A novel 2D Pulsed Arterial Spin Labeling Protocol for Pediatric Cases with Brain Tumor

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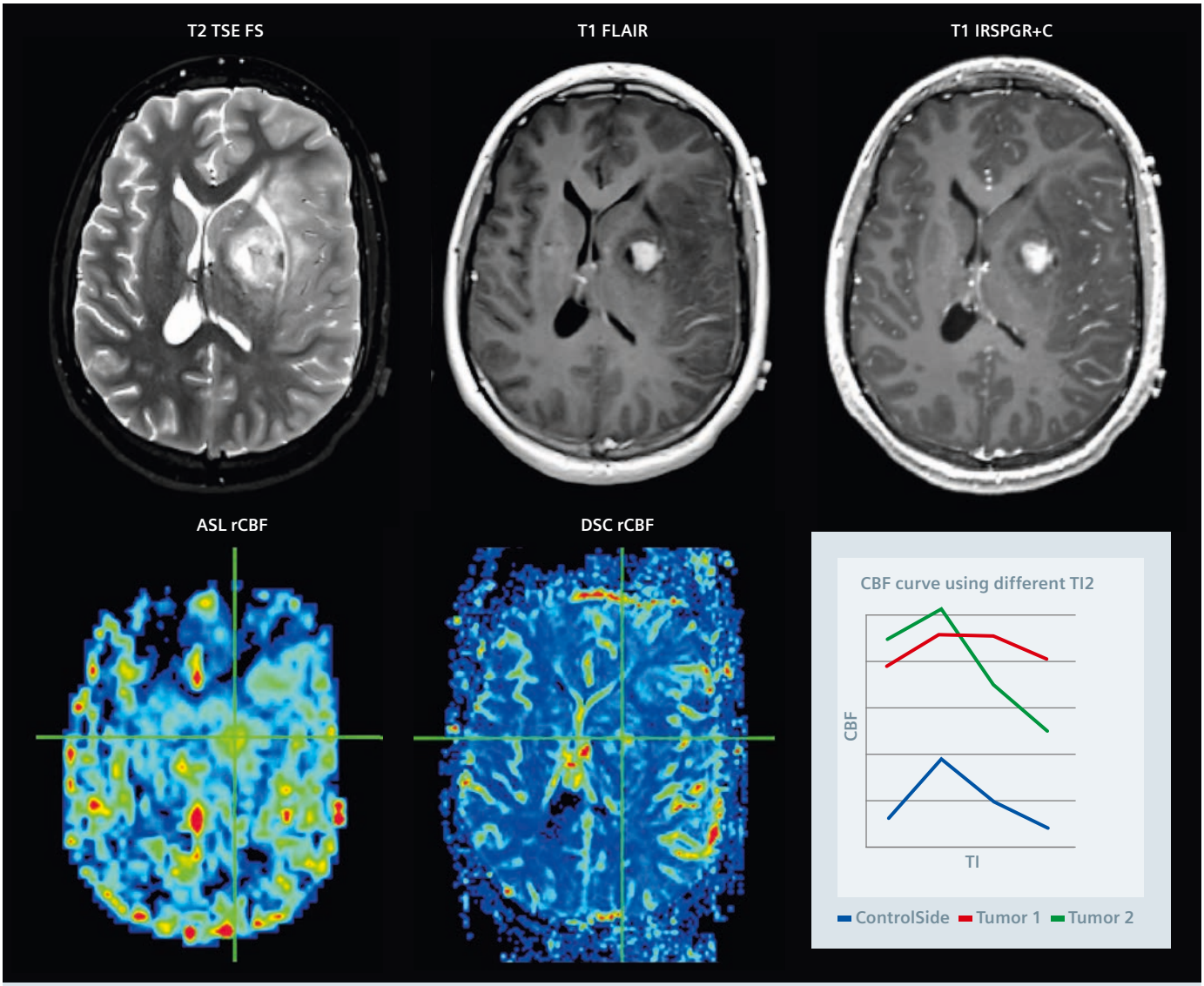

1 rCBF curve using different TI allows assessment of the rCBF considering pathological alteration in regional arterial transit time.

