Concurrent measurement of brain perfusion, blood volume and blood brain barrier permeability using dynamic contrast enhanced T1-weighted MRI

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**Introduction:** The measurement of brain perfusion (CBF) and cerebral blood volume (CBV) is important when diagnosing and treating vascular, degenerative and neoplastic diseases. These diseases are often associated with an increase of blood brain barrier (BBB) permeability. One clinical application relates to the discrimination between tumor recurrence and tissue degradation following radiation therapy. Despite the widespread use of MR perfusion imaging based on bolus tracking a concurrent estimation of CBF, CBV and permeability has proved difficult to achieve. Using dynamic contrast enhanced (DCE) MRI (1,2,3), an estimation of perfusion has not been possible and an estimation of the CBV has been problematic (4). In dynamic susceptibility contrast (DSC) MRI the effect of BBB leakage may compromise the estimation of CBV, partly due to a mixing effect of $T_1$ and $T_2^*$ relaxation (5). Generally, if CBV is estimated as the volume of distribution of the tracer an overestimation will occur in areas with BBB leakage. We present a methodology whereby a concurrent estimation of CBF, CBV and the permeability surface area (PS) product can be obtained. The method is based on DCE-MRI (6) and fundamental tracer kinetic principles. We demonstrate the method in patients with a brain tumor.

**Theory:** Basic tracer kinetic theory states that $C_a(t) = C_F C_i(t) R(t)$ where $R(t)$ is the residue impulse response function and $C_i(t)$ and $C_a(t)$ are tissue and arterial concentration curves. This equation requires linearity only and is independent of the exact distribution of the tracer in the compartments. $R(t)$ and CBF can be determined using deconvolution. The mean transit time MTT is the time integral of $R(t)$, and the volume of distribution of the tracer $V_d$ is calculated from the central volume principle as $V_d = CBF MTT$. If the BBB is intact, $V_d$ should represent the cerebral blood volume. If leakage occurs then we expect $V_d$ to become larger than the CBV as accessible extravascular compartments are included. The BBB permeability and vascular volume can be estimated independently using Patlaks method (7). Here the tissue is modelled as a reversibly accessible (blood) compartment, and an irreversibly accessible (extravascular) compartment. If plotting $C_i(t)/C_i(0)$ as a function of $\int_0^t C_i(\tau) d\tau/C_i(0) (t)$ the slope represents the unidirectional influx constant $(K_i)$, and the intercept represents the volume of the vascular compartment (denoted $V_a$). For a low permeating tracer, $K_i$ approximates the PS product.

![Fig. 1](image1.png)

**Results:** Perfusion in gray and white matter was 72±16 and 31±4 ml/100g/min, respectively, and 56±45 ml/100g/min in tumors. The corresponding values for CBV were 6±2, 4±1, and 7±6 ml/100g, and the PS products were 0.9±0.4, 0.9±0.3 and 2.2±2.1 ml/100g/min. Fig. 1 shows examples of parameter estimation using deconvolution (a) and the Patlak plot (b). Remark the overestimation of blood volume in (a) compared to (b). In (c) we compare the two estimates of CBV, $V_d$ and $V_a$. They agree for normal gray matter, whereas $V_d$ tends to be larger in tumor tissue. Finally, Fig. 2 shows maps of CBF, $K_i$, $V_a$ and $V_d$ for a tumor patient with a large glioblastoma.

**Discussion:** The present study shows that it is possible to estimate perfusion, blood volume and permeability from a single bolus injection, even in cases with a deficient BBB, when using $T_1$-weighted DCE-MRI. Our results point to the importance of considering the effect of leakage on the CBV estimation. We addressed this by explicitly including the extravascular compartment in the tracer kinetic modelling. The methodology shown here can be applied to determine both CBV and BBB permeability in tumor patients. This study is to our knowledge the first to report on the permeability of the normal BBB for a Gd containing contrast agent. Unexpectedly, $K_i$ was consistently found to be larger than zero. This issue needs to be studied further.


![Fig. 2](image2.png)