ORIGINAL

Tissue oxygenation index reflects changes in forearm blood flow after brief ischemia

Hiroyuki Kinoshita[1,2], Takahiko Akahori[1], Emi Nakamura[1], Hazuki Okawa[1], Shinji Kawahito[2], Hiroshi Kitahata[3], and Yoshihiro Fujiwara[1]

[1]*Department of Anesthesiology, Aichi Medical University School of Medicine, 1-1 Yazako Karimata, Nagakute 480-1195, Japan, Departments of Anesthesiology[2] and Dental Anesthesiology[3], Tokushima University Hospital, Tokushima, 3-18-15, Kuramoto, Tokushima 770-8503, Japan*

Abstract : Whether the near-infrared spectroscopy (NIRS) technology correctly detects the changes in oxygenation related to ischemia and reperfusion of organs and tissues other than brain remains unclear. The present study examined how different tissue oxygenation parameters derived from NIRS reflect the changes in the forearm blood flow (FBF) according to the brief ischemia and the subsequent reperfusion, and whether values of these parameters move in parallel with the medial and lateral sides of FBF. Thirteen volunteers underwent the prospective observational study. The tissue oxygenation index (TOI), regional saturation of oxygen (rSO_2), skin tissue oxygenation (StO_2), and FBF values were evaluated in the forearm. Medial rSO_2 values at 1 to 3 minutes after the termination of brief ischemia were higher than lateral rSO_2 and respective TOI values. FBF and StO_2 values quickly increased according to the cessation of brief ischemia, whereas the medial and lateral values did not differ during and after the brief ischemia. TOI and StO_2, but not rSO_2, reflected changes in FBF of both medial and lateral sides simultaneously in response to the reperfusion after brief ischemia. The muscle tissue oxygenation during reperfusion favors the use of TOI and StO_2, but not rSO_2, as the surrogate parameter. J. Med. Invest. 64 : 228-232, August, 2017

Keywords : *Forearm blood flow ; near-infrared spectroscopy ; regional saturation of oxygen ; tissue oxygenation index*

INTRODUCTION

The tissue oxygenation represents the balance between the local oxygen delivery and consumption, which relates to both the organ's metabolic activity and its blood flow (1). Near-infrared radiation is capable of transmitting through the body tissues due to the property which is scarcely absorbed by water and hemoglobin, and the scatter of the radiation is less than that of ultraviolet or visible radiation (2). The analysis of the near-infrared spectrum, i.e. near-infrared spectroscopy (NIRS), therefore, allows clinicians to evaluate the oxygenation in human brain tissues, which have some distance from the scalp (2). Similar to transcranial Doppler sonography or stump pressure measurements, NIRS accurately reflects changes in cerebral blood flow, indicating that the methodology is a clinically meaningful, non-invasive monitoring method in the population, which, is potentially suffered from cerebral ischemia (3). However, whether the NIRS technology can correctly detect the changes in oxygenation related to ischemia and reperfusion of organs and tissues other than brain remains unclear.

The changes in both temperature and blood flow of the surface skin are known to modify the value of cerebral regional saturation of oxygen (rSO2), which is determined by the NIRS employing the Beer-Lambert law (4). On the other hand, the tissue oxygenation index (TOI) defined by the NIRS using the spatially resolved spectroscopy appears more reliable than rSO2 in the evaluation of cerebral oxygenation because the tissue hemoglobin concentration, situation of cutaneous circulation, skull thickness, and the area of the cerebrospinal fluid layer affect rSO2, but not TOI, at least in the brain (5, 6). However, whether the tissue oxygenation parameters derived from different NIRS technologies similarly reflect the changes in forearm blood flow (FBF) caused by the brief ischemia and the subsequent reperfusion remains unknown.

