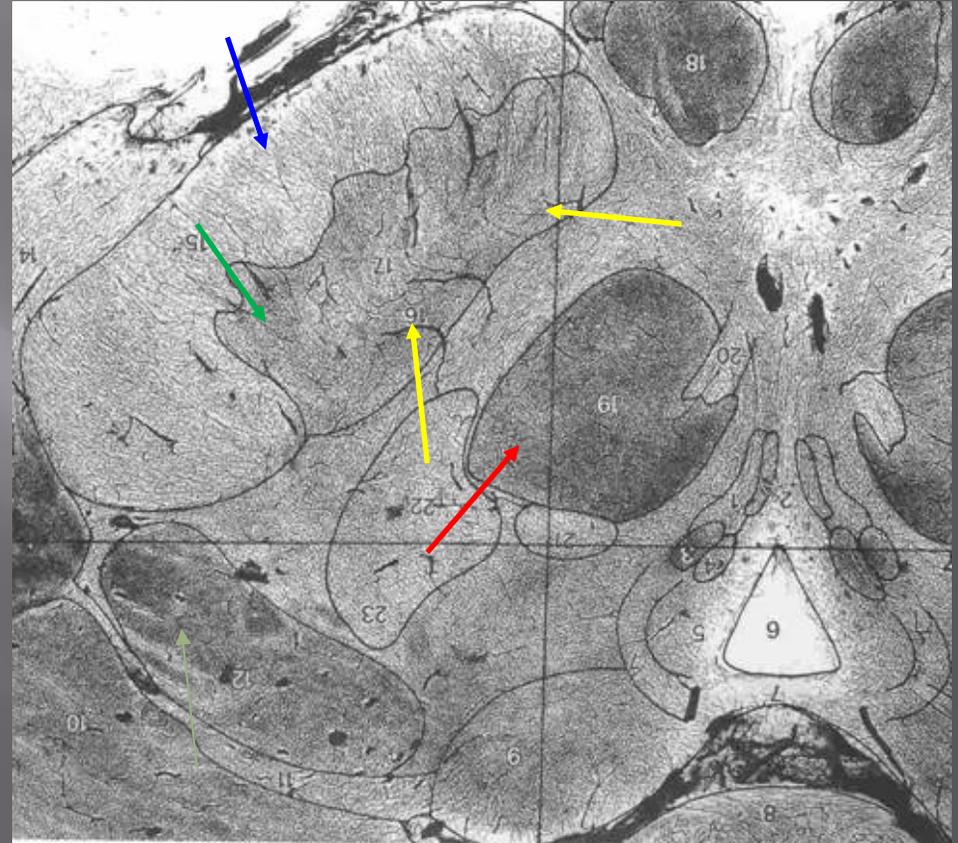


MIP Iterative SWIM over 4 slices

SWIM versus Cadaver Brain Staining

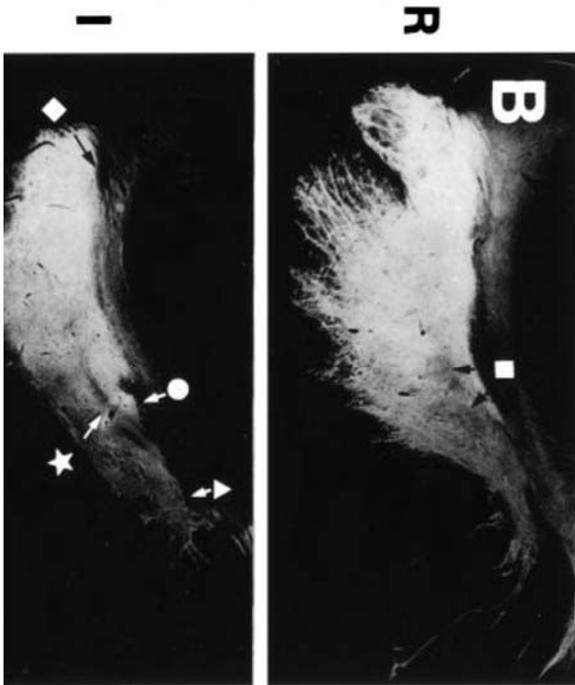
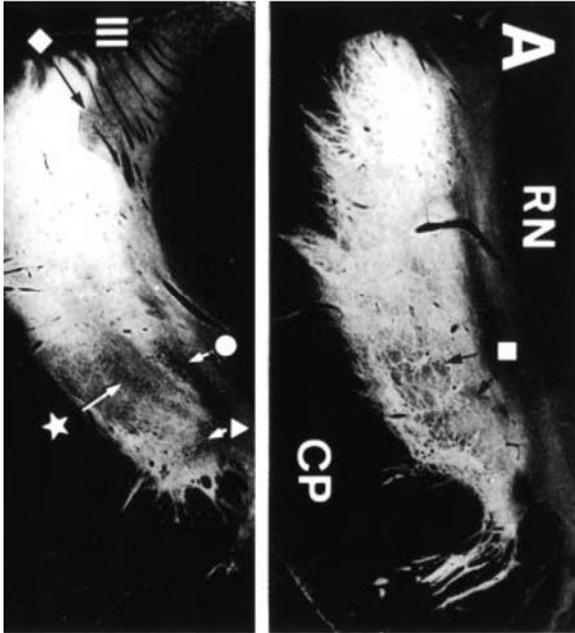


