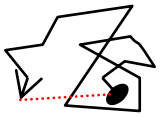
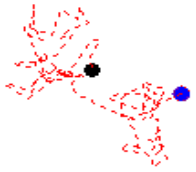
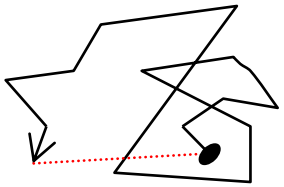
WHAT IS DIFFUSION?

- Random translational motion of molecules driven by their internal thermal energy (Brownian motion) (Einstein, 1905).

RMS distance travelled in a fixed time would be a measure of diffusion. $R = \sqrt{6\,D\,t}$







FACTORS AFFECTING DIFFUSION

- *Diffusion depends on*
  - *Type of particle or molecule under study*
  - *Temperature*
  - *Environment in which diffusion takes place*
- *Diffusion is very high in gases, intermediate in liquids and low in solids.*

Diffusion MRI

- *Based on the ability to visually depict the micro movement of the water molecules present within a voxel. These motions encounter different obstacles in the body (cell membranes, proteins, macromolecules, fibers…), which vary according to the tissues and certain pathological modifications (intracellular edema, abscess, tumors…).*

Main Role of Diffusion MRI

- *Diffusion MRI has revolutionized the management of acute brain ischemia (stroke), saving life of many patients and sparing them significant disabilities*

The birth of water diffusion MRI *Le Bihan*

The world's first diffusion images of the brain were made public in August 1985 at the Society of Magnetic Resonance in Medicine (SMRM) meeting in London. First diffusion MRI paper appeared in 1985 in the journal of the French Academy of Sciences (Le Bihan & Breton, 1985).

Diffusion MRI: what water tells us about the brain

Denis Le Bihan

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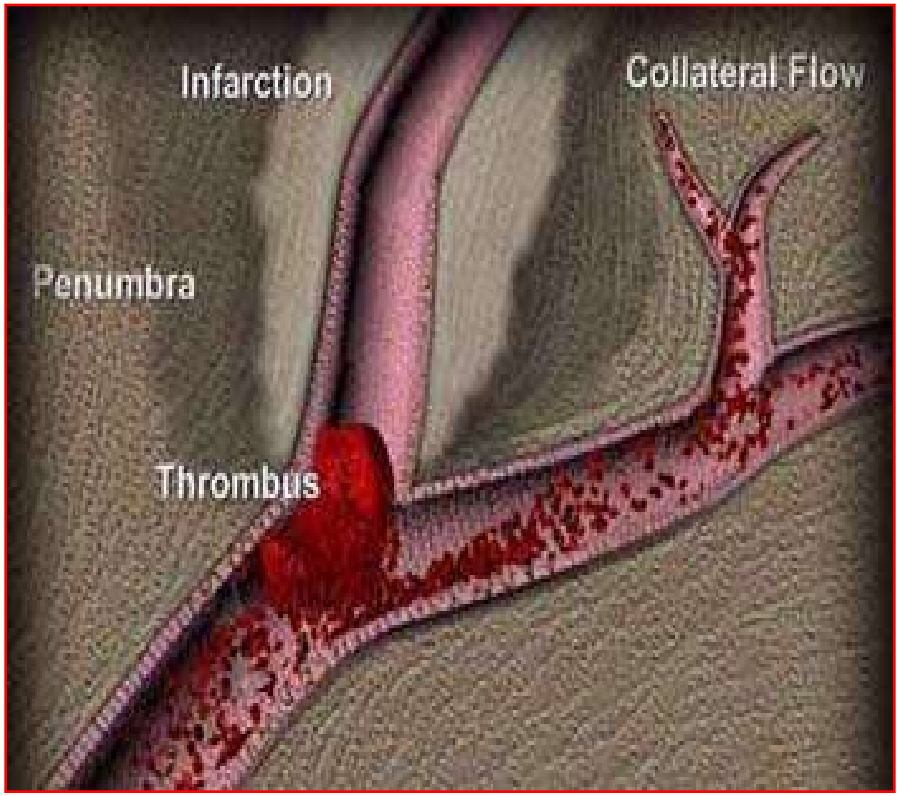
Ischemic Stroke

caused by occlusion of a blood vessel that disrupt the flow of blood to the brain .

infarct

When a stroke occurs, it kills brain cells in that immediate area. This area of dead cells is called an infarct



Penumbra

The blood supply in the area surrounding the infarct is compromised, but not completely cut off. This area is called the penumbra.

Without prompt treatment the penumbra, will also die.

Role of DWI Assessment of acute stroke.

In case of non hemorrhagic stroke

CT is negative for the first 12 hours to 24 hours after symptom onset.

Conventional MR sequences also do not show early changes in ischemic stroke until 6-12hours.

Diffusion weighted Imaging can detect infarct within 1-2 hours.

Therapeutic options for Ischemic Stroke

Intravenous(IV) with recombinant tissue plasminogen activator (rt-PA)

Studies have shown that patients may benefit from artery re-canalization only if therapy is started within first 3 hours after occlusion.

Intra-arterial (IA) rt-PA must be given within 6 **hours** of onset

Both have strict inclusion and exclusion criteria

- Ischemia

  Ischemic tissue exhibits reduced diffusion.

  Intracellular water

  - low (restricted) diffusion.

  Extracellular water

  - higher diffusion.

ischemia

⇓

cytotoxic edema

⇓

reduction in extracellular volume fraction

⇓

reduction in overall diffusion

.

Free diffusion

The water molecules displace freely in all spatial directions. A typical example of this corresponds to fluids such as cerebrospinal fluid.

Restricted isotropic diffusion

Water molecule displacement is restricted, in whatever spatial direction, by numerous obstacles (proteins, cells)
Example: abscess, tumor at high cell density

Restricted anisotropic diffusion

Certain structured tissues create obstacles that orientate the motion of the water molecules (tendency to displace themselves in one or several particular directions). Diffusion is only restricted in certain spatial directions.
Example : nerve fibers (organization in bundles of axons running in parallel, with concentric layers of myelin restricting transversal diffusion)

How Diffusion is measured ?

With plain diffusion MRI, diffusion is fully described using a single (scalar) parameter, the diffusion coefficient, D.

- *Stejskal and Tanner equation*

  $S = S_o \exp(-b \cdot D)$

S_o is Signal Intensity of T_2W or b = 0 image

S is signal Intensity under gradient field

D is diffusion coefficient

b is constant

DIFFUSION TENSOR

In the presence of anisotropy, diffusion can no longer be characterized by a single scalar coefficient, but requires a tensor, D, which fully describes molecular mobility along each direction and correlation between these directions

ADC is actually a tensor quantity or matrix

$$ADC = \begin{matrix} ADC_{XX} & ADC_{XY} & ADC_{XZ} \\ ADC_{yx} & ADC_{YY} & ADC_{YZ} \\ ADCzx & ADC_{ZY} & ADC_{ZZ} \end{matrix}$$

DIFFUSION TENSOR Contd..

Diagonal elements of this matrix can be combined to give information about the magnitude of the ADC (apparent diffusion coefficient)

Magnitude of ADC = ⅓ (ADC_{XX} ADC_{YY} ADC_{ZZ})

HOW DIFFUSION IS MEASURED IN MRI?

