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Technology

Intraoperative monitoring of cerebral blood oxygenation and hemodynamics during extracranial-intracranial bypass surgery by a newly developed visible light spectroscopy system

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Abstract

Background: Cerebrovascular reconstruction procedures run the risk of changing the balance between oxygen supply and consumption during surgery. We assessed the value of visual light spectroscopy for detecting changes in cerebral blood oxygenation (CBO) during superficial temporal artery–middle cerebral artery (STA-MCA) anastomosis.

Methods: We developed a VLS monitoring system which permits continuous monitoring of CBO changes during surgery. Using the VLS, we evaluated the CBO changes in the MCA territory on the lesion side in 18 patients who underwent STA-MCA anastomosis.

Results: Temporary occlusion of the MCA (M4 portion) did not change the CBO in 17 patients. However, in the patient with dissecting aneurysm, it caused decreases of oxyhemoglobin and cortical oxygen saturation ($CoSO_2$) associated with an increase of deoxyhemoglobin, although these CBO changes were normalized by STA blood flow. In 5 patients, STA blood flow increased the oxyhemoglobin and $CoSO_2$ and decreased the deoxyhemoglobin, indicating that cortical blood flow (CoBF) was increased. The $CoSO_2$ before anastomosis was significantly low in the patients who showed an increase of $CoSO_2$ by STA blood flow (63.0% ± 2.5%) as compared with those who did not (72.0 ± 6.1%, $P = .024$).

Conclusion: Temporary occlusion of a cortical artery during bypass surgery did not affect the CBO in patients who had chronic cerebral ischemia, but caused acute ischemia in the patient who did not. STA blood flow increased the CoBF during surgery more frequently in patients who showed a low perfusion pressure. The VLS monitoring system is considered useful for evaluating bypass function and facilitates safe and accurate bypass surgery.

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Keywords: EC-IC bypass; Cerebral ischemia; Laser-Doppler flowmetry; Moyamoya disease; STA-MCA anastomosis; Visible light spectroscopy

1. Introduction

Although the International EC-IC Bypass Study Group reported failure of EC-IC bypass surgery to prevent stroke [24], EC-IC bypass is still an important operative technique in neurosurgery. A number of studies have demonstrated that EC-IC bypass surgery can prevent stroke in patients with TIA caused by hemodynamic compromise [1,6,10,19,25] and moyamoya disease [7,8,18,22]. In addition,

Abbreviations: CBO, cerebral blood oxygenation; CoBF, cortical blood flow; $CoSO_2$, cortical oxygen saturation; EC-IC, extracranial-intracranial; HHb, deoxyhemoglobin; ICA, internal carotid artery; LDF, laser-Doppler flowmetry; NIRS, near-infrared spectroscopy; O_2Hb, oxyhemoglobin; STA-MCA, superficial temporal artery–middle cerebral artery; tHb, total hemoglobin; TIA, transient ischemic attack; VLS, visual light spectroscopy.

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EC-IC bypass is recognized as an important element in the treatment of complex cerebral aneurysms and cranial base tumors [16,20,26].

To perform EC-IC bypass surgery safely and accurately, the following problems need to be considered and resolved during surgery. First, occlusion of the graft artery must be corrected during surgery. Intraoperative graft occlusion usually occurs for technical reasons or because of a hypercoagulable state. Second, cerebral ischemia caused by the temporary occlusion of the recipient artery such as the MCA may result in cerebral infarction after surgery. Finally, an increased perfusion pressure induced by EC-IC bypass can cause hyperperfusion syndrome in the chronically hypoperfused brain, particularly in the case of high-flow bypass [23]. To resolve these problems, various intraoperative monitoring techniques have been developed to evaluate the hemodynamic changes or patency of the graft during surgery including EC-IC bypass [3,4,9,14,15].

Recently, NIRS, an optical method for measuring CBO changes, has been applied to intraoperative monitoring in craniotomy [2,17]. Monitoring of CBO changes, which reflect the balance between oxygen supply and consumption, can provide important information concerning the efficacy and complications of EC-IC bypass to the operators. However, it is difficult to monitor CBO changes continuously during craniotomy by NIRS, because near-infrared light from the surgical microscope migrates into the NIRS detector through the brain tissue, leading to interference with its measurements. In contrast, VLS, which measures CBO changes by means of the absorption spectra of hemoglobin in the visible light range [5,12], is more suitable for intraoperative monitoring during craniotomy than is NIRS, because visible light can easily be shaded during surgery.

