Evaluation of non-invasive MRI based measurement of blood oxygenation in malignant glioma

J. den Hollander¹, C. Prebisch¹, A. Förschler¹, J. Gemp², H. Kooijman³, C. Zimmer ¹

¹ Department of Neuroradiology, ²Department of Neurosurgery, Technische Universität München, Munich; ³Philips Healthcare, Hamburg

Introduction

Hypoxia has been linked to tumor progression and therapeutic resistance. New studies show that a hypoxic microenvironment promotes the self-renewal and development of tumor stem cells within malignant glioma, suggesting that these cells may contribute to tumor maintenance and recurrence [1]. Emerging MRI techniques for non-invasive measurement of blood oxygenation [2] might allow in vivo detection of hypoxic areas within malignant glioma and may help to improve therapeutic strategies in the future. In our study, we seek to evaluate measurements of blood oxygenation levels within malignant tumors based on the theory of Yablonski & Haake [3].

Methods

The fractional cerebral blood oxygenation $Y$ is related to the transverse relaxation rates $R_1 = 1/T_1$ and $R_1^* = 1/T_1^*$:

$$Y = 1 - \frac{R_1^*}{C\cdot CBV}; \quad R_1^* = \frac{I}{T_1^*} - \frac{I}{T_1}$$

($CBV$: cerebral blood volume; $C = 4g\cdot \alpha\cdot \beta_\gamma$, const.)

Quantitative maps of transverse relaxation times $T_2$ and $T_2^*$ were obtained from exponential fits of multi-echo signals of spin and gradient echo sequences (Fig. 1).

Subjects: Quantitative $T_2$ and $T_2^*$ maps were obtained from 6 patients with malignant glioma (4 male, 2 female, 61±9 a).

Instrumentation: 3 T whole body scanner (Philips Achieva): body coil for transmit; 8-channel head coil for receive

Imaging Parameters:

- Spatial resolution for all measurements: 10 slices, matrix 112x106, voxel size 2x2x3 mm³
- $T_2$ measurement: GRASE with EPI factor 7 and SENSE factor 2, 6 echoes, TE = [20,120] ms, TR = 2146 ms, $\alpha = 90^\circ$, duration 34 s
- $T_2^*$ measurement: multi-GE: 8 echoes, TE = [6,51,5], TR = 1000 ms, $\alpha = 30^\circ$, duration 94 s

Postprocessing:

Evaluation was performed with custom programs written in MATLAB und SPM8 [5] and comprised exponential fit for $T_2$ and $T_2^*$, spatial coregistration and calculation of $R_1^*$.

Results and Conclusion

Fig. 2 summarizes preliminary results in 4 patients. Increased $R_1^*$ values indicate areas with low blood oxygenation levels within viable tumor tissue. These results indicate that a non-invasive measurement of oxygen saturation within malignant glioma might be feasible in a clinical setting.

However, further effort is needed to validate these results:

- Inclusion of quantitative CBV measurement [4] to control for blood volume effects and enable calculation of $Y$
- Correlation with immunohistochemical analyses of biopsy specimen to validate hypoxic areas
- Higher spatial resolution for better delineation of anatomical features
- Correlation with clinical outcome of $R_1^*$ positive and negative patients could identify $R_1^*$ as a prognostic factor

References: