Comparison of a data processing method accounting for contrast agent extravasation with the pre-load approach in bolus-based CBV estimates in tumors

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Introduction Estimate of relative Cerebral Blood Volume (rCBV) obtained with dynamic susceptibility-contrast MR methods suffers from contrast agent (CA) extravasation in brain tumors: competing T1 effect occurs and leads to rCBV underestimation (1). A CA preload is therefore advised (2). However this doubles the dose of CA that the patient receives. Alternatively, various methods have been proposed in order to account for CA extravasation (1-3). The aim of this study is to compare a data processing method accounting for CA extravasation (3) with the pre-load approach (2) in brain tumor patients.

Subjects and Methods Nine patients with cerebral tumor (5 glioblastomas, 2 oligodendrogliomas, 1 meningioma, 1 irradiated metastasis) were scanned at 1.5T. On each patient, a dynamic susceptibility contrast protocol (Gradient-echo EPI, TE/TR = 30/500ms, $\alpha = 45°$, tacq = 60 sec, bolus of 0.1 mmol/kg Gd-DOTA) was performed twice with an interscan delay of 6 to 12 minutes. rCBV maps were computed using two analysis protocols:
- protocol "gamma": fit of a gamma-variate to the data;
- protocol "dilution": fit of a (gamma-variate + CA dilution in the circulation) to the data (3).
For both protocols, rCBV was eventually computed as the area under the gamma-variate curve. Regions of interest were drawn in the tumoral region with maximum CA extravasation on the first scan (tumor), and in the contralateral white matter (WM) for each scan, each method and each patient. rCBV variations between both methods were also calculated.

Results In all cases, the "dilution" protocol fitted perfectly the data. This was not the case for the "gamma" protocol. Fig. 1 shows the data (blue), the "gamma" fit (red) and the "dilution" fit (green). The two components of the "dilution" fit (gamma and dilution parts) have also been explicitly represented. In this tumor, the "dilution" protocol yields a gamma-variate component wider than that of the "gamma" protocol and therefore a larger rCBV (Fig. 1). For the 2nd the second injection, the post-bolus baseline is above the pre-bolus baseline and "gamma" and "dilution" fits yield close rCBV values (data not shown).
Mean rCBV estimates from the 2nd injection are larger than those obtained from the 1st injection, for both analysis protocols and ROIs, but this is not the case for each patient. Variations in rCBV estimates between the 1st and the 2nd injection are less pronounced for the "dilution" protocol and for both ROIs (WM: +11.8% in rCBV for "dilution" vs +20.8% in rCBV for "gamma"; tumor: +20.3% vs +28.4%), suggesting that the "dilution" protocol compensates in part for the CA extravasation. Mean rCBV estimates derived from the 1st injection using the "dilution" protocol are however not correlated to that derived from the 2nd injection with the "gamma" protocol (R^2=0,12), suggesting that the "dilution" protocol does not perform as a CA preload.

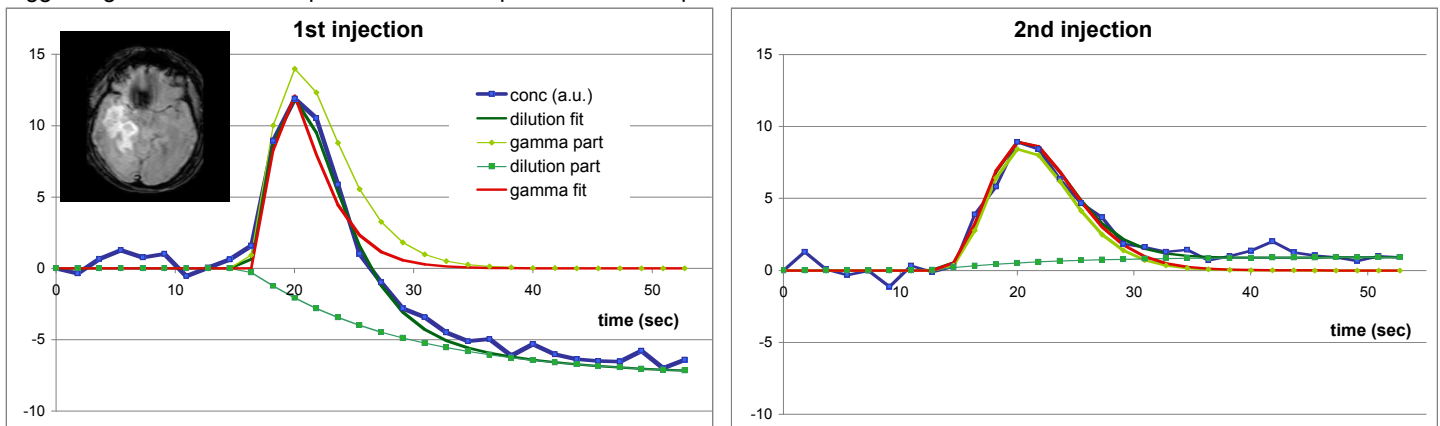Figure 1: Concentration versus time curves in the tumor from 1st and 2nd injections.

Discussion
It has been shown that a CA preload increases rCBV estimates where CA extravasates (1). We observed that, in our experimental conditions, this is not the case for each tumor bearing patient. We also observed that rCBV estimates in WM are also increased by the CA preload. An analysis of the 1st injection data accounting for the CA extravasation does not yield rCBV estimates that correlate to those obtained after CA preload. Further investigations are required to understand the effect of preload in WM and to evaluate the accuracy of rCBV estimates in tumor before and after preload. This could be achived by a comparison between rCBV estimates obtained with MRI and X-ray computed tomography. This study also suggests that normalization of rCBV estimates by WM values should be handled with care.

References
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