Inverted SWIM image



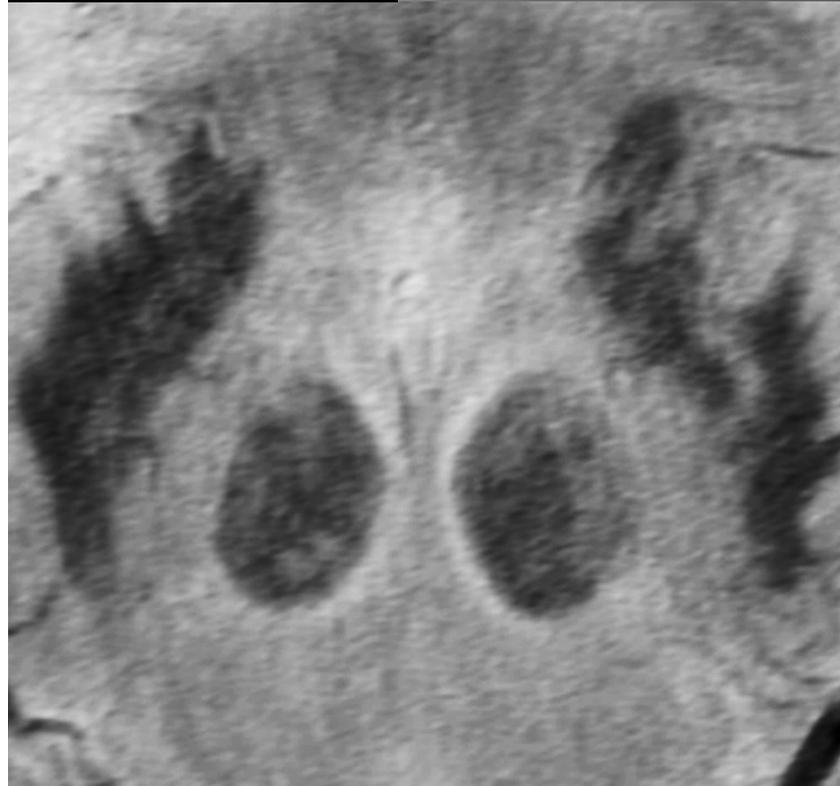
India ink stained brain

Red = RN, Yellow = SNc, Green = SNr, Blue = Crus Cerebri



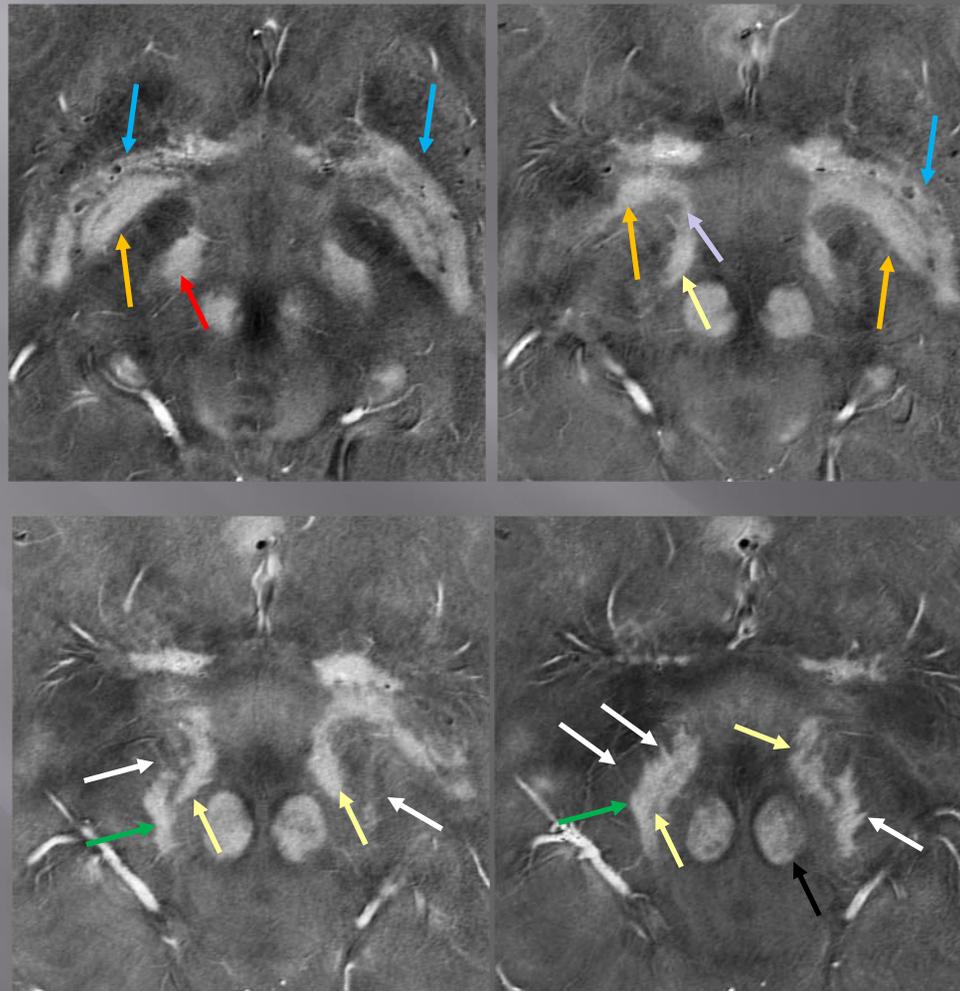
Left: Inverted QSM 100 μ x200 μ x1250 μ
 Right: Calbindin D28k immunostaining

Damier et al.
 Brain 122, 1437, 1999.



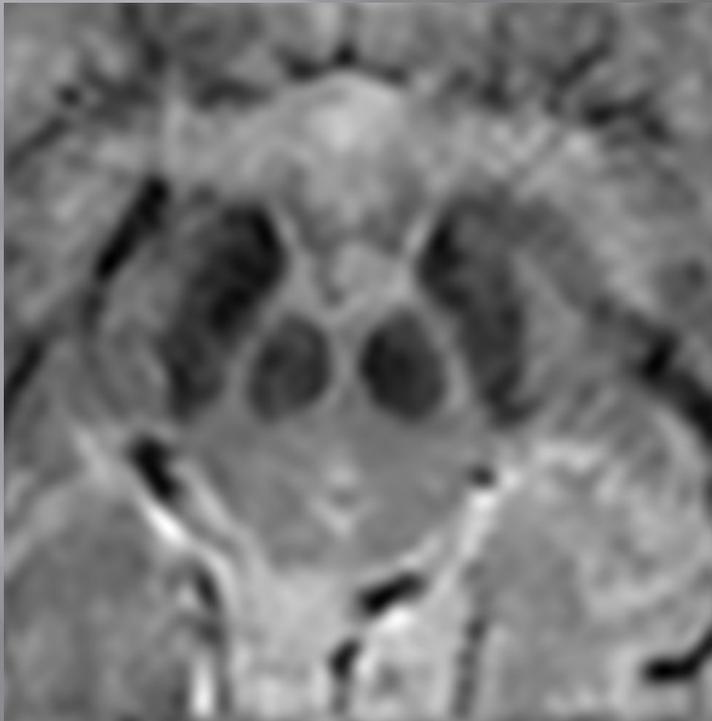
Basal ganglia to midbrain connections STN to SNpc to merging with SNpr

100 μ x 200 μ x 1250 μ

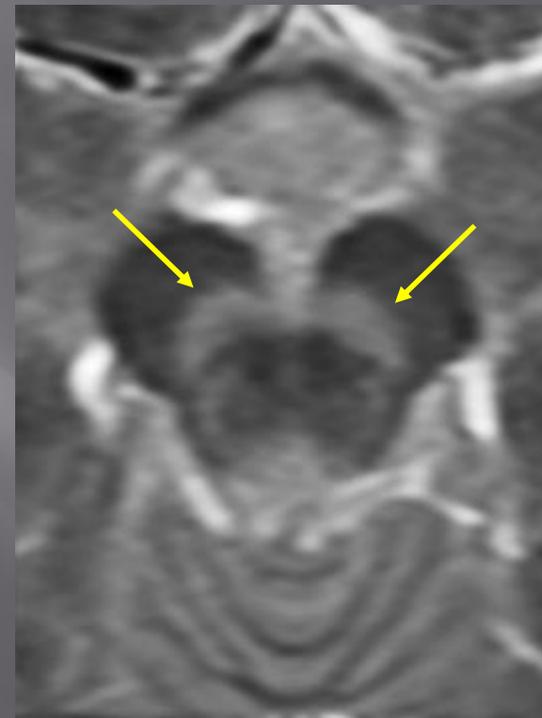


Red = STN, Yellow = SNpc, Green = SNpr, Orange = GPi, Dark Blue = GPe,
Black = RN, White = SN filaments through the CP, Light Blue = Nigrostriatal pathways

Gradient echo imaging of the midbrain



Panda sign



Santa Claus mouse

Yellow = Neuromelanin

Part 4: Questions

- 1) Why is high resolution good for studying the midbrain?
- 2) Why is the signal from the SN dark?
- 3) What's the difference between a Panda and Santa Claus?

MICRO Imaging

- ▣ SWI can image vessels down to 50 microns with a resolution of only 200 microns thanks to T2* and phase masking
- ▣ Arteries generally can't be seen because they are fully oxygenated
- ▣ How can we see arteries with SWI?

MICRO Imaging

The answer is to change the susceptibility of the arteries by using a USPIO contrast agent.

Now we can shift the arterial susceptibility to be the same as that for the veins and hence if we can see 50 micron veins without the contrast agent we should be able to see 50 micron arteries with it.

We use Ferumoxytol to do this, an FDA approved agent for treating anemia.