The present study was designed to examine how different tissue oxygenation parameters derived from NIRS (TOI and rSO2), and a white light spectroscopy method (skin tissue oxygenation ; StO_2) reflect the changes in FBF according to the brief ischemia and the subsequent reperfusion, and whether values of these parameters move in parallel with the medial and lateral sides of forearm. Therefore, the results of the current study suggest if TOI and rSO_2 values are available as surrogate parameters when secure recanalization and reperfusion have to be non-invasively monitored in the clinical conditions including those after vascular bypass surgery and the use of the tourniquet in the extremities.

METHODS

After institutional approval from Aichi Medical University School of Medicine (the approved no. 13-134), this study was registered in the UMIN Clinical Trial Registry (UMIN000026435). The informed consent was obtained from healthy enrolled volunteers (n=13, 24-35 years of age). The work described has been carried out under Declaration of Helsinki. Subjects with the history of redness or rash on their forearm were excluded from this study.

Equipment for measurements

NIRO-200NX™ (Hamamatsu Photonics, Hamamatsu, Japan), INVOS 5100C™ (Covidien, Tokyo, Japan), C9183™ (Hamamatsu

Received for publication April 5, 2017 ; accepted May 7, 2017.

Address correspondence and reprint requests to Hiroyuki Kinoshita, M.D., Ph.D. Department of Anesthesiology, Aichi Medical University, School of Medicine, 1-1 Yazako Karimata, Nagakute 480-1195, Japan and Fax : +81-561-63-6621.

Photonics, Hamamatsu, Japan) or MoorFLPI-2™ (Moor Instruments, Axminster, Devon, UK) was employed to determine the continuous TOI (%), rSO_2 (%), StO_2 (%) and FBF (arbitrary perfusion unit) values, respectively. NIRO-200NX™ uses three wavelengths of near-infrared light (735, 810 and 850 nm) and the sensor contains two photodiodes. The monitor adopts the spatially resolved spectroscopy methodology, which combines multidistance measurements of optical attenuation (7, 8). The method makes NIRO-200NX™ possible to calculate TOI as a ratio of oxyhemoglobin to total hemoglobin concentration. INVOS 5100C™ utilizes the Beer-Lambert principle to evaluate differences in absorption of photons returning from deep and superficial tissues using the near infrared light at the wavelength of 730 and 810 nm (4). C9183™ employs a white light-emitting diode as the light source, which has the wavelength of the visible light at 520 to 580 nm, and the monitor can detect the oxygenation only at the 1-2 mm depth from the skin surface [The personal communication with Hamamatsu Photonics, Hamamatsu, Japan]. The laser-speckle imaging monitor MoorFLPI-2™ that is equipped with the class 1 near-infrared laser source with the wavelength of 758 nm is capable of evaluating the tissue blood flow at a distance of 30 cm above the skin surface, and the monitor expresses tissue blood flow as the relative value (9). The blood flow imager uses the laser speckle contrast technique to deliver real-time, high-resolution blood flow images (9).

Protocol of Measurements

The primary outcome to measure in the current study was to evaluate whether values of parameters including TOI and rSO_2 similar to changes in the FBF according to the brief ischemia and the subsequent reperfusion move in parallel with the medial and lateral sides of the forearm. The measurement areas (25 mm^2) were at 3 cm distal from an elbow joint, and both 2 cm lateral at brachioradialis muscle above the radial artery and 2 cm medial at flexor carpi radialis muscle above the ulnar artery from the midline of the ventral forearm. Our preliminary study verified that the changes of FBF obtained by the MoorFLPI-2™ were same between these 2 areas (n = 3). The measurement area in the use of NIRO-200NX™ and INVOS 5100C™ was set in the center between the photodetection and irradiation probes and these probes always lined parallel to avoid the photodetection interference by each irradiation probe.

