Perfusion and Diffusion Imaging

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Outline (Accelerated)

- **Perfusion MRI**
  - With Exogenous Contrast
    - Dynamic Contrast Enhanced (DCE) MRI - T1
    - Dynamic Susceptibility Contrast (DSC) MRI - T2/T2*
  - Without Exogenous Contrast
    - Arterial Spin Labeling (ASL)
- **Diffusion MRI**
  - Isotropic (3 dimensional) Diffusion Weighted Imaging (DWI)

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MR Contrast Agents

- MR Contrast agents are unique among diagnostic imaging agents:
    - MR signal is *not* a direct measure of contrast agent concentration
    - Depends on the effects of the contrast agent on relaxivity (T1, T2, T2*)

- In order to properly understand contrast agent studies, an understanding of water movement on the MR signal is necessary
    - Water Exchange across boundaries between different compartments
    - Water Diffusion within biological compartments

- Similar to other pharmacokinetic (non-MR) tracer studies, the proper application of a tracer kinetic model is necessary for proper application and interpretation

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Perfusion MR Imaging

- **Two Main "Flavors" of Perfusion Imaging with Contrast Agents:**
  - **<u>"Relaxivity" (T1) Methods</u>:**
    - Dynamic Contrast Enhanced (DCE) MRI
      - Perfusion Parameters (Extraction Fraction, Extracellular Volume Fraction, Blood Volume)
  - **<u>"Susceptibility" (T2/T2*) Methods</u>:**
    - Dynamic Susceptibility Contrast (DSC) MRI
      - Perfusion Parameters (Blood Volume, Blood Flow, Mean Transit time)

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Tracer Kinetic Principles

- **<u>Tracer Kinetics</u>** - Concept of measuring movement of a diffusible chemical (tracer) to and from various biological compartments using external detection methods

- Since the exchange of diffusible tracers between blood and tissue occurs in vessels with a larger surface area, this approach primarily measures capillary blood flow

- <u>General Assumptions</u>:

    1. Tracer molecules do not become metabolized
    2. Tracer injection does not disturb the system
    3. System is linear and time-independent (LTI)

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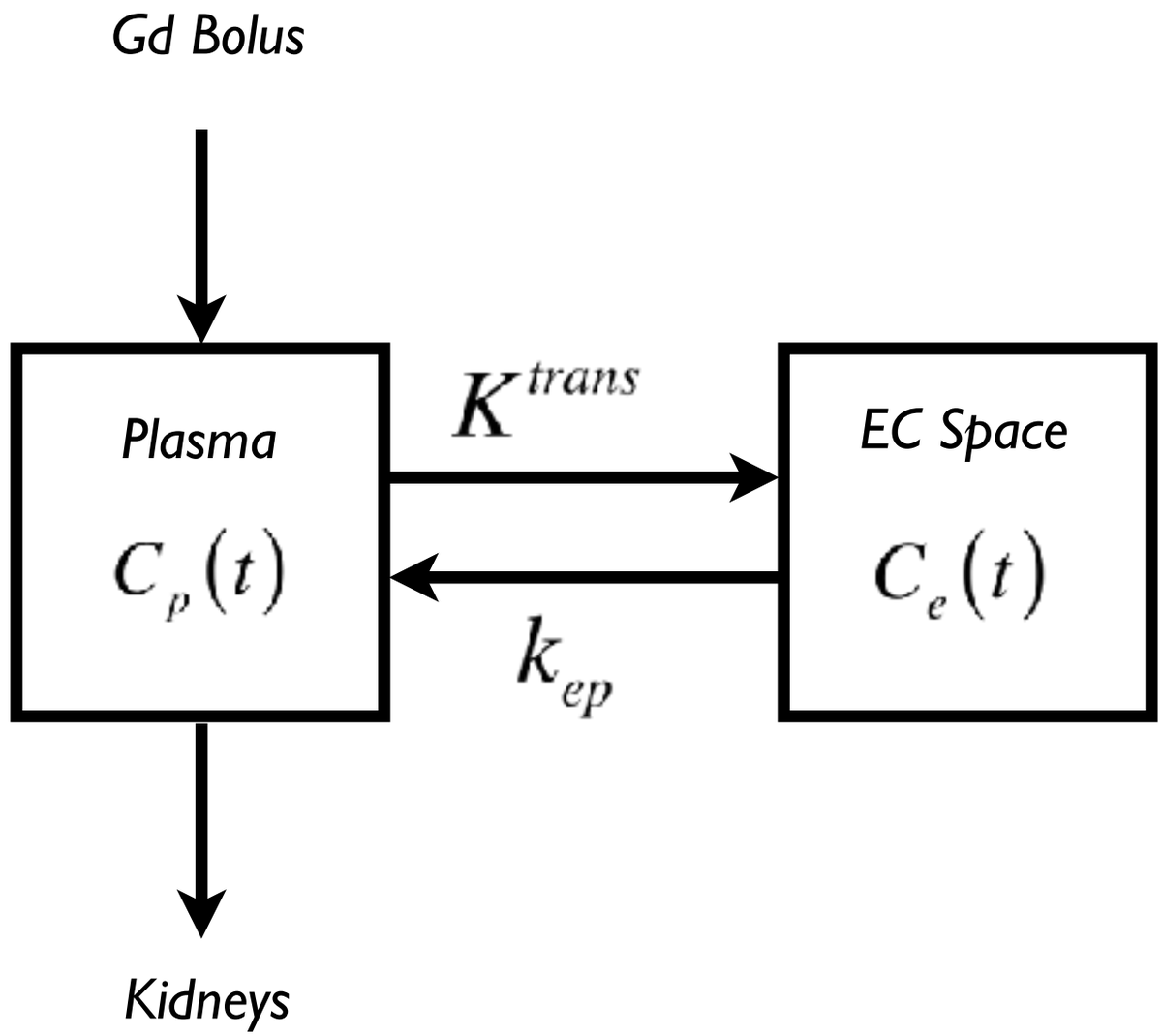
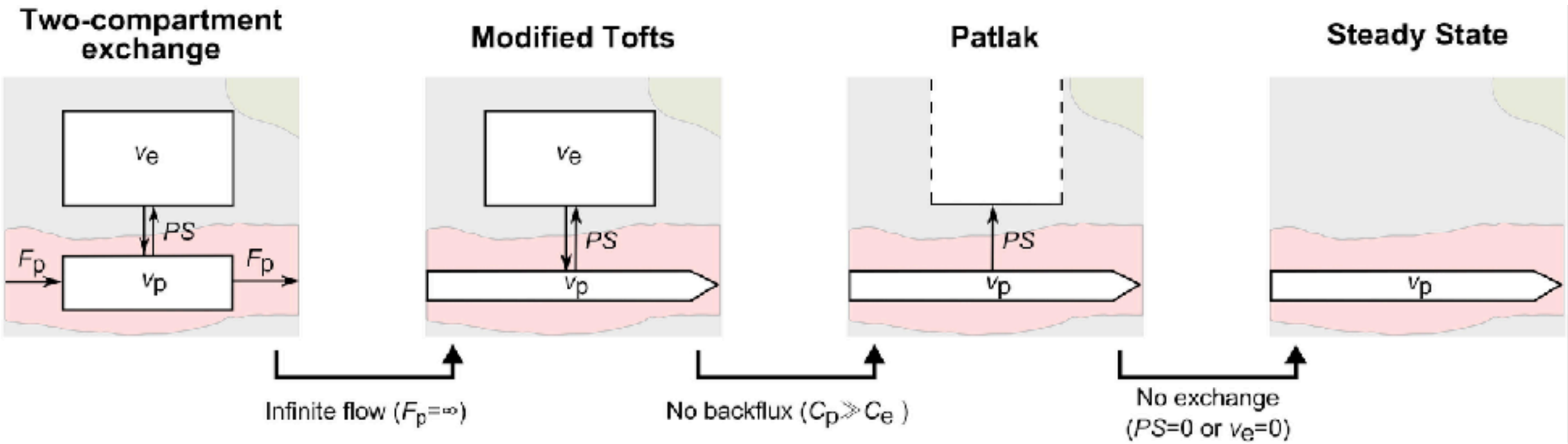
Dynamic Contrast Enhanced (DCE) MRI



Simplifications to the Full Pharmacokinetic Model



Heye AK et al, *Neuroimage* 2016; 125: 446-455.

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Simplifications to the Full Pharmacokinetic Model

- **<u>Tofts Model:</u>**
  - Assumes equilibrium of the contrast media between the plasma and the EES
  - <u>Original Tofts Model</u>: *Assumes <u>Plasma Compartment is Negligible</u>*
    - One compartment, two parameters

$$C_{tissue}(t) = K^{trans} \int_0^t C_p(\tau) e^{-k_{ep}(t-\tau)} \, d\tau$$

  - <u>Modified (Extended) Tofts Model</u>:
    - Two compartment, three parameters

$$C_{tissue}(t) = v_p C_p(t) + K^{trans} \int_0^t C_p(\tau) e^{-k_{ep}(t-\tau)} \, d\tau$$

↑ *"Observed Concentration"*

Tofts PS. *J Magn Reson Imaging* 1997; 7(1): 91-101.
Tofts PS., et al., *J Magn Reson Imaging* 1999; 10(3): 223-232.
Leach MO, et al., *Eur Radiol* 2012; 22(7): 1431-1464

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Simplifications to the Full Pharmacokinetic Model

- **<u>Tofts Model:</u>**
  - Advantages - Biological relevant, most accurate
  - Disadvantages - Need to acquire a lot of data points, computationally intensive

$$C_{tissue}(t) = v_p C_p(t) + K^{trans} \int_0^t C_p(\tau) e^{-k_{ep}(t-\tau)} d\tau$$

"Observed Concentration"

Tofts PS. *J Magn Reson Imaging* 1997; 7(1): 91-101.
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Simplifications to the Full Pharmacokinetic Model

- **<u>Patlak Model</u>**: Measure slope of "wash-in" curve
  - Special Case of the Toft Model that ignores back flow into the EES
  - Advantages - Quick, no need for mathematics (also known as the graphical method...just measure the slope). No need for a lot of data (only wash in)
  - Disadvantages - In tissues with nonzero wash out rate, Patlak model is highly inaccurate.

Plasma Negligible

$$C_{tissue}(t) = K^{trans}\int_0^t C_p(\tau)\,d\tau$$

Plasma Non-Negligible

$$C_{tissue}(t) = v_p C_p(t) + K^{trans}\int_0^t C_p(\tau)\,d\tau$$

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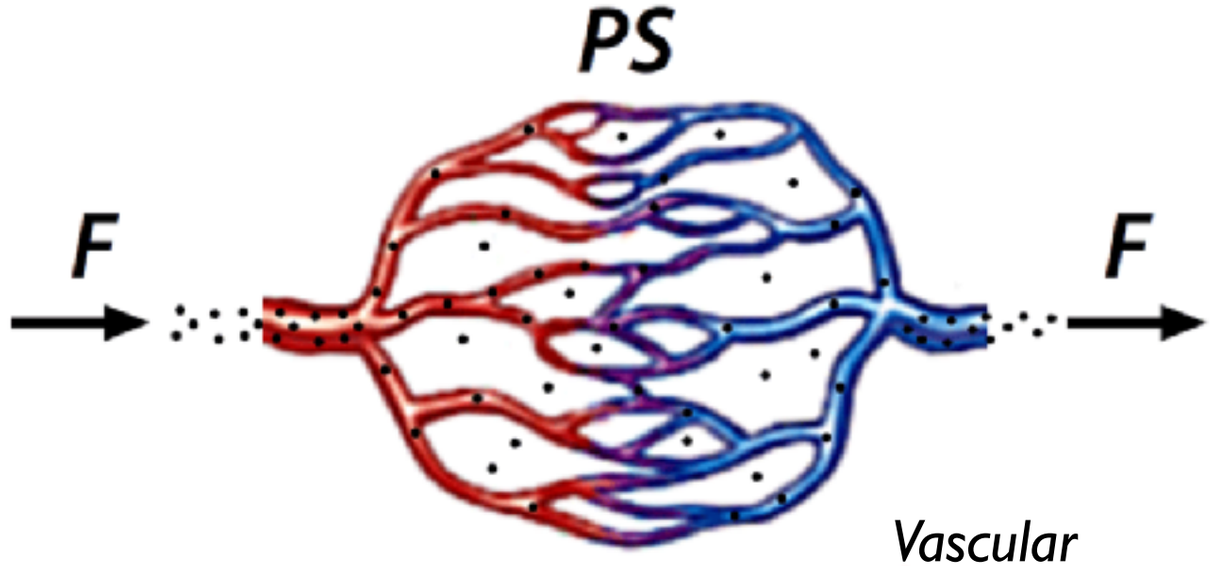
Dynamic Contrast Enhanced (DCE) MRI

Note on K^{trans}



$$K^{trans} = F \cdot \left(1 - e^{-\left(\frac{P \cdot S}{F} \right)} \right)$$

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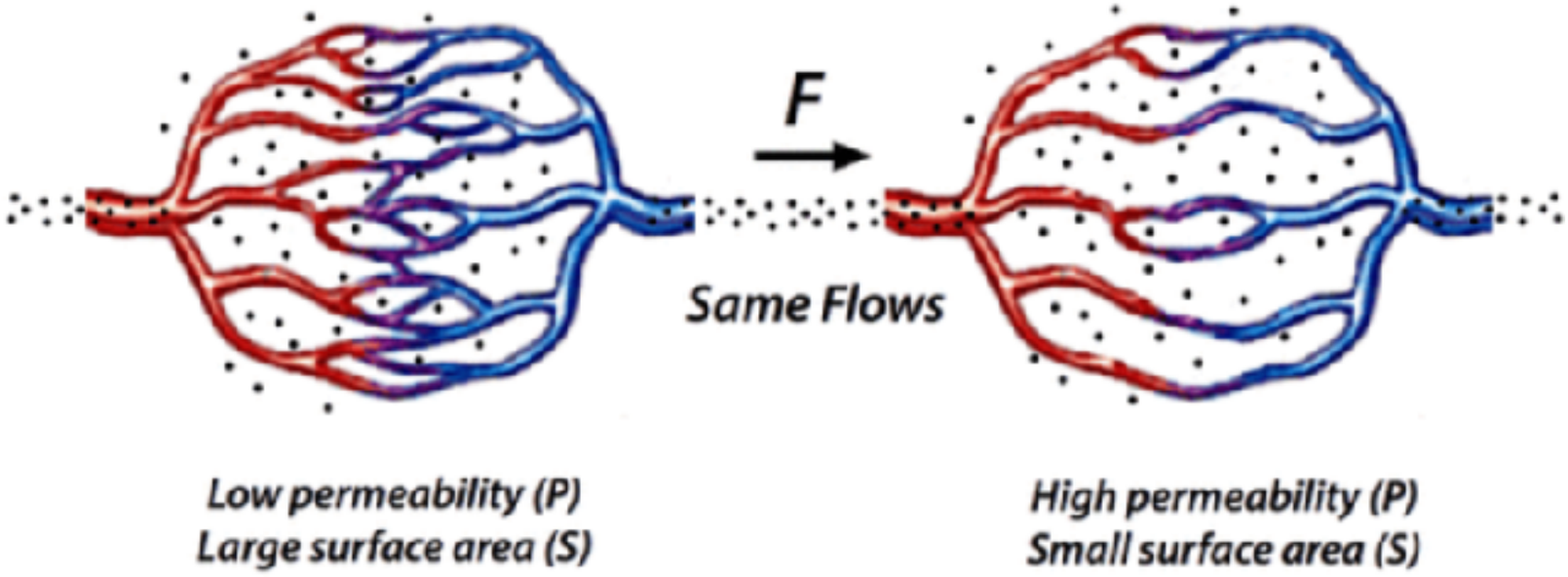
Dynamic Contrast Enhanced (DCE) MRI

Note on K^{trans}

- **<u>Permeability/Surface Area Limited</u>**
- Plasma blood flow (F) is much greater than P x S product.
- Large amount of gadolinium is available within the tissue, so amount of enhancement depends primarily on size and permeability of the capillary bed

$$P \cdot S \ll F \qquad\qquad K^{trans} \approx P \cdot S$$



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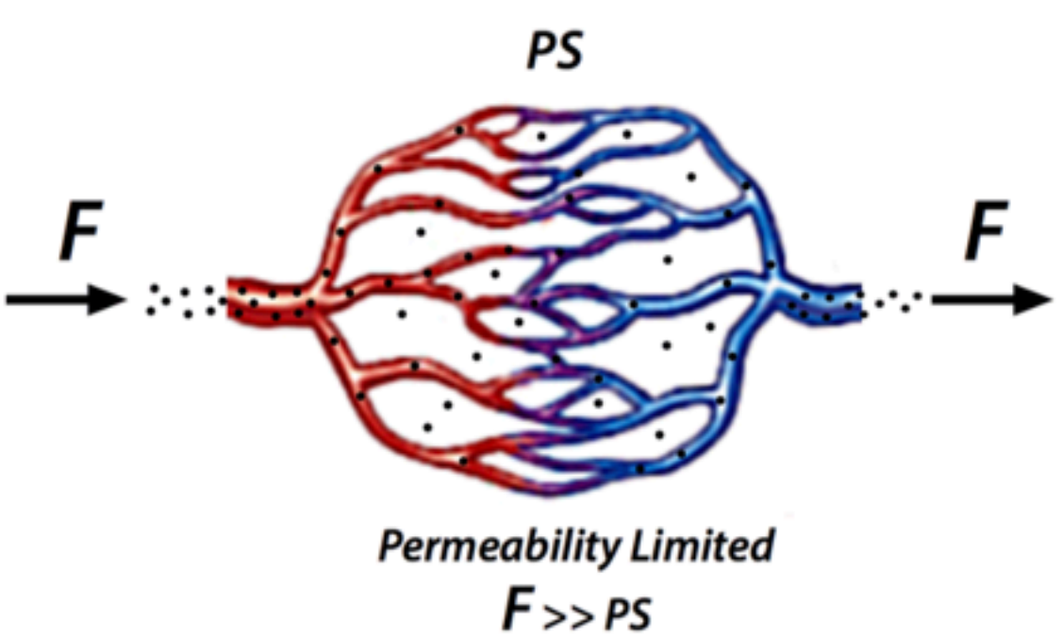
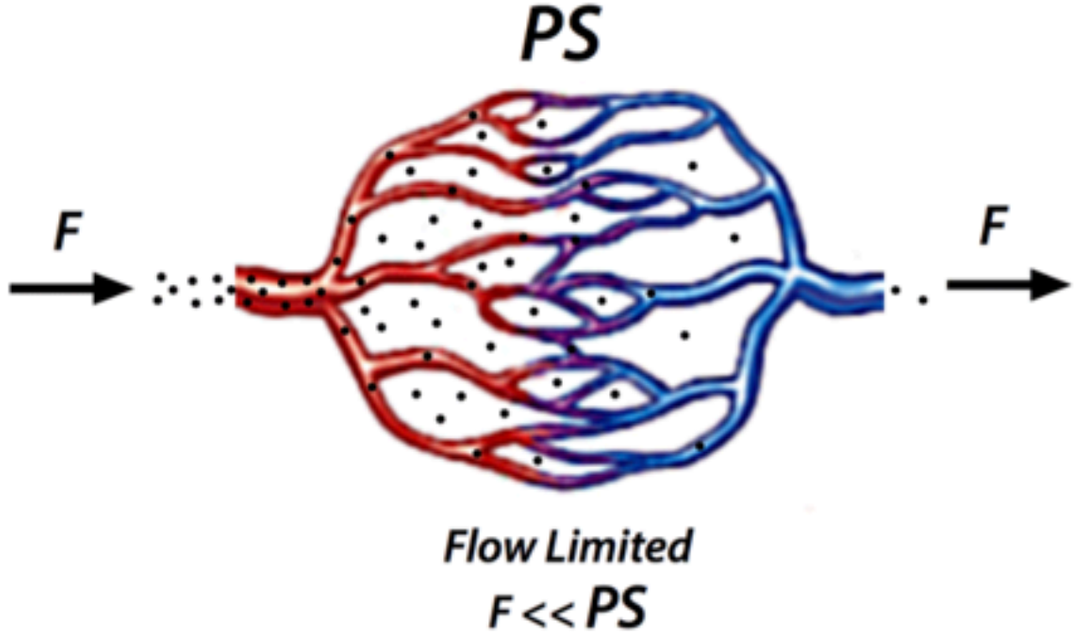
Dynamic Contrast Enhanced (DCE) MRI

Note on K^{trans}

- **<u>Flow Limited</u>**
- Plasma blood flow (F) is smaller than P x S product.
- Most of the contrast leaks into the extracellular space before reaching the venules

$$P \cdot S \gg F \qquad\qquad K^{trans} \approx F$$





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Dynamic Contrast Enhanced (DCE) MRI

1. <u>Pre-Contrast T1 Map from Multiple Flip Angle Data</u>:

Linear Scale Factor (coil coupling, proton density, $e^{-TE/T2}$)

$$S(\theta) = \frac{A \cdot \sin\theta\left(1 - e^{-TR/T1}\right)}{\left(1 - \cos\theta \cdot e^{-TR/T1}\right)}$$

2. <u>Convert to Relaxation Rate, $R_1(0) = 1/T1$</u>

3. <u>Using the same TE, TR, θ, collect dynamic data during contrast injection S(t)</u>

4. <u>Convert S(t) to $R_1(t)$</u>

$$S(t) = \frac{A \cdot \sin\theta\left(1 - e^{-R1(t)\cdot TR}\right)}{\left(1 - \cos\theta \cdot e^{-R1(t)\cdot TR}\right)}$$

$$e^{-R1(t)\cdot TR} = \frac{S(t) - A \cdot \sin\theta}{\left(S(t) \cdot \cos\theta - A \cdot \sin\theta\right)}$$

$$R1(t) = -\frac{1}{TR}\ln\left(\frac{S(t) - A \cdot \sin\theta}{\left(S(t) \cdot \cos\theta - A \cdot \sin\theta\right)}\right)$$

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Dynamic Contrast Enhanced (DCE) MRI

5. Calculate $\Delta R_1(t)$

$$\Delta R1(t) = R1(t) - R1(0) = \frac{1}{TR}\left[\ln\left(\frac{S(0) - A\cdot\sin\theta}{\left(S(0)\cdot\cos\theta - A\cdot\sin\theta\right)}\right) - \ln\left(\frac{S(t) - A\cdot\sin\theta}{\left(S(t)\cdot\cos\theta - A\cdot\sin\theta\right)}\right)\right]$$

6. Convert From Relaxation Rate to Concentration

$$C_{tissue}(t) = \frac{1}{r_1}\Delta R1(t)$$

Relaxivity of Contrast Agent

7. Use arterial input function as $C_{in}(t)$

8. Fit the concentration vs. time curve for each voxel with pharmacokinetic model using nonlinear least-squares regression

$$C_{tissue}(t) = v_p C_p(t) + K^{trans}\int_0^t C_p(\tau)e^{-k_{ep}(t-\tau)}\,d\tau$$

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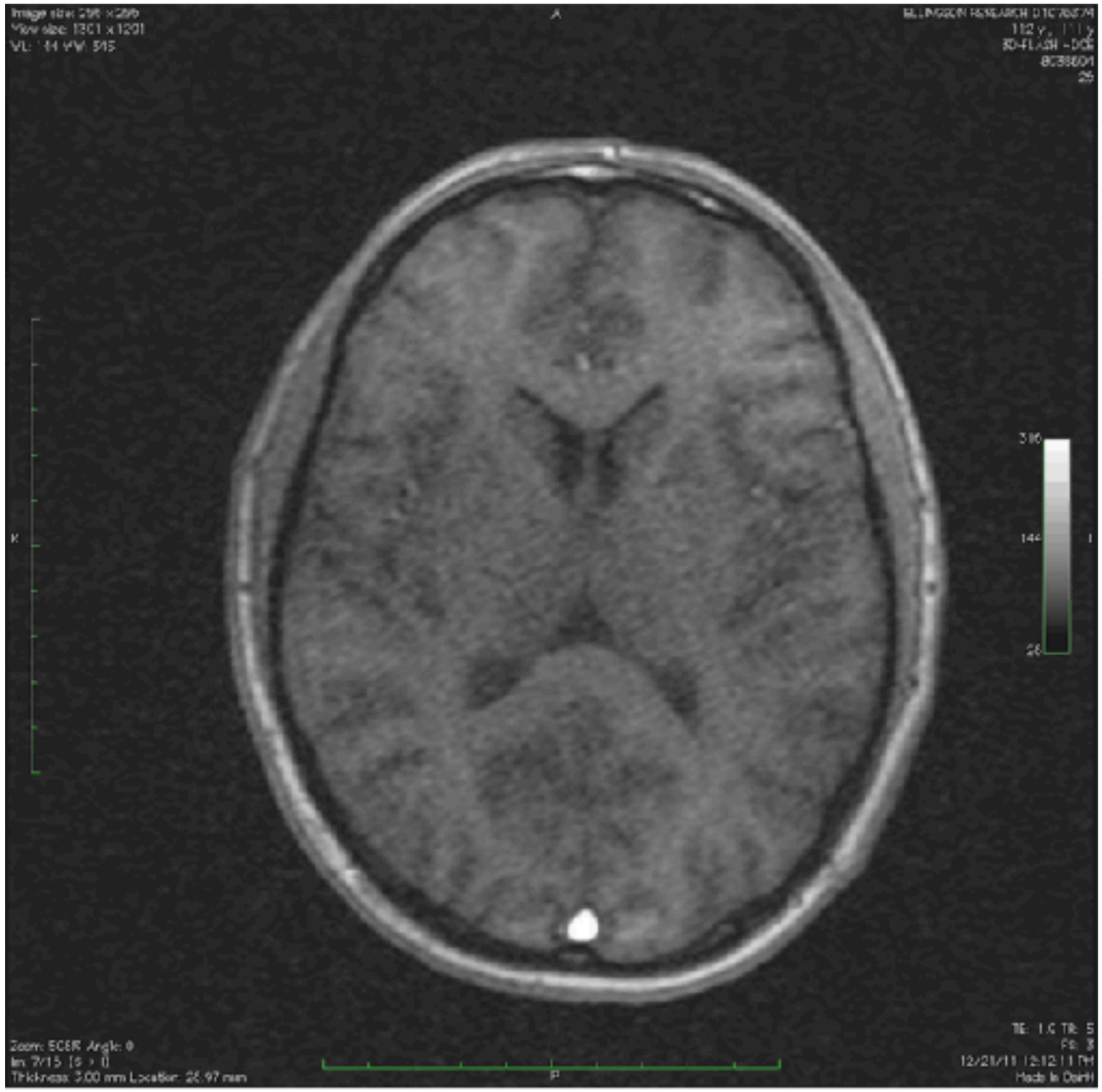
Dynamic Contrast Enhanced (DCE) MRI



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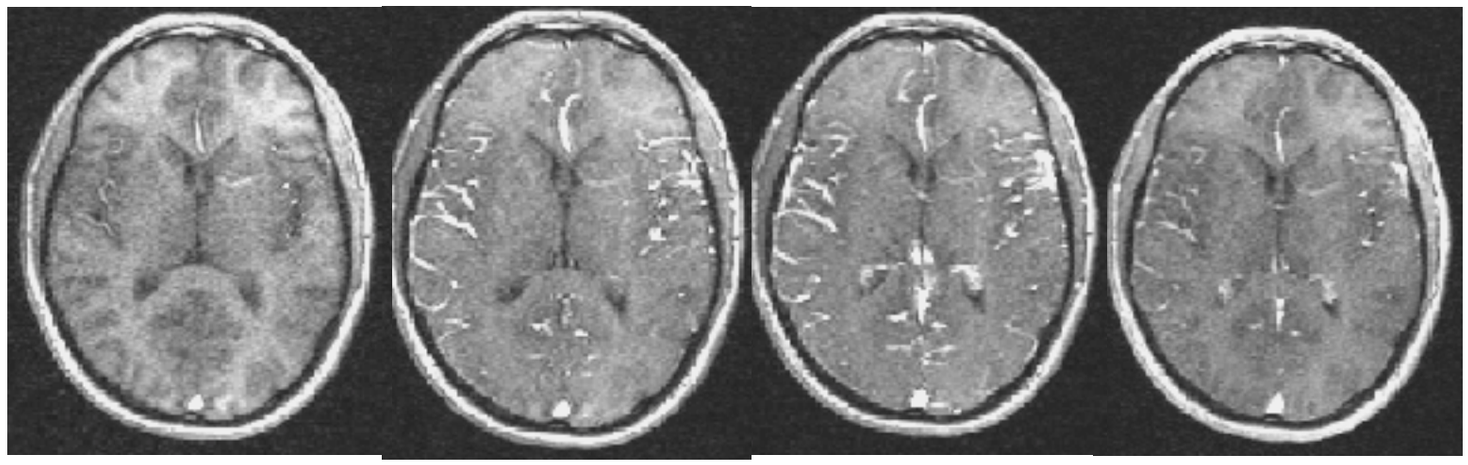
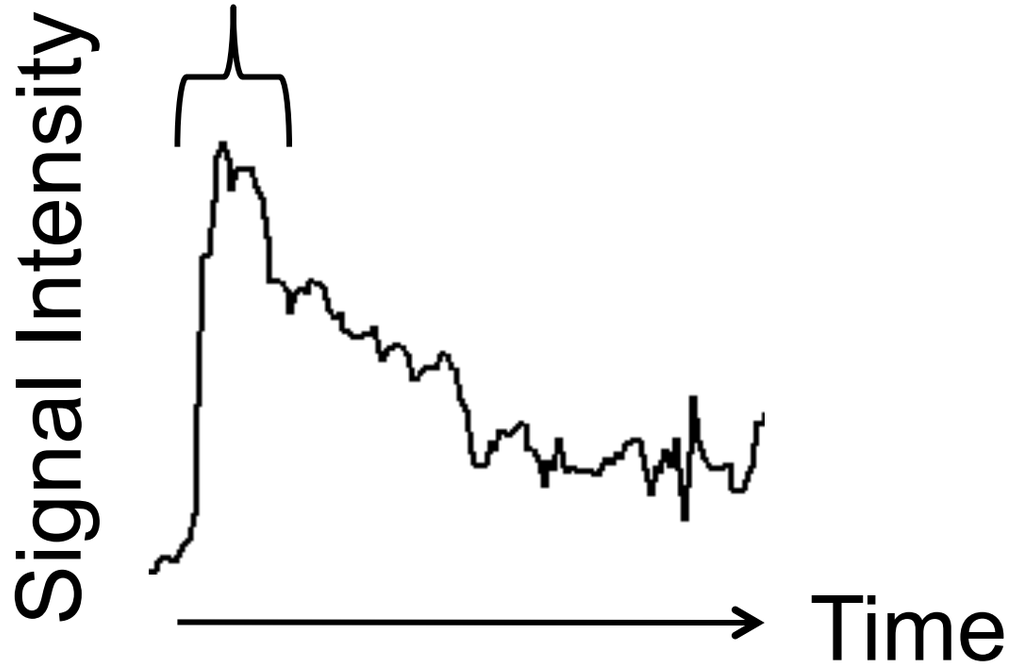
Dynamic Contrast Enhanced (DCE) MRI





