# Quantitative Measurement of Spinal Cord Blood Volume (SCBV) in Humans using Vascular-Space-Occupancy (VASO) MRI

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**INTRODUCTION:** Spinal cord hemodynamics is a key component in the pathophysiology of many related diseases, such as spinal stenosis, spinal tumor and spinal cord injury. While perfusion measurement techniques for brain are well established, a reliable method for spine cord perfusion estimation in humans is still lacking. PET methods suffer from a relatively low intrinsic spatial resolution, making it difficult for measurements in small structures such as spinal cord. MRI is capable of high spatial resolution and dynamic susceptibility contrast (DSC) MRI has been used widely for brain perfusion. However, DSC MRI typically uses single-shot EPI image acquisition schemes and it suffers from significant image distortions in body imaging in comparison with the brain. Here we present the first report of quantitative measurement of spinal cord blood volume (SCBV) in humans. This technique uses pre- and post-contrast Vascular-Space-Occupancy (VASO) images and is based on the T1-shortening effect of the Gd-DTPA contrast agent. A unique advantage of this technique is that the quantification of SCBV does not require the knowledge of the arterial input function, allowing accurate estimation of absolute BV values in physiological units (ml blood per 100ml tissue).

**METHODS Theory:** The VASO sequence is a non-slice-selective inversion recovery (IR) sequence, where the inversion time (TI) is chosen to null the blood signal. This technique was originally designed to map the relative changes in cerebral blood volume (CBV) during brain activation (1). More recently, the VASO technique has been combined with the Gd-DTPA contrast agent for the measurement of absolute CBV (2). The present study is an extension of this method to the study of spinal cord BV. The theoretical framework for the SCBV calculation is similar to that used for CBV and is detailed previously (2). Briefly, the method is based on the fact that the $T_1$ of pre-contrast blood is known, and that the contrast agent injection significantly reduces blood $T_1$ but has no effect on the extravascular tissue $T_1$ (due to the blood-brain-barrier (BBB)). The pre-contrast signal is given by:

$$S_{pre} = S_{tissue} + S_{blood} = M_0 \cdot [C_{tissue} \cdot (1-V) \cdot (1-2 \cdot e^{-TI/T_{1,t}}) + 0] \quad (1)$$

where $M_0$ is the equilibrium MR signal per unit volume of water proton; $C_{tissue}$ is the water density of the tissue; V is the SCBV in ml blood per ml tissue; $T_{1,t}$ is the tissue $T_1$ value. Note that the blood term is 0 because of the optimal TI to null the blood. The post-contrast signal is given by:

$$S_{post} = S_{tissue} + S_{blood} = M_0 \cdot [C_{tissue}(1-V) \cdot (1-2 \cdot e^{-TI/T_{1,t}}) + V \cdot C_B \cdot (1-2 \cdot e^{-TI/T_{1,b,post}})] \quad (2)$$

where $C_B$ is the water density of blood; $T_{1,b,post}$ is the blood $T_1$ value after contrast agent injection. Note that the first term in Eq 2, the tissue signal, is the same as in Eq 1 because the contrast agent is restricted in the blood, whereas the second term, the blood signal, is non-zero because the contrast agent has significantly shortened the blood $T_1$ and the TI used does not null the blood signal any longer. Therefore, the signal difference between post-contrast and pre-contrast is given by: $S_\Delta = S_{post} - S_{pre} = M_0 \cdot V \cdot C_B \cdot (1-2 \cdot e^{-TI/T_{1,b,post}})$

When $T_{1,b,post}$ is small (<200ms), the above equation becomes: $S_\Delta = M_0 \cdot V \cdot C_B$. Then SCBV can be computed from: $V = S_\Delta / (M_0 \cdot C_B)$

The normalization factor, $M_0$ ,is estimated from the pre-contrast CSF signal intensity as: $M_0 = S_{CSF} / (1-2 \cdot e^{-TI/T_{1,CSF}} + e^{-TR/T_{1,CSF}})$, based on the inversion recovery signal equation. $C_B$ is assumed to be 0.87ml water/ml blood (3).

**Experiment:** Experiments were performed on a 1.5T MR system (Siemens Medical Solutions). Six subjects with no known spinal cord pathology gave written consent to participate in the study. The pre- and post-contrast VASO scans were positioned to cover the C1-C7 spinal levels and used identical parameters: body coil for transmission and neck coil for reception, TR=6000s, TI=920ms, FOV=140mm, matrix=128x128, gradient-echo, segmented EPI factor 5, TE=6ms, 5 slices, slice thickness 10mm, scan duration 1'48". After 3D motion correction between pre- and post-contrast images, signal subtraction was performed on a voxel-by-voxel basis. A region-of-interest containing pure CSF was manually outlined for the calculation of $M_0$.

