BRAIN BYTES

Perfusion MRI: a brief overview

Introduction

The evaluation of brain hemodynamics is a cornerstone in researching diseases of the brain and psyche. Traditionally, cerebral perfusion measurements have been made using radiation-based techniques such as positron emission tomography, single photon emission computed tomography and Xenon-enhanced computed tomography. Advances made using Magnetic Resonance Imaging (MRI)-based techniques now offer advantageous non-ionizing alternatives for the evaluation of brain perfusion in a number of pathological conditions and in healthy volunteers. Perfusion MRI (pMRI) is increasingly applied in preclinical and clinical settings because of the widespread accessibility of MRI scanners and the lower level of invasiveness that MRI offers.

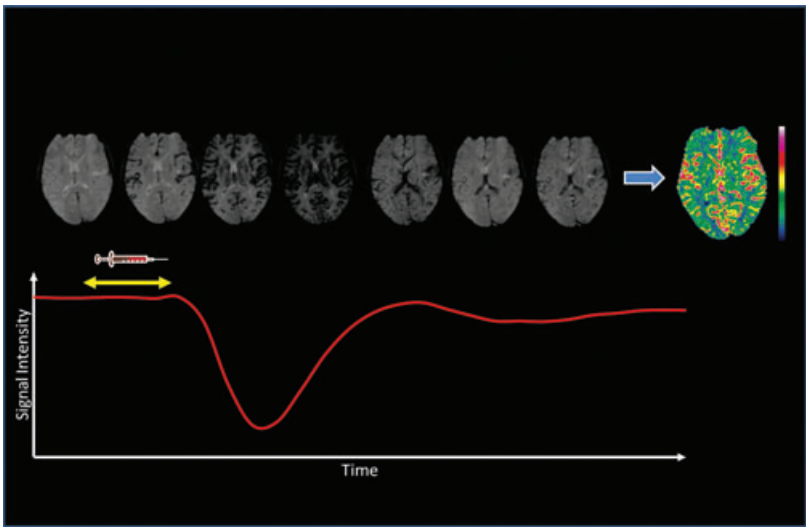

Fig. 1. Basic principle of an DSC-MRI perfusion imaging experiment. Bolus injection of a gadolinium chelate results in a dynamic signal drop in the MR image during the passage of the contrast agent. This dynamic signal change can be converted to physiological parameters like relative CBV and relative CBF using established tracer kinetics theory.

Methodological principles

The most commonly applied methods in pMRI are the dynamic contrast enhancement (DCE) approach, which uses an injected exogenous contrast agent as a flow tracer, and arterial spin-labelling (ASL), which uses magnetically tagged water protons in arterial blood as an endogenous flow tracer.

DCE-MRI utilizes injectable gadolinium chelates as a non-diffusible paramagnetic tracer in combination with ultra-fast MR imaging sequences to measure either a decrease in signal intensity (T2/T2*-weighted; dynamic susceptibility contrast, DSC) (Fig. 1) or an increase in signal intensity (T1-weighted DCE) during the first passage of the injected tracer through the cerebral vascular bed. Signal-to-noise (SNR)-levels using this technique are excellent, and a whole-brain pMRI experiment using voxels of 15–20 mm^3 takes about 2 min to perform, where the repetition time of the imaging sequence is kept at 1–2 s. The resulting time series are analysed using tracer kinetic theory (1) using commercially available software packages to estimate relative hemodynamic parameters such as cerebral blood volume (CBV), cerebral blood flow (CBF), usually presented as parametric maps overlaid high-resolution MRI.

In ASL-MRI, the protons of blood water flowing into the brain are magnetically tagged at the level of the feeding arteries using a radio frequency pulse (Fig. 2). The magnetically labelled blood water protons decays with T1 relaxation, with a half-life of 1–2 s, depending on magnetic field strength. The effects of ASL are measured by subtracting images acquired with and without magnetic labelling, and the signal difference directly reflects local perfusion. From the signal difference absolute CBF may be quantified using analytical framework based on diffusible tracer clearance theory (2). SNR levels using ASL are low (0.5–1.5% signal change), and therefore an image acquisition time of 5–10 min is needed to robustly determine full brain CBF. A large number of different spin-labelling schemes with accompanying exciting acronymic names exist (3) and new versions with improved performance appear continuously. ASL-MRI is preferably performed using higher field strengths for several reasons. As the T1 relaxation time increases with field strength, a higher magnetic field enables a longer time window to measure the signal of interest. Also, because the by subtracting images acquired with and