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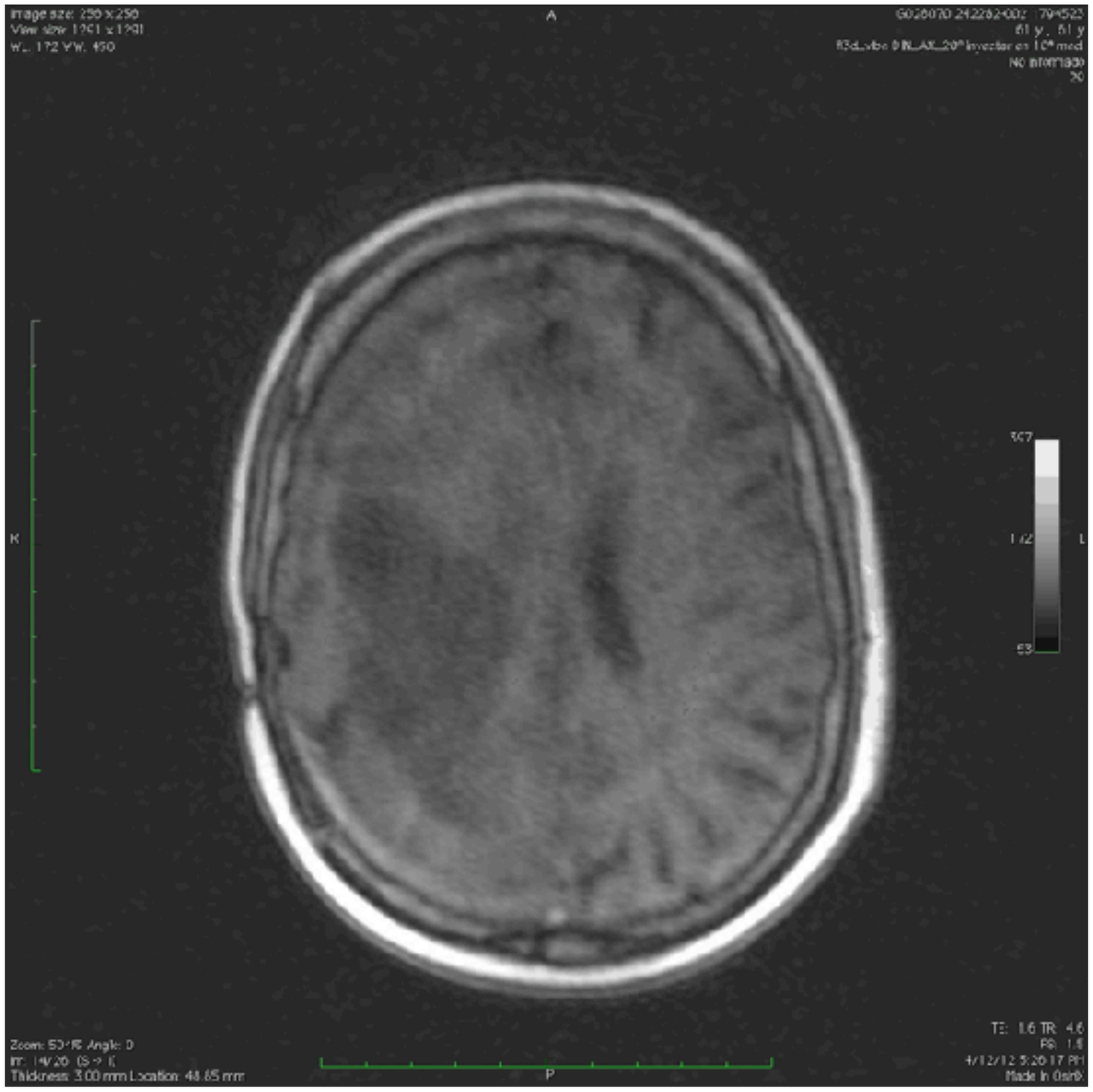
Dynamic Contrast Enhanced (DCE) MRI



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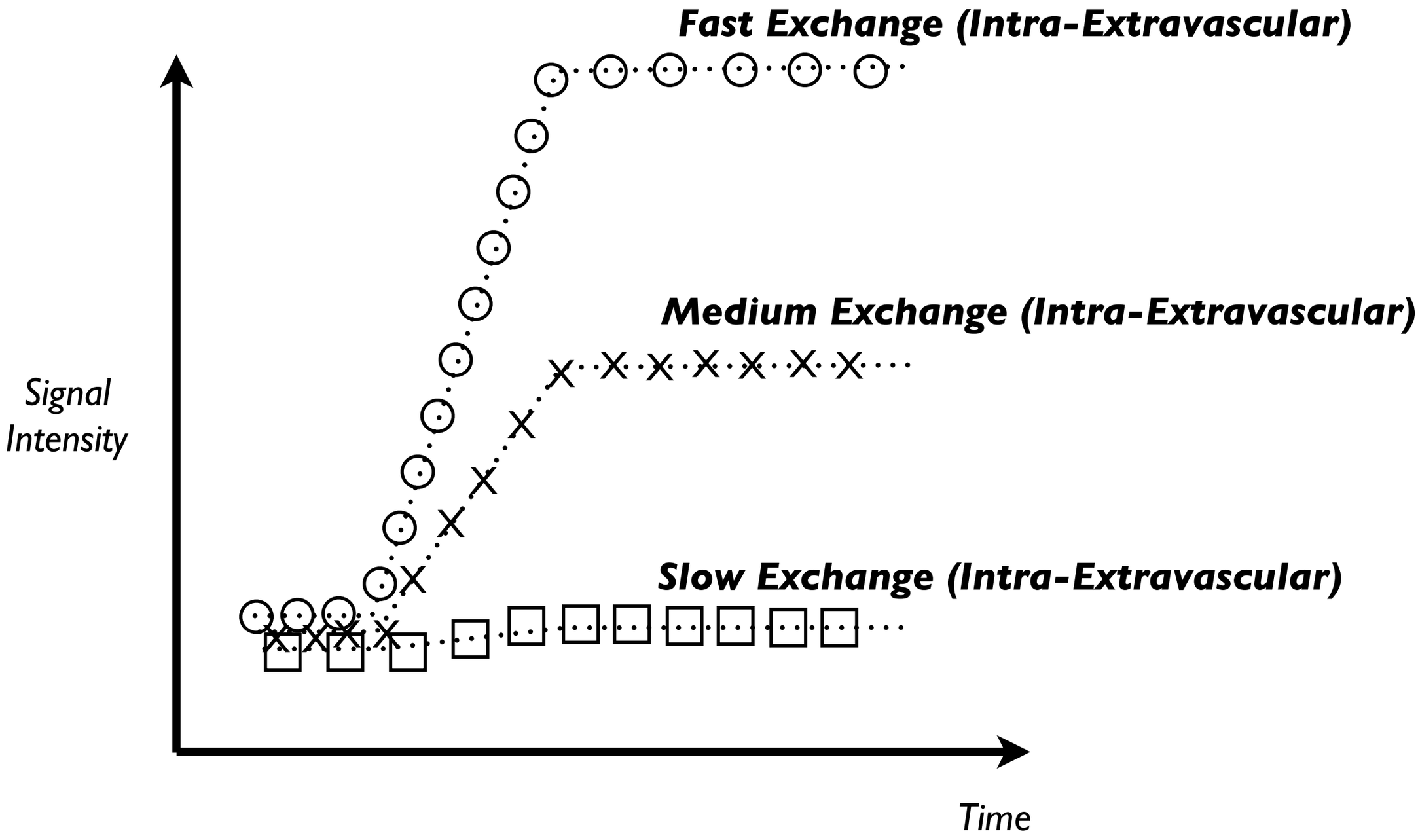
Dynamic Contrast Enhanced (DCE) MRI



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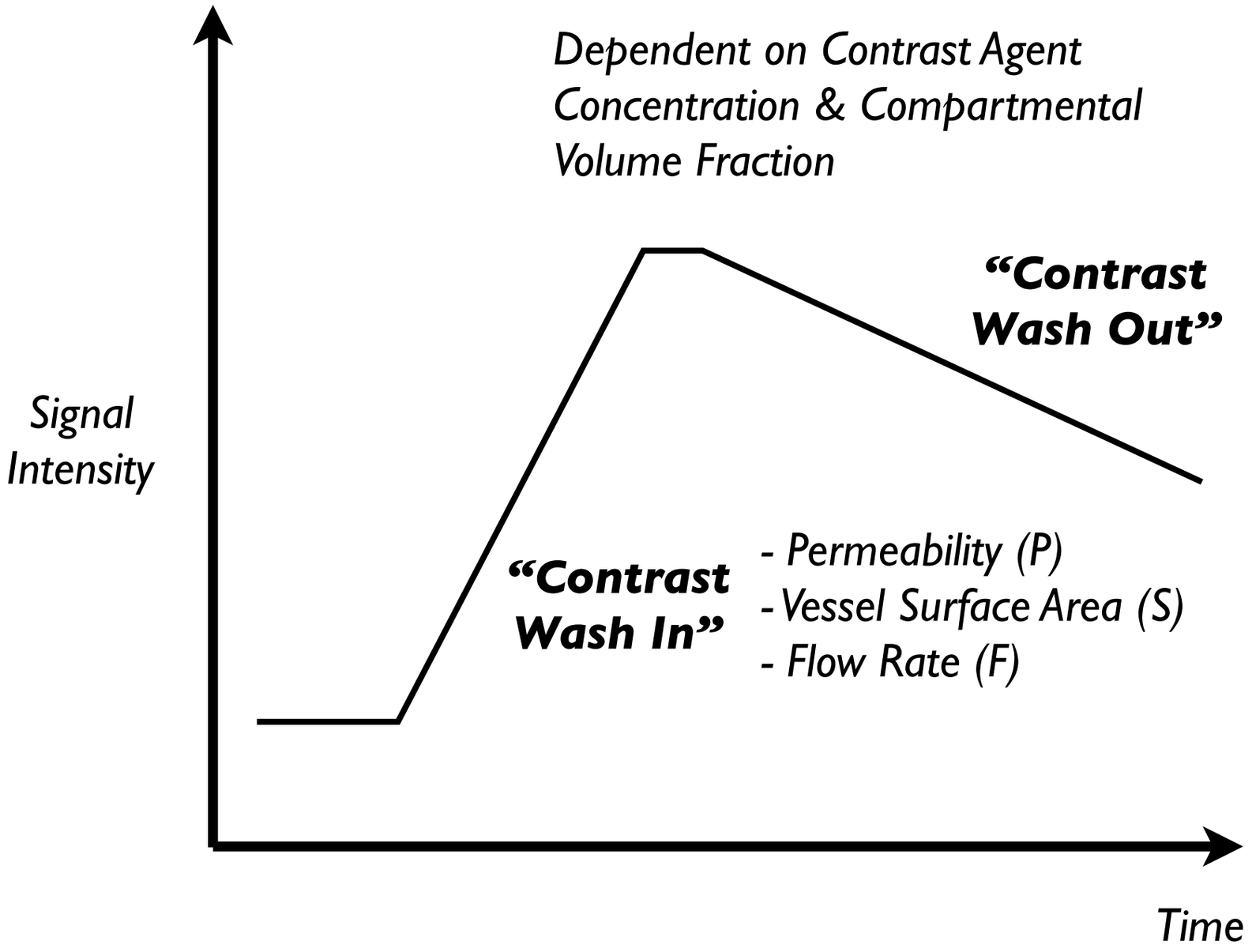
Dynamic Contrast Enhanced (DCE) MRI



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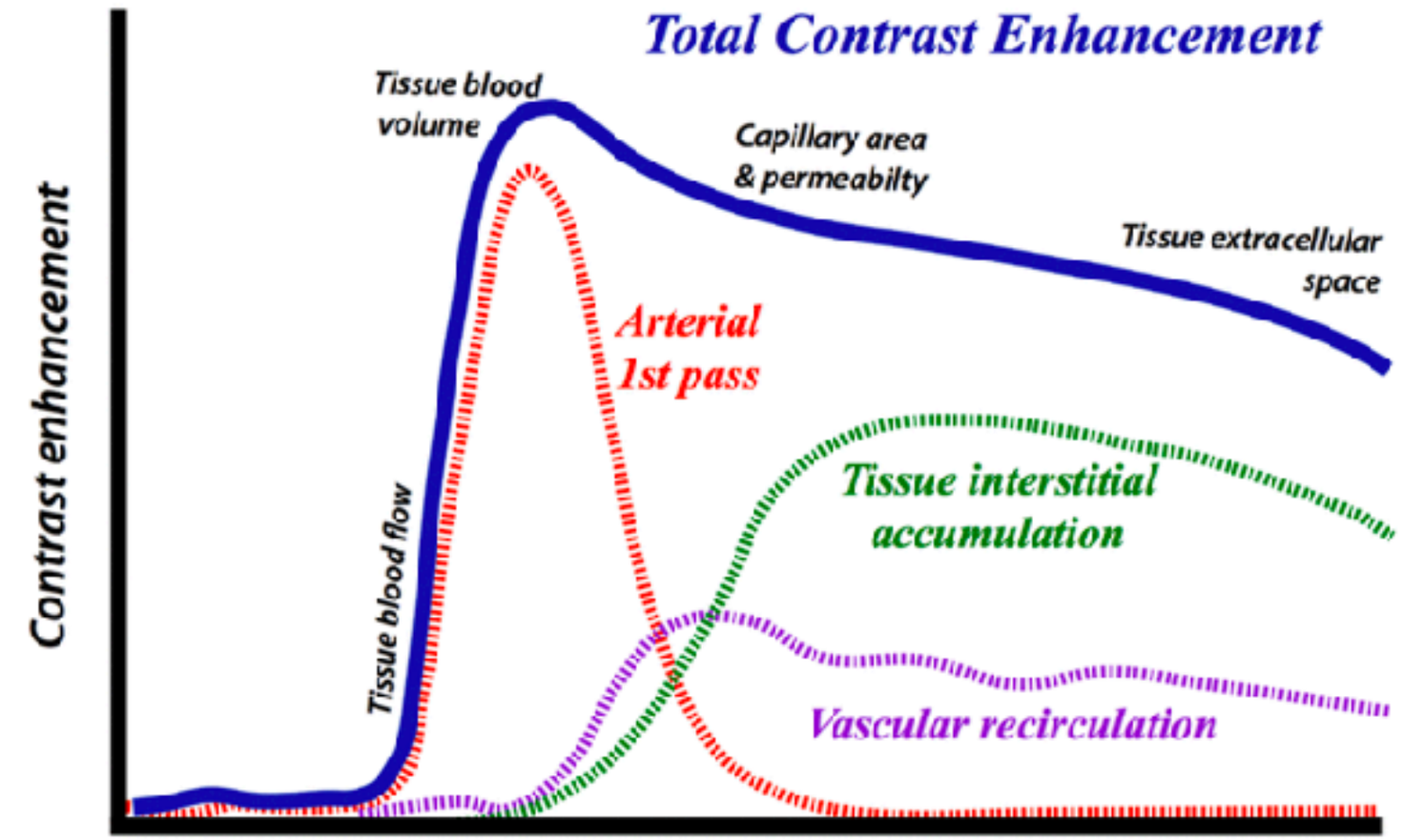
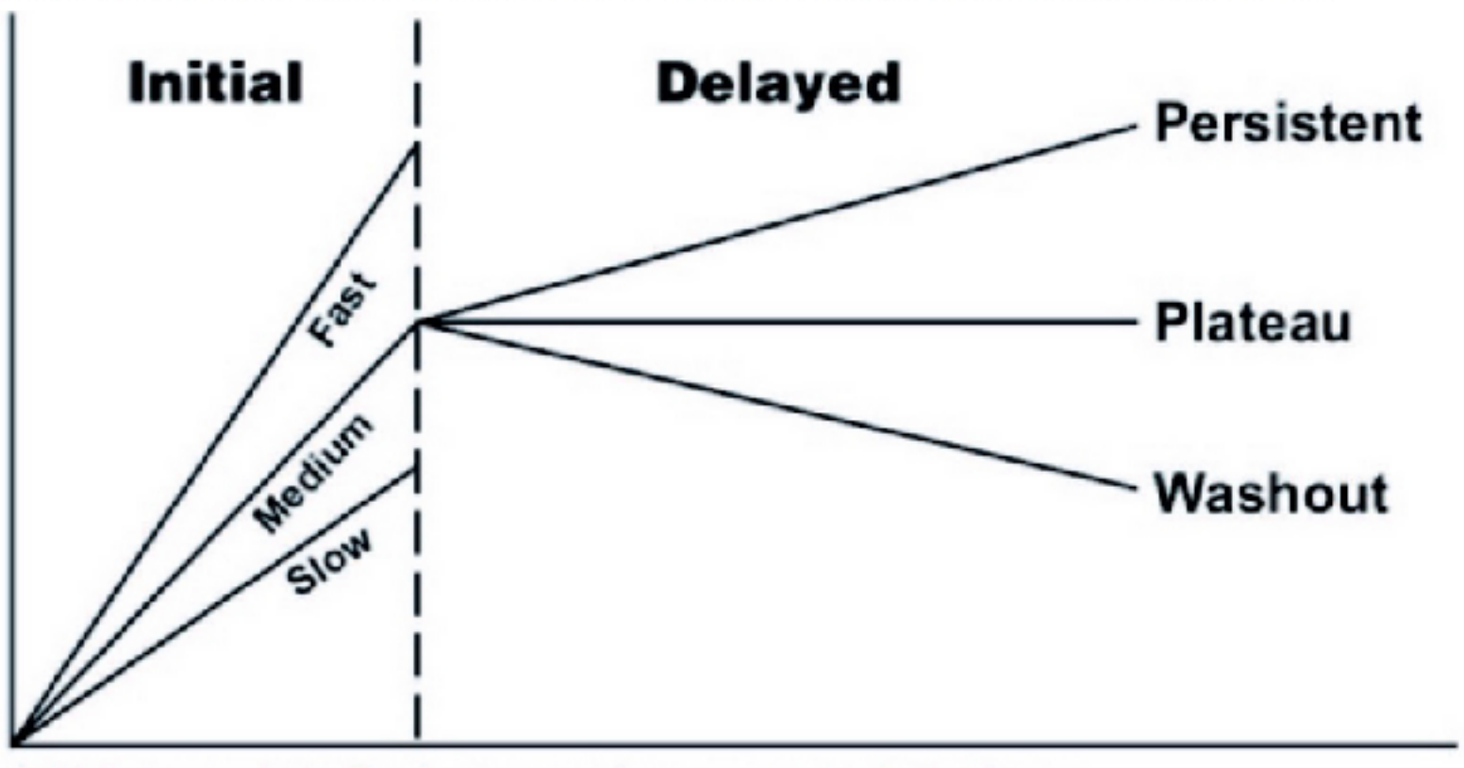
Dynamic Contrast Enhanced (DCE) MRI





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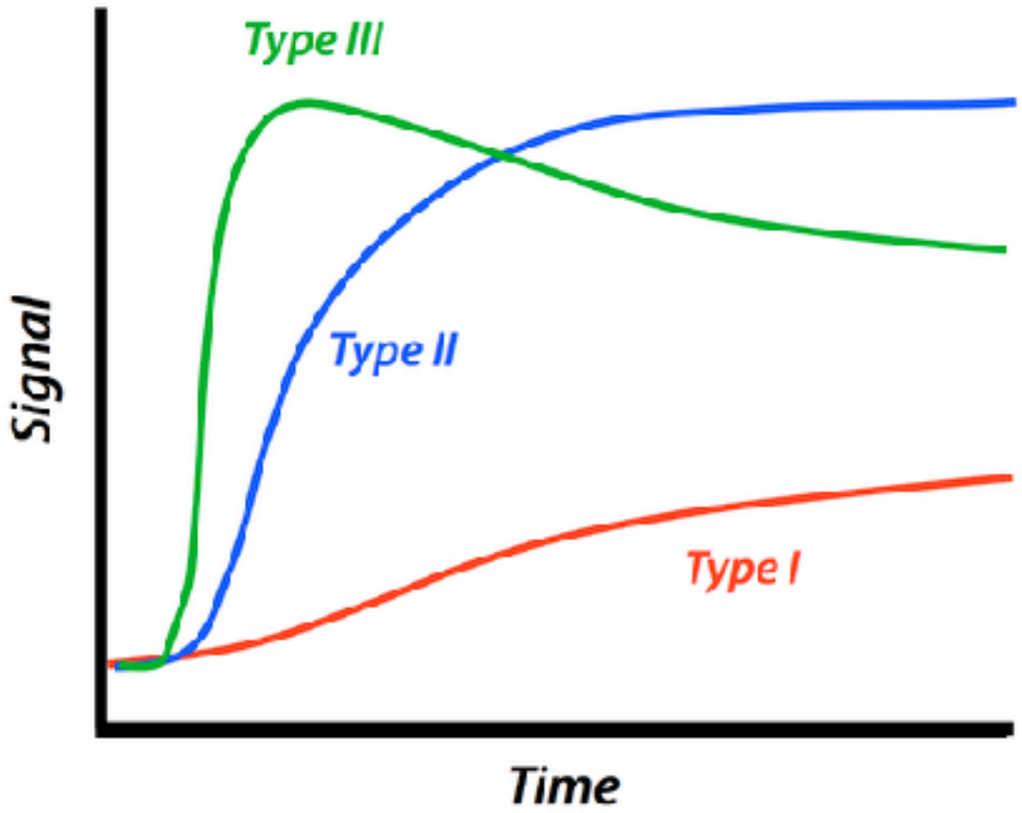
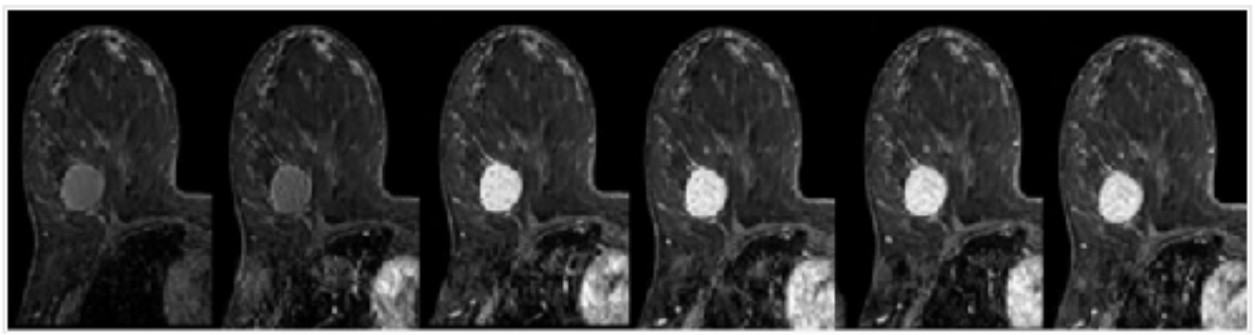
Dynamic Contrast Enhanced (DCE) MRI

Breast Cancer Risk

Subtypes





- **Type I:** More likely to be benign
- **Type II:** Intermediate Risk
- **Type III:** More likely to be malignant

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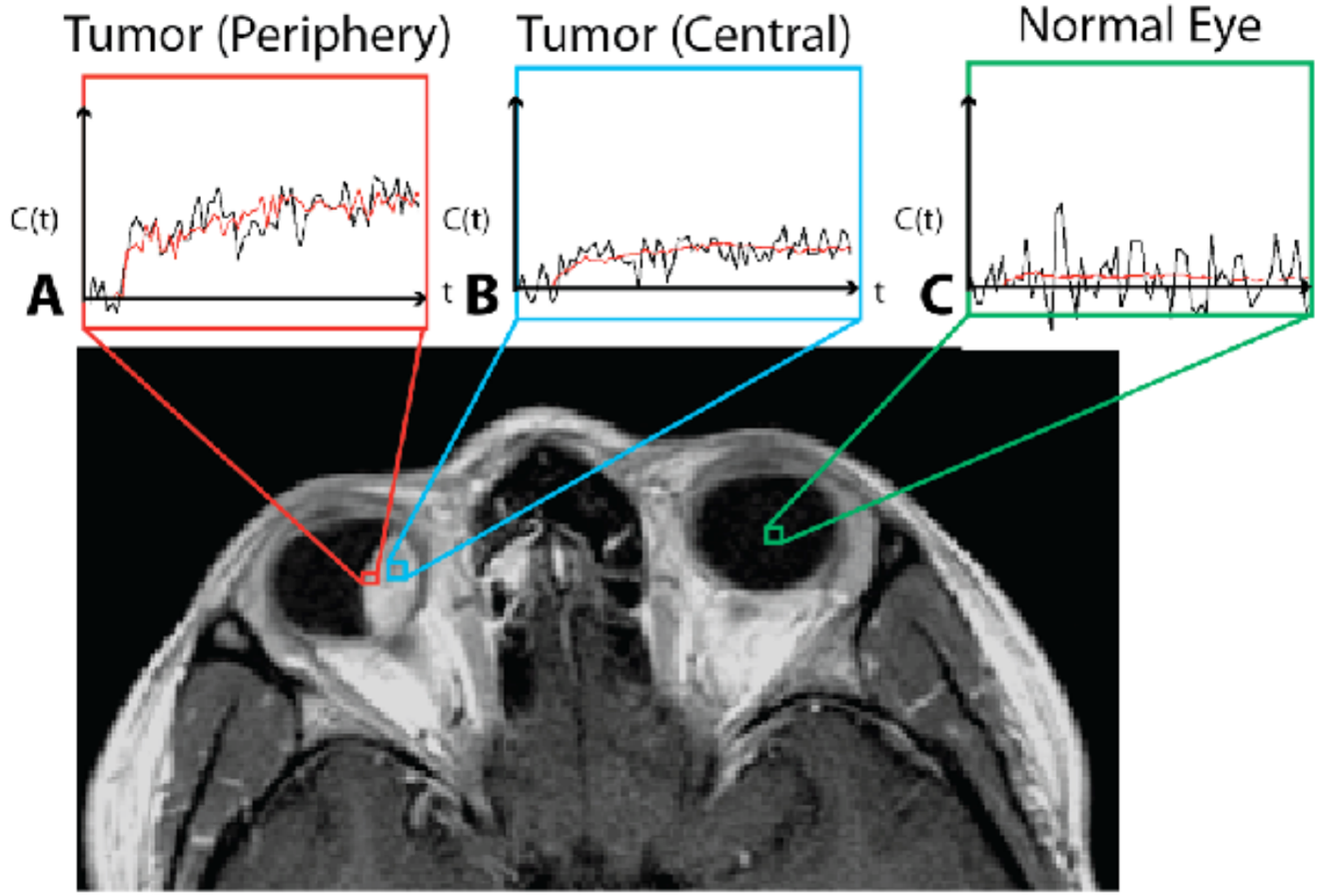
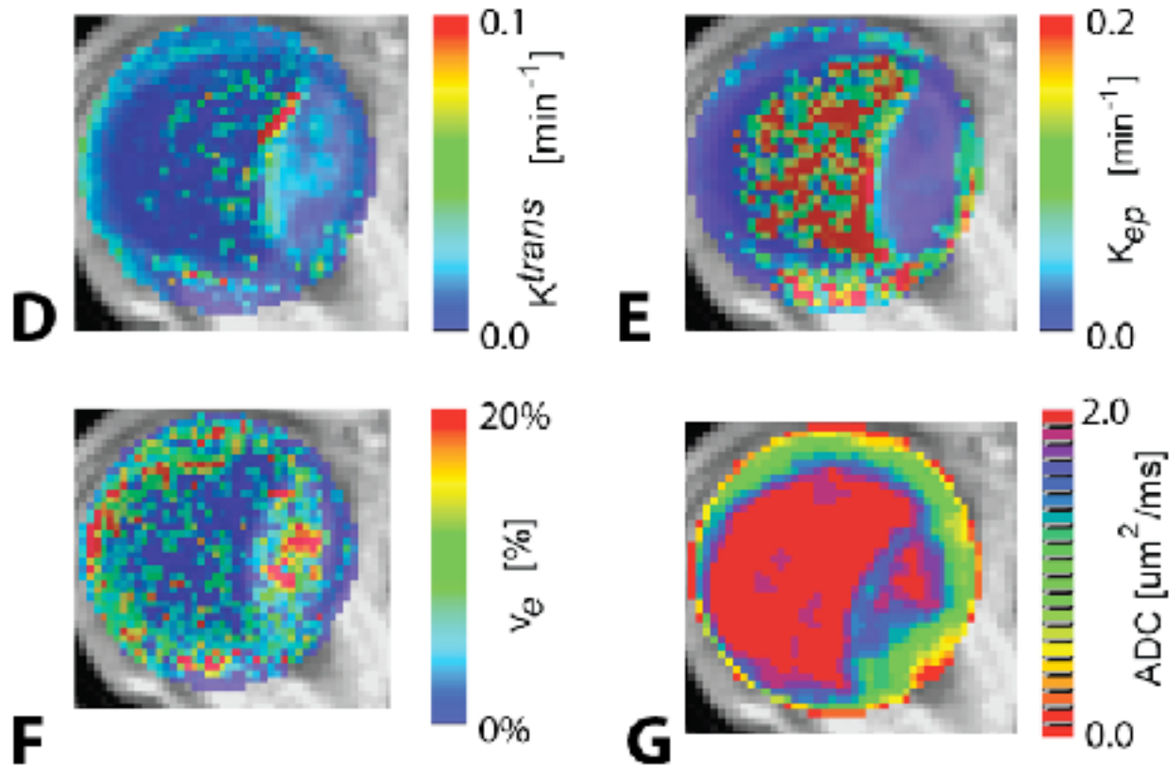
Uveal Melanoma - Rare intraocular tumor





Kamrava M[1], Sepahdari AR, Leu K, Wang PC, Roberts K, Demanes DJ, McCannel T, Ellingson BM.