$S = S_0 \exp(- b.\ ADC)$

$\mathbf{b = \gamma^2 G^2 \Delta^2 (T - \Delta / 3)}$

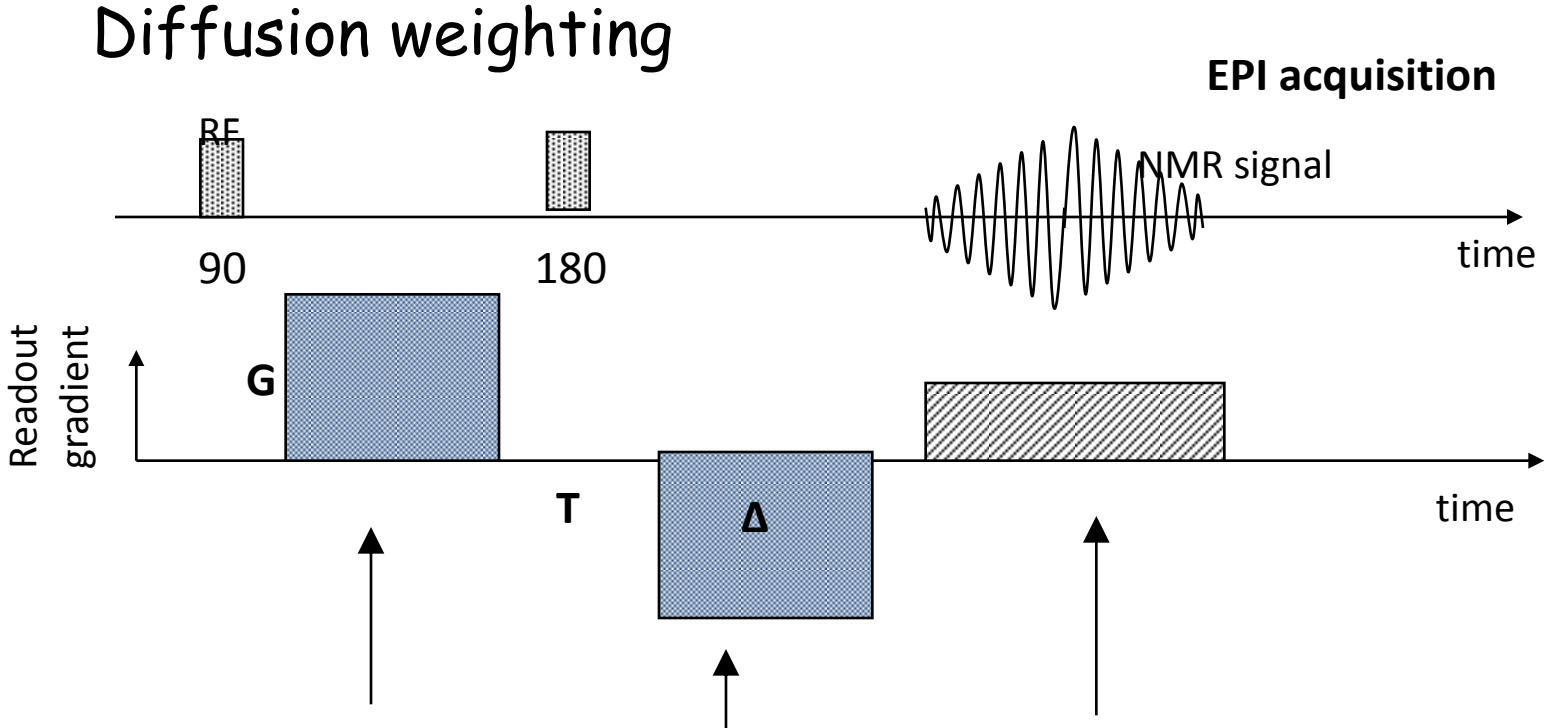
G Gyromagnetic ratio of the proton

G Strength or amplitude of gradients

Δ Duration of each gradient pulse

T Time interval between gradient pulses

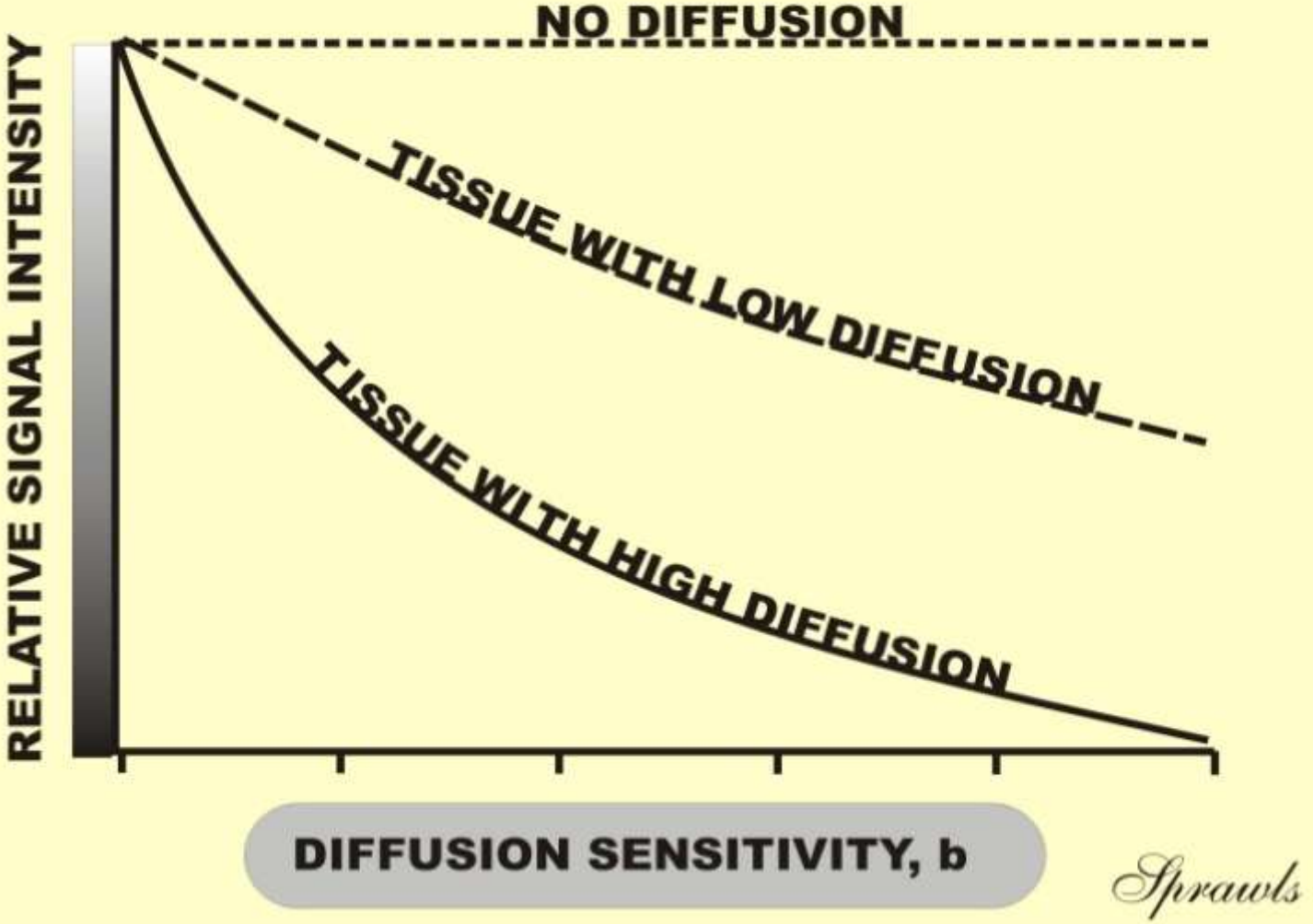
MR Pulse sequences in DWI



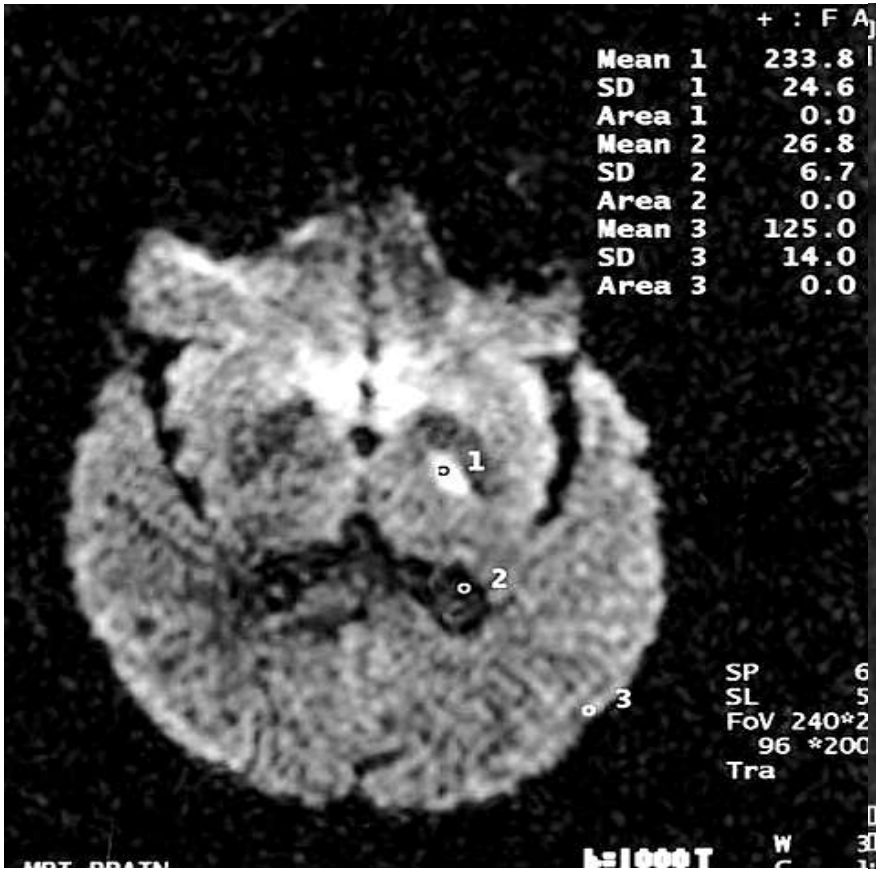
Stationary: nucleus	dephased	rephased	echo contributes to signal
Diffusing: nucleus	dephased	not fully reduced	loss of signal
High ADC			

Diffusion Gradients

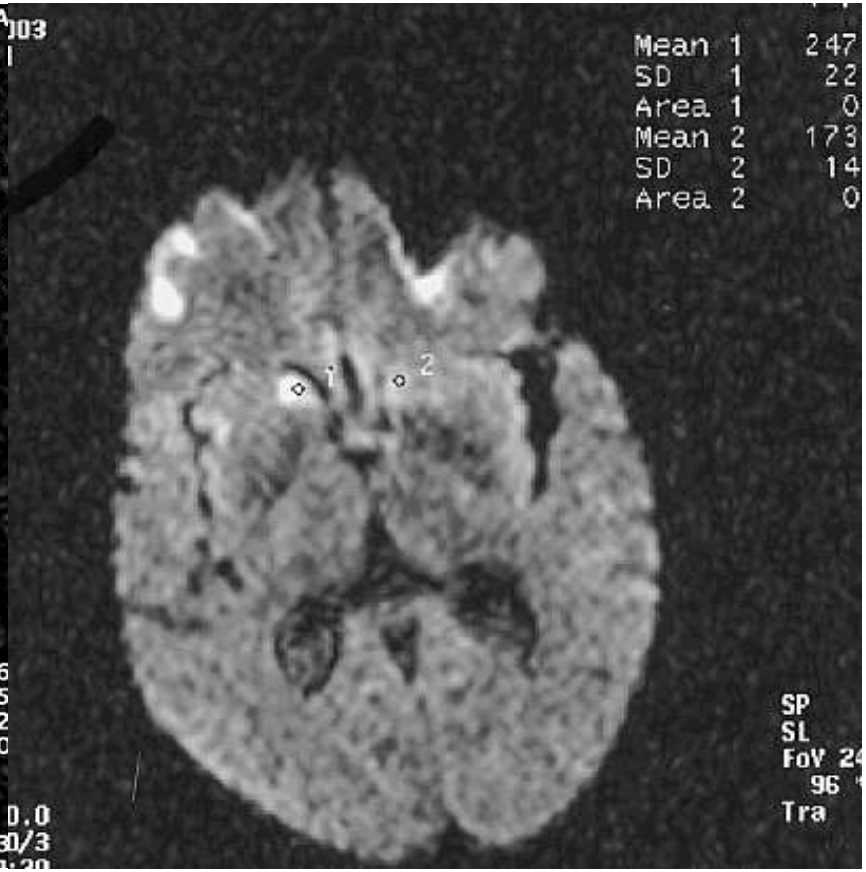
DIFFUSION IMAGING



Sprawls



DW IMAGE AT b=1000s/mm2 SHOWING Lt INTERNAL CAPSULE INFARCT (TIME8 Hrs



DW IMAGE AT b=1000s/mm2 SHOWING Rt Caudate Nucleus (TIME: 8 HRS)

DWI

ADC Map

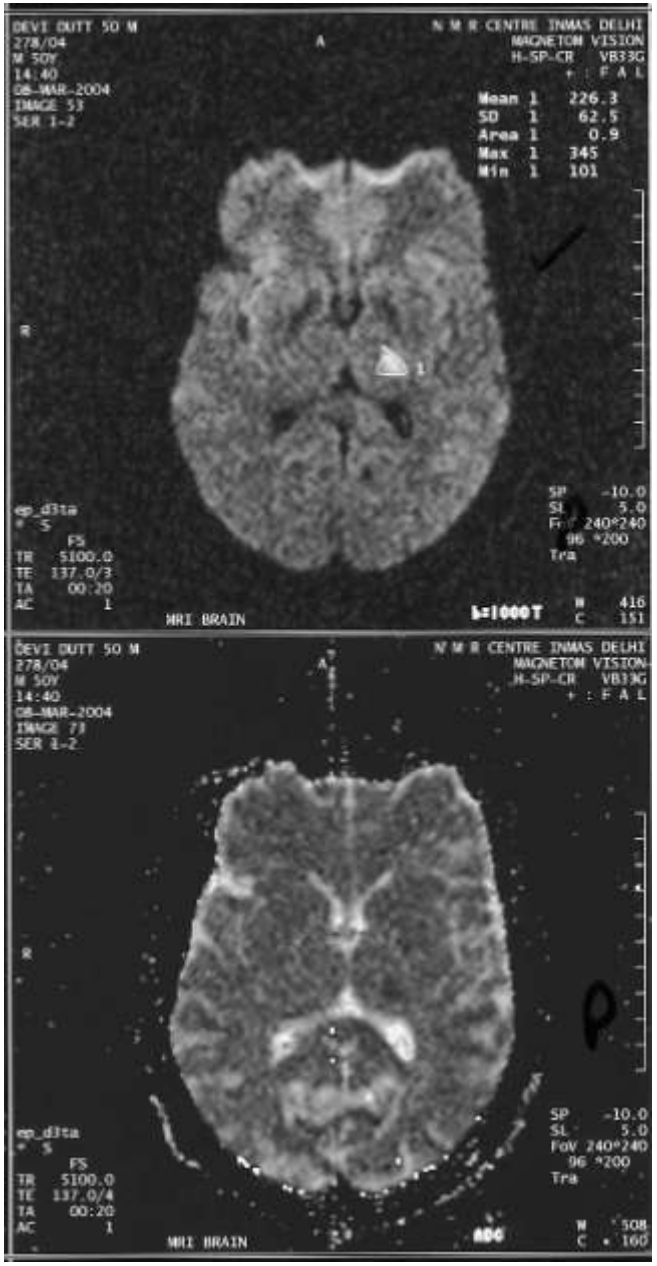

DEVI DUTT 50 M
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IMAGE 53
SER 1-2
N M R CENTRE INMAS DELHI
MAGNETOM VISION
H-SP-CR VB33G
Mean 1 226.3
SD 1 62.5
Area 1 0.9
Max 1 345
Min 1 101
R
ep_d3ta
FS
TR 5100.0
TE 137.0/3
TA 00:20
AC 1
SP -10.0
SL 5.0
FOV 240*240
96 *200
Tra
MRI BRAIN
b=1000T
W 416
C 151
DEVI DUTT 50 M
278/04
M SOY
14:40
08-MAR-2004
IMAGE 71
SER 1-2
N M R CENTRE INMAS DELHI
MAGNETOM VISION
H-SP-CR VB33G
R
ep_d3ta
FS
TR 5100.0
TE 137.0/4
TA 00:20
AC 1
SP -10.0
SL 5.0
FOV 240*240
96 *200
Tra
MRI BRAIN
ADC
W 508
C 160