Ferumoxytol enhanced MRAV

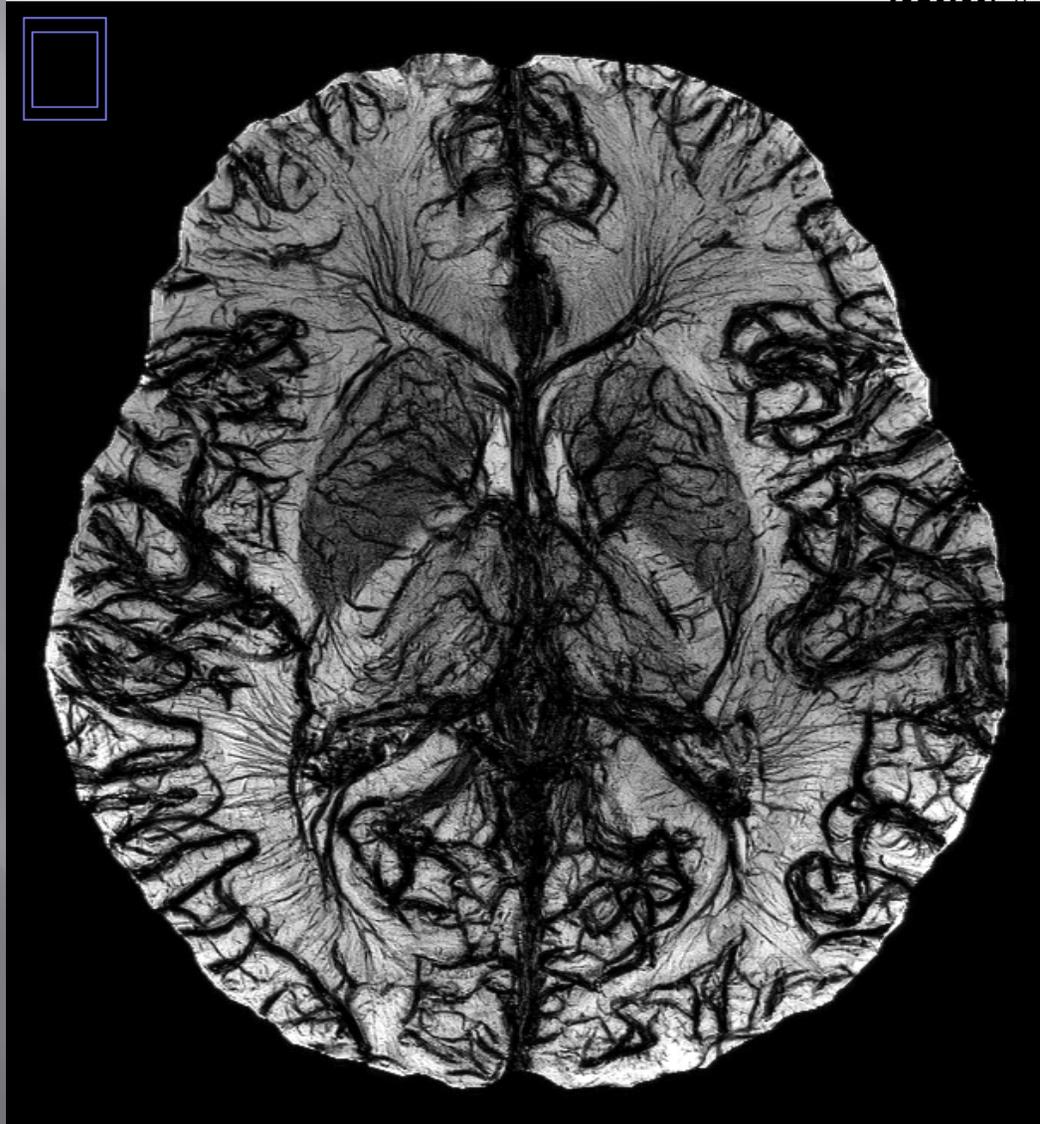
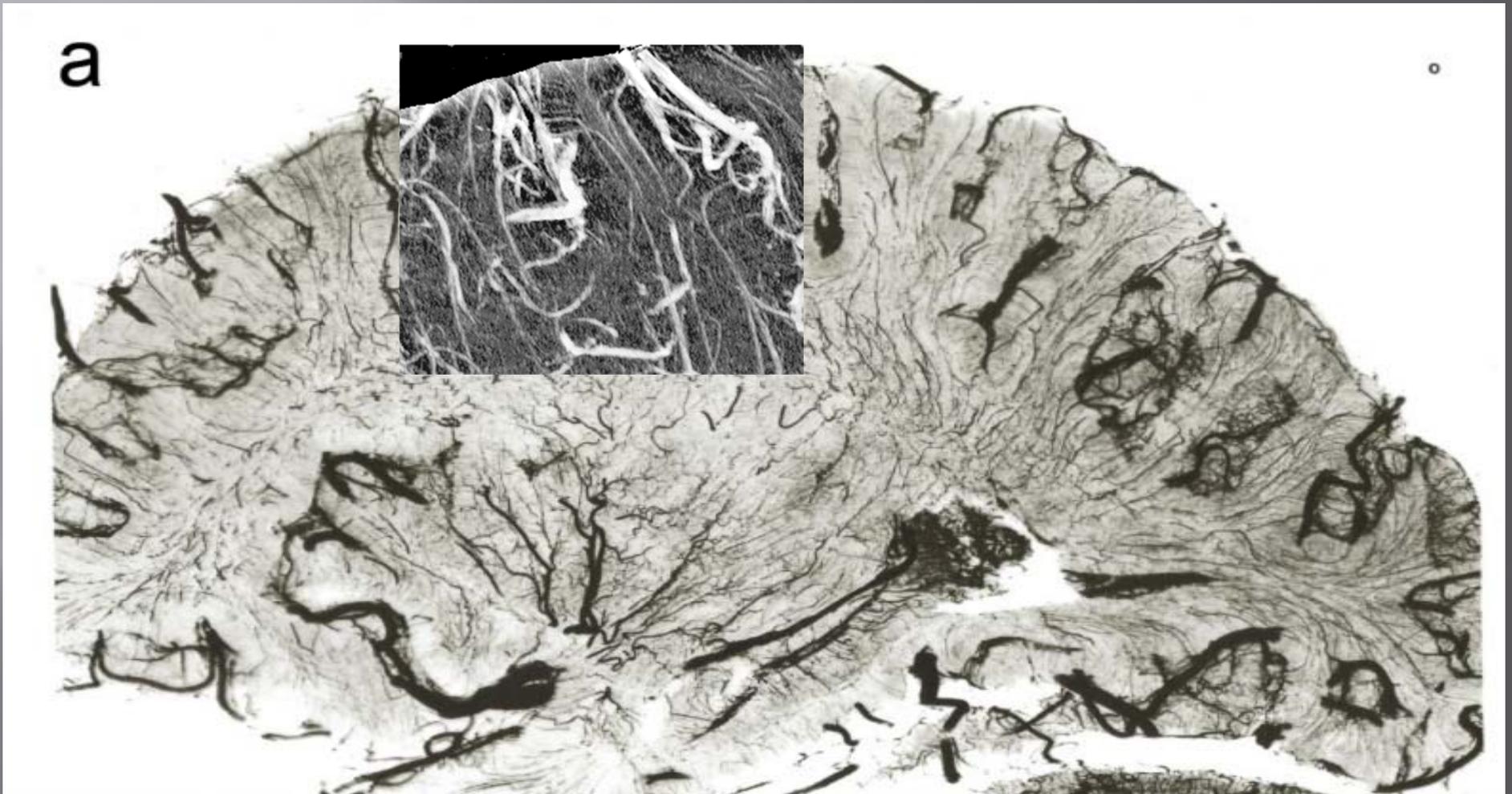