**RESULTS and DISCUSSION:** Figs. 1a and b show the pre- and post-contrast VASO images, respectively. Note that, for most regions, the post-contrast image is considerably brighter than the pre-contrast image. This is because those regions do not have BBB and the Gd-DTPA enters the extravascular space. In the cord regions, however, the contrast agent is restricted to the intravascular space and the signal enhancement is much smaller. Fig. 1c shows the absolute SCBV map in units of ml blood/100ml tissue. High BV voxels are likely to contain gray matter and low BV, white matter. The surrounding CSF regions are mostly close to zero. For each subject, the center 3x3 voxels in the spinal cord are averaged for ROI analysis. The results are listed in Table 1. Our study shows an averaged SCBV value of 4.12±0.65 ml blood/100ml tissue (mean±SD) in the cervical spinal cord, which is in a similar range to the BV values in brain (4). Our spatial resolution is not sufficient for clear delineation of gray-white matter boundaries. However, from the location of the ROIs, they are expected to be largely gray matter but will also contain some white matter. To our knowledge, there are no previous reports on the absolute values of SCBV in humans and the reports in animals are also scarce. Hoy et al. measured plasma volume of spinal cord in dogs using radioactively labeled plasma proteins and found to be 0.85 ml plasma/100 g tissue. After accounting for the hematocrit and blood density, this corresponds to 1.56 ml blood/100ml tissue, which is considerably lower than the values obtained in this study. A possible reason is that the tissue radioactivity was measured after the spine dissection, at which time the signal may have decayed significantly. In summary, we have developed an MR approach for quantitative measurement of SCBV in humans. It is capable of achieving relatively high spatial resolution without the confounding EPI distortions. These features make this method a useful technique for in vivo studies of spinal cord hemodynamics.

**REFERENCES:** 1) Lu et al. MRM 50: 263 (2003); 2) Lu et al. MRM 54: in-press (2005); 3) Herscovitch et al. JCBFM 5: 65 (1985); 4) Rostrup et al. NeuroImage 24: 1 (2005).

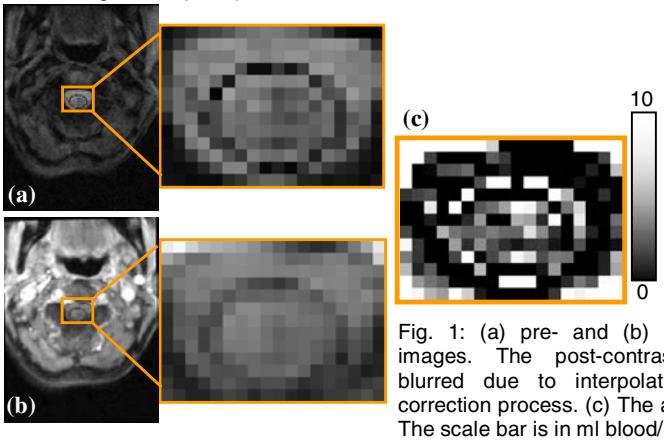


Fig. 1: (a) pre- and (b) post-contrast VASO images. The post-contrast image appears blurred due to interpolation in the motion correction process. (c) The absolute SCBV map. The scale bar is in ml blood/100 ml tissue.

| Subject | Pre-contrast | Post-contrast | Difference | M0 (from CSF) | SCBV (ml blood/ml tissue) |
|---|---|---|---|---|---|
| 1 | 143.3 | 156.2 | 12.9 | 460.3 | 3.22 |
| 2 | 386.4 | 442.8 | 56.4 | 1477.1 | 4.39 |
| 3 | 380.5 | 430.2 | 49.7 | 1452.3 | 3.93 |
| 4 | 356.3 | 401.3 | 45.0 | 1214.3 | 4.26 |
| 5 | 445.9 | 532.5 | 86.6 | 1932.1 | 5.15 |
| 6 | 416.9 | 471.1 | 54.1 | 1640.2 | 3.79 |
| **mean** | **354.9** | **405.7** | **50.8** | **1362.7** | **4.12** |
| **std** | **108.2** | **130.1** | **23.6** | **501.7** | **0.65** |

Table 1: Summary of SCBV results in six subjects. An ROI containing 3x3 voxels was used for each subject.