Effect of Sevoflurane Concentration, Blood Pressure, Arterial Carbon Dioxide Tension, Temperature, and Stimulation on Spinal Cord Blood Flow in Patients Undergoing Spinal Surgery: An Exploratory Study

To the Editor:

WE used laser speckle contrast imaging during spinal surgery to investigate how spinal cord blood flow responds to intraoperative factors relevant to anesthesia. Laser speckle contrast imaging is a noninvasive optical technique that generates high-resolution, full-field blood flow maps.[1] The principle of laser speckle contrast imaging is illustrated in Supplemental Digital Content figure S1, A and B (https://links.lww.com/ALN/E358). We investigated the effect of anesthetic agent, arterial carbon dioxide tension ($PaCO_2$), mean arterial pressure (MAP), and temperature on spinal cord blood flow. We also sought evidence of autoregulation and neurovascular coupling in the human spinal cord. This observational study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (see supplemental content https://links.lww.com/ALN/E364).

Patients undergoing elective laminectomies were included, as well as patients recruited into Duroplasty for Injured cervical Spinal Cord with Uncontrolled Swelling (DISCUS; ClinicalTrials.gov NCT04936620) and Injured Spinal Cord Pressure Evaluation (ISCoPE; ClinicalTrials.gov NCT02721615), which are clinical studies recruiting patients with acute, severe traumatic spinal cord injuries. After surgical resection/decompression, we exploited various intraoperative protocols used in our department to address our questions. Spinal cord blood flow was assessed using a portable laser speckle contrast imaging machine. For details, see Supplemental Digital Content methods (https://links.lww.com/ALN/E363). This is an exploratory study. Patient cohorts were small, analyses were not predefined, and the aim is signal finding and parameter estimation for future studies rather than confirmation of mechanism.

Thirty-five patients who underwent laminectomies, with or without dural opening, were included. We previously showed that an intact dura and cerebrospinal fluid have little influence on spinal cord blood flow measurements with laser speckle contrast imaging.[1] Propofol and remifentanil were administered to 24 (68.6%) patients, while 11 (31.4%) patients received sevoflurane. Demographics are shown in Supplemental Digital Content tables S1 to S3 (https://links.lww.com/ALN/E365). Two patients undergoing craniotomy were used as controls to validate the technique, *i.e.,* to investigate whether laser speckle contrast imaging detects increased cerebral blood flow in response to increasing sevoflurane minimum alveolar concentration (MAC) or increasing $PaCO_2$. No patient experienced intraoperative awareness. The Supplemental Digital Content flowchart (https://links.lww.com/ALN/E362) shows patient numbers in each experimental protocol.

In the two craniotomy patients, increasing sevoflurane MAC caused progressive increase in cerebral blood flow (Supplemental Digital Content fig. S1E, https://links.lww.com/ALN/E358), in agreement with earlier studies.[2,3] In contrast, figure 1 shows that increasing sevoflurane concentration caused no significant change in spinal cord blood flow. During these assessments, MAP and $PaCO_2$ were kept constant. Our findings suggest that human spinal cord vessels are less responsive to sevoflurane than cerebral vessels.

In the two craniotomy patients, increasing $PaCO_2$ caused a progressive increase in cerebral blood flow (Supplemental Digital Content fig. S1D, https://links.lww.com/ALN/E358). Figure 1 shows that increasing $PaCO_2$ also causes a significant increase in spinal cord blood flow. This response of spinal cord blood flow to changes in $PaCO_2$ was seen in the patients who received propofol and in those who received sevoflurane (Supplemental Digital Content table S4, https://links.lww.com/ALN/E365). Thus, carbon dioxide is a potent vasodilator in the spinal cord and increases spinal cord blood flow, analogous to its effect on cerebral vasculature.[4] During these assessments, MAP and anesthetic

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). M.C.P. and S.S. contributed equally as senior authors.

The article processing charge was funded by the Neurosciences Research Foundation.