Image courtesy of Yulin Ge and NYU. 59

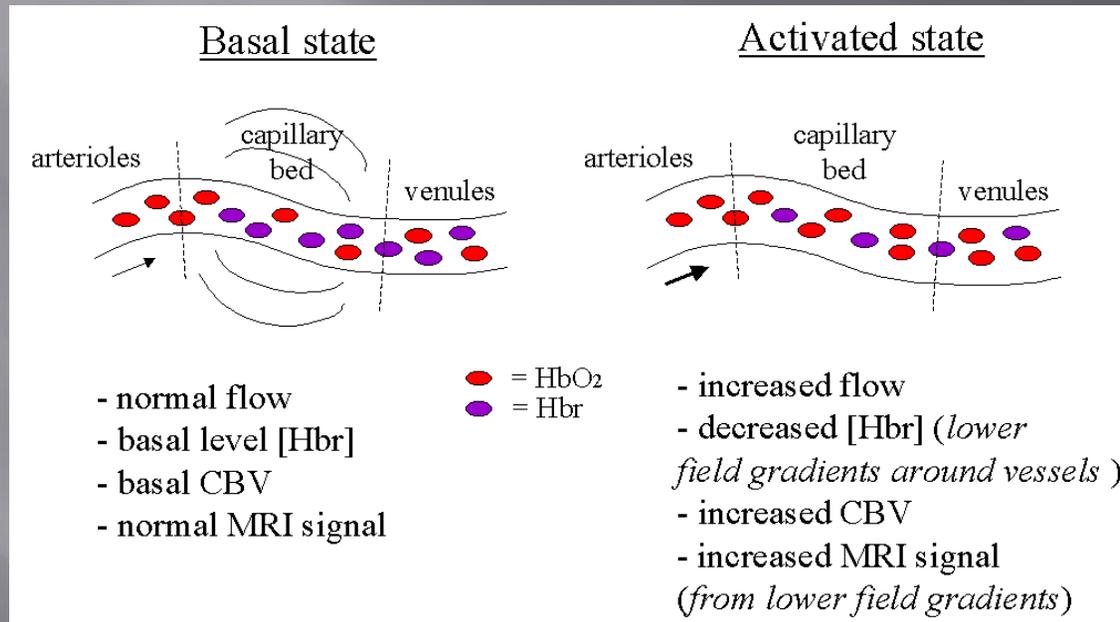
In vivo MICRO imaging compared to cadaver brain imaging: Imaging the cerebral arteries



Part 5: Questions

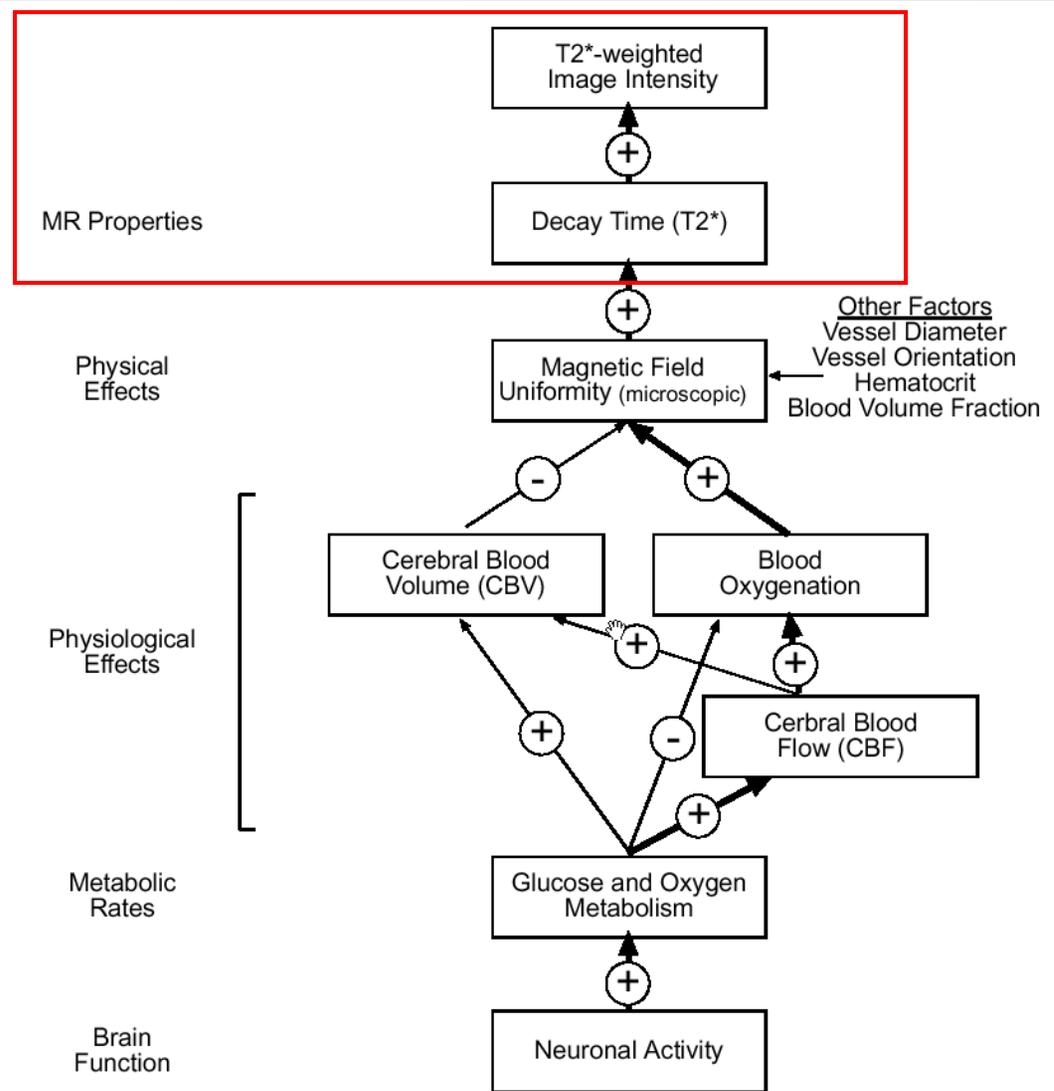
- 1) Why are arteries usually not visible in SWI?
- 2) Why can they be seen with Ferumoxytol?
- 3) How big are the cerebral arteries?

BOLD signal



Possible functional Contrasts for fMRI

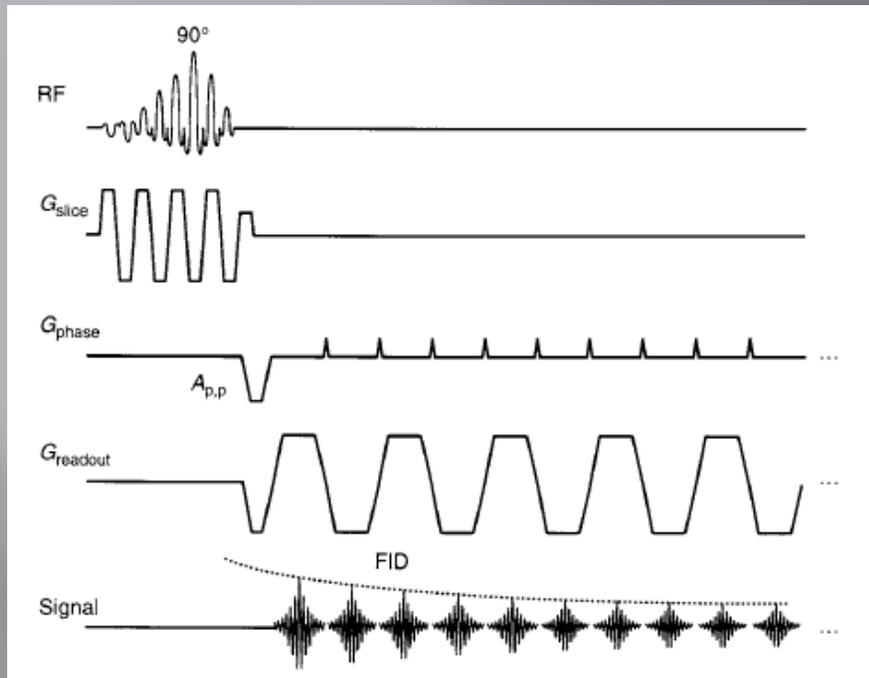
- ▣ BOLD (Blood Oxygenation Level Dependent)
- ▣ CBF
- ▣ CBV
- ▣ Frequency
- ▣ Diffusion
- ▣ Neuronal currents
- ▣ Susceptibility
- ▣ ...



