BOLD MRI evaluation of vessel reactivity to CO_2 and O_2 enrichment: implementation in brain tumor patients

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Background/ Aims:

The switch of tumors from avascular to the vascular phase marks a critical checkpoint in tumor progression. Clinical studies have demonstrated that the degree of angiogenesis is correlated with the malignant potential of several human cancers[1]. Previously we developed a method for *in-vivo* mapping of tumor vessel functionality and maturation by MRI[2]. Vascular maturation, a process which can render the vessels resistant to anti-angiogenic therapy is detected by enhanced relaxation due to changes in blood flow in response to hypercapnia (5% CO_2), while vascular functionality is detected by the change of T_2* in response to hyperoxia (95% O_2) as described[2] . Our earlier studies prove the feasibility of this method to detect anti-angiogenic effects in laboratory animal tumor models[2,3]. In the present study we demonstrate preliminary results of applying this method in brain tumor patients.

Methods:

MRI was performed on 3T VH/i and 1.5T echo-speed GE system (Milwaukee, WI, USA). Nine control subjects and one patient with recurrent oligodendroglioma grade 3 were scanned. MRI protocol included T_1 and T_2 weighted images, and functional mapping (GE-EPI) in a block design paradigm while inhaling either air-5% CO_2, or oxygen-5% CO_2 with air as a blank (Figure 1D, E respectively). Data analysis was done using home written IDL software (Research Systems Inc.).

Results and Discussion:

In healthy subjects we observed differences in the MRI response of gray and white matter to oxygen and CO_2, as expected from their different vessel density (Figure 1B, C). We have optimized the protocol by separating the paradigm into two separate experiments of CO_2 and oxygen, since the response to CO_2 was reduced after breathing O_2. We have also optimized parameters, such as number of repeats during each gas saturation (1.5min for CO_2 and 1min for O_2) and air interval (1.5-2 min alternatily), which depend on the physiological response to the gases. Representative results from a 27 years old volunteer are shown in Figure 1.

Using the chosen optimal paradigm and parameters we applied this method to a 33 year old patient with recurrent brain oligodendroglioma. Vessel reactivity was elevated in the tumor area compared to healthy tissue in the same patient. Results from CO_2 and O_2 reactivity clearly highlighted the tumor from normal brain tissue (Fig 2). This tumor was not enhanced with Gd. This can explain the reactivity to CO_2 in this tumor.

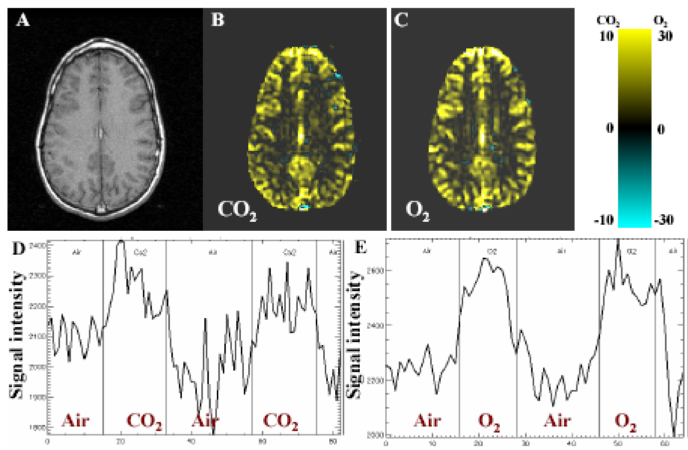

Figure 1: T_1 SE slice from a 27 years old volunteer obtained by 1.5T MRI. CO_2 reactivity (B) and O_2 (C) maps are given as % change of signal intensity (scale bar). Representative BOLD signal response to CO_2 (D) and O_2 (E) paradigm.

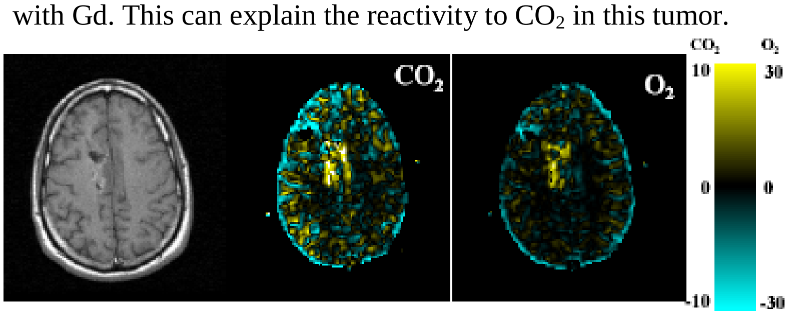

Figure 2: Representative T_1 SE slice from a 33 years old patient with recurrent oligodendroglioma obtained by 1.5T MRI. CO_2 reactivity and O_2 maps are given as % change of signal intensity (scale bar).

In conclusion, we have shown preliminary results of the application of a breathing paradigm method for a patient with brain tumor. This method clearly highlighted the tumor from normal brain tissue and might add additional information regarding classification, grading of brain tumors and optimizing treatment.

References

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