Introduction

Arterial spin labeling (ASL) is a non-invasive MRI technique that does not rely on ionizing radiation for measuring regional cerebral blood flow (rCBF). ASL can be applied as an attractive alternative method for measuring perfusion in pediatric[#] brain tumor patients where it is desirable to minimize the use of ionizing radiation and Gd-based contrast agents. Compared with conventional dynamic susceptibility contrast (DSC) techniques, ASL can be quantitative enabling the measurement of global hypo- or hyperperfusion as well as absolute perfusion changes in longitudinal studies. However, to date ASL has not been widely utilized in clinical practice.

Quantification of rCBF using ASL perfusion MRI requires several experimental and physiological parameters to be properly accounted for. Variable bolus transit time and post-labeling delay are two confounding factors that may compromise the quantitative accuracy of perfusion estimates [3]. While the widely used PICORE Q2TIPS method of pulsed ASL (PASL) with a fixed temporal width tagging bolus enables quantitative estimates of rCBF from measurements taken at a single inversion time (TI), one of the key assumptions of Q2TIPS is that TI is sufficiently long for the trailing edge of the tagged bolus to have reached the imaging voxel [4]. Empirical observations suggest that transit time can be altered in different physiological and/or pathological conditions [1, 3, 5]. Therefore, we have developed a new PASL protocol[§] that fits the single compartment model to multiple TI acquisitions to reduce artifacts caused by spatially variable bolus transit times[&].

Theory

PASL uses an inversion pulse and a tag saturation module to define the temporal duration of the tag (e.g. QUIPSS or Q2TIPS methods) [8], where a single compartment model can be used to estimate rCBF [2].

$$\begin{aligned} \Delta M &= 0 && TI_2 < t_A \\ \Delta M &= 2 f M_0 \alpha (TI_2 - TI_1) e^{-\left(\frac{t}{T1b}\right)} && t_A < TI_2 < t_A + TI_1 \\ \Delta M &= 2 f M_0 \alpha \; TI_1 e^{-\left(\frac{t}{T1b}\right)} && t_A + TI_1 < TI_2 \end{aligned}$$

In this model ΔM is the signal difference between label and control images, TI_2 is the total inversion time between the label pulse and the readout of the proximal slice, TI_1 is bolus cut off time (also defines bolus duration), t_A is the arterial transit time (ATT) referring to the time it takes the arterial blood to travel from the labeling site to the capillaries in the issue being imaged, T_{1b} is the longitudinal relaxation time of blood, α is the inversion efficiency and M_0 is the acquired map of equilibrium magnetization of arterial blood. This model assumes no exchange of labeled blood water into the tissue. Using this model, the rCBF map can be calculated using equation (1) [7], where λ = blood/tissue water partition coefficient, τ = bolus cut off time (also defines bolus duration).

$$f = \frac{\lambda \Delta M}{2 \alpha M_0 \tau \exp(-TI_2 / T_{1b})} \qquad (1)$$

In this model as proposed by Buxton et al. [2], different slices are measured at different inversion times TI_2^{SLICE} due to the acquisition duration of a slice using 2D fast imaging methods like EPI, so that rCBF estimates that account for different TI_2^{SLICE} can be made by applying an inverted factor $\Delta M^{CORRECTED} = \Delta M.exp(\Delta TI_2^{SLICE} / T_{1b})$, which normalizes the different TI_2^{SLICE} for different slices to the first slice with $TI_2^{SLICE\_1}$. In line with the shape of PASL kinetic curves shown by Gallichan et al. [3], after a transit time Δt, the first inverted blood spins of the bolus arrive at the slice. During the time $(\Delta t + \tau)$, the bolus accumulates in the slice and give the increase in perfusion signal ΔM according the function $\Delta M \sim t.exp(-t/T1')$. At the time $(\Delta t + \tau)$, the perfusion signal ΔM reaches a maximum. After the time $(\Delta t + \tau)$ the perfusion signal ΔM undergoes longitudinal relaxation modeled with an effective relaxation time $T1'$ according the function $\Delta M \sim exp(-t/T1')$. $T1'$ is a function of $T1$ in tissue and blood. This approach minimizes bias in rCBF values if the bolus arrives in time in all regions of the slice with minimal temporal dispersion. In brain regions with altered bolus transit times due to pathology or biological differences, the bolus transit times are larger than $(TI_2^{SLICE} - \tau)$, then the standard model calculation will underestimate the true rCBF.