Other role of Diffusion imaging

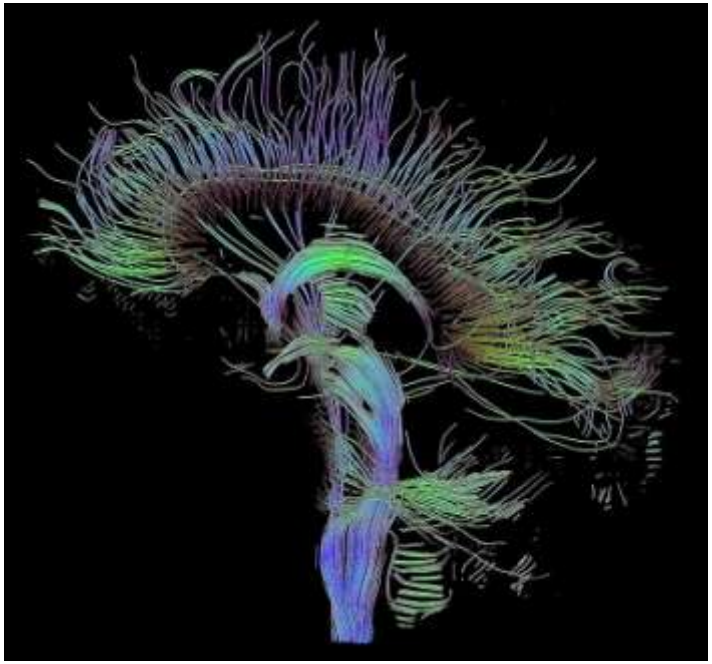
- *Tumoral: cerebral lymphoma (reduced ADC), epidermoid and cholesteatoma cysts (hypersignal in diffusion).*
- *Infectious: pyogenic brain abscess (reduced ADC, providing differential diagnosis from a necrotic tumor in which the ADC is increased),*
- *herpes encephalitis*
- *Degenerative: Creutzfeldt-Jakob's disease (aid to early diagnosis)*
- *Inflammatory: MS*
- *Traumatic*

Diffusion Tensor Imaging

Diffusion tensor imaging enables the in-vivo study of tissue microstructure. It gives indications about possible nerve fiber anomalies in white matter or the spinal cord that are not visible in conventional imaging

Fiber tractography

- to analyze brain maturation and development (myelinization),
- assist in the preoperative check-up for brain tumors (corticospinal bundle) or for medullary compression.
- Alzheimer’s disease,
- certain psychiatric affections,



Summary of DWI

- *DWI (Diffusion Weighted Images) are acquired by combining EPI*
- *Fast gradient echo sequence with two large gradient applied after excitation*
- *The gradient pulses are designed to cancel each other out if spins do not more whilst moving spins experience pulse shift.*
- *Signal attenuation therefore occurs in normal tissues with random motion and high signal appears in the tissue with restricted diffusion.*

PERFUSION

- Volume of blood delivery of oxygen / nutrients / contrast agents (gadolinium) to cells via capillaries bed of a block of a tissue in a given period
- Affected by pathological and physiological conditions, such as tumor angio-genesis, stroke and infarct, vascular wall changes.

CBF Thresholds for preservation of function and structure

above 60 ml/100 g/min hyperperfusion

40-60 ml/100g/min normal range

40-20 ml/100g/min olgemia

20-12 ml /100 g /min penumbra

12 ml/100g/min threshold for ischemia

MR Perfusion Techniques

1. Dynamic susceptibility Contrast (DSC)

- GRE-EPI (T2* weighted) widely used
- SE-EPI (T2 weighted)

2. Dynamic contrast-enhanced perfusion

- Spoiled Fast Gradient Echo T1-imaging after Gd bolus, measures vascular permeability

3. Arterial Spin Labeling (ASL): uses magnetically tagged endogenous water as tracer (no Gd)

Parameters for DSC

Single shot GRE-EPI or SE-EPI

- TE = 30 – 60 ms (GRE-EPI) or 50 – 80 ms (SEEPI)
- TR = min. (< 2 sec depends on number of slices)
- TA = 90 - 120 sec. or ~ 100 time points •

Contrast dose = 0.1 – 0.2 mmol/kg •

Injection rate: 3 – 5 ml/sec with 20 ml saline flush

GRE-EPI vs SE-EPI DSC

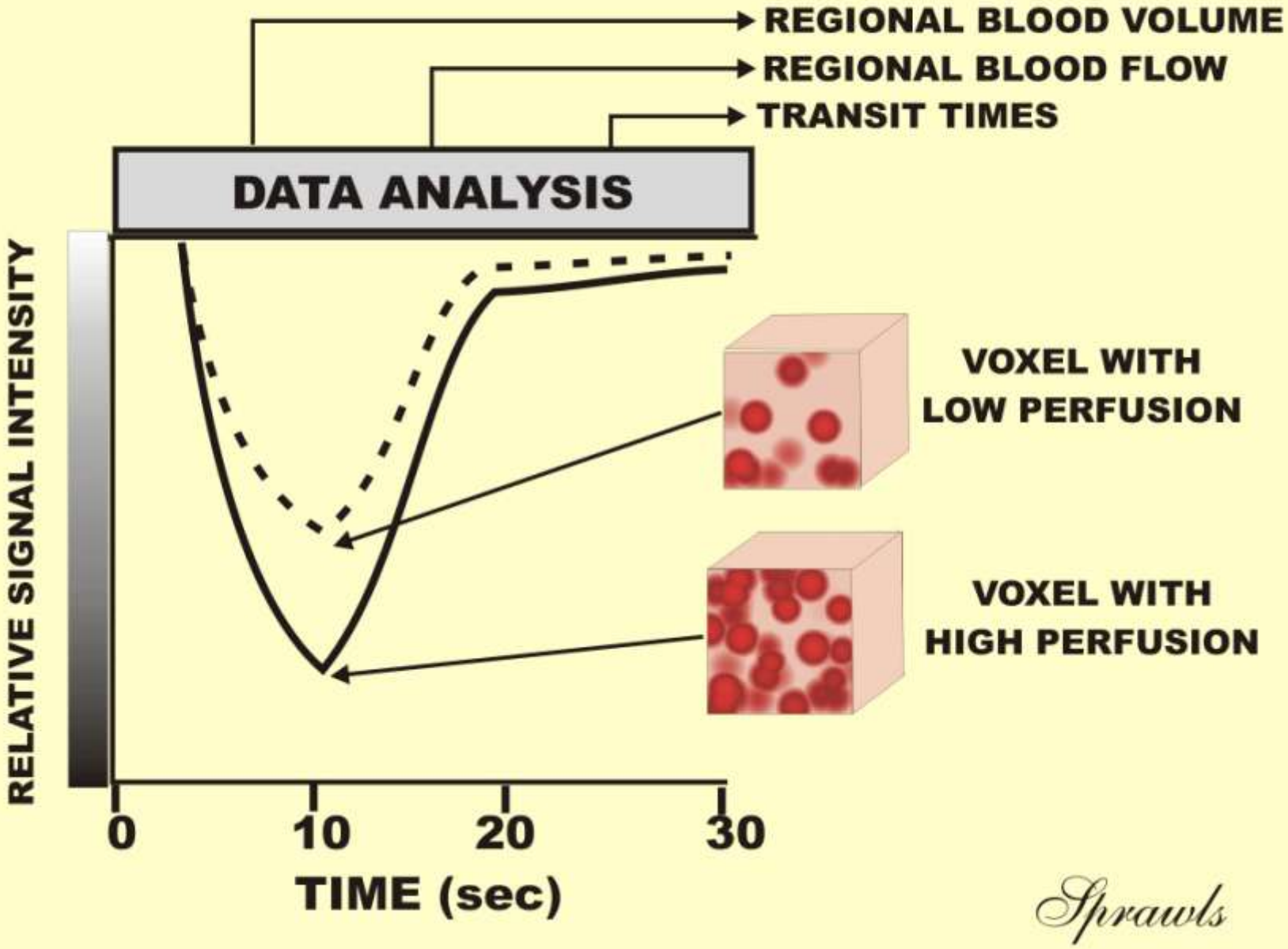
- *SE-EPI signal (T2 dependent) is more specific to microvasculature while GRE EPI signal (T2* dependent) is also sensitive to larger vessels.*
- *GRE-EPI provides greater sensitivity and coverage (more slices for same TR).*

Dynamic susceptibility Contrast

- based on dynamic monitoring of the passage of paramagnetic material Gd-DTPA through susceptibility effect.

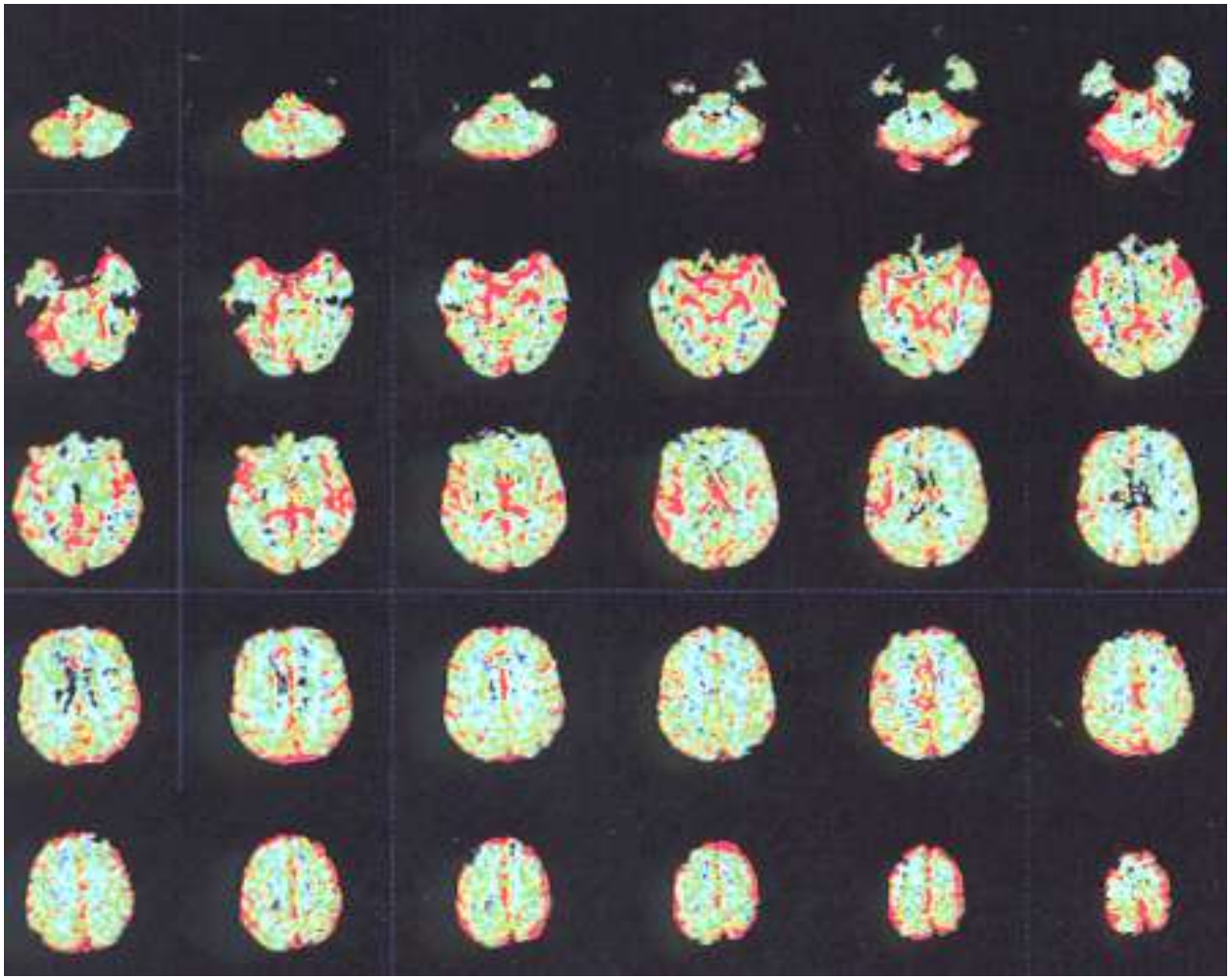
- by combining the simultaneous use of paramagnetic contrast material and ultra fast imaging
- The degree of drop in MR signal caused by the susceptibility effects of gadolinium is assumed to be proportional to the tissue concentration of gadolinium, so that relative concentration-time curves can be obtained (delta R2 curves) .