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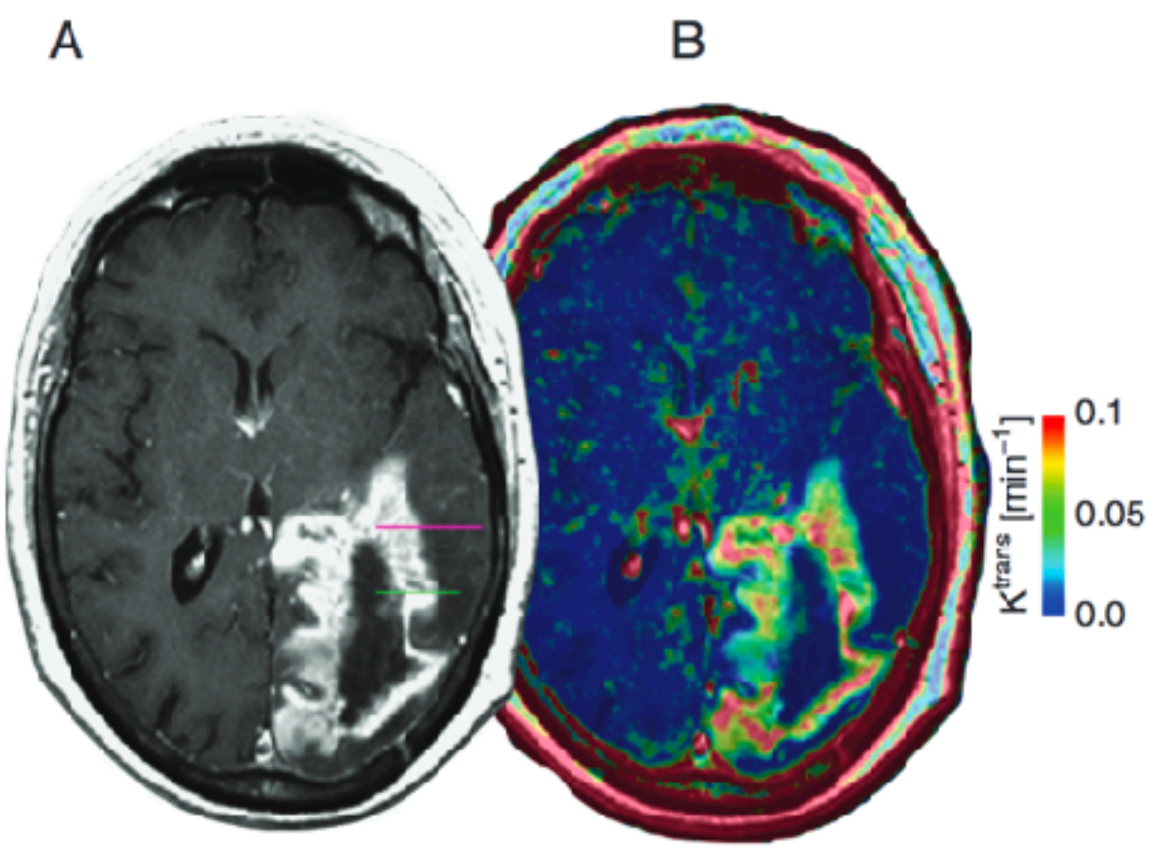
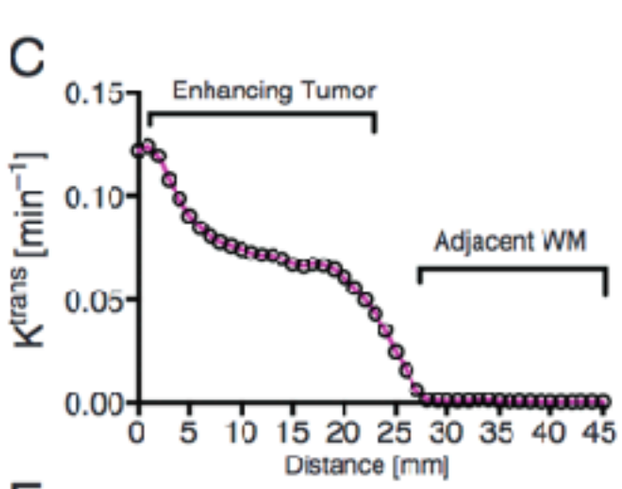
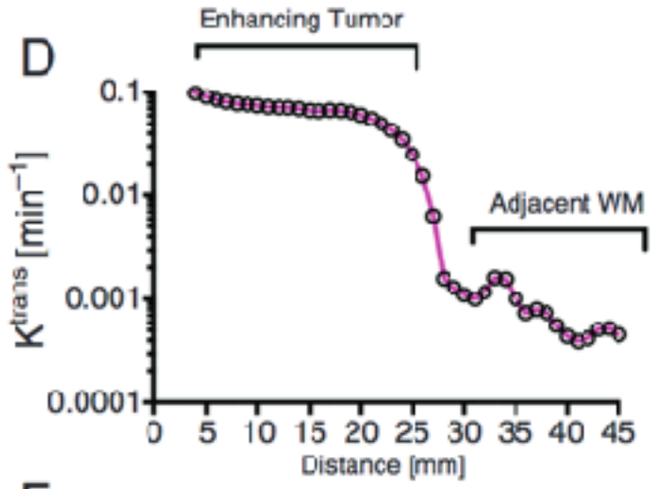
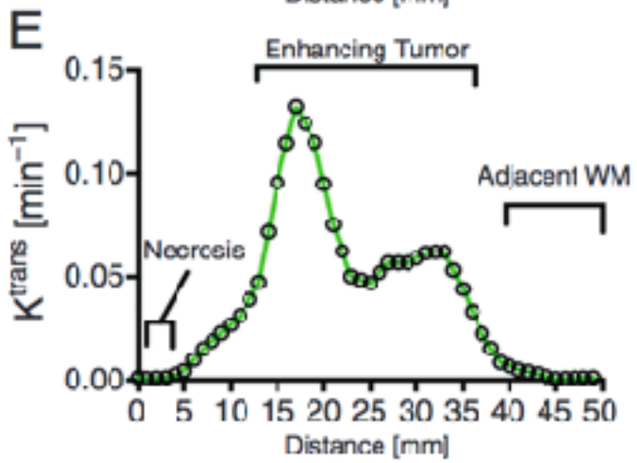
Dynamic Contrast Enhanced (DCE) MRI

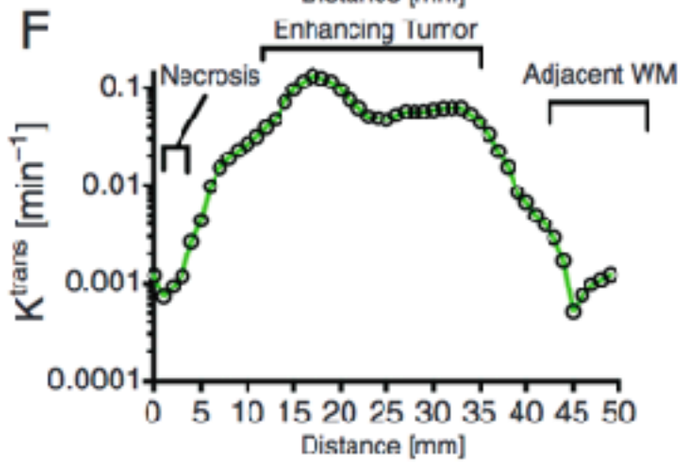
Gadolinium Brain Penetrance











Levin VA[1,2], Ellingson BM[3]. **Understanding brain penetrance of anticancer drugs** Neuro Oncol. 2018 Apr 9;20(5):589-596.

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Dynamic Contrast Enhanced (DCE) MRI

Gadolinium Brain Penetrance

Table 1 Collation of Gd-contrast transfer constant, K^{trans}, and tumor extracellular space, *Ve*, for different grades of glioma

K^{trans} / min^{-1}					*Ve*				Reference
Brain	Grade I	Grade II	Grade III	Grade IV	Grade I	Grade II	Grade III	Grade IV	
0.004	0.066	0.093	0.190	0.214	0.27	0.43	0.63	0.72	22
		0.032	0.102			*0.07*	0.35		23
		0.019	0.108			*0.03*	0.32		24*
		0.026	0.096	0.135		*0.12*	0.48	0.52	25
0.004	*.066*	*0.042*	*0.124*	*0.174*	*0.27*	*0.43*	*0.44*	*0.62*	*Average*

*Study was limited to oligodendroglioma tumors.

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Perfusion MR Imaging

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  - **<u>"Relaxivity" (T1) Methods</u>:**
    - Dynamic Contrast Enhanced (DCE) MRI
      - Perfusion Parameters (Extraction Fraction, Extracellular Volume Fraction, Blood Volume)
  - **<u>"Susceptibility" (T2/T2*) Methods</u>:**
    - Dynamic Susceptibility Contrast (DSC) MRI
      - Perfusion Parameters (Blood Volume, Blood Flow, Mean Transit time)

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Susceptibility (T2/T2*) Methods

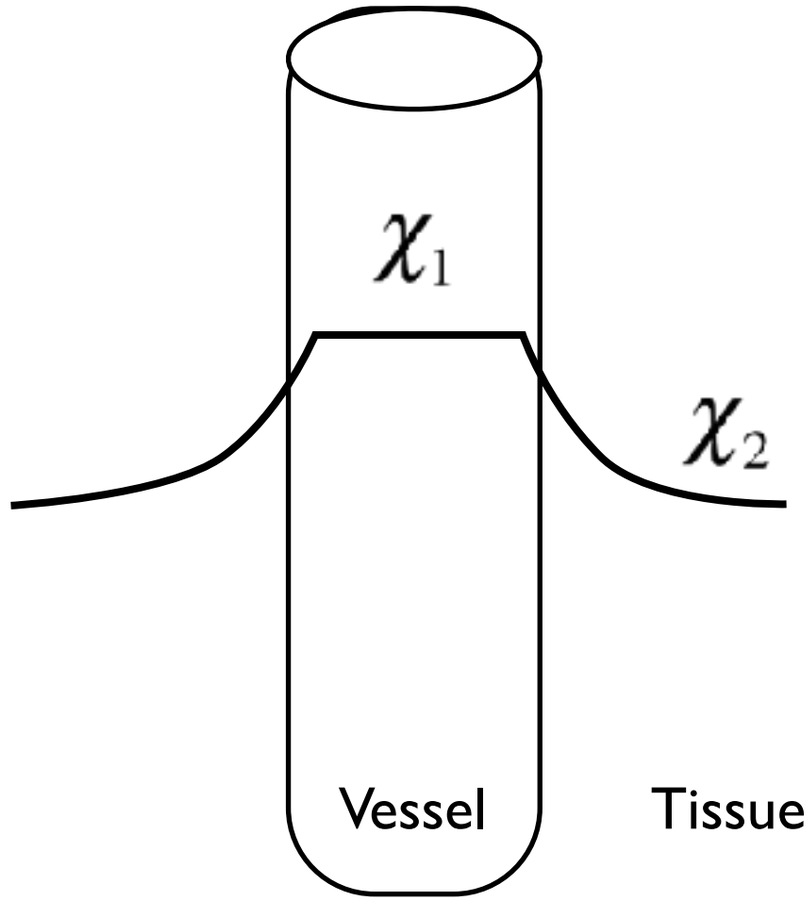
- All susceptibility methods require a magnetic susceptibility gradient be present between the vasculature and extracellular, extravascular space

- Susceptibility contrast agents have much higher magnetic moments, which leads to higher magnetic susceptibilities χ compared to body tissues = *susceptibility agents*

- These agents set up a concentration gradient between the intravascular and extravascular spaces

- Diffusion of water molecules through these gradients alters the phase of the associated protons, resulting in transverse relaxation.

- Therefore, these are also called *spoiling* agents (decrease T2/T2*)



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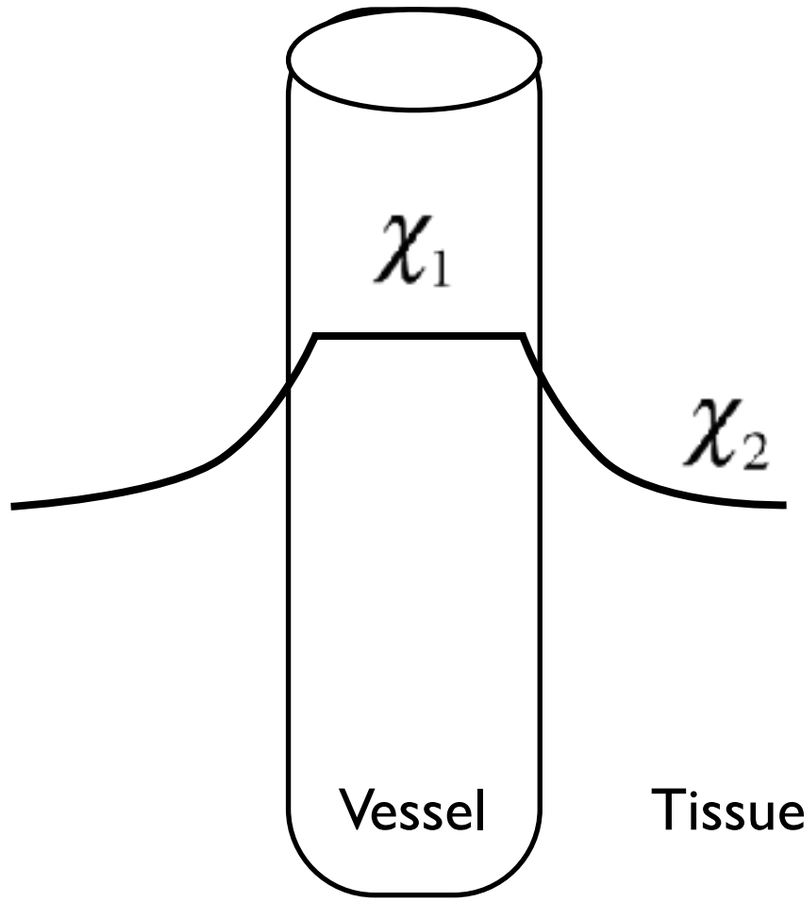
Susceptibility (T2/T2*) Methods

- Susceptibility contrast agents are typically:
  - Superparamagnetic (MION, SPIOs)
  - Highly concentrated paramagnetic (bolus of Gd-chelated CA)



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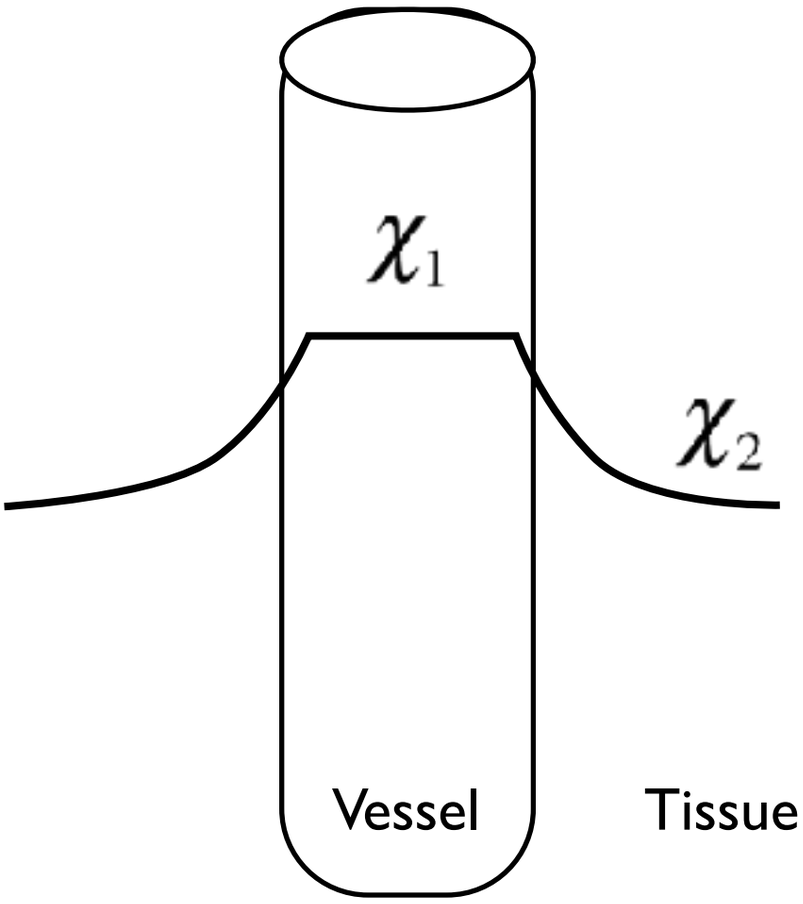
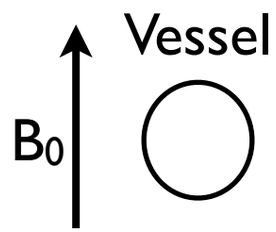
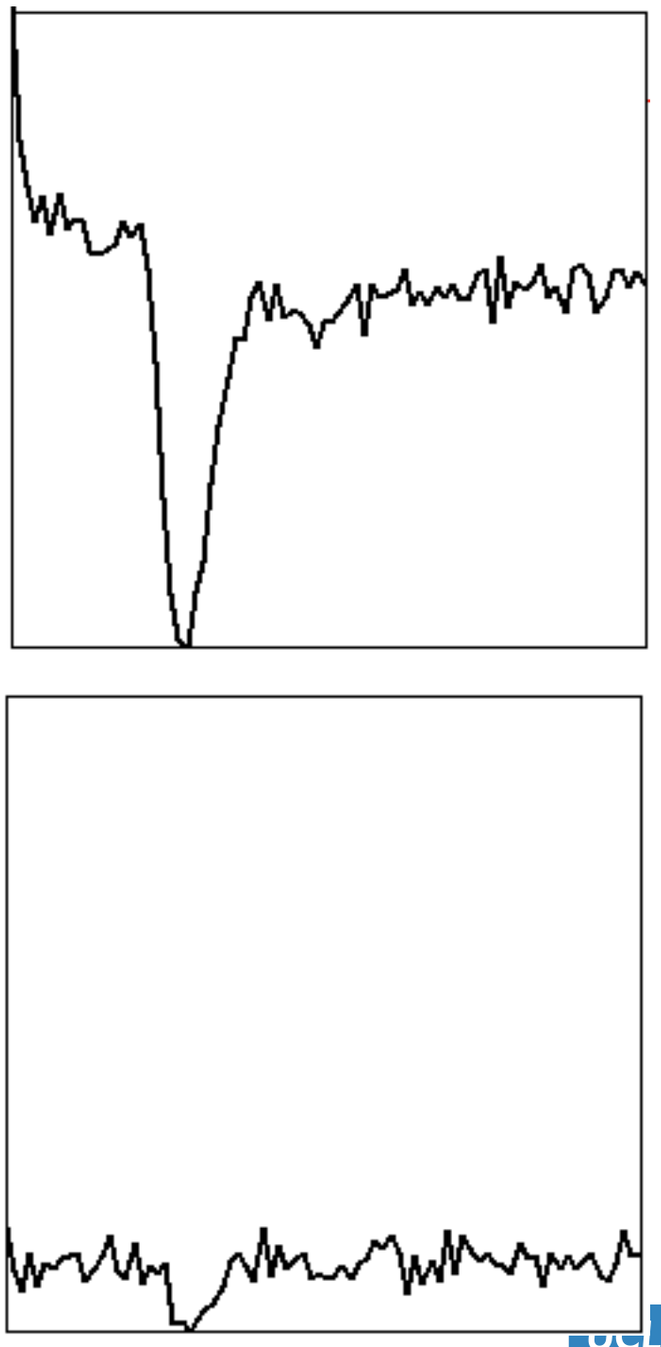
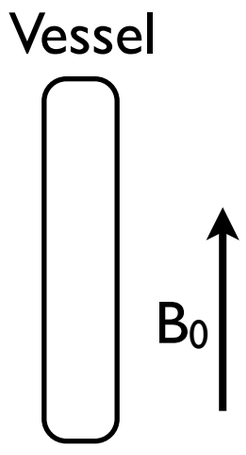
Susceptibility Effects Depend on Vessel Orientation Relative to B_0 Field









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Dynamic Susceptibility Contrast (DSC)-MRI

- Based on the "indicator-dilution" theory (Stewart, 1894)
- "The volume of solution necessary to dilute the injected indicator (Observed Concentration) is exactly equal to the volume of blood that had diluted the injectate over the time interval in which the indicator was recovered."
- Assumptions:
    - Single in-flow and single out-flow
    - Recirculation does not occur
    - Indicator/contrast agent perfusion is representative of the native fluid
    - System must exhibit "stationarity"
        - The distribution of particle transit times is constant during the experiment

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Dynamic Susceptibility Contrast (DSC)-MRI

$$CBV \propto \int_{0}^{t=\infty} C(t)\,dt$$

- Substituting Relaxation Rate R2* for concentration:

$$C(t) = \frac{1}{r_2^*}\Delta R2^*(t)$$

$$CBV \propto \int_{0}^{t=\infty} \Delta R2^*(t)\,dt$$

$$CBV = CBF \cdot MTT$$

$$CBV \propto -\int_{0}^{t=\infty} \left(\frac{1}{TE}\ln\frac{S(t)}{S(0)}\right)dt$$

$$volume = \frac{volume}{time} \cdot time$$

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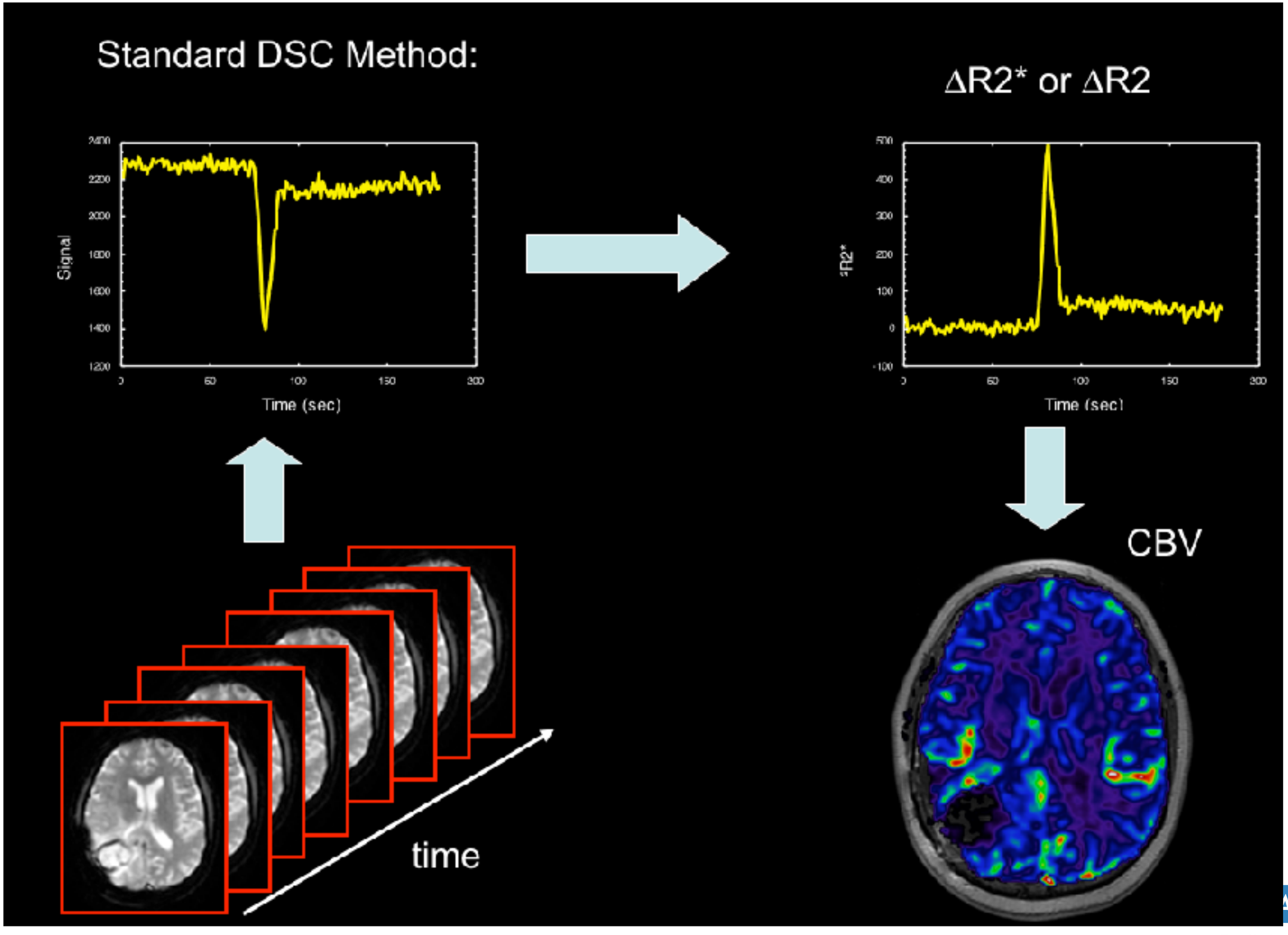
Dynamic Susceptibility Contrast (DSC)-MRI



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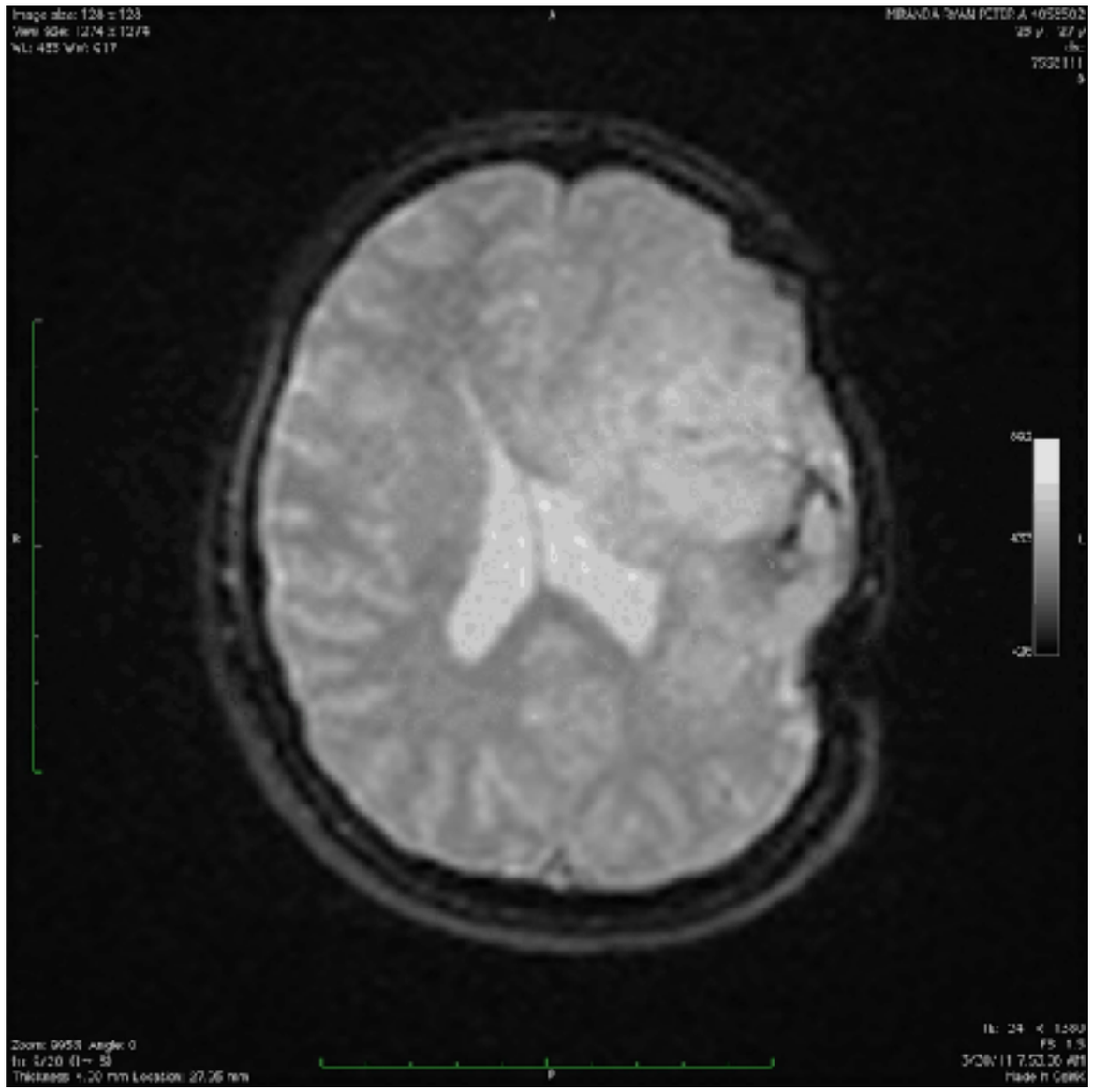
Dynamic Susceptibility Contrast (DSC)-MRI



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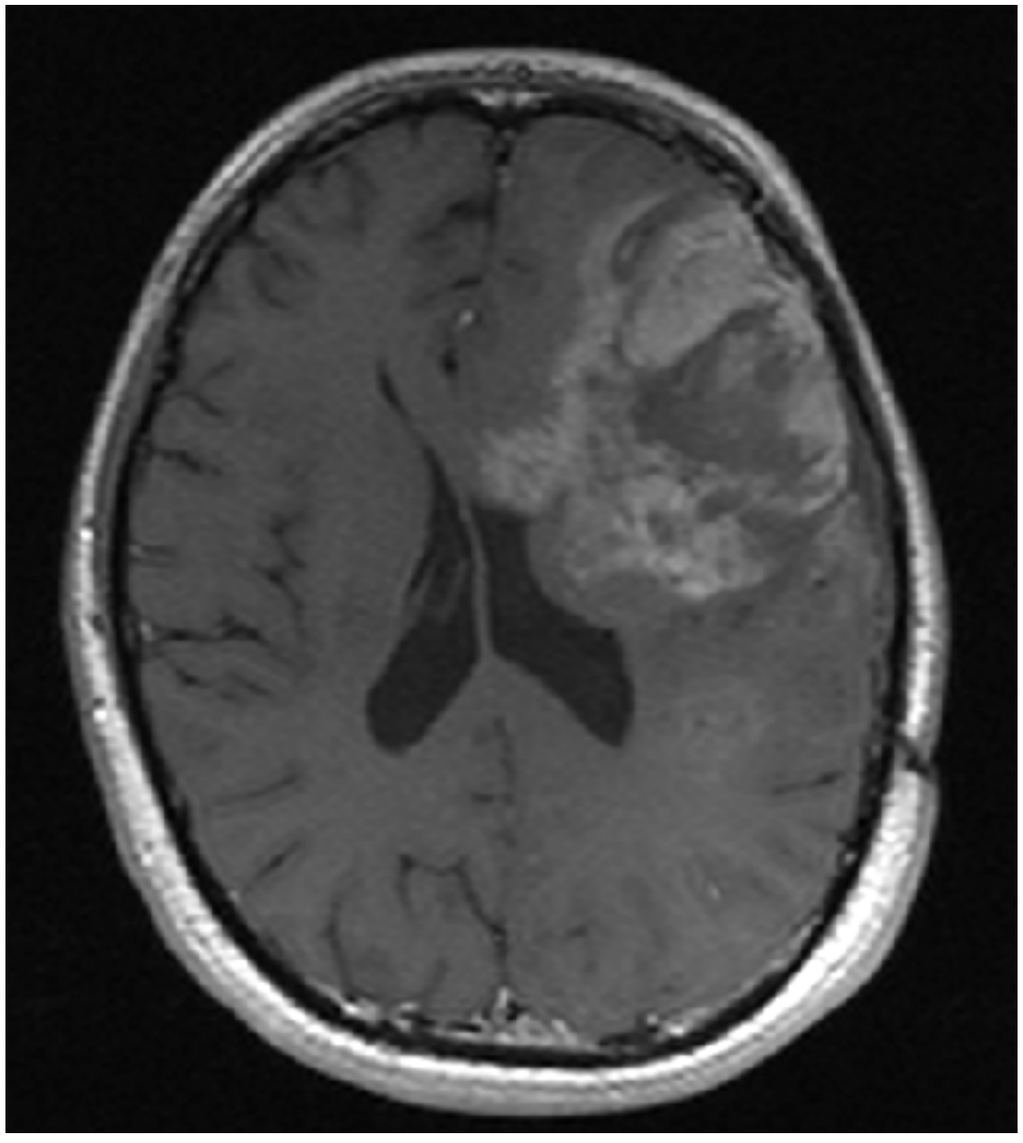
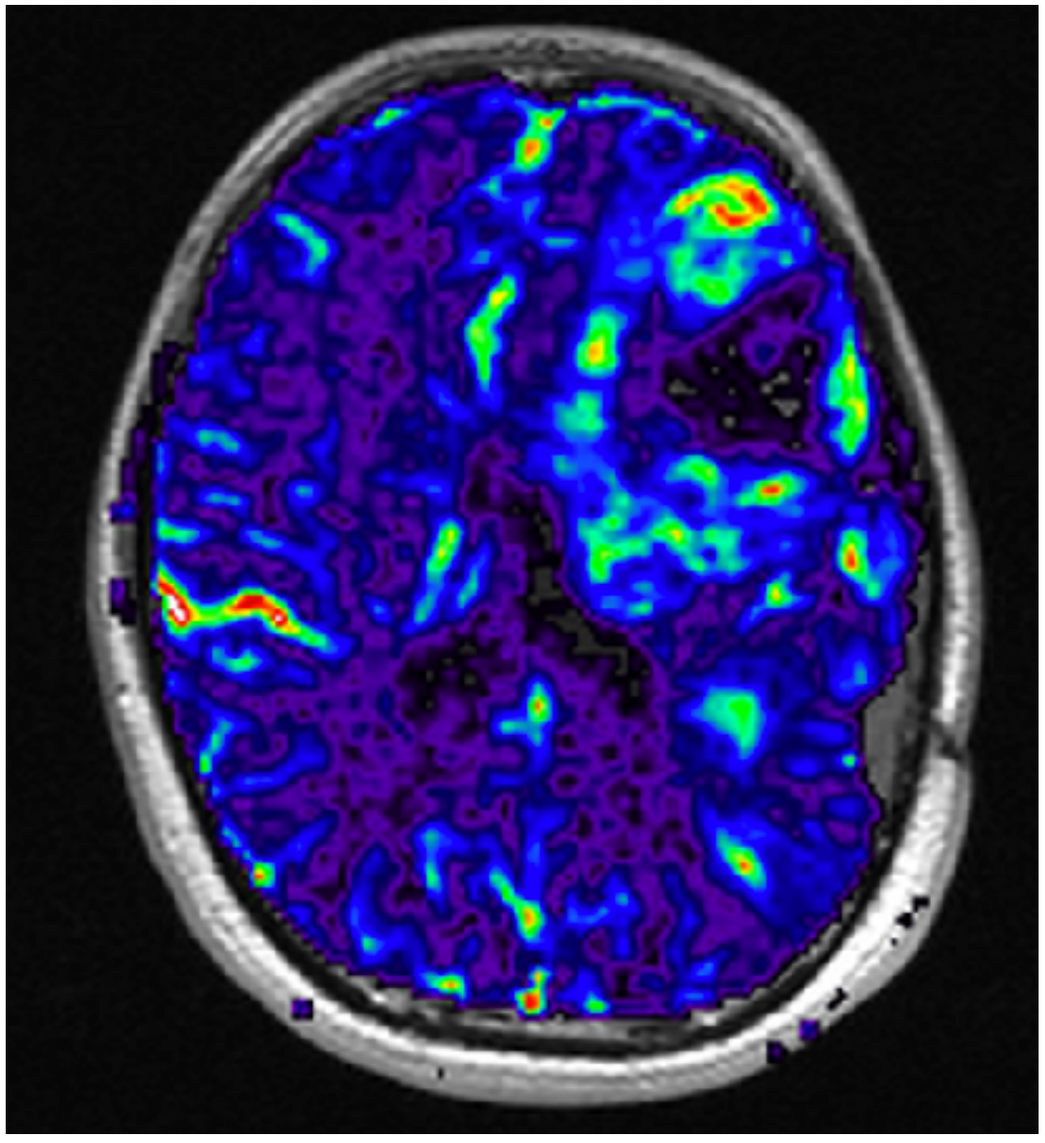
Dynamic Susceptibility Contrast (DSC)-MRI

