

# MRI Applications

## A few details on the following terms « Flow », « Perfusion » and « Diffusion » from the imaging point of view

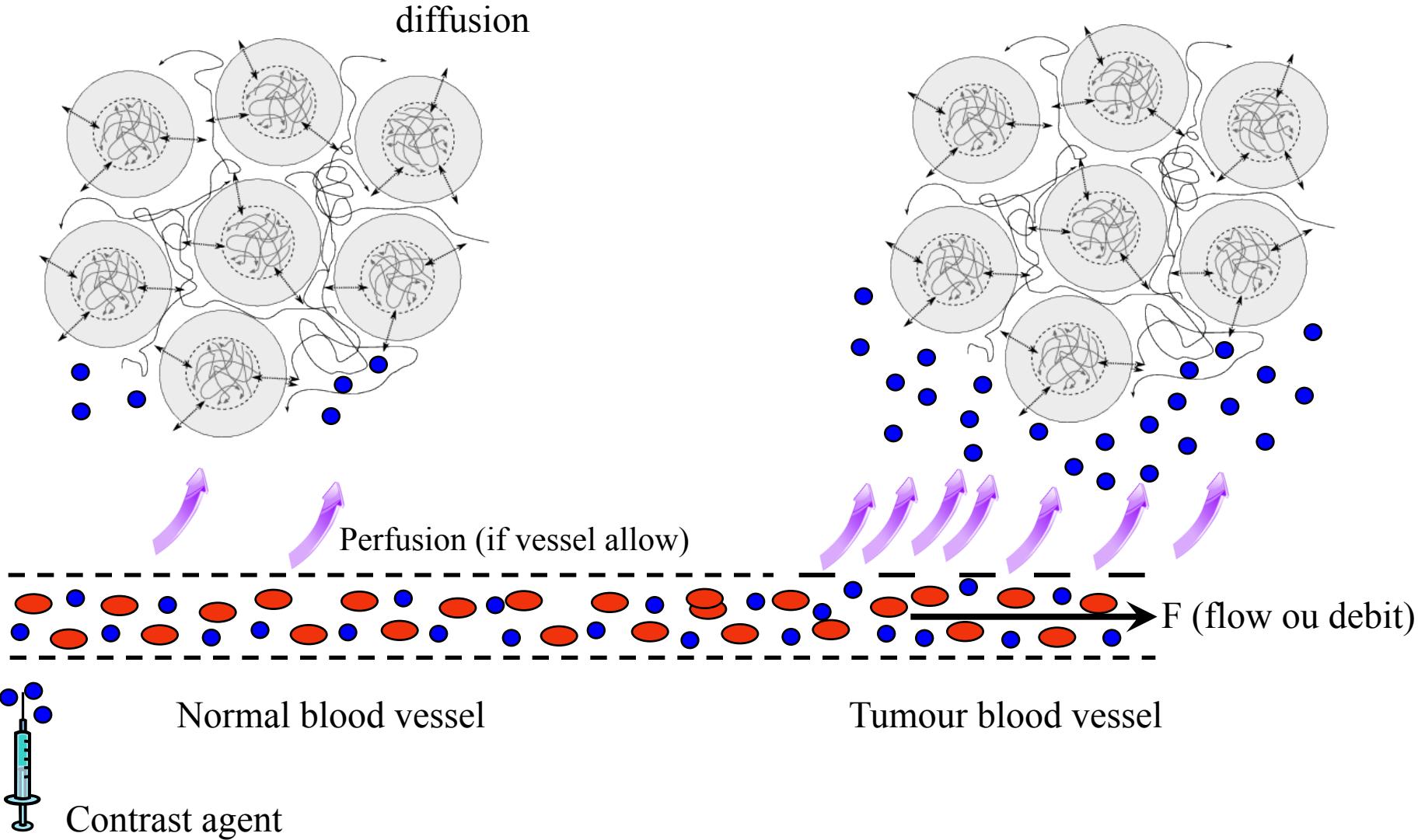
**Flow** : transport of liquid, essentially blood within the blood vessels – flow is characterized within a vessel as a velocity (eg. cm/s) or as a debit (eg. mL/min)

**Diffusion** : random movement of a molecule within a given space – concerns essentially the movement of water molecules within the intra- and extra-cellulaire space. It is expressed in  $\text{cm}^2\text{s}^{-1}$ .

**Perfusion** : transit of a molecule (contrast agent, water, tracer etc..) from blood vessel towards intra- et extra-cellulaire compartments. One can measure the microvascular permeability (eg. *Study of angiogenesis in tumours*)

**Specific case of the brain:** the healthy BBB prevents the transit of contrast agents and we can only measure capillary permeability and blood volume

# A few details on the following terms « Flow », « Perfusion » and « Diffusion » from the imaging point of view

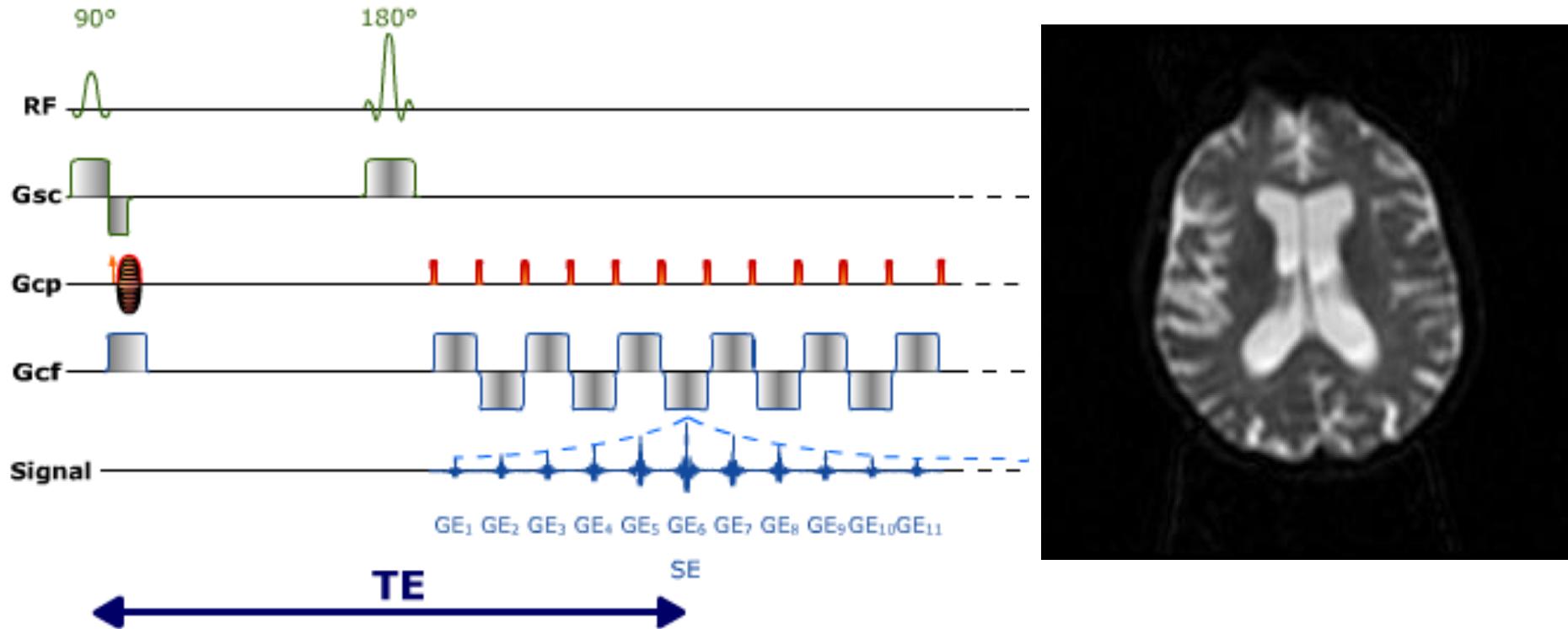


# Echo Planar Imaging (EPI)

The Ultimate in UltraFast Imaging

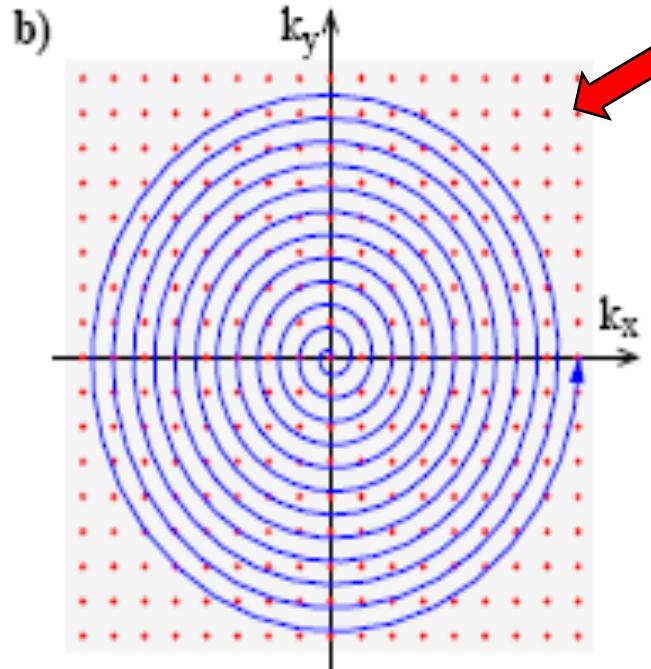
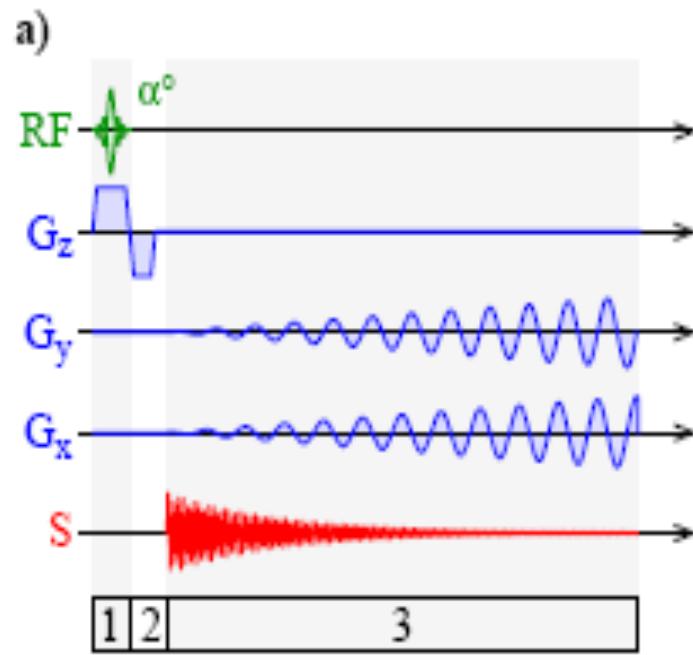
Echo Planar Imaging was “dreamed of” in the late 1970s, but only some very important technological developments have allowed this ultra-fast technique to become a reality.

It is based on a single-shot acquisition with very rapidly switching gradients.



# K-space filling

Fourier space can be filled in a number of ways and one very efficient technique is the « spiral » method where the gradients oscillate in order to cover more efficiently the k-space grid.

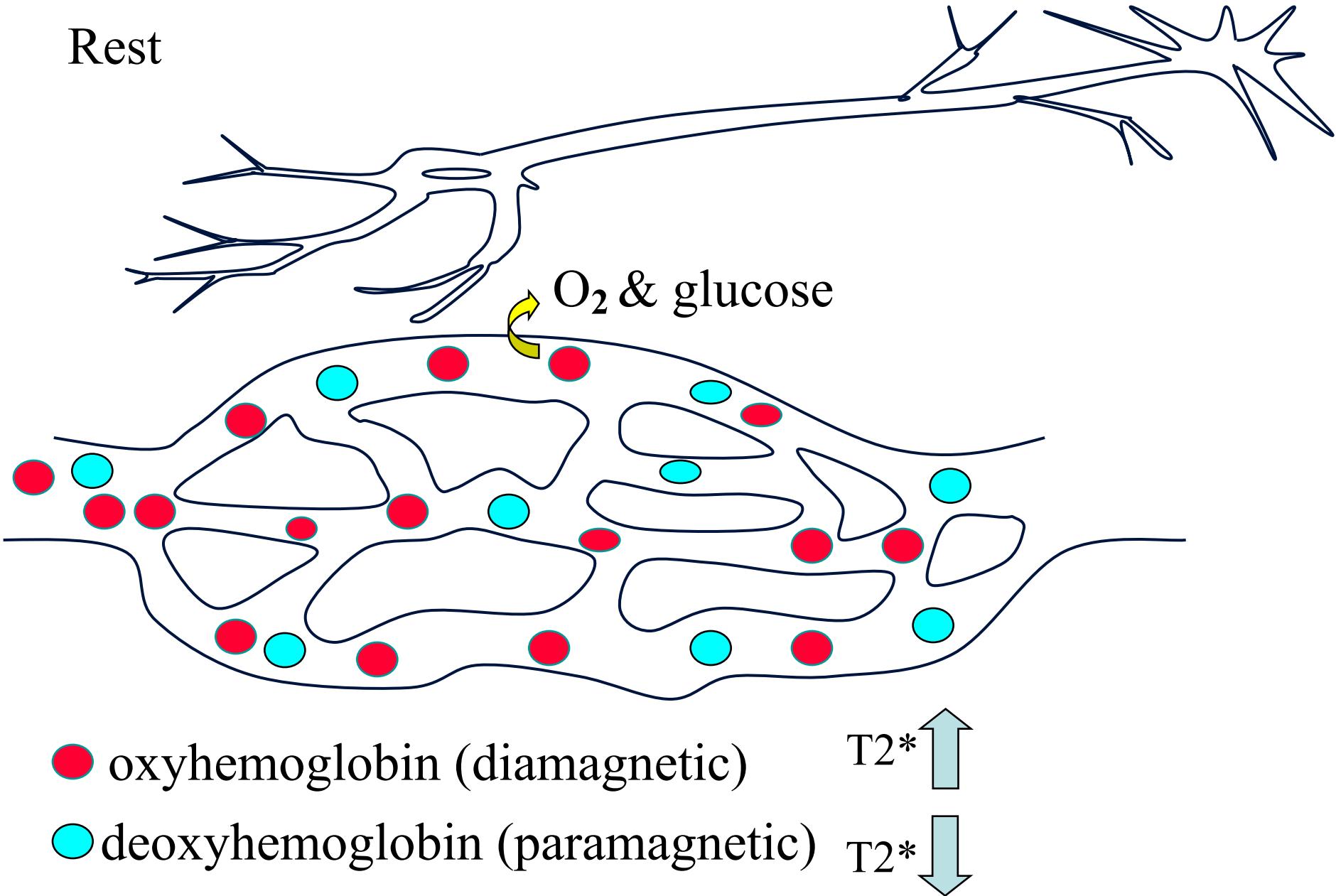


Loss of data on periphery compensated by extrapolation

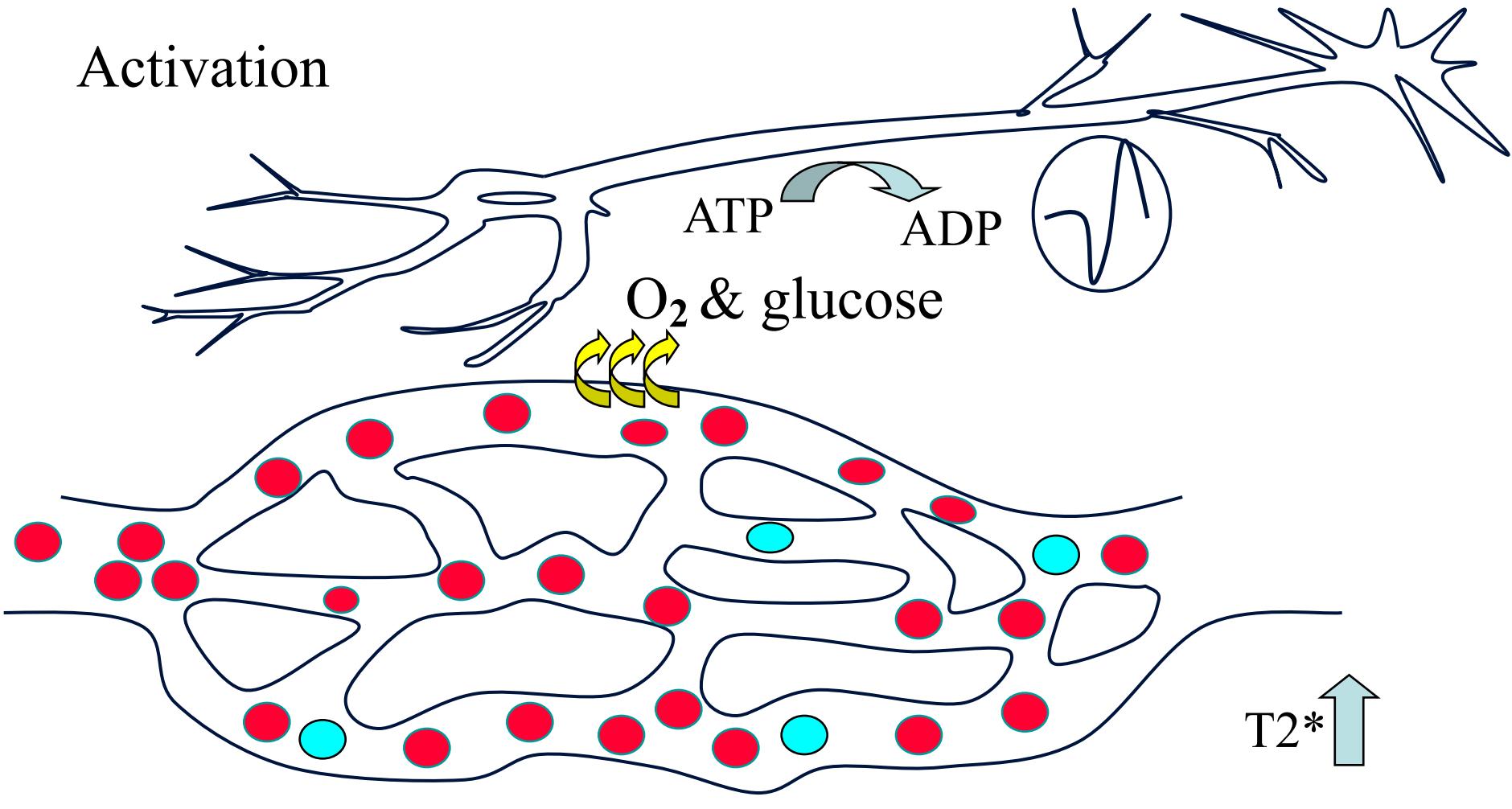
# The BOLD effect

## (Blood Oxygen Level Dependent)

Rest



Activation



↑ Blood flow

'over-compensation'

↑ % $O_2$

↑ "BOLD" signal

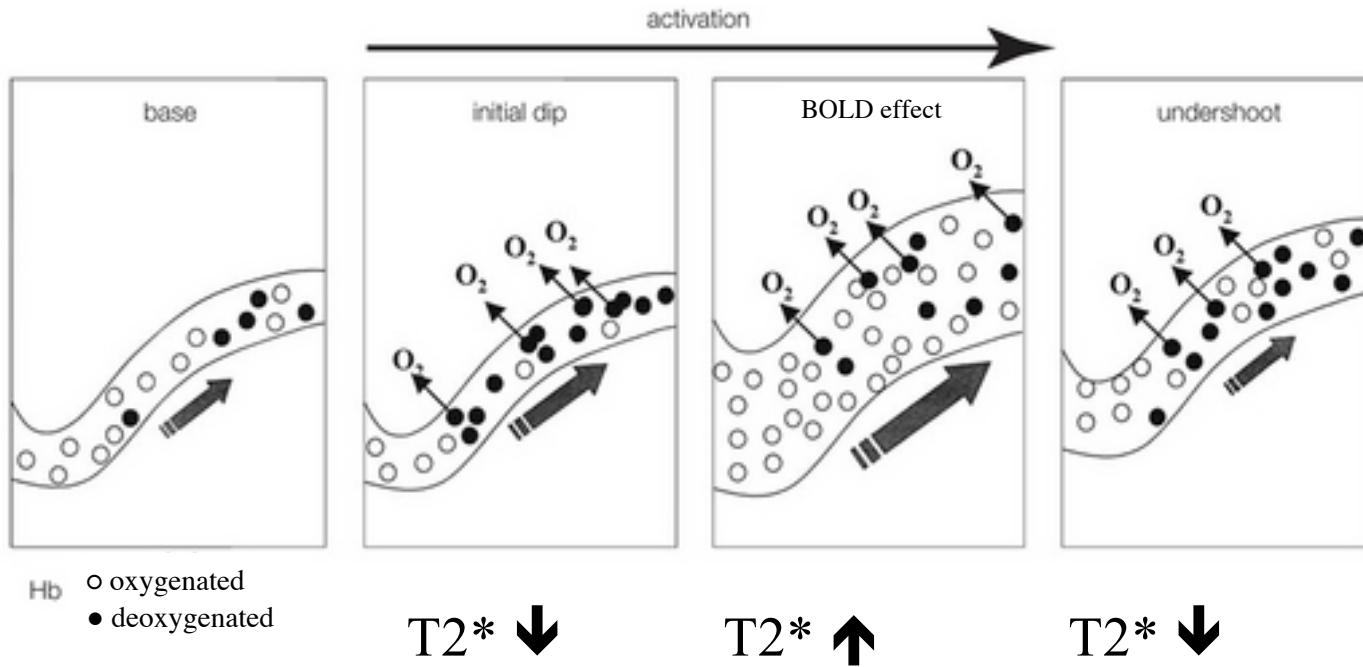
# Cerebral Activation Imaging or functional MRI (fMRI)

## *Blood Oxygen Level Dependent Functional MRI (BOLD fMRI)*

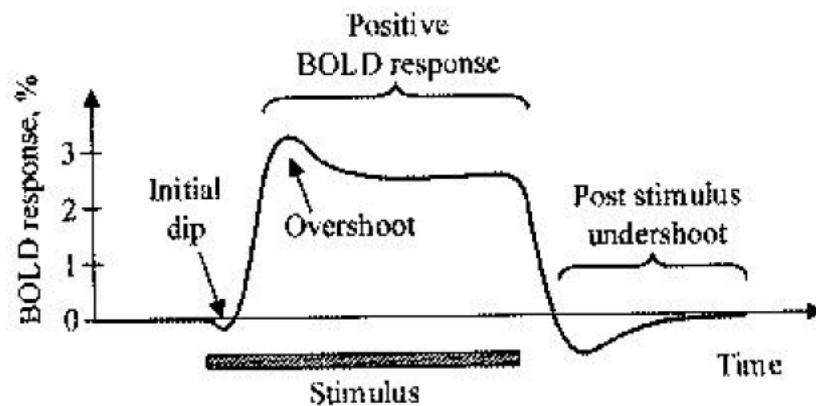
- Cerebral areas that are **active** possess increased regional blood flow
- Oxygen use increases but does not follow the increase in blood flow



- Modification of ratio *oxyhemoglobin* to *deoxyhemoglobin*
- Increased NMR signal from blood protons (reduced T2\* effect)
- Global signal increase  $\sim 2\text{-}5\%$  ( $\rightarrow 1,5\text{ T}$ ) because blood  $\sim 6\%$  of gray matter – at 3.0 T, signal increase  $\sim 10\%$



In practice, the BOLD response looks like this .....