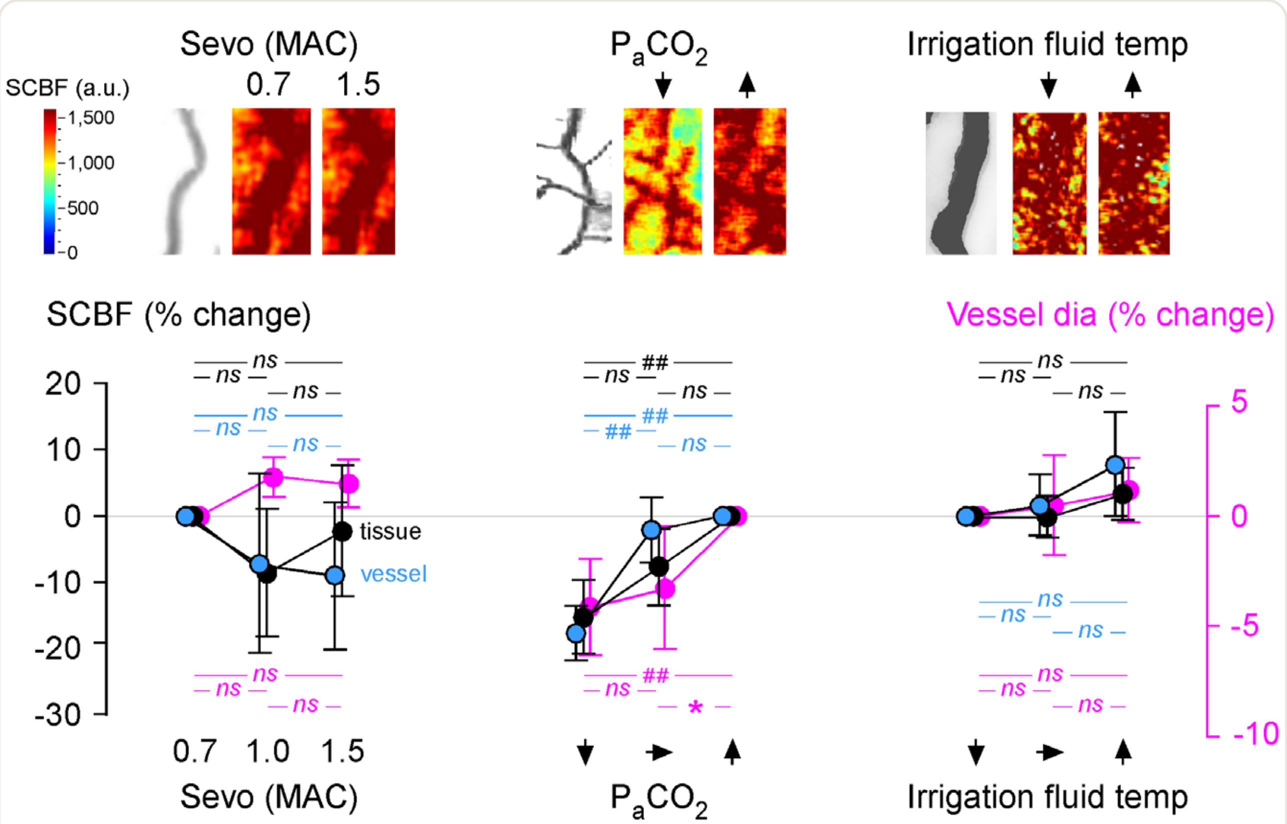

Fig. 1. Effect of sevoflurane minimum alveolar concentration (MAC), $PaCO_2$, and irrigation fluid temperature on spinal cord blood flow (SCBF). Shown are spinal cord vessels: photograph and corresponding laser speckle contrast imaging at sevoflurane (Sevo) MAC 0.7 *versus* 1.5, photograph and corresponding laser speckle contrast imaging at low (↓) *versus* high (↑) $PaCO_2$, and photograph and corresponding laser speckle contrast imaging at cold (↓) *versus* warm (↑) irrigation fluid temperature (temp). Also shown is spinal cord blood flow scale (arbitrary units [a.u.]): percent change in vessel blood flow (*blue*), tissue blood flow (*black*), and vessel diameter (dia) (*purple*) at sevoflurane MAC 1.0 or 1.5 *versus* 0.7, low (↓) or normal (→) *versus* high (↑) $PaCO_2$, and cold (↓) or room temperature (→) *versus* warm (↑) irrigation fluid. Mean ± 95% CI; paired Student's *t* tests with Bonferroni corrections, *$P < 0.05$, ##$P = 0.001$; ns, not significant.

concentration were kept constant. Interestingly, increasing sevoflurane MAC rendered the spinal cord blood flow more sensitive to $PaCO_2$; *i.e.,* the same change in $PaCO_2$ produced a larger change in spinal cord blood flow (Supplemental Digital Content fig. S2, https://links.lww.com/ALN/E359). During these assessments, the MAP was kept constant.

