

Specialty area: Perfusion in the Brain, Heart & Body

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Highlights:

- **Consensus recommendation proposes pseudo-continuous labeling, background suppression, and segmented 3D readout as workhorse ASL-sequence**
- **New sequences and post-processing approaches for mapping of oxygen extraction fraction**
- **Methods to obtain information on microvascular functioning and architecture beyond cerebral blood flow**
- **Techniques to image flow territories and cerebrovascular disease-induced changes**

Title: Cerebral Perfusion Imaging

Target audience: clinical and technical oriented neuroscientists, neuroradiologists, neurologists

Objective: To describe recent innovations in cerebral perfusion MRI

Background: Whereas the brain represents only about 2% of the body weight, it accounts for 20% of the body's total energy consumption. Since the brain lacks almost any form of energy storage, all energy needs to be transported into the brain by means of cerebral perfusion, and regulation of perfusion has to be tightly coupled to neuronal activation. Even short interruptions of the blood supply have been estimated to lead to a dramatic loss of neurons (1 million per minute), synapses (14 billion per minute) and myelinated fibers (12 km per minute) (1). Fortunately, the human brain has many reserve mechanisms to sustain sufficient delivery of oxygen and nutrients, such as large vessel collaterals (e.g. via the Circle of Willis), local control of microvascular resistance, and systemic control. In the last 25 years, two main MRI techniques for measuring cerebral perfusion have emerged. The first, arterial spin labeling MRI (ASL) exploits inversion of arterial blood magnetization as an endogenous tracer, whereas the second technique, named dynamic susceptibility contrast MRI (DSC-MRI), relies on dynamic monitoring of the first passage of contrast agent through brain tissue. Recent new developments and their application will be presented.

Consensus on clinical implementation of ASL: In the last 20 years a plethora of new ASL labeling methods, readout options and quantification approaches have been proposed. Many of these were highly important steps in the maturation of the ASL-technique towards clinical quality perfusion maps in a clinically acceptable scan-time. However, the high amount of different sequences did also result in a rather slow clinical and commercial acceptance of ASL, due to uncertainty of what sequence to use. In the last two years, the perfusion studygroup in collaboration with the EU COST-action "ASL in dementia" has had numerous discussion-sessions to achieve a consensus recommendation on ASL, resulting in a recommended default implementation consisting out of pseudo-continuous labeling, background suppression, segmented 3D readout without vascular crushing gradients, and calculation and presentation of both tag/control difference images and cerebral blood flow in absolute units using a simplified model (2). By using acquisitions similar to the

recommended sequence, ASL has been successfully applied in e.g. acute stroke (3,4), brain tumours (5), Alzheimer's disease (6), Moyamoya disease (7), vascular reactivity measurements in large vessel disease patients (8), resting state fMRI (9), cognitive studies (10) and pharmacological MRI (11).

Oxygen extraction fraction (OEF) measurements: In the end stage of cerebral autoregulation, more oxygen is extracted from the blood, which proves a strong indicator of chronic hemodynamic impairment, as shown e.g. by PET with ^{15}O -oxygen as tracer (12). Many MRI-based methods have been proposed to obtain OEF-maps, either by exploiting phase changes due to the magnetic susceptibility of deoxyhemoglobin (13), differences in T_2 and T_2^* (14), and by combined hypercapnic and hyperoxia challenges (15,16). Moreover, in the last few years techniques have been proposed that first isolate venous signal by applying velocity selective or traditional ASL techniques, followed by an MLEV-T2 measurement module (17-19).

Microvascular structure and functioning: By monitoring the first pass of contrast agent with combined gradient and spin echo imaging, it is possible to obtain information on the mean vessel size of the microvasculature (20). More recent studies into the differences between gradient and spin echo signal changes induced by contrast agent, result in more information on the microvascular architecture and oxygenation-status, which seems especially helpful in characterization of neo-vasculature in brain tumours as well as treatment responses (21-24). Whereas traditionally only the maximum value (CBF) and the area-under-the-curve (CBV) of the residue function is exploited in DSC-MRI (note that the residue function is obtained by deconvolving the tissue passage curve with the arterial input function), the shape of the residue function has received more attention lately, since it can provide the distribution of transit times through the microvasculature (25,26). This capillary transit time distribution is hypothesized to change in brain diseases, such as Alzheimer's Disease and acute stroke, to guarantee sufficient supply of oxygen (27,28).

Flow territory mapping: Restricting the labeling in ASL to a single vessel or by varying the labeling efficiency in multiple scans, enables imaging of the downstream flow of labeled spins in a single artery, which can be exploited for vessel-selective angiography as well as for depiction of arterial flow territories. Applications of flow territory mapping have shown considerable changes in territories due to cerebrovascular disease and first studies are looking into the coupling between the vasculature and the neuronal networks (29,30). Last year a new technique, VENTI, was proposed to measure the venous territories (31).

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