PERFUSION IMAGING



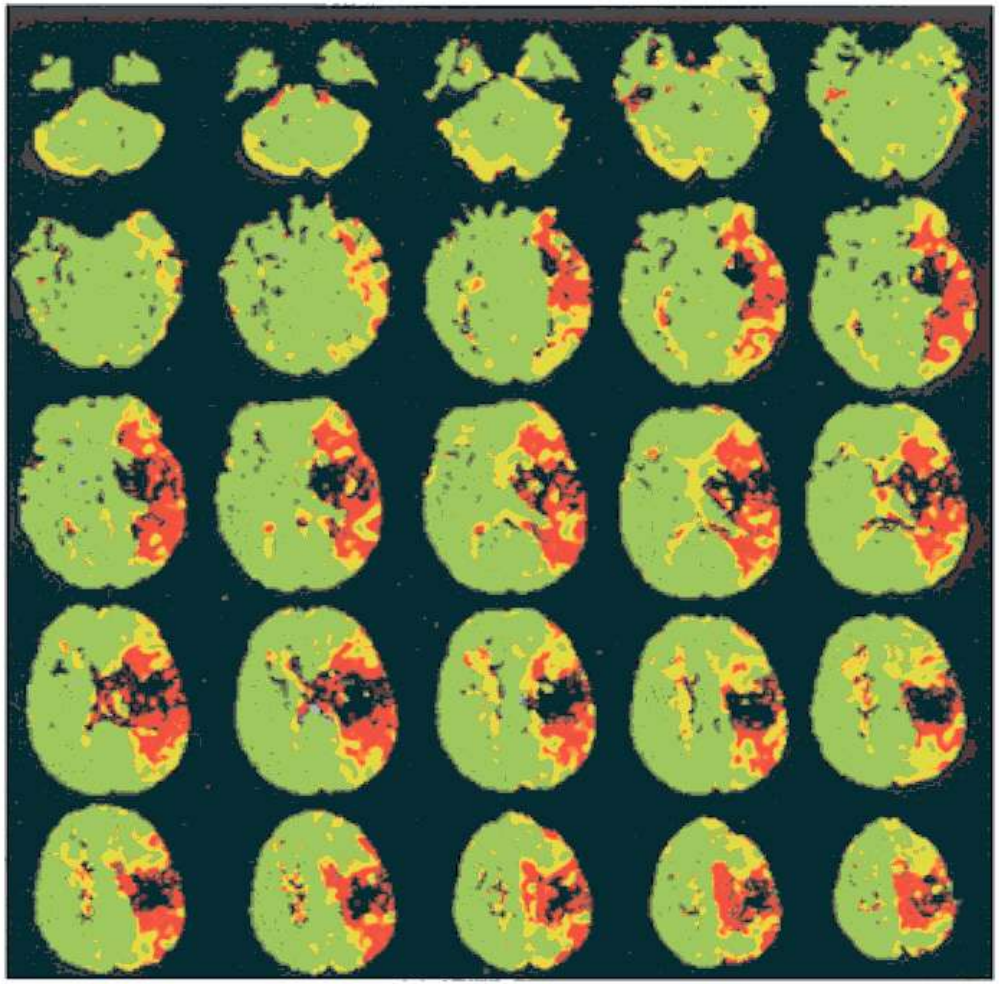
Sprawls

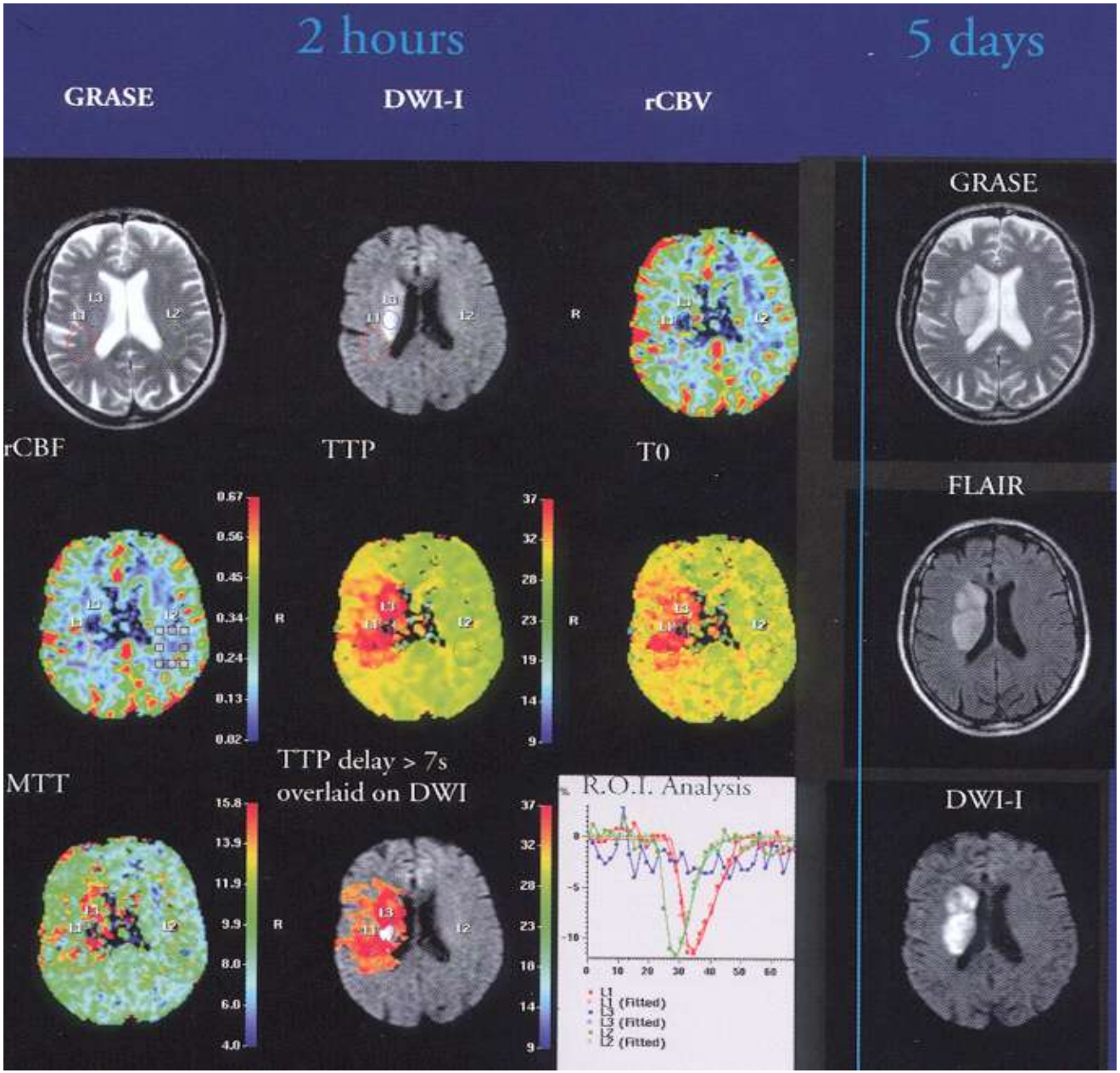
Regional Cerebral Blood Volume



Time To Peak Images

Stroke Patient




2 hours
5 days
GRASE
DWI-I
rCBV
GRASE
rCBF
TTP
T0
FLAIR
MTT
TTP delay > 7s
overlaid on DWI
R.O.I. Analysis
DWI-I

2. T1-weighted dynamic contrast-enhanced perfusion

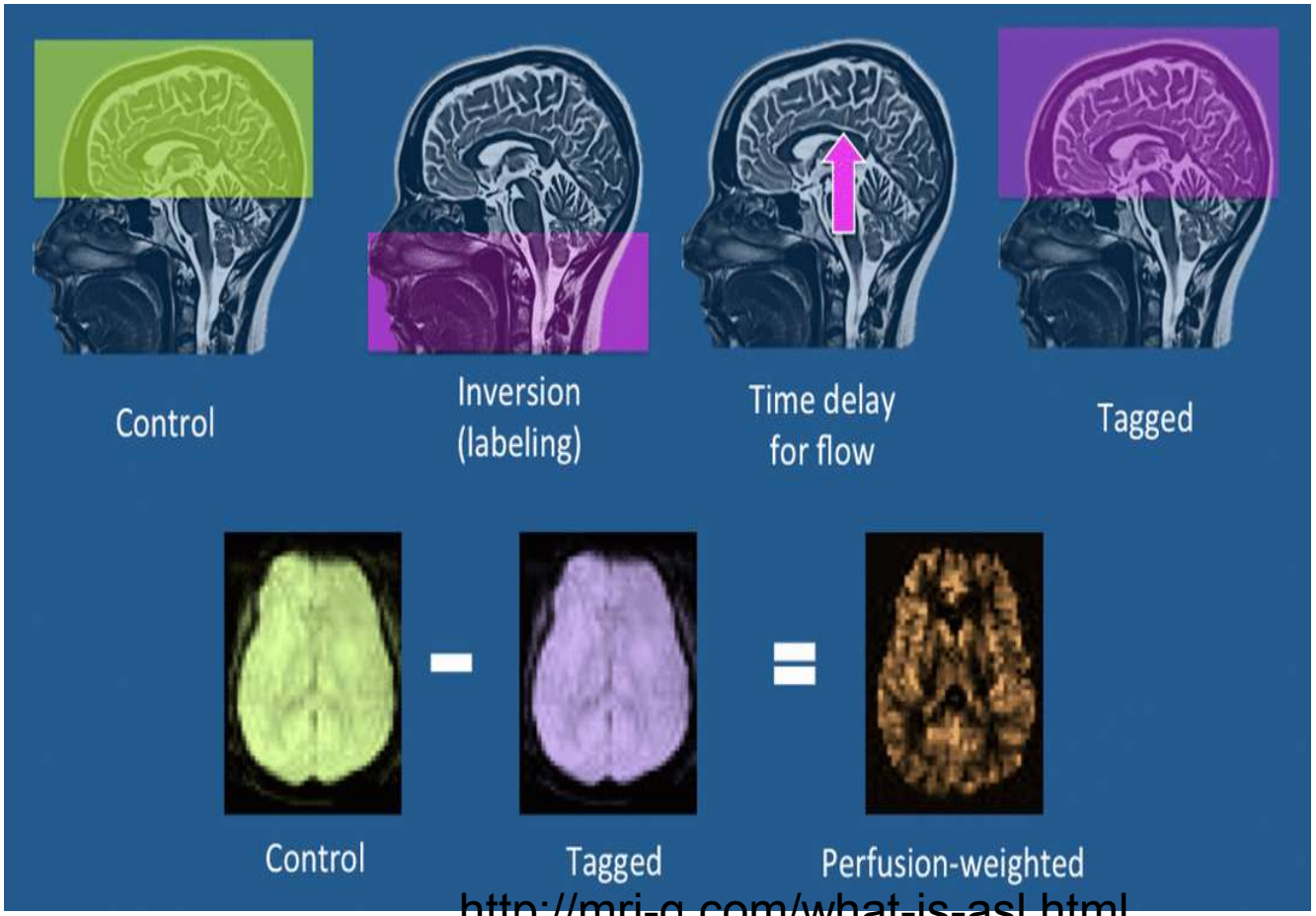
DCE MR perfusion, also widely referred to as “permeability” MRI, is based on the acquisition of serial T1-weighted images before, during, and after administration of extracellular low-molecular-weight MR contrast media, such as a gadolinium-based contrast agent. The resulting signal intensity–time curve reflects a composite of tissue perfusion, vessel permeability, and extravascular-extracellular space