# Activation Imaging ou fMRI

Study of cognitive and motricity functions. Characterization of functional cerebral zones.

Study the physiological response of specific tasks ;

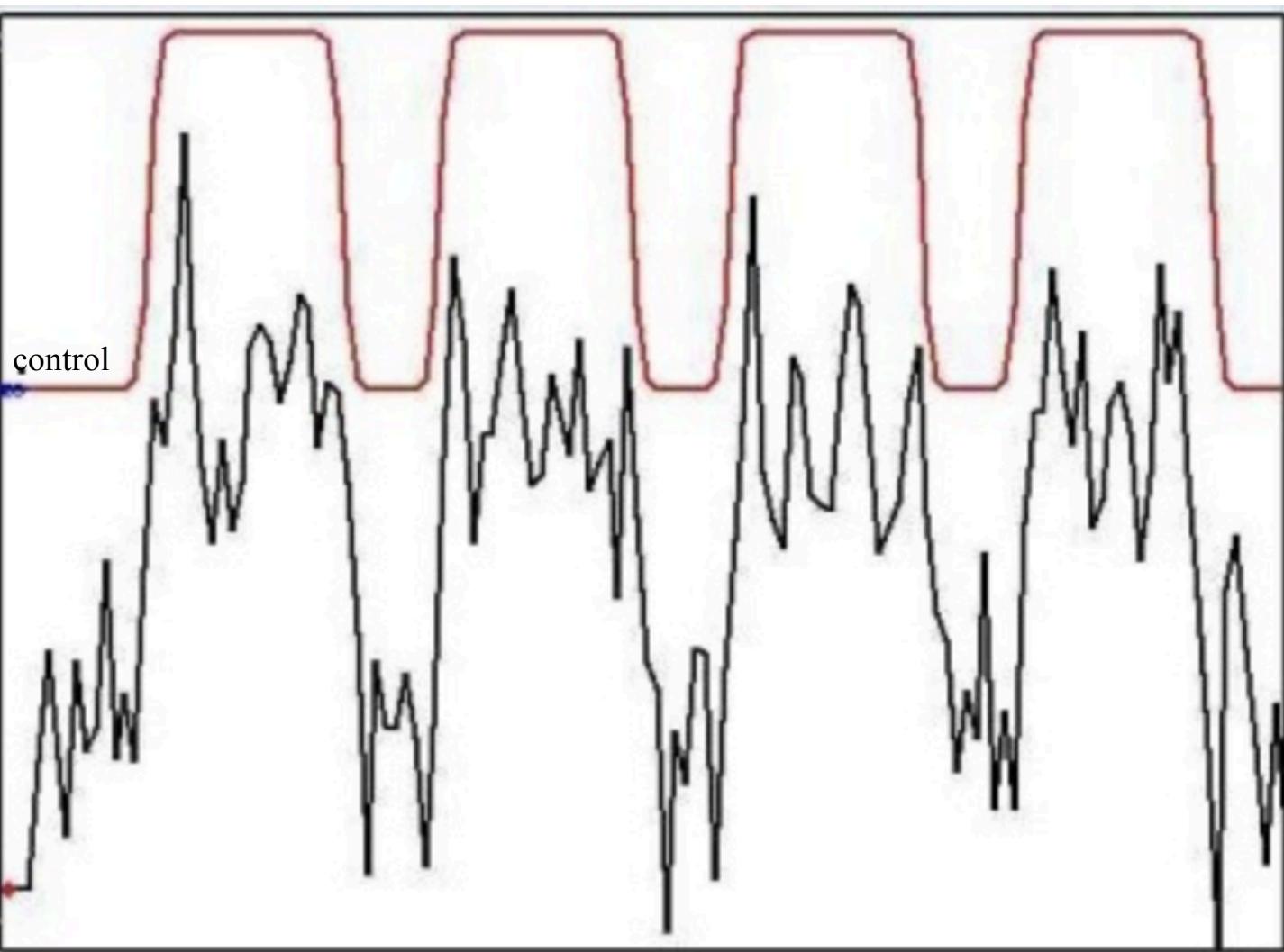
Motricity Cortex : movement of fingers, finger tapping

Visual Cortex : blinking light source

Language Cortex : « mental » construction of sentences

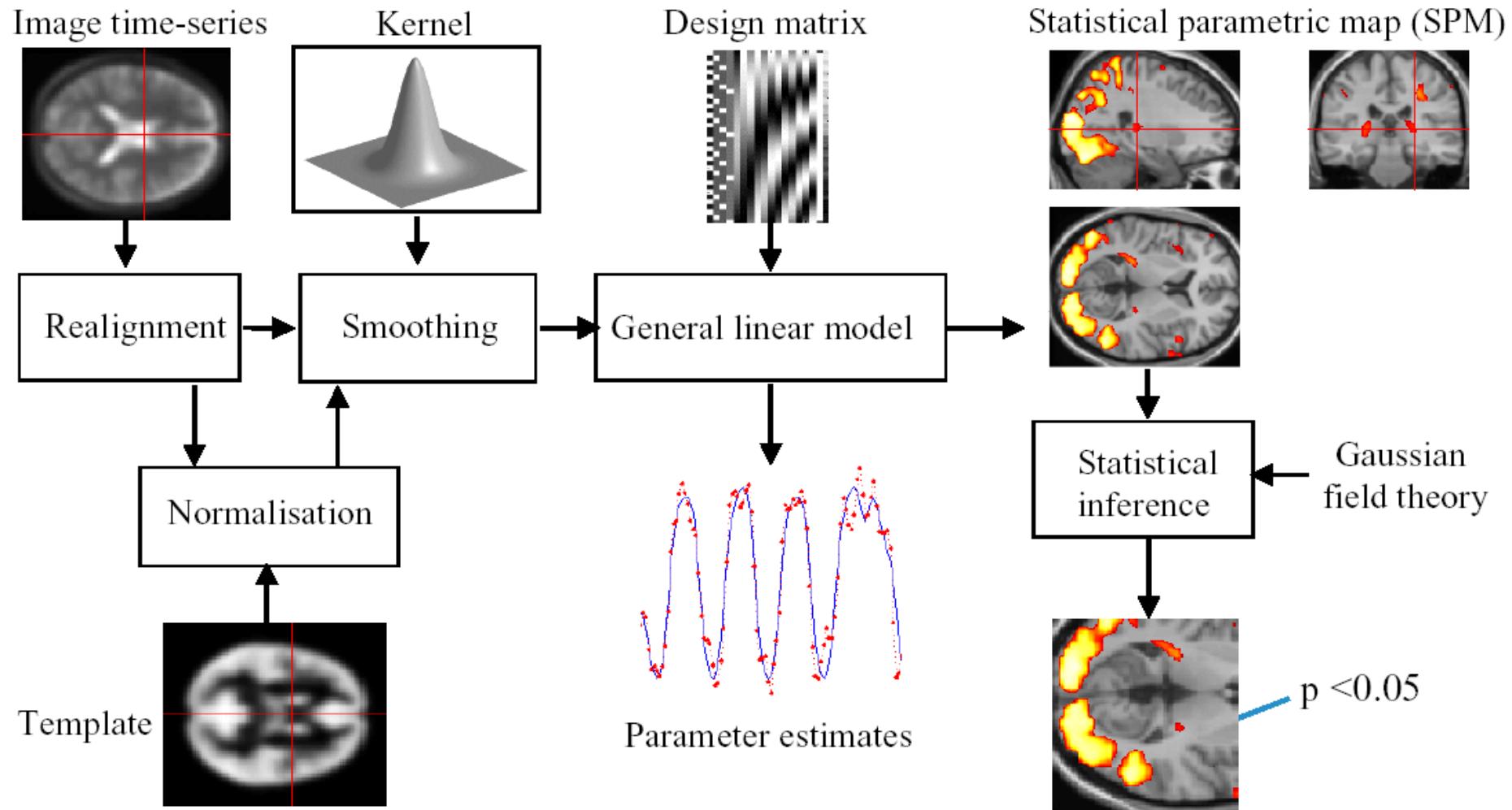
task

Intensity of  
pixel signal

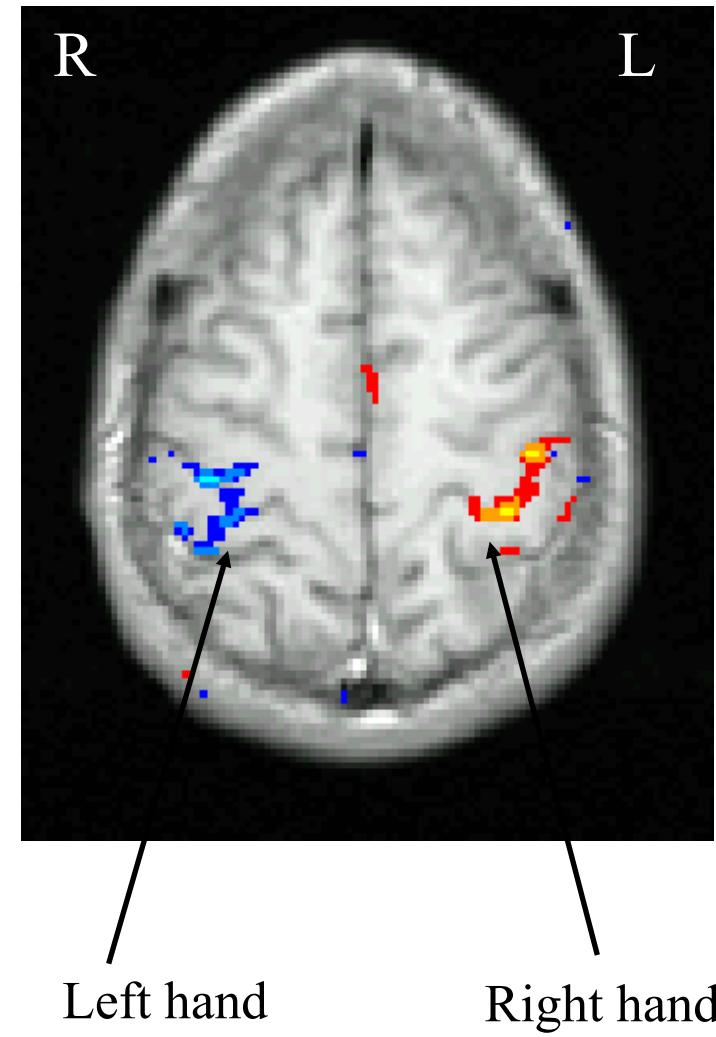
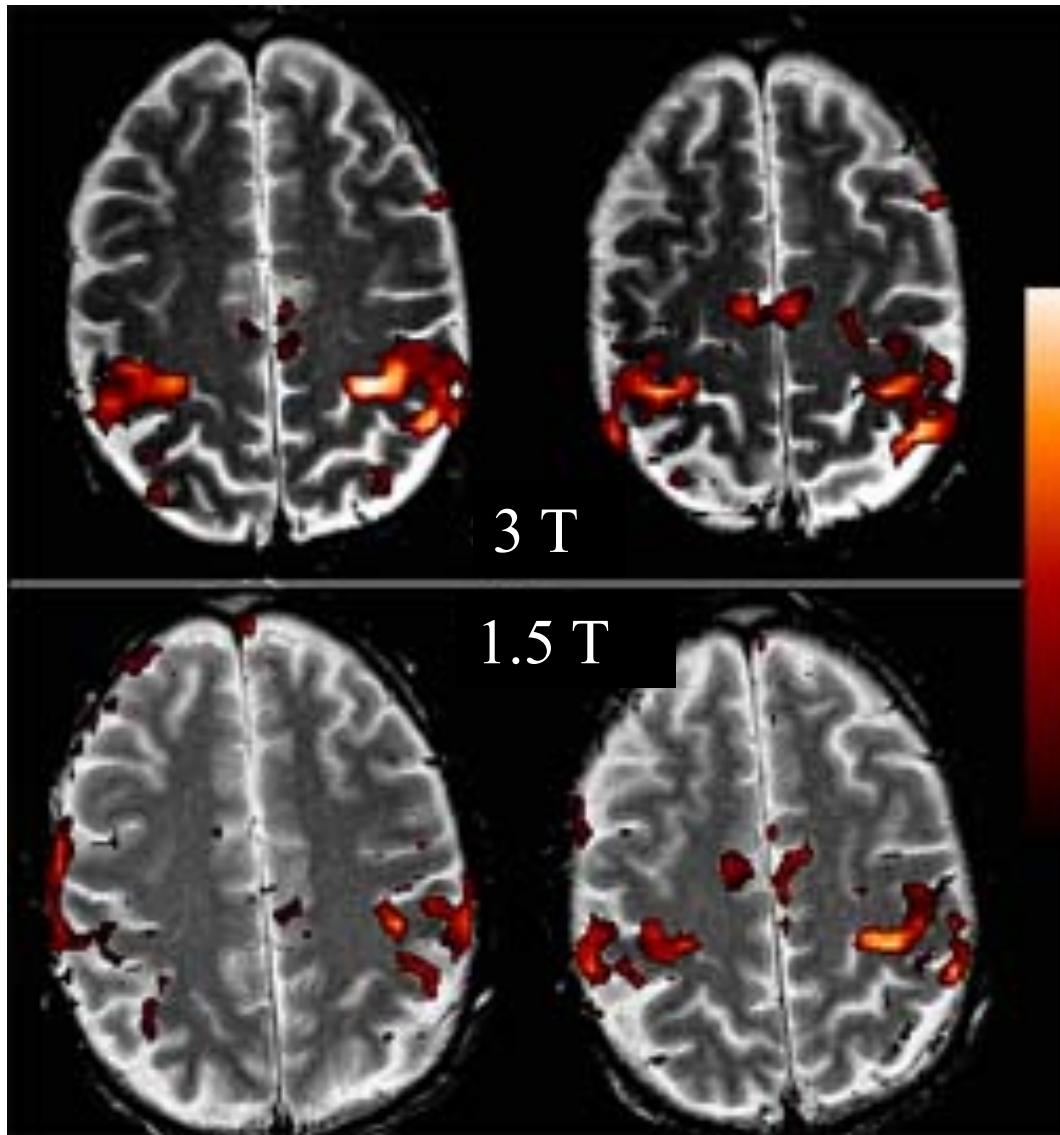