Post-Contrast T1w



rCBV



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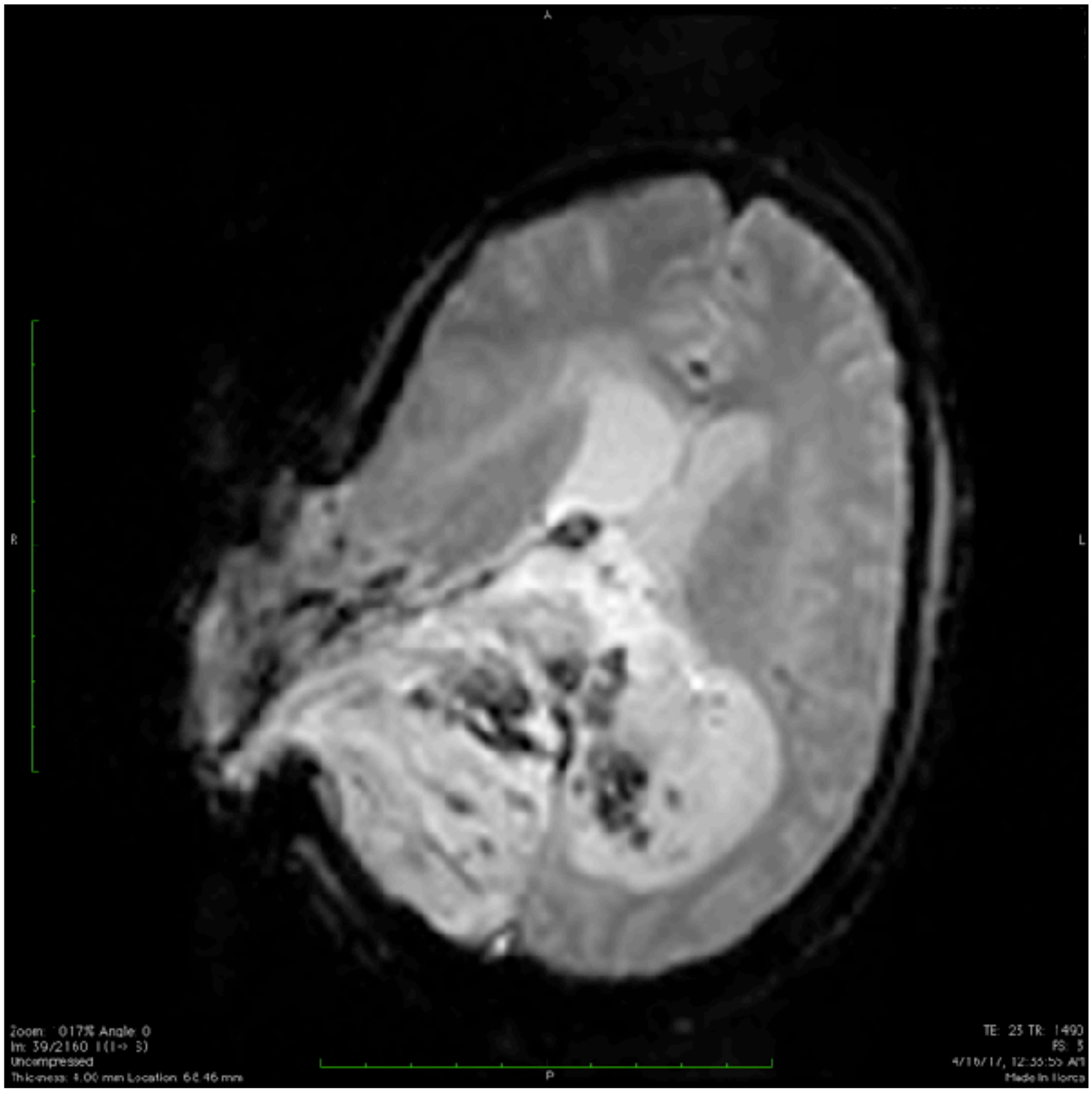
Dynamic Susceptibility Contrast (DSC)-MRI

Raw Time Series



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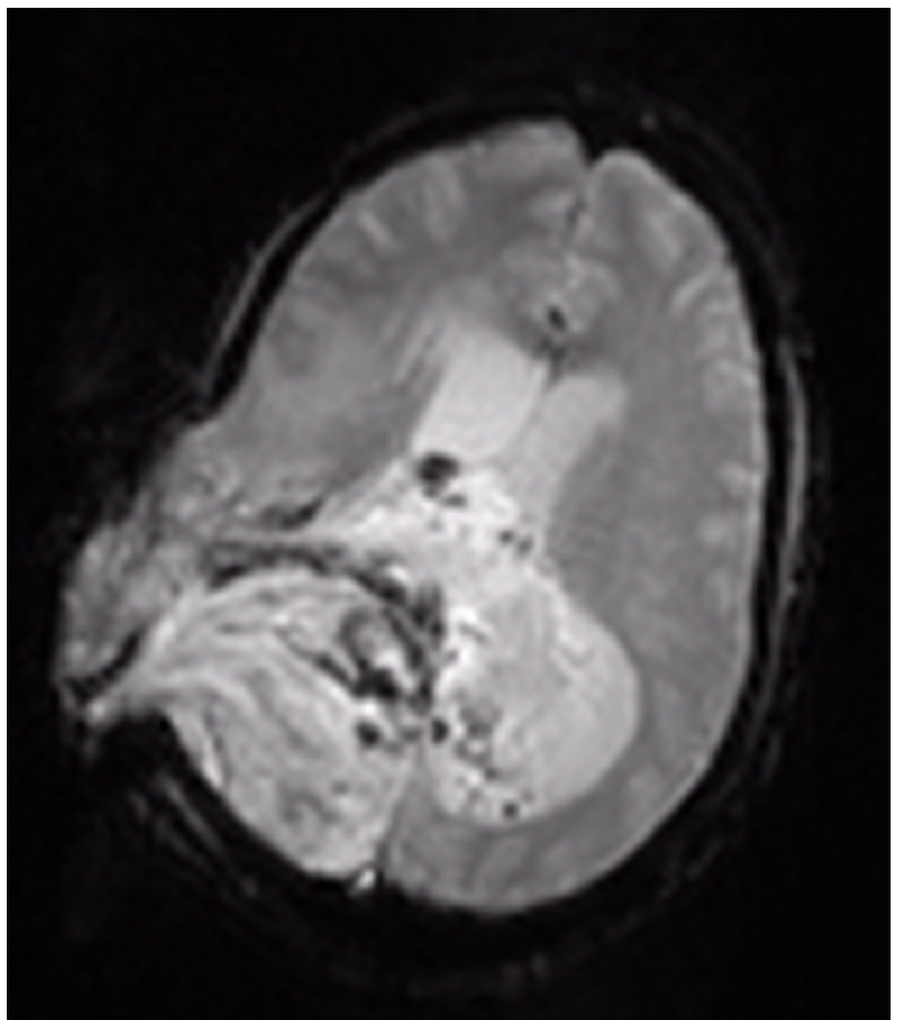
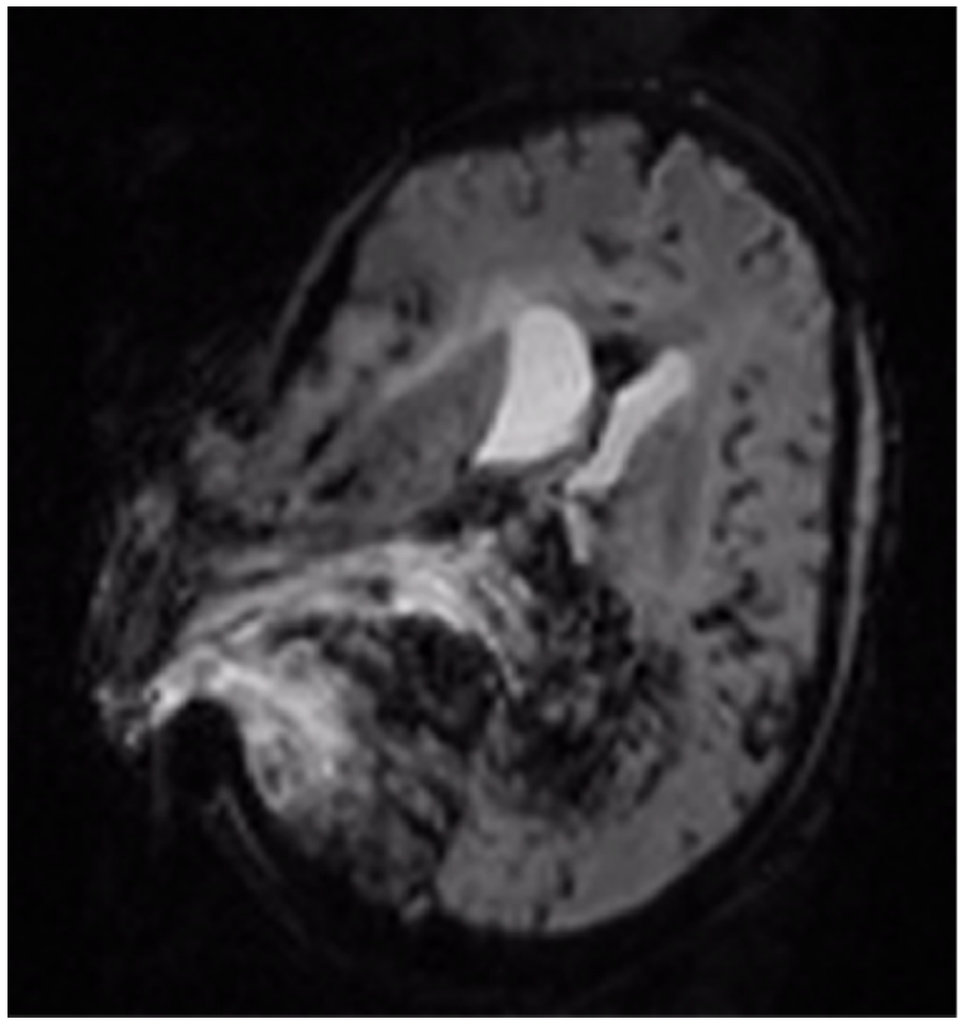
Dynamic Susceptibility Contrast (DSC)-MRI

Raw Time Series

Baseline



Bolus Peak



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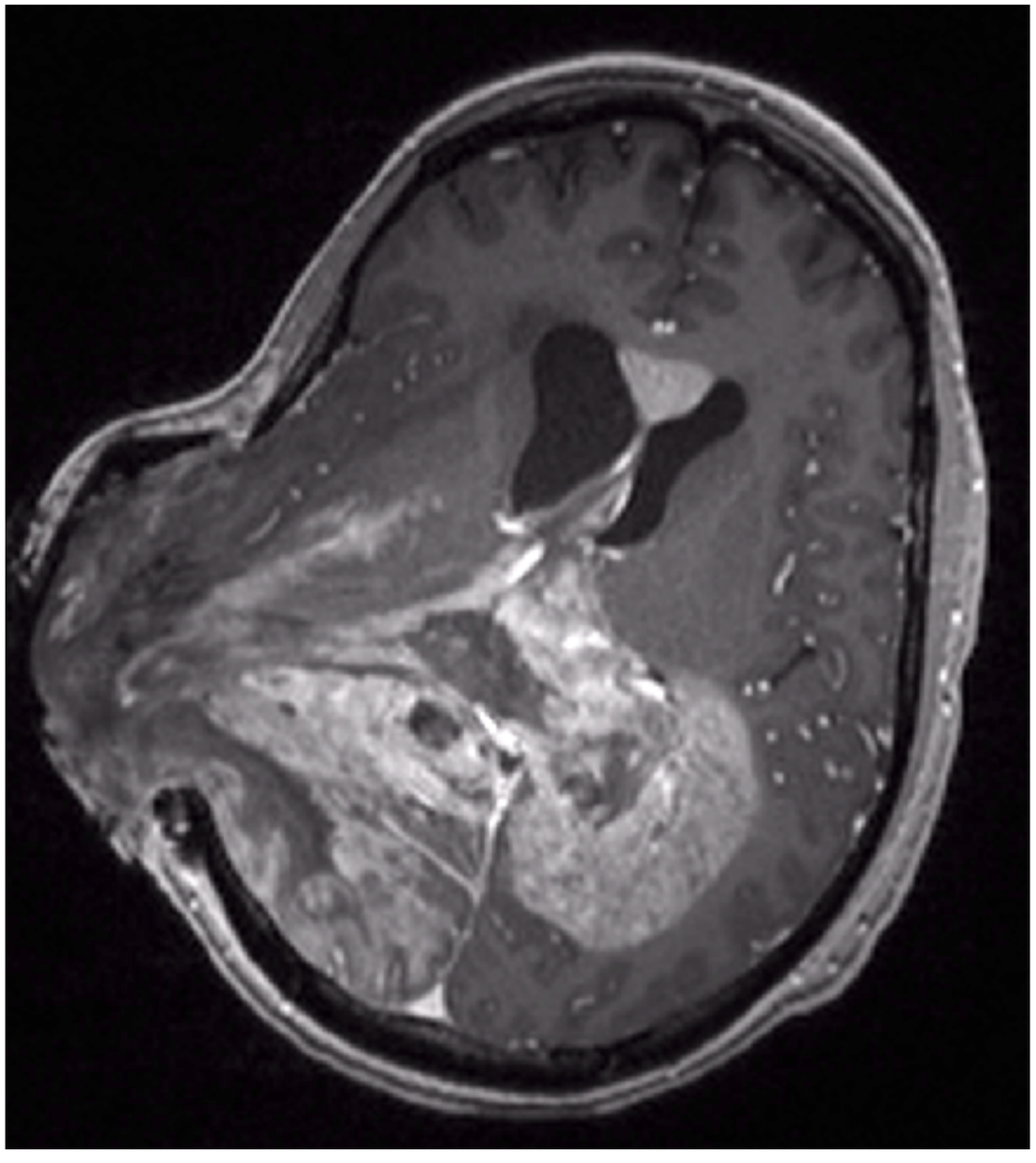
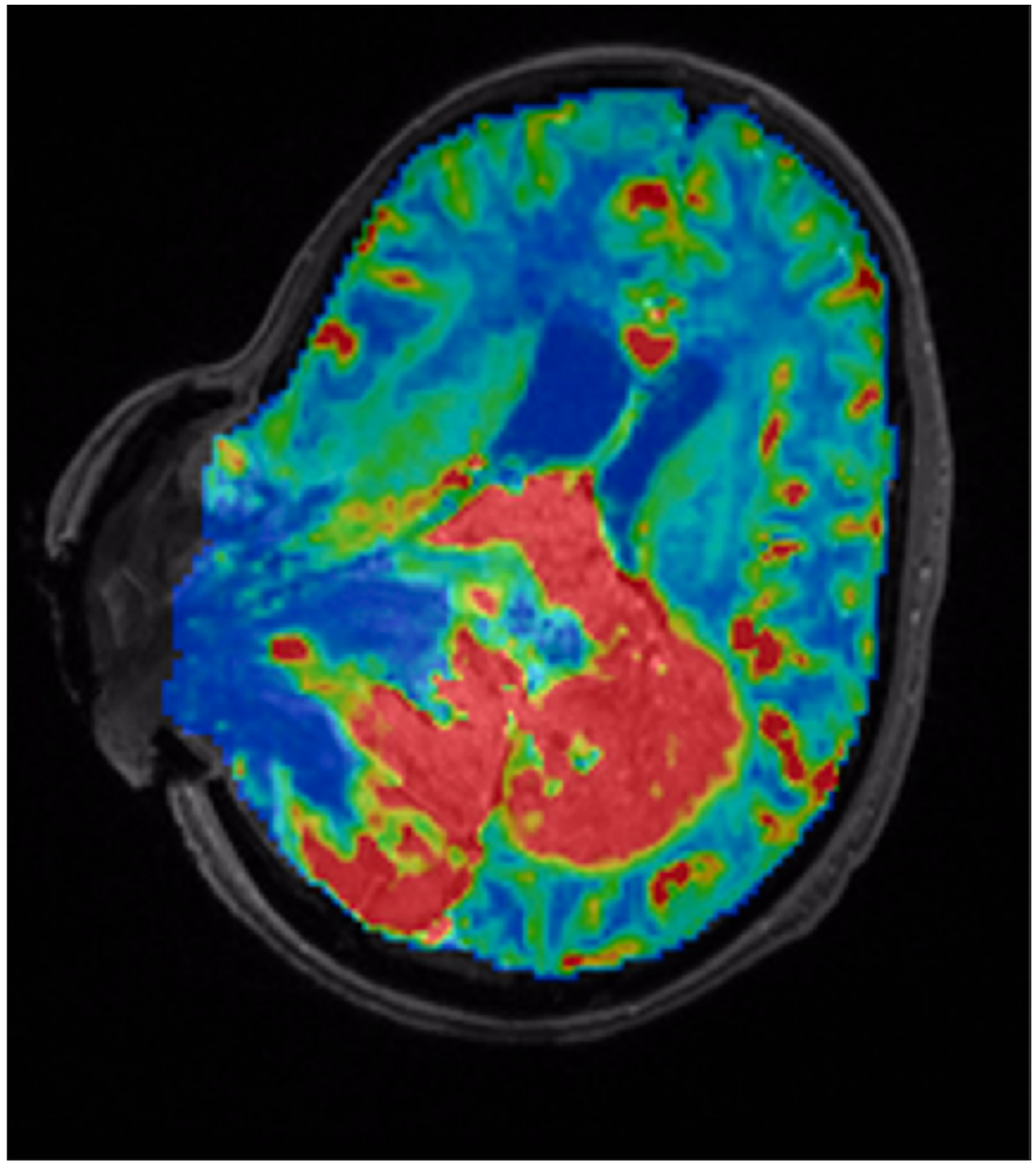
Dynamic Susceptibility Contrast (DSC)-MRI

Post-Contrast T1w



rCBV



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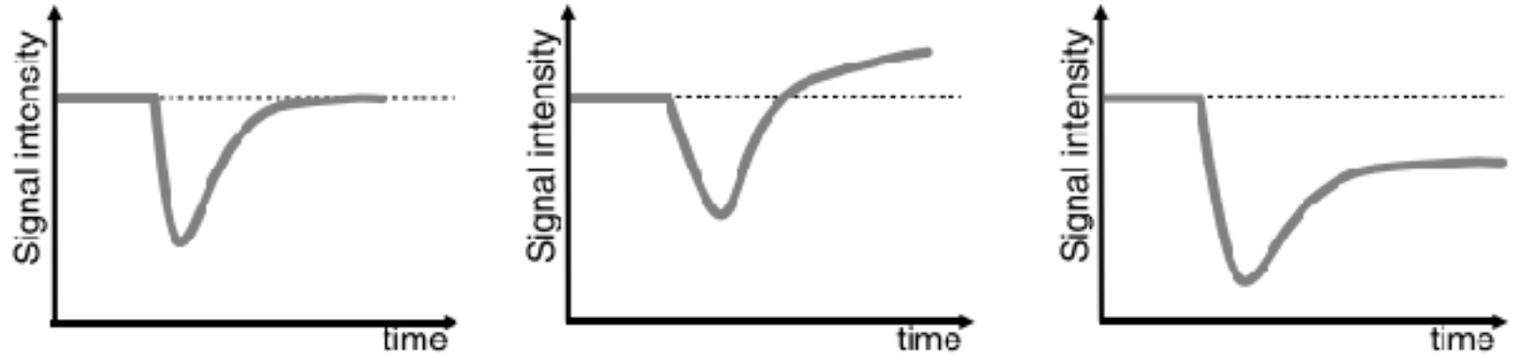
Contrast Agent Extravasation - Leakage Correction

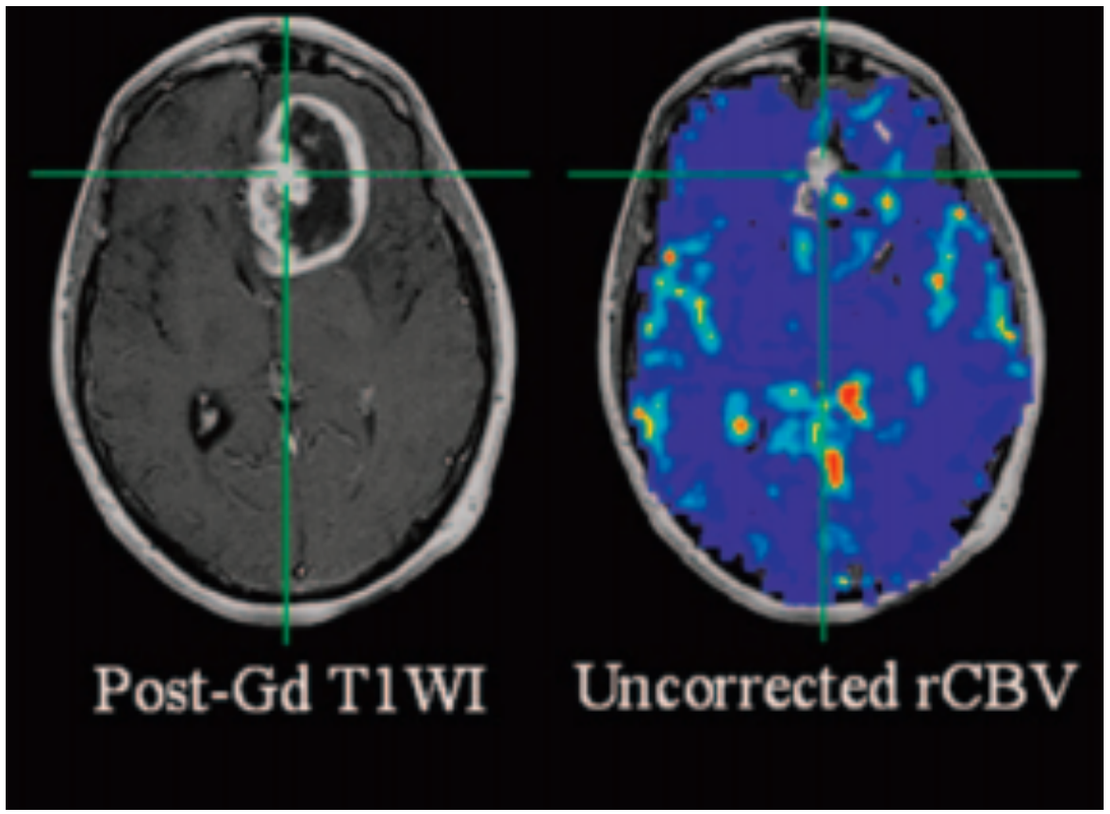
- DSC assumes that contrast agent stays in the blood vasculature
- If it doesn't (e.g. Brain Tumors), the result is over or under/over estimation of CBV/CBF



Intact BBB (Negligible T_1 effect)

BBB leakage (T_1 effect dominates)

BBB leakage (T_2^* effect dominates)



Calamante, Top Magn Reson Imaging, 2010

Boxerman, AJNR, 2006

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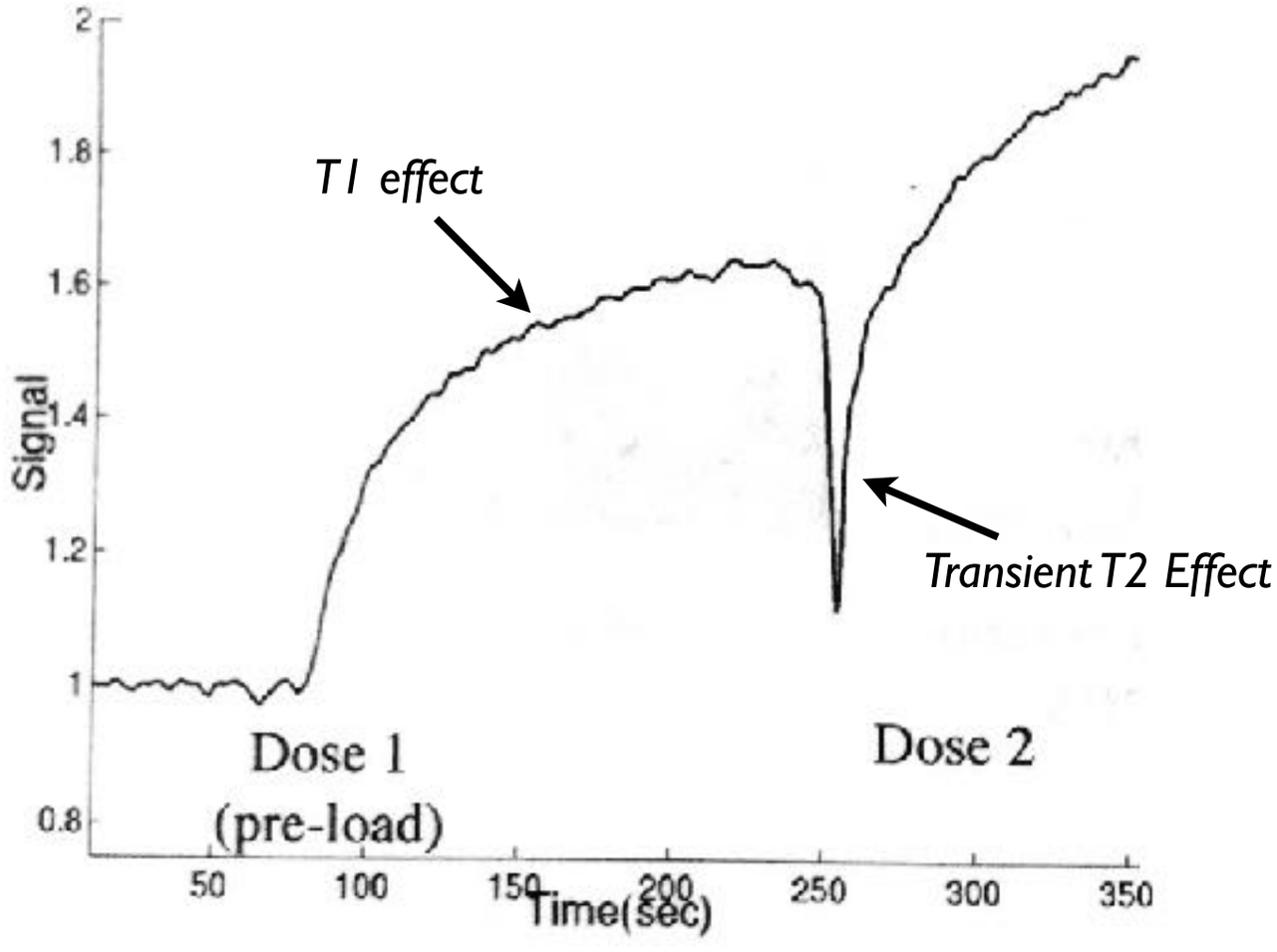
Contrast Agent Extravasation - Leakage Correction

- There are two main ways to deal with this (now the "standard" practice in tumors):
  - Deliver a "pre-load" of contrast agent
    - *Lowers concentration gradient between intravascular and extracellular space*



Courtesy of Kathleen Schmainda, Medical College of Wisconsin

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Contrast Agent Extravasation - Leakage Correction

- There are two main ways to deal with this (now the "standard" practice in tumors):
  - Deliver a "pre-load" of contrast agent
    - *Lowers concentration gradient between intravascular and extracellular space*
  - Post-processing correction of the T1 or T2* (leakage) effect

Boxerman, AJNR, 2006

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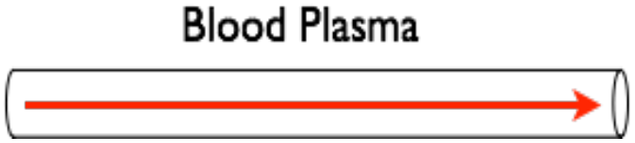
NEW Post-Hoc Leakage Correction Theory (Bidirectional)

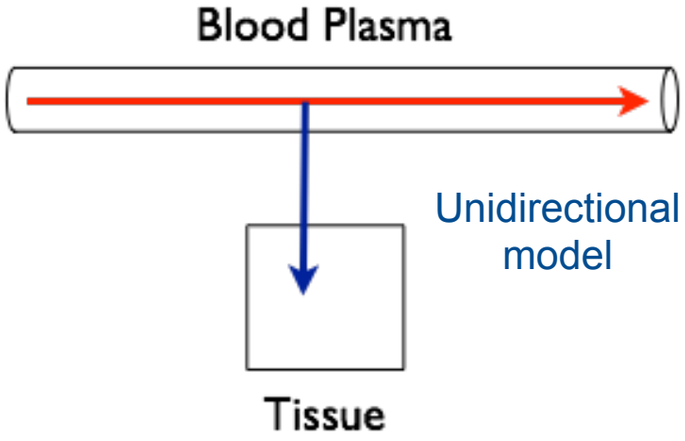
Leu et al., AJNR 2016; JMRI 2016; AJNR 2017

Uncorrected rCBV



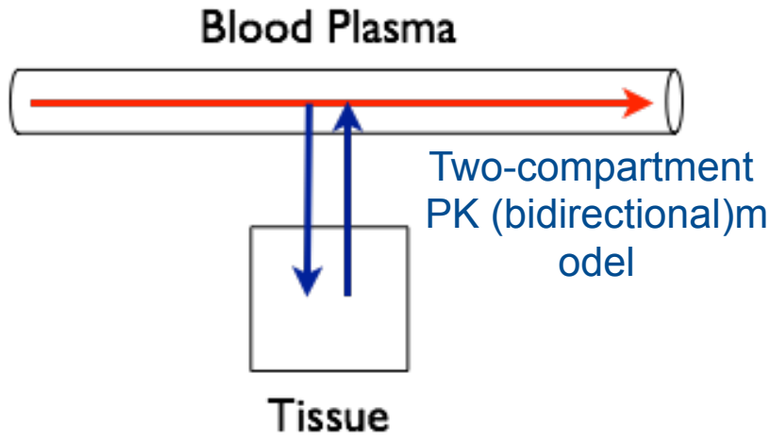
$$\Delta\tilde{R}_2^*(t) = -\frac{1}{TE}\ln\left(\frac{S(t)}{S_0}\right)$$

Current Leakage Correction Model (Unidirectional)



$$\Delta\bar{R}_2^*(t) = K_1 \cdot \Delta\bar{R}_2^*(t) - K_2 \int_0^t \bar{R}_2^*(\tau)d\tau$$

