# Altering the inspired oxygen concentration differentiates vascular lesions from parenchymal lesions: a study using susceptibility weighted imaging in a mouse model of multiple sclerosis

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**Target audience:** Those working in MRI in multiple sclerosis (MS) and in animal models of MS, and those developing susceptibility weighted imaging (SWI) as a clinical tool.

**Purpose:** To test the usefulness of changing inspired oxygen levels for differentiating vascular lesions (caused by intravascular deoxyhemoglobin) from parenchymal lesions (due to iron deposition and demyelination) on SWI using an animal model of MS, experimental autoimmune encephalomyelitis (EAE). This builds on our previous work in the EAE model where we showed that although SWI did detect iron-based lesions in the parenchyma, many lesions were due to deoxyhemoglobin in the blood.[1] We hypothesized that altering the inspired oxygen concentration would change hemoglobin saturation enough to differentiate between vascular and parenchymal (non-vascular) lesions. If successful, we will have established an *in vivo* method that can be used to investigate deoxyhemoglobin as a cause of SWI lesions.

**Methods:** Female C57BL/6 mice were immunized with EAE.[2] A 9.4T Bruker Avance console with a 20mm surface coil was used for imaging. Lumbar spinal cords of EAE mice at peak disease (n=6) and naive control mice (n=5) were imaged using 3D GE with flow compensation (matrix=192x128x32, FOV=0.92cmx1.28cmx1.28cm, TE/TR/α=4ms/50ms/15°, NEX=17, voxel size=48x100x400μm). Animals were imaged using a standard gas mixture of 30% $O_2$/70% $N_2$; then the gas mixture was changed to being 100% $O_2$ (no $N_2$) with ten minutes allotted for the 100% $O_2$ to fill the gas line, and then animals were imaged again with the 100% $O_2$. SPIN software (MRI Institute, Detroit, MI) was used to process the magnitude and phase images,[3] using a 32x32 Hanning filter and multiplying the negative phase mask into the magnitude data four times to create SWI images.

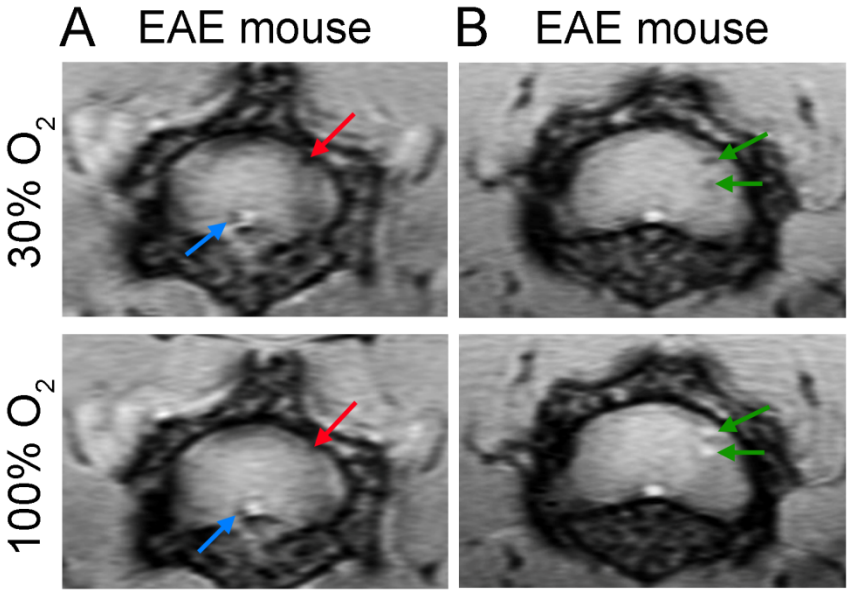


**Figure 1. Vascular-based SWI lesions visible with 30% $O_2$ either disappear or become hyperintense upon administration of 100% $O_2$ in EAE mice. A** shows a hypointensity visible with 30% $O_2$ that disappears with 100% $O_2$ (red arrows). A parenchymal lesion remains in the white matter (blue arrows), which is not due to deoxyhemoglobin. **B** shows two hypointensities seen with 30% $O_2$ that become hyperintense with 100% $O_2$ (green arrows).

**Results:** In EAE mice, vascular lesions visible with 30% $O_2$, particularly those at the grey/white matter boundary of the spinal cord, showed different responses upon administration of 100% $O_2$ (**Fig. 1**). Some lesions seen with 30% $O_2$ disappeared with 100% $O_2$ (**Fig. 1A**); some appeared hypointense with 30% $O_2$, but became hyperintense with 100% $O_2$ (**Fig. 1B**), while some lesions were less hypointense with 100% $O_2$ than with 30% $O_2$, but did not disappear completely (data not shown). Parenchymal lesions that were observed in the ventral white matter were visible with both 30% $O_2$ and 100% $O_2$ (**Fig. 1A**).

**Discussion:** Comparing images acquired with a low percent concentration of inspired oxygen (30%) with those obtained with a high percent concentration of inspired oxygen (100%) enabled us to differentiate between vascular lesions and parenchymal lesions that were not vascular in origin. The different responses observed upon administration of 100% $O_2$ are likely related to the initial deoxyhemoglobin saturation. Larger changes with $O_2$ may reflect regions that were relatively more hypoxic, but that had sufficient blood flow to respond to changes in arterial saturation. Parenchymal lesions remaining after administration of 100% $O_2$ are likely due to iron deposition and demyelination, as shown previously by our group.[1]

**Conclusion:** Changing inspired oxygen concentrations can be used to differentiate lesions that are vascular in origin from those that are not, and so can help us better understand the pathophysiology of MS detected with SWI. We can quantify the number of lesions due to deoxyhemoglobin *in vivo* which can be useful for time course studies. Use of a high percent concentration of oxygen is the underlying principle for hyperbaric oxygen therapy, or high-dose oxygen therapy, which has been used in those with MS safely.[4] Therefore, this method could be applied in MS patients to help differentiate between sources of lesions seen in SWI in MS patients.

**References:**

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