Real-time monitoring of spinal cord blood flow with a novel sensor mounted on a cerebrospinal fluid drainage catheter in an animal model

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Objective: The aim of our study was to develop a novel monitoring system for spinal cord blood flow (SCBF) to test the efficacy of the SCBF sensor in an animal model.

Methods: The sensor system consisted of 2 optical fibers, a pedestal for fiber fixation, and a mirror for the laser reflection and was incorporated into a cerebrospinal fluid drainage catheter. In vivo studies were performed in a swine model (n = 10) to measure SCBF during spinal cord ischemia induced by clamping the descending thoracic aorta and supra-aortic neck vessels, when necessary. A temporary low cardiac output model was also created by inflow clamping of the inferior vena cava to analyze the quantitative changes in SCBF during this maneuver.

Results: The developed SCBF monitoring catheter placed intrathecally could detect SCBF in all the swine. The SCBF after aortic crossclamping at the fourth intercostal level exhibited diverse changes reproducibly among the swine, with a >25% reduction in SCBF in 5 pigs, an increase in 3, and no significant changes in 2. Consistent reductions were recorded during inferior vena cava occlusion. The mean SCBF decreased by 32% after inferior vena cava occlusion when the cardiac output had decreased by 27%.

Conclusions: We have developed a novel SCBF sensor that could detect real-time changes in spinal cord perfusion in a swine model. The device holds promise to detect imminent ischemia or ensure acceptable blood perfusion in the spinal cord and could further enhance our understanding of spinal cord circulation. (J Thorac Cardiovasc Surg 2014;148:1726-31)

Thoracoabdominal aortic aneurysm (TAAA) repair carries a significant risk of spinal cord injury that will result in poor early and long-term outcomes.[1-3] Although diverse strategies to prevent spinal cord injury have been used, the incidence of paraplegia and paraparesis has remained significant and has reportedly been 2.7% to 11.4%.[4-7] The difficulty in avoiding such a devastating complication can essentially be attributed to the lack of a reliable direct monitoring system for spinal cord ischemia. The difficulties that preclude real-time monitoring of spinal cord perfusion encompass the anatomic location of the spinal cord, which is surrounded by the solid vertebral column, and the complexity of the blood supply. Thus, the development of an intraoperative continuous monitoring device for SCBF would be highly desirable.

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The aim of our study was to develop a novel real-time monitoring system for spinal cord blood flow (SCBF) to test the efficacy of the SCBF sensor in an animal model.

METHODS

SCBF Sensor Development

We elected to adopt the principal of laser Doppler flowmetry to put the theory into our practice.[8,9] To create a novel sensor for SCBF designed for use in the intrathecal space, microelectromechanical system technology was applied.

Our SCBF sensor system consists of 2 optical fibers, a pedestal for fiber fixation, and a cerebrospinal fluid (CSF) drainage catheter (Silascon, inner diameter 0.9 mm, outer diameter 1.65 mm; Kaneka Medix Co, Osaka, Japan; Figure 1). The pedestal consisted of a 4-in. silicon wafer (0.525 mm × 0.7 mm × 3 mm) using a dicing technique, and a mirror was attached to the tip of the pedestal for right-angled reflection of the laser. Two optical fibers were situated in 2 grooves on the upper surface of the pedestal. The sensor probe was fixed on a CSF drainage catheter using epoxide-based adhesive, and the 2 optical fibers were passed through the CSF drainage catheter and connected to a flowmeter with fiberoptic connections. With this system, the blood flow can be noninvasively monitored from an intrathecal space while simultaneously incorporating continuous CSF drainage capabilities.

Ex Vivo Evaluation of SCBF Sensor

We evaluated the SCBF sensor and compared it with a commercially available blood flow sensor (ST-N probe; Omegawave, Inc, Tokyo, Japan) in an ex vivo experiment. A noncontact blood flowmeter (FLO-N1; Omegawave, Inc, Tokyo, Japan) was chosen for this evaluation, because it is necessary to detect SCBF without coming in contact with the spinal cord

Abbreviations and Acronyms

CSF	= cerebrospinal fluid
IVC	= inferior vena cava
MEP	= motor evoked potential
SCBF	= spinal cord blood flow
TAAA	= thoracoabdominal aortic aneurysm

to avoid direct tissue injury. The calibration was completed by simply pressing the button on the measurement console before usage.

In a simple evaluation, the blood flow was measured at the tip of a human subject's finger. A blood pressure cuff was placed on the humerus of the left arm, and 2 blood flow probes were set to measure the blood flow. Under stable conditions, the cuff was inflated $\leq$250 mm Hg to interrupt the arterial blood flow of the left index finger for 30 seconds. The pressure of the cuff was then released to re-establish the blood flow. We monitored the sequential changes in blood flow 3 times in 1 person to evaluate the reliability of this SCBF sensor compared with that of the commercially available ST-N probe. In addition to blood flow, using this method, we could measure the blood volume, which represents the hemoglobin content in the tissue, and the flow velocity.

