Organ-specific effects of oxygen and carbogen gas inhalation on tissue longitudinal relaxation times

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Introduction Molecular oxygen (O_2) is weakly paramagnetic and shortens tissue longitudinal relaxation time (T_1), providing a mechanism for detecting signal modulation in plasma and tissue fluid that contain dissolved oxygen. Small but significant T_1-shortening due to inhaling high O_2 concentrations has been identified in arterial blood, the spleen and renal cortex, but no change has been demonstrated in liver[1, 2]. We investigated the T_1-shortening effect of dissolved molecular oxygen in upper abdominal organs in healthy volunteers and compared the T_1 reduction observed with 100% oxygen to that achieved with carbogen (95% O_2/5% carbon dioxide) which is believed to counteract oxygen-induced vasoconstriction.

Method 16 healthy normal volunteers (six female and ten male; mean age 30.4 years) were studied. Smokers and individuals with significant heart or lung disease were excluded. All experiments took place on a Philips Intera system (Philips Medical Systems, Best, Netherlands) at 1.5 Tesla. Volunteers inhaled medical air (21% oxygen) followed by 100% oxygen and then carbogen in the same order and time schedule at 15 l/min through a non re-breathing circuit with reservoir mask. 3D fast field echo images were acquired for a 9.9 cm volume slab through the upper abdomen (TR 3.5 ms, TE 0.9 ms, α = 2°/ 8°/ 17°, 3 signal averages, FOV 384 mm, imaging matrix 128 x 128, 3 mm slice thickness). T_1 maps were created every 76.8 s using the variable flip angle method[3]. Six baseline measurements were collected while breathing medical air, followed by 12 on 100% oxygen, 12 on carbogen and a further 6 – 12 back on medical air. Volumes of interest (VOI) were drawn within each organ by one observer (JOC). Mean T_1 values, change from baseline and change in relaxation rate ($1/T_1\,(t) - 1/T_{1\,(baseline)}$ hereafter denoted $\Delta 1/T_1$ – a quantity proportional to regional oxygen concentration – were calculated for all time points. Group mean $\Delta 1/T_1$were plotted for each VOI to evaluate wash-in of oxygen/carbogen and the wash-out of carbogen. Differences in mean $\Delta 1/T_1$ were tested using a one-way analysis of variance with a post-hoc Bonferroni correction. Liver VOI analysis split subjects according to fasting status (fasted for ≥ 4hrs v eaten within 4hrs) and was tested by a two-sided independent samples t-test.

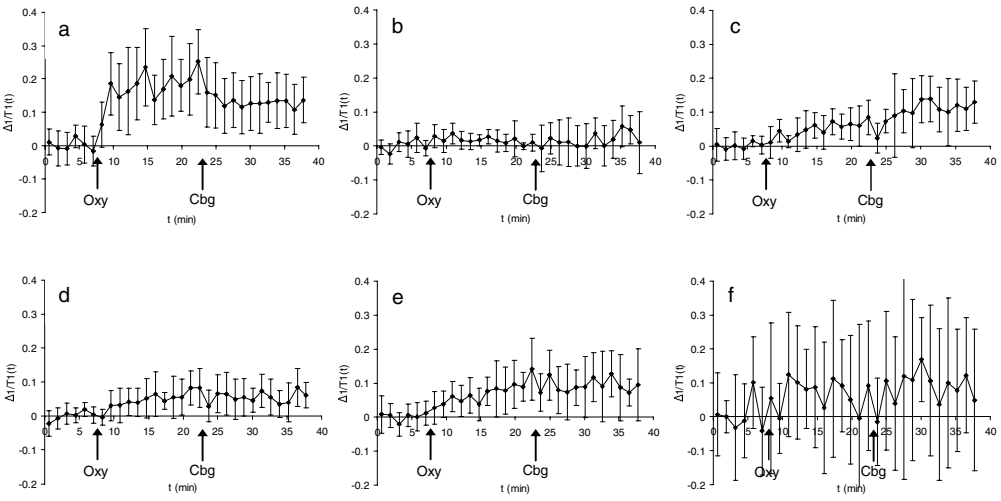
Results VOI were drawn in the spleen, liver, renal cortex, para-spinal muscle (PSM) and subcutaneous fat in each subject where possible. Data were excluded from two volunteers (one due to circuit failure and one where motion between acquisitions made VOI comparison unreliable). 13 subjects experienced dyspnoea breathing carbogen, which resulted in curtailing the examination one volunteer. No other adverse events were reported.

