MAGNETIC RESONANCE IMAGING OF *IN VIVO* FLOW PHENOMENA

So far we have seen that magnetic resonance can

- *Locate the positions of spins (mainly water) with the aid of one or multiple field gradient: MRI*
- *Characterize other metabolites by virtue of their different chemical shifts: MRS*

Magnetic resonance can also be exploited for

- *THE NON-INVASIVE MONITORING OF DISPLACEMENTS.*

Under *in vivo* monitoring conditions, this leads to

1. **MAGNETIC RESONANCE IMAGING OF FLOW IN ARTERIES – MAGNETIC RESONANCE ANGIOGRAPHY (MRA)**
2. **MAGNETIC RESONANCE IMAGING OF FLOW IN MICROVACULARIZATIONS – PERFUSION MRI**
3. **MAGNETIC RESONANCE IMAGING OF RANDOM DISPLACEMENTS: DIFFUSION MRI AND DIFFUSION TENSOR IMAGING (DTI)**

Each of these modalities has its preferred area of clinical/research application. In general

1. **MAGNETIC RESONANCE ANGIOGRAPHY IS USED TO IMAGE LARGE-VOLUME FLOW IN ARTERIES AND VEINS. This is analogous to what used to be done by injecting X-ray opaque dies or radioactive agents and taking plaques. MRA is more expensive, but less invasive and better for distinguishing blood flow rates.**
2. **PERFUSION MAGNETIC RESONANCE IMAGING TARGETS THE DEGREE OF MICROVASCULARIZATION OF A SPECIFIC ORGAN. Since microvascularization depends on the nature of the organ, particularly depending on weather tissue is ischemic or not and highly angiogenic or not, it serves as marker of stroke-affected regions, tumor growth, inflammations, etc.**
3. **DIFFUSION MRI IS MOSTLY USED TO MONITOR THE EARLY EFFECTS OF STROKE; DTI IS MOSTLY USED TO STUDY THE STRUCTURE OF TISSUES, PARTICULARLY FOR NEURON TRACKING.**

There are various ways by which MRI allows one to monitor all these phenomena. MRA in particular uses methodologies that later find use both in perfusion MRI (e.g., injection of relaxation agents) as well as in diffusion MRI (e.g., uses of gradient echoes, bipolar gradients, etc). We therefore begin by focusing on all main methods used in MRA, and discuss later their adaptations to the remaining problems.

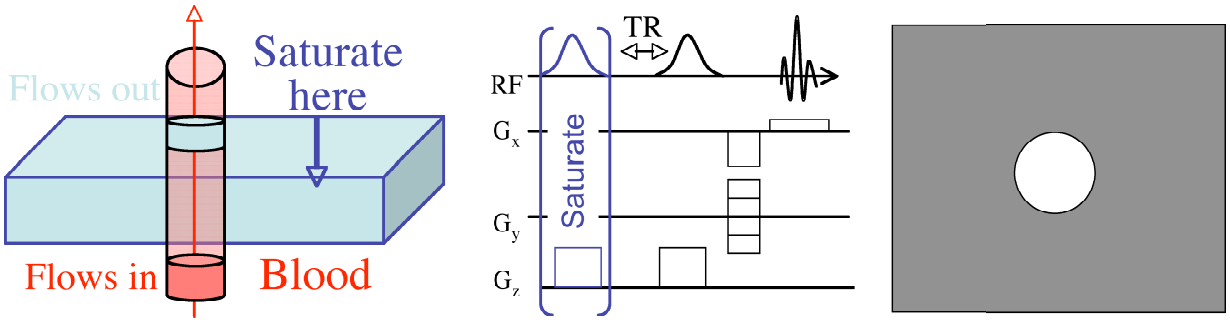
1. THREE MAIN EFFECTS ARE EXPLOITED TO OBTAIN MRA INFORMATION: (A) TIME-OF-FLIGHT EFFECTS. (B) FLOW-INDUCED PHASE EFFECTS/DISTORTIONS. (C) EFFECTS INDUCED BY ADDITION OF EXOGENOUS CONTRAST AGENTS

A. Time-of-Flight Effects

Time-of-flight effects exploit the fact that blood in arteries/veins is moving –in a relatively homogeneous way, at high speeds, and in large amounts. To visualize this movement by MR one can do many MRI-based experiments, and then extract the velocity of the fluid's physiological flow based on time-of-flight parameters. That means, of flow-derived changes affecting the MR signal within either times T1 or T2.