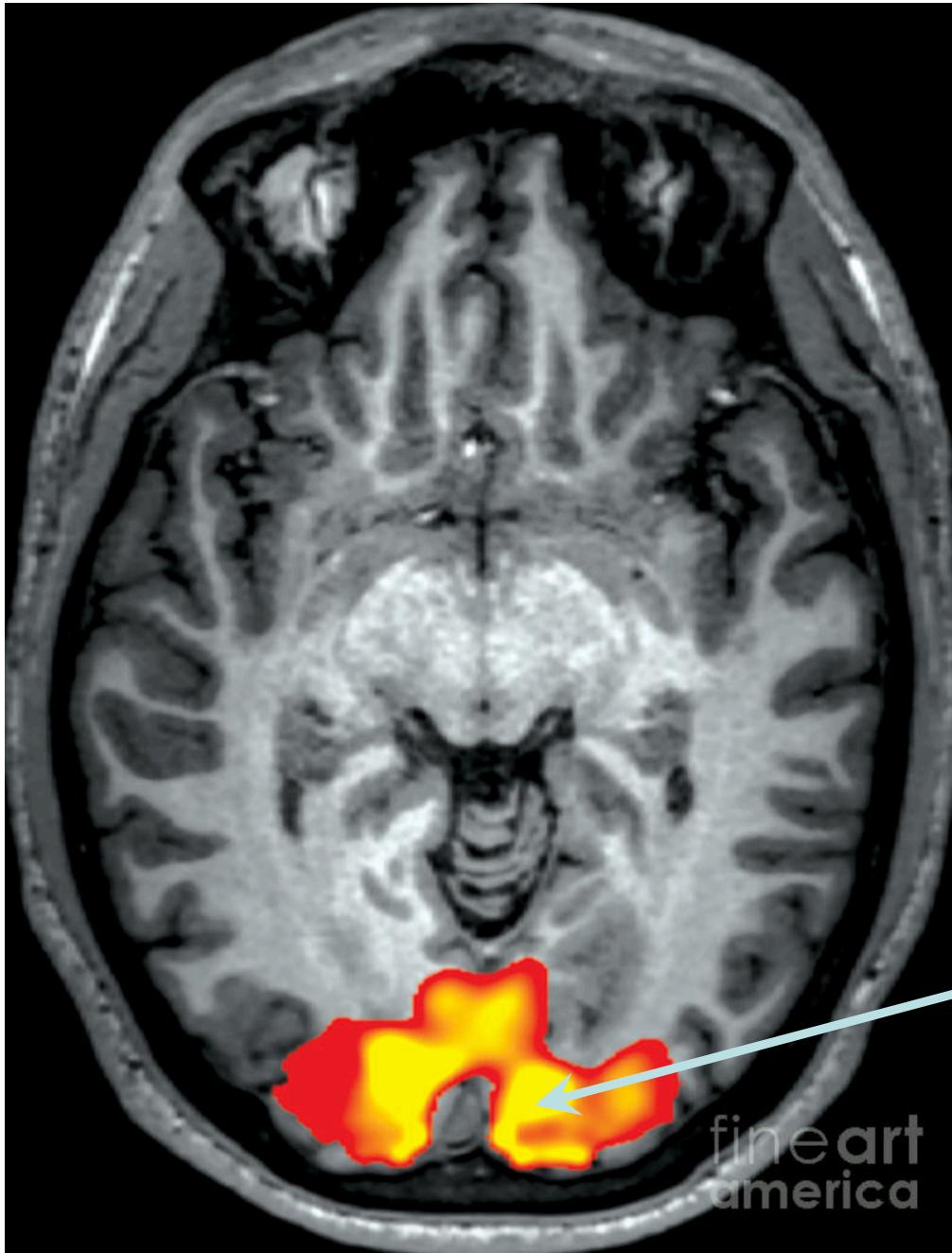
time

# Statistical Parametric Mapping (SPM)



# Paradigm : finger tapping

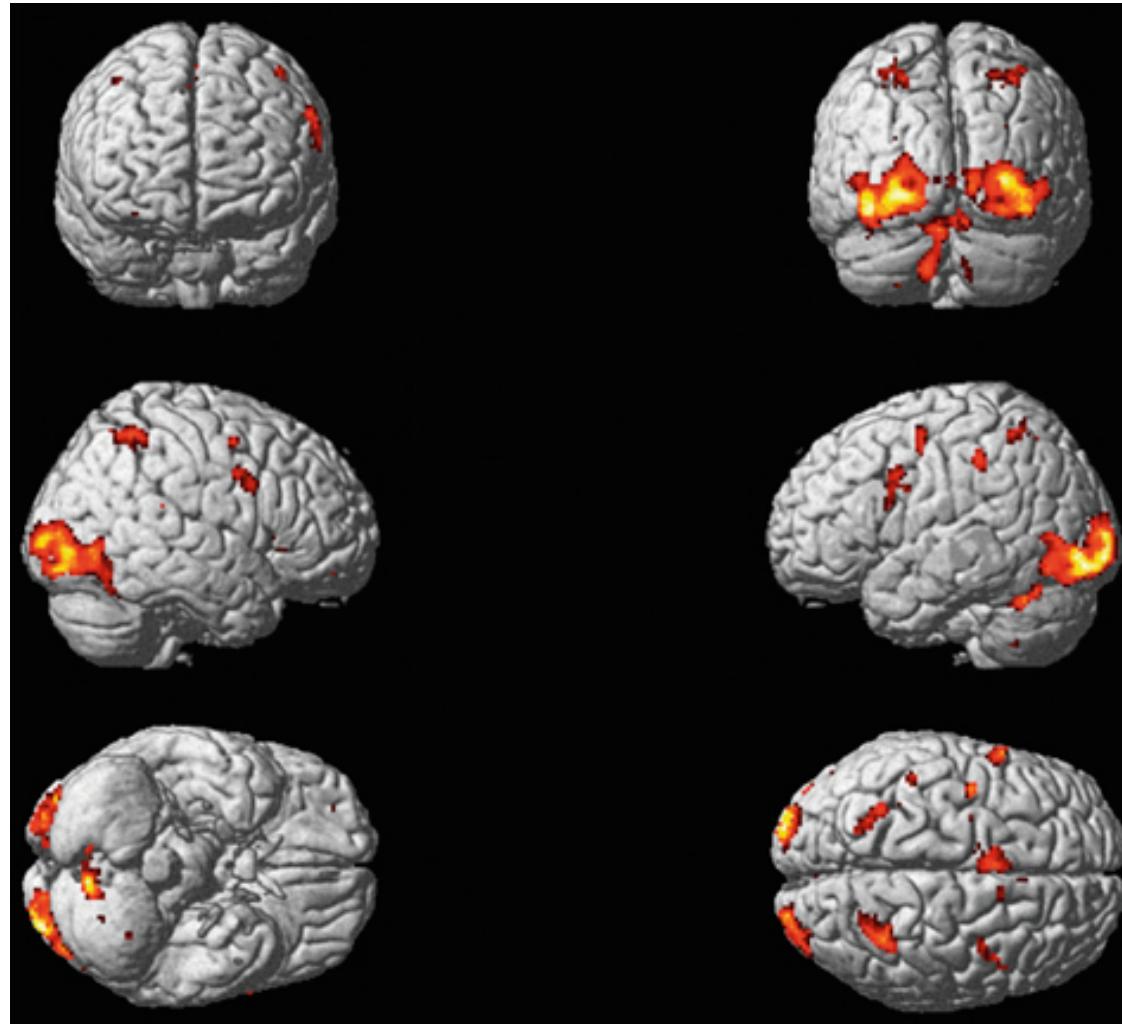




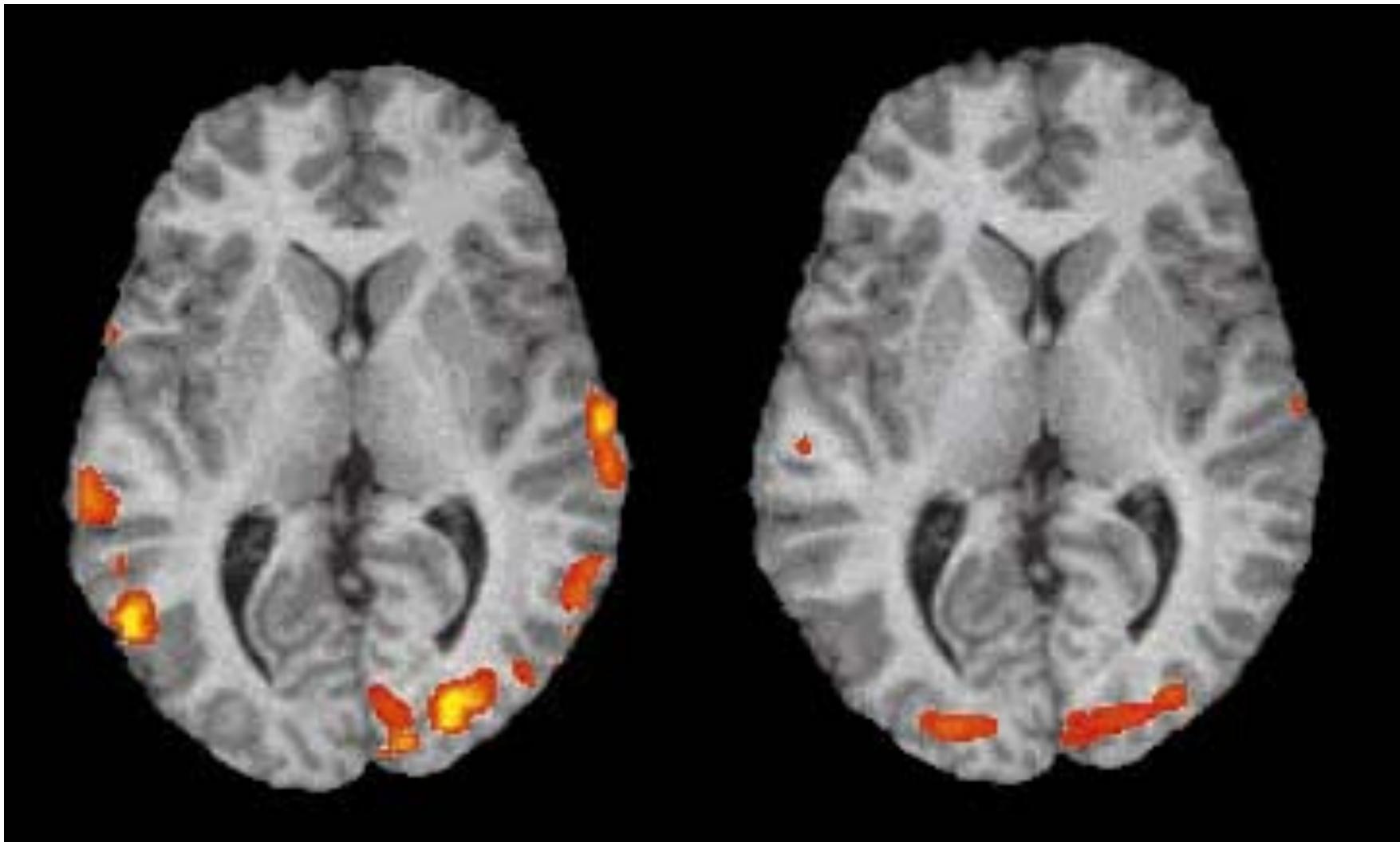
Paradigm : visual stimulus

Occipital region  
of brain

## Paradigm : Eyes following light point source



Paradigm : reading

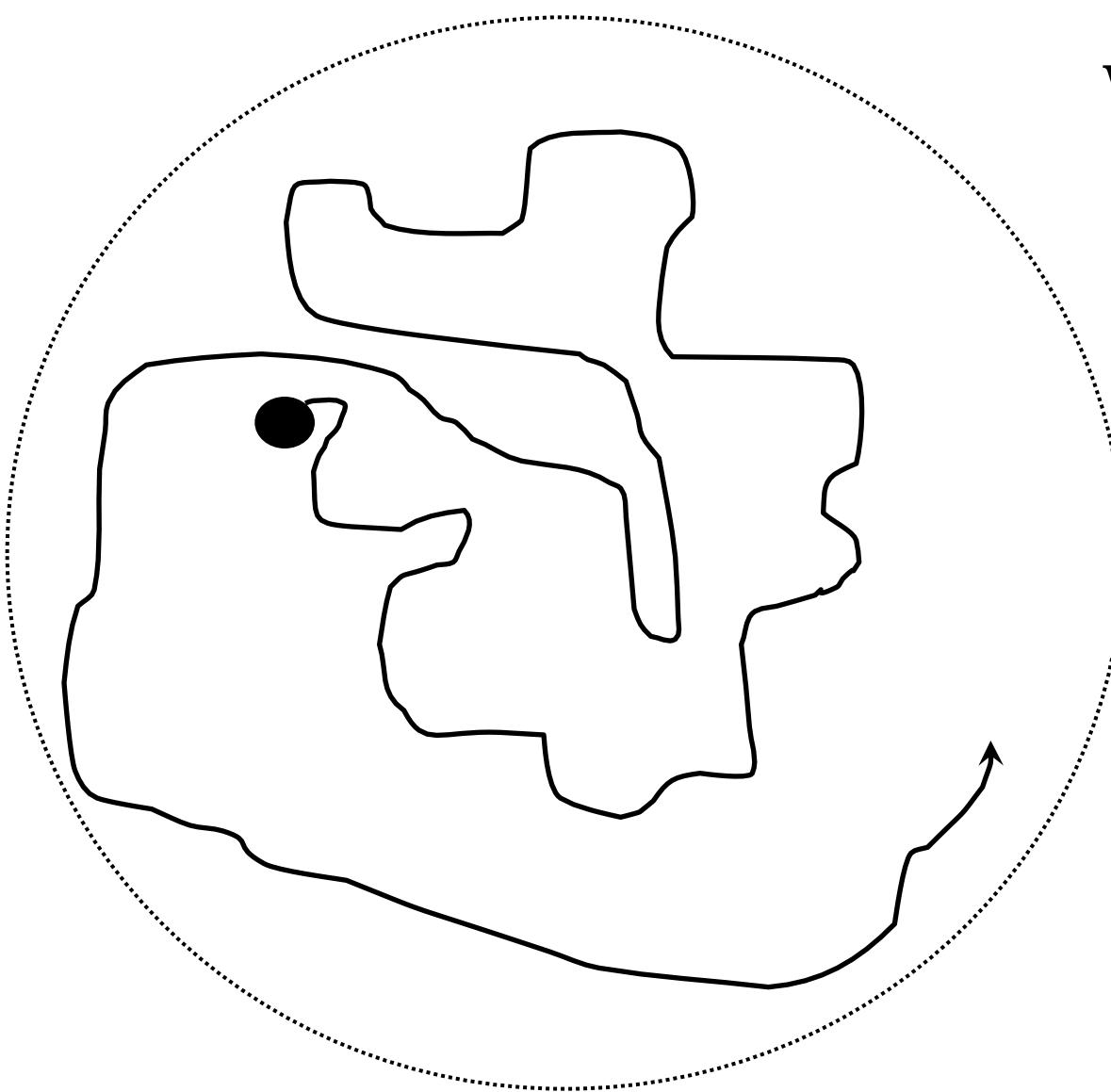


Normal suject

Dyslexic Suject

# Diffusion Imaging

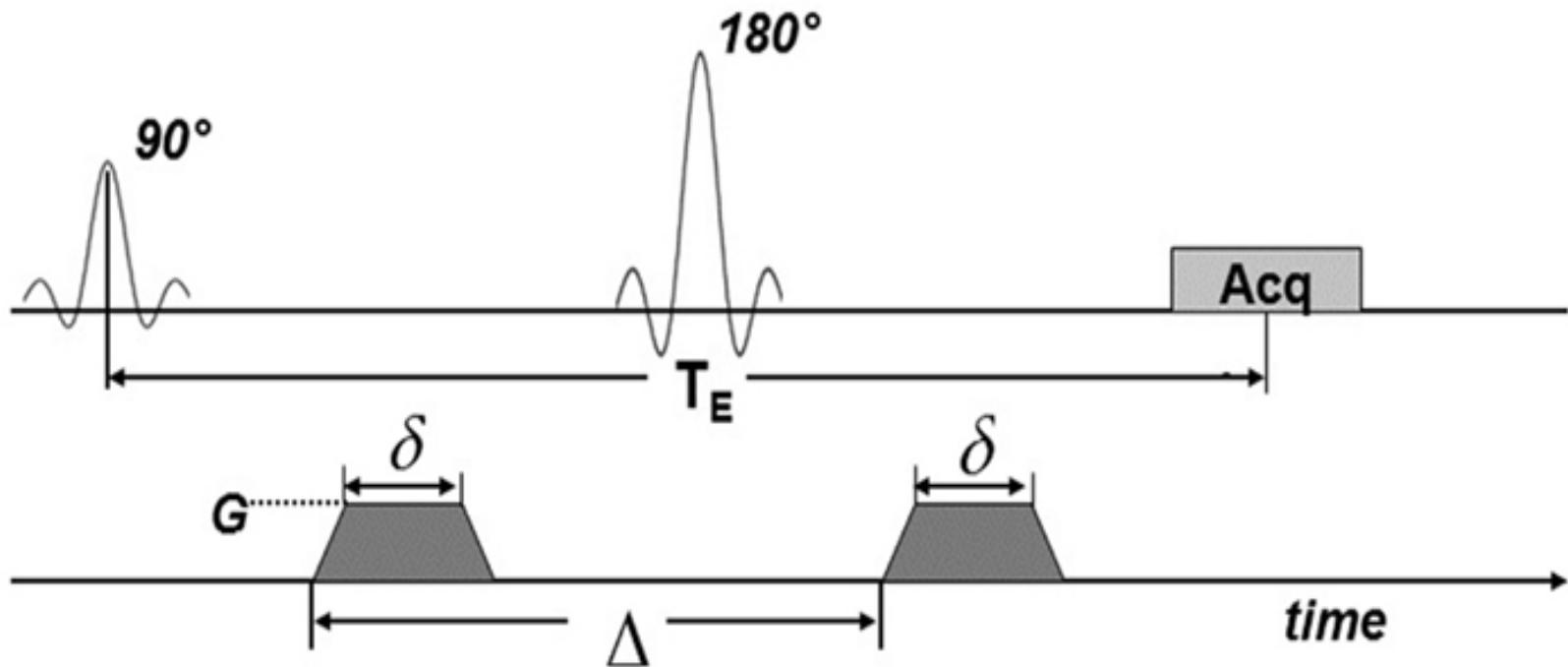
Water Motion



« Brownian » Movement - isotropic and random :  $D$  ( $\text{cm}^2/\text{s}$ )

# Diffusion sequence

$$b = -\gamma^2 G^2 \delta^2 (\Delta - \delta/3)$$

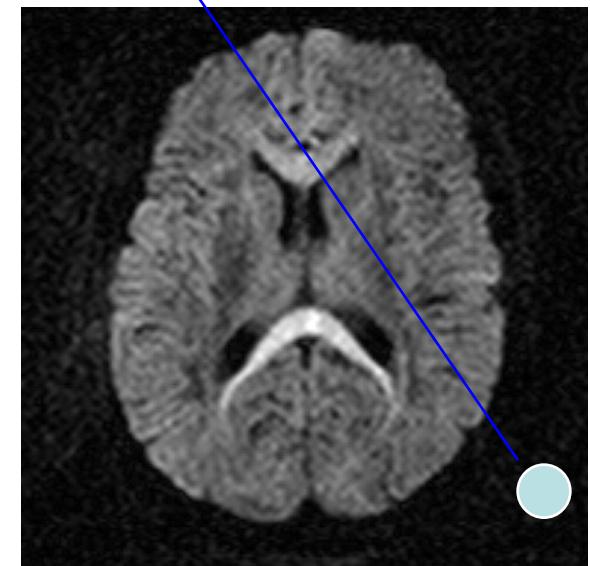
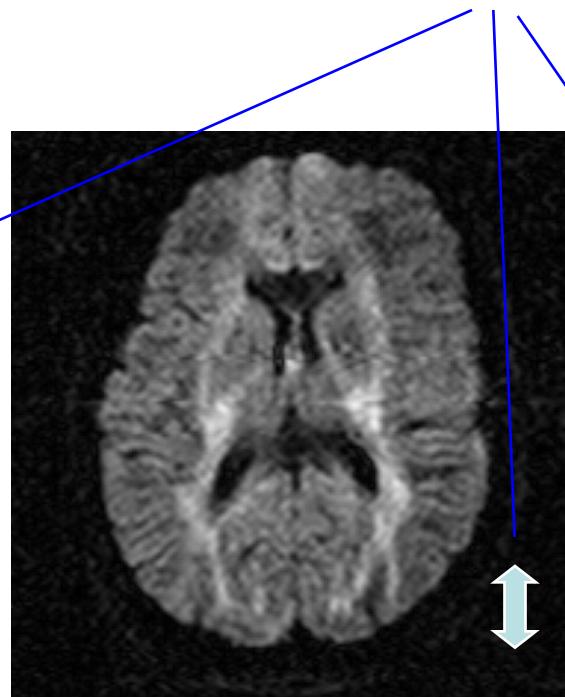
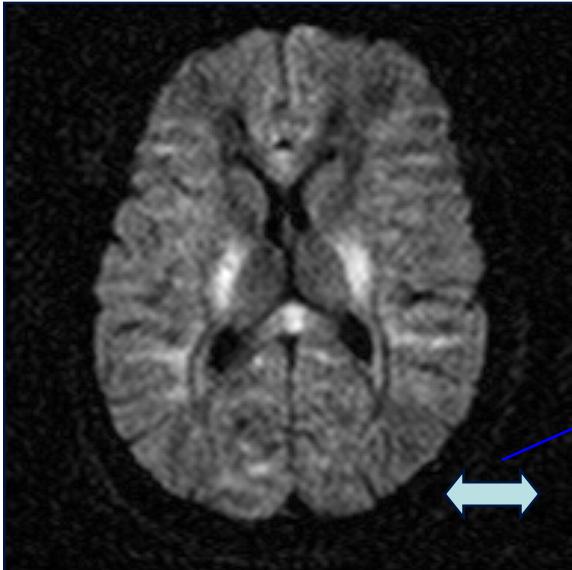


Bipolar gradients reduce the signal of mobile water molecules.

The greater the motion, the greater the signal loss will be ...

# Diffusion Imaging

Signal Intensity sensitive to the direction of water molecular motion

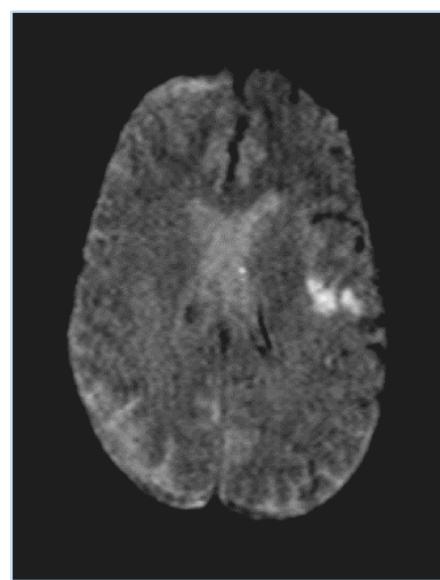


More the water molecular motion is restricted, more the signal intensity on the image will be high (and vice versa)

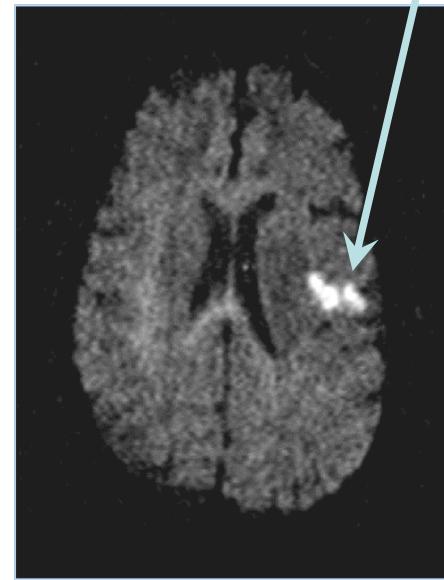
# EPI DIFFUSION



$b=0 \text{ s/mm}^2$



$b=500 \text{ s/mm}^2$

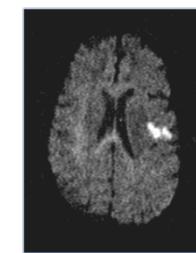
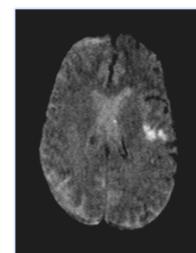
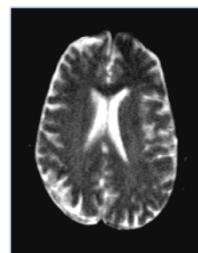
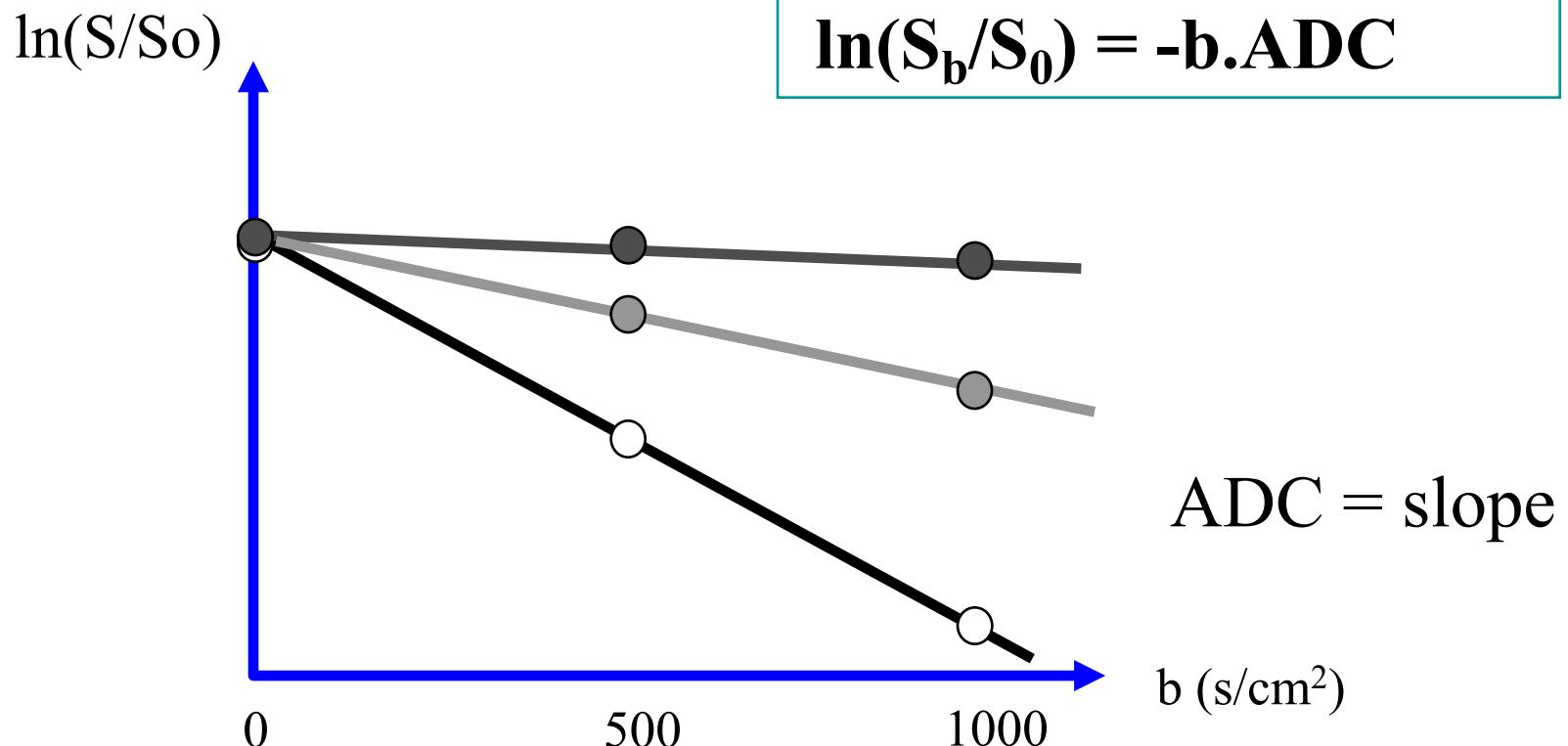


Area of restricted diffusion

$b=1000 \text{ s/mm}^2$

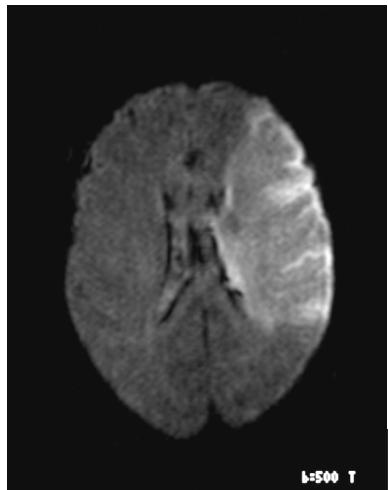
# EPI DIFFUSION

## Apparent Diffusion Coefficient

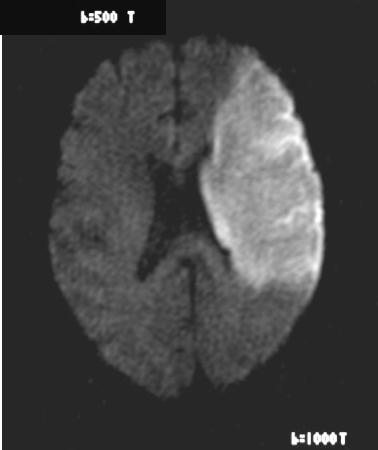


# EPI DIFFUSION

Create an ADC map :