In the present study, we developed an intraoperative VLS monitoring system for undertaking continuous measurements of CBO changes during the entire course of surgery. Initially, we evaluated the accuracy of the VLS monitoring system in in vitro and in vivo experiments. Then, using the VLS monitoring system, we evaluated the effects of temporary occlusion of the recipient artery (ie, the MCA) and the blood flow of the donor artery (ie, the STA) on the CBO in the MCA territory on the lesion side during STA-MCA anastomosis.

2. Materials and methods

2.1. Patients characteristics

We investigated 18 patients undergoing craniotomy for STA-MCA anastomosis during the period from March 2002 to March 2005. The subjects included 7 patients with moyamoya disease, 6 patients with occlusion of the ICA, 4 patients with occlusion of the MCA, and 1 patient with dissecting aneurysm of the ICA. Among the patients with moyamoya disease, 5 had multiple episodes of TIA, although magnetic resonance imaging did not demonstrate cerebral infarction in these patients. The other 2 patients with moyamoya disease had cerebral hemorrhage. Single-photon emission computed tomography (SPECT) revealed a reduced regional CBF (rCBF) at rest (≤30 mL per 100 g/min) and vasoreactivity to acetazolamide (≤10%) in the MCA territory on the lesion side in all of the patients except for the patient with dissecting aneurysm of the ICA

Table 1
Individual patient profiles and intraoperative physiological parameters

Case no.	Age (y)/sex	Clinical type of stroke	Cause of stroke	Side	Intraoperative physiological parameters						
					SBP/DBP (mm Hg)	BT (°C)	HR (bpm)	SO_2 (%)	PO_2/PCO_2 (mm Hg)	Hb (g/dL)	Ht (%)
1	35/M	TIA	Moya	R	148/92	34.4	58	100	216/36	14.2	41.7
2	23/M	TIA	Moya	R	148/62	34.3	65	100	242/39	13	39.4
3	14/F	TIA	Moya	L	125/70	34.5	73	100	214/42	13.2	38.4
4	14/F	TIA	Moya	R	120/65	35.1	58	100	293/38	12.4	36.4
5	23/F	TIA	Moya	R	145/80	35.5	65	100	251/41	13.2	38.5
6	64/M	CH	Moya	R	120/65	36	62	100	188/40	11.5	33.8
7	26/F	CH	Moya	L	140/90	34.7	65	100	182/36	12.5	36.4
8	45/M	LI	ICA-O	R	135/84	34.4	63	100	314/42	14.1	41.1
9	71/M	LI	ICA-O	R	143/80	35	65	100	171/38	13.5	40.5
10	74/M	AE	ICA-O	L	150/65	34.5	75	100	183/42	13.4	39.1
11	48/M	TIA	ICA-O	L	130/65	35.7	85	100	135/38	12.8	37.6
12	55/M	BI	ICA-O	L	140/80	35.1	55	100	169/44	14.5	43.1
13	48/F	LI	MCA-O	R	115/68	35	60	100	189/45	13.1	37.8
14	49/F	BI	MCA-O	R	130/75	35.7	69	100	213/36	10.7	31.8
15	61/M	LI	MCA-O	L	165/80	35	58	100	244/37	13.4	39.4
16	49/F	TIA	MCA-O	R	130/80	35	75	100	125/43	12.6	37.6
17	68/M	LI	ICA-O	R	130/60	36	55	100	251/40	10.4	32.2
18	52/M	SAH	ICA-D	R	152/72	36.5	74	100	135/38	13.5	41.5

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; BT, body temperature; bpm, beats per minute; Hb, hemoglobin; Ht, hematocrit; CH, cerebral hemorrhage; LI, lacunar infarct; AE, artery-to-artery embolism; BI, border zone infarct; SAH, subarachnoid hemorrhage; moya, moyamoya disease; ICA-O, ICA occlusion; MCA-O, MCA occlusion; ICA-D, ICA dissection.

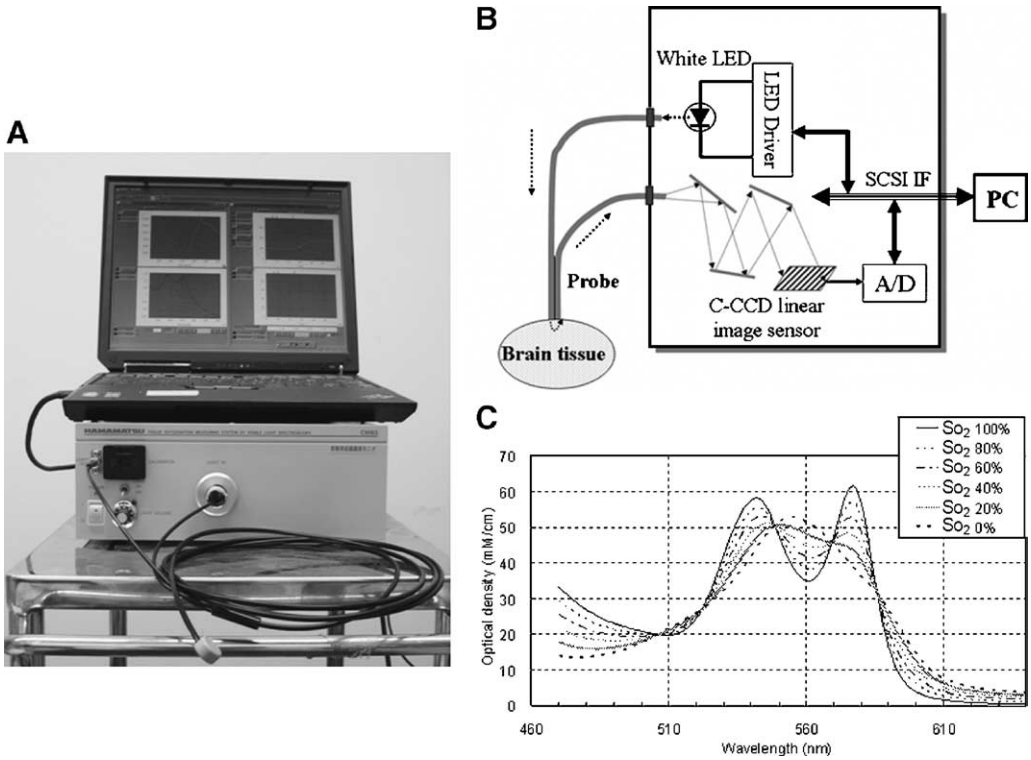

Fig. 1. A: Photograph of the VLS system. B: Block diagram of the VLS system. C-CCD indicates cooled charge-coupled device. C: Absorption spectra of hemoglobin at various oxygen saturations (0%-100%). The ordinates indicate the optical density (mmol/L per centimeter); the abscissa indicates the wavelength (nm).

(patient 18). Postoperative angiography demonstrated patency of the anastomosed STA in all patients. Table 1 summarizes the individual patient profiles. The present study was approved by the Committee for Clinical Trials and Research on Humans. The patients gave informed consent for all procedures described herein to be performed. The ethical committee of our university hospital approved the protocol of the study.

2.2. Intraoperative VLS monitoring system

We have developed an intraoperative CBO monitoring system using VLS (C9183, Hamamatsu Photonics KK, Hamamatsu, Japan). Fig. 1A shows a block diagram of the present monitoring system. The VLS measures changes of the O_2Hb and HHb concentrations in the cerebral vessels by means of the characteristic absorption spectra of hemoglobin in the visible light range (Fig. 1B). Changes in total hemoglobin (tHb; sum of O_2Hb and HHb) indicate blood volume changes. White light from the light-emitting diode was directed at the tissue through a fiberoptic bundle, and the reflected light was transmitted to a cooled charge-coupled device spectrometer. The diameter of the fiberoptic bundle was 1 mm, and the distance between each fiberoptic bundle was 2 mm; the estimated measurement area was approximately 2 mm in width and 1 mm in depth [21]. To eliminate the effects of external light such as the light of the operative microscope, the LED was regulated by a PC

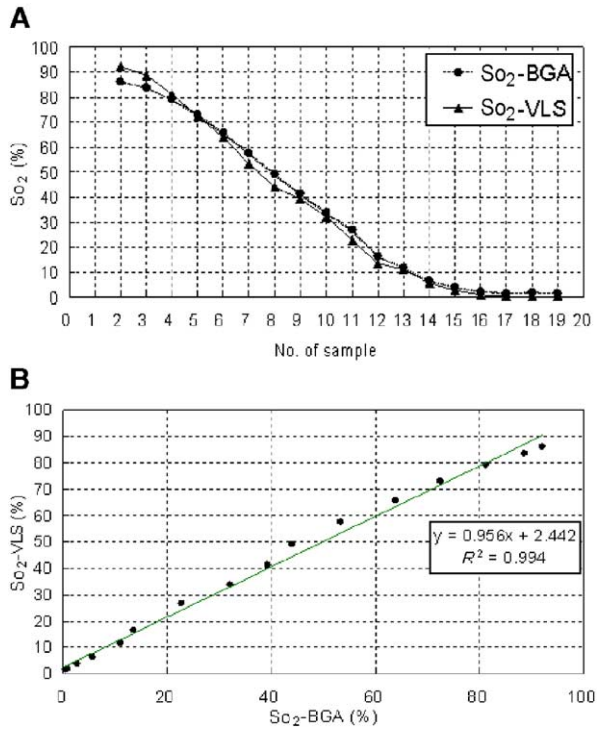

Fig. 2. A: Changes in oxygen saturation measured by the VLS system and by the blood gas analyzer. B: Relation between the oxygen saturation values measured by the VLS system (ordinate) and by the BGA (abscissa). BGA indicates blood gas analyzer.

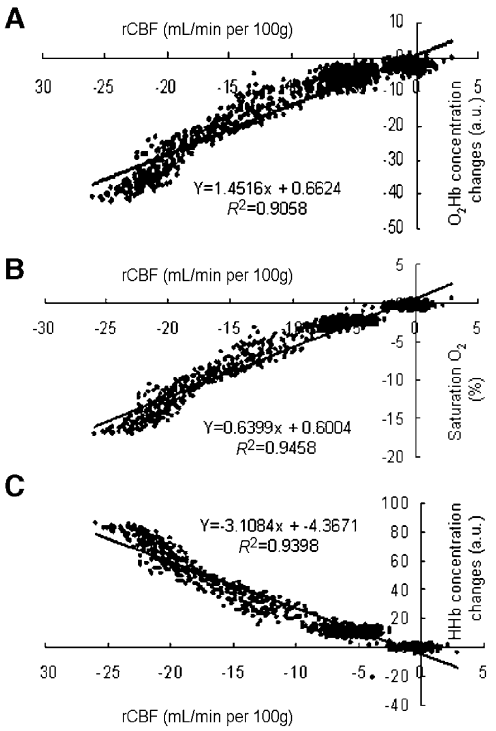

Fig. 3. Relations between the rCBF measured by LDF and the O_2Hb (A), $CoSO_2$ (B), and HHb (C) measured by VLS in the rat global ischemia model. Significant positive correlations existed between the CoBF and the $CoSO_2$ and O_2Hb (A, B), and a negative correlation between the CoBF and HHb (C). a.u., arbitrary unit.

to emit white light on/off at 2 Hz; the spectrum with light-on was adjusted by subtraction of the spectrum with light-off. The relative concentration changes in O_2Hb and HHb were calculated by least square error curve-fitting based on the differential spectrum; the analyzed wavelength range was 520 to 580 nm. The sampling rate was 0.5 seconds. The ratio of $O_2Hb/[O_2Hb + HHb]$ indicates the cortical oxygen saturation ($CoSO_2$).

$$\frac{\partial A}{\partial \lambda} = k_1 \cdot \frac{\partial O_2Hb}{\partial \lambda} + k2 \cdot \frac{\partial HHb}{\partial \lambda} + C.$$

where A (λ) represents the absorption spectrum at λ nm; k_1, the relative concentration of O_2Hb; and k_2, the relative concentration of HHb; and C, constant.

2.3. Preliminary assessment of accuracy of the VLS monitoring system

To evaluate the accuracy of the SO_2 measured with the present system, we undertook simultaneous measurements by the VLS system and a blood gas analyzer (NOVA Biomedical, Waltham, MA, STAT profile 2) using phantoms containing human whole blood, intralipid, and water (0.96% Dulbecco phosphate-buffered saline). The container of phantom was placed in a temperature-controlled reservoir to keep the phantom temperature at 37°C. The oxygenation in the phantom was changed by yeast and oxygen bubbling. The recording probe was placed in the phantom, and the SO_2 was monitored continuously, while a small amount of the phantom was periodically sampled for blood gas analyzer measurement of the true SO_2. A strong correlation was noted between the SO_2 values measured by the VLS system and the blood gas analyzer (Fig. 2).

In addition, we evaluated the relation between the CBO changes measured by VLS and the CoBF measured by LDF in a rat global ischemic model. The animal experiments were carefully performed in accordance with the guiding principles for the care and use of laboratory animals approved by Nihon University School of Medicine.

Sixteen male Wistar rats (Charles River Co, Ltd, Ibaraki, Japan) weighing 300 to 380 g were used for these experiments. The rats were anesthetized with 40 mg/kg IP pentobarbital and mounted in a stereotactic frame after insertion of catheters into the femoral artery and vein; anesthesia was maintained with 2% inspired halothane in O_2-supplemented room air. For simultaneous measurements of the VLS and LDF (FLO-NI, OMEGA WAVE, Tokyo, Japan), 2 small burr holes (diameter, 3 mm) were cut at 4 mm posterior to the bregma and 3 mm lateral to the sagittal suture. The recording probes of the VLS and LDF were placed on the cortical surface via the burr holes on the right and left sides, respectively.

After control recordings had been made for 60 minutes, diltiazem was administered intravenously to reduce the systemic blood pressure. When the systolic blood pressure was reduced to approximately less than 70 mm Hg, the

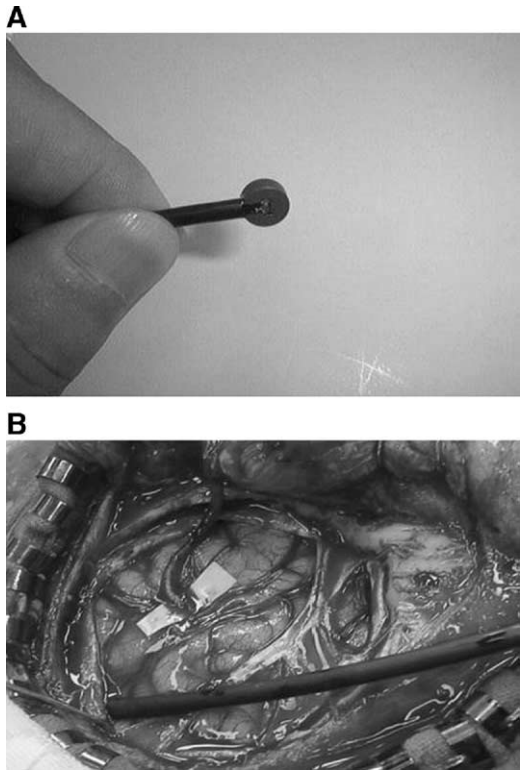

Fig. 4. A: Recording probe of the VLS system. B: Recording setting during surgery. The probe was placed under the subdural space, at a position 15 to 20 mm apart from the site of anastomosis.

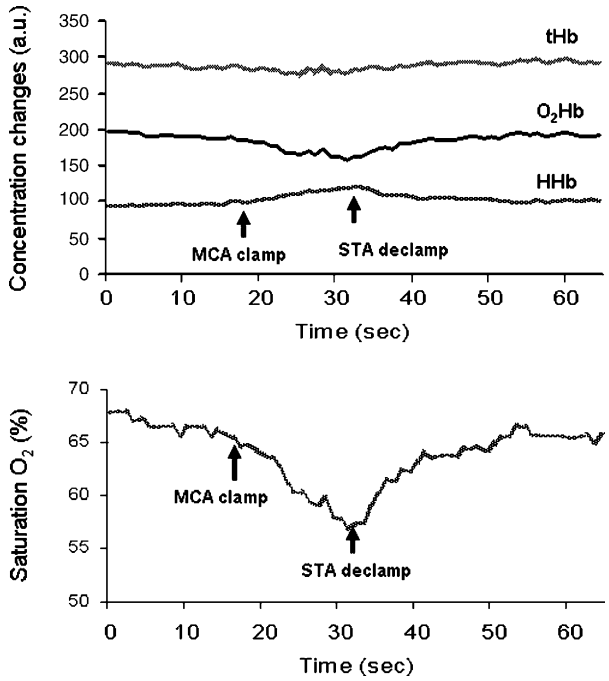

Fig. 5. Effects of temporary occlusion of the MCA on the CBO in the patient with dissecting aneurysm of the ICA (patient 18) during STA-MCA anastomosis. The ordinates indicate concentration changes of O_2Hb, HHb, and tHb in arbitrary units (upper) and $CoSO_2$ in % (lower). Note that temporary occlusion of the MCA caused ischemic changes (ie, decreases of O_2Hb, tHb, and $CoSO_2$ with an increase of HHb); however, the ischemic changes were normalized by declamping of the STA.

CoBF exhibited a decreasing tendency. The $CoSO_2$ and O_2Hb decreased in association with the decrease in CoBF. On the other hand, the HHb increased with these changes, indicating the occurrence of an increase in oxygen extraction during cerebral ischemia. We observed significant positive correlations between the CoBF and the $CoSO_2$ and O_2Hb (Fig. 3A and B), and a negative correlation between the CoBF and HHb (Fig. 3C).

2.4. Intraoperative monitoring procedures

The STA was carefully isolated from the reflected skin flap and anastomosed end-to-side to the M4 portion of the MCA. In the patients with moyamoya disease, encephalo-myo-synangiosis was performed after the STA-MCA anastomosis. The physiological parameters during surgery were within the reference ranges in all of the patients (Table 1).

For continuous monitoring of the CBO changes in the MCA territory on the side of anastomosis, the recording probe (outer diameter, 7 mm; distance between the emitter and receiver fiberoptic bundles, 1.5 mm) was placed under the subdural space so that the probe and optical fiber did not interfere with the surgical procedure, 15 to 20 mm distal to the part of the M4 portion where the STA was anastomosed (Fig. 4). After completion of the anastomosis, we repeated clamping and declamping of the MCA to evaluate the effects of MCA occlusion on the CBO; the STA was clamped during this test. We then repeated clamping and

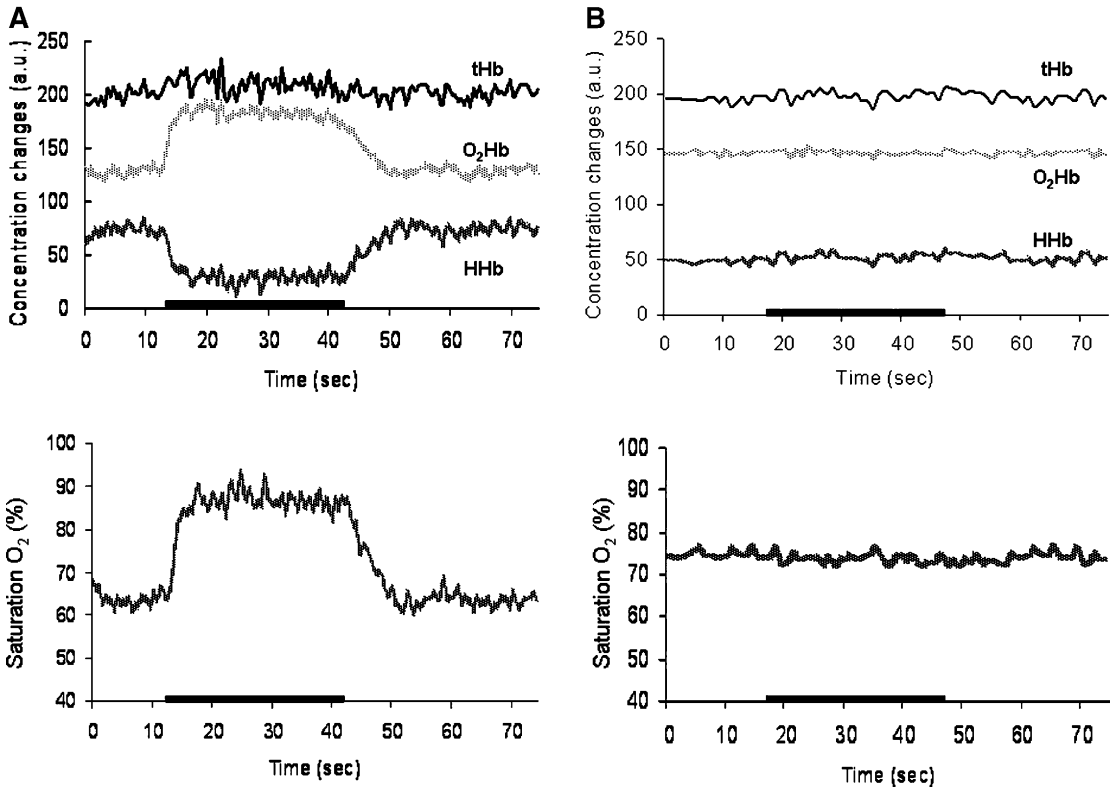

Fig. 6. Changes in hemoglobin concentrations (upper) and $CoSO_2$ (lower) caused by declamping of the STA during surgery. The ordinates indicate concentration changes of O_2Hb, HHb, and tHb in arbitrary units (upper) and $CoSO_2$ in % (lower). Note that the STA declamping caused increases of O_2Hb and $CoSO_2$ associated with a decrease of HHb in A, but no changes in B.

declamping of the STA to evaluate the effects of STA blood flow on the CBO; the MCA was declamped during this test.

2.5. Data analysis

To evaluate the effects of the STA blood flow and the MCA occlusion on the MCA territory on the lesion side, we compared the VLS parameters (ie, O_2Hb, HHb, tHb, and $CoSO_2$) during a 10-second period of control with those observed during declamping of the STA or clamping of the MCA for a 10-second period. In addition, we compared the VLS parameters, preoperative rCBF as measured by SPECT, and STA blood flow between the MD and non-MD patients using the unpaired *t* test.

3. Results

Temporary occlusion of the MCA did not change the CBO significantly in 17 patients. However, in the patient with dissecting aneurysm of the ICA (patient 18), it caused decreases of O_2Hb and $CoSO_2$ associated with an increase of HHb, indicating the occurrence of cerebral ischemia. These CBO changes induced by occlusion of the MCA returned to the control level after declamping of the STA (Fig. 5).

In 4 patients with moyamoya disease and 1 patient with MCA occlusion, declamping of the anastomosed STA caused increases of O_2Hb and $CoSO_2$ associated with decreases of HHb; tHb did increase significantly, but the degree of tHb increase was much smaller than that of the O_2Hb increase (Fig. 6A). These CBO changes indicate that the STA blood flow increased the CoBF with small changes in cerebral blood volume. Other patients did not exhibit significant CBO changes induced by the STA blood flow during bypass surgery (Fig. 6B).

Fig. 7 compares the $CoSO_2$ before anastomosis between these patients who showed CBO changes (ie, increases of O_2Hb and $CoSO_2$ and decreases of HHb) by STA blood flow and those who did not. The $CoSO_2$ before anastomosis was significantly low in the patients with CBO changes (63.0% ± 2.5%) as compared with those without them (72.0% ± 6.1%, $P = .024$). There were no significant differences in preoperative rCBF, percent of vasoreactivity to acetazolamide, and STA blood flow between the 2 groups.

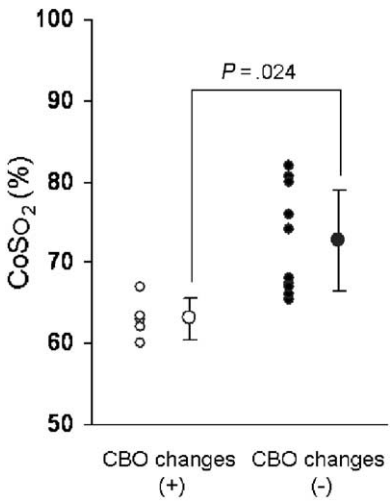

Fig. 7. Comparison of the preanastomosis $CoSO_2$ between patients who showed CBO changes (ie, increases of O_2Hb and $CoSO_2$ associated with a decrease of HHb) during STA declamping and those who did not. The ordinate represents the $CoSO_2$ in %.

4. Discussion

In preliminary experiments, a strong correlation was noted between the SO_2 values measured by the VLS monitoring system and the blood gas analyzer in the in vitro model. Moreover, in the rat cerebral ischemia model, significant positive correlations existed between the O_2Hb and $CoSO_2$ measured by the VLS and the CoBF measured by LDF. These findings indicate that the present VLS system allows us to monitor dynamic changes in CBO caused by hemodynamic alterations during surgery. Meyer et al [12], using a VLS system (ie, EMPHO), mapped the distribution of CBO changes surrounding the arteriovenous malformation; however, it is not suitable for continuous monitoring. In contrast, our monitoring system permits continuous monitoring of dynamic changes in CBO during craniotomy with a high time resolution.

The present VLS monitoring system does, however, have the following limitations. First, the system measures the CBO changes at a single small area in the cortex. For this reason, the CBO changes occurring outside the recording site may be overlooked. First, the present VLS system measures the CBO changes at a single small area in the cortex; the measurement area of VLS is limited to the cortical surface area (ie, approximately 1 mm in depth and 2 mm in width). The VLS system, therefore, may not detect CBO changes outside the measurement area, including the subcortex area. Therefore, even if the VLS does not show significant changes in CBO during surgery, an infarction may have occurred in these areas. Such a limitation, however, also exists in other intraoperative monitoring methods, including LDF and the thermal diffusion method. Scanning of the cortical surface by moving the VLS light guide [12] or the use of NIRS [2,17] may increase the measurement area, but these methods do not allow continuous monitoring during surgery. Second, the values for the hemoglobin concentration are expressed as relative values, not absolute values, because the optical path length in the brain tissue is not known. We therefore did not compare these values among the subjects except for the $CoSO_2$. Finally, the present system does not allow direct measurements of mitochondrial function, which can be evaluated by monitoring the nicotinamide adenine dinucleotide oxidation-reduction state [11].