(Doug Noll's primer)

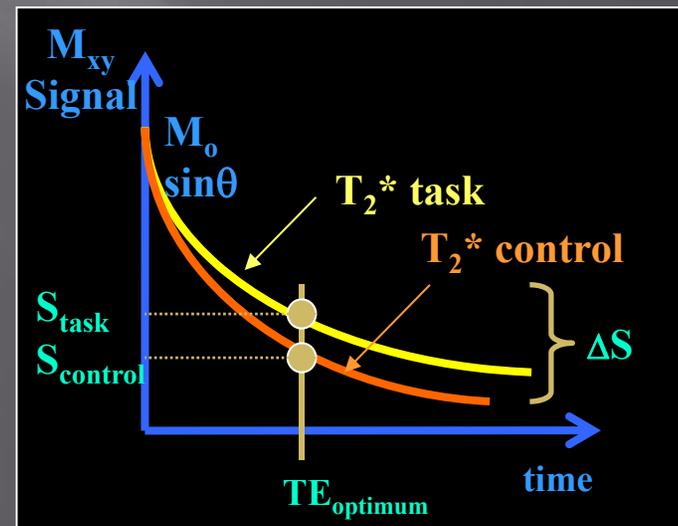
GE-EPI

↑neural activity → ↑ blood flow → ↑ oxyhemoglobin → ↑ T2* → ↑ MR signal



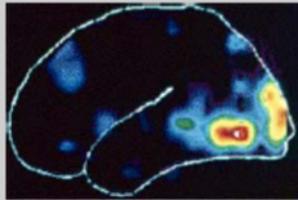
(Handbook of MRI pulse sequences, M.A.Berstein)

- Mainly T2* contrast
- High CNR, low SAR, fast scanning
- Low resolution(64x64)
Low specificity
Signal dropouts
Image distortion
...
- Nevertheless, still the most widely used fMRI sequence

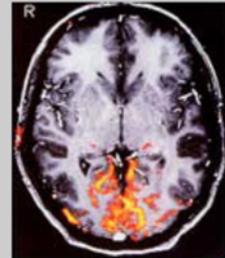


(Source: Jorge Jovicich)

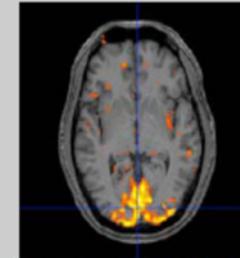
Activated Brain



H_2O^{15+} PET

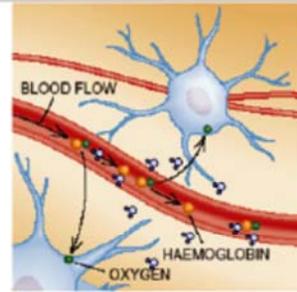
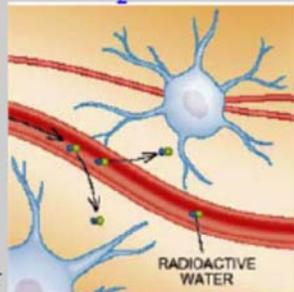


BOLD fMRI

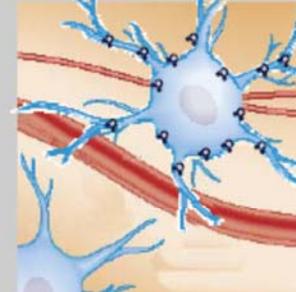
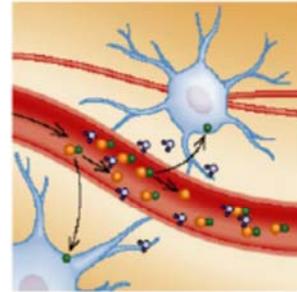
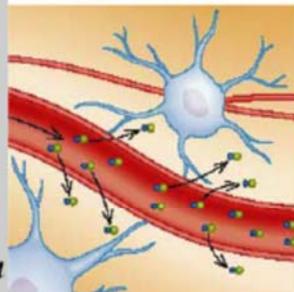


DIFFUSION fMRI

Rest



Activation



- ↗ blood flow
- ↗ quantity of radioactive water in activated tissues

Radioactive water

- ↗ blood flow & oxygenation
- ↘ magnetized water relaxation in/near vessels

Magnetized water

- ↗ cell size and membrane surface
- ↘ diffusion of water near membranes

Plain brain water

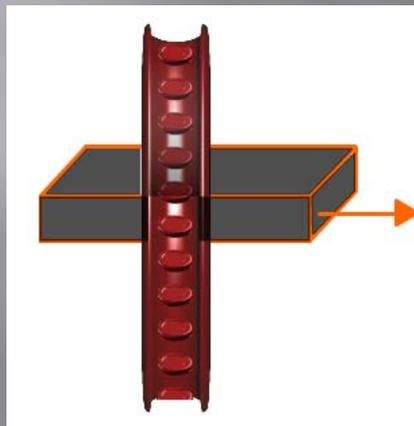
Part 6: Questions

- 1) What happens to blood flow when the brain is activated?
- 2) Why does the signal increase as blood flow increases?

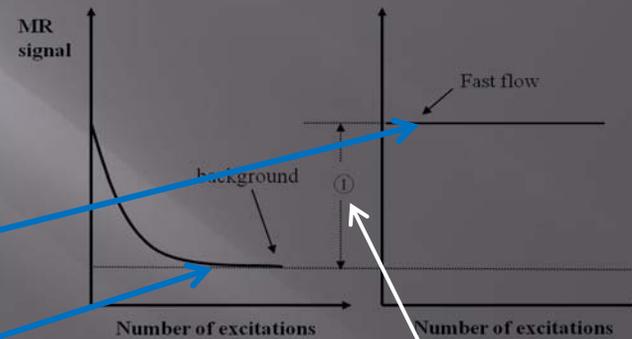
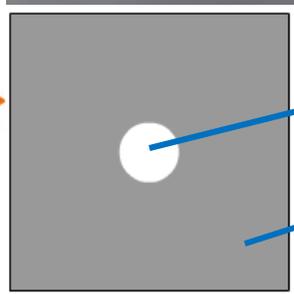
MRA AND FLOW QUANTIFICATION

The Basics of Flow in MRI

- Between each excitation, new blood that is fully magnetized enters the slice, it will have maximum signal each excitation.



[from www.imaio.com]

