

# Vasoreactivity Mapping using Dynamic (C)O<sub>2</sub> Enhanced MRI

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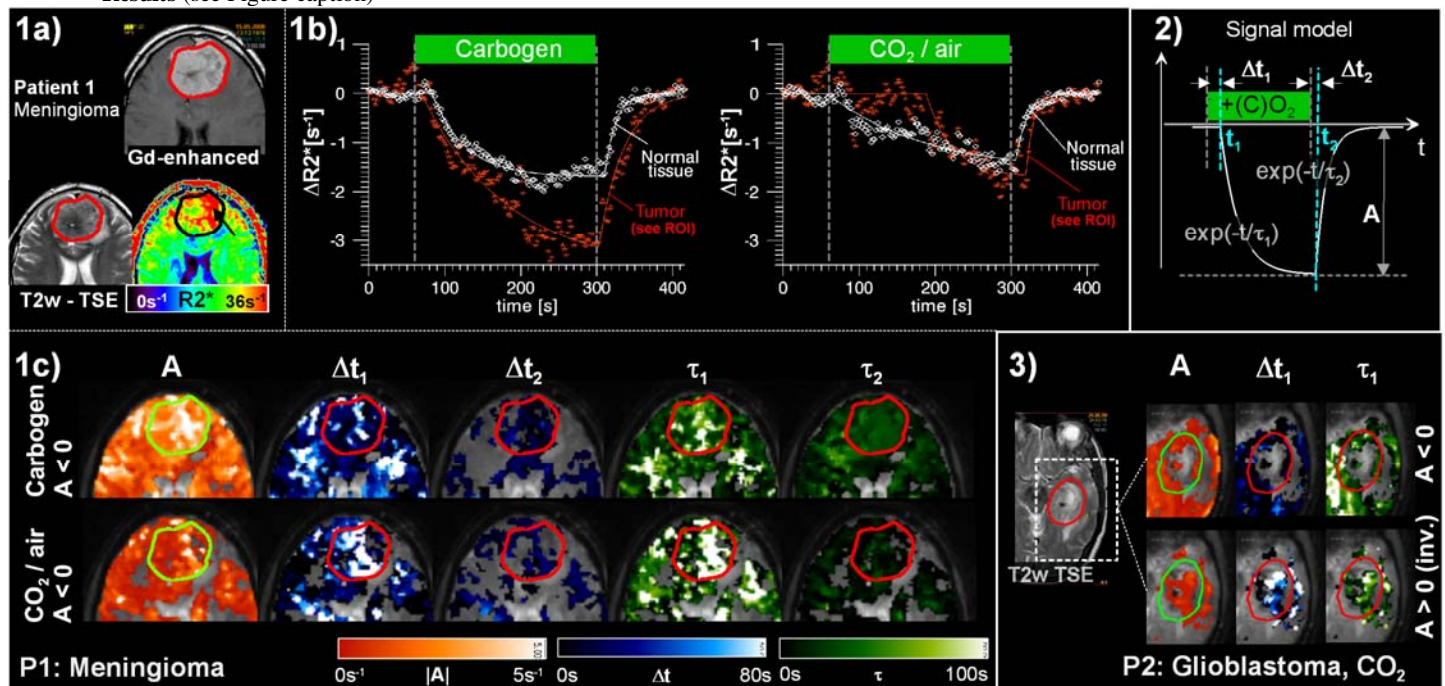
## Introduction

In dynamic (C)O<sub>2</sub> enhanced MRI, the patient inhales O<sub>2</sub> and/or CO<sub>2</sub>-enriched air, which results in a modulation of oxygenation, blood flow and volume in mature and functional vessels. The MR-feedback on pathologic vasoreactivity, in return, supports therapy selection and monitoring in oncologic applications (1-4). The MR response is generally depicted as the amplitude change in the MR signal or R2\*, induced by the respiratory challenge. This approach presumes that the vessel reaction on the stimulus is only reflected by the response amplitude. This is not generally true, as indicated by our own findings that also revealed a tissue-dependent temporal behavior of the response. To enable appropriate and accurate dynamic (C)O<sub>2</sub> enhanced MR imaging, we therefore suggest 1.) to dynamically measure the change in R2\* ( $\Delta R2^*$ ) during the respiratory challenge, 2.) to fit a signal model to the recorded  $\Delta R2^*$  time series at each voxel, and 3.) to depict the result parameters of this fit in separate vasoreactivity maps.