In the patient with dissecting aneurysm of the ICA (patient 18), temporary occlusion of the MCA caused decreases of O_2Hb and tHb associated with an increase of HHb, indicating the occurrence of acute cerebral ischemia. In this patient, the STA-MCA anastomosis was performed to prevent ischemic stroke after permanent occlusion of the

ICA; thus, the patient did not have chronic cerebral ischemia before the surgery. It should be noted that the ischemic changes caused by occlusion of the MCA were normalized by declamping of the STA, indicating that the anastomosed STA supplied blood flow to the ischemic region. The surgeon was therefore able to perform the bypass surgery safely and accurately with CBO monitoring.

In contrast, there were no significant CBO changes during the MCA occlusion in other patients who had chronic cerebral ischemia before surgery. The most likely explanation for this is the presence of extensive cortical anastomotic channels in patients who had chronic cerebral ischemia. The present results are consistent with those obtained by the thermal diffusion method [4]. These observations suggest that temporary occlusion of the cortical branch during STA-MCA anastomosis does not cause acute cerebral ischemia in cases who have chronic cerebral ischemia before surgery. The present monitoring system may therefore be particularly useful in EC-IC bypass for the treatment of complex aneurysms or cranial base tumors [16,20,26].

We observed increases of O_2Hb and $CoSO_2$ associated with a decrease of HHb after declamping of the anastomosed STA in 6 patients. Such CBO changes indicate an increase of CoBF because changes in O_2Hb and $CoSO_2$ correlate positively with changes in CoBF, and HHb changes correlate negatively with CoBF changes (Fig. 2). In contrast, the other 12 patients did not exhibit significant changes in CBO after declamping of the STA. It should be emphasized, however, that an absence of CBO changes does not necessarily mean occlusion of the graft, because postoperative angiography demonstrated patency of the anastomosed STA in the patients. Using NIRS, we have observed that the bypass comes to maintain the CBO gradually within 1 year in many patients [13]. These findings suggest that the bypass did not supply blood flow during surgery but began to maintain the CBO in the ischemic lesion after surgery in these patients.

Interestingly, the $CoSO_2$ before anastomosis was significantly low in the patients who showed CBO changes after declamping of the STA as compared with those who did not (Fig. 6). We found a significant positive correlation between the $CoSO_2$ measured by VLS and the CoBF measured by LDF before anastomosis (Fig. 3A), suggesting that the CoBF might be low in patients with low $CoSO_2$. These findings suggest that the STA may supply more blood flow to the ischemic lesion with a lower perfusion pressure. However, we did not observe significant differences of rCBF in the MCA territory on the lesion side as measured by SPECT before surgery. We have reported that the STA blood flow failed to maintain CBO in 20% of patients with STA-MCA anastomosis [13]. Further studies are needed to clarify the underlying mechanisms of differences in bypass function.

5. Conclusions

The VLS system can monitor dynamic changes in CBO during STA-MCA anastomosis. Temporary occlusion of the MCA (M4 portion) is safe in patients who have chronic cerebral ischemia before surgery, but not in patients who do not. An increase of CoBF induced by STA blood flow was observed more frequently in patients who showed a low $CoSO_2$ before surgery. Finally, it should be emphasized that CBO monitoring by VLS may be useful for evaluating bypass function and facilitates safe and accurate bypass surgery.

Acknowledgments

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Commentary

The temporary occlusion of the recipient cortical artery during STA-MCA anastomosis may cause cerebral infarction in that territory after surgery. In addition to that, an increased perfusion pressure after surgery caused by high-flow bypass can induce hyperperfusion syndrome. The reliable intraoperative detective methods for cerebral infarction and hyperperfusion syndrome have not been developed yet. The authors described that VLS monitoring system was considered useful for evaluating bypass function, which could contribute to a safe and accurate bypass surgery. They investigated the accuracy and reliability of VLS in in vitro and in vivo studies.

As the authors stated in the discussion, there are some limitations. Among them, the most critical is that the system can only measure the CBO of a single small territory in the superficial cortex. It hardly detects the CBO in the subcortex area which the cortical artery supplies. Therefore, even if the VLS does not show any significant changes of CBO during surgery, an infarction may occur in the subcortex area. Moreover, the authors have never applied their method to the patients who needed the EC–proximal MCA bypass. The VLS would not be applicable in such cases because the probe cannot measure the CBO in the wide area supplied by proximal MCA.

The authors showed that the $CoSO_2$ before anastomosis was significantly low in the patients who showed CBO changes after declamping of the STA as compared to those who did not. They speculated that the STA might supply more blood flow to the ischemic lesion with a lower perfusion pressure. To support the speculation, the intraoperative measurement of the blood flow is required.

The VLS monitoring has several limitations that I mentioned above. By further improvement, however, it will be a useful modality to assess bypass function for safe and precise bypass surgery.

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