For instance one can

- **Saturate all spins in a plane and then let the in-flow of fresh blood to reinstate the MRI signal over times TR<T1**



Features

_ Simple & non-invasive

_ The strength of the signal depends on vascular velocity and orientation of the explored vessel (the vascular signal will be better if the slice is perpendicular to the axis of the vessel) => can be modeled & quantified

_ The sequence has "play" parameters: TR, saturation, slice thickness, etc.

Limitations

The main limitations of this time-of-flight MRA are:

_Signal loss linked to spin dephasing when flows are complex or turbulent (stenosis)

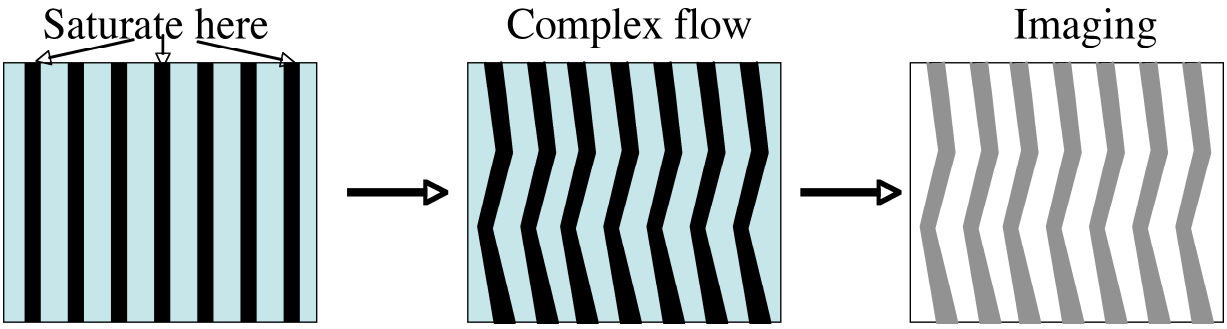
_ Flows cannot be followed if too slow or oriented parallel to the slice plane

_Poor signal suppression of the stationary tissues with short T1 relaxation time (fat, atheroma, hematoma, thrombus) leads to poor flow contrast.

- **In a related sequence, one saturate spins in one plane, and monitor where this plane has moved at a later time TR < T1.**

To do so one would take the previous sequence, and make the saturated and the monitored *z*-slices different.

- **Besides doing 1D saturation patterns of this kind, one could do a 2D-patterned (or even 3D patterned) saturation, and see how this has changed at a later time TR < T1.**

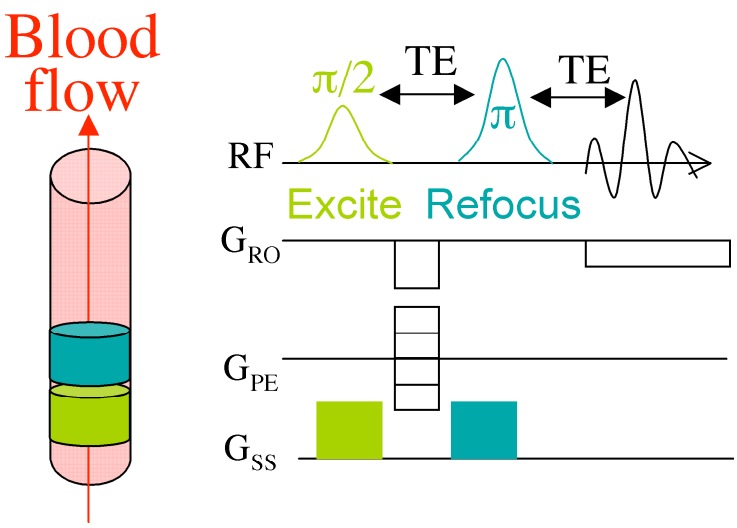


This is more complicated to do than the sequence described earlier. But it has two main advantages:

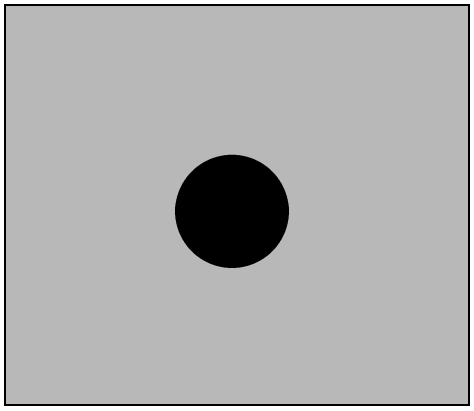
_ can deal better with motions even when they happen in the plane of the saturation/labeling

_ can deal with smaller displacements.