NEW Leakage Correction Model (Bidirectional)



$$\Delta\hat{R}_2^*(t) = K_1 \cdot \Delta\bar{R}_2^*(t) + (K_2 + k_{ep} \cdot K_1)\int_0^{t_k} \Delta\bar{R}_2^*(\tau)d\tau - k_{ep} \cdot \int_0^{t_k} \Delta\hat{R}_2^*(\tau)\,d\tau$$

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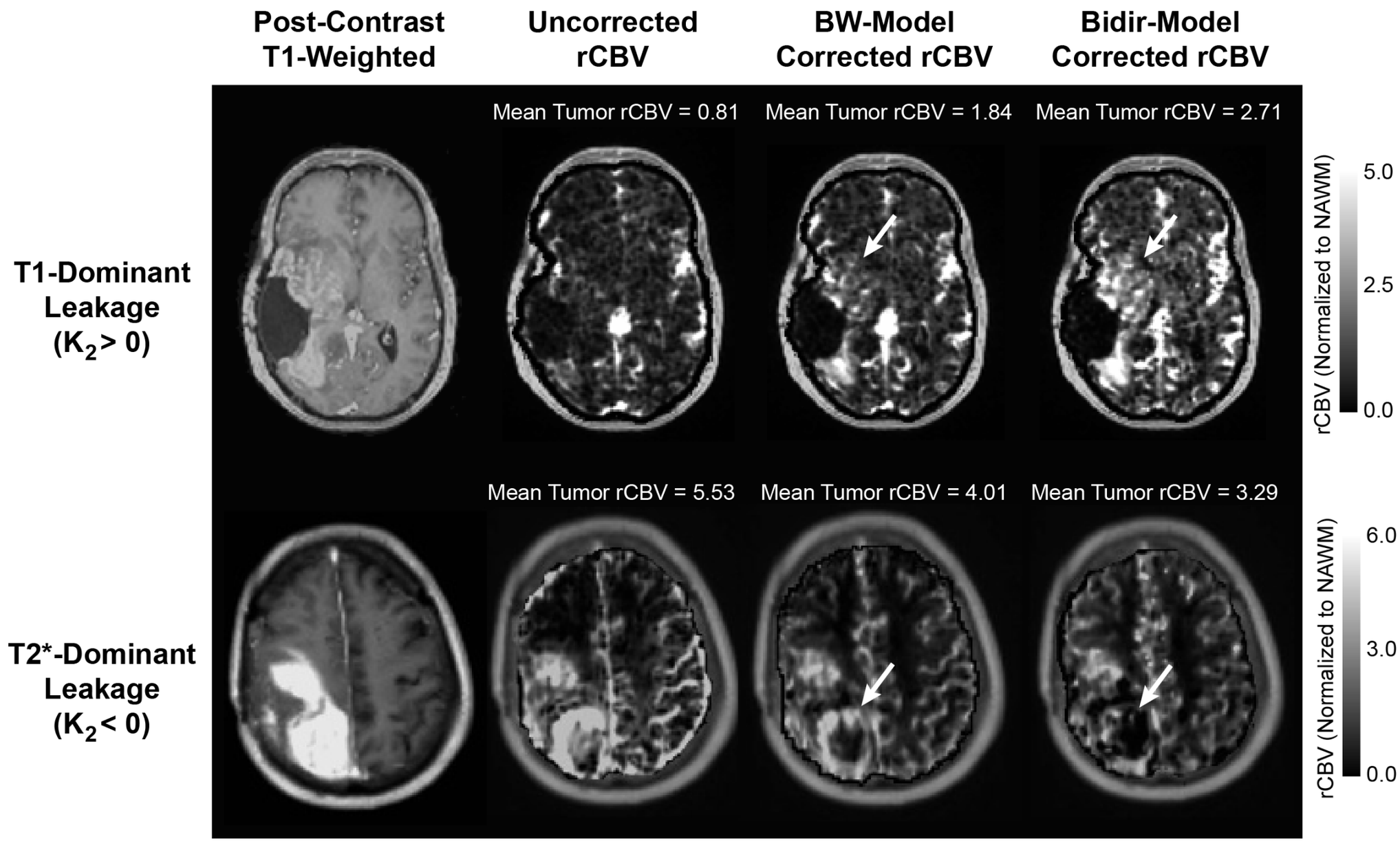
NEW Post-Hoc Leakage Correction Theory (Bidirectional)

Leu et al., AJNR 2016; JMRI 2016; AJNR 2017



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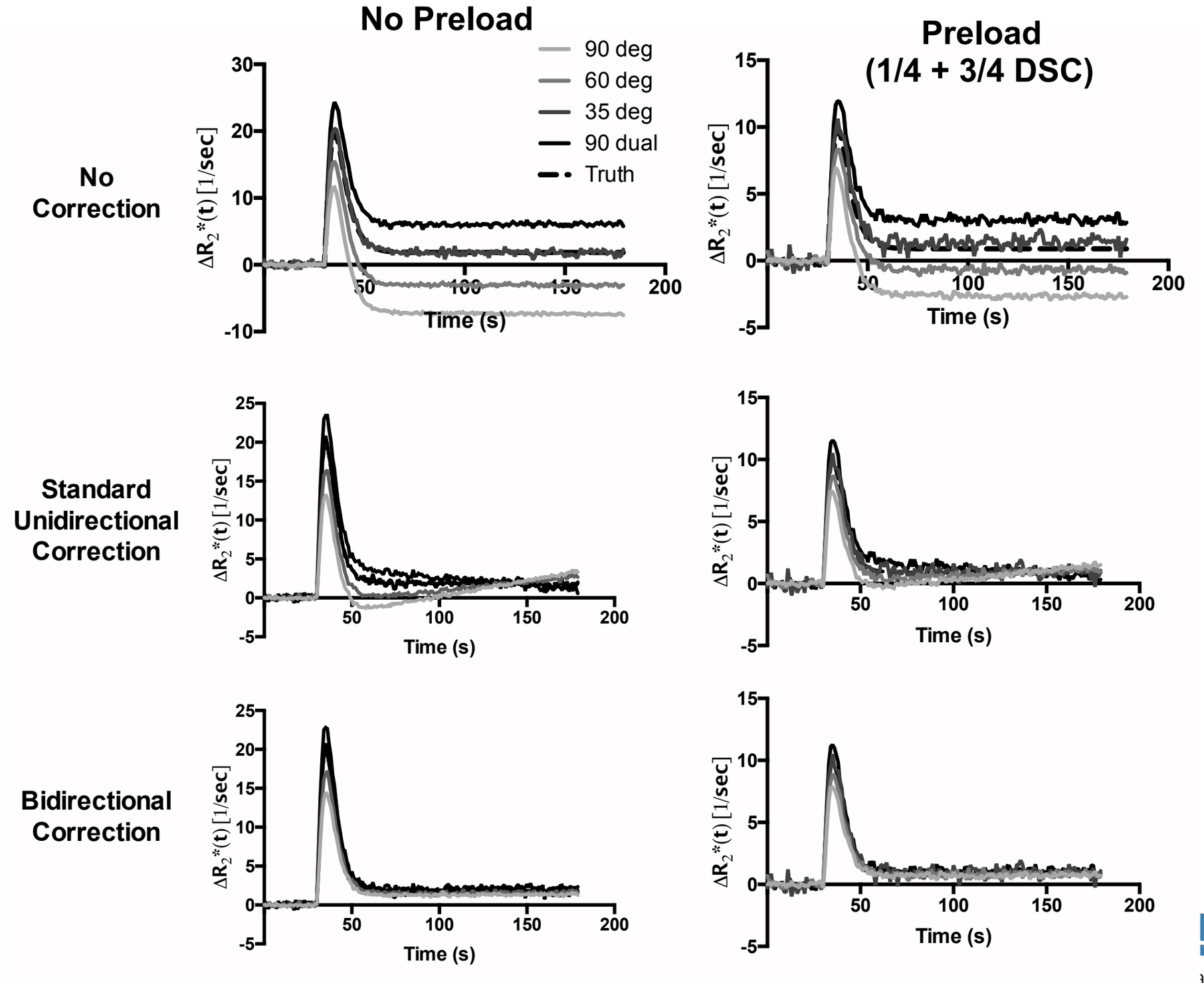
NEW Post-Hoc Leakage Correction Theory (Bidirectional)

Leu et al., AJNR 2016; JMRI 2016; AJNR 2017



Arterial Spin Labeling (ASL)

- Arterial Spin Labeling (ASL) is a type of *perfusion MRI* that *does not* utilize exogenous contrast agents
- Perfusion = delivery of nutrients/oxygen to tissues through blood flow
  - Volume of blood flowing through capillary bed within a set volume of tissue in a specified period of time
- Measured in **mL Blood/min/100g Tissue**

- Perfusion indicates the relative condition of the vascular network
- Indirectly reflects the metabolic activity of tissue
- Detects tissue that may be at risk of ischemic insult
- Can be used to reflect brain activity (fMRI)

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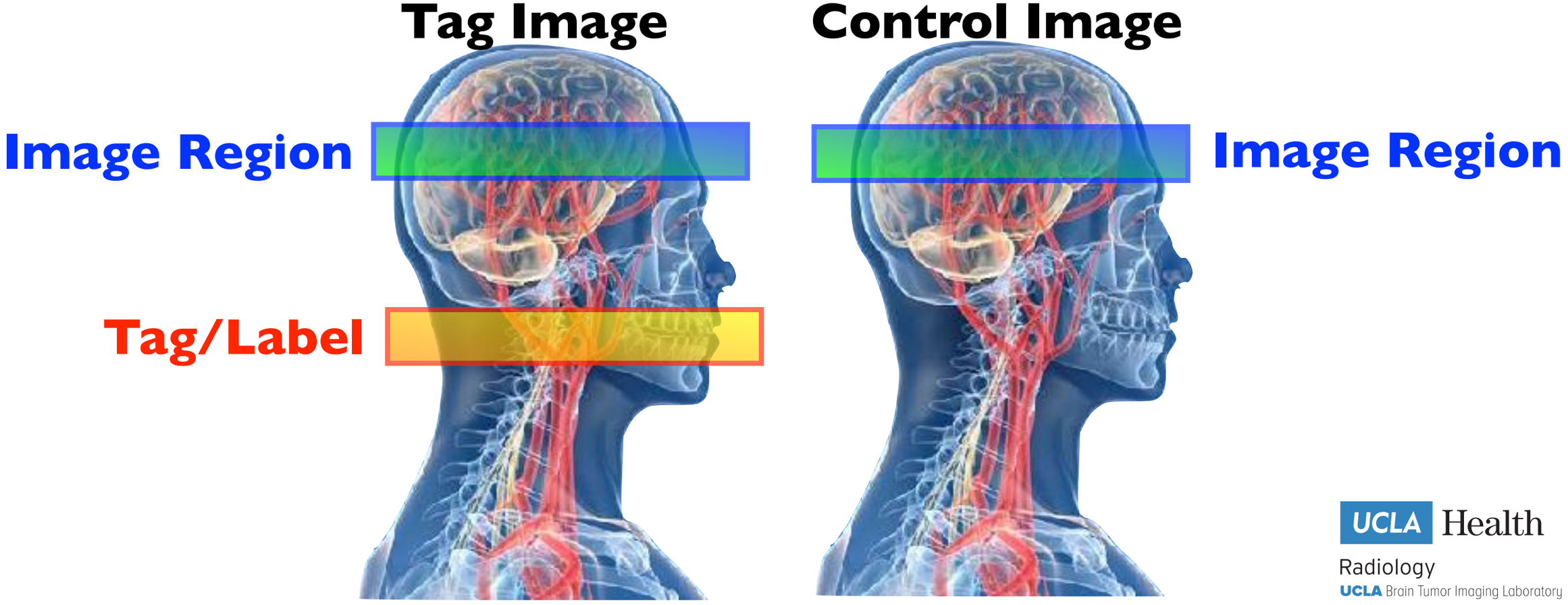
Arterial Spin Labeling (ASL)

- Inflowing blood proton spins are inverted or saturated before entering the image slice (endogenous contrast)
- Imaging is performed after a specified delay, allowing labeled blood to flow into tissue
- "Labeled" image is subtracted from "control" image with no tagging
- Change in magnetization is proportional to CBF



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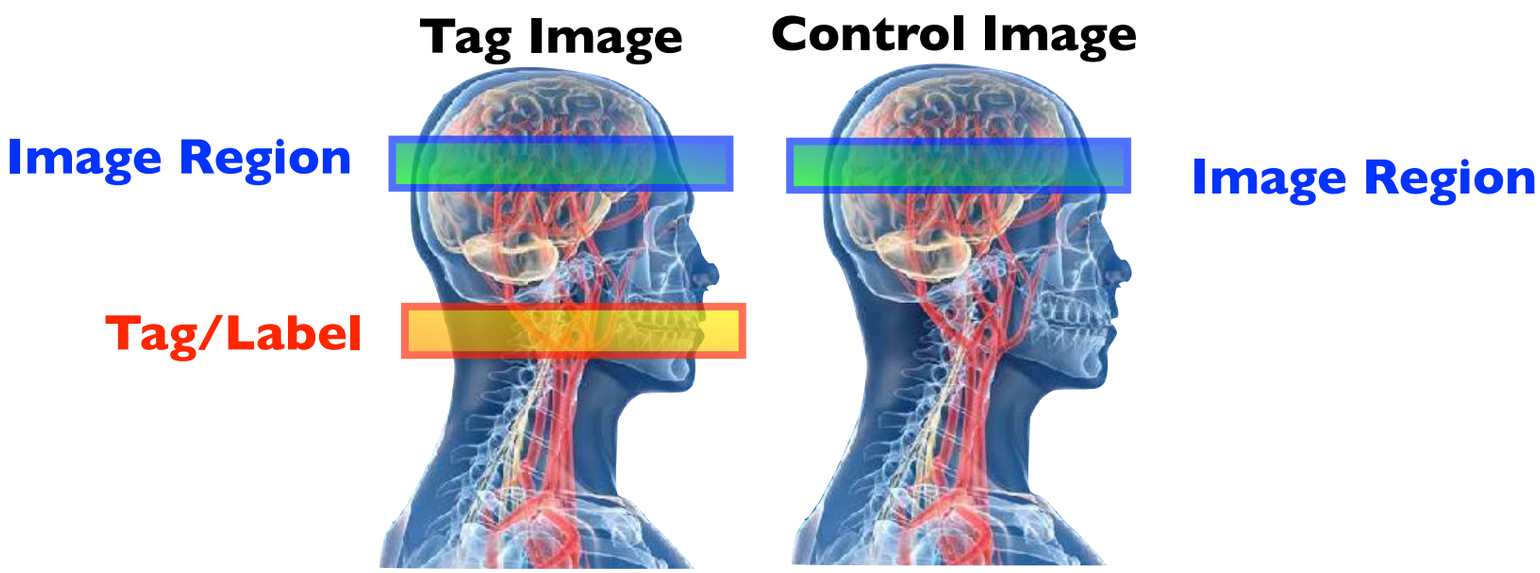
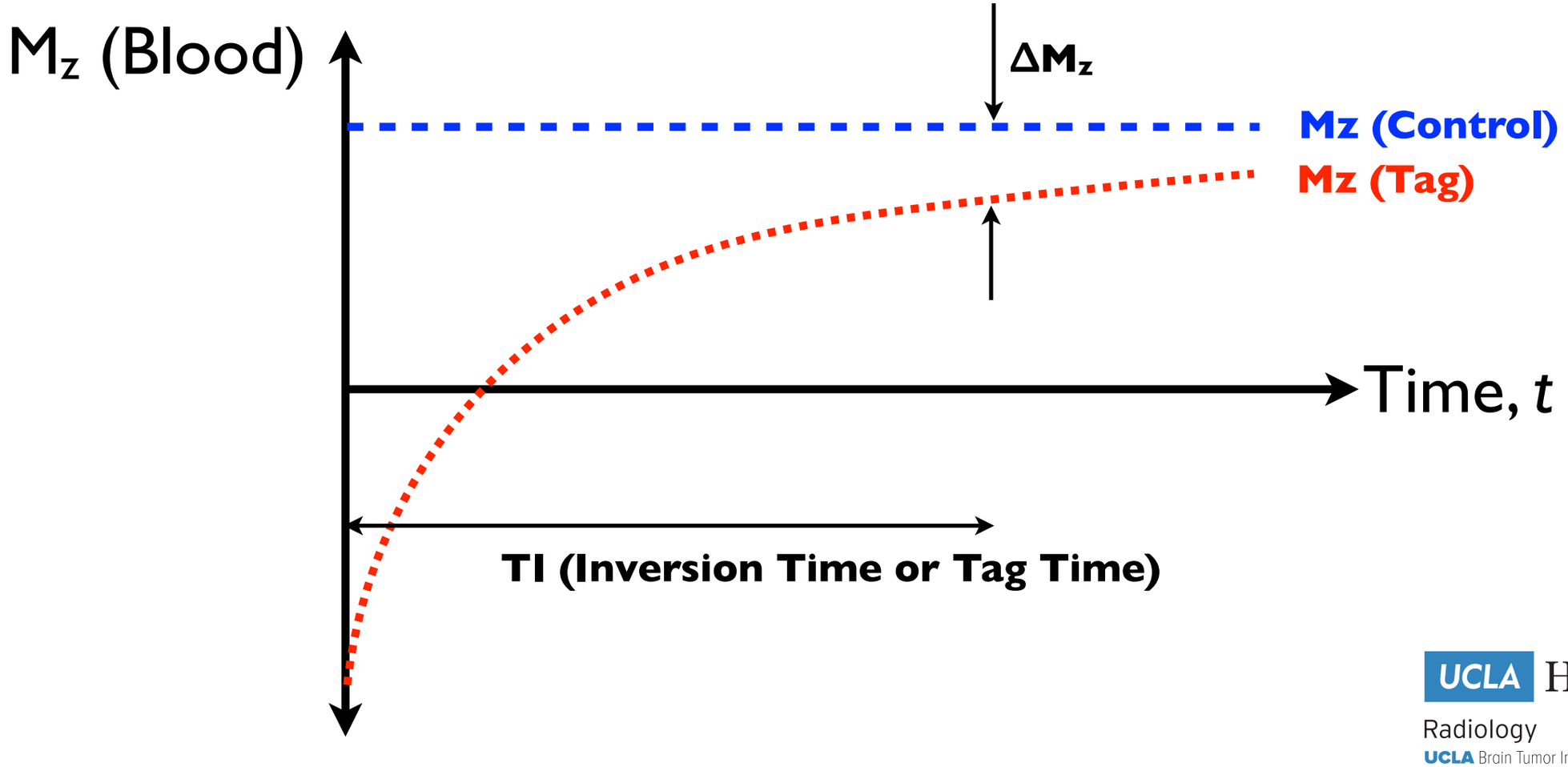
Arterial Spin Labeling (ASL)





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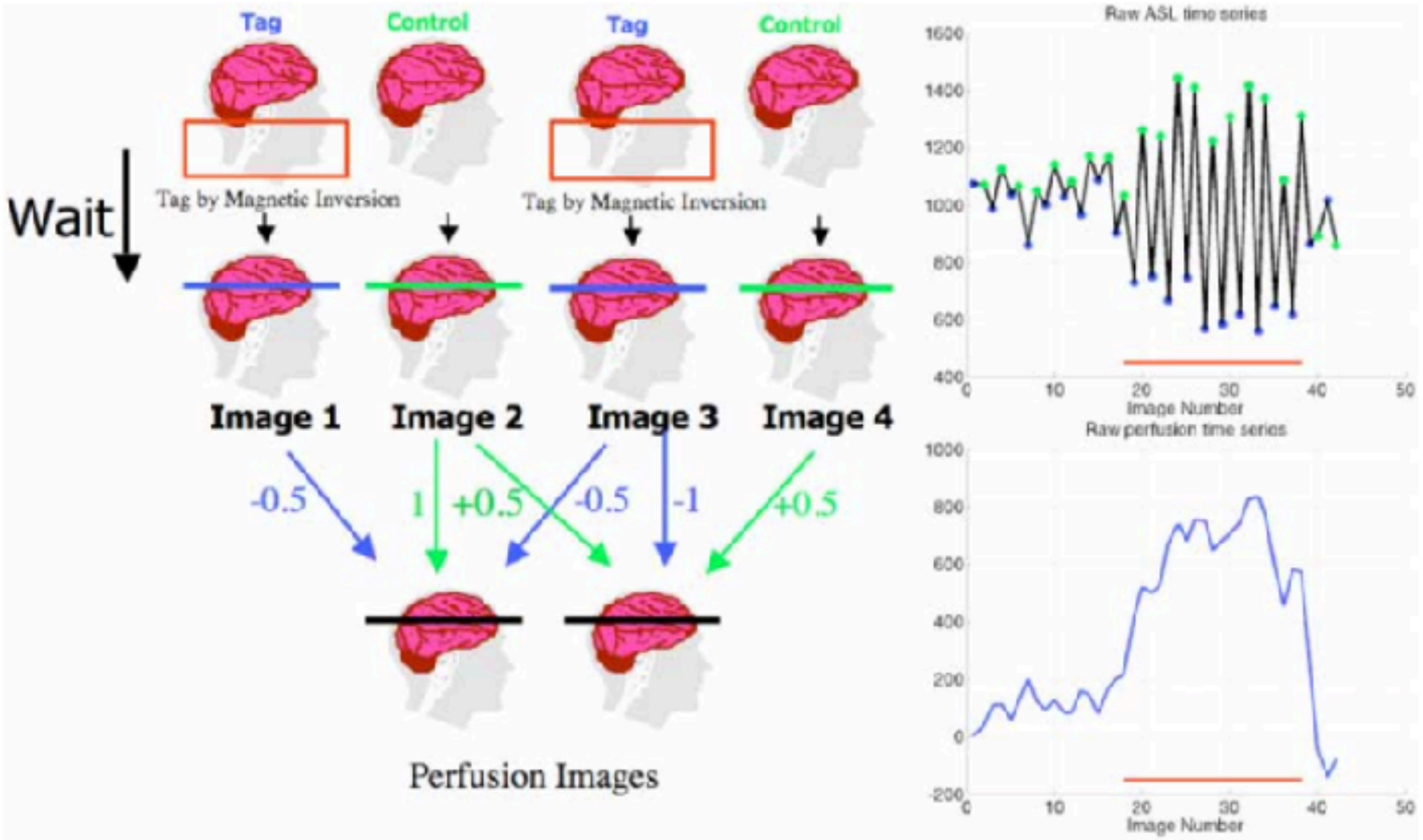
Arterial Spin Labeling (ASL)



Liu and Brown, 2007

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Arterial Spin Labeling (ASL)

- Types of ASL
  - **PASL** = Pulsed ASL
  - **CASL** = Continuous ASL
  - **PCASL** = Pseudocontinuous ASL
  - **VS-ASL** = Velocity Selective ASL

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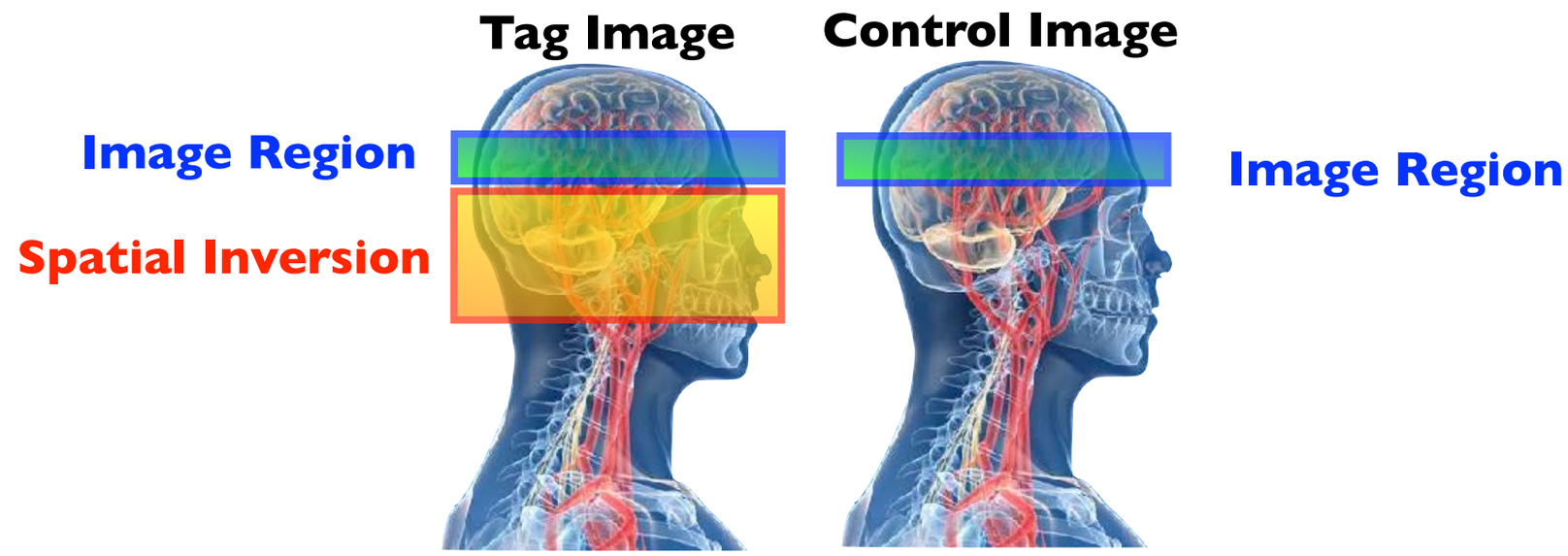
Pulsed ASL (PASL)

- Short (5-20ms) RF pulses are used to saturate or invert a slab of spins (both static and flowing) in the "tagging region", proximal to the imaging slice in the region of interest (Edelman et al., 1994)

- Advantage: High inversion efficiency and little RF use (low SAR)

- Disadvantage: Depends on coverage and uniformity of the transmit RF field to determine geometry of applied tag



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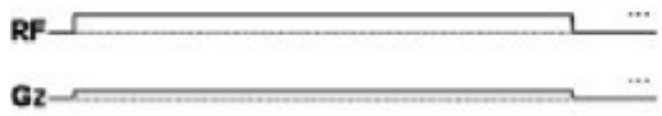
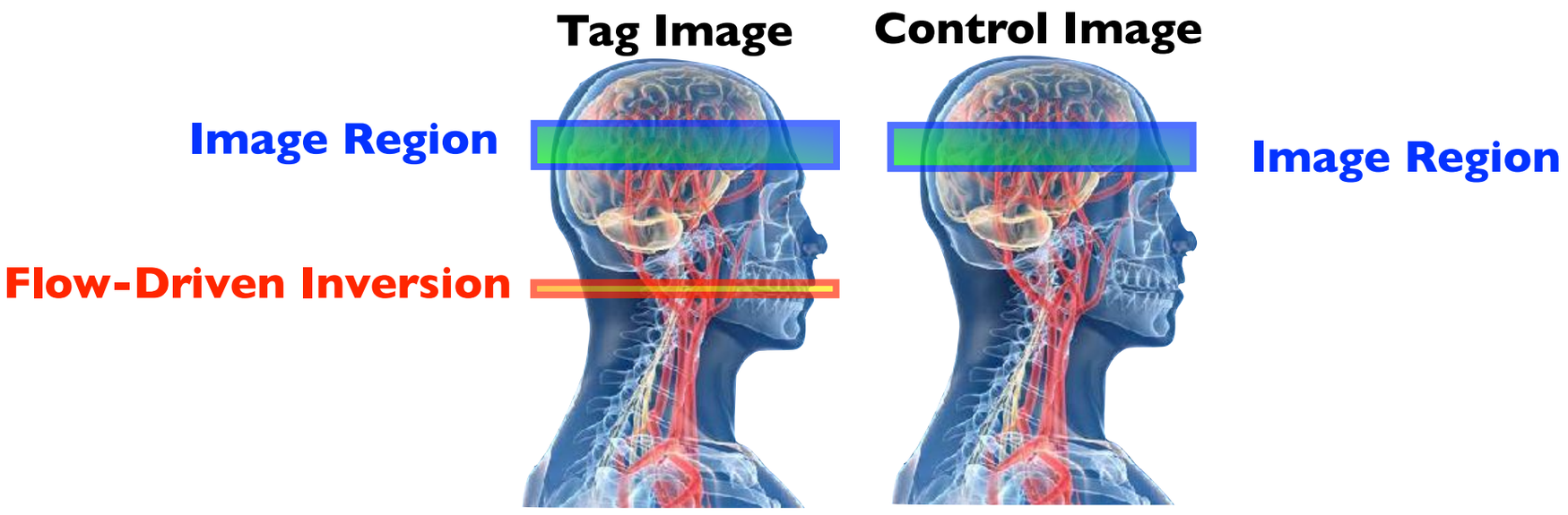
Continuous ASL (CASL)

- Tagging is based on location *and* velocity
- Long (1-3 second) RF pulses are used with a constant gradient field to irradiate a narrow plane of spins with RF energy



- Inflowing spins within a physiological range of velocities are labeled based on **flow-driven adiabatic inversion** (Williams et al., 1992)
- Labeling must be faster than T2 but slower than precession around B_1
- Advantage: Higher overall SNR compared with PASL
- Disadvantage: Larger amount of RF power (higher SAR)



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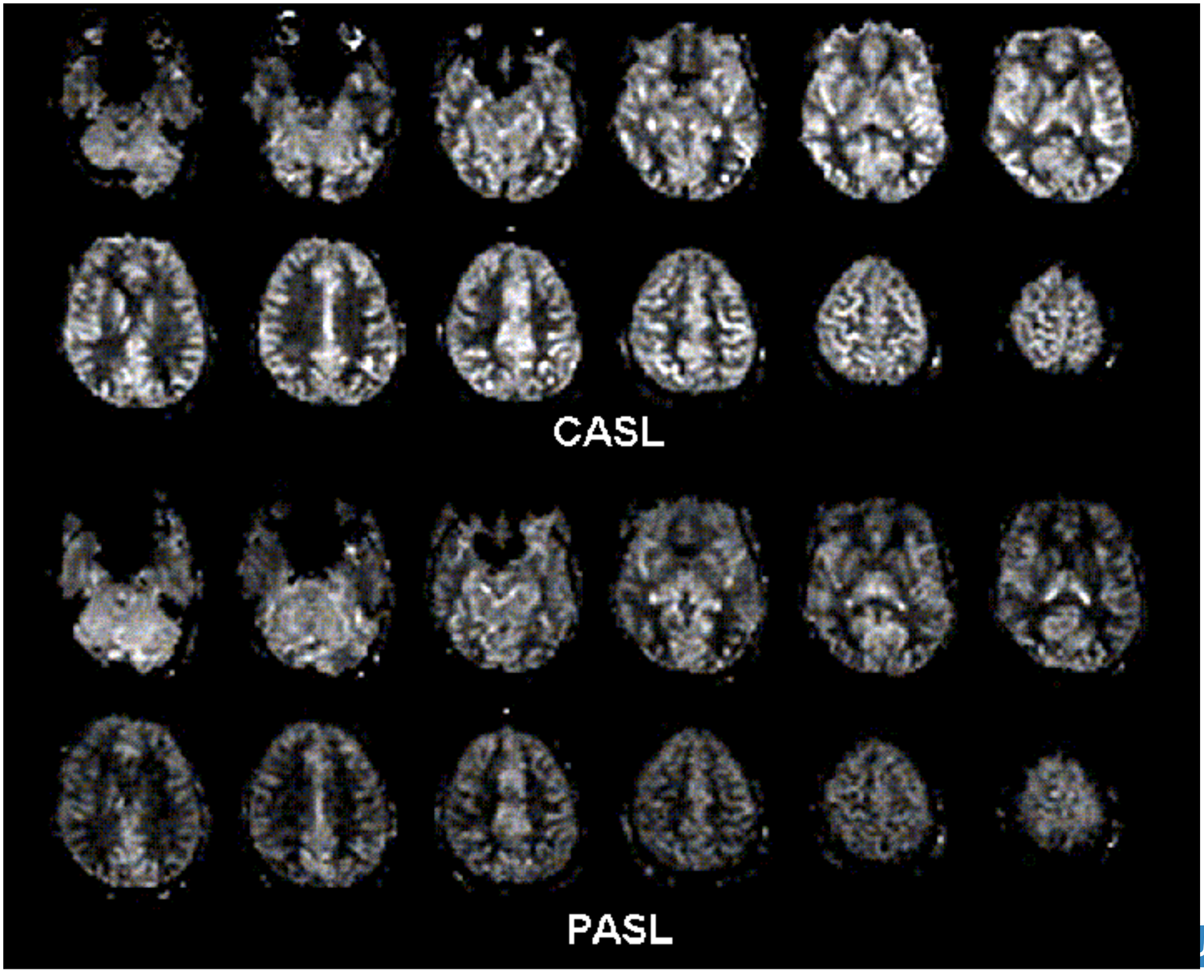
PASL vs. CASL at 3T