$b=500 \text{ s/mm}^2$

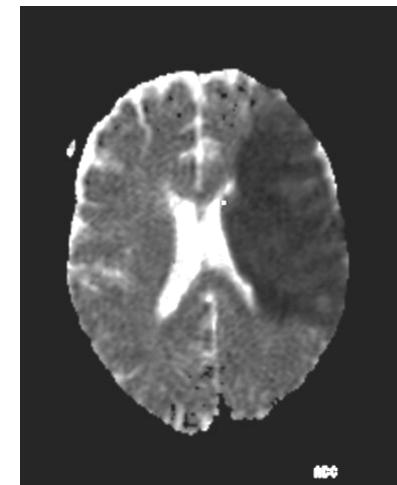


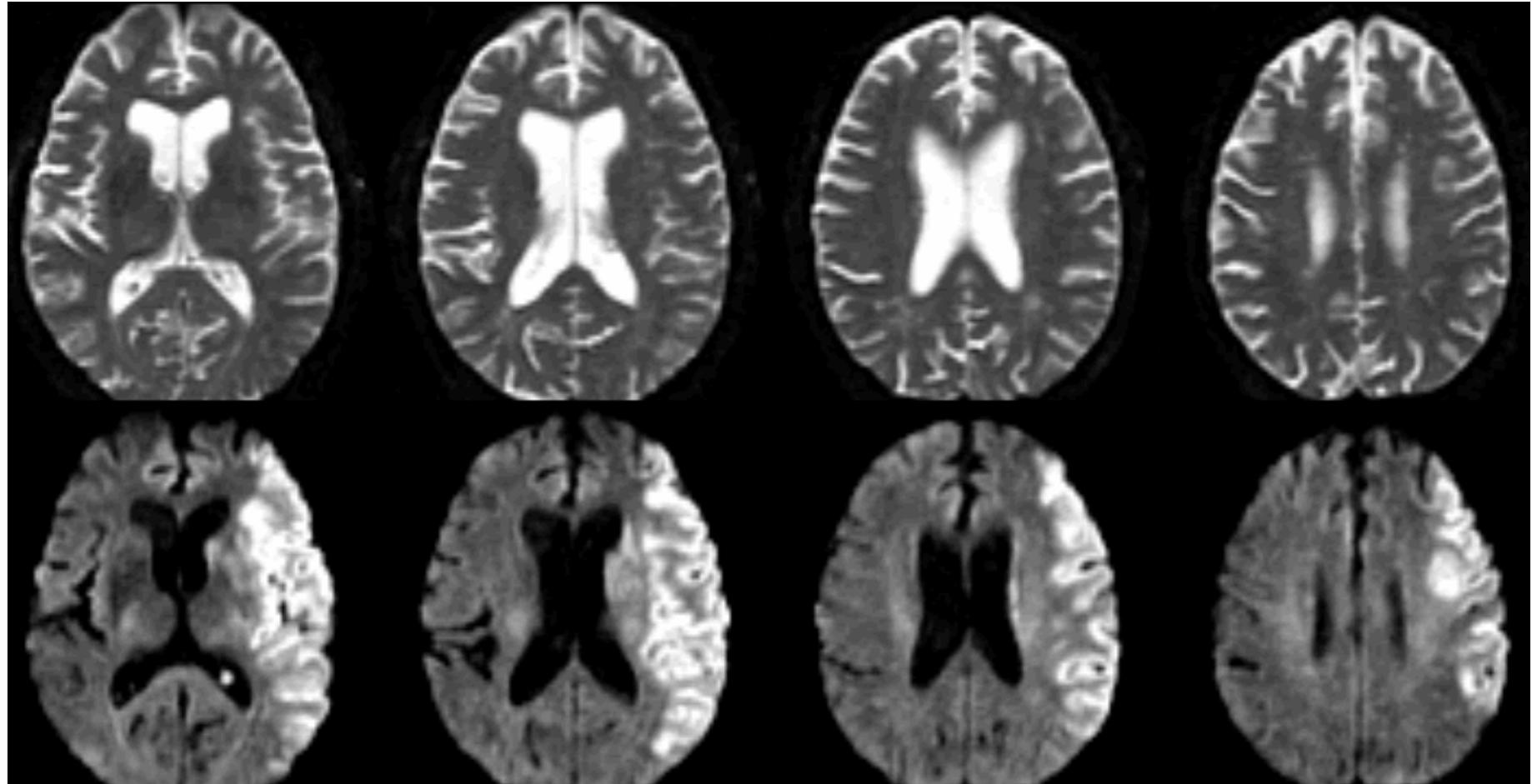
$b=1000 \text{ s/mm}^2$

Post-Processing



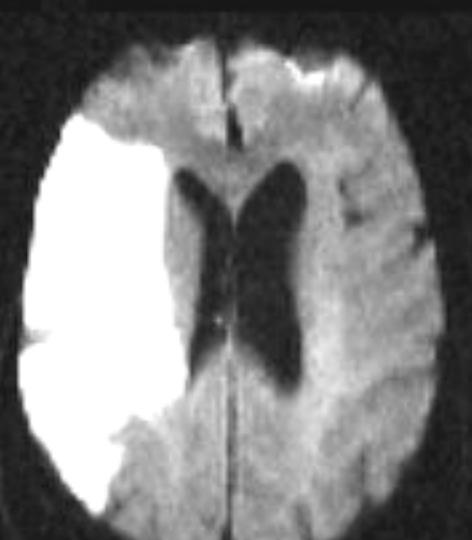
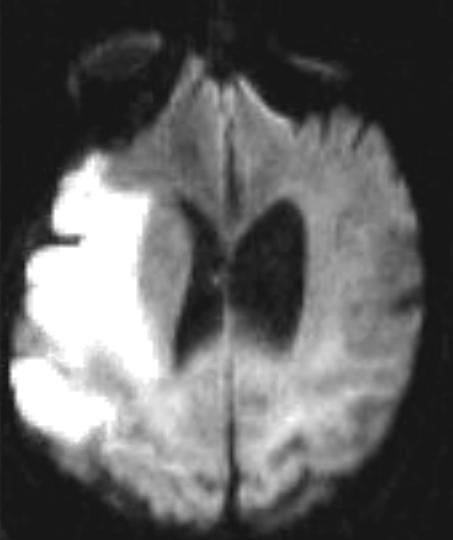
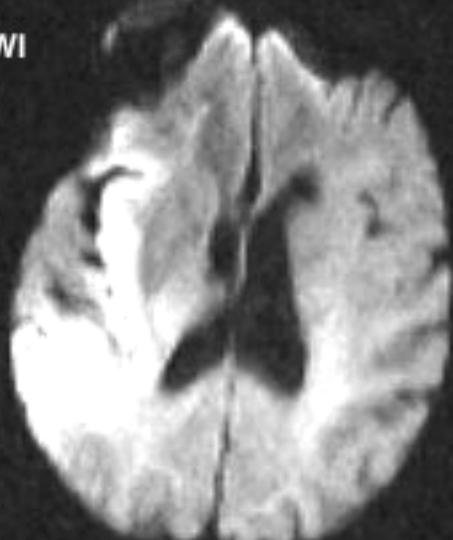
ADC Image



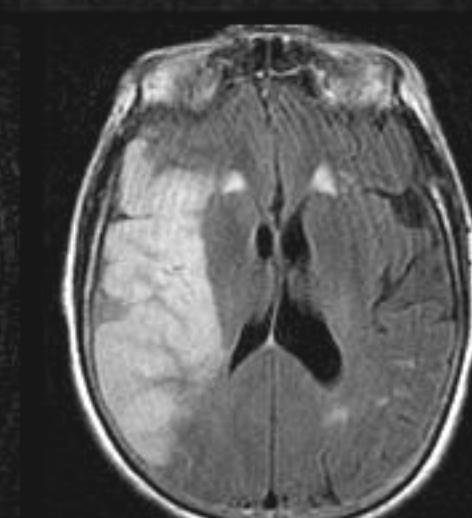
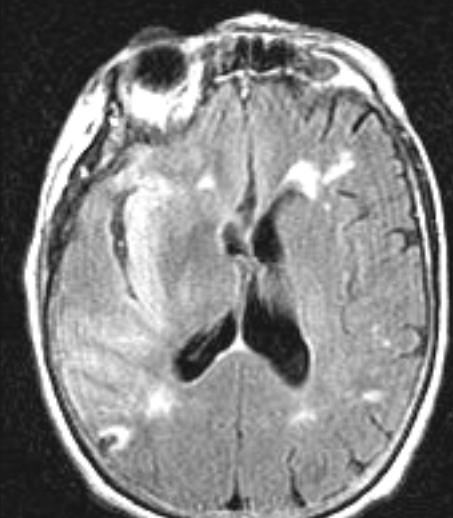
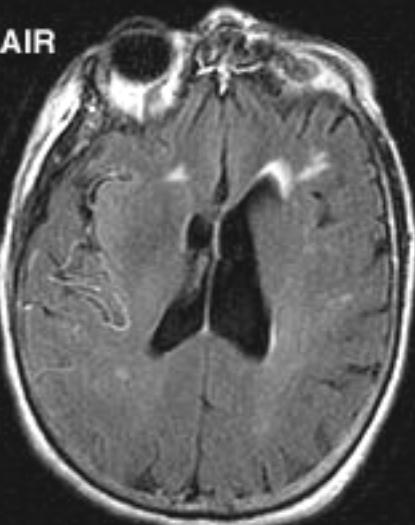


Acute stroke 4 h

DWI



FLAIR



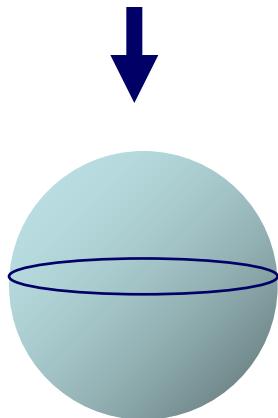
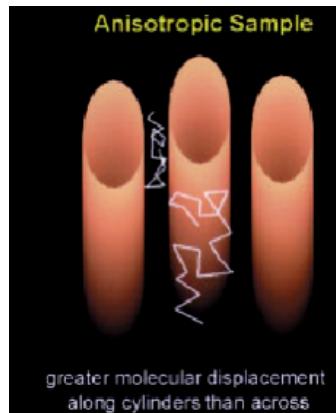
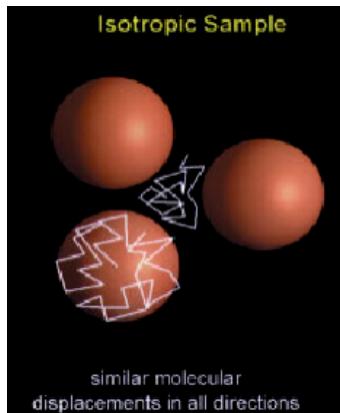
2 Hours

10 hours

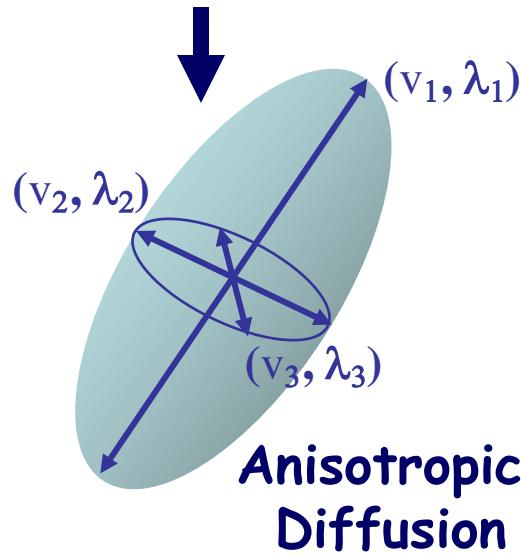
36 hours

# Isotropic and Anisotropic Diffusion of Water Molecules

## Diffusion of water molecules



Isotropic Diffusion

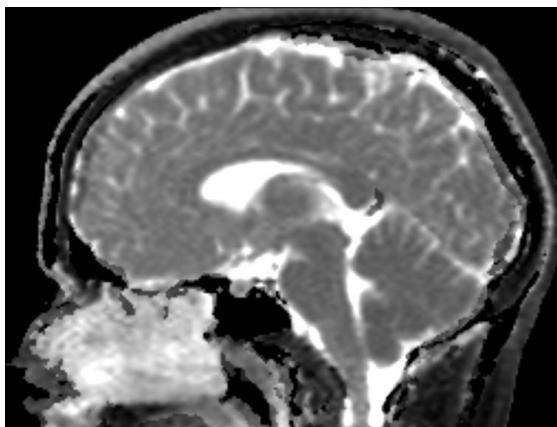


- Isotropic vs Anisotropic diffusion
- Underlying structures of the tissues
  - Faster diffusion along fibres than perpendicular to them
  - Water diffusion anisotropy used to track fibers, estimate white matter integrity

- Tensor model
  - $v_i$  : principal directions of diffusion
  - $\lambda_i$  : associated diffusivities

# Diffusivity & Fractional Anisotropy

## Mean Diffusivity



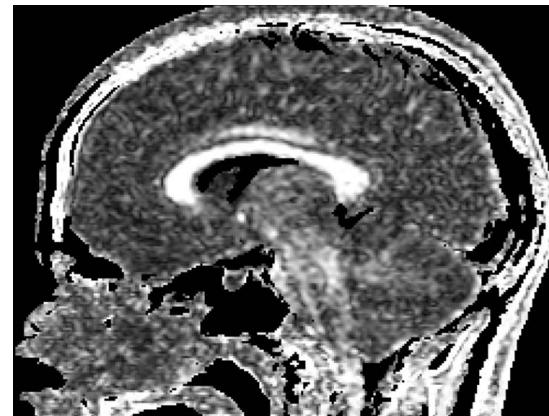
$$\frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

Addition of eigenvalues



**Overall diffusion**

## Fractional Anisotropy



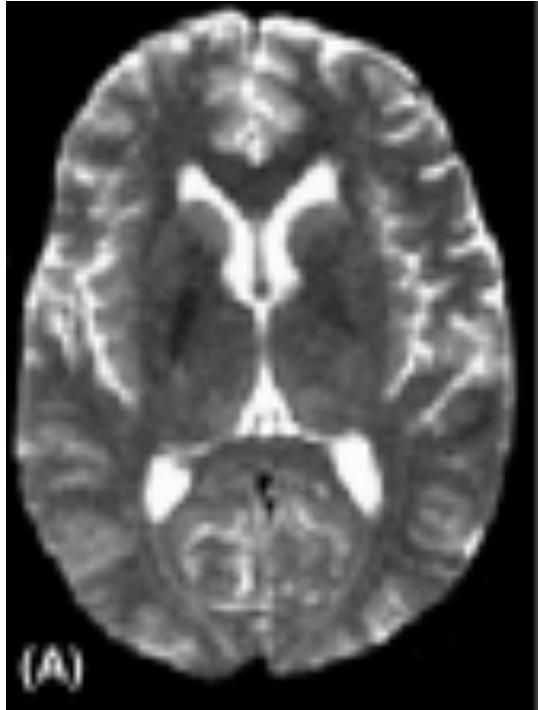
$$\sqrt{\frac{3}{2}} \frac{\sqrt{(\lambda_1 - \hat{\lambda})^2 + (\lambda_2 - \hat{\lambda})^2 + (\lambda_3 - \hat{\lambda})^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

Difference in eigenvalues



**Directional diffusion**

# Fractional Anisotropy Maps



T2-weighted



FA map

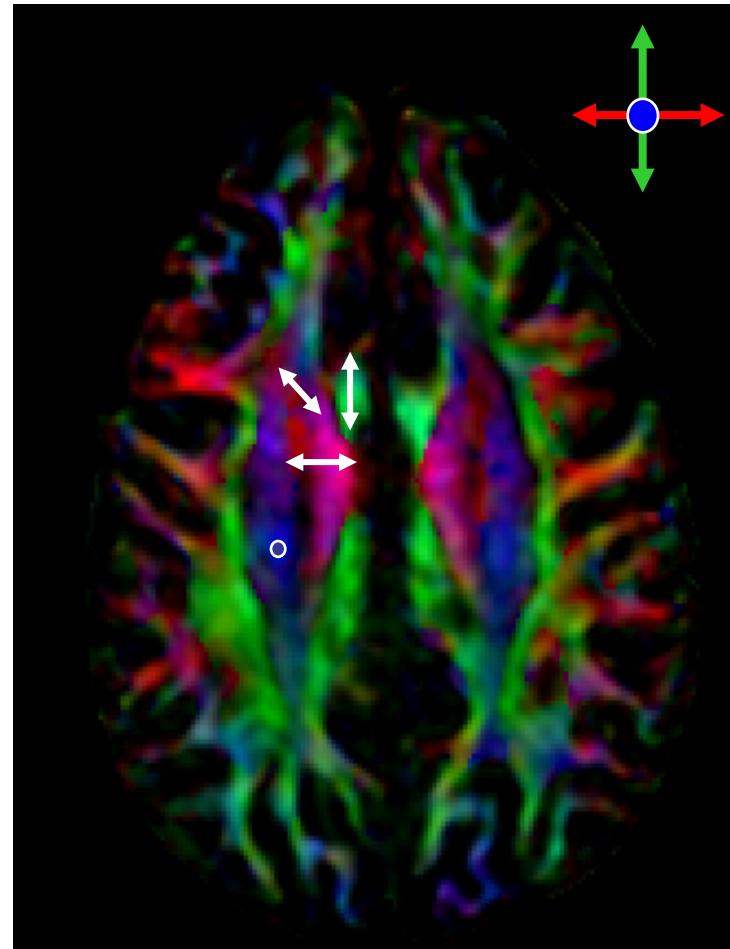
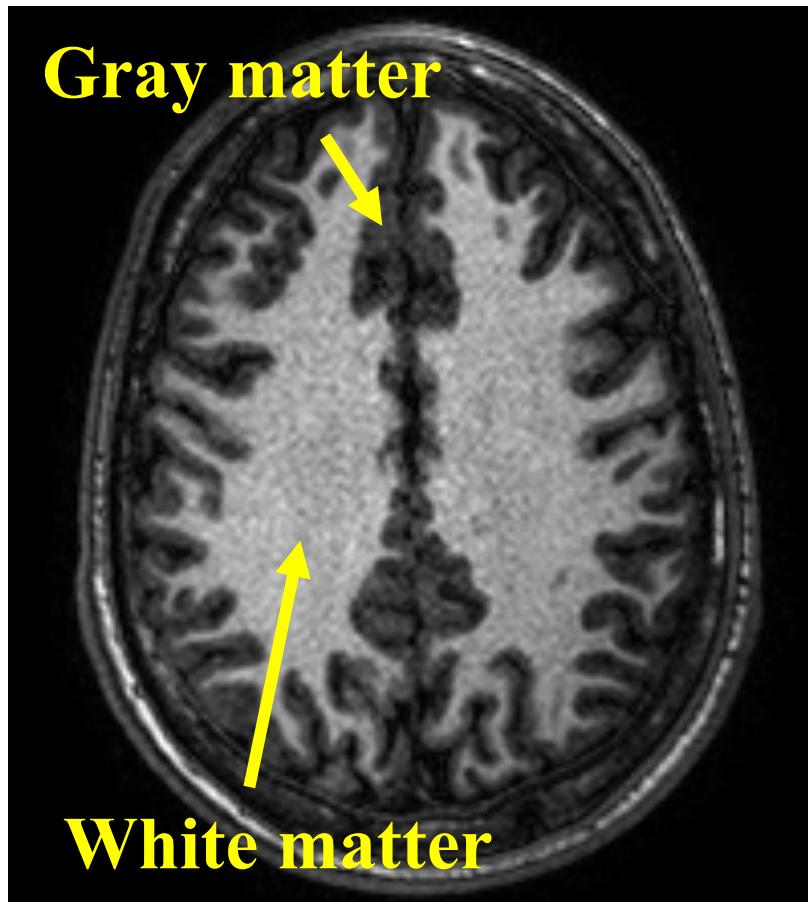
FA maps better depict  
the white matter fibres.

T2\* & FA: Moseley et al. (2002) *Brain & Cognition*; 50:396-413.