- **Do a special kind of 90-TE-180-TE pulsed spin echo sequence, where the initial 90° pulse affects spins positioned in one slice and the later 180° pulse addresses spins in another plane. Only when the flow has taken the spins from their initial 90° excitation position to the latter 180° refocusing position during the time TE, will we get a full echo.**



This method uses a spin-echo sequence where a slice selective 90˚ pulse excites spins in one plane, and the 180˚ pulse refocuses spins in another plane. In the absence of flow, no signal is seen because no spins experience both the 90˚ and 180˚ pulses. In the presence of flow and the correct TE time, blood from the 90˚ plane flows into the 180˚ plane and produces an echo.



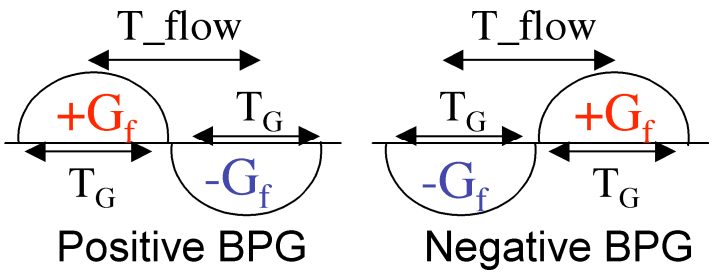
If the 90˚ and 180 ˚ pulses are applied at the same frequency, the 2D MRI signal will look dark. In general, this is not the "best" of observables – one would rather have a stronger signal from the targeted vessels, than a darker one. Another complication of this (and of many other) flow MRA methods, is their need to achieve a more-or-less complete suppression of the background tissue in order to lead to an MRA image. Usually this is all achieved by data post-processing.

B. Flow-induced Dynamic Phase Effects: Phase-contrast MRA

Phase contrast angiography is based on the different dynamics that stationary vs. moving spins will exhibit under the action of bipolar magnetic field gradients (BPG) pulse. In other words: so far we have used the phase evolution of the spins to encode their positions or their chemical shifts. Phase-contrast MRA uses the phase evolution of the spins to encode their ***displacements.***

A bipolar gradient is in essence a gradient-echo block: a gradient which is turned on in one direction for a period of time then turned on in the opposite direction for an equivalent amount of time. A positive bipolar gradient pulse has the positive lobe first and the negative lobe immediately thereafter; a negative bipolar gradient pulse has the

negative lobe first and the positive thereafter. In either case, the areas under the first lobe of the gradient pulse must equal that of the second:



A bipolar gradient pulse has no net effect on stationary spins. For example, a stationary spin exposed to the first lobe of a positive BPG will acquire a phase in radians given by

