Perfusion Imaging

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What is Perfusion

- Perfusion describes the amount of blood delivered to the capillary beds of a block of tissue in a certain time period.
- Transport of oxygen, glucose and other nutrients from blood to tissue.
- Occurs at the capillary level (radius ~ 5 μm)
- It is typically characterized by three quantities: cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT). The typical imaging voxel contains several thousand capillaries.
- CBF and MTT measurements necessarily rely on techniques sensitive to motion (for instance, bolus tracking techniques), CBV may be measured with other methods (for instance, in a steady state).

Cerebral Perfusion: measurable parameters

- CBF: rate at which blood flows through the microvasculature of a region of tissue.
- In gray matter 40-60 ml/100g/min
- – In white matter 20 ml/100g/min

$$\mathrm{rCBF} = \frac{\text{Net blood flow through the voxel}}{\text{Mass of the voxel}}.$$

Cerebral Perfusion: measurable parameters

- CBV: fraction of volume of tissue occupied by blood (~3%).
- Dependent of MRI technique (sensitivity to vessel size)
- – In gray matter 4 ml/100g tissue
- – In white matter 2 ml/100g tissue

$$\mathrm{rCBV} = \frac{\text{Volume of blood in a voxel}}{\text{Mass of the voxel}}.$$

$$\mathrm{rCBV}\ (\%) = 100\,\frac{\text{Volume of blood in a voxel}}{\text{Volume of the voxel}}.$$

Cerebral Perfusion: measurable parameters

- MTT: Mean transit time, average time that blood spends passing through the blood volume with a region of tissue before it exits though the venous system.

$$\mathrm{rMTT} = \frac{\mathrm{rCBV}}{\mathrm{rCBF}}.$$

Advantages of MRI over CT, PET & SPECT

MRI has the advantages of

- high temporal and spatial resolution
- using no radioactivity,
- being almost noninvasive
- and offering combination studies using other MR techniques (diffusion, spectroscopy, angiography, structural imaging).

Types of Perfusion Imaging

MR perfusion imaging is divided into categories:

(1) Exogenous based techniques either

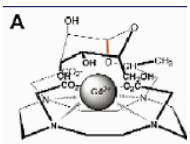
(a) using intravenous bolus injection of paramagnetic contrast agent, dynamic susceptibility contrast magnetic resonance imaging (DSC-MRI). or

(b) Steady State techniques

(2) Endogenous - arterial spin labeling of protons in blood.

Contrast enhancement with Blood pool agents

- Blood pool tracer perfusion imaging is carried out with exogenous paramagnetic contrast agents, such as gadolinium chelates.
- A nondiffusible contrast agent does not cross the intact BBB and remains in the intravascular compartment, where it changes the blood T1 and T2.
- Although the agent is confined to the vascular space, its effects extend to the extravascular space as well, due to magnetic susceptibility effects and to water exchange between blood and tissue.
- As a result, the presence of a nondiffusible contrast agent within the vascular bed may also change the relaxation times in the adjacent tissue



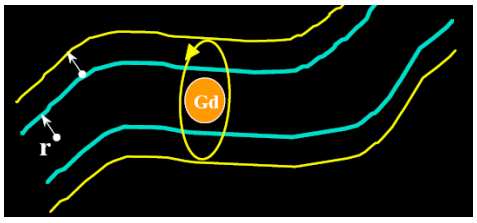
Gadolinium

- Gadolinium is a lanthanide metal being paramagnetic property due to seven unpaired electrons. Due to toxicity gadolinium is chelated to different compounds: Gadolinium-DTPA
- Gadodiamide (Gadolinium DTPA) provides greater contrast between normal tissue and abnormal tissue in the brain and body.
- Gd is non radioactive.
- Before the imaging takes place it is injected into a vein and then accumulates in the abnormal tissue.
- An important feature of using gadodiamide as a contrast agent is that the only known adverse side effects are mild headaches, nausea, local burning at entry site

Susceptibility

- Magnetic Susceptibility is the degree of magnetization of a material in response to a magnetic field.
- the magnetic field is strengthened by the presence of the paramagnetic material
- Paramagnetic contrast agent within the vasculature
- Distorts the magnetic field
- Reduces T2 around the vessel

$$\vec{B} = \vec{B}_0(1 + \chi),$$



Changes in T1 relaxation

- The effect of MR contrast agents on T1 relaxation is caused by so-called dipole-dipole interactions i.e. on direct interaction of protons in the water molecules with the dipole moment of the unpaired electrons of the paramagnetic contrast agent.
- Gadolinium-compounds in the brain are intravascular when the blood brain barrier is intact. T1 shortening produces signal enhancement in the blood volume, that contributes about 5% of the total brain volume.
- The change in blood water longitudinal relaxation rate may be easily obtained from the relaxivity r1 and the blood concentration cb of the contrast agent:
- R1 = 1/T1 and $R1^0$ is the intrinsic blood water relaxation