Trace: Molko et al. (2001) *Stroke*; 32(9) 2049-54

# Diffusion Tensor MRI (DT MRI)

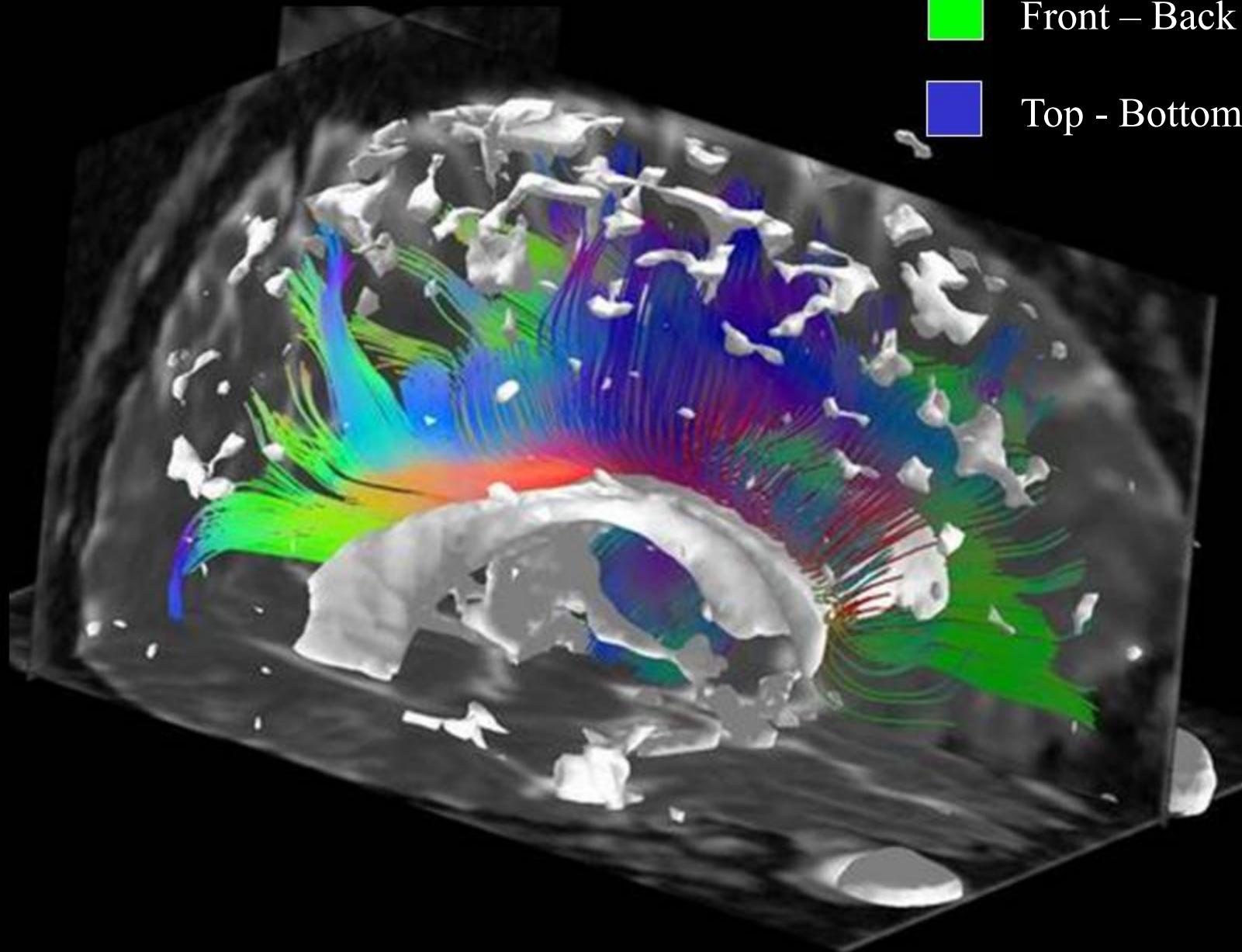
- Reveals white matter structure



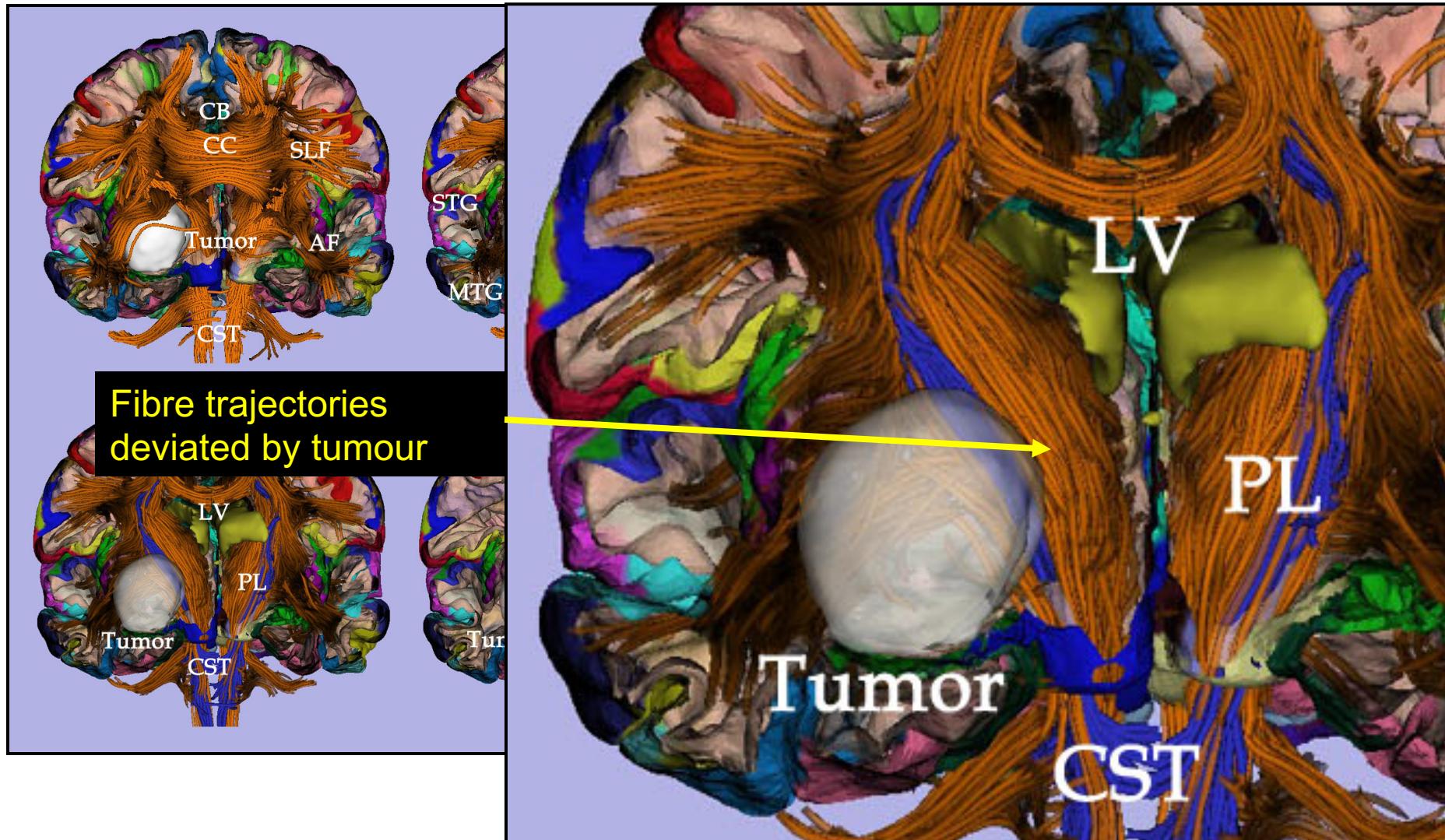
 Right – Left

 Front – Back

 Top - Bottom



# Possible Application in Neurosurgery



# MRI Perfusion using a contrast agent

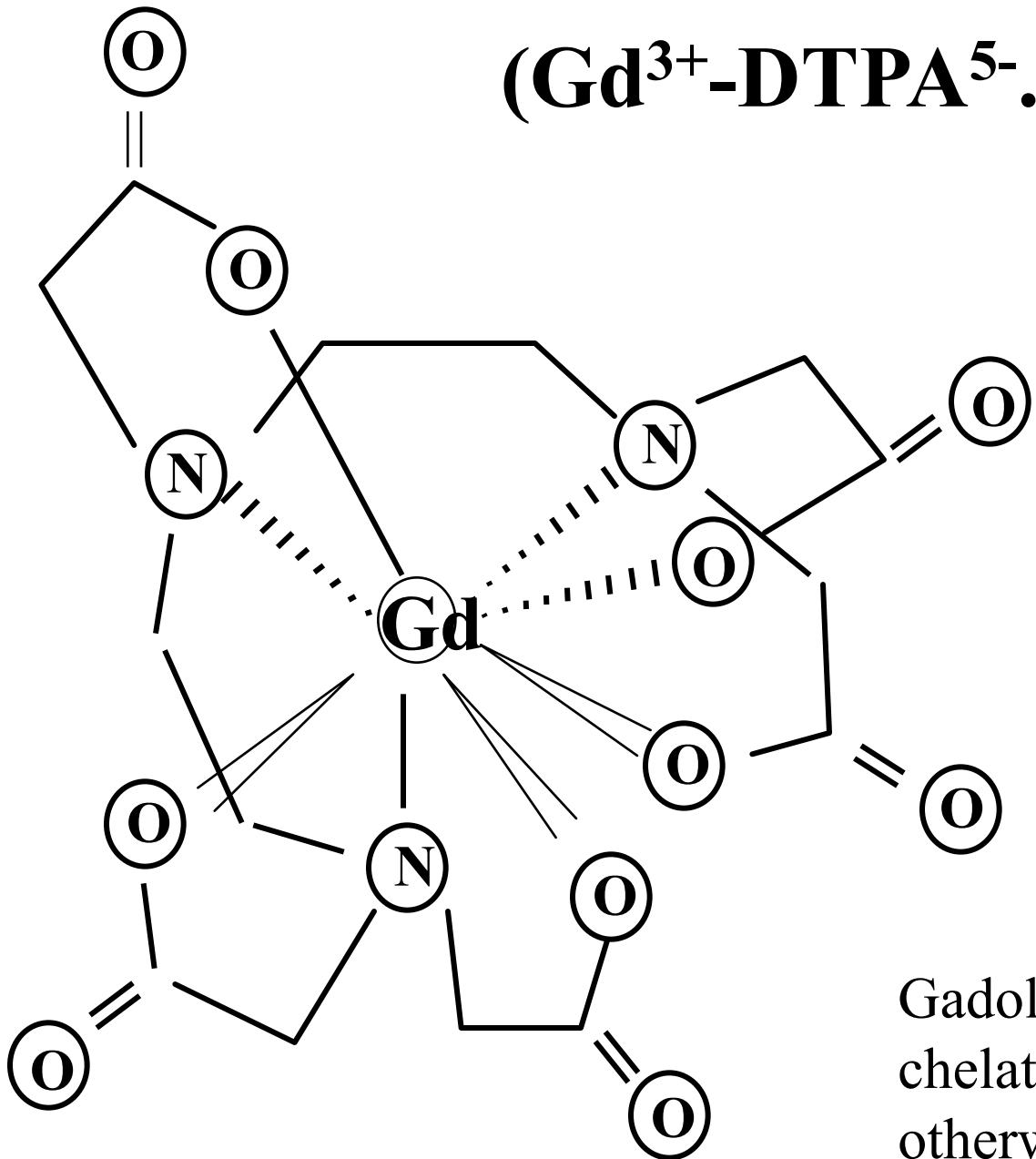
# Paramagnetic Effect

The relaxation times ( $T_1$ ,  $T_2$  and even  $T_2^*$ ) are very sensitive to the presence of paramagnetic ions.

- paramagnetic ion possesses an unpaired electron (deep orbital)
- electron dipole is x1000 that of  ${}^1\text{H}$
- presence of ions reduces massively relaxation times

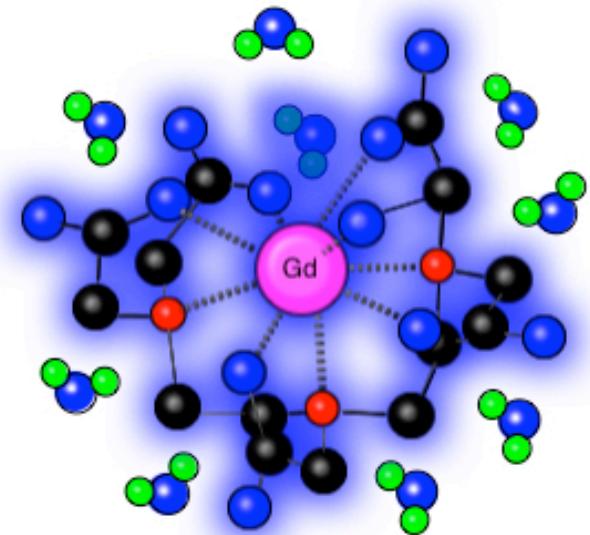
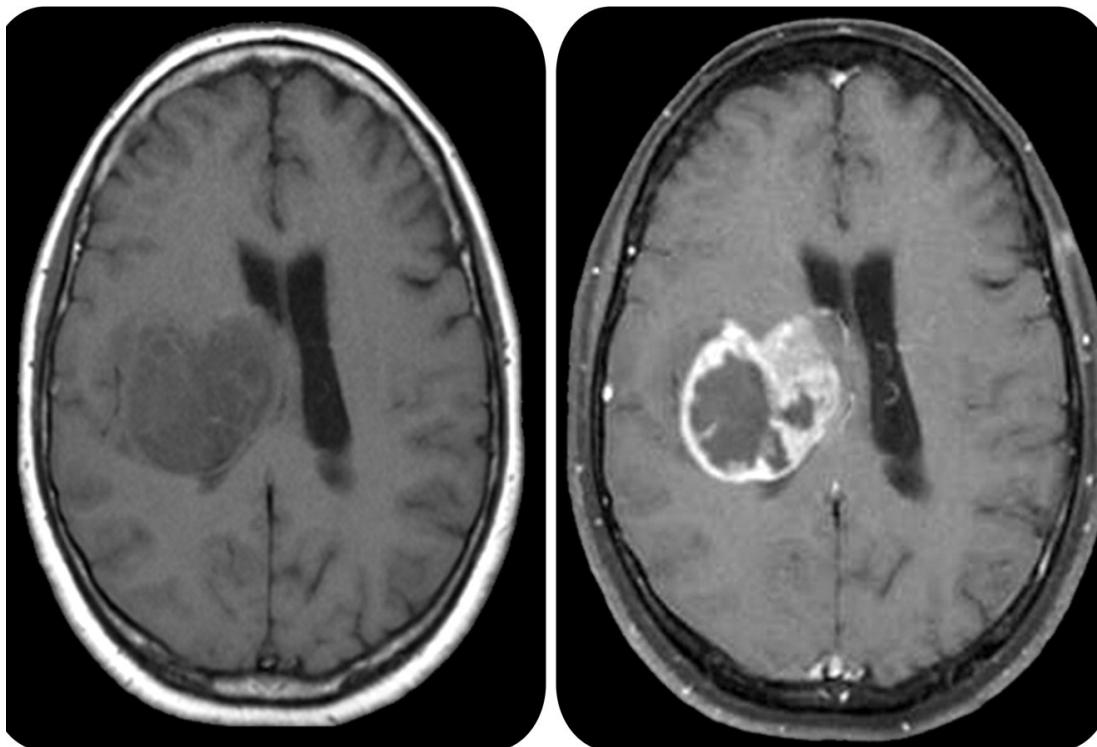
$$1/T_1 = 1/T_{1o} + r_1 \cdot [\text{Agent}]$$

where  $r_1$  is the relaxivity associated with the ion



Gadolinium must be chelated (eg. to DTPA) – otherwise toxic !

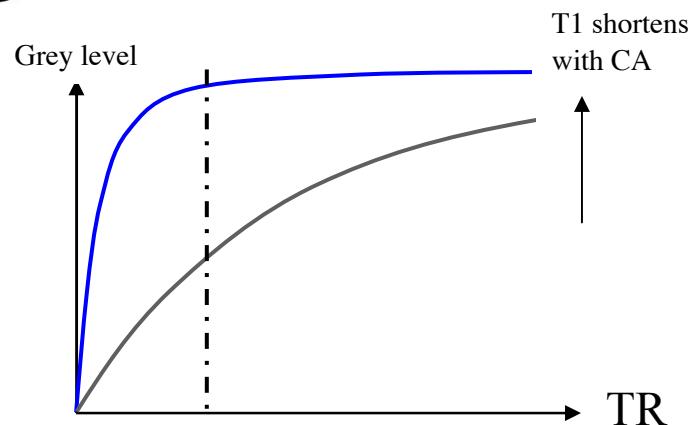
# T1 weighted MRI with Gd contrast agents



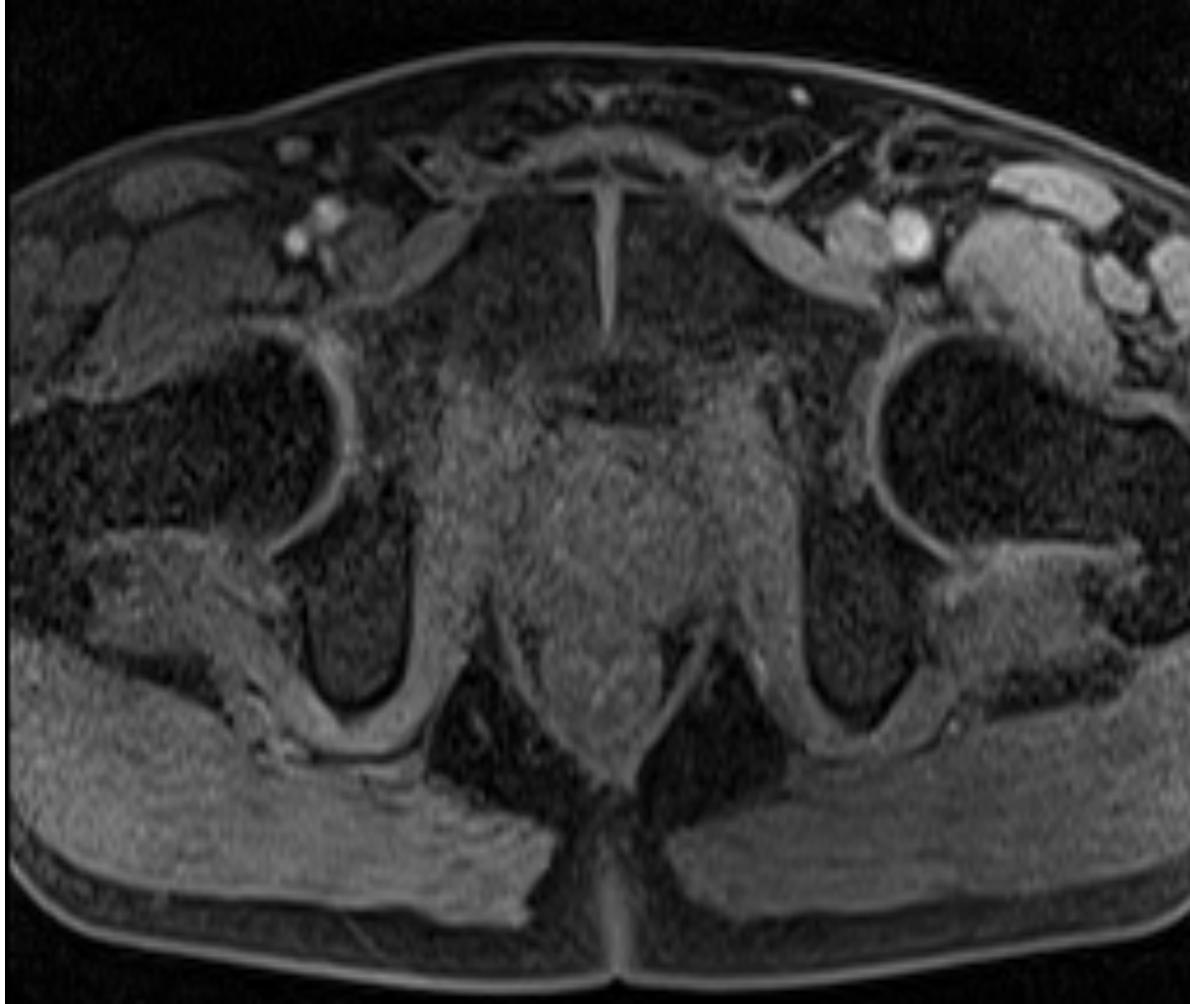
Intravenous injection of paramagnetic agent :

- Drop in T1 of water molecules in blood
- Drop in T1 of water molecules in extracellular space

Drop in T1 = ↑ in signal on T1 image



This sequence is T1 weighted and gives « positive contrast »

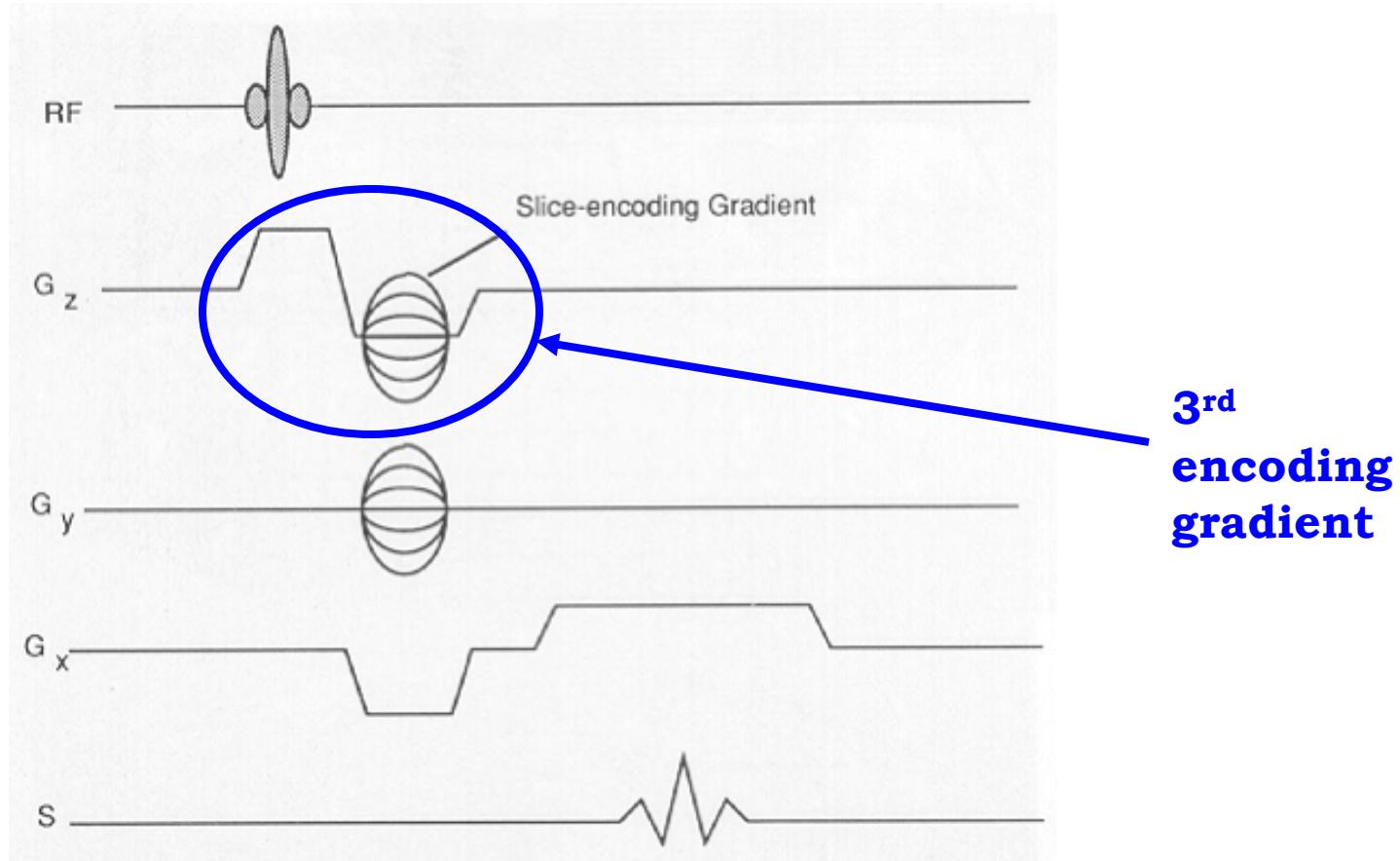


## Cancer of the Prostate

Perfusion Imaging  
using fast 3D T1-  
weighted sequence  
(gradient echo)

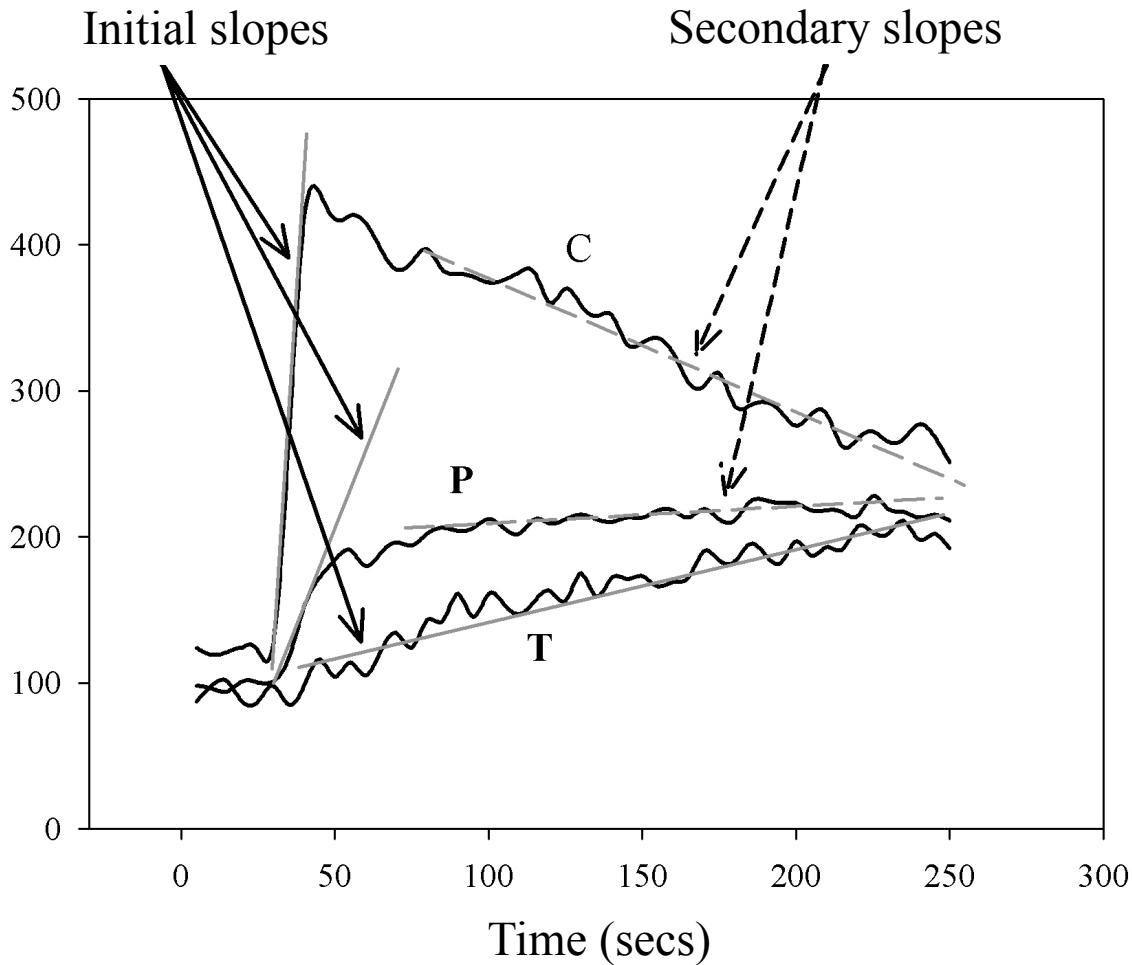
3D block of 16  
slices acquired  
every 6 secs

# Generic 3D GE sequence



$$\text{Scan time} = \text{TR} \cdot N_{\text{phases}} \cdot N_{\text{slices}} \cdot N_{\text{EX}}$$