Parameters

- Spoiled 2D or 3D gradient echo (SPGR or FLASH)
- TE = min. • TR = min. (typically 4 – 10 sec)
- FA = 30 – 40 deg
- TA = several minutes.
- Contrast dose = 0.1 – 0.2 mmol/kg
- Injection rate: 3 – 5 ml/sec with 20 ml saline flush.
- Measure baseline T1 with different FAs

Arterial Spin Labeling methods

- Inverted magnetization of flowing blood exchanges magnetization with static tissues, reducing equilibrium magnetization by 1-2%



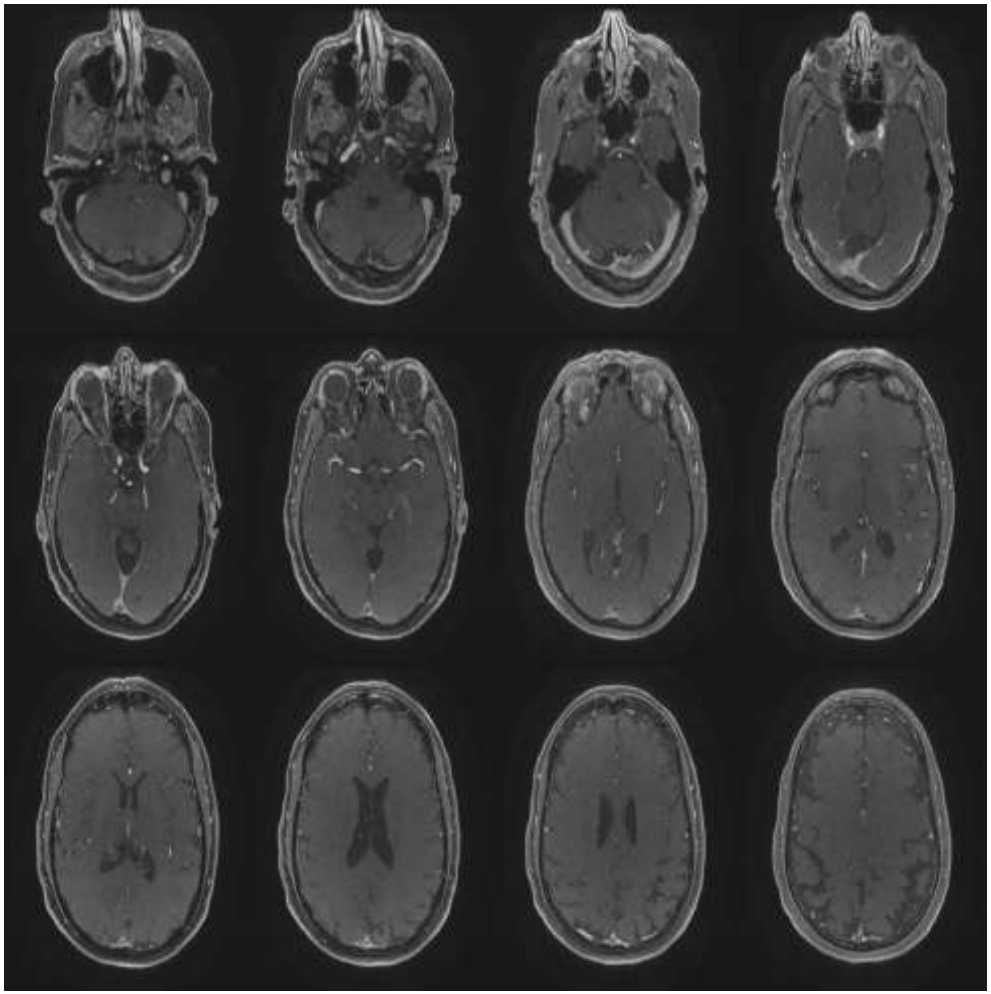
http://mri-q.com/what-is-asl.html

Perfusion Contrast methods: Summary

	DSC	DCE	ASL
Name	Dynamic Susceptibility Contrast	Dynamic Contrast Enhanced	Arterial Spin Labeling
Uses Gadolinium?	YES	YES	NO
Data Acquisition	1st pass of intravascular Gd through regional circulation	1st pass plus continuous accumulation of Gd in extracellular space	Continuous arrival and diffusion of labeled H_2O into cells and interstitum
Imaging Sequence	T2* weighted rapid GRE or EPI	T1-weighted rapid GRE or EPI	Custom interleaved 2D/3D EPI or FSE hybrid readout with proximal inversion/saturation module
Acquisition Time	Short (1-2 min)	Long (5-10 min)	Intermediate (3-5 min)
Clinical Use	Most widely used for brain (strokes/tumors) and heart (ischemia)	Most widely used for evaluating tumors/response to therapy in brain, breast, pelvis	Used to measure blood flow of brain, heart, kidney, muscle

http://mri-q.com/what-is-asl.html

MR Angiography: TOF Images

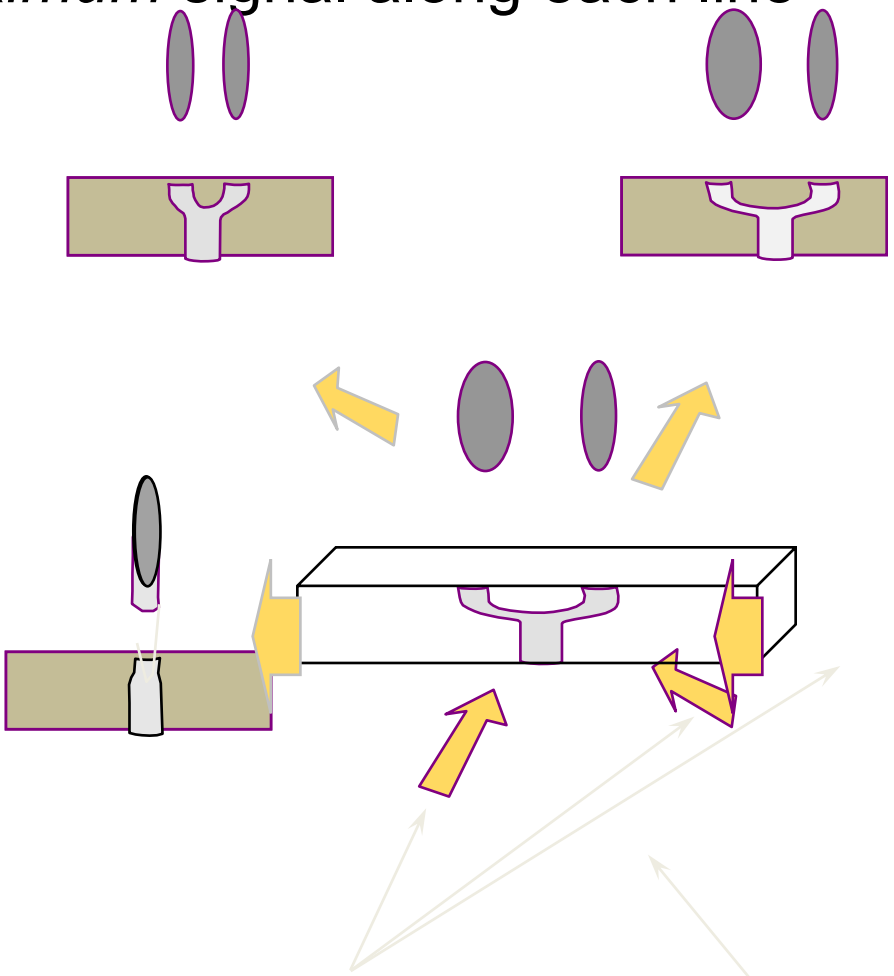


2-D Time of Flight Images

- Blood flow enhancement by detecting moving blood
- *Unsaturated* blood into imaged volume produces a bright signal
- Detection range is limited by the eventual saturation of tagged blood

Maximum Intensity Projection: MIP

Projections cast through the image stack; project *maximum* signal along each line