Mean T_1 values on air were consistent with those reported in the literature. No significant difference was found between liver baseline T_1 for the fasting (594 ± 35, n=6) and non-fasting (570 ± 60, n=5) groups (p=0.314). Changes in mean T_1 values while breathing each gas (excluding pre-equilibrium time points – the first 2 time points on oxygen and carbogen breathing) and mean group wash-in $\Delta 1/T_1$ are shown in Table 1 and Figure 1. Both oxygen and carbogen induced highly significant increases in relaxation rate (reductions in T_1) in the spleen, liver (fasted subjects (F)), renal cortex and PSM (all p<0.001). Magnitude of $\Delta 1/T_1$ for both air-oxygen and air-carbogen was equal in muscle (p=1.0) and renal cortex (p=0.471). In the spleen, the $\Delta 1/T_1$ was significantly greater with oxygen inhalation than with carbogen (p<0.001). In contrast, $\Delta 1/T_1$ in the liver (fasted subjects (F)) was significantly greater during the carbogen phase of breathing (p<0.001). Significant $\Delta 1/T_1$ was also seen in the subcutaneous fat for oxygen (p=0.011) and carbogen (p=0.002), although greater noise was present. No significant $\Delta 1/T_1$ was measured in the liver in subjects who eaten within the last 0-4 hours (non-fasted (N)).

Organ	Mean T_1 values (ms)			Mean $\Delta 1/T_1$ (s^{-1})	
	Air	Oxygen	Carbogen	Oxygen	Carbogen
Spleen	926 ± 26	795 ± 24	836 ± 25	0.188	0.127
Liver (N)	570 ± 27	566 ± 27	561 ± 21	0.016	0.019
Liver (F)	599 ± 13	580 ± 11	562 ± 15	0.053	0.113
PSM	736 ± 16	709 ± 16	709 ± 19	0.055	0.057
Renal	945 ± 15	883 ± 9	873 ± 22	0.076	0.092
Fat	236 ± 8	232 ± 8	231 ± 8	0.077	0.091

Table 1. Mean ± standard error T_1 values of air, oxygen and carbogen inhalation for each organ VOI and mean change in $1/T_1$ from air-to-oxygen and air-to-carbogen. In the case of the liver, N indicates not fasted and F indicates fasted subjects.

Examination of breathing air following the air-oxygen-carbogen protocol (wash-out phase) revealed a negative $\Delta 1/T_1$ in the spleen that was highly significant (p<0.001). Measurements for air at the beginning and end of the experiment showed no statistical difference (p=0.407) supporting the notion that the effect of hyperoxic gases is real but short lived in the spleen. In contrast, there was no change in relaxation rate in the liver of fasted subjects during the second set of acquisitions on air from that of carbogen (p=1.0) but this phase was highly significantly different from the original baseline measurements (p<0.001).



Discussion Oxygen inhalation produces repeatable changes in organ T_1 times of greater magnitude than previously described. Contrary to previous findings, the liver does exhibit oxygen-induced reduction in T_1, but only in the fasted state, possibly due to a higher fraction of arterial: portal venous blood supply. Changes were also measured in PSM and subcutaneous fat, with measurements of $\Delta 1/T_1$ indicating comparable dissolved oxygen concentrations in most tissues. Carbogen inhalation produced variable and opposed modulation of the T_1-shortening effect in different organs. Further work is required to elicit the physiological correlates of change in $1/T_1$ after hyperoxic gas inhalation and its potential use as a biomarker of tissue oxygenation and perfusion.

Figure 1a. Spleen, b. Liver (non-fasted), c. Liver (fasted), d. para-spinal muscle, e. renal cortex and f. fat. Mean $\Delta 1/T_1$ for each organ (error bars are standard deviation across individuals). Equivalent scale has been used to emphasise differences in the magnitude of changes and the confidence in measured values for each organ.

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