Measurement of CBF and PS product in brain tumor patients using T1 w dynamic contrast enhanced MRI at 3 tesla

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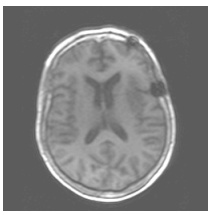
Introduction: Dynamic contrast enhanced MRI perfusion measurement of the brain is commonly performed by using T2* weighted sequences. However, several problems are associated with this method: the inherent image distortion due to susceptibility, especially in patients having undergone neurosurgery; systematic overestimation of perfusion because of different relaxivity of paramagnetic contrast agent (CA) in larger vessel (from which the input function is obtained) and in the capillaries; often problems of defining a good input function because of low spatial resolution on T2* weighted EPI, and finally a problem of estimating a deficient blood brain barrier (BBB), because the relaxivity of CA is different when confined in a small compartment compared with a distribution in the interstitial space. For this reason we investigated whether dynamic contrast enhanced MRI perfusion measurement using a T1 weighted sequence was possible. At 1.5 tesla the effect of such sequences is low; therefor the study was carried out at 3 tesla.

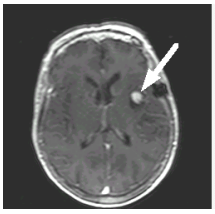
Purpose: 1) to estimate cerebral perfusion quantitatively pixelwise (CBF map) and in ROI's in normal brain 2) and in cases of BBB deficiency (tumor patients) to estimate the permeability surface area product (PS product) quantitativily.

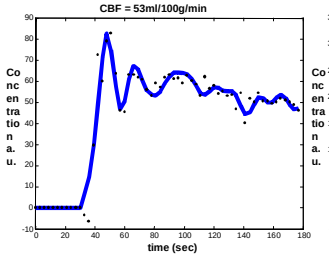
Methods: The study was carried out using a Philips 3 tesla Intera Achieva whole body scanner with a transmit/receive circular polarized head coil, on 10 brain tumor patients having MRI for clinical reason, either diagnostic or as part of a follow up. A dose of 0.1 mmol/kg gadodiamide inj. (Omniscan, GE Health) was injected in a peripheral vein during dynamic imaging. The sequence consisted of a 3D fast field echo sequence, where each phase step in kz was preceded by a non selective 90 degree pulse, having an interval between this pulse and the first alfa pulse of 20 ms (TI). The time between alfa pulses (nutation angle 12 degree) to generate xy magnetization for image generation (TR) was 4.1 ms, and TE was 2.1 ms. Matrix 78 x 128, FOV 230 mm. Six slices were obtained with a frame rate of one frame pr 3 sec. The selected sequence was linear in signal versus R_1 for the relevant concentration level of CA. Furthermore the short TI preclude a significant effect of water exchange between various compartments (1).

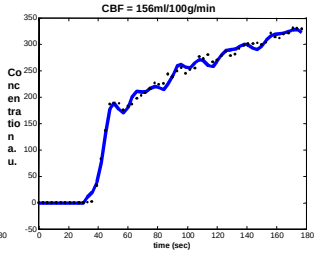
From one bolus injection both CBF and PS was estimated independently of each other: Having obtained the input function from a ROI placed inside the clearly visible middle cerebral artery, ROI's were placed in normal gray matter / tumor tissue lesions to obtian signal versus time curves (input function and tissue signal function respectively). Both the input function and tissue signal function were baseline corrected by subtracting the baseline signal i.e. before arrival of contrast agent. CBF was calculated using a general singular value decomposition having an additional side constrain consisting of the first order derivation of the residue impulse response (RF) function as a function of time, in order the decrease oscillation of the RF. CBF was also calculated pixelwise. From the same data the PS product was estimated from a Patlak plot, plotting the ratio of instant tissue concentration/ instant arterial concentration versus integrated arterial concentration/ the instant arterial concentration. The unidirectional influx constant, K_i, was calculated as the slope of the linear part of data in such plot and finally the PS product was calculated from the Crone-Reenkin equation: $K_i = CBF(1-exp(-PS/CBF))$.

Results: Fig.1 shows an axial slice in a brain tumor patient before and after CA injection (Fig.2) obtained with the 3D dynamic sequence. Note the relative good gray-white matter contrast before injection, and the enhancing lesion (inserted arrow).









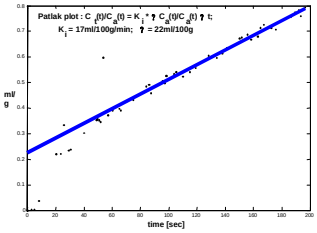
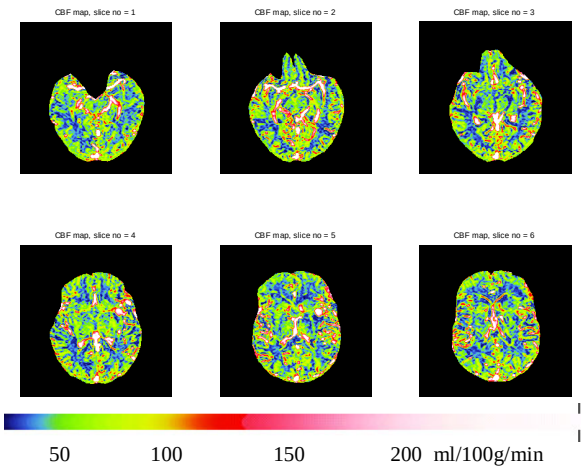


Fig.1 Fig.2 Fig.3 Fig.4 Fig.5

Fig.3 shows an example of tissue enhancement curve from a ROI placed in normal frontal gray matter, and Fig.4 from a ROI placed in the lesion shown in Fig.2. The perfusion model is fitted to data, and CBF values are inserted in the figures. Note that the first pass of the bolus is clearly differentiated from slower leakage of CA out of the vascular space. Fig.4 shows a Patlak plot from this lesion; the regression line is a fitted line to the linear part of the curve, with a K_i (slope) of 17 ml/100g/min. PS is calculated to 18 ml/100g/min.

Fig.6 shows an example of CBF map for the 6 slices. Gennerally, gray matter CBF for ROI's placed in frontal, temporal and occipital gray matter was 70± 21, and CBF of white matter was 12 ± 10, and CBF of the lesions found in patients was 92± 32 ml/100g/min. PS ranged 8- 24 ml/100g/min.

Fig.6



Conclusion: In this study we have shown that CBF measurenent and quantification of the permeability of the BBB is possible from the same set of data, using dynamic contrast enhanced T1-weighted MRI at 3 tesla. The method is robust, the input function is easily obtained from susceptibility and distortion free images, which easily can be fused with other images. The CBF and the deficient BBB is clearly separated and calculated independently of each other in 4 min. and no manipulation is required to obtain both the CBF and PS results.

1.Larsson HB et al. Quantification of the effect of water exchange in dynamic contrast MRI perfusion measurements in the brain and heart. MRM 2001;46:272-281.