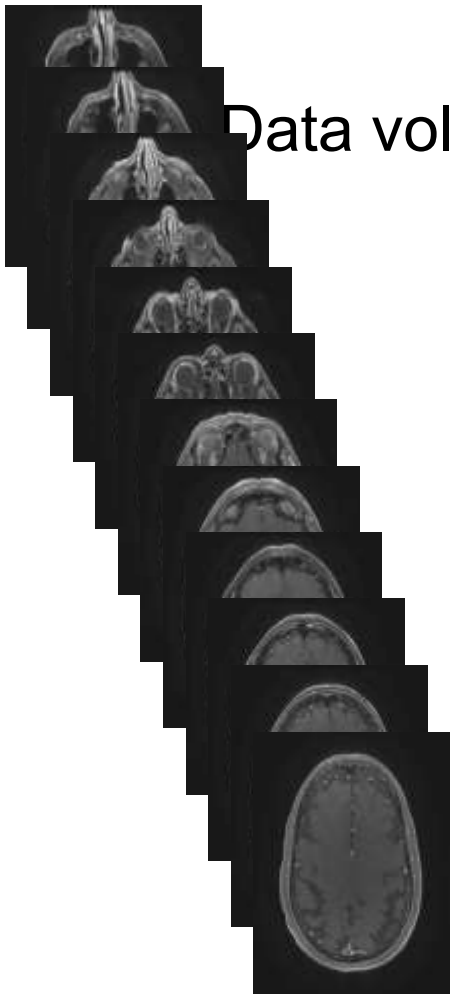


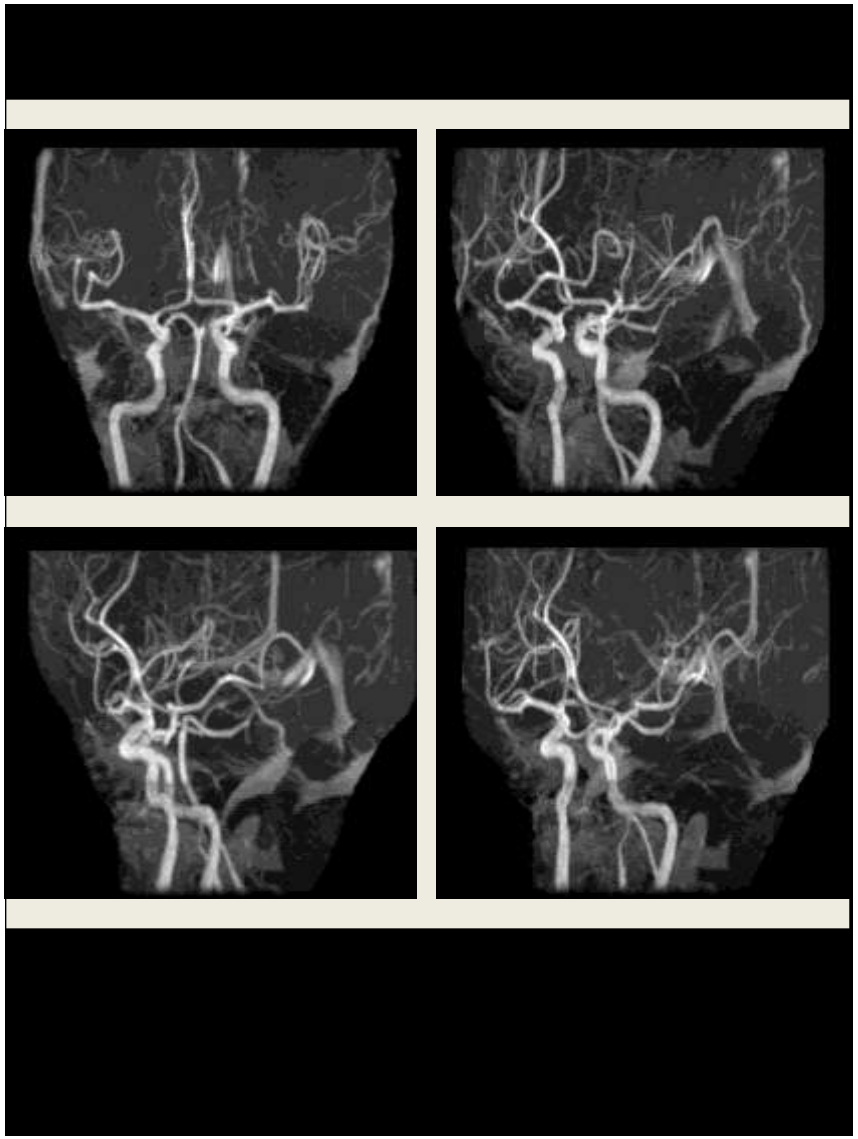
MIP images

Projection angles

Volume of 2D Images

2D Projection Angiograms from MIP





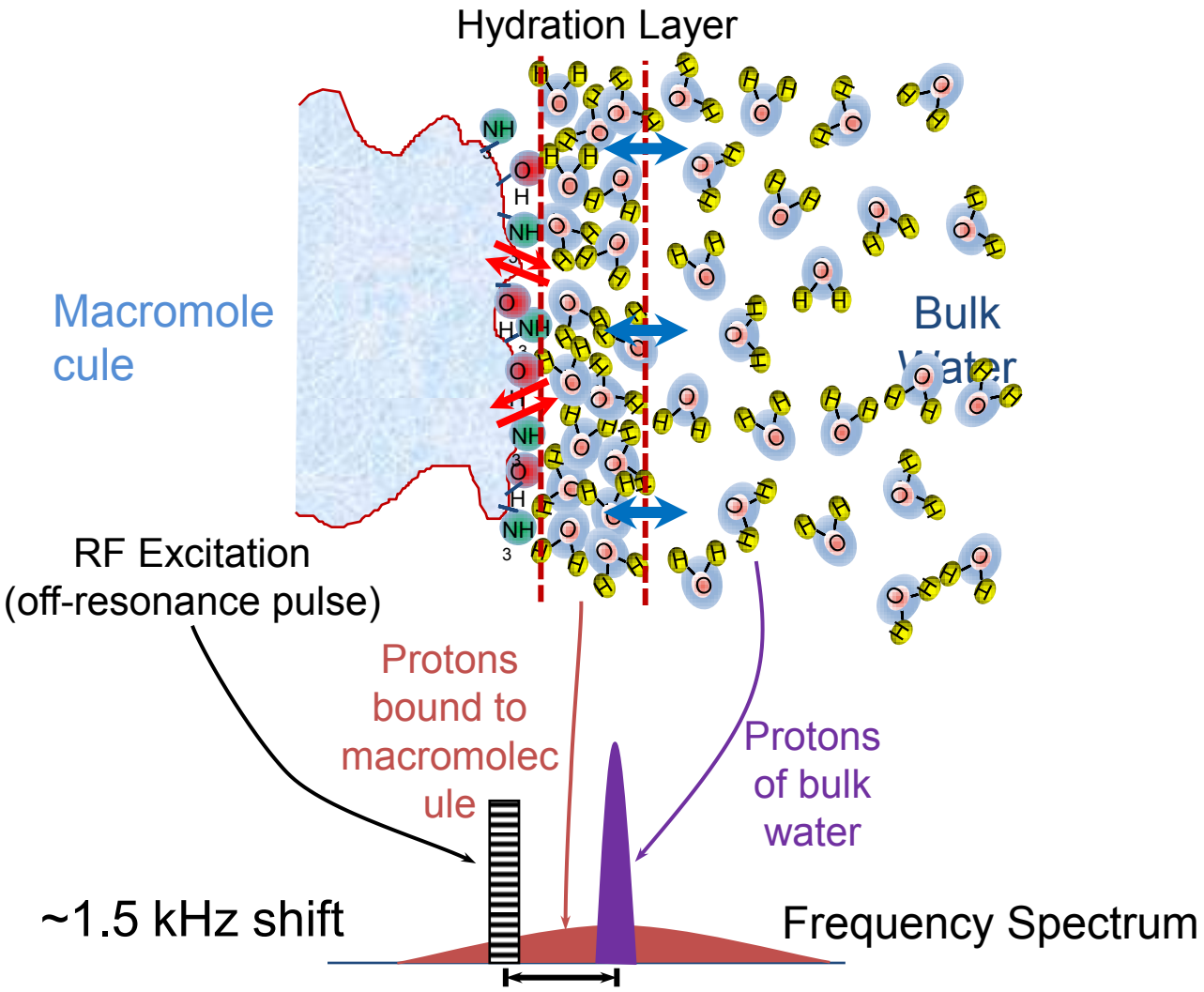
MRA (MR Angiography)

- Technique for visualization of MR signal from flowing blood located in a vascular network.
- Utilizes bright blood technique (blood is assigned largest pixel value in the image)
- Uses both 2D and 3D technique
- Two major classes
  - Time of flight
  - Phase contrast

Magnetization Transfer Contrast

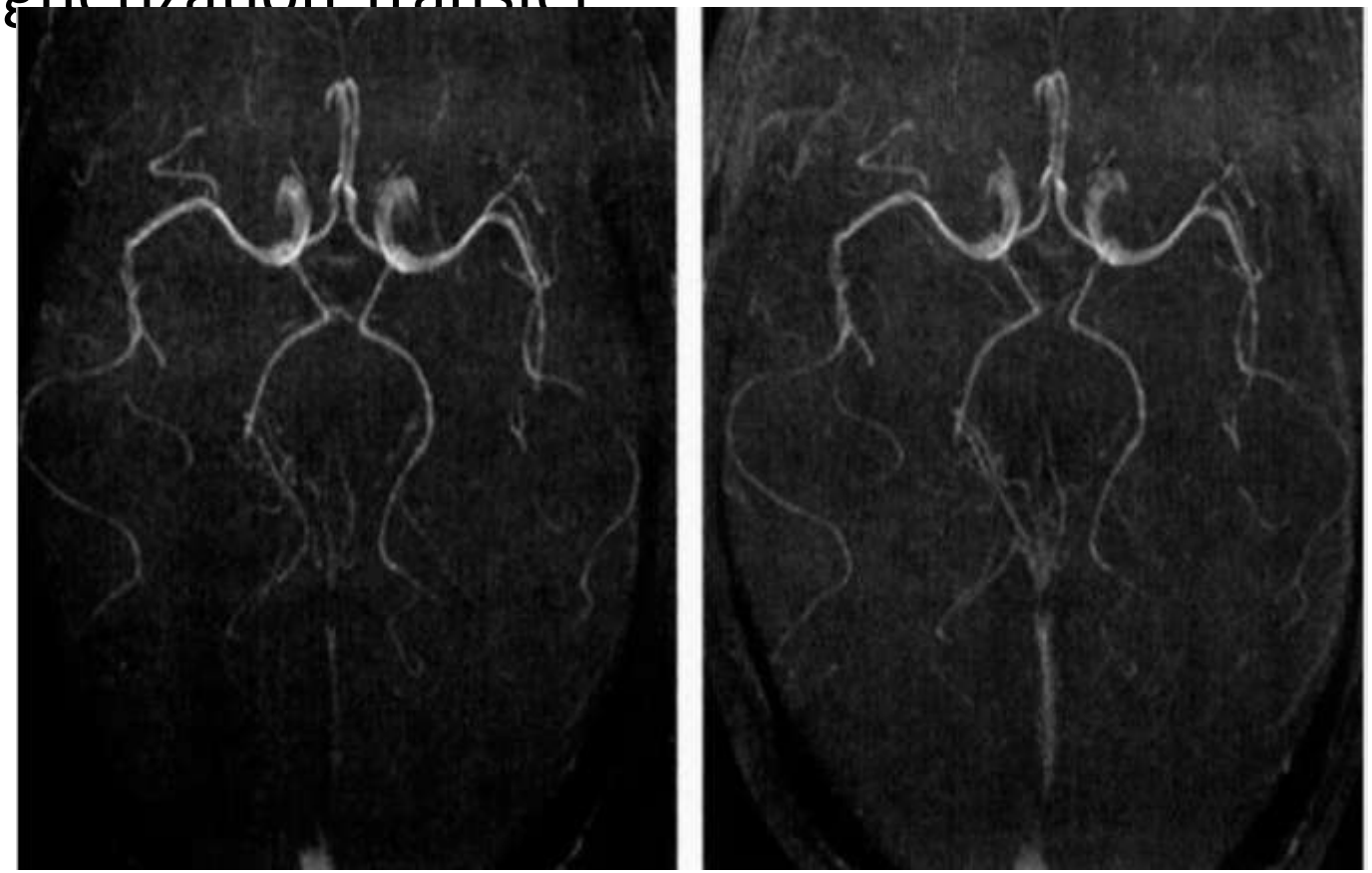
- Protons in macromolecules have different precessional frequency than protons in adjacent free (bulk) water
- Selective excitation of the macromolecule protons
- Magnetization transfer occurs via coupling (hydration layer) and partially saturates bulk water
- The “saturation label” affects *only those protons having a hydration coupling or chemical exchange*
- Image contrast improves **by reducing background signals**
- Uses: heart, eye, multiple sclerosis, knee cartilage, MR angiography

Magnetization Transfer Contrast



Magnetization Transfer Contrast

- TOF MR angiography comparison — much better visualization of small vessels with Magnetization Transfer