In Vivo Evaluation of SCBF Sensor in a Swine Model

We evaluated the SCBF sensor for clinical applications, in particular as a continuous blood flow-monitoring device for use in TAAA repairs. A CSF drainage catheter is routinely placed into an intrathecal space at the L4–L5 vertebral level before TAAA repair. The location of the front edge of the CSF drainage catheter is confirmed using fluoroscopy and computed tomography. However, the resolution of these modalities has not been sufficient to detect the sensor head direction because of the small sensor size (3 mm $\times$ 0.7 mm $\times$ 0.525 mm) and radiolucency of the sensor head. Therefore, the sensor head direction could be misdirected when percutaneously inserted into the intrathecal space. The determined values would be unreliable if the sensor head were not facing the spinal cord. To address this issue, we performed 3 different validations in an animal model.

In the first experiment, we evaluated the relationship between the directional characteristics of the sensor head and the intensity of the reflected signals from the SCBF. The sensor head direction was arranged under direct vision from face-to-face placement to the opposite direction gradually with the changes in the SCBF recorded.

The second experiment was designed to observe the changes in SCBF when the aorta was crossclamped at the fourth intercostal level. The supra-aortic neck vessels were also clamped when no significant changes in SCBF were observed during aortic crossclamping.

Finally, a temporary low cardiac output model was also created by inflow clamping of the inferior vena cava (IVC) to analyze the quantitative changes in SCBF during this maneuver.

Animal Experiments

Domesticated swine weighing approximately 40 kg were used for these experiments. The swine were fed a normal diet and received humane care in compliance with "The Guiding Principles in the Care and Use of Animals" from the Ministry of Education, Culture, Sports, Science and Technology in Japan (publication no. 71 in 2006). The animal care committee of the Tohoku University Graduate School of Medicine approved the experimental protocol (protocol no. 2013-127).

After anesthetic induction with an intramuscular injection of midazolam (0.2 mg/kg) and medetomidine (0.05 mg/kg), endotracheal intubation was performed. The swine were mechanically ventilated during the experiment. Intraoperative anesthesia was maintained with inhaled sevoflurane (0.5%-3.0%) and a continuous infusion of fentanyl (5 μg/kg/h) and ketamine (15 mg/kg/h). If the sedation was not sufficient to keep the swine stable, periodic propofol injections (2-4 mg/kg) were administered. The right carotid or radial arterial blood pressure, heart rate, and oxygen saturation were monitored during the procedures.

The swine was placed in a prone position, and the spinous process was exposed at the level of T9. The SCBF sensor was positioned in the intrathecal space. After repositioning in the right lateral position, an incision was made, and the descending aorta and brachiocephalic and left subclavian arteries were isolated. Finally, in a cranial direction, the SCBF sensor was inserted into the intrathecal space $\leq$ 5 cm in length at the T9 level.

Directional Characteristics of SCBF Sensor

The SCBF was measured using the SCBF sensor while changing the sensor head direction. The relationship between the spinal cord and the sensor head direction was defined as follows: face-to-face position, 0°; the opposite position, 180°; and in between, 90°. Additionally, the torquability of the CSF drainage catheter with 2 optical fibers was evaluated to rotate the catheter inserted through subcutaneous fat tissue 15 cm in length toward the spinal cord. Also, the SCBF was recorded while rotating the catheter externally to change the sensor head direction.

SCBF Assessment After Aortic Crossclamping and IVC Clamping

The SCBF was measured using the SCBF sensor after aortic crossclamping at the level of T4 and IVC clamping. The supra-aortic neck vessels were also clamped to ensure spinal cord ischemia when the SCBF did not decrease after aortic crossclamping, because significant collateral flow will be provided by the internal mammary arteries in some swine. A temporary low cardiac output model was also created by inflow occlusion using IVC clamping to analyze the quantitative changes in the SCBF during this maneuver. These maneuvers were conducted in 3 pigs to ensure reproducible observations.

RESULTS

Ex Vivo Evaluation of SCBF Sensor

The results of the ex vivo experiment are shown in Figure 2. The performance of the commercially available ST-N sensor and the new SCBF sensor was equivalent in measuring blood flow (SCBF sensor, nonischemia, 20.1 $\pm$ 1.3 mL/min/100 g and ischemia, 1.47 $\pm$ 0.3 mL/min/100 g; ST-N sensor, nonischemia 19.9 $\pm$ 0.6 mL/min/100 g and ischemia 0.99 $\pm$ 0.3 mL/min/100 g). These results are expressed as the mean $\pm$ standard deviation. The coefficient of correlation between these 2 sensors was 0.98.

In Vivo Evaluation of SCBF Sensor in a Swine Model

Effect of direction on SCBF sensor results. Figure 3 shows the difference in SCBF at each sensor direction (angles, 0°, 90°, and 180°); the mean $\pm$ standard deviation values are also listed in Table 1. The SCBF sensor accumulated the reflected signals more effectively at 0° than at the other directions and thus detected the SCBF adequately. Furthermore, the apparent pulsatile flow, according to each heart contraction, was observed at the 0° angle. However, the baseline blood flow and pulsatile flow at the 90° angle were obviously decreased compared with those at 0°, and the SCBF sensor at 180° could only detect the

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