Heat causes vasodilation, and cold causes vasoconstriction.[5] Figure 1 shows that increasing the temperature of the irrigating saline caused little or no change in spinal cord blood flow, which suggests that spinal cord temperature during surgery is primarily determined by the core temperature rather than the temperature of the irrigation fluid. During these assessments, MAP, $PaCO_2$, and anesthetic concentration were kept constant.

Next, we sought evidence of autoregulation, *i.e.,* whether spinal cord blood flow stays constant despite changes in MAP. A sudden increase in MAP caused a transient increase in spinal cord blood flow in patient 5 with return to baseline spinal cord blood flow (fig. 2) but a persistent increase in spinal cord blood flow in patient 30 recorded from within the injured cord (Supplemental Digital Content fig. S3, https://links.lww.com/ALN/E360), indicating intact and impaired autoregulation, respectively. Supplemental Digital Content table S5 (https://links.lww.com/ALN/E365) shows that, in patients without traumatic spinal cord injuries, autoregulation was generally preserved. In contrast, autoregulation was impaired in many patients with traumatic spinal cord injuries. Thus, the human spinal cord autoregulates, akin to brain autoregulation.[6] As with brain autoregulation,[7] spinal autoregulation is preserved in patients receiving propofol or sevoflurane. The existence of spinal cord autoregulation and its disruption in traumatic spinal cord injury support the concept of optimum spinal cord perfusion pressure, defined as the perfusion pressure that optimizes autoregulation,[8] which can be targeted to rationalize the management of traumatic spinal cord injuries by avoiding cord hypo- and hyperperfusion.

In the brain, increased neuronal activity elicits a localized increase in cerebral blood flow, thus coupling energy