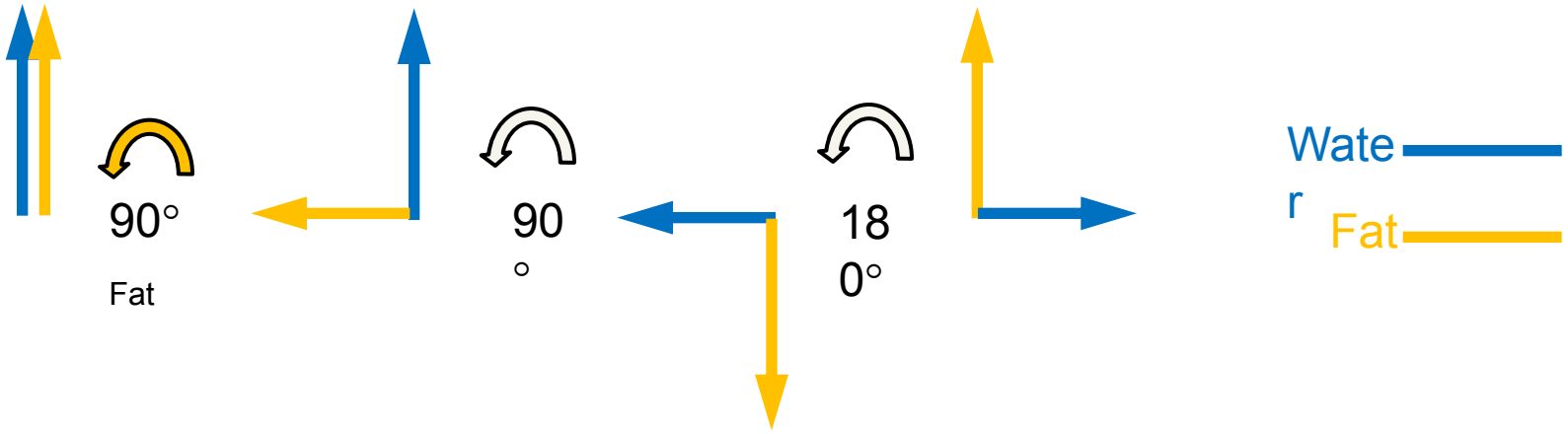


Without MT

With MT

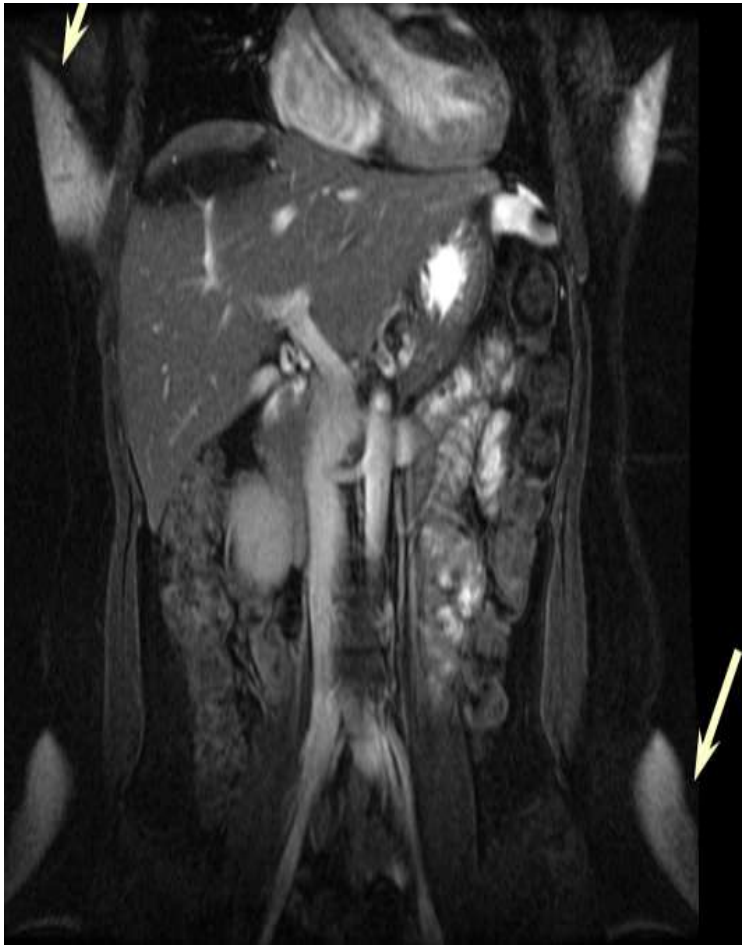
Chemical Saturation

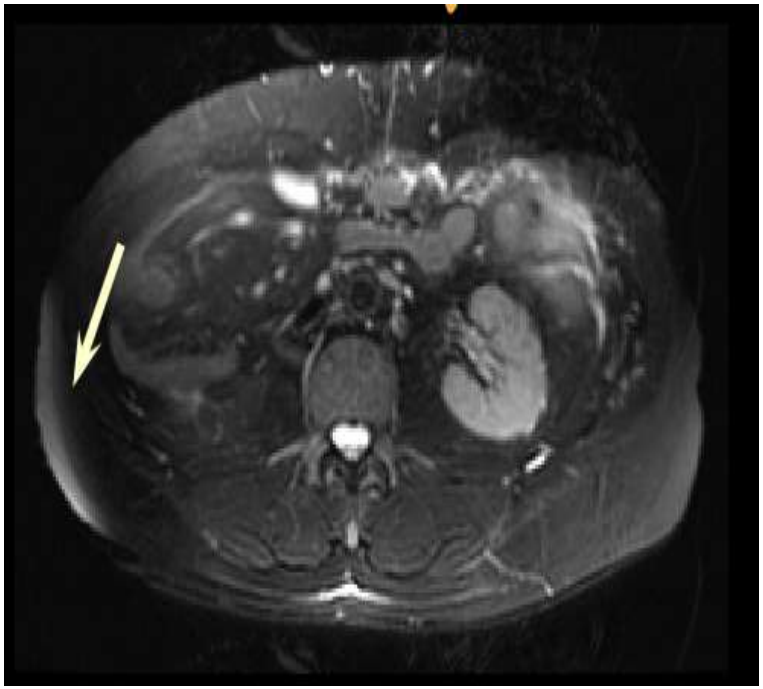
- "Chem-sat" or "fat-sat" techniques suppress the fat signal
  - Fat suppression is achieved by using different resonance frequencies of fat and water (There is ~215 Hz separation at 1.5 T)
  - Typically accomplished by preceding a SE or FSE sequence with a 90° pulse that is frequency, not spatially, selective.



Effect of Inhomogeneity on FatSat

- FatSat failure due to field inhomogeneities (arrows)



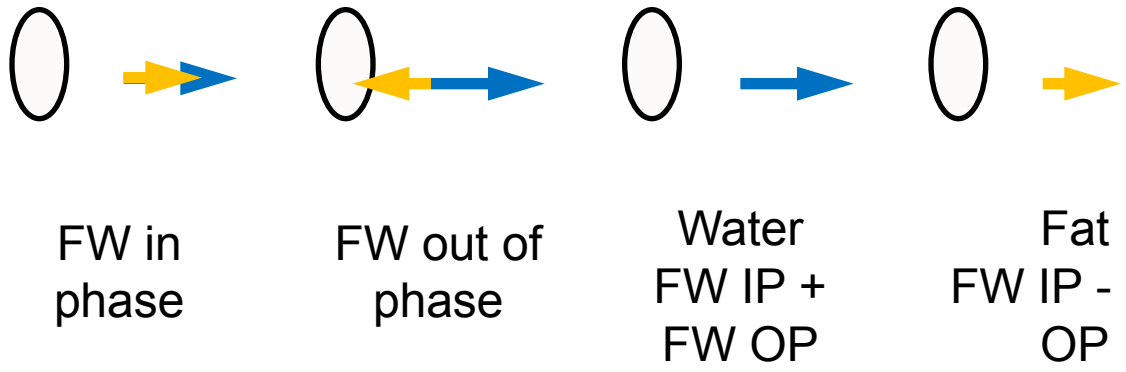


Dixon Technique

- Water and fat do not resonate at the same frequency
- Frequency difference results in phase difference, $\Delta\phi = 2\pi \Delta f t$, where f is frequency difference between fat and water – 215 Hz at 1.5 T; 430 Hz at 3.0 T
- 3 point Dixon: acquires images at 0, 180 and 360 degree phase shifts – extra image used to correct phase shifts
- $\Delta\phi = n\pi$ when
  - TE = 2.33n ms for n = 1, 2, … (1.5T)
  - TE = 1.16n ms for n = 1, 2, … (3.0T)
- Add and subtract images to get fat-suppressed and fat-only images
- Also get *in-phase* images and *out-of-phase* images

Dixon Technique

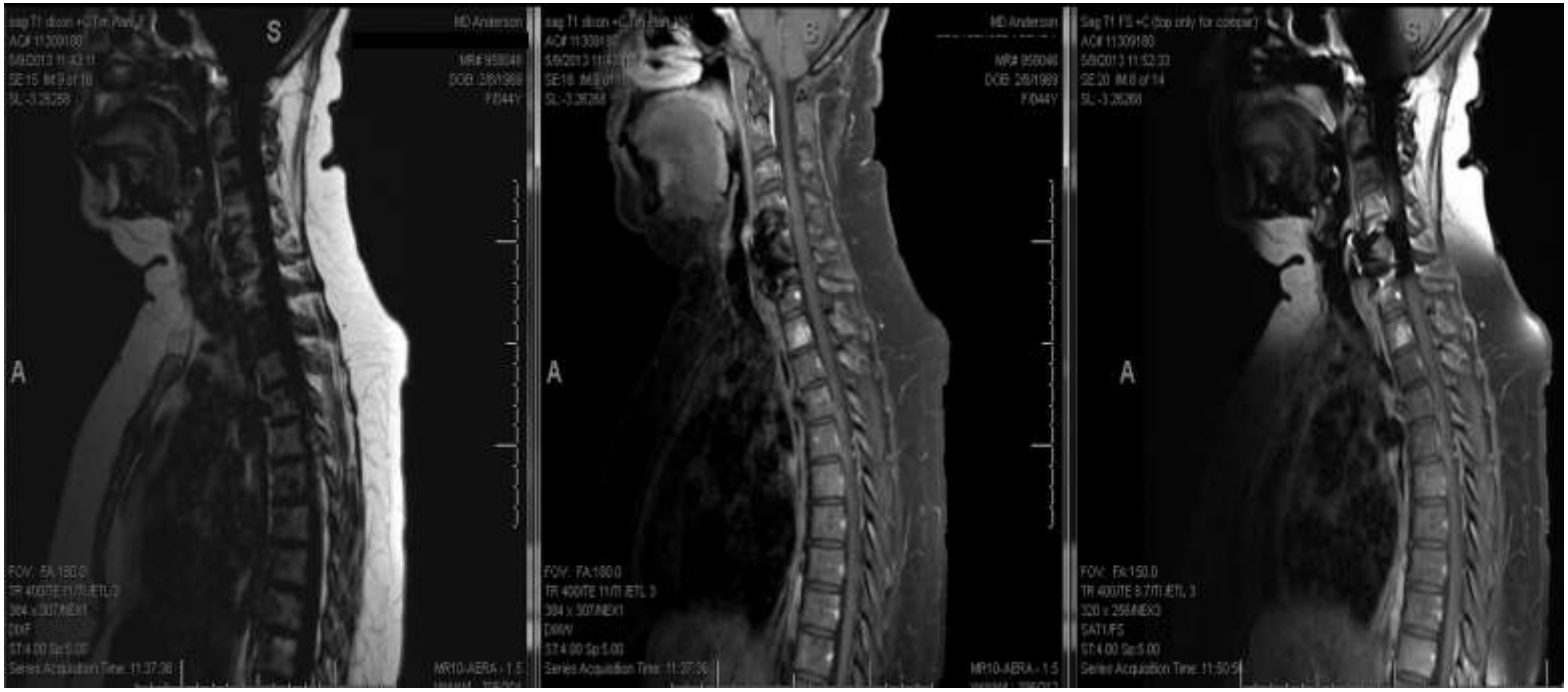
- Acquisition -- Four image sets – two derived



- Advantage of Dixon: Much less sensitive to field inhomogeneities than FatSat
- Disadvantage of Dixon: Longer acquisition time (two image sets are required) – however can also use multi-echo acquisition

Dixon Technique

- Post Gd T1 images



Dixon Fat Image

Dixon Water Image

Fat Sat Image

MRI Artifacts

- Positive or negative signal intensities that do not accurately represent the anatomy
- Can obscure or mimic pathological processes or anatomy
- In some cases can help with the differential diagnosis by providing extra information
- Origins:
  - Machine
  - Patient
  - Processing

Most common MRI Artifacts

- Motion-induced (e.g., blood flow, respiration)
- Aliasing or “wrap-around” artifact
- Metal object artifacts
- Truncation artifacts
- System-related artifacts
  - Distortions (gradient & static field inhomogeneities)
  - RF coil problems and RF interference
  - Receiver / memory / array processor problems