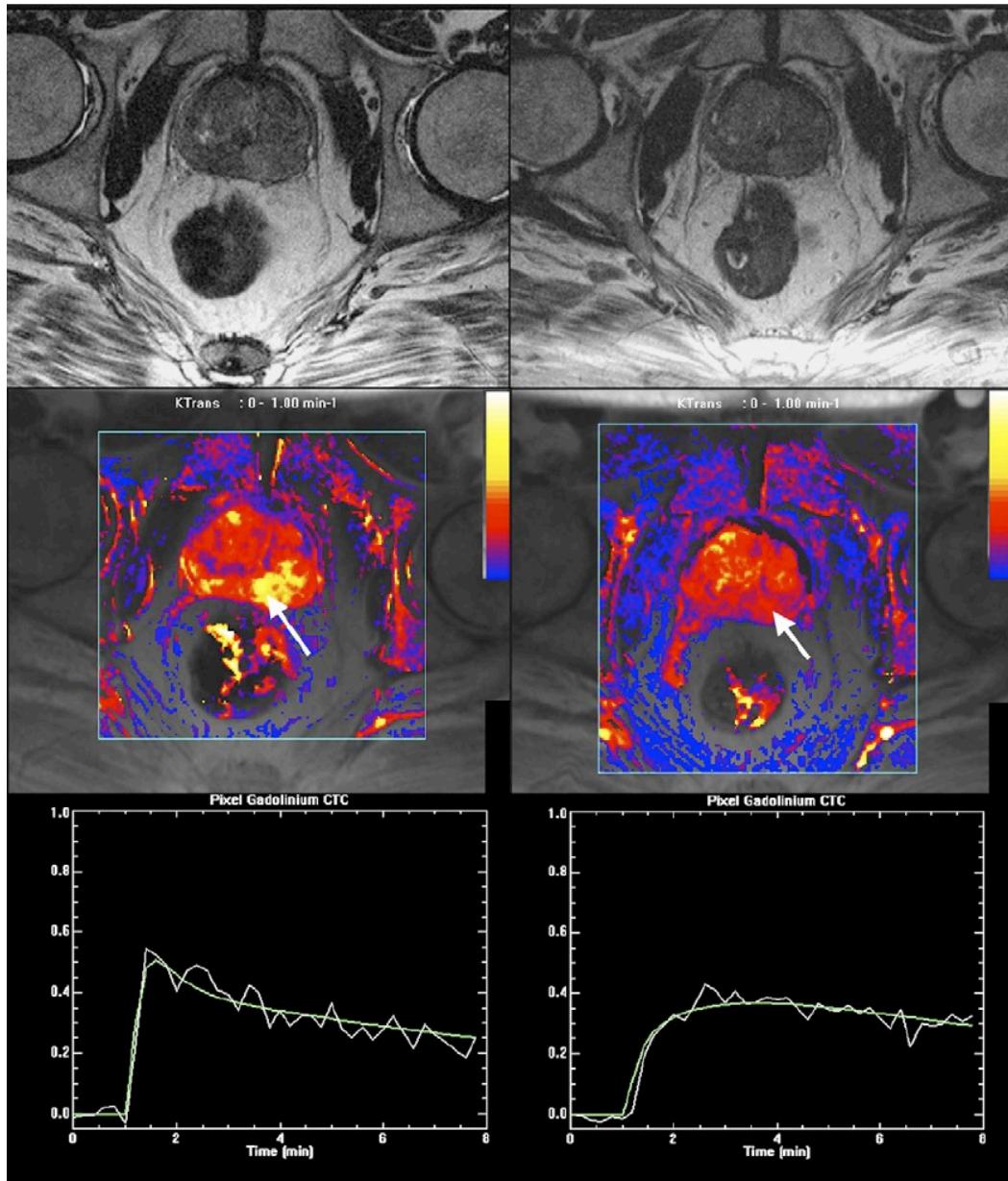
# Typical Curves of Prostate Tissue and of Cancer



Results show differences between

- Max Augmentation of signal
- Initial (wash-in) slopes
- Secondary (washout) slopes

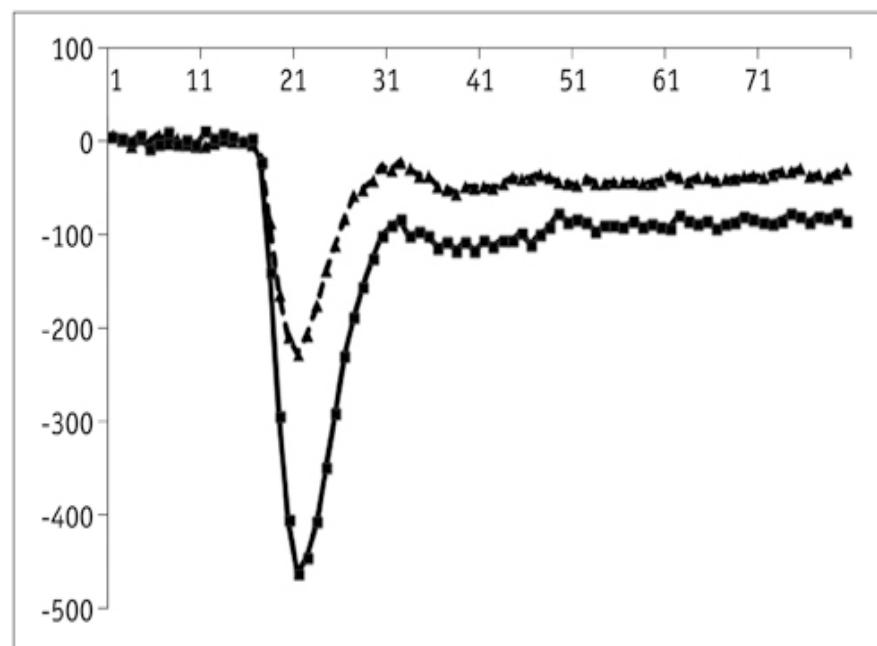
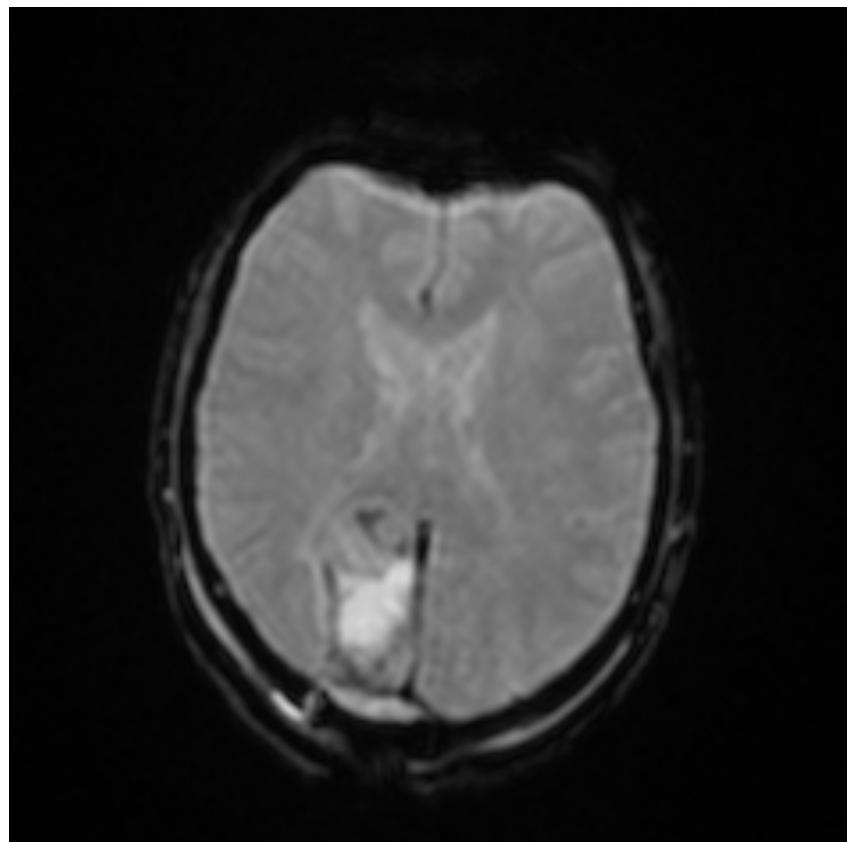
Parametric images of  $K_{trans}^{tr}$  acquired before and 1 month after anti-androgen therapy.



# EPI for T2\* weighted perfusion MRI

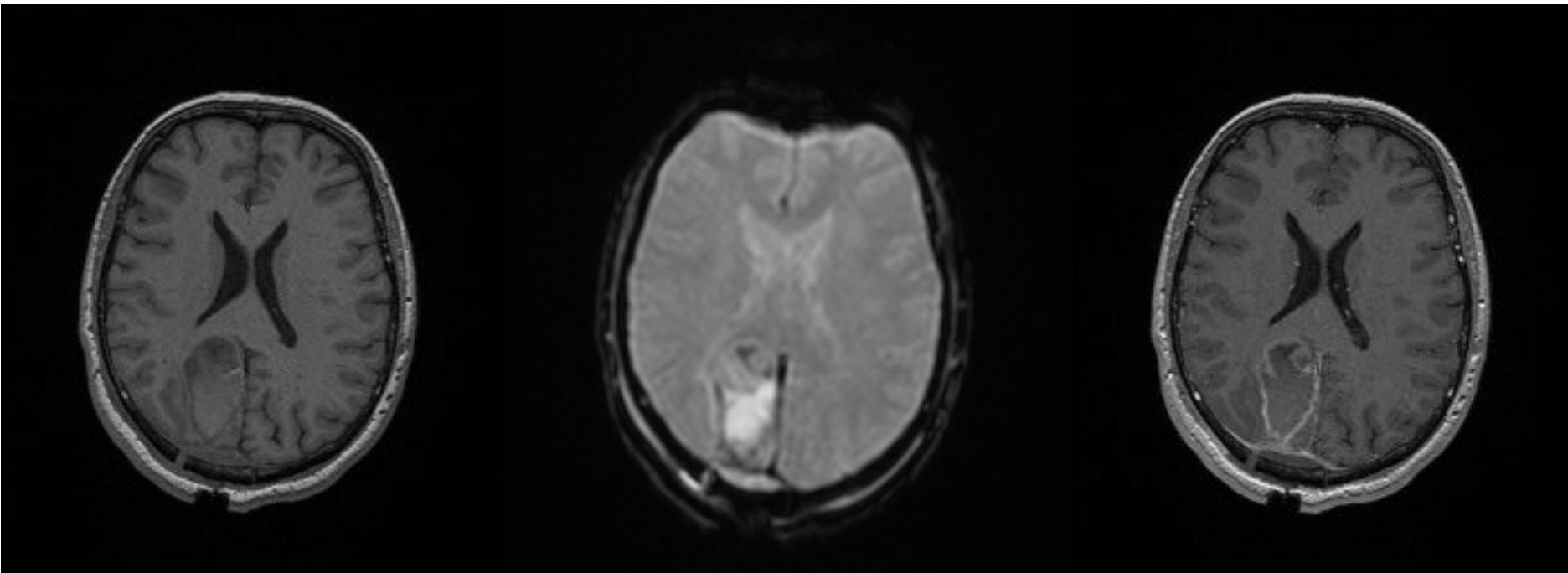
This sequence is T2\* weighted and gives « negative contrast »

Cerebral perfusion is studied using T2\* because the contrast agent cannot pass the BBB. Perfusion studied indirectly with respect to normal vessels.



In practise, we acquire :

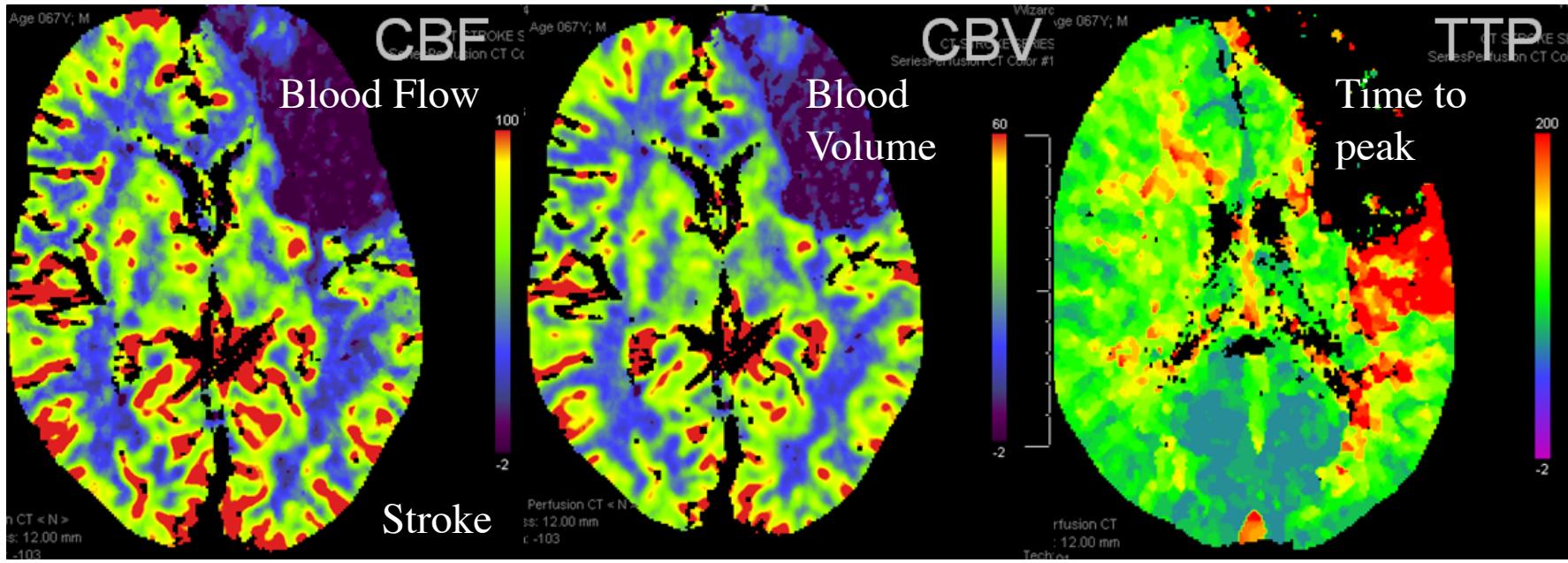
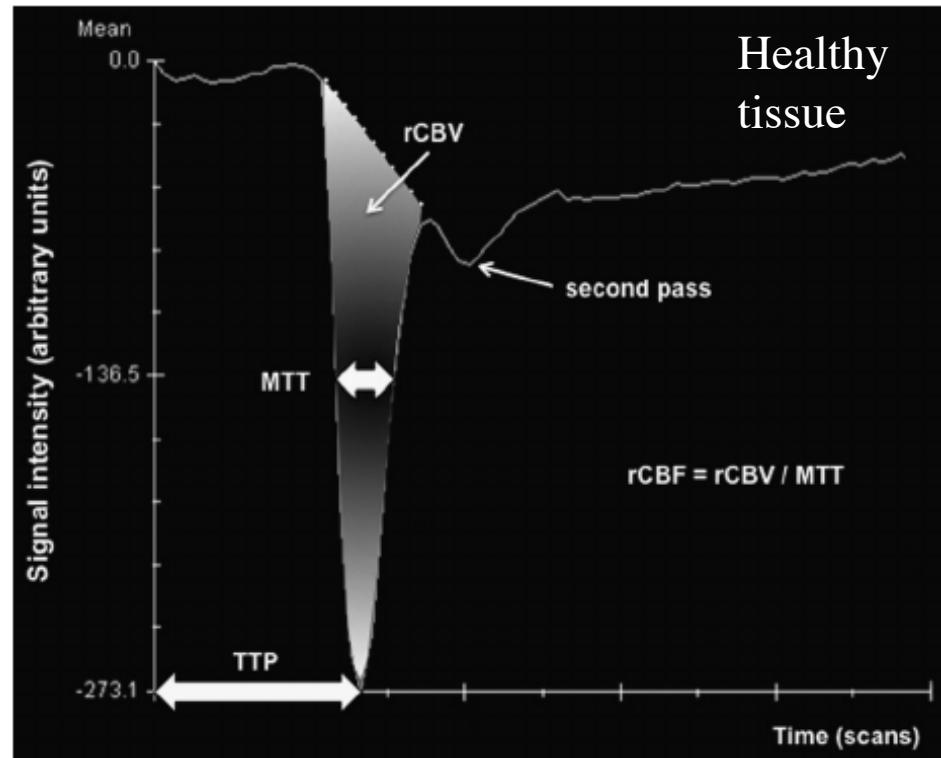
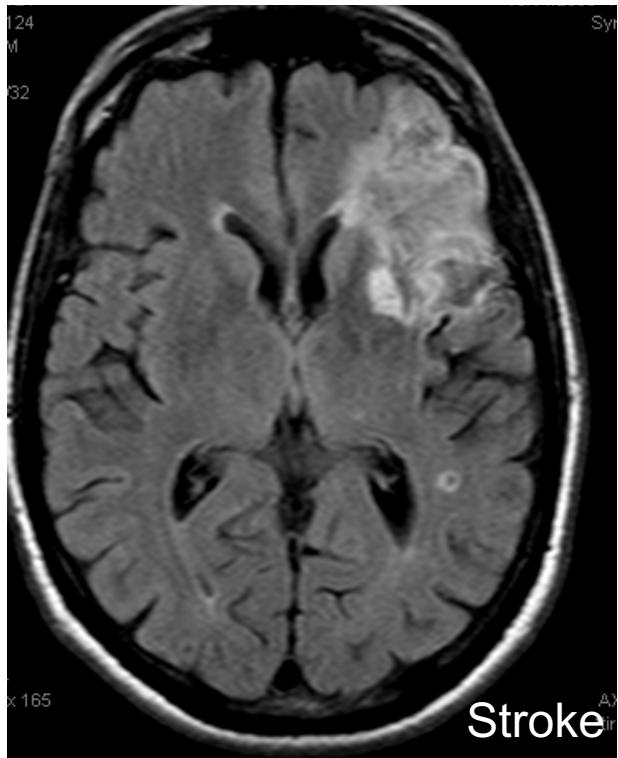
- T1 weighted sequence before Gd injection
- T2\* weighted sequence during Gd perfusion
- T1 weighted sequence after Gd injection



3D T1 GE pre-Gd

Tumour

3D T1 GE post-Gd



# NMR Spectroscopy

# Introduction to NMR spectroscopy

Nuclear magnetic resonance spectroscopy only concerns certain nuclei.

Among these nuclei, those that offer some biological interest are ;

$^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$ ,  $^{23}\text{Na}$  et  $^{31}\text{P}$  for the nuclei with an odd atomic mass number

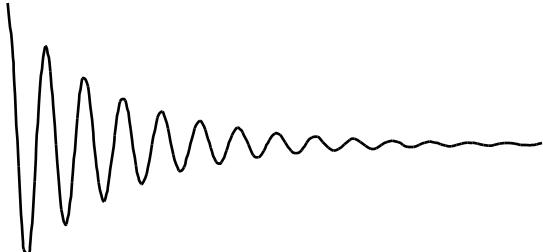
# Relative Sensitivity (ou Receptivity)

Isotope	$\gamma$ ( $10^7 \text{ rad T}^{-1}\text{s}^{-1}$ )	C (%)	D <sub>p</sub>	Frequency (MHz) at 1.5 T
<sup>1</sup> H	26.752	99.985	1.000000	63.8
<sup>13</sup> C	6.728	1.108	0.000176	16.0
<sup>19</sup> F	25.181	100	0.834	60.1
<sup>31</sup> P	10.841	100	0.0665	25.9
<sup>23</sup> Na	7.080	100	0.0185	16.9

Receptivity D = |  $\gamma^3 C$  | , where  $\gamma$  is the gyromagnetic ratio et C is the natural abundance of the nucleus.

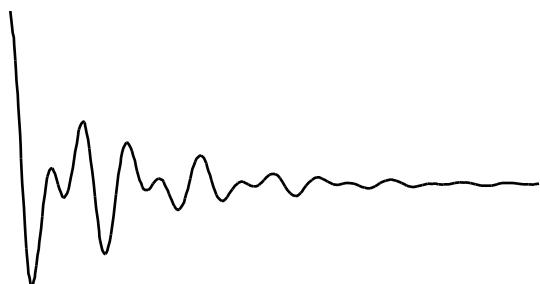
# The NMR signal

After exciting the « spins » via a radio-frequence pulse, the signal is captured by the probe in the form of a damped sinusoidal emission.



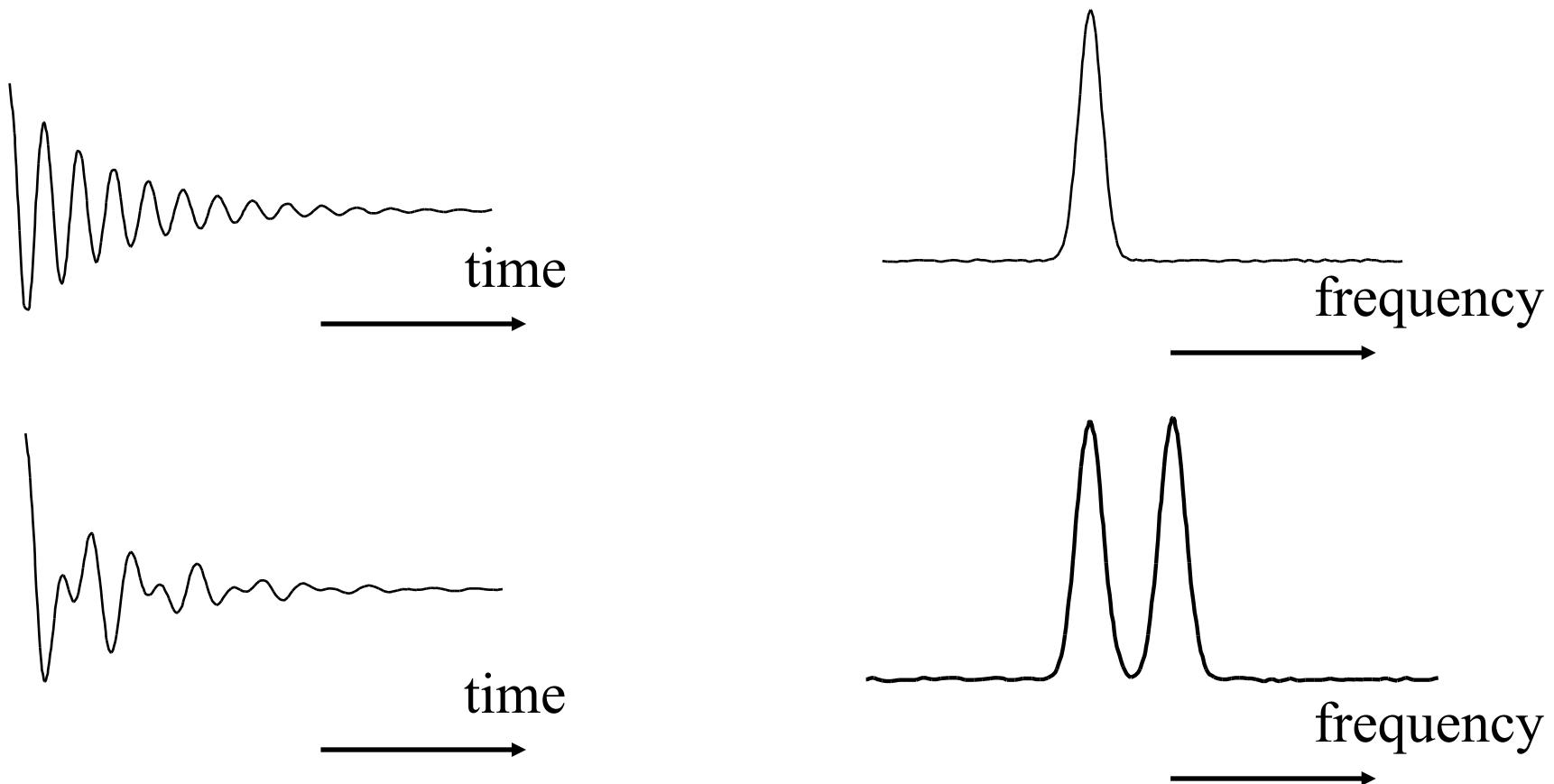
The Free Induction Decay (ou FID) is characterised by