$$R_1 = R_1^0 + r_1 c_b,$$

T1 in adjacent tissues

- In the normal brain the BBB prevents diffusion of contrast agents out of the intravascular spaces.
- However, water exchange induces a change in extravascular T1. The residence time of water in capillaries has been considered to be on the order of 500 msec.
- Water exchange is slow with respect to MR measurement times, resulting in a limited shortening of tissue T1.
- "T1 maps" have poorer contrast-to-noise ratios than corresponding T2-weighted maps
- T1 change is relatively small and the method has not found broad applications.

Transverse Relaxation Rates

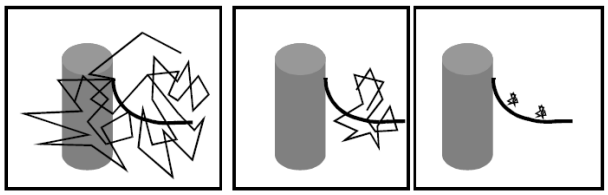
- The transverse relaxation of blood is predominantly due to diffusion of water protons through field gradients arising from the susceptibility difference between red blood cells (RBC) and plasma

$$\Delta\chi_{\mathrm{RBC/plasma}} = \chi_{\mathrm{RBC}} - (\chi_{\mathrm{plasma}} + \chi_{\mathrm{CA}}),$$

- Since RBC susceptibility depends on the oxygenation, changes in the relaxation rate(R2) due to the injection of the contrast agent, also depend on the oxygenation level.
- For fully oxygenated blood, the injection of contrast agent increases susceptibility difference, resulting in a decreased blood T2. With deoxygenated blood, the contrast agent causes an increase in blood T2.

Changes in T2 and T2* in Adjacent Tissue

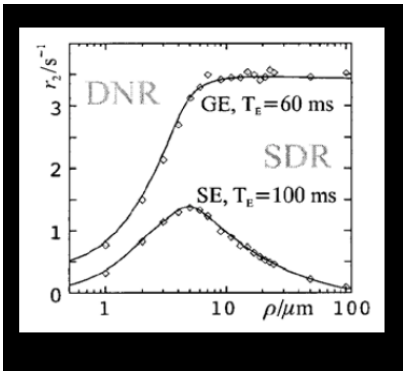
- The echo time in gradient-echo or spin-echo experiments is generally smaller than 100 msec, Thus, here also water exchange between intra- and extravascular compartments is slow, and it does not contribute significantly to T2 changes.
- The changes in tissue T2 and T2* are mainly due to the dephasing of the extravascular spins in the spatially non uniform field created by the magnetic susceptibility differences between vascular and extravascular compartments.
- This susceptibility difference causes magnetic field distortions in the vicinity of blood vessels, resulting in a decrease of the transverse relaxation times of protons in the extravascular compartment.
- The presence of microscopic magnetic field heterogeneities creates a distribution of resonance frequencies.



Vessel size and susceptibility effects

- The signal change caused by a paramagnetic compound also depends on how many different magnetic fields the spins experience during the duration of the pulse sequence.
- Around a larger vessel, water molecules will only experience the same "static" magnetic field because the distance travelled by diffusion is small in relation to the characteristic distance of field inhomogenity. Dephasing due to static inhomogenity leading to signal loss will occur in a gradient-echo experiment but not in a spin-echo experiment.
- Around smaller vessels, the water molecules will experience varying magnetic field gradients due to diffusion (around the vessel and around the neighboring vessels), this will lead to dephasing and signal loss in a gradient-echo as well as in a spin-echo experiment.

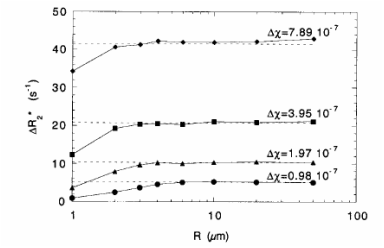
- Spin echo sensitive to microvasculature
- Gradient echo sensitive to all vessel sizes



Gradient Echo Experiments

- At large doses of contrast agent, all the vascular components are on the plateau and gradient-echo experiments can measure the total vascular volume. It has been shown that at the long echo times usually employed and at a high concentration of contrast agent, the enhancement in relaxation rate is given by

$$\Delta R_2^* = \frac{4}{3}\,\pi\gamma\chi_{CA}^{m} c_b B_0 \mathrm{CBV},$$



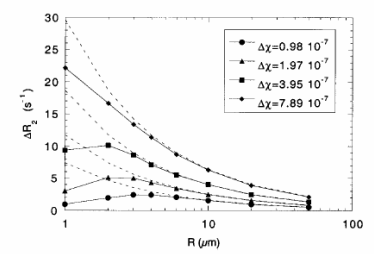
Spin Echo Experiments

- In spin-echo experiments, the dephasing resulting from static local differences in Larmor frequencies is refocused and diffusion effects become more visible.