$$\phi_{initial} = 2\pi\,\gamma\,G_f\,T_G\,z_{initial}$$

whereas in the second lobe it will gain a phase

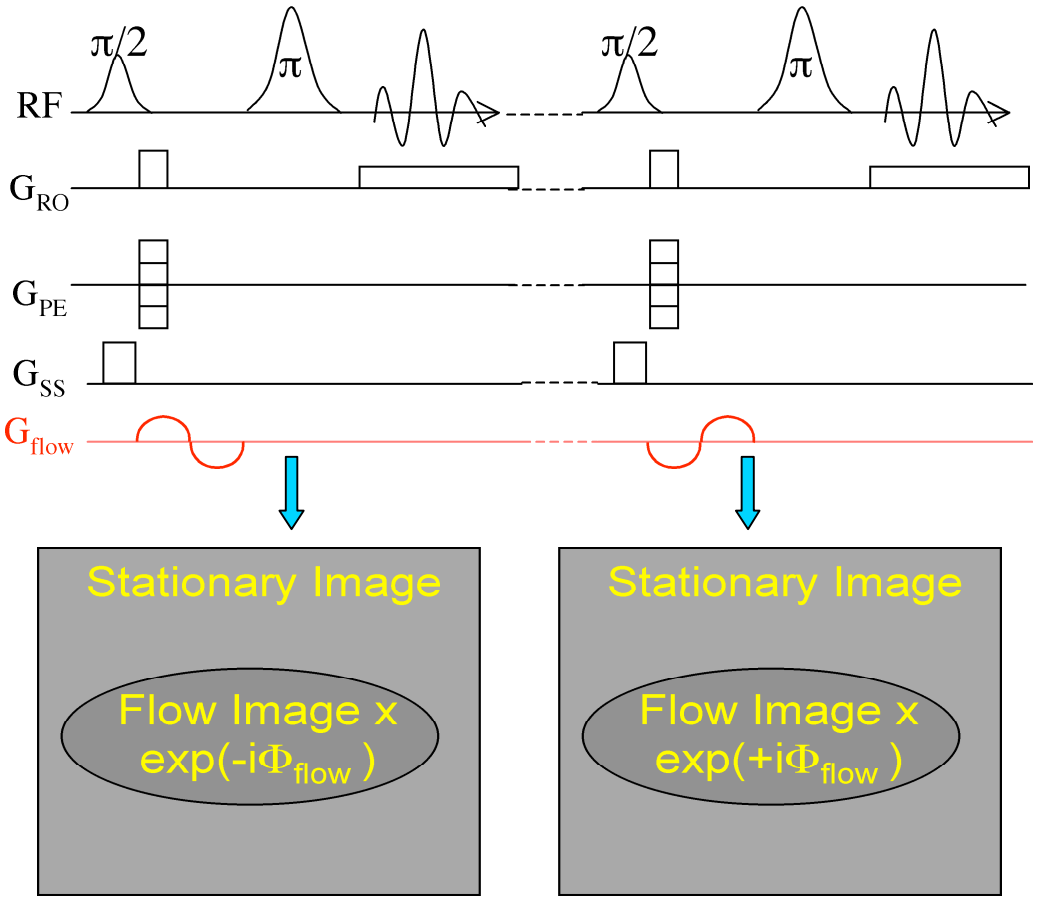
$$\phi_{final} = -2\pi\,\gamma\,G_f\,T_G\,z_{final}$$

Since the z coordinates in the initial and final phases are identical, this leads to an overall zero phase $\Phi = \phi_{initial} + \phi_{final}$

By contrast, spins that have a velocity component in the direction of the BPG will be affected by the gradient pulse. In fact they will gain an overall phase which depends on their displacements $\Delta z = velocity\,T\_flow$ along the gradient's axis:

$$\Phi_{flow} = \phi_{initial} + \phi_{final} = 2\pi\,\gamma\,G_f\,T_G\,(z_{initial} - z_{final})$$
$$= -2\pi\,\gamma\,G_f\,T_G\,T\_flow\,velocity$$

If a BPG is inserted in any one imaging sequence, in addition to all the other gradients, it will not affect the image: all it will do is impart a phase shift to the moving spins. This constant phase will propagate into the final MRI image, but since an image is usually given by a magnitude representation of the FT(k) data, this will lead to no visible effect. However if two imaging sequences are performed sequentially: one in which BPG employs a positive bipolar gradient pulse and a second using a negative BPG, then we have a good flow-derived contrast mechanism.



If the images arising from two such experiments are subtracted (or otherwise manipulated), the signals from the stationary spins will cancel and those arising from the flowing blood will add. The net result will be an image of the flowing spins.

Limitations

Main limitations of phase-contrast MRA include:

_Signal addition will only be maximized when Φ_{flow} is "tuned" to be $\pi/2$. Small displacements are associated to small dephasing effects and therefore poor contrast.

_ Flows can only be followed along the direction of the flow-encoding gradient.

