Quantification of hyperoxia induced changes in normal tissue and intracranial glioma using SWAN imaging

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Introduction: Changes due to elevated levels of tissue O_2 consumption in tumor gives information of vascular growth, hemodynamic changes in the response to treatments, vasoreactivity, vascular function and vessel maturation. Increased oxygen imparts radiation sensitivity while hypoxic tumors are insensitive towards radiation. Relaxation time (R2*) is sensitive indicator of tissue oxygenation which provide indirect estimates of tissue O2 for monitoring tumor oxygenation. Oxygen-dependence of R2* is primarily based on the magnetic properties of deoxyhaemoglobin (Hb) and oxy-haemoglobin (HbO2) where increased levels of paramagnetic Hb generate additional local susceptibility field gradients and increase R2*, whereas decreased Hb levels, typically related to increased levels of diamagnetic HbO2, tend to decrease R2*[1]. For quantification of tumor R2*, blood oxygenation level dependent (BOLD) MRI imaging based on changes in deoxyhemoglobin concentration have been used2. This offers a non-invasive approach to assess tumour oxygenation and vasoreactivity without exposure to ionising radiation. In this study the effect of hyperoxia on quantitative R2* and phase using T2* weighted Angiography (SWAN) in various grades of glioma is presented.

Materials & Methods: ***Subjects:*** Fifteen (11 male and 4 female; mean age=43 yrs) treatment naive consecutive patients (10 high grades & 5 low grades on histopathology) with definitive diagnosis of glioma were included in this study. ***Data acquisition:*** All patients underwent conventional MRI on a 3.0T scanner (Signa HDxt, General Electric, Milwaukee, USA) using a 12 channel head coil after the approval from the institutional ethics committee. Conventional MRI was performed in the axial plane with a field of view (FOV) = 240 × 240 mm^2, slice thickness = 3 mm, interslice gap = 0.0mm. In addition, SWAN imaging with TR/TE/Flip Angle/slice thickness: 47/25/15/2.4mm and acquisition matrix of 320x224 was performed while breathing normal air and after 4 minutes of breathing 100% oxygen[2]. The data was acquired using 7 echoes with a central-echo time of 25.024 ms and an echo-spacing of 4.008 ms (the 7 acquired echo times used were: 13 ms, 17.008 ms, 21.016 ms, 25.024 ms, 29.032 ms, 33.04 ms and 37.048 ms). ***MRI data processing and quantitative analysis:*** Complex data consisting of real and imaginary parts was collected using a multiecho SWAN imaging. The phase calculation removing the susceptibility artifacts was done as per Haacke et al[3] using a 64 × 64 low pass filter to remove the low spatial frequency component of background field. A linear fit was used to calculate the R2* from the same multi echo SWAN data. ***Statistical analysis:*** Paired t-test was used to look for the parameters with significantly different values in normal and hyperoxic condition in tumor, necrosis, edema, hemorrhage and normal brain regions. Student's independent t-test was used to observe the changes in ΔMagnitude, ΔPhase and ΔR2* in tumor and normal tissue region. A p-value ≤0.05 was considered as significant.

Results: Hyperoxic conditioned showed significant changes in the values of R2* in peri-tumoral edema, tumor, hemorrhagic regions in the cellular tumor, tumor necrosis and normal (contra-lateral of tumor) tissue whereas cellular tumor and necrotic regions showed significant change in the phase values compared to normoxic data from the same regions. Magnitude values of susceptibility weighted images changed significantly in tumor hemorrhage, tumor necrosis and normal brain region (Table 1). A significant change in difference of magnitude and phase was observed between tumor and normal brain tissue region.

	Magnitude(in Signal Intensity) (Mean±SD)			Phase(in radian) (Mean±SD)			R2*(in $msec^{-1}$) (Mean±SD)		
	Hyperoxia	Normoxia	p-value	Hyperoxia	Normoxia	p-value	Hyperoxia	Normoxia	p-value
Edema	7698.9±1067.6	7841.8±1582.5	0.161	0.0155±0.02	0.0127±0.02	0.065	0.0184±0.00	0.0156±0.00	0.001
Tumor	5505.9±804.3	5403.0±934.0	0.214	-0.009±0.07	-0.0005±0.07	0.006	0.0340±0.02	0.0301±0.01	0.000
Hemorrhage	616.7±265.3	882.98±659.1	0.000	0.1749±1.17	0.1143±1.06	0.631	0.0678±0.04	.0865±.03618	0.000
Necrosis	9629.8±3041.2	8908.9±3065.9	0.000	0.002±0.02	0.005±0.02	0.011	.0064±.00457	.0100±.00844	0.000
Normal	4011.5±727.9	4181.6±853.8	0.000	0.004±0.04	0.004±0.04	0.779	0.0470±0.01	0.0417±0.01	0.000

Table1: Showing mean and standard deviation of magnitude, phase and R2* values at hyperoxia and normoxia in edema, tumor, hemorrhage, necrosis and normal brain region.

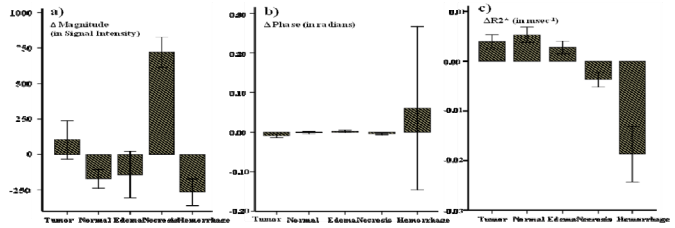

Fig1: Shows difference between hyperoxia and normoxia in a) magnitude b)phase c) R2* of different regions of tumor and normal brain parenchyma.

Discussion: Edema, cellular tumor, hemorrhage, necrosis and normal tissue region showed significant changes after hyperoxia in R2* values (Table1), however ΔR2* was significantly different in edema, necrosis and hemorrhagic region as compare to normal brain region(Fig1). Insignificant difference of ΔR2* values of cellular tumor from normal region may indicate equi reactive vasculature in tumor as well as normal parenchyma. Edema showed significant change in ΔR2* from normal ($p<0.037$) values may be due to vasculature compression by the interstitial edema. In necrosis and hemorrhagic region ΔR2*<0 indicating good venous vascularization and "normal" vasoreactivity[4]. Δ phase of tumor region is significantly different from normal brain region ($p< 0.023$) and Δmag of tumor ($p<0.003$)and necrosis region($p<0.000$) is significantly different from normal brain region indicating alteration of vessel function in pathological tissue type from normal. Our preliminary study demonstrates that there is differential response to different tumor tissue type to hyperoxia and this information may be of value for tissue classification in brain tumor tissue type in future.

Reference:1. Winter et al. 2011,Phys. Med. Biol;56:1225–1242, 2.Muller et al. 2011, Eur Radiol;21:786-798, 3. Haacke et al. 2004, MRM;52: 612-618,4. Müller et al. 2009 ISMRM 17