In this study, we introduce a novel protocol to acquire two consecutive PASL scans with identical parameters, one in ascending and another in descending slice order. Each slice now has two average perfusion maps with different TI_2^{SLICE} times. The two maps and corresponding TI_2^{SLICE} can be interpolated, e.g. an average $TI_2^{compensated} = (TI_2^{SLICE\_1,1} + TI_2^{SLICE\_1,2}) / 2$ is assumed. Then, all slices have the same average TI_2, while signal-to-noise ratio (SNR) per unit time is preserved. No further assumptions, as in the standard model, are required, because all maps for different slices are quantified with $TI_2^{average}$. This approach minimizes bias in rCBF estimates if the bolus arrival time varies between brain regions. In addition, a model validity map can be calculated from the rCBF maps at different TI_2^{SLICE}: the experimental signal difference at different TI_2^{SLICE} is set in ratio (A / B) to the theoretical model: $\Delta M(TI_2^{SLICE\_1,1}) / \Delta M(TI_2^{SLICE\_1,2})$=:A compared to $\exp(-(TI_2^{SLICE\_1,1} - TI_2^{SLICE\_1,2}) / T1')$ =:B.

Moreover, we collected data using four different inversion times (TI_2) with a fixed bolus cut off time (TI_1), then fitted those four different datasets with the theoretical perfusion curve of the single compartment model, in order to estimate rCBF and regional ATT [3].

Methods

PASL data were acquired using PICORE Q2TIPS sequence on a 3T MRI scanner (MAGNETOM Verio, A Tim System, Siemens Healthcare, Germany).

A 32-channel head receive coil was used to increase SNR. Scan parameters: 16 slices, 5 mm thickness, dist. factor 20%, matrix 64 × 64, field-of-view (FOV) 24 cm, 6/8 partial Fourier, BW 2298 Hz/Px, TR 3000 ms, TE 13 ms, TI_1 700 ms, four different TI_2 (1200 ms, 1500 ms, 1800 ms, 2100 ms) were applied twice with one scan in ascending and another one in descending slice order, each scan with 32 acq. pairs plus one M_0 image, total scan time of the protocol about 11 min. Inline 3D Prospective Acquisition

Correction (PACE) was used during all PASL scans to minimize head motion artifacts [6]. In post-processing, perfusion-weighted images were calculated for each TI2 acquisition and combined from two scans with different slice order. Then four different perfusion-weighted images were fitted into the single compartment model to estimate ATT and rCBF, as described elsewhere [1, 3].

Case report

A 16-year-old male presented with slurred speech and blurred vision. MR morphological imaging shows a heterogeneously enhancing tumor centered in the left putamen with a final pathologic diagnosis of primitive neuroectodermal tumor (PNET). Both PASL and DSC perfusion are concordant in demonstrating regional increased CBF within the tumor, consistent with a high grade neoplasm. Using our novel PASL protocol, we were able to generate different rCBF maps at different TI, and more precisely assessed the rCBF, considering the pathological alteration in regional ATT (Fig. 1).

Conclusion

The development of a robust, quantitative ASL protocol is critical for estimation of CBF in research and clinical applications. A number of studies have measured multiple TI times for the same slices and demonstrated in healthy human brain that the model provides unbiased rCBF estimates in some regions, but in other regions considerable bolus dispersion and latency have been observed [3]. Moreover, acquisition of multiple TI will considerably increase the exam time and might not be feasible in some clinical applications. In this report, a novel PASL multiple-TI protocol is introduced using a 32-channel coil to preserve SNR at clinically acceptable measurement durations. Brain tumors remain the second most common tumor in the pediatric age group after leukemia. It is well known that malignant brain tumors typically cause neoangiogenesis due to increased metabolic demand, resulting in an increase in rCBF. By developing a robust, quantifiable ASL protocol tumor grading – and therefore clinical management – can be more accurately accomplished without the use of gadolinium injection. The novel PASL multiple-TI method enables us to more accurately estimate rCBF in pediatric tumor cases at clinically acceptable examination time. Future research is needed to determine whether this method may be useful for doctors in making treatment decisions and monitoring patients' response to treatment.

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[#]MR scanning has not been established as safe for imaging fetuses and infants under two years of age. The responsible physician must evaluate the benefit of the MRI examination in comparison to other imaging procedures.
[§]WIP – Works in progress: The new PASL protocol is currently under development; it is not for sale in the U.S. Its future availability cannot be ensured.
[&]Patent US 2010/0141254 A1 by J. Pfeuffer using this technique was filed on Oct 22, 2009.