Abstract  Absolute quantification of cerebral blood flow, cerebral blood volume and mean transit time is desirable in the determination of tissue viability thresholds and tissue at risk in acute ischaemic stroke, as well as in cases where a global reduction in cerebral blood flow is expected, for example, in patients with dementia or depressive disorders. Absolute values are also useful when comparing sequential examinations of tissue perfusion parameters, for example, in the monitoring and follow-up of various kinds of therapy. Regardless of the method employed, a number of assumptions and approximations must be made to obtain absolute measures of perfusion. Furthermore, the different stages of data acquisition and processing are associated with various degrees of uncertainty. In this review, the problems of particular relevance to absolute quantification of cerebral perfusion parameters using dynamic susceptibility contrast magnetic resonance imaging are discussed, and possible solutions are outlined.

Keywords  Perfusion · Cerebral blood flow · Dynamic susceptibility contrast MRI · Arterial input function · Quantification

Introduction

The term ‘perfusion’ normally refers to the capillary blood flow in tissue, i.e. the volume of blood passing through a given volume or mass element of tissue per unit time. Other haemodynamic parameters related to tissue blood supply are the blood volume, often expressed in relative terms as the blood volume fraction (in per cent by volume) or as the volume of blood in a given mass element of tissue, and the mean transit time (in units of time) of blood through the local capillary network from the arterial to the venous side. Since the blood carries oxygen and nutrition to the tissue through the capillaries, perfusion is important in maintaining tissue viability. The study of brain perfusion has several clinical applications, since changes in perfusion can be associated with a number of neurological diseases.

In the clinical environment, cerebral perfusion is often assessed by dynamic magnetic resonance imaging (MRI) in combination with an exogenous contrast agent [1,2]. By tracking the first passage of the contrast agent bolus through the blood vessels in the brain using rapid susceptibility-weighted imaging, and by applying kinetic models for intravascular tracers [3,4], perfusion parameters such as cerebral blood flow (CBF) in ml/(min 100 g), cerebral blood volume (CBV) in ml/100 g and mean transit time (MTT) in seconds can, in principle, be calculated (Fig. 1). This approach is known as dynamic susceptibility contrast MRI (DSC-MRI), and it relies on the fact that the exogenous paramagnetic contrast agent produces local magnetic field gradients that extend from the vascular compartment into the surrounding tissue, even if the contrast agent is not present in the extravascular space. These local magnetic field gradients lead to a reduction in the magnetic resonance (MR) signal in the images obtained with a $T_2^*$-weighted
The relationship between the signal, contrast agent, C, is proportional to the change in diffusion in the contrast agent-induced magnetic field gradients.

due to intravascular T2 shortening in combination with spin signal is also seen in spin-echo (SE) pulse sequences due to an infinitely short arterial bolus. Instead, the measured concentration-versus-time curve in the tissue is the convolution of a kernel, given by CBF · R(t), and the concentration-versus-time curve in the tissue-feeding artery, i.e. the arterial input function (AIF) [7–9]. A correction factor given by $k_H = [1 - H_{\text{large}}]/[\rho(1 - H_{\text{small}})]$, where $H_{\text{large}}$ and $H_{\text{small}}$ are the haematocrit values in large and small vessels, respectively, and $\rho$ is the density of brain tissue [8], is normally introduced. The incorporation of haematocrit values into the correction factor is due to the fact that the tracer is distributed in the plasma volume rather than in the whole-blood volume:

$$k_H C(t) = \text{CBFR}(t) \otimes \text{AIF}(t)$$

By monitoring the signal in an appropriate tissue-feeding artery separately over time, to measure the tracer concentration in the artery as a function of time, the CBF can be determined by deconvolution, as the initial height of the product of CBF and $R(t)$, due to the fact that $R(0) = 1$. Furthermore, the MTT can be determined by Zierler’s area-to-height relationship, according to Eq. 6 [10]:

$$\text{MTT} = \frac{\int_0^\infty R(t)dt}{\max[R(t)]}$$

where $\max[R(t)]$ is the peak value (theoretically the initial value) of the tissue impulse residue function. Furthermore, according to the central volume theorem [3,11], the blood volume can be calculated as the product of the blood flow and the mean transit time.

$$\text{CBV} = \text{CBF} \cdot \text{MTT}$$