

**Introduction** Vessel size imaging (VSI) is a relatively new MRI technique that relates the contrast agent-induced changes of transverse relaxation rates, $R_2$ and $R_2^*$, to each other [1,2] to obtain an index that provides information about the size of vessels within a voxel of interrogation. Ideally, such measurements require the simultaneous acquisition of multiple gradient-echo (GE) and a spin-echo (SE) signals. However, limiting the acquisition to just one GE and SE induces $T_1$-related errors in the estimation of the vessel size [1]. This problem can be solved by acquiring multiple GE/SE-signals (Fig.1), from which one can derive $T_1$-independent estimates of $R_2$ and $R_2^*$ from before and during contrast-agent passage. The parameter estimates can then be used to improve accuracy in VSI.

**Theory and Methods** A spin-and gradient-echo (SAGE) echo-planar imaging (EPI) pulse sequence [3] with parallel imaging was used for bolus-perfusion measurements with the capabilities to detect $R_2$ and $R_2^*$, as well as $AR_2$ and $AR_2^*$, the bolus-induced changes in these values. Assuming static dephasing for $AR_2^*$ determination [4] and slow-diffusion approximation for $AR_2$ [5], the vessel size index can be calculated according to [1,2] via:

$$ R = 0.867 \cdot \sqrt{\frac{D}{\Delta R_2^*}} \cdot \frac{\Delta R_2^*}{\Delta R_2^*_{\text{pre}}} $$

Both the diffusion coefficient $D$ and the volume fraction of blood in tissue $\zeta$ are spatially varying and should ideally be included for accurate calculation of the VSI. In this study, we used relative cerebral blood volume (CBV) maps determined from the bolus-perfusion experiment as an approximation for $\zeta$:

$$ \zeta = k \cdot \text{CBV} = \frac{k}{TR} \int \left( R_2^*(t) - R_{2,\text{pre-bolus}}^* \right) dt $$

Here, $k$ is a correction factor that is necessary to relate CBV to the absolute volume fraction of blood. With dynamic susceptibility-contrast perfusion weighted imaging (DSC-PWI), an absolute value for $k$ cannot be determined; therefore all the calculations in this study are based on relative values. Moreover, we used the simplified assumption of a constant $D$ across the brain. Changes in $R_2$ and $R_2^*$ were calculated as follows:

$$ \Delta R_2 = \frac{1}{TR} \int \left( R_2^*(t) - R_{2,\text{pre-bolus}}^* \right) dt $$

From the substitution of $\Delta R_2$ and $\Delta R_2^*$ in Eq. (1) by Eq. (3) follows:

$$ R = 0.867 \cdot \sqrt{\frac{D}{\Delta R_2^*}} \cdot \frac{\Delta R_2^*}{\Delta R_2^*_{\text{pre}}} $$

$R_2(t)/R_2^*(t)$ were calculated through least-squares fit of the characteristic signal equations [6]:

$$ S(t) = S_{0} \cdot e^{-R_2^* t} $$

with $S(t)$ measured at 4 different $TE$ using the SAGE-EPI sequence. This method has the advantage of inherently $T_1$-insensitive $R_2$ estimations (same as the non-EPI measurements in [1]) performed in animals measured in steady-state, but opposed to the single gradient-echo EPI acquisitions in [2] that cannot reveal an absolute measure of $R_2^*$. Also, $R_2^*$ is free from $T_1$-biases as opposed to the two-point techniques for $AR_2^*$ estimation used in [1,2].

Imaging parameters were chosen as follows: field strength = 3T, 4 EPI echo trains ($R = 3$) were acquired with $TE = 16.8, 38.3, 87.2$, and $107$ ms; $TR = 1800$ ms, $14$ slices with $5$ mm slice thickness; in-plane resolution = $96\times96$, FOV = $24$ cm; $60$ dynamic time-points. $19$ ml Gd-DTPA were injected into the right hand of a tumor patient at a flow rate of $5$ ml/s, followed by $25$ ml saline flush.

**Results and Discussion** Fig.2 shows $R_2$ and $R_2^*$ maps in a tumor patient after surgical treatment. Fig.3 gives a glance at the relative cerebral blood volume (rCBV), as well as the vessel size index VSI. We were able to acquire a qualitative measure of the mean vessel size per voxel with multi-echo SAGE-EPI, with $R_2$ and $R_2^*$ being estimations of relaxation rates free of $T_1$-biases.


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**Fig.1:** Spin- and gradient-echo (SAGE) EPI sequence [3] used in this study for $T_1$-independent estimation of $R_2$ and $R_2^*$

**Fig.2:** Comparison of $R_2$ (left) and $R_2^*$ (right) in a brain-tumor patient. The scale on the right is in $ms^{-1}$. $R_2$ and $R_2^*$ were calculated using the characteristic signal equations (Eq. 5).

**Fig.3:** Cerebral blood volume (left) and vessel size index (right). Both maps show relative number numbers indicated on the scale on the right.

**Fig.4:** Histogram of the vessel size index for the slices shown in Fig.3.