- a) its frequency composition
- b) a decay modulated by  $T_2^*$

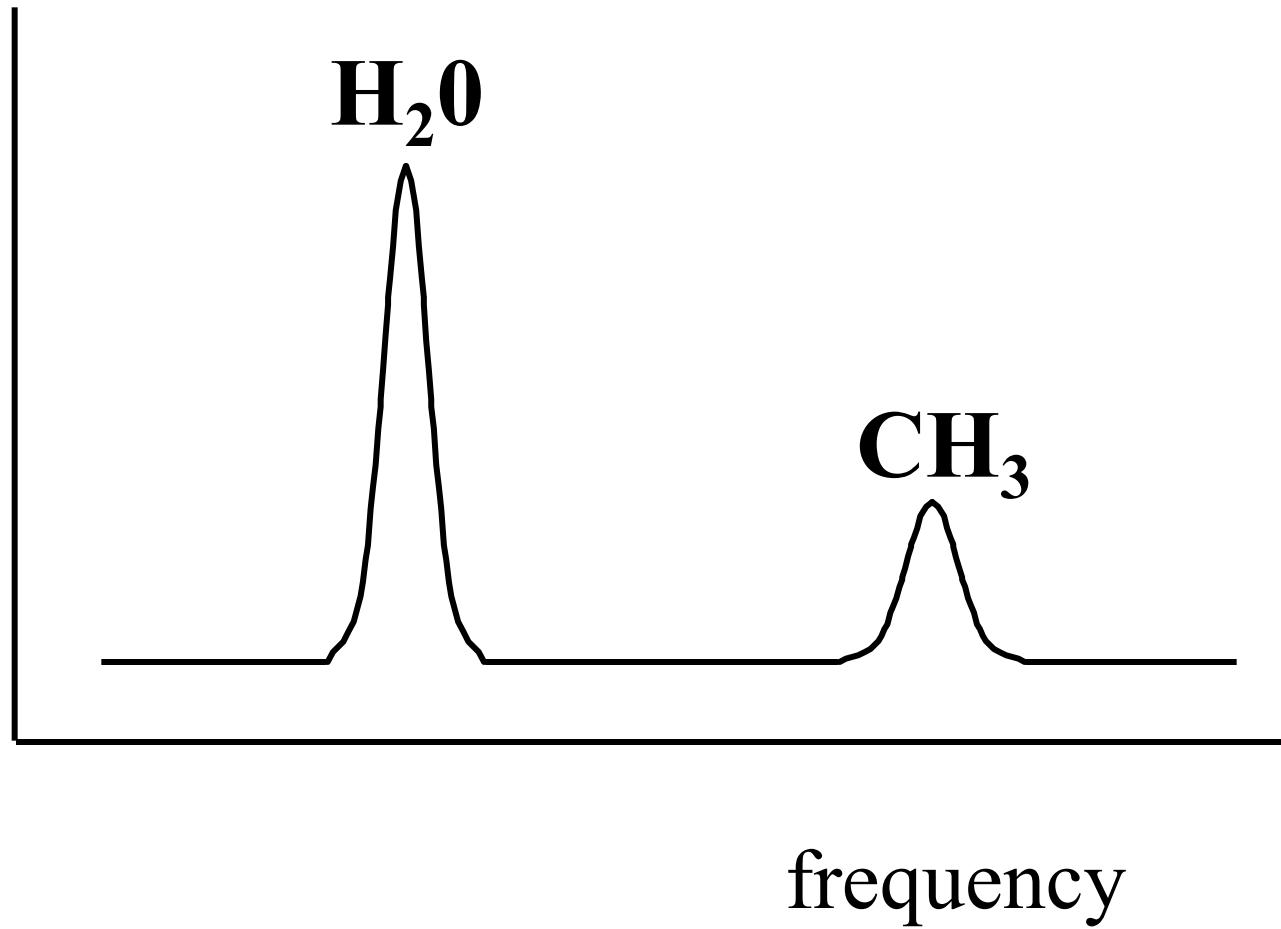


# The Fast Fourier Transform

Reading the FID is not simple for the human eye and in order to afin extract frequency information from the signal, one needs to convert this time-varying signal into the frequency domain.



# Chemical Shift



# Frequency composition and the chemical shift

Consider the case of a single nuclear species ie. the  $^1\text{H}$  nucleus.

The Larmor frequency ( $\nu$ ) of the nucleus is proportional to the strength of the external magnetic field ( $B_o$ ) felt by the nucleus.

$$\nu = \gamma B_o / 2\pi$$

However, this external magnetic field,  $B_o$ , may be different according to the particular chemical environment around the nucleus.

Around each nucleus there is an electron cloud specific of the atom.

In the presence of  $B_o$ , electron movement is such that a supplementary small intensity magnetic field is created and in opposition with respect to the principal external magnetic field  $B_o$ .

Depending on the electronic density distribution and on the chemical bonds formed in proximity to the nucleus, the latter will be influenced by an effective magnetic field that will be slightly different from  $B_o$ .

$$\nu = \gamma (B_o - \sigma B_o) / 2\pi = \gamma B_o (1 - \sigma) / 2\pi$$

where  $\sigma$  is the screening constant and depends on the specific environment around each nucleus.

If the chemical environment varies from one nucleus to the next, the effective magnetic field  $B_{\text{eff}}$ , and thus the resonance frequency, will differ for each nucleus.

This phenomenon is called « chemical shift » and is expressed in p.p.m (parts per million) in order to render it independant of the absolute value of the main field  $B_0$ .

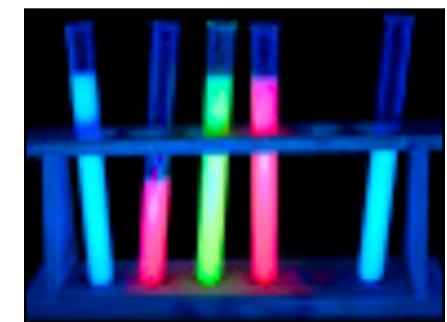
$$\delta = [(\nu - \nu_{\text{ref}}) / \nu_{\text{ref}}] \times 10^6 \text{ ppm}$$

but  $\nu_{\text{ref}} \sim \nu_0$ , the nominal frequency

$$\delta = [(\nu - \nu_{\text{ref}}) / \nu_0] \times 10^6 \text{ ppm}$$

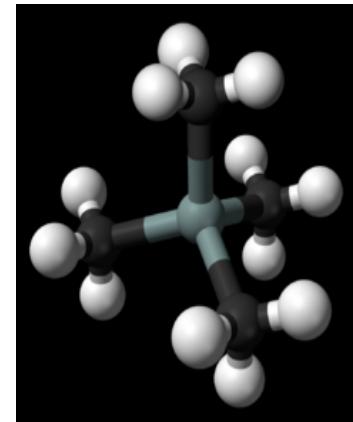
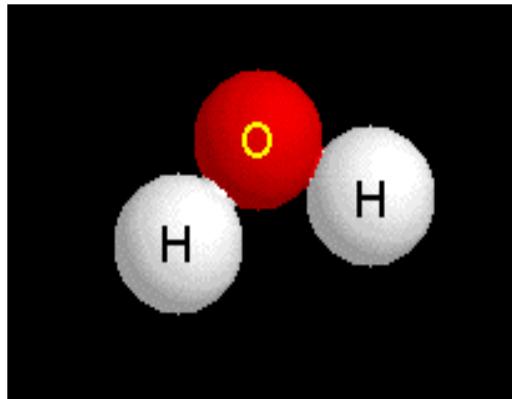
$\text{H}_2\text{O}$

$\text{Si}(\text{CH}_3)_4$



4.7 ppm

0.0 ppm

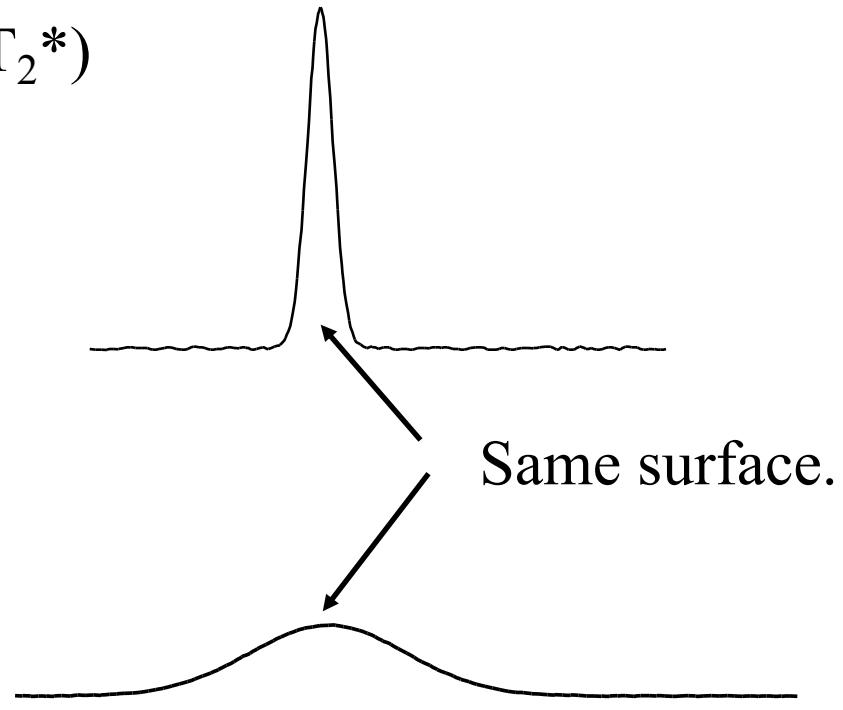
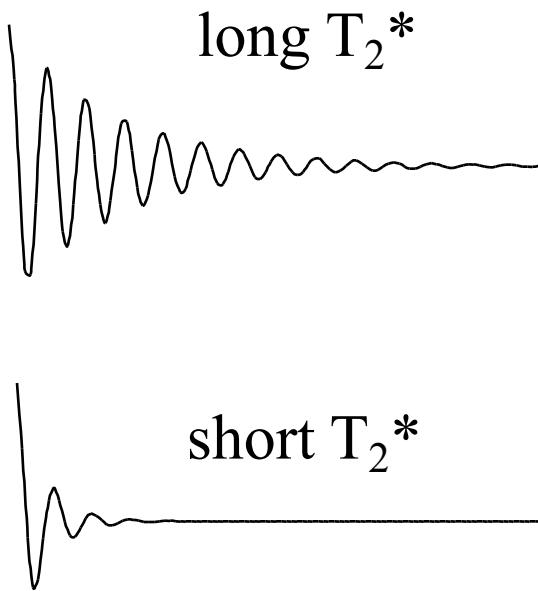


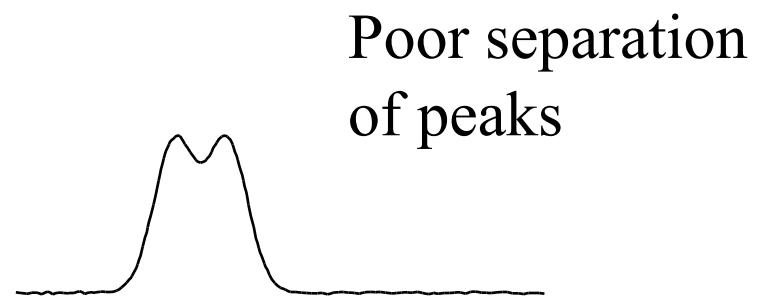
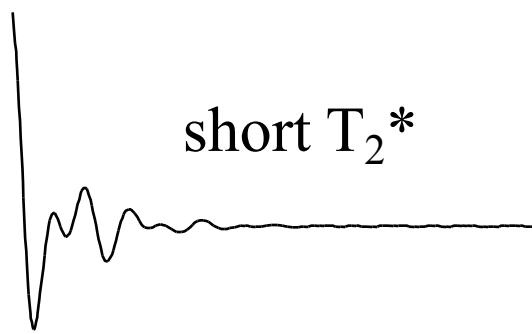
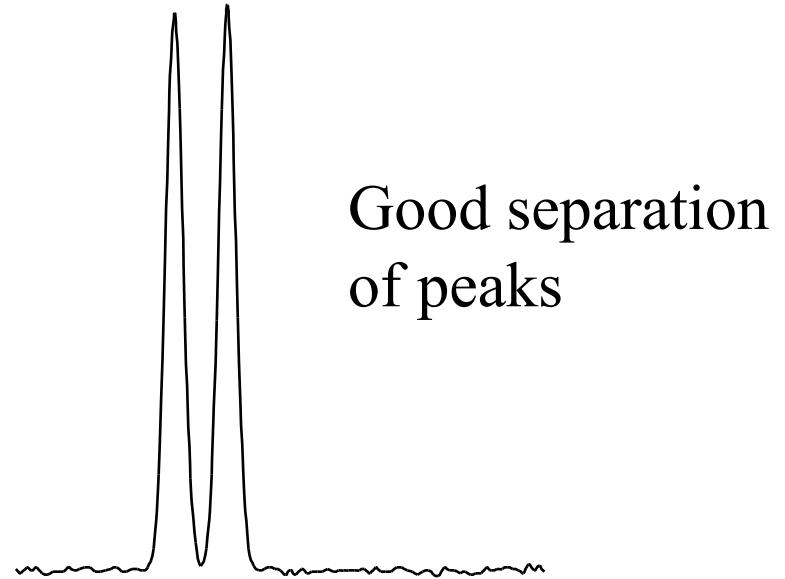
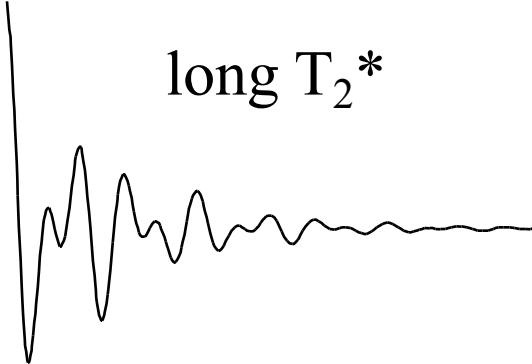
TMS

# Basic characteristics of the spectra : $T_2^*$

The relaxation time  $T_2^*$  is related to the heterogeneity of the principal magnetic field  $B_0$ . This parameter influences the width of the resonant peaks.

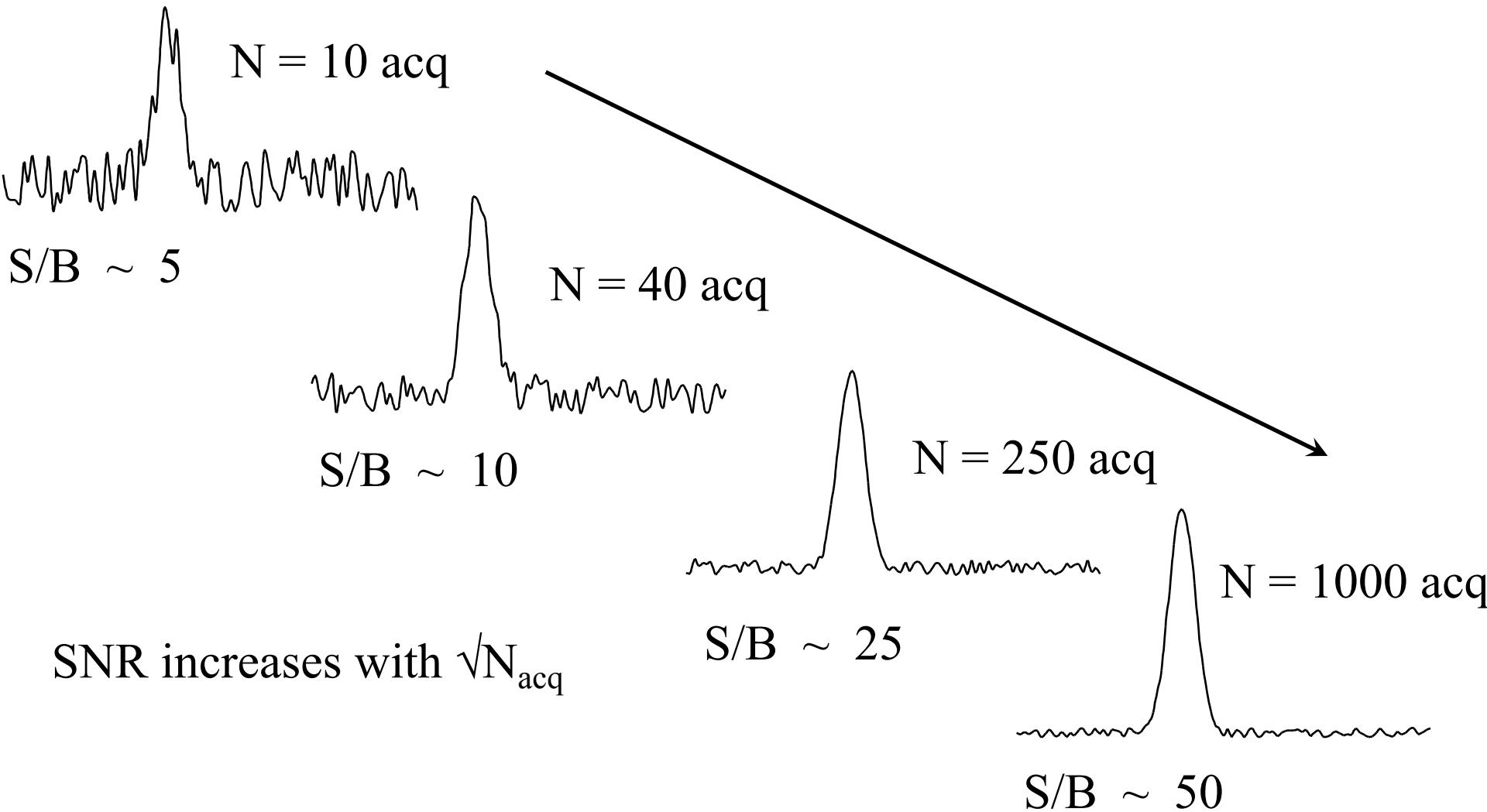
$$\nu_{1/2} = 1/(\pi T_2^*)$$





Conclusion : Need a very good magnetic field homogeneity

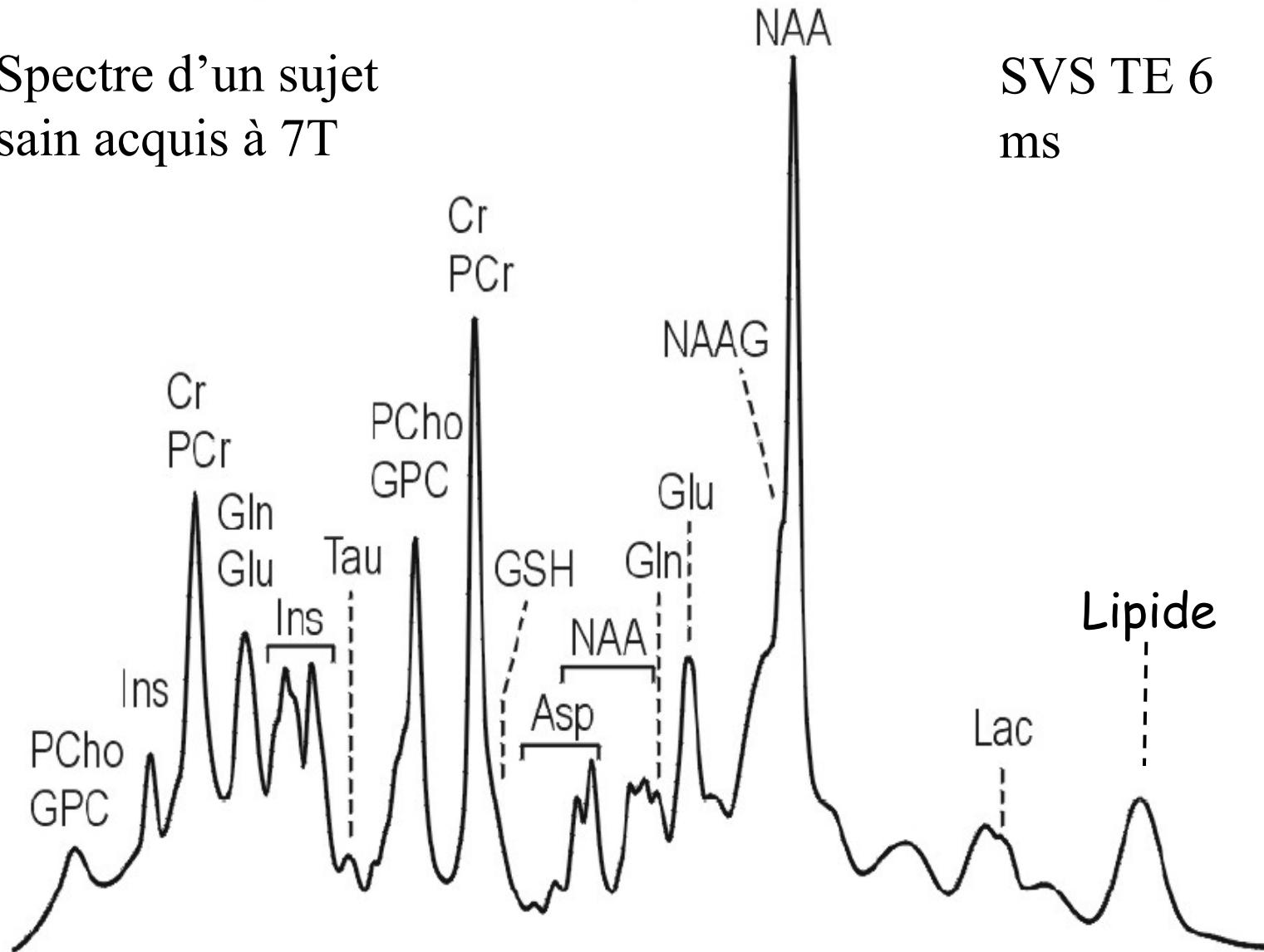
# Influence of signal/noise ratio (SNR)