- The phenomena that induce a change in transverse relaxation rates are closely related to the diffusion length during the experiment time TE. This diffusion length LD depends on the self-diffusion coefficient D of water in the vicinity of the vessel walls:

$$I_D = \sqrt{6DT_E}\ .$$

- The water molecules move through field gradients induced by the blood-tissue susceptibility difference.
- With large vessels one can assume that during the experiment time (TE) each diffusing water molecule experiences an approximately constant field gradient whose value depends on its initial position (slow diffusion approximation). An attenuation of the echo occurs (T2 decrease).
- For small vessels, a diffusing water molecule experiences a whole range of magnetic fields resulting in the averaging of phase differences (motional narrowing) and reduced signal attenuation. At a given rCBV, the change in R2 of a spin-echo experiment reaches a maximum for microvessels and decreases when vessel size increases.



Spin Echo v/s Gradient Echo

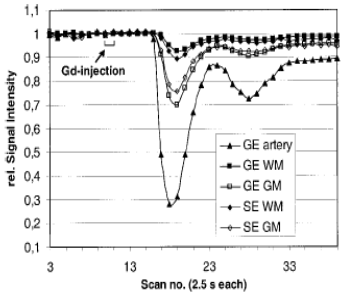


Figure 1. Signal-time course of the relative signal intensities for gray and white matter and the middle cerebral artery for the GE (black squares) and the SE method (gray diamonds). While the GE-based method shows a larger signal change in the gray matter (open symbols), the SE-based method shows a larger relative signal change in the white matter (solid symbols).

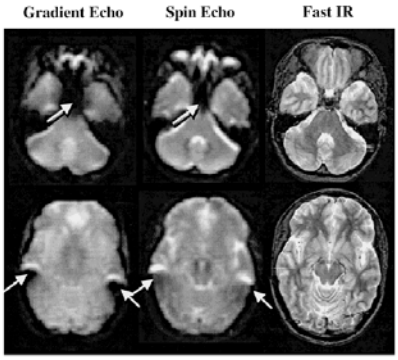
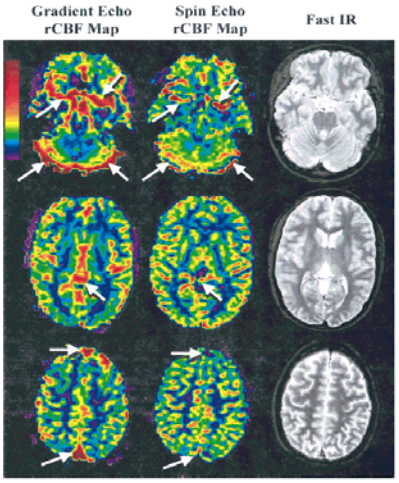


Figure 2. Source images for the gradient-echo method (left), the spin-echo method (middle), and the corresponding anatomic inversion recovery images. The more pronounced signal losses at the air-tissue boundaries in the gradient-echo images are visible (see arrows). The geometric distortions are equal since the acquisition parameters are kept constant for the two EPI-based methods.

Spin Echo v/s Gradient Echo



Figures 3. rCBF maps calculated from the gradient-echo (left), the spin-echo (middle), and the corresponding anatomic inversion recovery (right) images. The appearance of large vessels is markedly reduced in the spin-echo images (arrows), resulting primarily in a representation of capillary perfusion.

Spin Echo v/s Gradient Echo

- spin-echo(SE)-based perfusion MRI yield a better estimate of capillary tissue perfusion.
- In computer simulations, the sensitivity of a GE based method is relatively independent of the size and distribution of vessels and capillaries within a given voxel, whereas SE-based methods show a maximum sensitivity for vessels between 5 and 10 mm diameter, the size of capillaries in the human brain.
- The apparent advantage of the GE technique is its higher contrast-to-noise ratio (CNR) compared with the SE technique.

References

- Methodology of Brain Perfusion Imaging: Emmanuel L. Barbier, PhD,1,2 Laurent Lamalle, PhD, and Michel De´corps, PhD

- Perfusion MRI of the Human Brain With Dynamic Susceptibility Contrast: Gradient-Echo Versus Spin-Echo Techniques: Oliver Speck, PhD, Linda Chang, MD, N. Menaka DeSilva, MD, and Thomas Ernst, PhD