Advantages

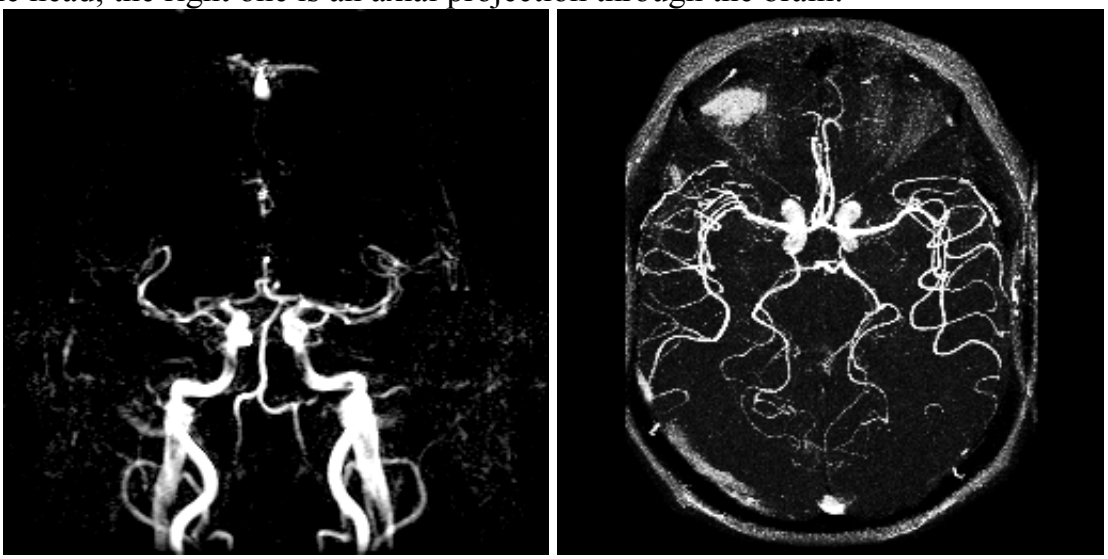
Main advantages of phase-contrast MRA include:

_Relatively fast and simple

_Better resolution than time-of-flight methods (good for looking at small vascularization)

_Good signal suppression of the stationary tissues

Here are two examples of MRA images: The left one is a coronal projection of the flow in the head; the right one is an axial projection through the brain:



C. Contrast-Enhanced MRA (CE MRA)

Contrast enhanced angiography is based on the difference in the T_1 relaxation time of blood and the surrounding tissue when a paramagnetic contrast agent is injected into the blood. This agent reduces the T_1 relaxation times of the fluid in the blood vessels relative to surrounding tissues. When the data is collected with a short TR value, the signal from the static tissues surrounding the blood vessels is very small: its relatively long T_1s and the short TR used will saturate static tissues. By contrast, the blood vessels carrying the contrast agents appear bright in these short-TR sequences. ***The high quality of images arising from contrast enhanced MR angiography has made CE MRA the modality of choice for angiographic MRI.***

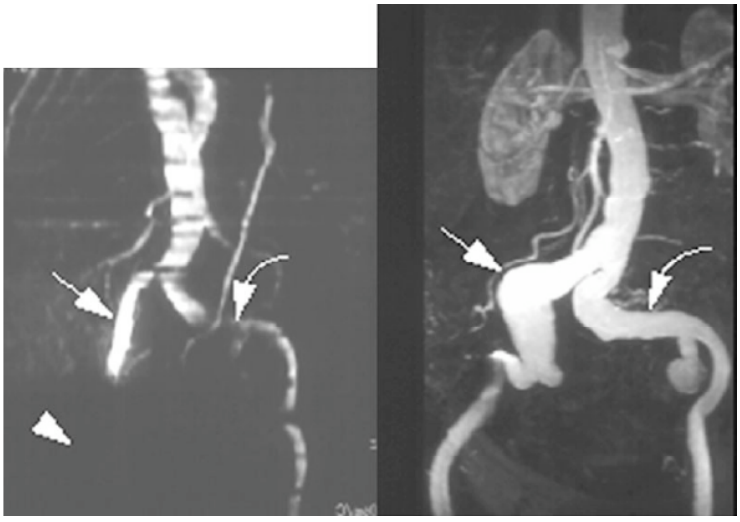


Figure 3. 2D TOF MRA (left) and 3D CE MRA (right) in the same patient show the advantages of 3D CE MRA which 1) eliminates slice misregistration and pulsatility artifacts; 2) reduces signal dropout from a right metallic hip (arrowhead); 3) more completely depicts slow flow in aneurysms (straight arrow); 4) reduces in-plane saturation artifact (curved arrow) and also shows a left internal iliac artery aneurysm. Courtesy of Thomas M. Grist; reprinted with permission from 3D Contrast MRA, 3rd edition, Springer Verlag; 2003. p 5.