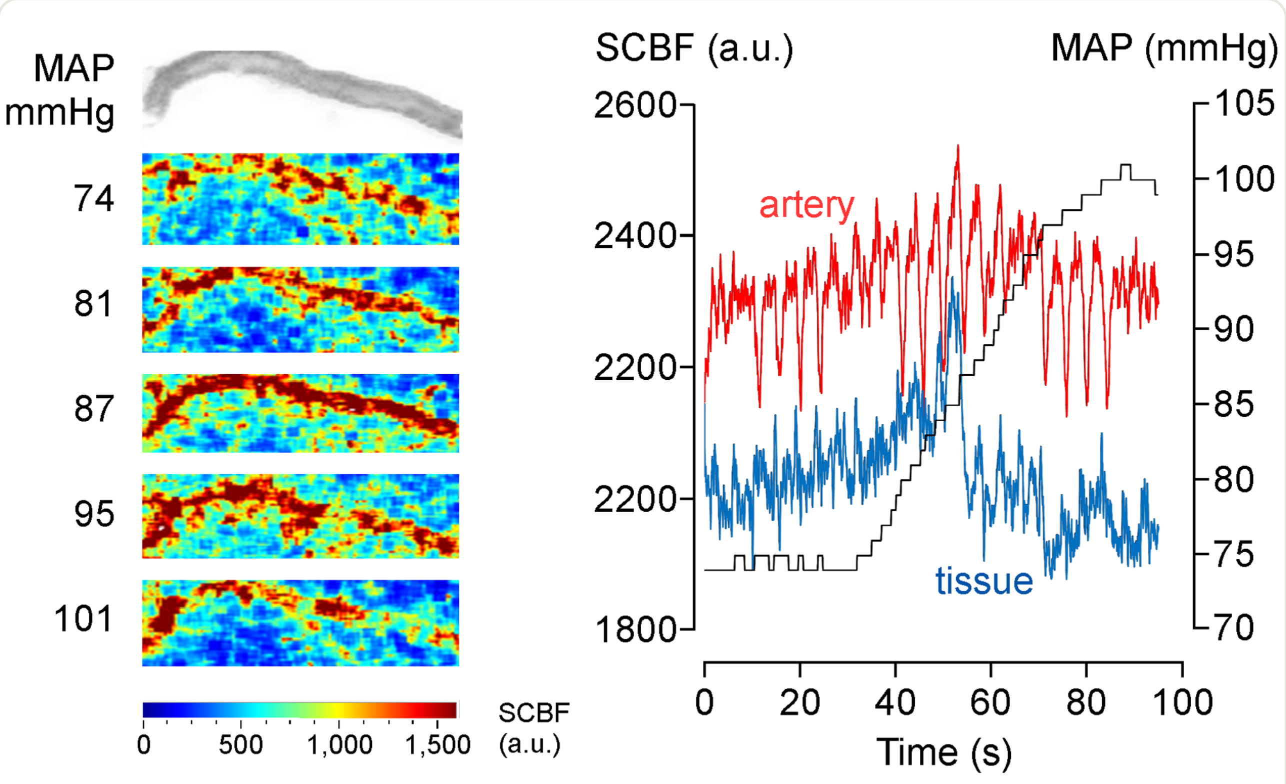

Fig. 2. Normal spinal cord autoregulation. Shown are a spinal cord vessel photograph and corresponding laser speckle contrast imaging with mean arterial pressure (MAP) at each time point shown. Also shown is a plot of mean arterial pressure (*black*), spinal cord blood flow (SCBF) in an artery (*red*), and tissue spinal cord blood flow (*blue*) *versus* time for patient 5. a.u., arbitrary units.

demand and energy supply.[9] In patients 34 and 35, direct electrical stimulation of one dorsal column was associated with an increase in spinal cord blood flow bilaterally that peaked within a second of stimulation onset and disappeared within a second of cessation of stimulation (Supplemental Digital Content fig. S4, https://links.lww.com/ALN/E361; Supplemental Digital Content video, https://links.lww.com/ALN/E366). This suggests that the spinal cord also exhibits neurovascular coupling. When one side of the cord is activated, commissural interneurons transmit information contralaterally to facilitate left–right upper limb coordination for object manipulation and left–right lower limb coordination for walking; this may account for the bilateral increase in dorsal column spinal cord blood flow in response to unilateral dorsal column stimulation. Our findings directly validate the previously reported functional magnetic resonance imaging findings of bilateral dorsal spinal cord blood flow increase during unilateral vibratory dermatomal stimulation.[10]

Our study has limitations. First, the number of patients is small. Second, only some patients were studied in each protocol, based on practical constraints, which may introduce selection bias. Third, the patients are heterogeneous. Fourth, laser speckle contrast imaging penetrates to a depth of 2 to 3 mm from the cord surface,[1] which monitors only the dorsal columns. Fifth, spinal cord oxygen demand was not measured to determine whether sevoflurane uncouples flow–metabolism matching.[7] Sixth, in each patient, autoregulation was studied as response of spinal cord blood flow to a single MAP change. Despite the limitations, our study offers clinically important insight into human spinal cord blood flow physiology. For example, based on our findings, in patients with cord compression, hypocarbia may be detrimental by causing hypoperfusion at the site of compression.

In conclusion, our data from this small patient cohort suggest that, in patients receiving sevoflurane or propofol, spinal cord blood flow exhibits autoregulation, carbon dioxide reactivity, and neurovascular coupling. Sevoflurane MAC and the temperature of irrigating saline had no significant effect on spinal cord blood flow. Future studies with larger, protocol-specific cohorts will be essential to confirm these observations and better define their clinical implications.

Research Support

This work was funded by the Wings for Life Spinal Cord Research Foundation (London, United Kingdom; research grant to Dr. Saadoun and Dr. Papadopoulos), the National Institute of Health Research (NIHR)

Efficacy and Mechanism Evaluation Program (EME, grant No. NIHR130048), and the Neurosciences Research Foundation (London, United Kingdom; McKissock fellowship to Dr. Asif). Dr. Asif's salary was funded by the EME, NIHR130048, and Dr. Boseta is partly funded by the NIHR Clinical Research Network.

Competing Interests

The authors declare no competing interests.