- CASL has >40% SNR of PASL at expense of higher SAR and duty cycle



Wang et al., Radiology 2005

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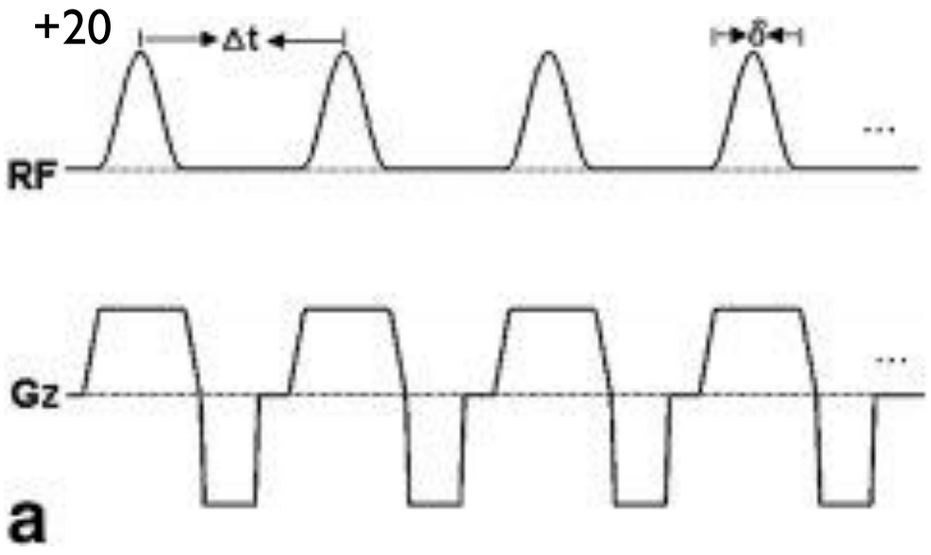
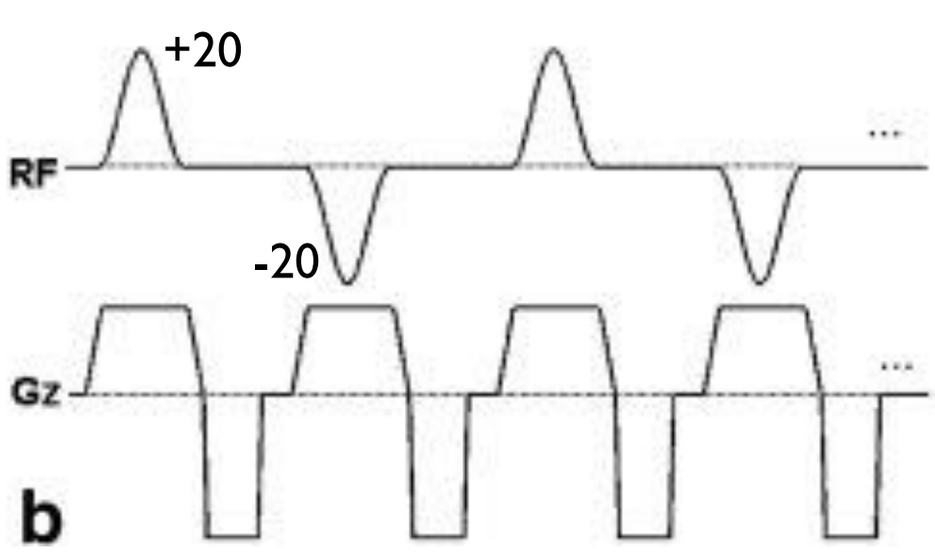
Pseudo-Continuous ASL (pCASL)

- Combination of pulsed and continuous ASL
- Combines advantages of both PASL and CASL
- Uses a long train of very short RF-pulses (~20 deg FA) to label spins in a narrow band
- Current ASL technique most used clinically

Tag Sequence



Control Sequence



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Diffusion MRI

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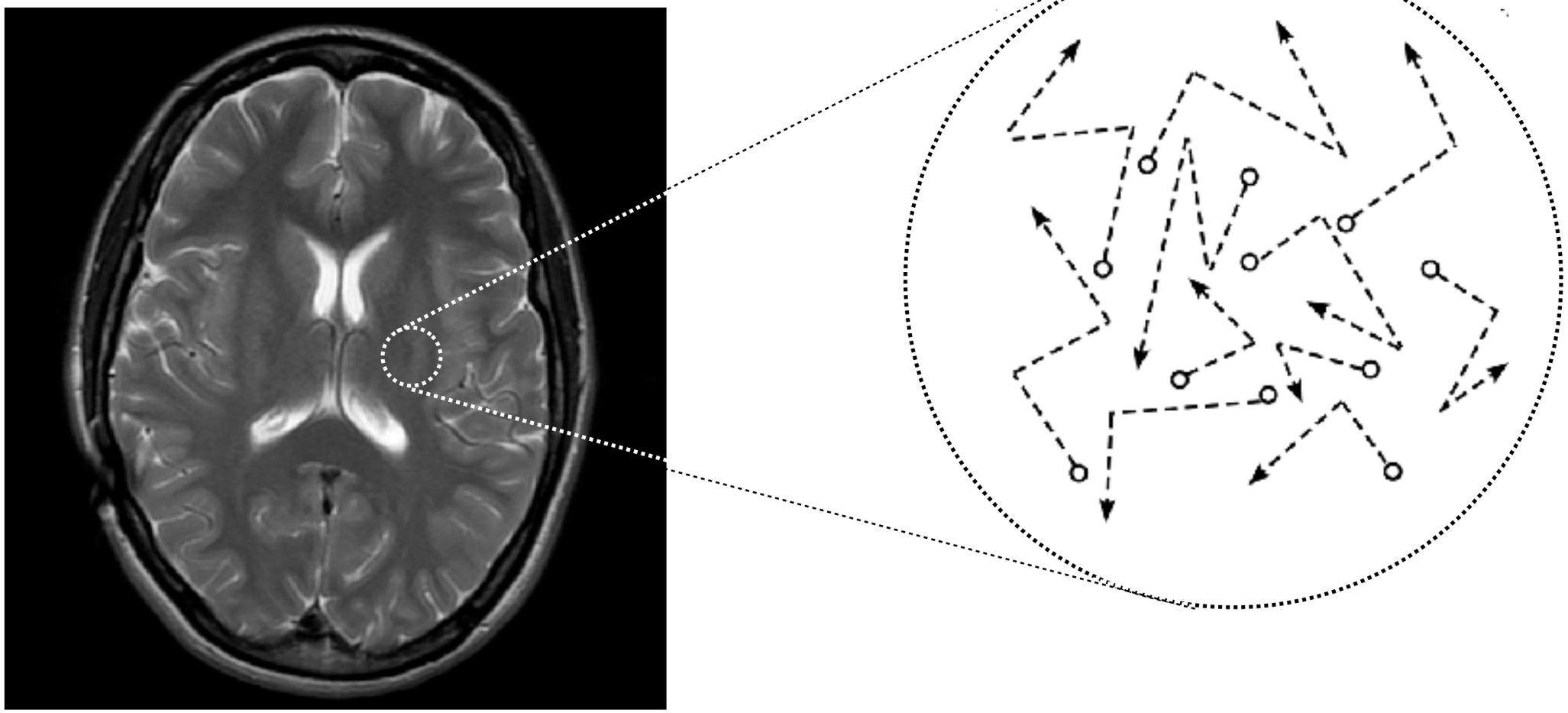
Diffusion Physics

- Water in the body is always in <u>random</u> motion due to <u>thermal agitation</u>



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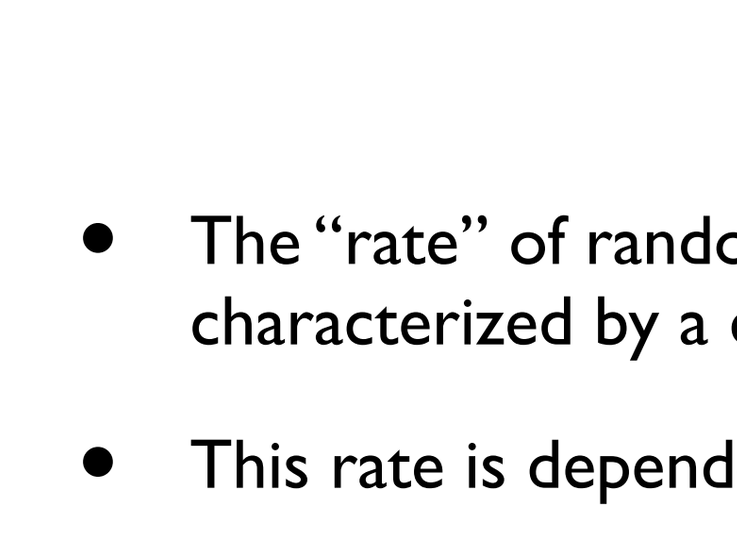
Diffusion Physics

- The "rate" of random <u>translational</u> water motion can be characterized by a diffusion coefficient **D**
- This rate is dependent on <u>Temperature</u> and <u>Viscosity</u>



Diffusion Coefficient
(rate of motion)

Temperature

$$D = \frac{kT}{6\pi\eta R}$$

Viscosity

Size of Molecule

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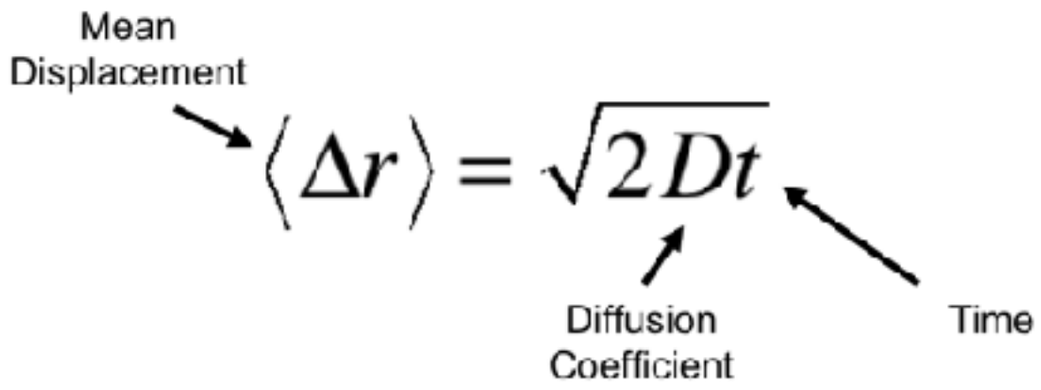
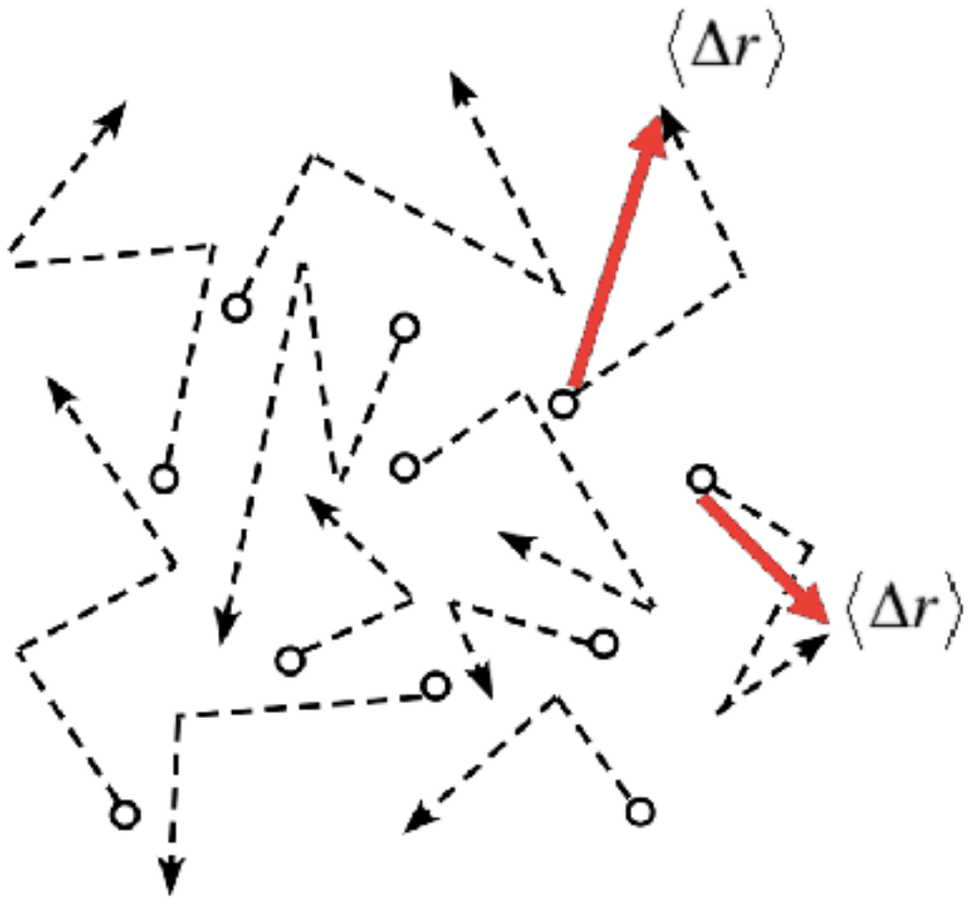
Diffusion Physics

- Mean displacement of water molecules is related to the diffusion coefficient **D** by Einstein's equation:





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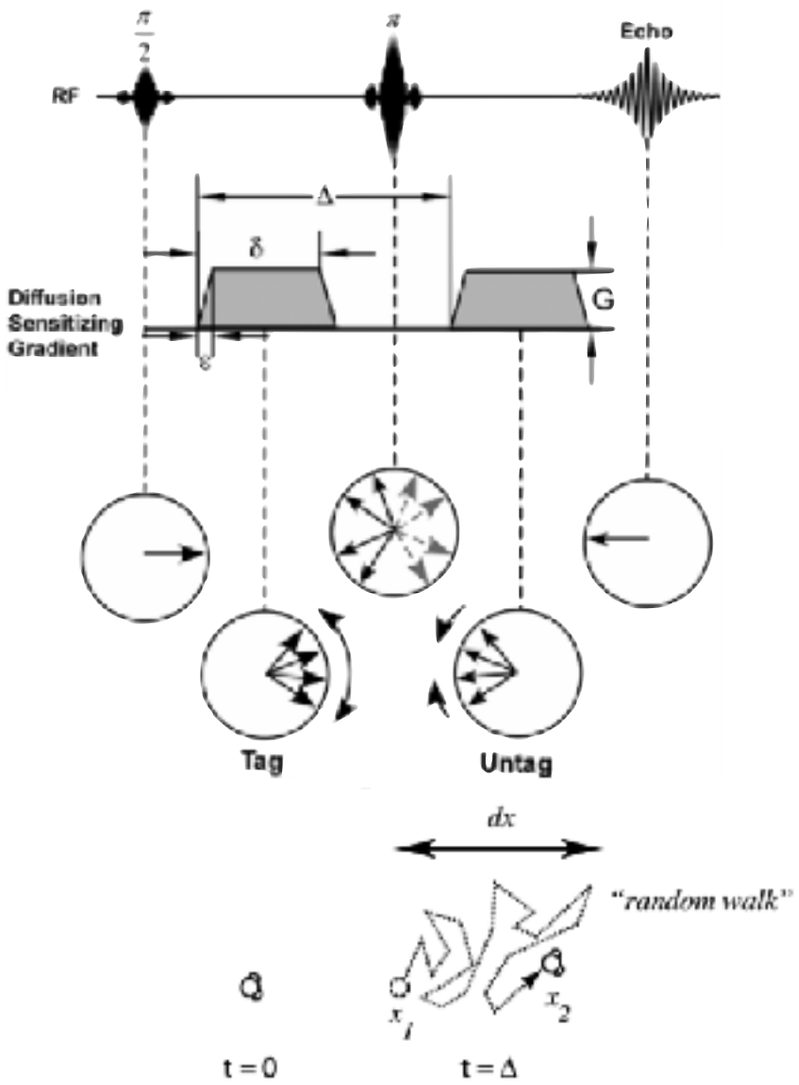
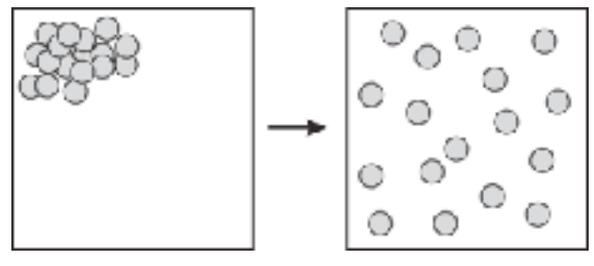
Measuring Displacement with NMR/MRI

- <u>Motion Probing Gradients (MPGs)</u> - Same gradients as imaging gradients
- Pulses to add phase, then subtract phase, from stationary spins
- Spins that have moved between pulses acquire phase





Ellingson *et al.*, *Concepts in MR*, 2008

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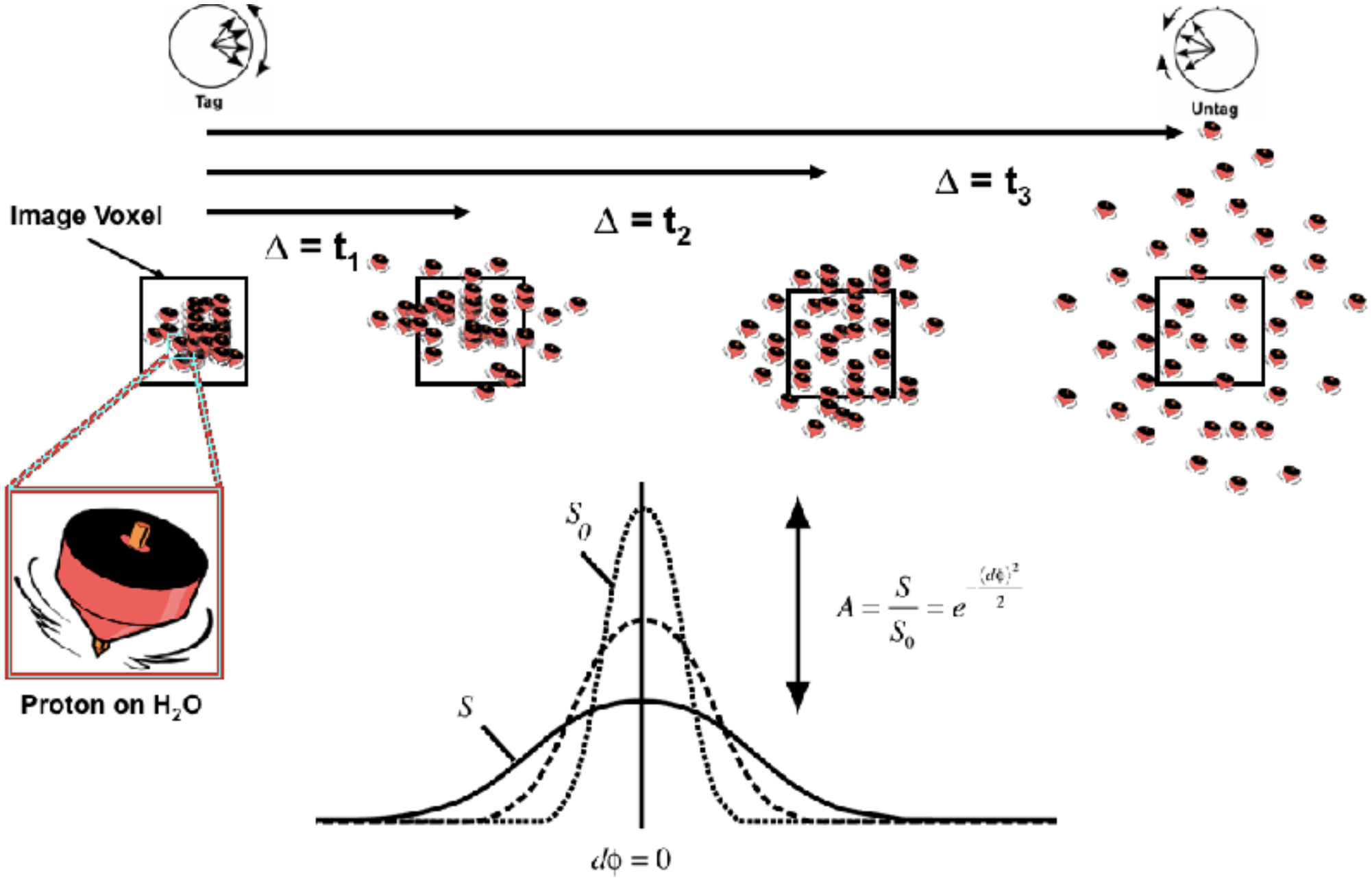
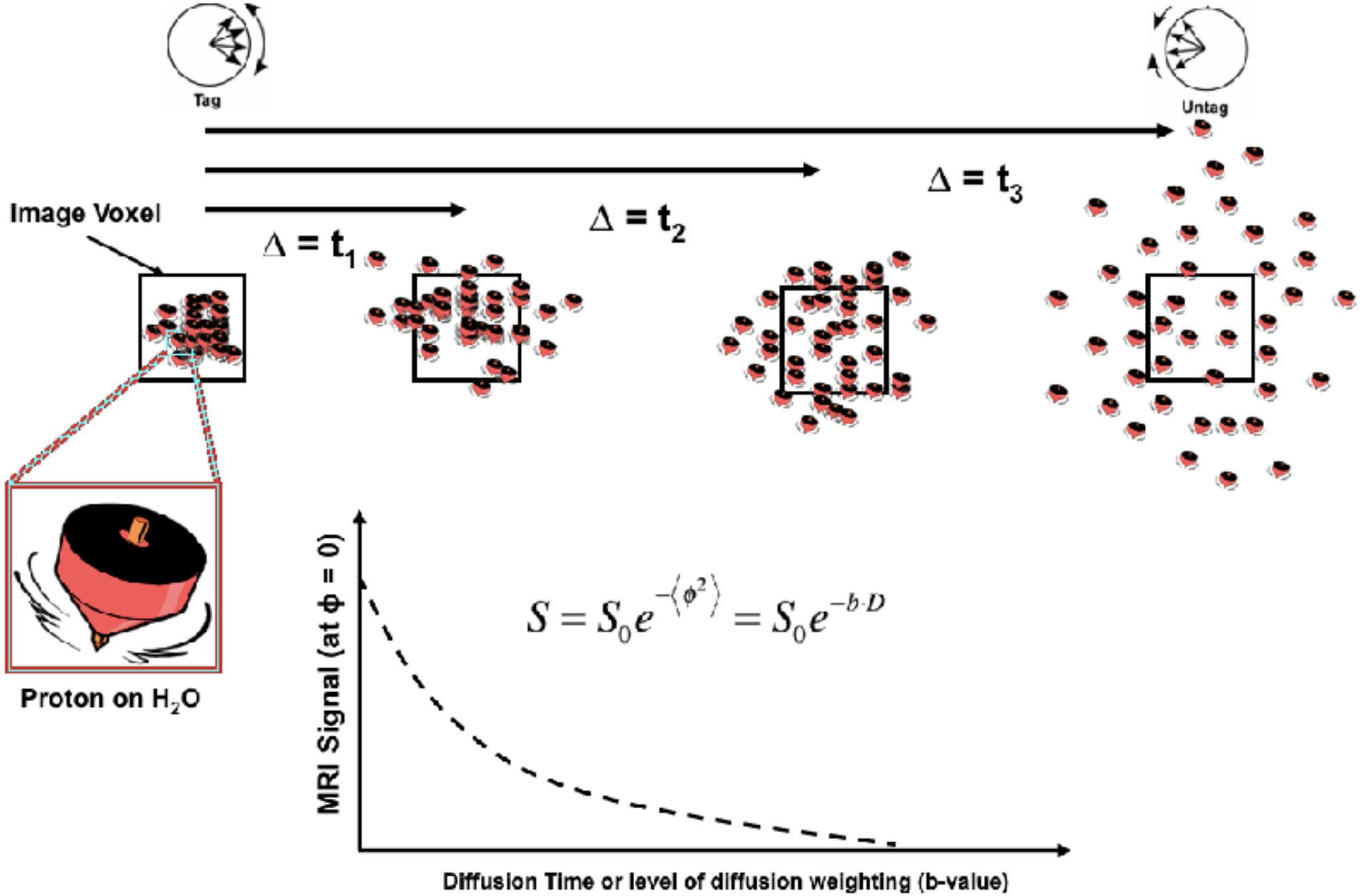
Measuring Displacement with NMR/MRI



Measuring Displacement with NMR/MRI



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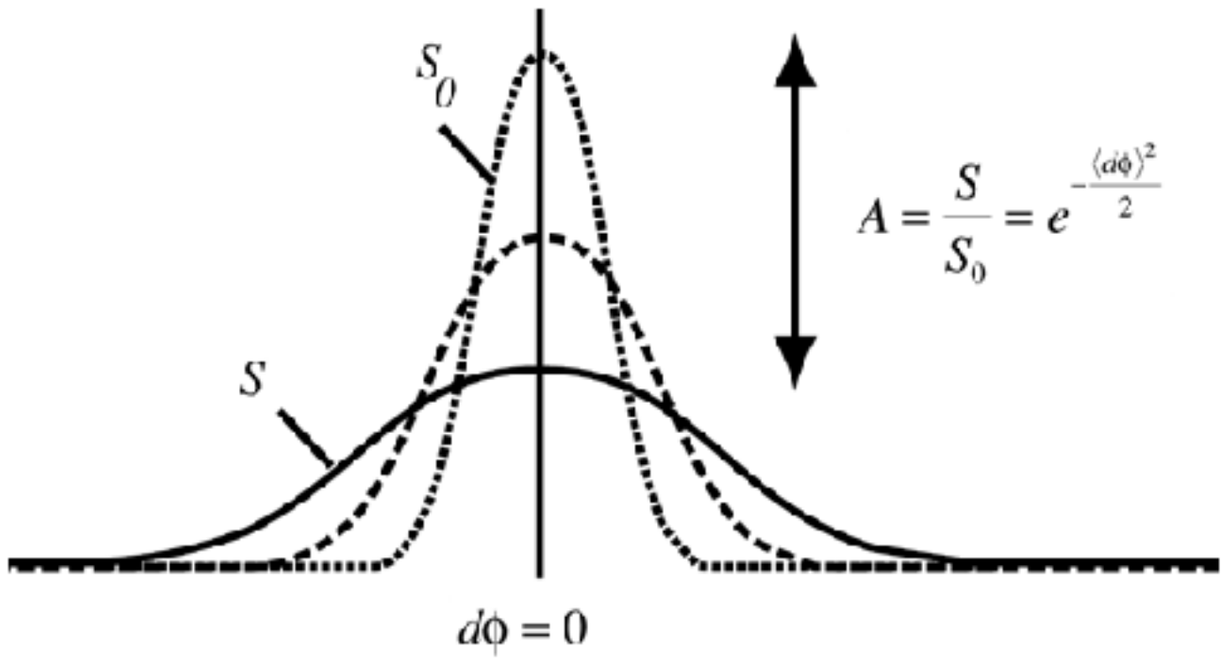
Measuring Displacement with NMR/MRI



Detected DWI Signal

Variability in Phase of "Tagged" H_2O

Level of Diffusion Weighting

$$S = S_0 e^{-\langle \phi^2 \rangle} = S_0 e^{-b \cdot D}$$

MRI Signal w/o Diffusion Sensitivity

Diffusion Coefficient

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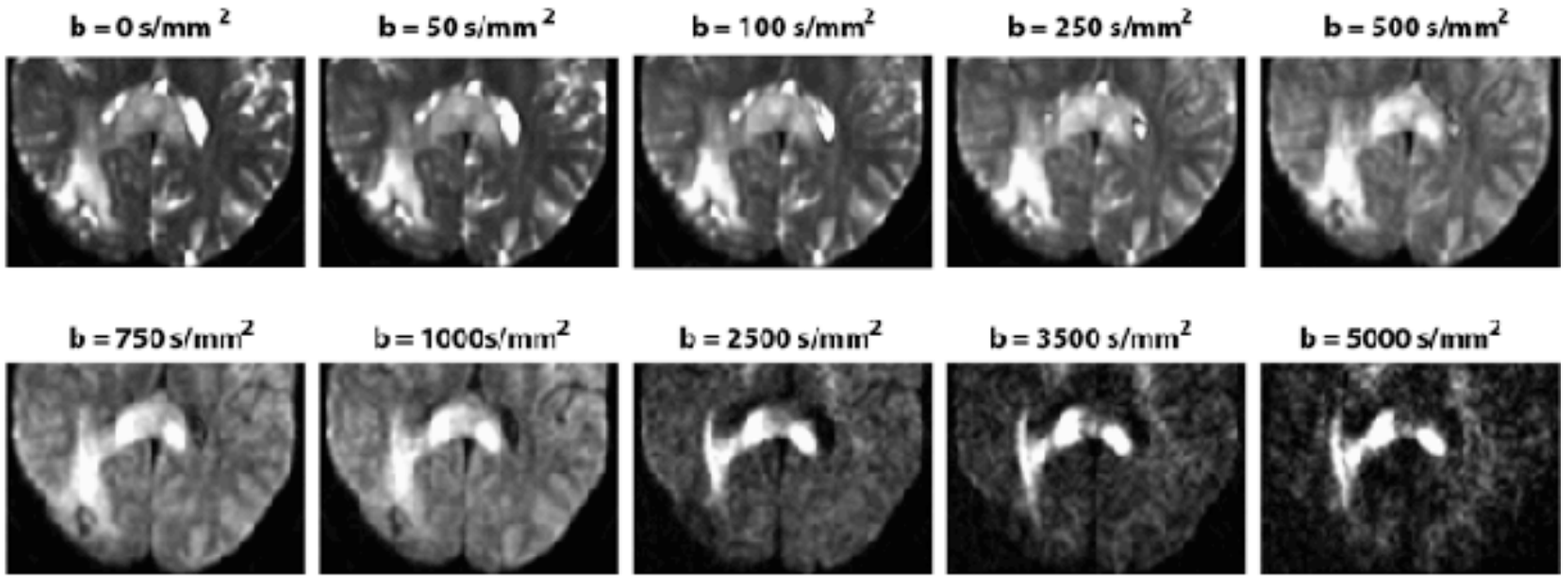
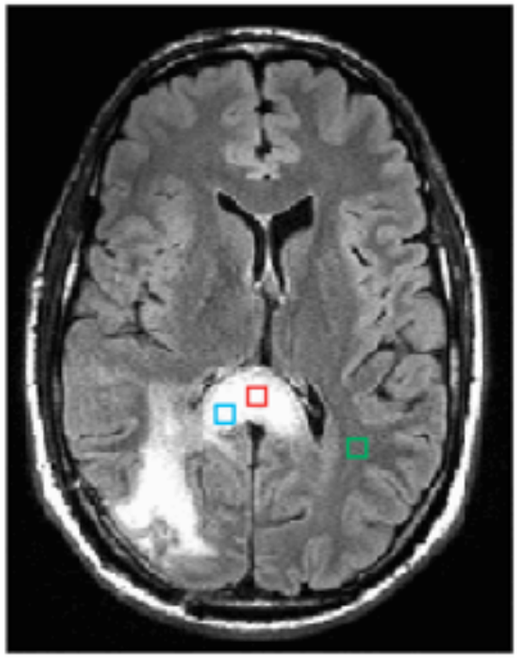
Measuring Displacement with NMR/MRI