# Spectre $^1\text{H}$ d'une acquisition à TE court

Spectre d'un sujet  
sain acquis à 7T

SVS TE 6  
ms

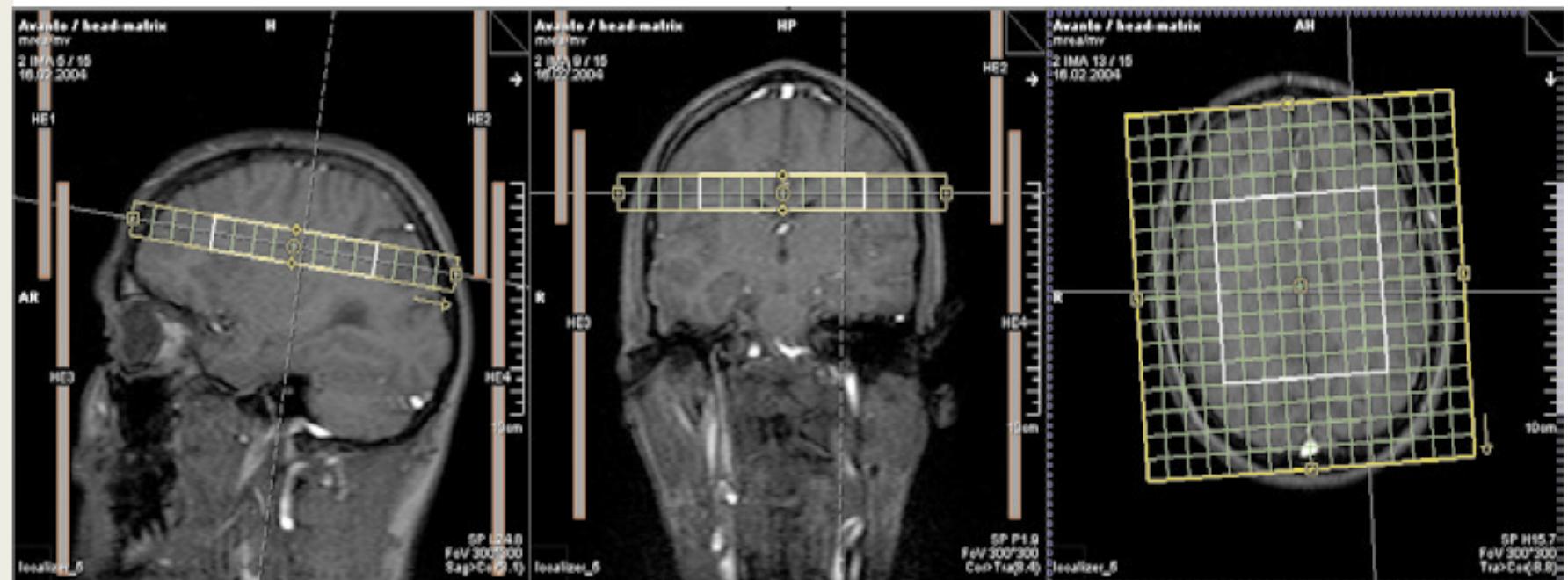


# MR Spectroscopy – in vivo metabolism

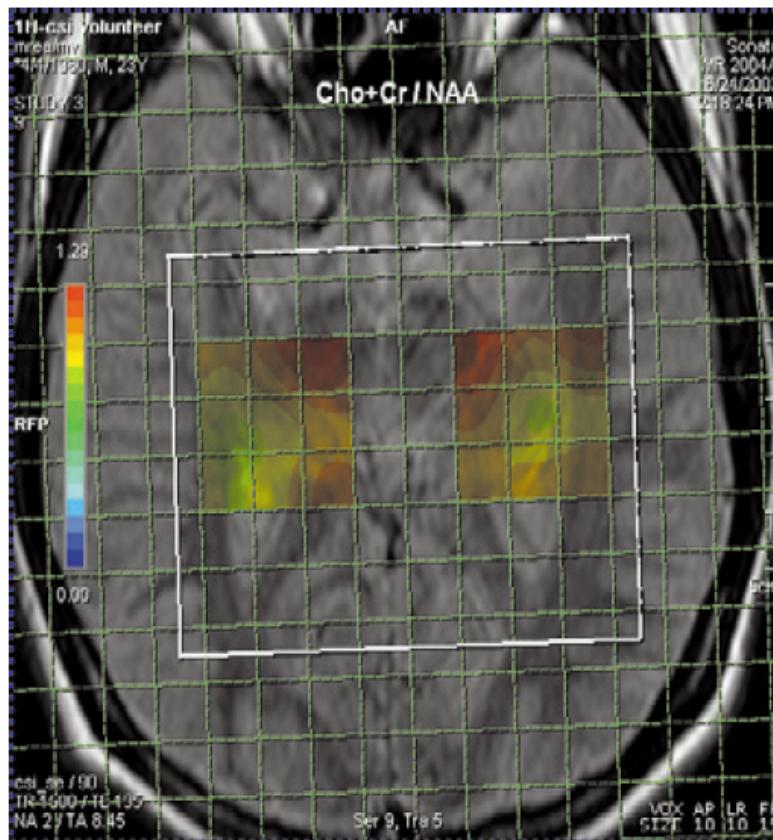
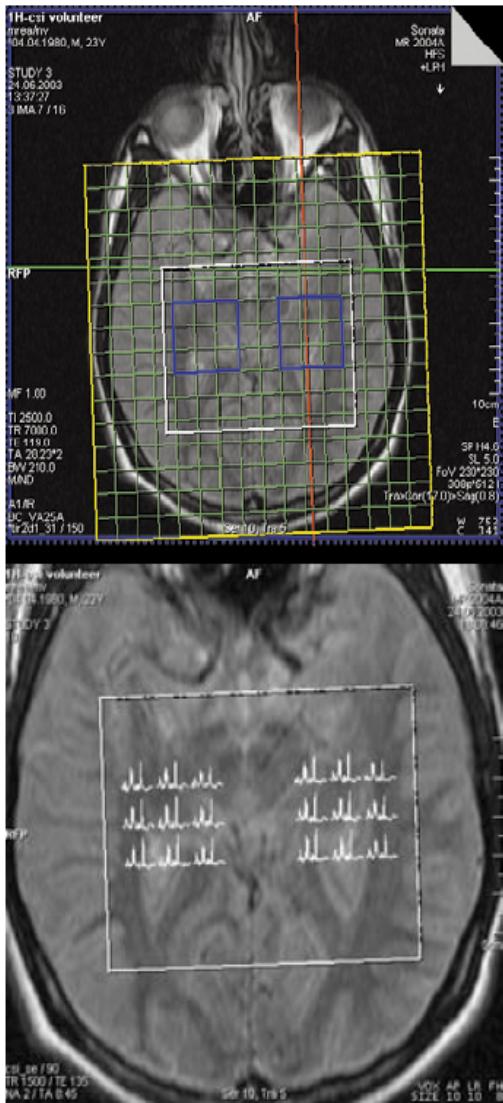
## **<sup>1</sup>H MRSI Metabolites**

	<b>Shift (ppm)</b>	<b>Biologic correlate</b>	<b>Surrogate marker</b>
<b>NAA</b>	2.01	Neuronal marker	Tumor infiltration Edema
<b>Cr</b>	3.03	Energetic	?
<b>Cho</b>	3.19	Membrane turnover	Tumor proliferation
<b>Lac</b>	1.31	Anaerobic metabolism	Hypoxia; radioresistance
<b>Lip</b>	0.9-1.2	Necrosis	Rapid tissue destruction

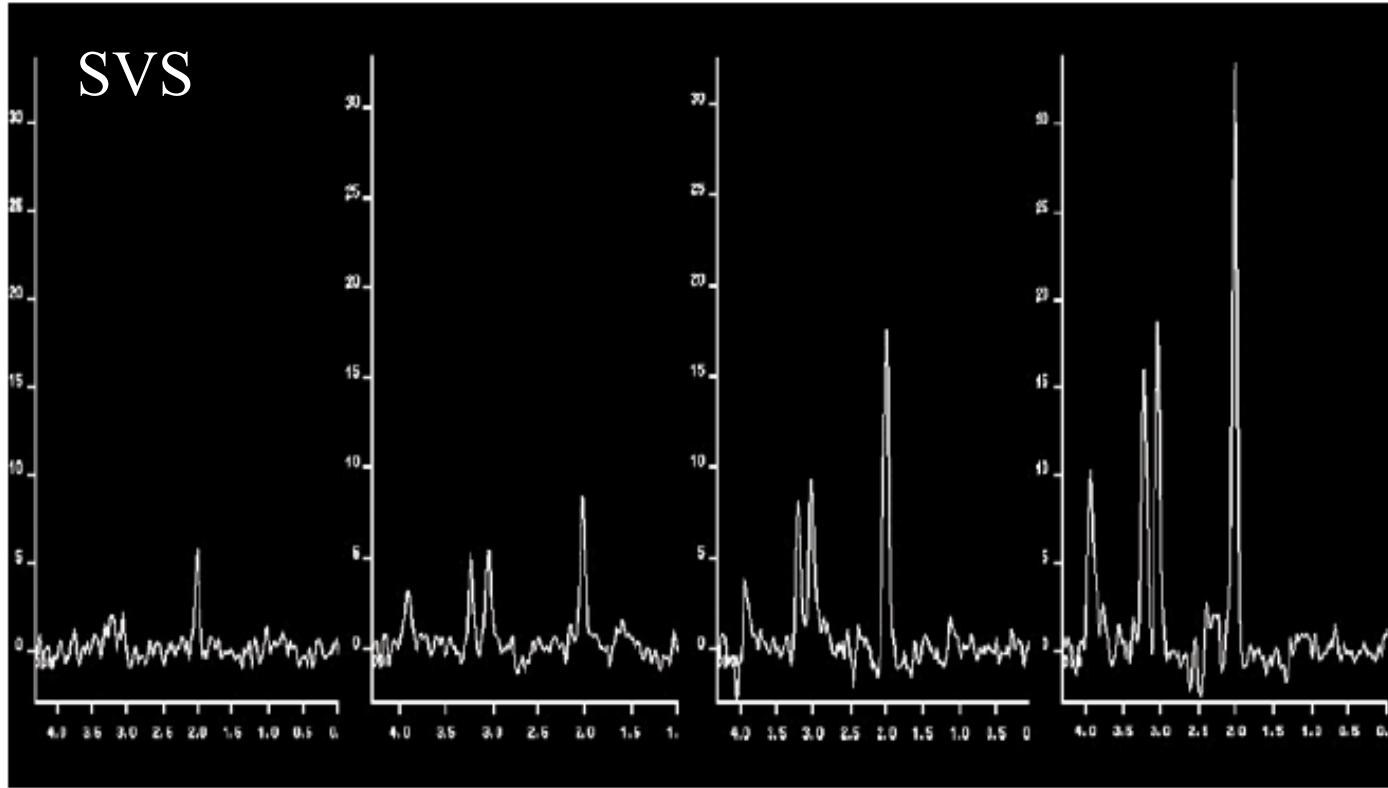
Easy positioning (translation, rotation etc.)  
using 2-3 image planes.



# Presentation of spectres in form of métabolite map



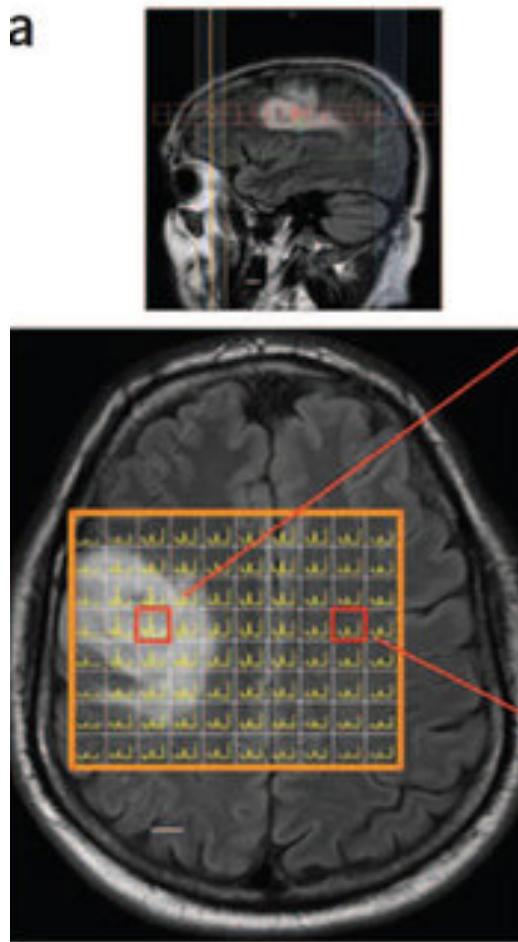
Voxel size plays a role in spectral quality



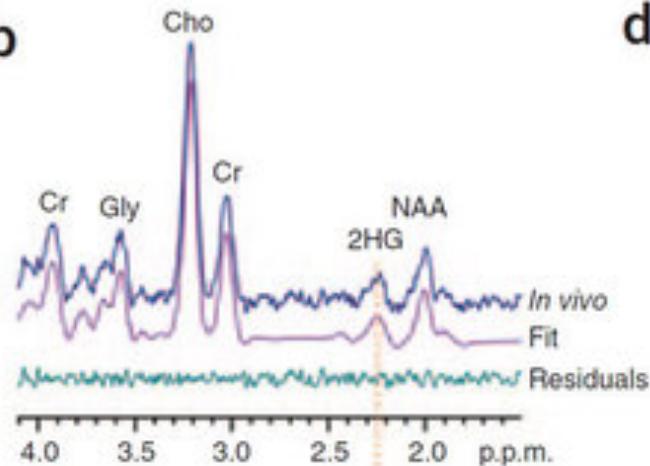
*Voxel size (from left to right):*  
 $1 \text{ cm}^3, 2 \text{ cm}^3, 4 \text{ cm}^3, 8 \text{ cm}^3$

# MR Spectroscopic Imaging in glioma

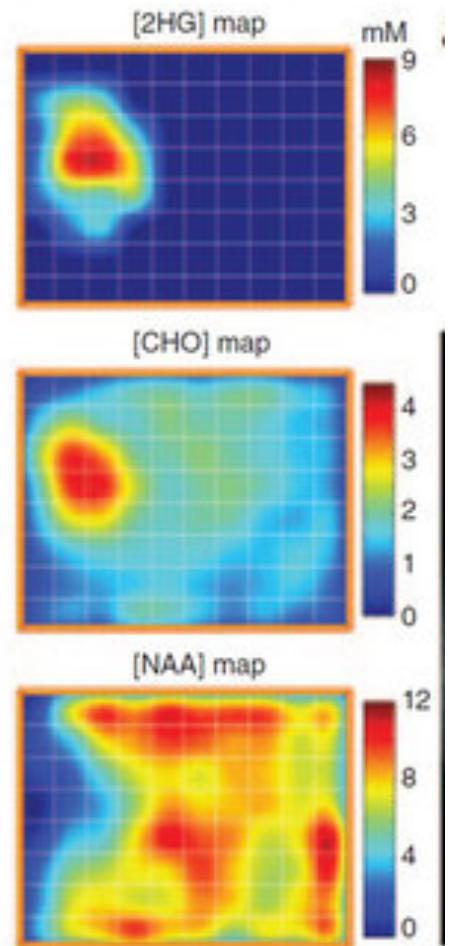
a



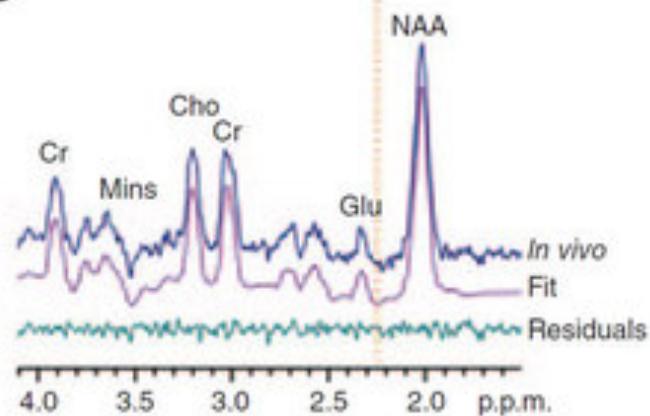
b



d



c



# Examples of characterization of cerebral gliomas

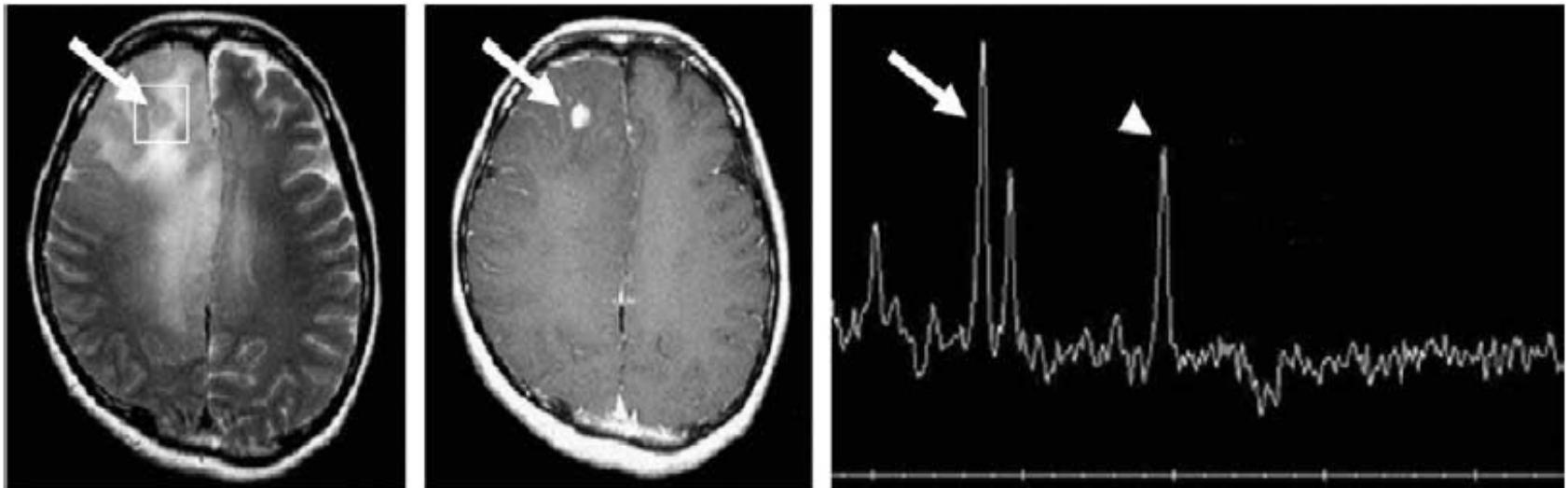
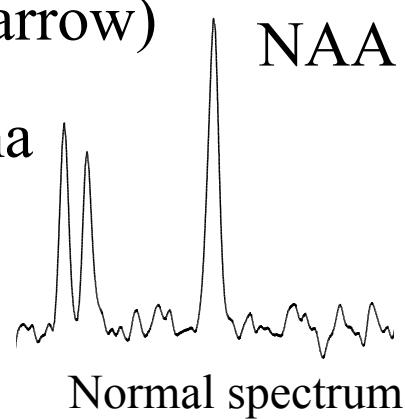


Image T2 : solid tumour with périphérique œdema (arrow)

Image T1 + Gd : Intense signal enhancement of lesion (arrow)

$^1\text{H}$  Spectrum : Cho  $\uparrow$ , NAA  $\downarrow$  suggest low grade glioma

*Biopsy : Grade II Glioma*



# Examples of characterization of cerebral gliomas

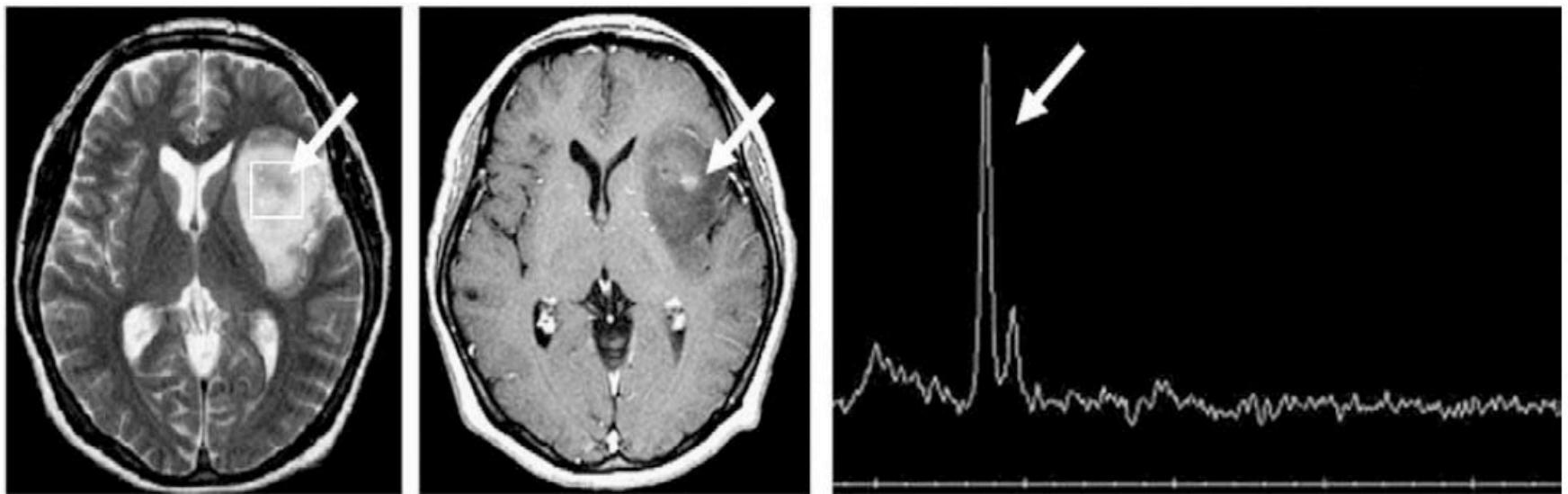


Image T2 : Voluminous homogeneous tumour (arrow)

Image T1 + Gd : Intense signal enhancement (centre) of lésion (arrow)

$^1\text{H}$  Spectrum : Cho ↑↑, NAA Ø suggest intermediary grade glioma

*Biopsy : Grade III Glioma*

# Examples of characterization of cerebral gliomas

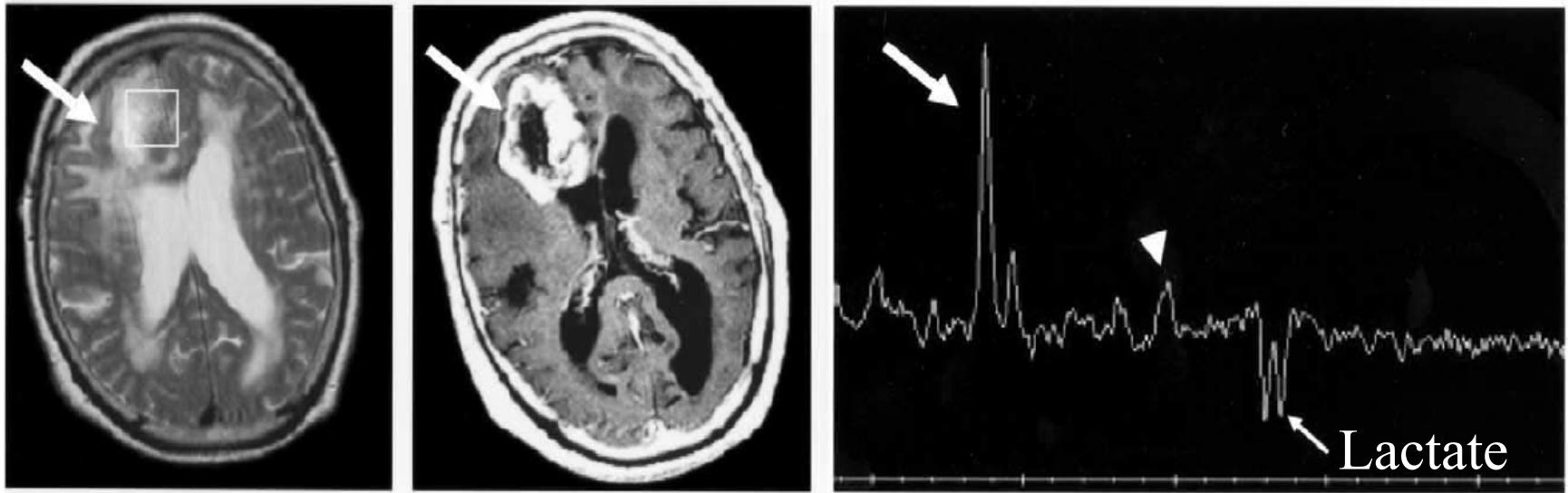


Image T2 : Voluminous heterogeneous tumour (arrow)

Image T1 + Gd : Intense peripheral enhancement (flèche)

$^1\text{H}$  Spectrum : Cho  $\uparrow \uparrow$ , NAA  $\sim \emptyset$ , Lactate suggest high grade glioma

*Biopsy : Grade IV Glioma*