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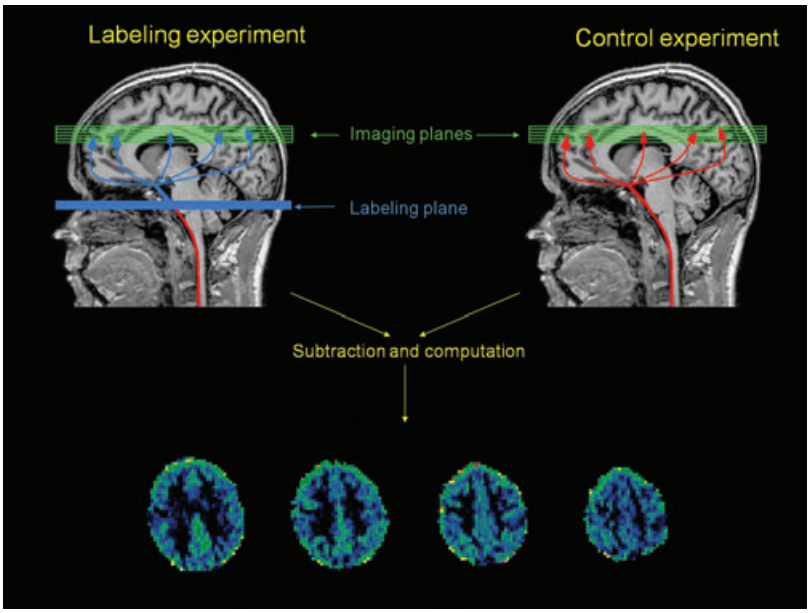

Fig. 2. Basic principle of an ASL-MRI perfusion imaging experiment. Two image sets are acquired: One in which the blood water protons are magnetically labelled proximally to the imaging slices using a radiofrequency pulse and one unlabeled control image set. Subtraction of the image sets produce a map of the distribution of labelled protons which is used to compute quantitative CBF maps. *ASL images courtesy of Dr. K. Emblem, Rikshospitalet.*

ASL-technique is relatively SNR-starved, it benefits from the general increase in SNR with increasing field strength. It is generally agreed upon that ASL-MRI-experiments should thus be performed using magnets of 3 T or higher field strengths.

Main limitations and advantages

Because of a non-linear relationship between the measured MRI-signal-changes and tracer concentration combined with other methodological challenges, robust quantitative determination of tissue perfusion with DSC-MRI is currently not feasible (4). Also, because the elimination of gadolinium chelates from the body is limited by renal clearance, in practice, only one measurement may be performed in a subject daily. The general utility of DSC-MRI is further limited in subjects with compromised kidney function, as the injection of gadolinium in rare instances may produce the potentially fatal condition 'nephrogenic systemic sclerosis'.

The complete non-invasiveness of ASL-MRI makes it very suitable for perfusion studies requiring repetitive follow-ups. The method, depending on an endogenous tracer, may be repeated infinitely. It gives reproducible absolute CBF measurements in cerebral grey matter, but is unsuitable for studying white matter. As the generated values are absolute, it is easy to compare results over sessions and subjects. Unfortunately, the sequences used for ASL and the postprocessing schemes are still relatively intricate and not routinely implemented on commercial scanners, therefore limiting its use to dedicated research settings.

Use of pMRI in neuropsychiatric research

In practice, the potential side-effects of gadolinium injections limit the use of DSC-MRI to strictly indicated clinical examinations in brain cancer and stroke.

ASL on the other hand, has numerous qualities making it a very attractive method in neuropsychiatric research. The repeatability and non-invasiveness of the method makes it very suitable for acute and longitudinal pharmacological validation studies (6). ASL may also be used as alternative approach to blood-oxygen-level-dependant (BOLD) functional MRI (fMRI). Contradictory to BOLD-fMRI, ASL-fMRI boasts high intra- and intersubject reproducibility. ASL-fMRI is also believed to localize activated brain regions more accurately than BOLD-fMRI (5), which is affected by oxygenation changes in draining venous vessels, generating activation signals from 'down stream' areas.

Conclusions

MRI-based methods for measuring cerebral perfusion are increasingly accessible, and present spatial and temporal high-resolution alternatives to radiation-based methods for assessing brain hemodynamics. ASL-MRI is the most suitable technique for performing neuropsychiatric studies, and should preferably be done on high-field magnets. Its implementation requires a certain level of dedication, as ASL still is not a standard on commercial scanner systems.

Inge Rasmussen Jr[1], Atle Bjørnerud[1,2]

[1]Interventional Center, Rikshospitalet University Hospital Oslo, Oslo, Norway; and
[2]Departement of Physics, University of Oslo, Oslo, Norway

Dr.Inge Rasmussen Jr
Interventional Centre,
Rikshospitalet,
Sognsvannsveien 20,
0027 Oslo,
Norway.
Tel: +47 23 07 01 11;
Fax: +47 23 07 01 10;
E-mail: inge@brainlab.no

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References

1. Meier P, Zierler KL. On the theory of the indicator-dilution method for measurement of blood flow and volume. J Appl Physiol 1954;**6**:731–744.
2. Kety SS, Schmidt CF. The nitrous oxide method for the quantitative determination of cerebral blood flow in man: theory, procedure and normal values. J Clin Invest 1948;**4**:476–483.
3. Barbier EL, Lamalle L, Decorps M. Methodology of brain perfusion imaging. JMRI 2001;**13**:496–520.
4. Boxerman JL, Hamberg LM, Rosen BR, Weisskoff RM. MR contrast due to intravascular magnetic susceptibility perturbations. Magn Reson Med 1995;**34**:555–566.
5. Duong TQ, Kim DS, Ugurbil K, Kim SG. Localized cerebral blood flow response at sub-milimeter columnar resolution. Proc Natl Acad Sci USA 2001;**98**:10904–10909.
6. Petersen ET, Mouridsen K, Golay X. The QUASAR reproducibility study, Part II: Results from a multi-center Arterial Spin Labeling test-retest study. Neuroimage 2009; (In Press).