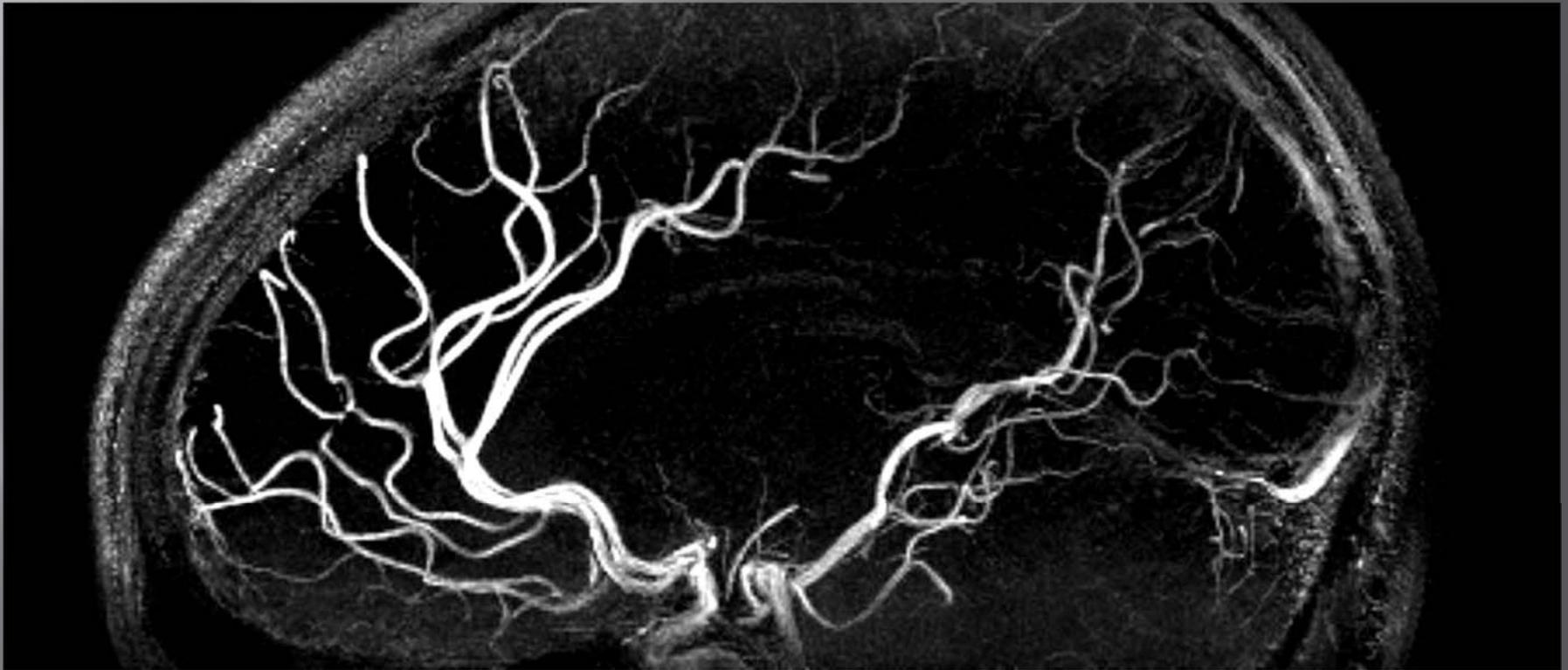


Contrast

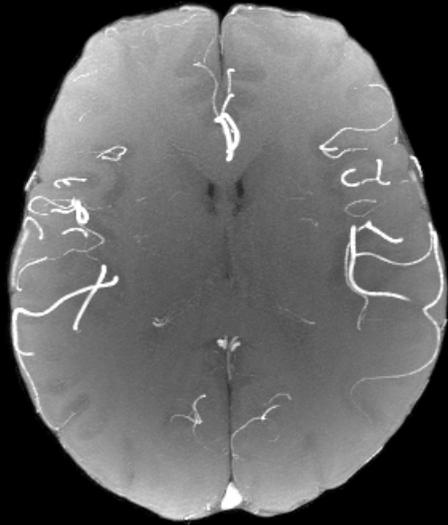
- ▶ This creates a contrast with the stationary surrounding tissue

High resolution MR angiography

Small arteries around 250 microns are beginning to become visible even without a contrast agent.
(0.5mm isotropic resolution)



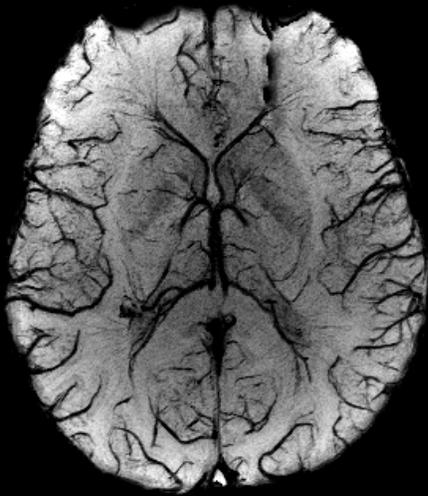
MRA short echo SWI



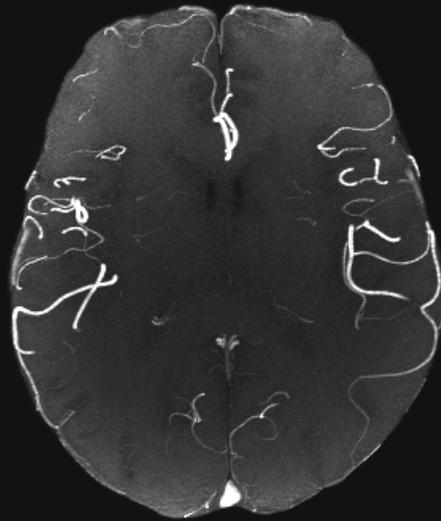
RP-DP MRA



SWI only veins



NLS MRA no veins

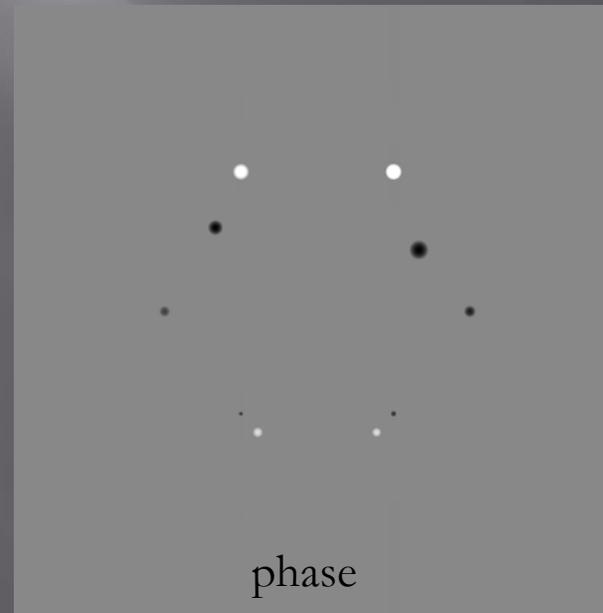
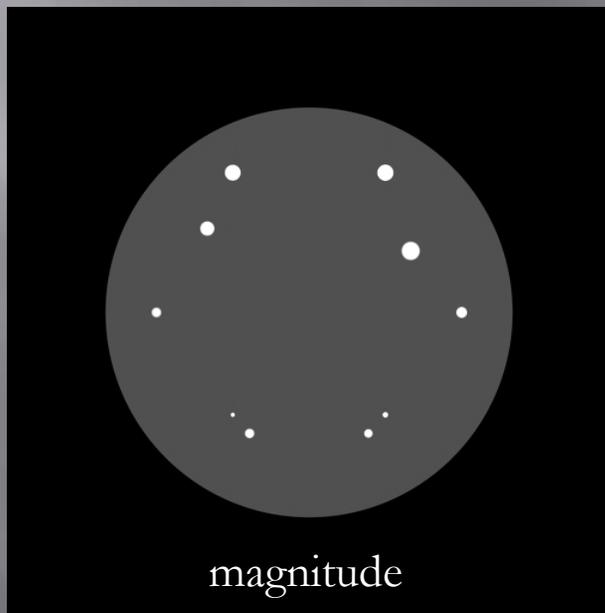


Simultaneous MRV
and MRI using a
double echo
interleaved SWI
rephased/dephased
sequence



The Basics of Flow in MRI

- ▣ Flowing fluid affects both MRI signal magnitude and phase in different ways
- ▣ These different effects can be used to both visualize and quantify flow

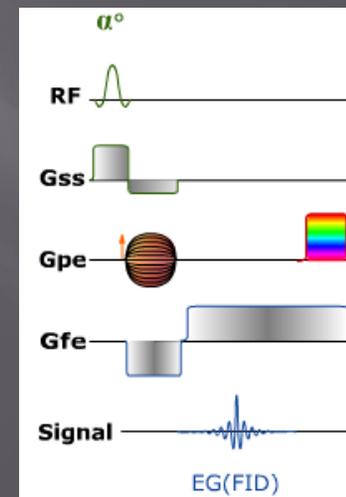


The Basics of Flow in MRI

- How fast must the blood be going to achieve maximum signal?
 - This value is referred to as the “threshold velocity” and is calculated from slice thickness (TH) divided by TR or TH/TR

- Bright Blood Imaging
 - Maximize In-Flow Effect
 - Saturate Surrounding Tissue
 - FLASH sequence
 - Smaller TR, Low Flip Angle
 - Flow Compensation – Null M1

Fast Low Angle Shot (FLASH) Sequence



[from www.imaios.com]

The Basics of Flow in MRI

- Some quick math behind this...
 - The phase of a spin with initial position x and velocity v is given as