- Multiple *b*-values in brain tumors

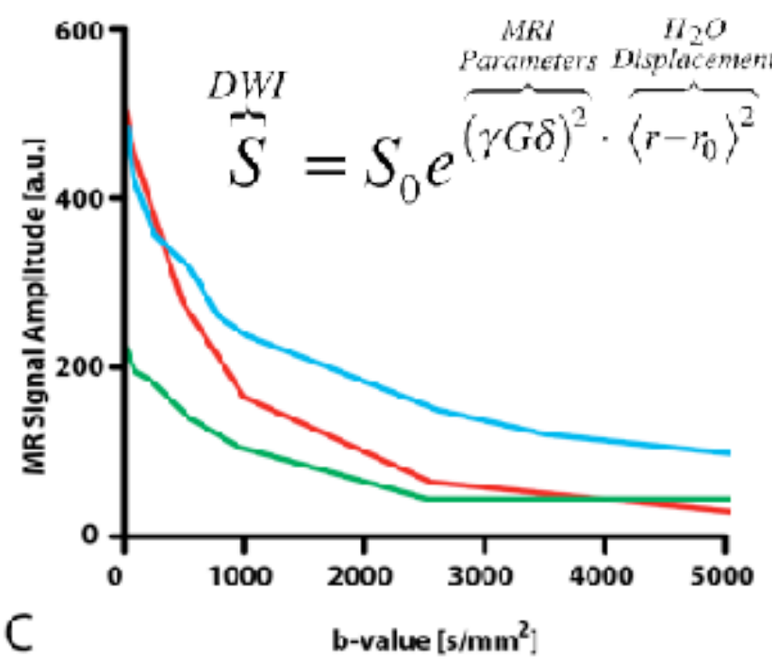
A



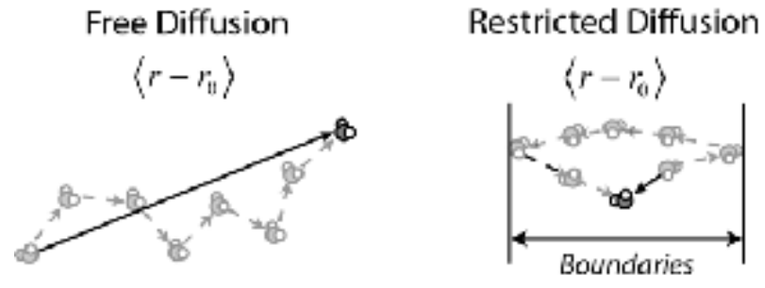
B



C



$$\vec{S}^{DWI} = S_0 e^{\overbrace{(\gamma G\delta)^2}^{MRI\ Parameters} \cdot \overbrace{\langle r - r_0 \rangle^2}^{H_2O\ Displacement}} = S_0 e^{-b \cdot ADC}$$



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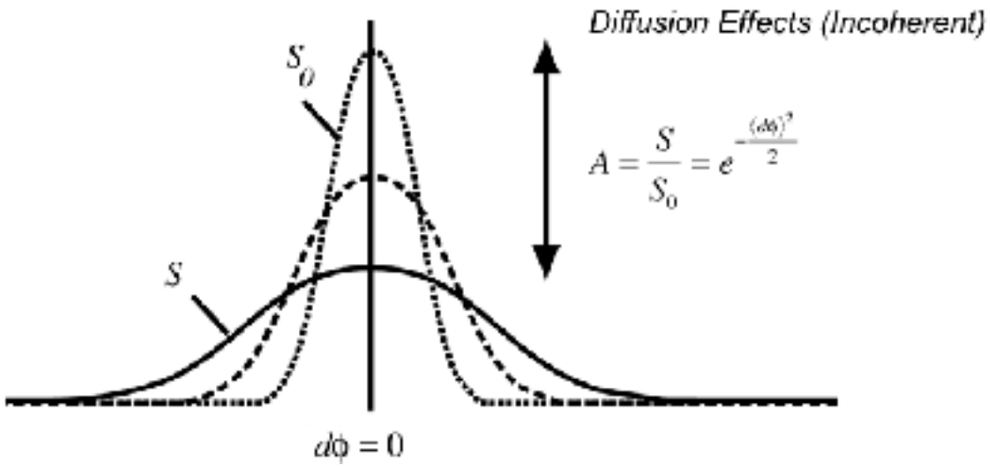
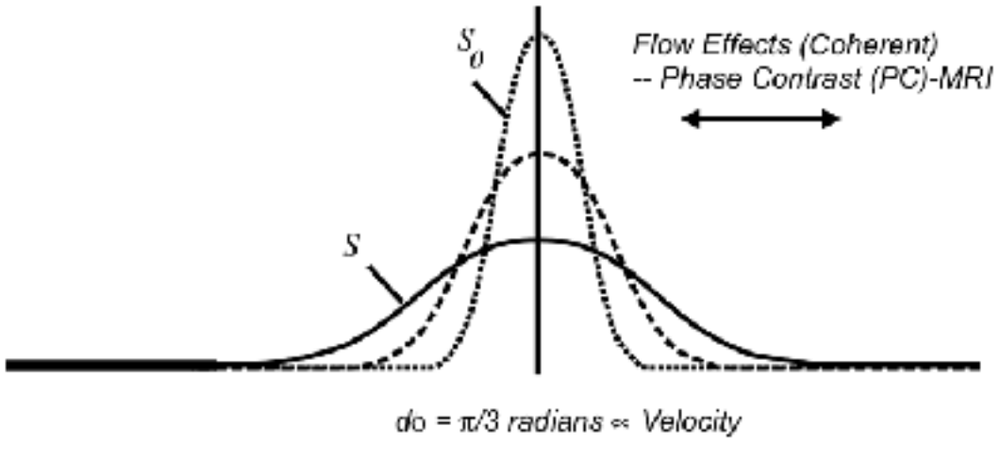
IVIM vs. IVCM

- **Intravoxel Incoherent Motion (IVIM) - *Diffusion***
  - Diffusion motion is <u>random</u> = <u>no net phase</u> but <u>signal attenuation</u>
- **Intravoxel Coherent Motion (IVCM) - *Perfusion/Flow***
  - Perfusion/flow is <u>not random</u> = <u>net phase</u> and <u>no signal attenuation</u>





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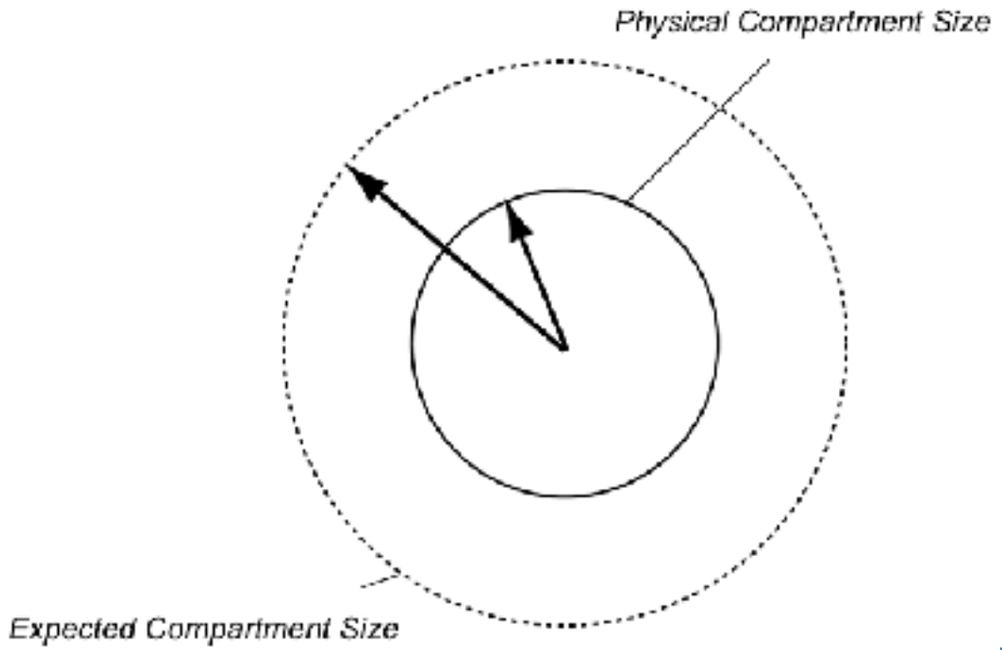
Factors that Affect Diffusion Measurements

- **<u>Size of the Compartments</u>**
  - We often assume *<u>free diffusion</u>* or Gaussian diffusion
  - The timing between tagging and untagging = *<u>diffusion (mixing) time</u>*
  - If this is large (e.g. clinical DWI), then spins will run into boundaries to diffusion (e.g. cells, extracellular matrix proteins, etc.)
  - Diffusion time sets limit to Δr, so we can only observe an <u>Apparent Diffusion Coefficient (ADC)</u>

$$ADC = \frac{\Delta r^2}{2t}$$



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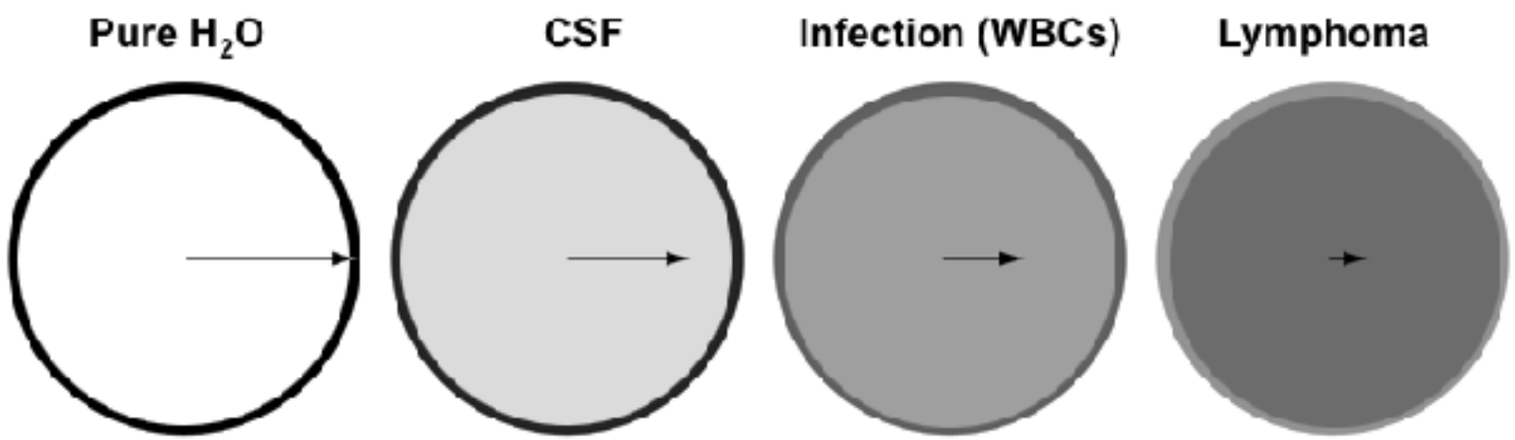
Factors that Affect Diffusion Measurements

- **<u>Viscosity</u>**
  - Higher viscosity tissues have lower ADC



Diffusion Coefficient
(rate of motion)

Temperature

$$D = \frac{kT}{6\pi\eta R}$$

Viscosity

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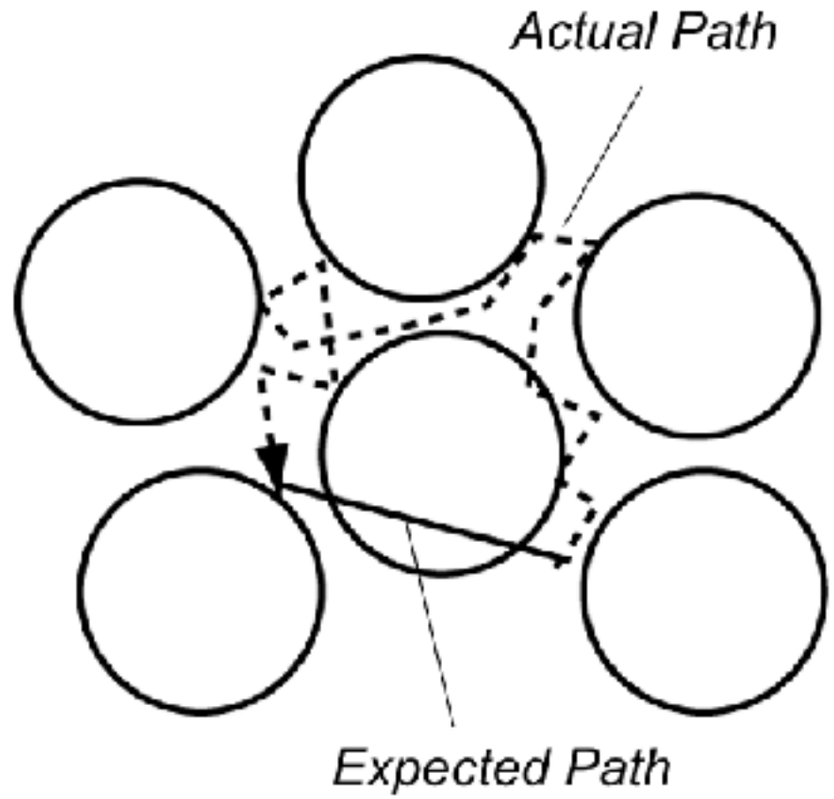
Factors that Affect Diffusion Measurements

- **<u>Tortuosity of the Environment</u>**
  - More tortuous paths *<u>look like slow diffusion</u>*

$$ADC = \frac{D}{\lambda^2} = \frac{D}{\left(\frac{L_{Path}}{L_{Expected}}\right)^2}$$

Tortuosity



Factors that Affect Diffusion Measurements

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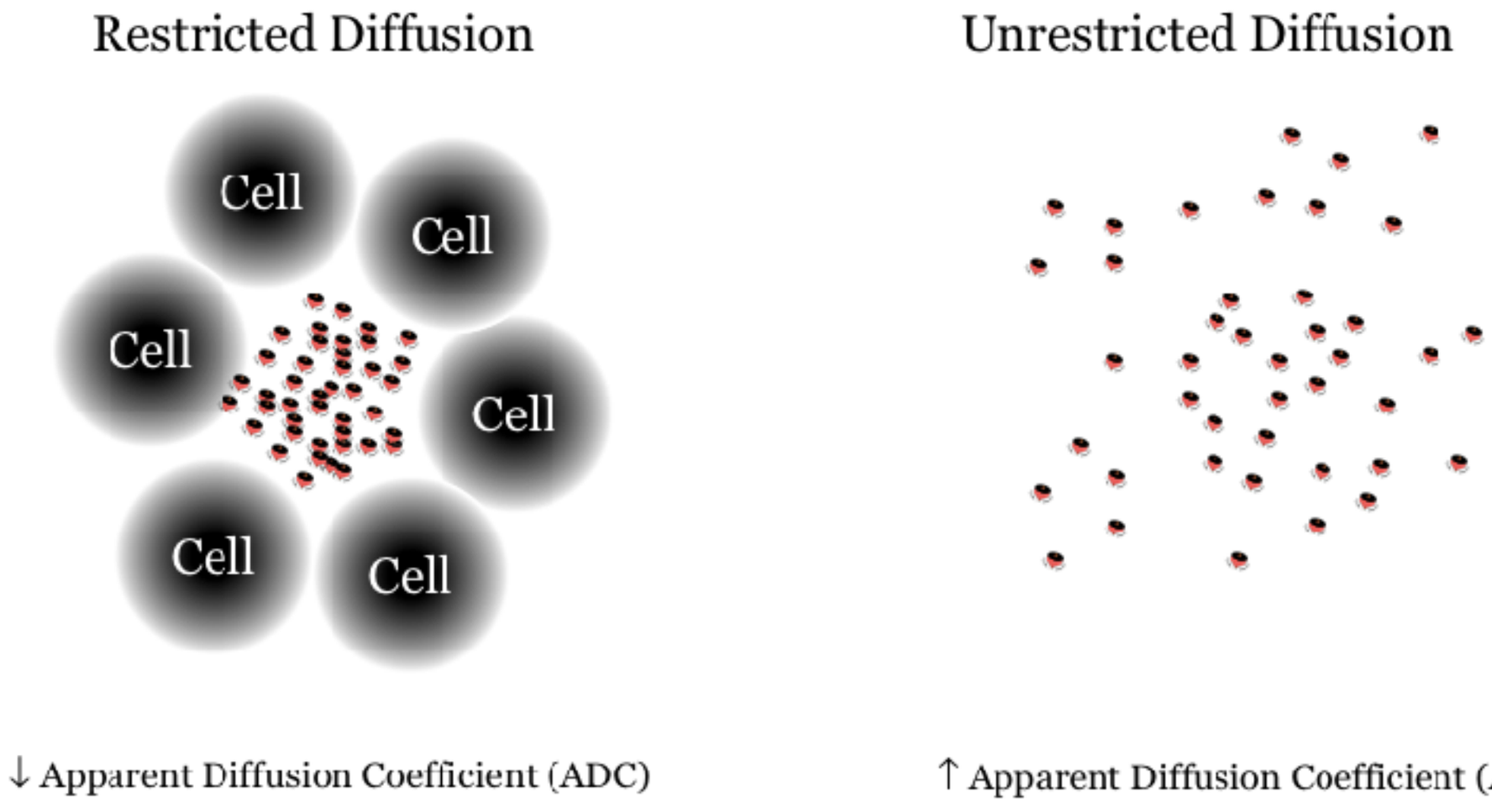

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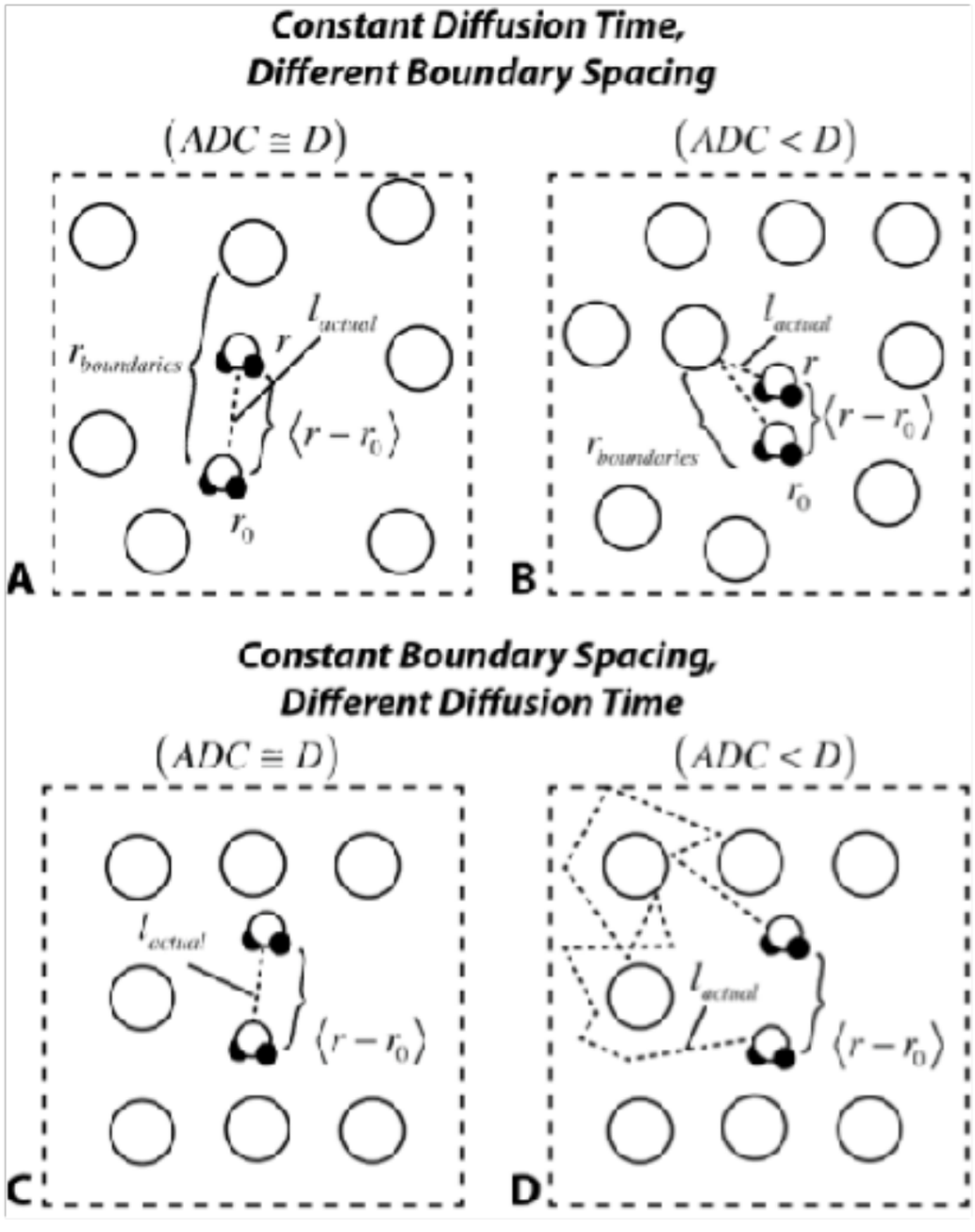
Factors that Affect Diffusion Measurements

- **<u>Tortuosity of the Environment</u>**
  - More tortuous paths *<u>look like slow diffusion</u>*



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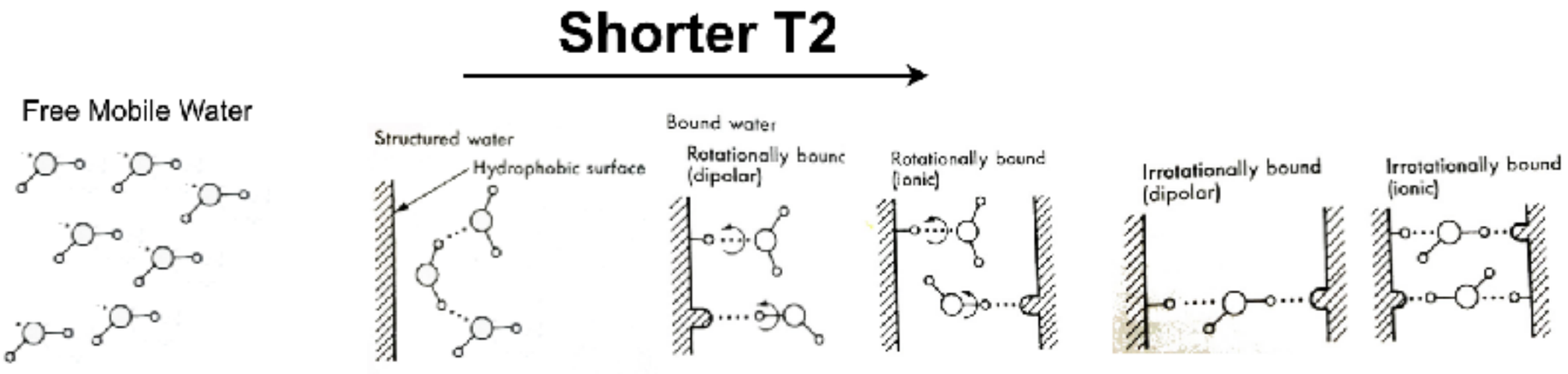
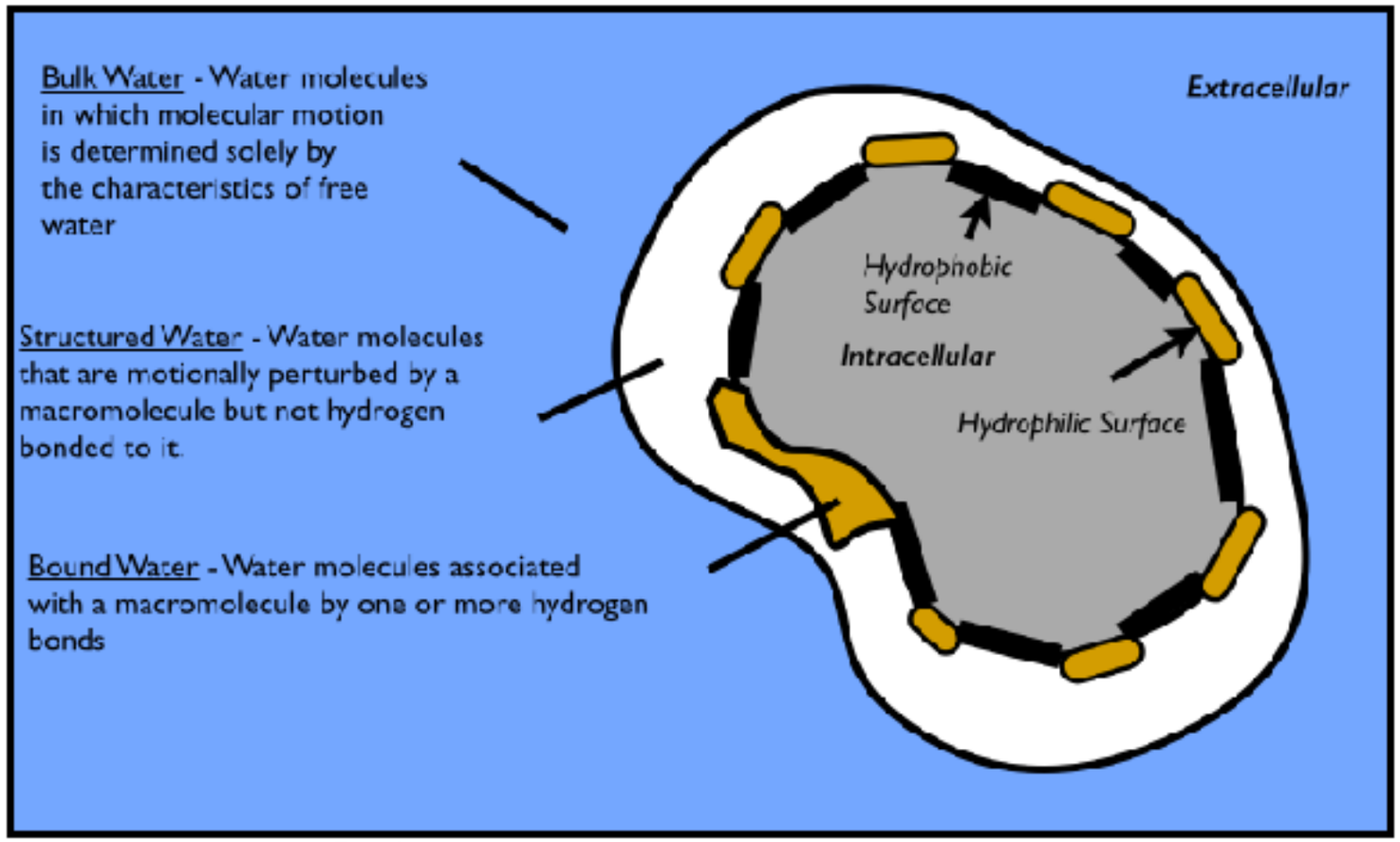
Factors that Affect Diffusion Measurements

- **<u>Echo Time (TE) - Determines water "species"</u>**





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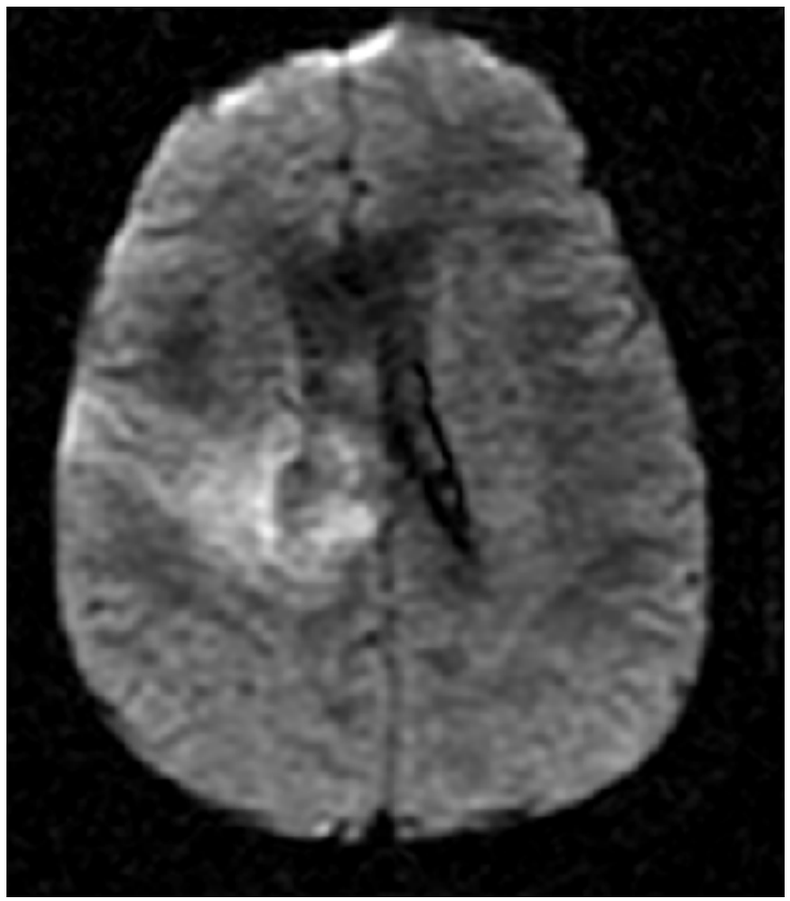
Diffusion MRI - Step-by-Step

1. Collect a diffusion-weighted image (DWI) (*b=1000 s/mm²* or *500 s/mm²*) by applying motion probing gradients in the x, y, and z directions, then averaging

    - Make sure TE is low and TR is long to maximize SNR

    - For higher resolution scans, use lower *b*-value for higher SNR



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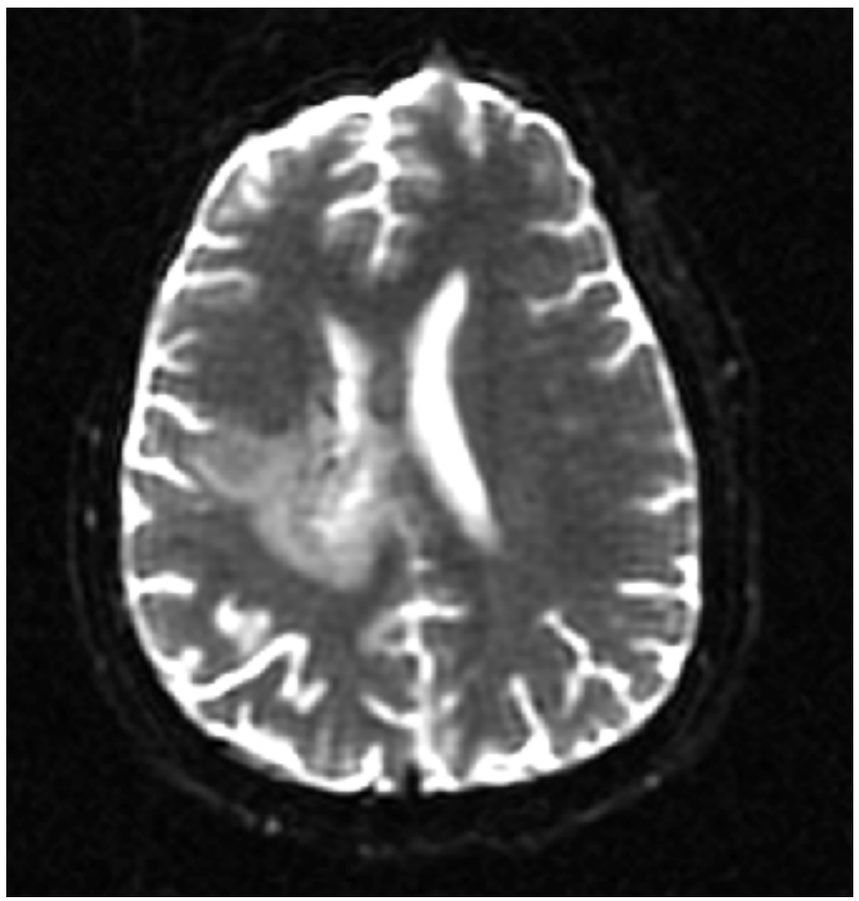
Diffusion MRI - Step-by-Step