Motion Artifacts

Cause

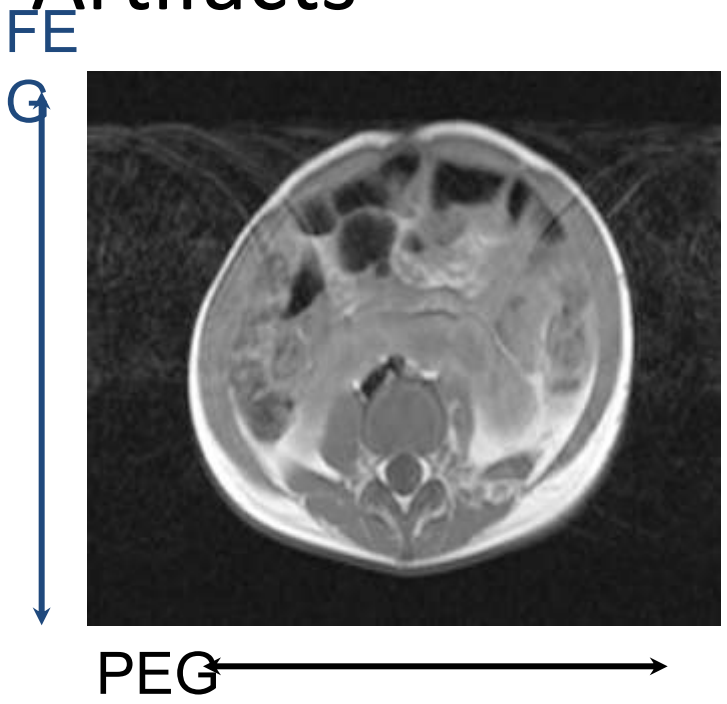
- Patient motion (respiratory, cardiac, swallowing, involuntary, peristalsis, blood or CSF flow …)

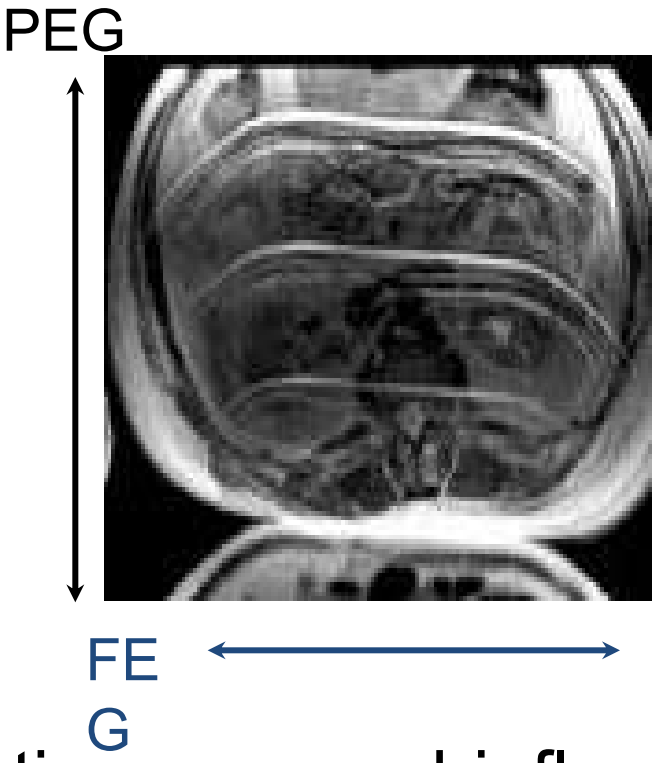
Results in *phase* mismapping in *k*-space

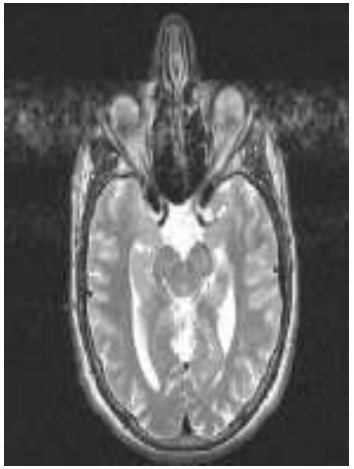
Appearance

- “Ghosts” of periodic motion (pulsatile flow, cardiac or respiratory motion) repeated along phase encoding direction
- Non-periodic motion (peristalsis, swallowing) generates diffuse noise in phase encoding direction

Motion Artifacts







Motion occurs chiefly along the **phase encode direction**

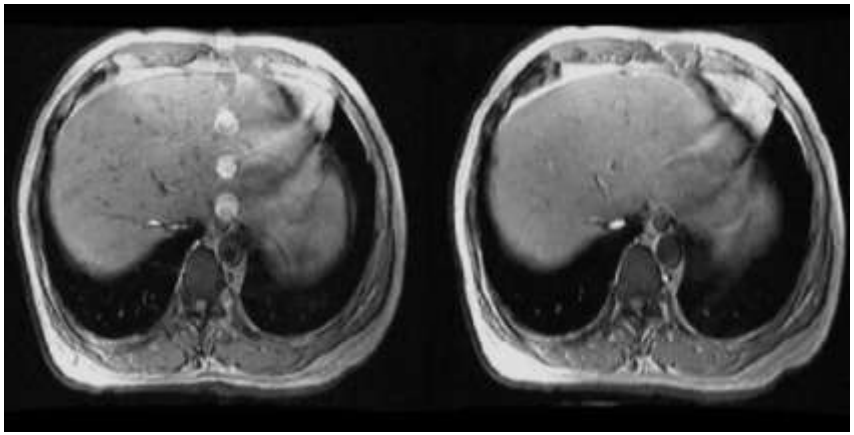
Motion can occur along FEG for *very* fast objects

Respiratory Artifact compensation

- Breath hold acquisitions –
  - Not appropriate for all sequences or for all patients
- Multiple averages (NEX, NAV, NSA, etc.)
  - Requires significant scan time!
- Respiratory compensation techniques
  - Respiratory trace to order the phase encoding steps reduces ghosting;
    poor compensation if breathing is irregular.)
- Respiratory triggering techniques
  - Acquire data only during consistent portions of the respiratory cycle
- Navigator echo techniques
  - Use rapid navigator techniques to track motion to correct phase ghosting errors

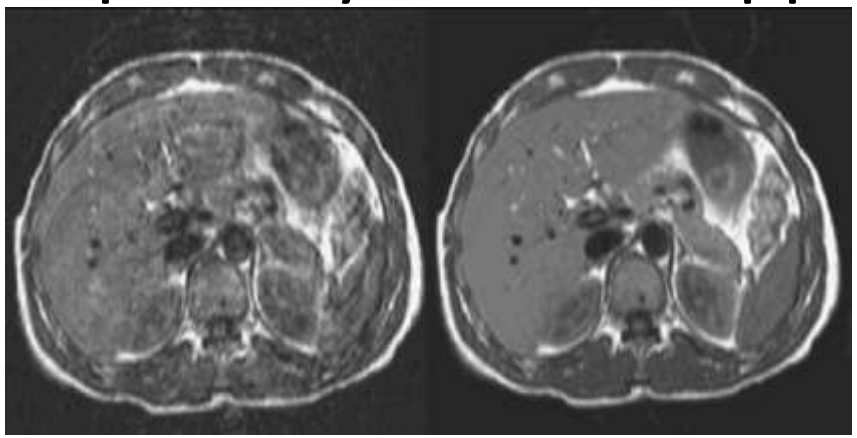
Motion Artifacts and suppression

- Flow artifact suppression



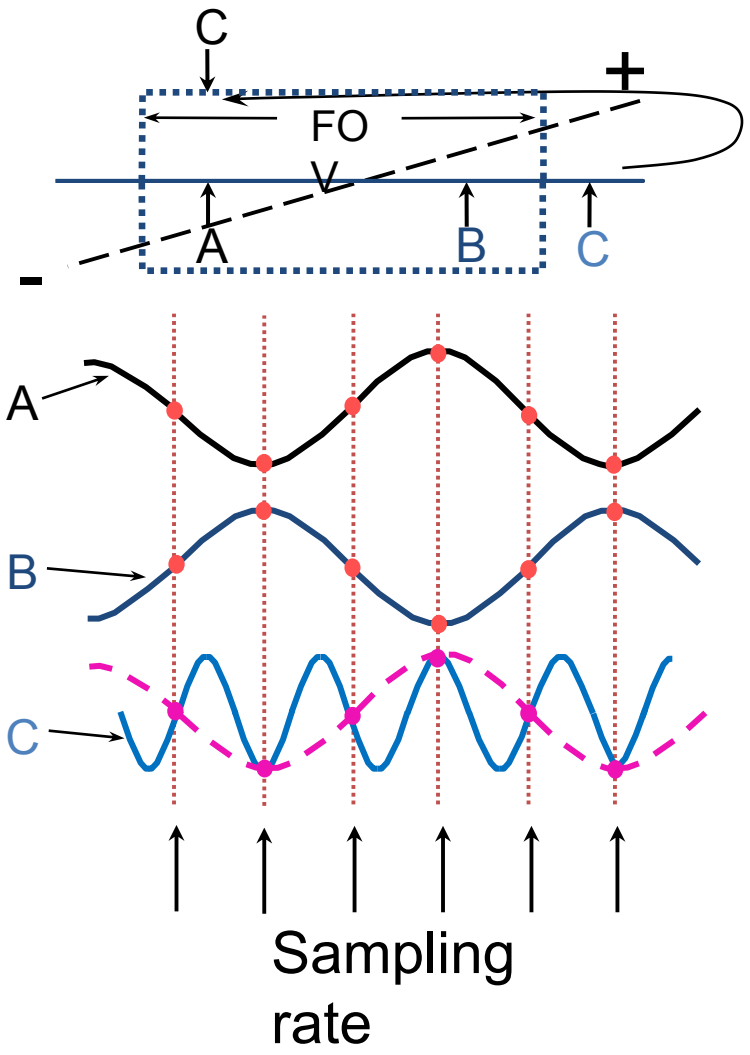
Blood Flow
Left: No correction
Right: Superior SAT pulse

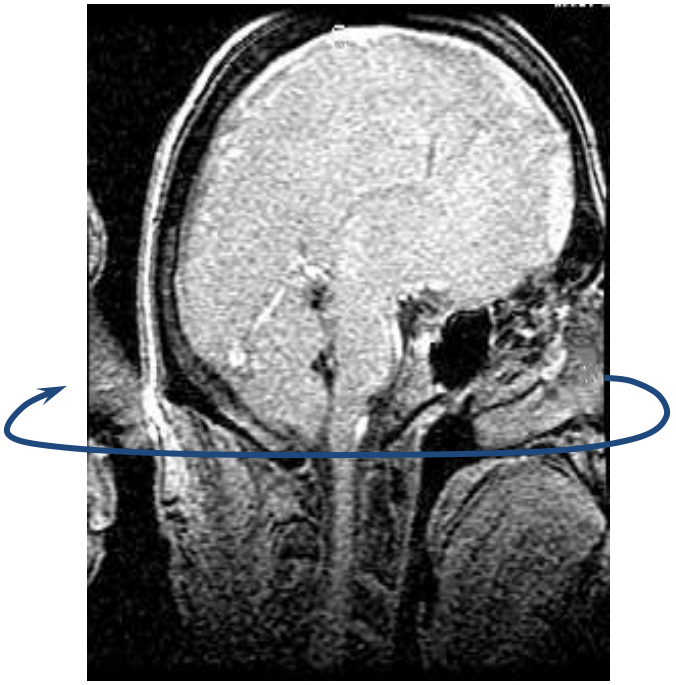
- Respiratory motion suppression



Respiration
Left: No correction
Right: Multiple NEX averaging

Aliasing: Wraparound Artifact





Wrap-
around

Cause: Insufficient sampling of highest spatial frequencies

Wraparound Artifact

- Possible solutions:
  - **Use larger FOV** (disadvantage: loss of spatial resolution)
  - **Use surface coil** (disadvantage: possible anatomic scan range limitations unless appropriate phased array is available)
  - **Use oversampling** or “no phase wrap” option
    - Increases FOV by 2x, but only displays the original FOV
    - Increases phase encode matrix by 2x for same resolution
    - Uses partial Fourier reconstruction to keep scan time similar
    - SNR remains unchanged given the 3 steps above

Role of Perfusion MRI techniques

- for quantitative assessment of specific pathophysiologic parameters,
- more accurate grading of intracranial tumors, and
- differentiation of tumours from normal tissue.