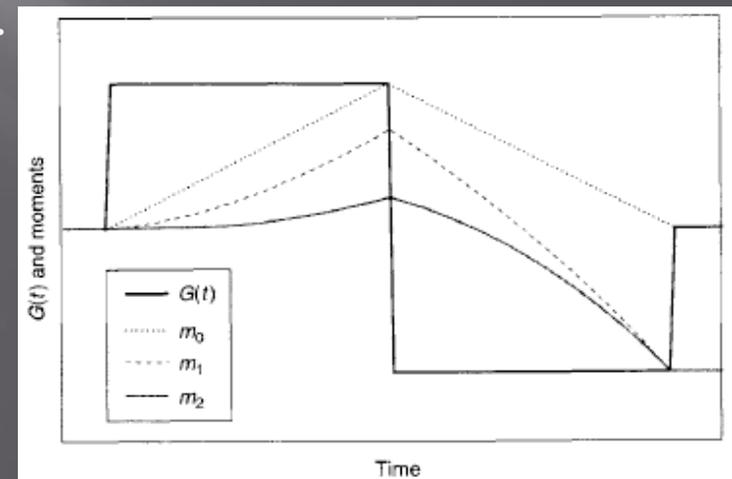
$$\phi = \phi_0 + \gamma x M_0 + \gamma v M_1$$

M_n refers to the n^{th} order moment of the gradient over time. ϕ_0 is background phase. Gamma is a constant

- For a bipolar gradient, $M_0=0$ and $M_1 \neq 0$.

$$\phi = \phi_0 + \gamma v M_1$$

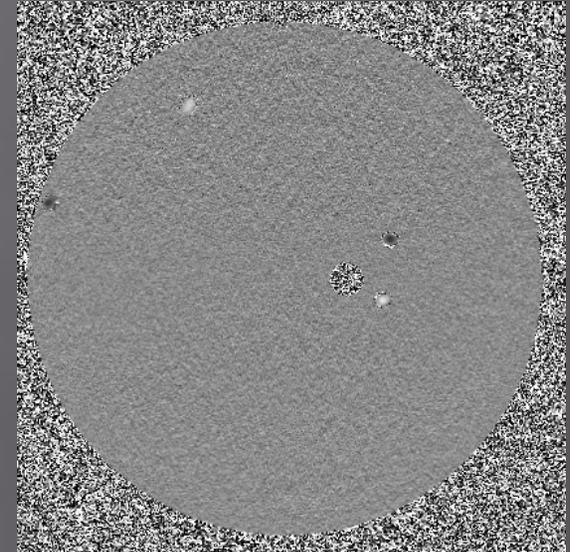
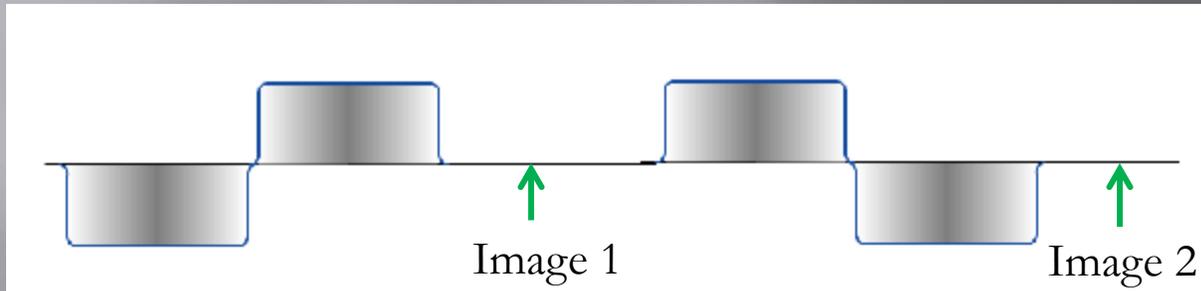
Phase is now a function of velocity



[Bernstein, M.A., et al, *Handbook of MRI pulse sequences*. 2004, Amsterdam; Boston: Academic Press. xxii, 1017 p.]

The Basics of Flow in MRI

- Use two images of opposite polarity for the bipolar gradients...



- And subtract 2 from 1... Now the resulting phase is

$$\Delta\phi = \gamma v \Delta M_1$$

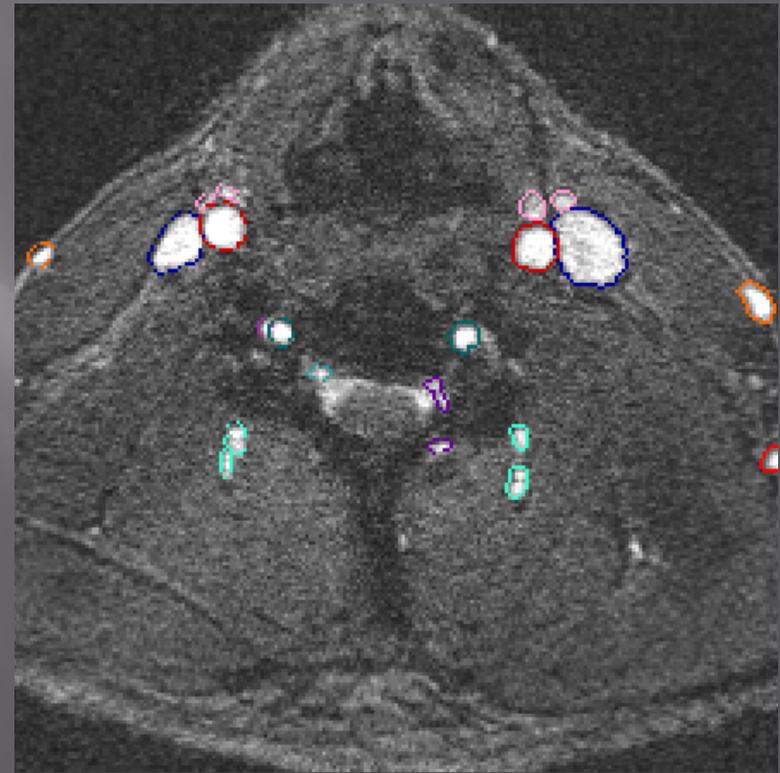
- Phase runs from $-\pi$ to π . Need scaling factor “venc”