2. Collect a reference (T2-weighted) dataset (b = 0 s/mm^2) with same TE, TR, resolution, etc.



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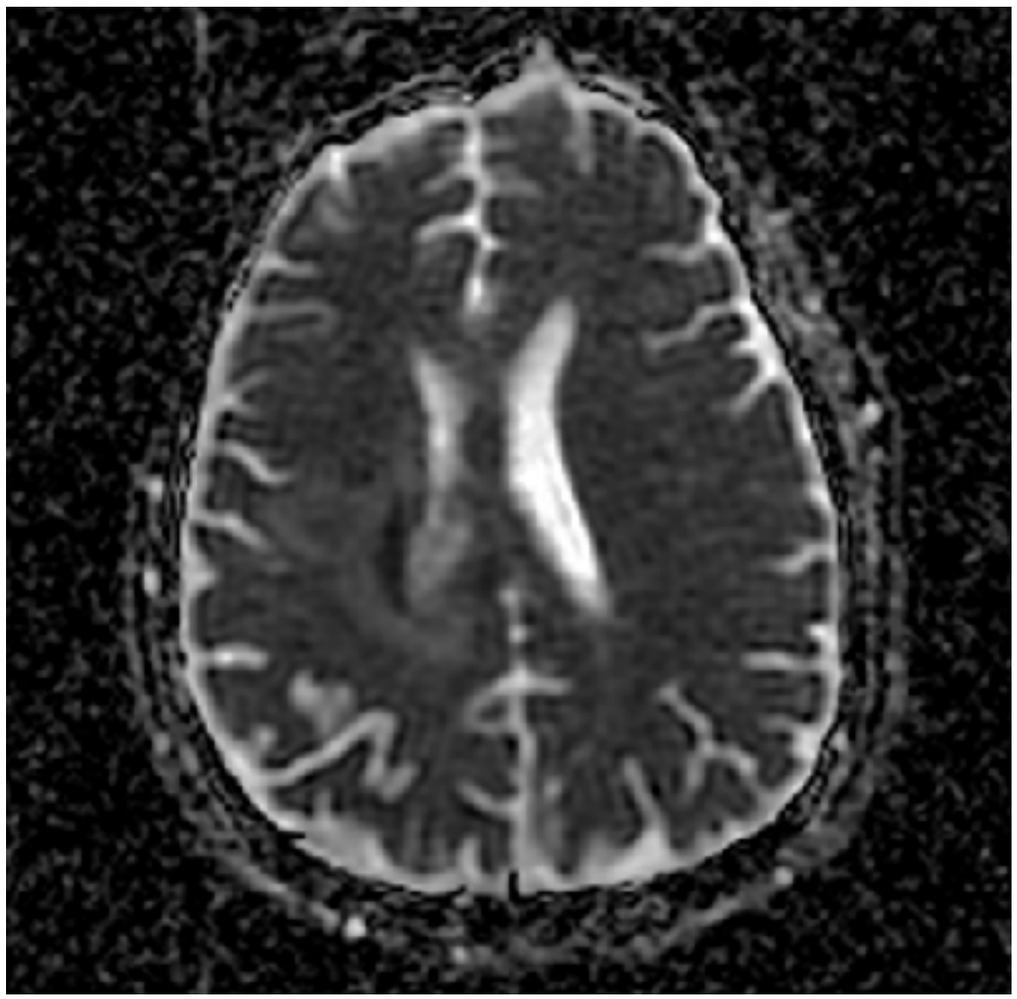
Diffusion MRI - Step-by-Step

3. Calculate ADC

$$ADC = -\frac{1}{b}\ln\left(\frac{S}{S_0}\right)$$ For *b*-values < 1000



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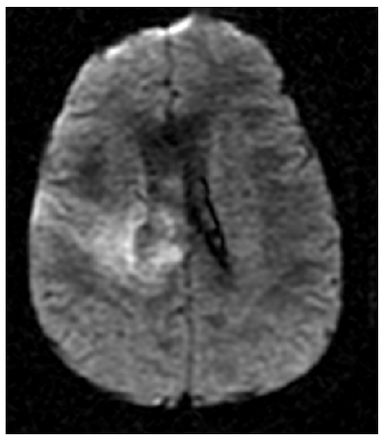
DWI vs. ADC

- **Diffusion Weighted Images (DWI)**
  - Images collected during application of "diffusion sensitizing gradients"
  - Contains T1, T2, and ADC effects
  - "Restricted Diffusion", long T2, and short T1 all influence DWI



$$DWI \propto \overbrace{\rho}^{\text{Proton Density}} \cdot \overbrace{e^{-1/T2}}^{\text{T2 Contrast}} \cdot \overbrace{\left(1 - e^{-1/T1}\right)}^{\text{T1 Contrast}} \cdot \overbrace{e^{-b \cdot ADC}}^{\text{Diffusion Contrast}}$$

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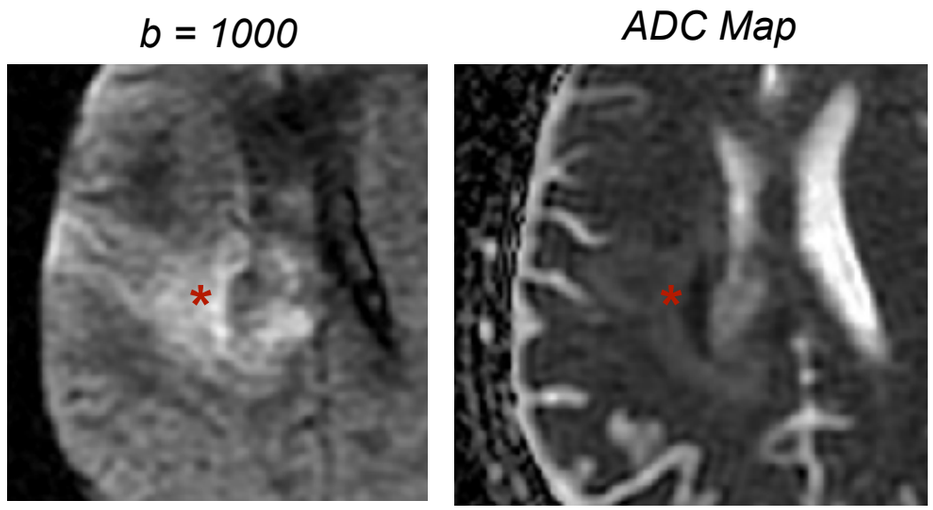
DWI vs. ADC

- **Diffusion Weighted Images (DWI)**
  - Influence of T2 in DWIs is known as "T2 shine through"



$$DWI \propto \overbrace{\rho}^{\text{Proton Density}} \cdot \overbrace{e^{-t/T2}}^{\text{T2 Contrast}} \cdot \overbrace{\left(1 - e^{-t/T1}\right)}^{\text{T1 Contrast}} \cdot \overbrace{e^{-b \cdot ADC}}^{\text{Diffusion Contrast}}$$

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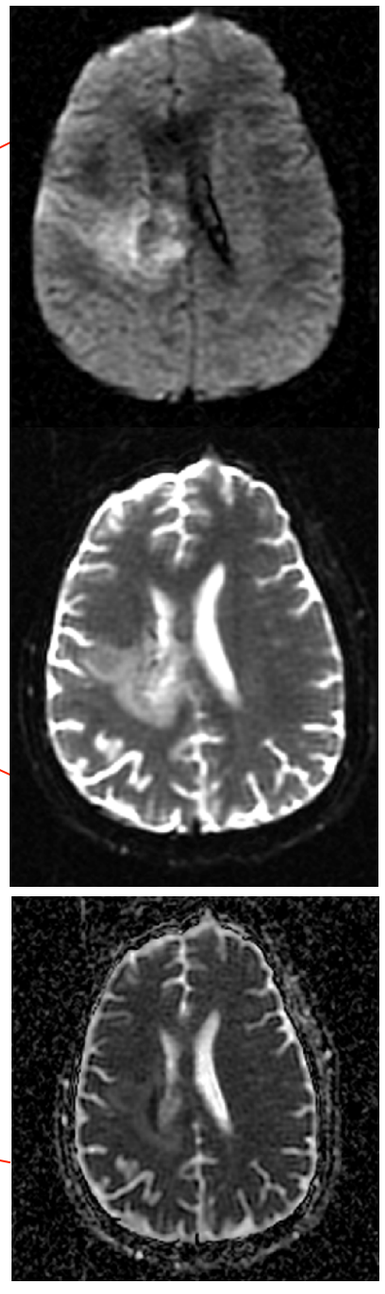
DWI vs. ADC

- **Apparent Diffusion Coefficient (ADC)**
  - Quantitative - Calculated from DWI and T2w (b=0) images
  - Reflects diffusion *<u>magnitude</u>*
  - Eliminates T1 and T2 effects

$$\frac{DWI}{T2_{b=0}} \propto \frac{\overbrace{\vec{\rho}}^{\text{Proton Density}} \cdot \overbrace{e^{-TE/T2}}^{\text{T2 Contrast}} \cdot \overbrace{\left(1-e^{-TR/T1}\right)}^{\text{T1 Contrast}} \cdot \overbrace{e^{-b\cdot ADC}}^{\text{Diffusion Contrast}}}{\underbrace{\vec{\rho}}_{\text{Proton Density}} \cdot \underbrace{e^{-TE/T2}}_{\text{T2 Contrast}} \cdot \underbrace{\left(1-e^{-TR/T1}\right)}_{\text{T1 Contrast}}} = \overbrace{e^{-b\cdot ADC}}^{\text{Diffusion Contrast}}$$

$$ADC = -\frac{1}{b}\ln\left(\frac{DWI}{T2}\right)$$



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Diffusion MRI Changes in Various Diseases

Disease	MR Signal Intensity		ADC	Cause
	DW Image	ADC Image		
Acute stroke	High	Low	Restricted	Cytotoxic edema
Chronic stroke	Variable	High	Elevated	Gliosis
Hypertensive encephalopathy	Variable	High	Elevated	Vasogenic edema
Cyclosporin toxicity	Variable	High	Elevated	Vasogenic edema
Hyperperfusion after carotid endarterectomy	Variable	High	Elevated	Vasogenic edema
HIV encephalopathy	Variable	High	Elevated	Vasogenic edema
Intraaxial mass				
Necrotic center	Variable	High	Elevated	Increased free water
Solid tumor	Variable	Variable	Variable	Depends on cellularity
Arachnoid cyst	Low	High	Elevated	Free water
Epidermoid mass	High	Low*	Restricted*	Cellular tumor
Pyogenic infection	High	Low	Restricted	Viscosity
Herpes encephalitis	High	Low	Restricted	Cytotoxic edema
Creutzfeldt-Jakob syndrome	High	Low	Restricted	Unknown
Diffuse axonal injury				
Majority of cases	High	Low	Restricted	Cytotoxic edema
Minority of cases	Variable	High	Elevated	Vasogenic edema
Hemorrhage				
Oxyhemoglobin	High	Low	Restricted	Intracellular
Deoxyhemoglobin	Low	Unknown†	Unknown†	Unknown†
Intracellular methemoglobin	Low	Unknown†	Unknown†	Unknown†
Extracellular methemoglobin	High	High	Elevated	Extracellular
Hemosiderin	Low	Unknown†	Unknown†	Unknown†
Multiple sclerosis				
Most acute lesions	Variable	High	Elevated	Vasogenic edema
A few acute lesions	High	Low	Restricted	Unknown
Chronic lesions	Variable	High	Elevated	Gliosis, neuronal loss

* Relative to that of cerebrospinal fluid (CSF).
† The ADC usually cannot be calculated.

Shaefer, Radiology, 2000

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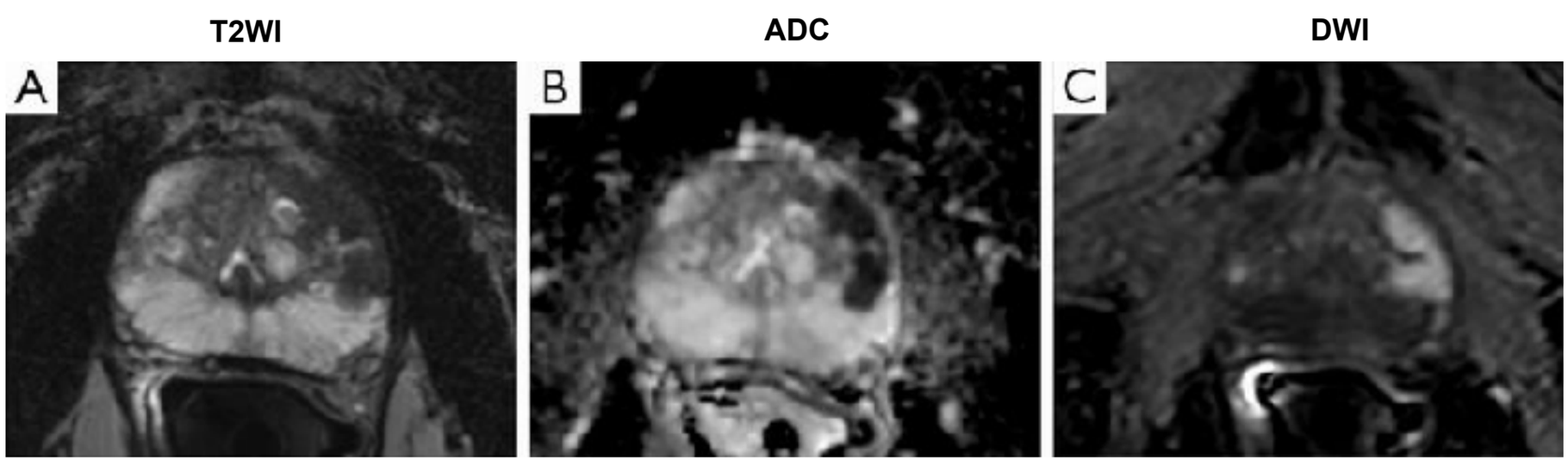
Diffusion MRI Changes in Various Diseases

Prostate

Table 1 Principles and characteristics of T2WI and functional sequences

Sequence	Principle	Finding of prostate cancer	Advantages	Drawbacks
T2WI	Water content of tissue	Low signal intensity	High resolution; sharp demarcation of the prostate capsule	Central or transition zone tumor detection
DWI	Proton diffusion properties	High signal intensity on DWI; low signal intensity on ADC map	Central or transition zone tumor detection; assessment of tumor aggressiveness	Poor resolution and image distortion
DCEI	T1WI with contrast medium	Enhance and wash out rapidly	Local recurrence detection after definite treatment	Long acquisition time
MRSI	Concentration of metabolites	Increased choline plus creatinine/citrate	Assessment of tumor aggressiveness	Needs more expertise; long acquisition time

T2WI, T2-weighted imaging; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient; DCEI, dynamic contrast-enhanced imaging; T1WI, T1-weighted imaging; MRSI, magnetic resonance spectroscopy imaging.



Loffroy et al., Quant Imag Med Surg 2015; 5(5):

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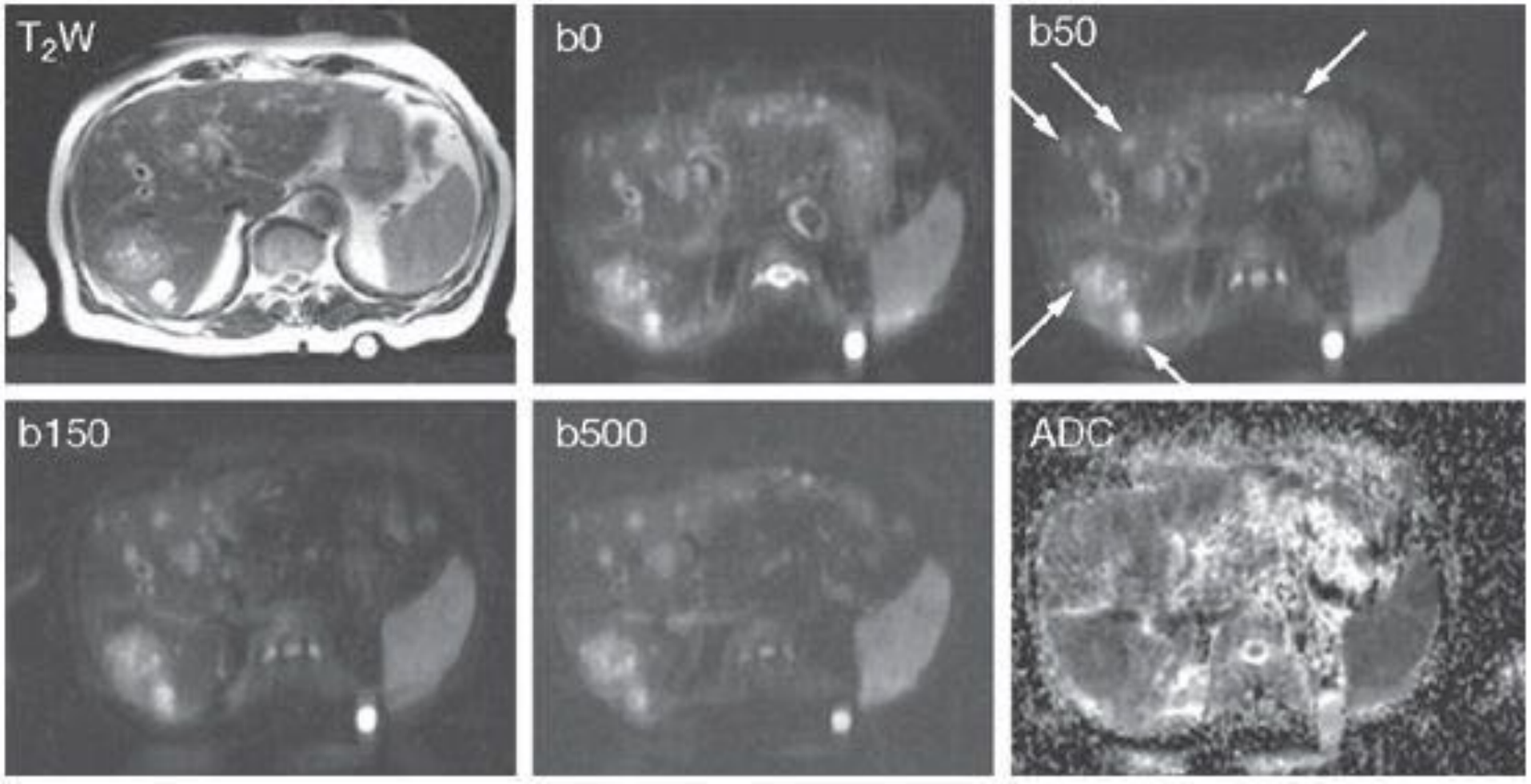
Diffusion MRI Changes in Various Diseases

Liver



Patterson, et al., Nat Clin Pract Oncol 2008; 5: 220-233.

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Diffusion MRI Changes in Various Diseases

Breast

Table 1 Apparent diffusion coefficient in benign and malignant lesions.

ADC values ($\times 10^{-3}$ mm^2/s)	Benign lesions ($n = 26$)	Malignant lesions ($n = 26$)	P
Mean	1.50	0.92	< 0.0001
Standard deviation	0.34	0.26	< 0.0001
Median	1.48	0.85	< 0.0001
Interquartile interval	1.31–1.68	0.77–1.03	< 0.0001

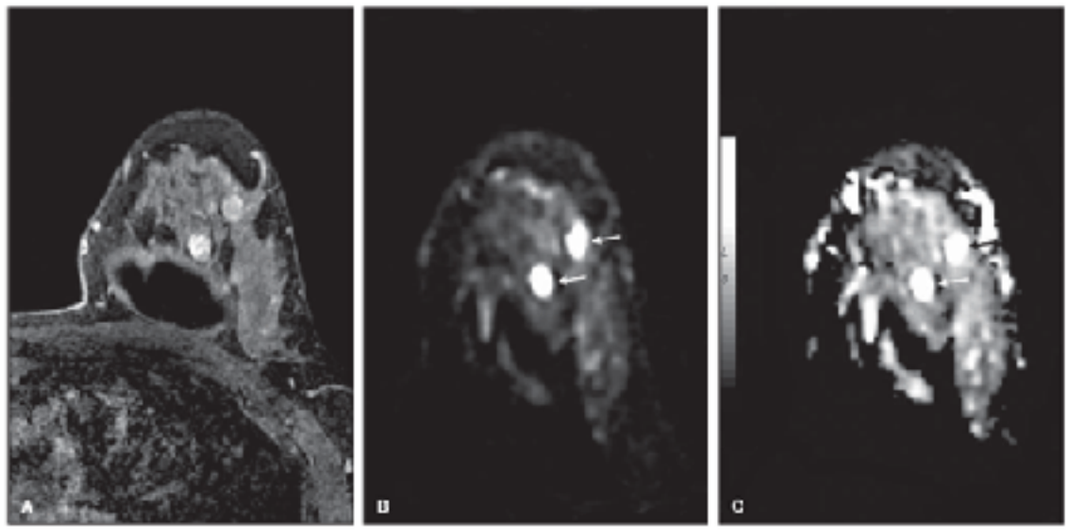

Figure 1. Female, 43-year-old patient presenting fibroadenomas in the left breast. Delayed phase contrast-enhanced 3D gradient, T1-weighted sequence with fat-suppression in the axial plane (**A**), diffusion weighted sequence (*b* 500 s/mm^2) in the axial plane (**B**), and apparent diffusion coefficient (ADC) black/white map in the axial plane (**C**) show two nodules with morphology and contrast-enhancement with benign appearance. Note that the nodules present high signal intensity on the diffusion (arrows) and on the ADC map (arrows) suggesting absence of water molecules diffusion restriction.

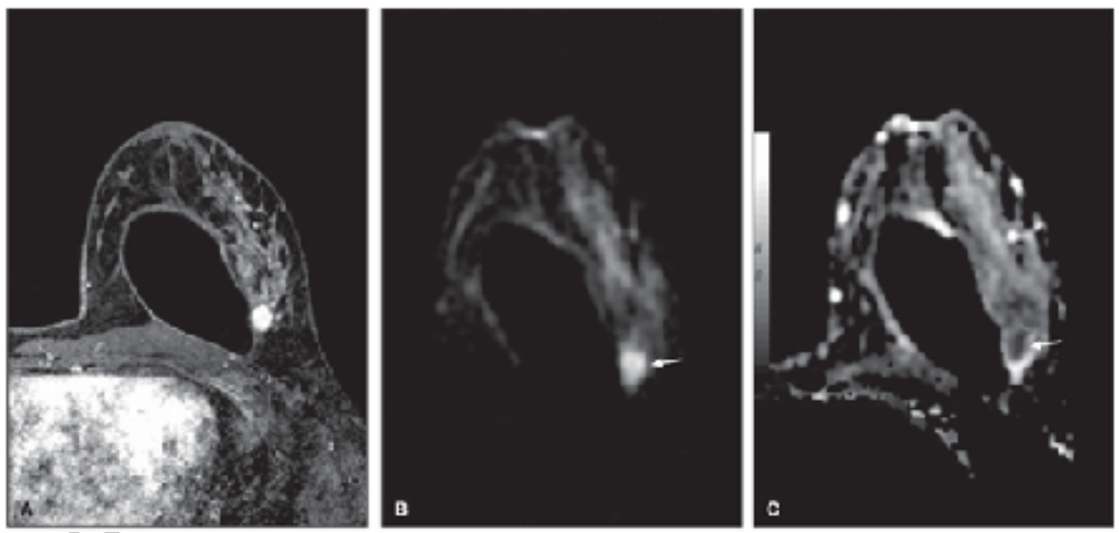

Figure 2. Female, 48-year-old patient presenting infiltrating ductal carcinoma in the left breast. Axial, 3D gradient T1-weighted sequence with fat-suppression at early postcontrast phase (**A**), diffusion-weighted sequence (*b* 500 s/mm^2) in the axial plane (**B**), and apparent diffusion coefficient (ADC) black/white map in the axial plane (**C**) show microlobulated nodule with suspicious contrast-enhancement. Note that the nodule presents high signal intensity on the diffusion (arrow) and signal loss on the ADC map (arrow), suggesting restricted diffusion of water molecules.

Pereira et al., Radiol Bras 2009; 42(5)

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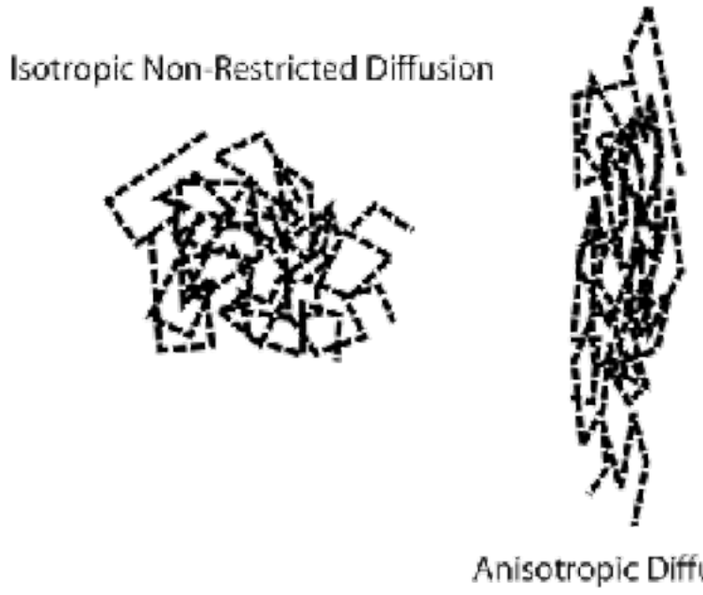
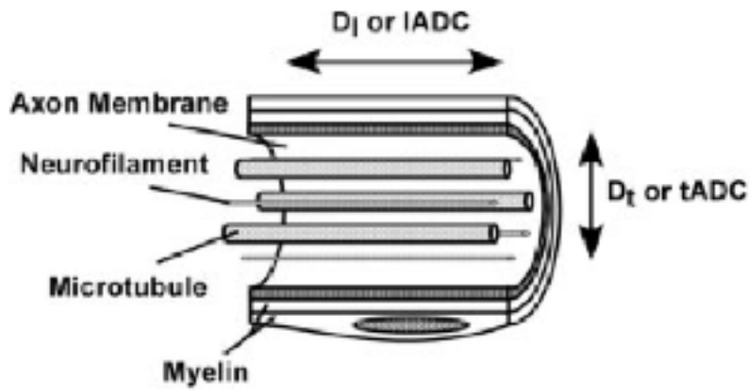
Assumptions of Isotropic Diffusion

Until now, we have assumed that diffusivity is uniform and have only measured diffusivity in 1 direction (or 3 directions, then averaged)

If diffusion is anisotropic (i.e. unequal in all directions) we may over/under estimate the diffusion coefficient if we measure only a single direction

In Diffusion Tensor Imaging (DTI) we make 1D diffusion measurements in multiple directions (>6 directions), then construct the mathematical 3x3 tensor field that describes the magnitude and direction of spin self-diffusion





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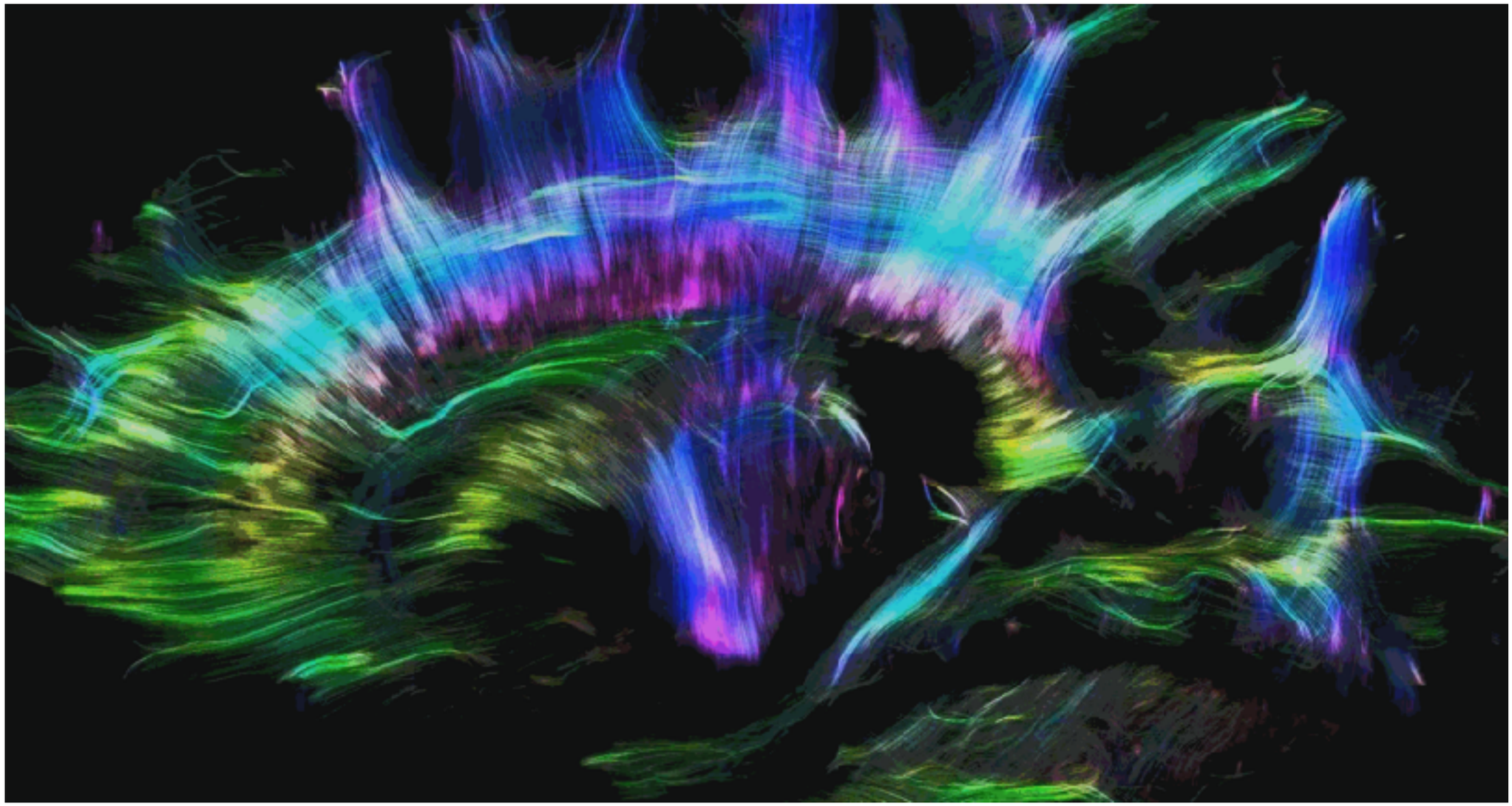
DTI Tractography



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Outline (Accelerated)

- **Perfusion MRI**
  - With Exogenous Contrast
    - Dynamic Contrast Enhanced (DCE) MRI - T1
    - Dynamic Susceptibility Contrast (DSC) MRI - T2/T2*
  - Without Exogenous Contrast
    - Arterial Spin Labeling (ASL)
- **Diffusion MRI**
  - Isotropic (3 dimensional) Diffusion Weighted Imaging (DWI)

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Quantitative Image Analysis
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