Hasan Asif, M.B., B.S.[1]
Samuel Ern Hung Tsan, M.D.[2]
Ellaine Boseta, B.Sc.[2]
Argyro Zoumprouli, M.D., Ph.D.[1,2]
Marios C. Papadopoulos, M.D.[1,2]
Samira Saadoun Ph.D.[1]*
[1]City St. George's, University of London, London, United Kingdom
[2]St. George's Hospital National Health Service Foundation Trust, London, United Kingdom
*ssaadoun@sgul.ac.uk

DOI: 10.1097/ALN.0000000000005911

Supplemental Digital Content

Supplemental Figure S1. Intraoperative laser speckle contrast imaging, https://links.lww.com/ALN/E358
Supplemental Figure S2. Effect of sevoflurane MAC on spinal cord blood flow CO_2 reactivity, https://links.lww.com/ALN/E359
Supplemental Figure S3. Impaired spinal cord autoregulation, https://links.lww.com/ALN/E360
Supplemental Figure S4. Neurovascular coupling, https://links.lww.com/ALN/E361
Flowchart, https://links.lww.com/ALN/E362
Supplemental methods, https://links.lww.com/ALN/E363
STROBE checklist, https://links.lww.com/ALN/E364
Supplemental tables, https://links.lww.com/ALN/E365
Supplemental video, https://links.lww.com/ALN/E366

References

1. Gallagher MJ, Hogg FRA, Zoumprouli A, Papadopoulos MC, Saadoun S: Spinal cord blood flow in patients with acute spinal cord injuries. J Neurotrauma 2019; 36:919–29. doi:10.1089/neu.2018.5961
2. Molnar C, Settakis G, Sarkany P, Kalman S, Szabo S, Fulesdi B: Effect of sevoflurane on cerebral blood flow and cerebrovascular resistance at surgical level of anaesthesia: A transcranial Doppler study. Eur J Anaesthesiol 2007; 24:179–84. doi:10.1017/S0265021506001335
3. Bundgaard H, von Oettingen G, Larsen KM, et al.: Effects of sevoflurane on intracranial pressure, cerebral blood flow and cerebral metabolism: A dose-response study in patients subjected to craniotomy for cerebral tumours. Acta Anaesthesiol Scand 1998; 42:621–7. doi:10.1111/j.1399-6576.1998.tb05292.x
4. Ainslie PN, Duffin J: Integration of cerebrovascular CO_2 reactivity and chemoreflex control of breathing: Mechanisms of regulation, measurement, and interpretation. Am J Physiol Regul Integr Comp Physiol 2009; 296:1473. doi:10.1152/ajpregu.91008.2008
5. Stretti F, Gotti M, Pifferi S, Brandi G, Annoni F, Stocchetti N: Body temperature affects cerebral hemodynamics in acutely brain injured patients: An observational transcranial color-coded duplex sonography study. Crit Care 2014; 18:552–7. doi:10.1186/s13054-014-0552-7
6. Meng L, Sun Y, Rasmussen M, et al.: Lassen's cerebral autoregulation plot revisited and validated 65 years later: Impacts of vasoactive drug treatment on cerebral blood flow. Anesth Analg 2024; 140:1426–38. doi:10.1213/ane.0000000000007280
7. Slupe AM, Kirsch JR: Effects of anesthesia on cerebral blood flow, metabolism, and neuroprotection. J Cereb Blood Flow Metab 2018; 38:2192–208. doi:10.1177/0271678X18789273
8. Werndle MC, Saadoun S, Phang I, et al.: Monitoring of spinal cord perfusion pressure in acute spinal cord injury: Initial findings of the injured spinal cord pressure evaluation study. Crit Care Med 2014; 42:646–55. doi:10.1097/CCM.0000000000000028
9. Kaplan L, Chow BW, Gu C: Neuronal regulation of the blood-brain barrier and neurovascular coupling. Nat Rev Neurosci 2020; 21:416–32. doi:10.1038/s41583-020-0322-2
10. Lawrence JM, Stroman PW, Kollias SS: Functional magnetic resonance imaging of the human spinal cord during vibration stimulation of different dermatomes. Neuroradiology 2008; 50:273–80. doi:10.1007/s00234-007-0338-6

(Accepted for publication December 1, 2025.)