## Methods

Informed consent was obtained from 5 patients (31-65 years old) with cerebral tumors (1 meningioma, 2 glioblastomas, 2 metastases). Imaging was done at 3T (Philips Achieva, The Netherlands): 2D, matrix 128x128, FOV 230x201mm, slice 5mm, flip angle 25°, 12 Echoes, TE 4-83ms, TR 97ms, 198 dynamics à 2.1s. Carbogen (Cb, 95% O<sub>2</sub>+5% CO<sub>2</sub>) and CO<sub>2</sub>-enriched air (CO<sub>2</sub>/air, 25% O<sub>2</sub> + 70% N<sub>2</sub> + 5% CO<sub>2</sub>) were delivered, using a protocol of 1/4/2min for breathing normal air/gas/air.  $\Delta R2^*$  with respect to the baseline is determined as in [5], including corrections for motion, B0 inhomogeneities and changes in T1. The signal model, fitted to the  $\Delta R2^*$  time series (Eq. 1, Fig. 2), has been obtained experimentally on data from respiratory challenges in volunteers [5]. A is the maximum change of the response function,  $\tau_1$  and  $\tau_2$  are the time constants of the rising and decaying monoexponential slopes, and  $t_1$  and  $t_2$  mark the start and end points of the response.  $\Delta t_1$  and  $\Delta t_2$  further denominate the delay of the response with respect to  $t_1$  and  $t_2$  (green bar, Fig.1b & 2). Voxels with positive and negative response amplitude are depicted in separate color-coded, median-filtered (3x3) maps.

Results (see Figure caption)



**Fig. 1** summarizes the results from the meningioma patient under Cb & CO<sub>2</sub>/air. **1a)** Anatomic reference scans & R2\*-map. **1b)** Global response curves of tumor and healthy tissue: Compared to normal brain, the global  $\Delta R2^*$  series in the tumor differs significantly in the amplitude and the temporal behavior. **1c)** The parameter maps for A,  $\Delta t_1$ ,  $\Delta t_2$ ,  $\tau_1$ ,  $\tau_2$  for pixels with  $A < 0$ . In parts of the meningioma, the response was higher in amplitude, slower and delayed, compared to normal brain tissue. This region partly coincides with areas of an increased baseline R2\* (1a, arrow), presumably reflecting a decreased baseline oxygenation. **1b+e)** The difference in amplitude is more pronounced during Cb, whereas the difference in the temporal behavior is more pronounced during CO<sub>2</sub>/air. **Fig. 2** Signal model (Eq.1). **Fig. 3** summarizes the results from a glioblastoma patient under CO<sub>2</sub>/air. The necrotic region of the glioblastoma and areas next to the tumor rim showed an inverse ( $A > 0$ ) and delayed response to CO<sub>2</sub>/air, possibly due to a vascular steal effect (lower row), whereas the tumor rim depicts normal vasoreactivity (upper row).

## Discussion/Conclusion

We presented a new technique for the localized, sensitive, and robust depiction of the temporal characteristics of the MR response to (C)O<sub>2</sub> respiratory challenges in vasoreactivity maps. With this approach, it is now possible to visually correlate the locally varying tumor characteristics with pathologically altered oxygenation and vasoreactivity. E.g. areas of high amplitude change during Cb (see meningioma case) may indicate high vessel density and/or function, and an inverse, delayed or decelerated response to CO<sub>2</sub> may indicate poor vessel reactivity or maturity (see glioblastoma case). We expect this method to considerably improve the interpretation of the MR findings in the upcoming field of oncologic research and to significantly increase the robustness and reproducibility of MR-monitored respiratory challenges in dynamic (C)O<sub>2</sub> enhanced studies.

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