Advantages

Main advantages of contrast-enhanced MRA include:

_Their need/reliance on fast-repetition sequences. This makes them fast, and capable of following flow in real-time:

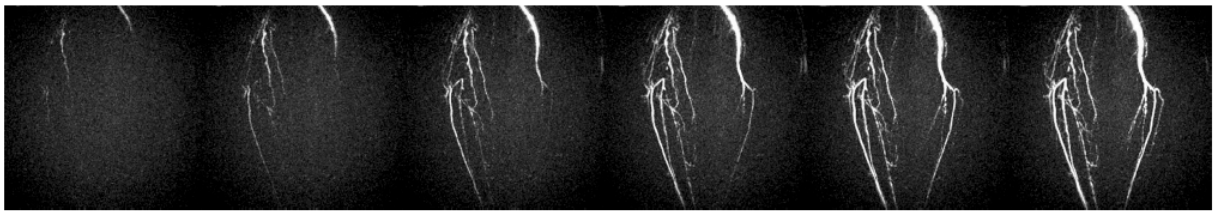


Figure 1. Time-resolved MIP images (2 seconds/frame), produced using a spiral acquisition and sliding window reconstruction, show differential flow rates between the right and left legs.

This in turn is related to "bolus tracking" experiments: acquisitions that are synchronized with the injection of the contrast agent

_ CE MRA can detect flow without any modification of existing MRI sequences; just by relying on the saturation of the non-contrasted tissues. This leads to higher resolutions than achievable by other methods

_CE MRA is not very sensitive to the direction or rate of flow.

Limitations

Main limitations of CE MRA include:

_Unlike the other approaches mentioned, which rely on intrinsic flow effects, this form of MRA requires the addition of an exogenous contrast agent

_The contrast agent washes away rapidly and hence fast MRI methods (e.g., EPI), with all their associated limitations, are almost a must

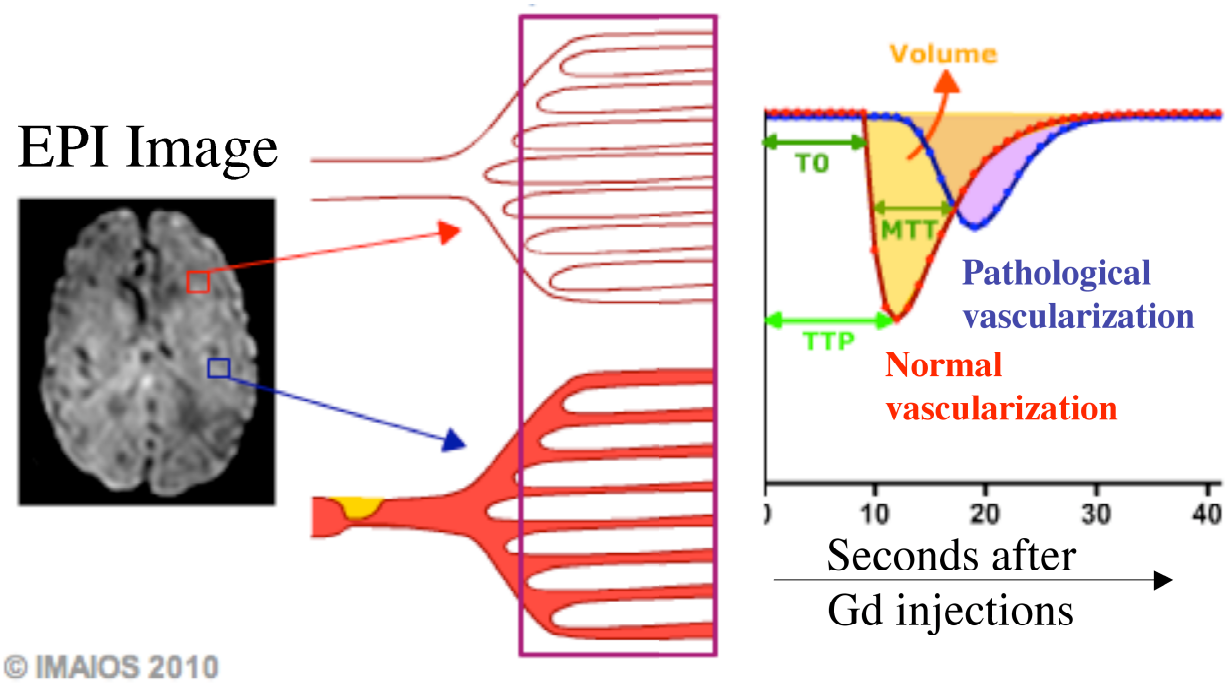
2. PERFUSION MRI

The methods used in MRA, particularly in CE MRA, find use in the study of micovascularization: **Perfusion MRI.**

Main features of this approach include

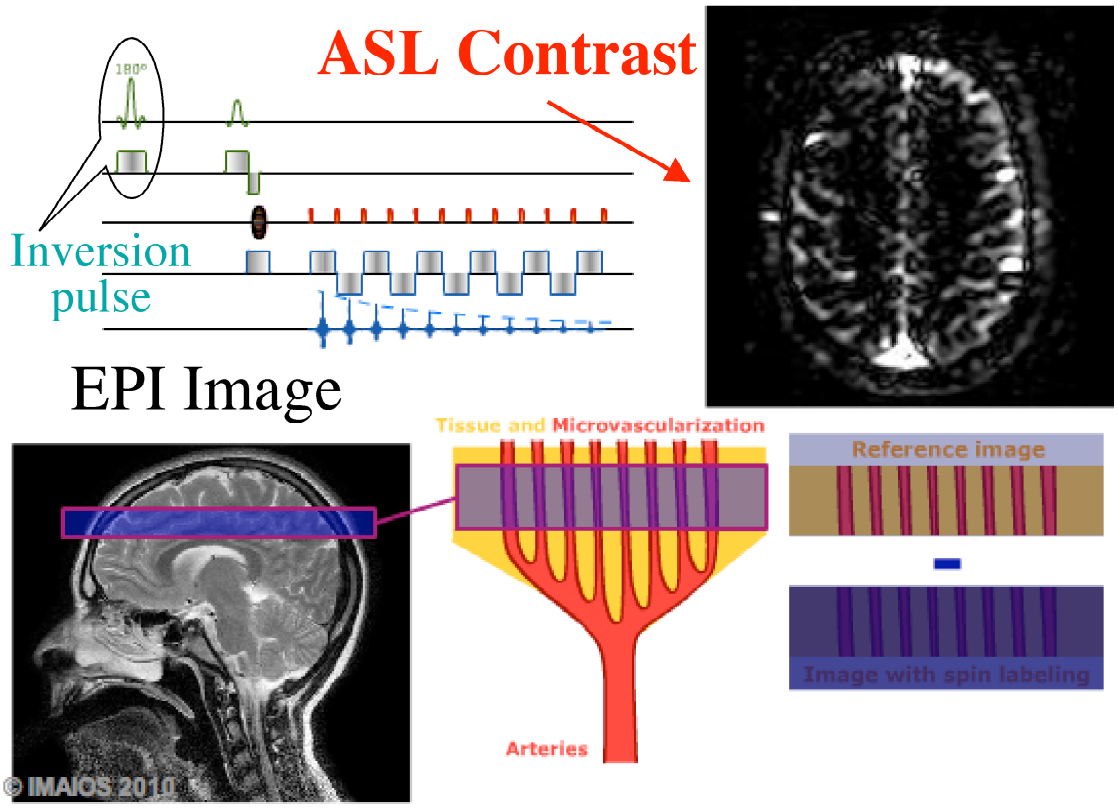
- Perfusion MRI provides a relative and/or absolute measurement of the parameters of cerebral microvascularisation: regional blood volume, mean transit time, regional blood flow.
- Perfusion MRI often relies on the use of an exogenous tracer (e.g., Gd-based or superparamagnetic-iron-oxide (SPION)-based particles as contrast agents) to achieve its contrast. These techniques exploits the magnetic susceptibility effects

that the Gadolinium chelates or SPION particles introduce, either in T2 weighting or on T2* weighting, in SE-EPI or GE-EPI sequences respectively. The quality of the injection and the timing of acquisition are of prime importance in obtaining a good examination - the method operates on the basis of spatially-resolved bolus tracking.



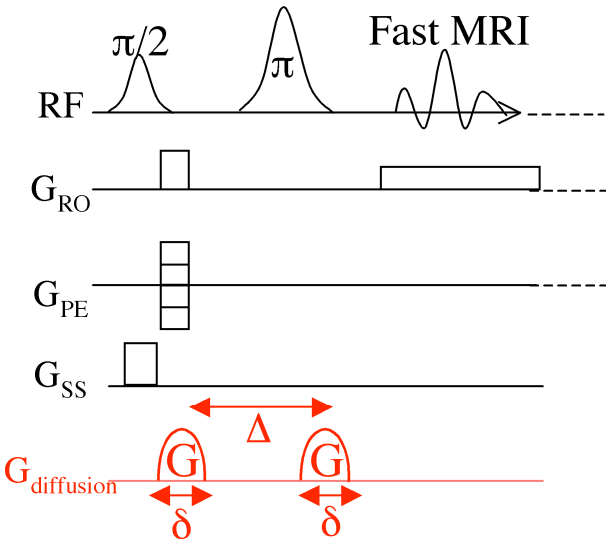
The drop in the signal during the first pass of the product allows perfusion parameters to be extracted after post-processing. Parameters indicative of stenosis is time-to-peak (TTP), and of ischemia is the overall volume