$$venc = \frac{\pi}{\gamma \Delta M_1}$$

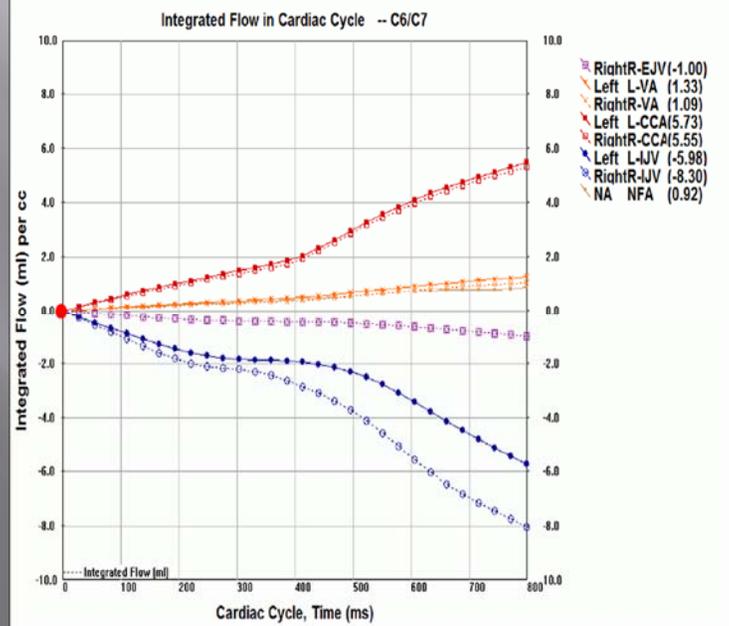
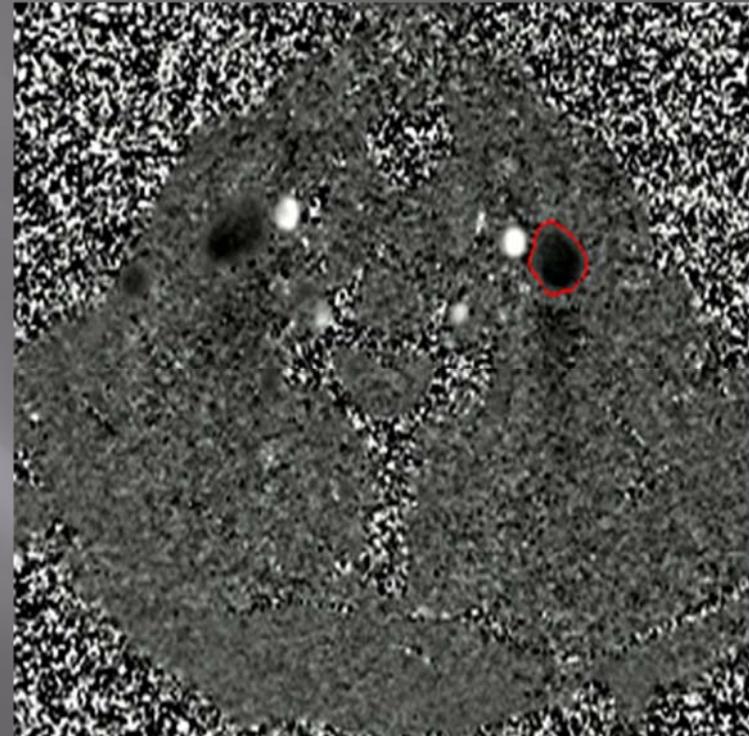
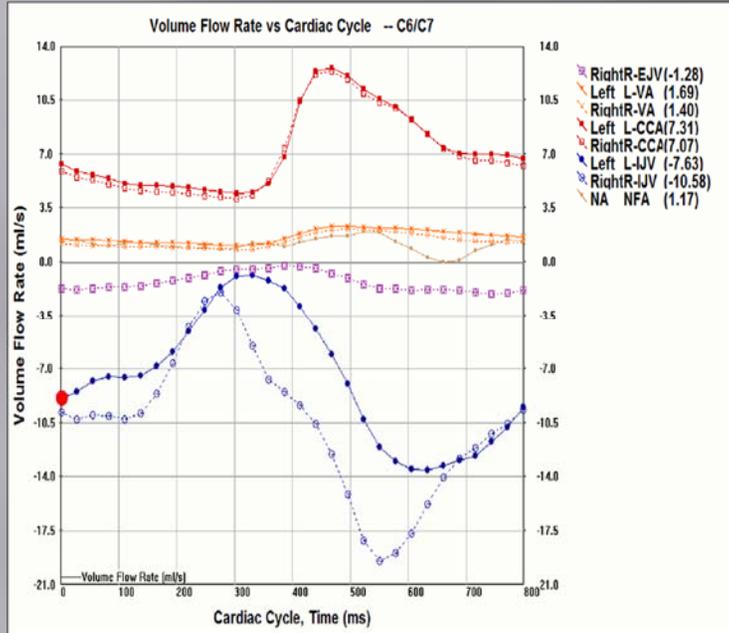
$$v = \frac{\Delta\phi}{\pi} venc$$

The Basics of Flow in MRI

- ▣ Flow can be quantified using special software
- ▣ This software must be capable of
 - Segmentation (automatic or manual)
 - Phase Unwrapping
 - Organizing/Exporting Results



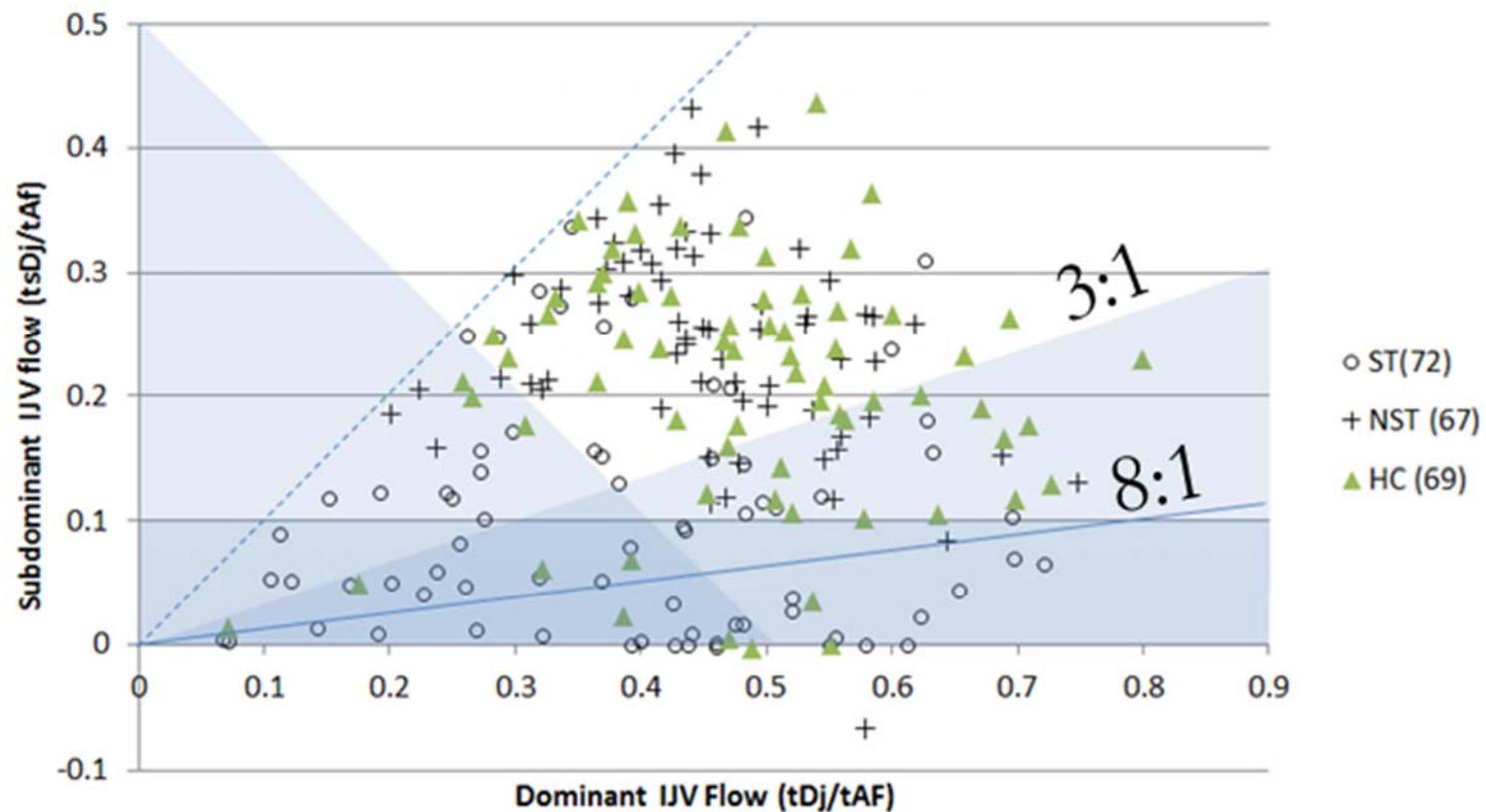
Flow change during a given cardiac cycle



Flow rate and integrated flow for the right internal jugular vein (RIJV). The red circle follows the darkening of the signal in the phase image above.

Dominant vs. Sub-dominant Venous Flow

Dominant IJV flow vs Subdominant IJV flow at the C6 level Normalized to Total Arterial Flow



Part 7: Questions

- 1) What is main principle behind TOF vascular imaging that makes the blood bright?
- 2) What is the principle behind flow encoding?
- 3) Why do you think low blood flow in the jugular veins may lead to a problem for MS and PD patients?

Potential Projects

- 1) Mapping out tissue properties in the brain.
- 2) Studying SWI in stroke to detect abnormalities.
- 3) Studying high resolution structural imaging at 7T.
- 4) Possible fMRI project.
- 5) Measuring blood flow changes in