- Arterial spin labeling (ASL) provides an alternative to carry out this kind of Perfusion MRI, which relies on an intrinsic contrast agent. In this technique the blood just upstream of the slice of interest is inverted or saturated; this "missing" signal then serves as a tracer. This inversion/saturation provokes a variation in the signal received in relation to an acquisition without prior saturation. An estimate of the local hemodynamic parameters can be deduced by comparing (subtracting) these two signals. Sensitivity to microvascularization is smaller than with contrast agents, but it is less invasive and easier to test under a variety of timing conditions. Besides, not all contrast agents can cross the blood-brain barrier!



- Main applications of Perfusion MRI include the monitoring of tumoral pathologies, the characterization of stroke and of ischemic tissues, hemorrhages and infections/inflammatory diseases.

3. DIFFUSION MRI



Diffusion imaging exploits many of the phase encoding concepts described for phase- contrasted angiography sequences –except that the Δz's are now smaller and random. Because of these major physical differences, the gradients must be increased in amplitude so as to image the much slower motions of water diffusion in the body. A typical diffusion-encoded MRI sequence is shown on the left

The intensity of the MRI signal is dependent on the "red parameters", as

$$S/So = exp[-\gamma^2 G^2 \delta^2 (\Delta - \delta/3) D] = exp[-b D]$$

where D is the apparent diffusion coefficient of the water along the $G_{diffusion}$ direction.

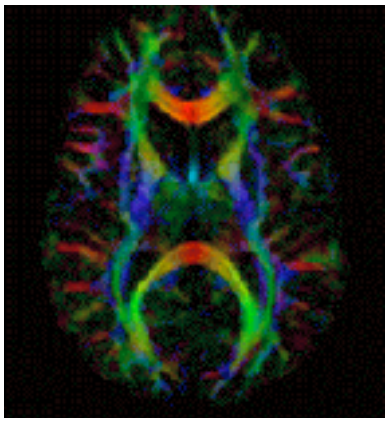
The apparent diffusion of water molecules may appear as being fast and free, as in cerebrospinal fluids; or restricted, as in cell membranes or fibers. Moreover, water molecules may move equally in all three spatial directions (isotropic diffusion); or they may diffuse more easily along a specific direction (anisotropic diffusion) as in nerve fibers or muscles/tendons. Each of these differences gives origin to another diffusion-based MRI approach.

A. DIFFUSION-WEIGHTED MRI (DW MRI)

DW MRI incorporates a high b-value into a regular pulse sequence, to distinguish regions of high/low water mobility. DW MRI is one of the most widespread and sensitive methods to diagnose stroke within the first hour of suspecting one.

Other applications of DW MRI include diagnosing other brain pathologies:

- Tumoral: cerebral lymphoma (reduced ADC), epidermoid and cholesteatoma cysts (hypersignal in diffusion).
- Infectious: 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



B. DIFFUSION-TENSOR MRI (DTI)

DTI measures numerous images, with different b-values and different orientations of the diffusion-encoding gradient. As the apparent diffusivity may be given by the morphology of the tissue, one can learn about directionality of tissues by monitoring the directionality of the random water diffusion. Getting this kind of data requires making several DW MRI experiments –not a quick acquisition unless using EPI

Main applications of DTI include

- The in-vivo study of tissue microstructure. This gives indications about possible nerve fiber anomalies in white matter or the spinal cord that are not visible in

conventional imaging.

- DTI can also be associated with functional MRI to study the interconnexions between nerve centers, can be used to analyze brain maturation and development (myelinization), assist in the preoperative check-up for brain tumors (corticospinal bundle) or for medullary compression.
- DTI can also be of interest in exploring Alzheimer's disease, certain psychiatric affections, inflammatory, tumoral, vascular, traumatic (irreversible comas) pathologies or drug-resistant epilepsies