On the day of measurements, volunteers were allowed to take clear fluids without caffeine freely until one hour before the measurements. Brief ischemia was achieved using a blood pressure cuff applied to the examined upper arm at 180 mmHg. Continuous measurements of medial (or lateral) TOI in combination with lateral (or medial) rSO2 were performed at the same time (Trial 1, n = 13) from the immediately before brief ischemia to 10 minutes after the release of a blood pressure cuff. Thirty minutes after the trial 1, the medial and lateral sides exchanged, and the continuous measurements were repeated (Trial 2, n = 13). During the measurements, noninvasive blood pressure in the upper limb, which was the other side of the tested arm at a 2.5-minute interval and continuous heart rate by the electrocardiogram in addition to pulse oximetry was monitored. Computer-generated random numbers were used for the randomization in the order of measurements. Measurements of StO_2 (n = 13) and FBF (n = 13) in the medial and lateral sides using two sensors were subsequently and simultaneously performed with a 30-minute interval.

Statistics

The data were expressed as mean ± SD. The power calculation was done using Sample Power 3.0™ (IBM Japan Inc., Tokyo, Japan). In the current study, a sample size of 13 gave 81% power to the detected rSO_2 change of 11% at a significance level of 0.05 (SD = 9.7). Statistical analysis using PASW Statistics 18™ (IBM Japan Inc., Tokyo, Japan) was performed by the repeated-measures analysis of variance followed by Scheffe's test. Differences were considered to be statistically significant when P is < 0.05.

RESULTS

Medial rSO_2 values at 1 to 3 minutes after the termination of brief ischemia were higher than lateral rSO_2 and respective TOI values (Figure 1). StO_2 and FBF values quickly decreased or increased according to brief ischemia and the termination, whereas the values did not differ between medial and lateral sides at any measurement period (Figures 2 and 3). TOI, rSO_2, StO_2 and FBF values demonstrated restoration at 10 minutes to the levels at the commencement of measurements according to reperfusion of the forearm (Figures 1, 2 and 3).

Mean blood pressure and heart rate did not change in response to brief ischemia and the termination in both the trials 1 and 2 and the values were within the normal range (Figure 4). No volunteer claimed health problems including redness or rash on the forearm related to this study.

DISCUSSION

Medial rSO_2 values at the initial phase of the forearm reperfusion were higher than lateral rSO_2, and respective TOI values whereas FBF values did not differ between the both medial and lateral sides during the measurements. These results suggest that the medial rSO2 values are modified by the forearm reperfusion after brief ischemia. The changes in skin oxygenation related to hyperthermia as well as vasoconstriction alter the value of cerebral rSO_2 from the Beer-Lambert NIRS, but not TOI evaluated by the spatially resolved methodology (4-6). However, the different skin perfusion in the medial and lateral sides of the forearm does not appear the cause of the NIRS value modification because StO_2 values between the both sides did not differ throughout the measurements. Previous studies proved that TOI is more reliable than rSO_2 measured by the Beer-Lambert Principle in cerebral NIRS parameters since the tissue hemoglobin concentration, skull thickness, and the area of the cerebrospinal fluid layer do not affect TOI (5, 6). The current results probably add an answer to the question why an oxygenation monitor, which is adopted the spatially resolved methodology, has long been used to determine the human skeletal muscle oxygenation in the physiological studies (10). However, the reason for the difference between TOI and rSO_2 in the current study remains unclear as the algorism of the NIRS technology employed in INVOS 5100C™ has not been opened to the public.

Some surrogate parameters should be essential to evaluate FBF when secure recanalization and reperfusion have to be non-invasively monitored in the clinical conditions including those after vascular bypass surgery and the use of the tourniquet in the extremities. Also, the noninvasive NIRS monitoring of skeletal muscle oxygenation is increasingly critical as a surrogate parameter to determine the cardiovascular and respiratory conditions of patients in the clinical practice, including the estimation of heart failure, the performance of ventilation, and successful remote preconditioning (11-13). Therefore, whether the NIRS monitor employs the Beer-Lambert or spatially resolved methodology is probably a significant determinant that one can achieve the accurate non-invasive evaluation of FBF using the technology. However, further studies are required to determine whether such a difference is clinically meaningful.

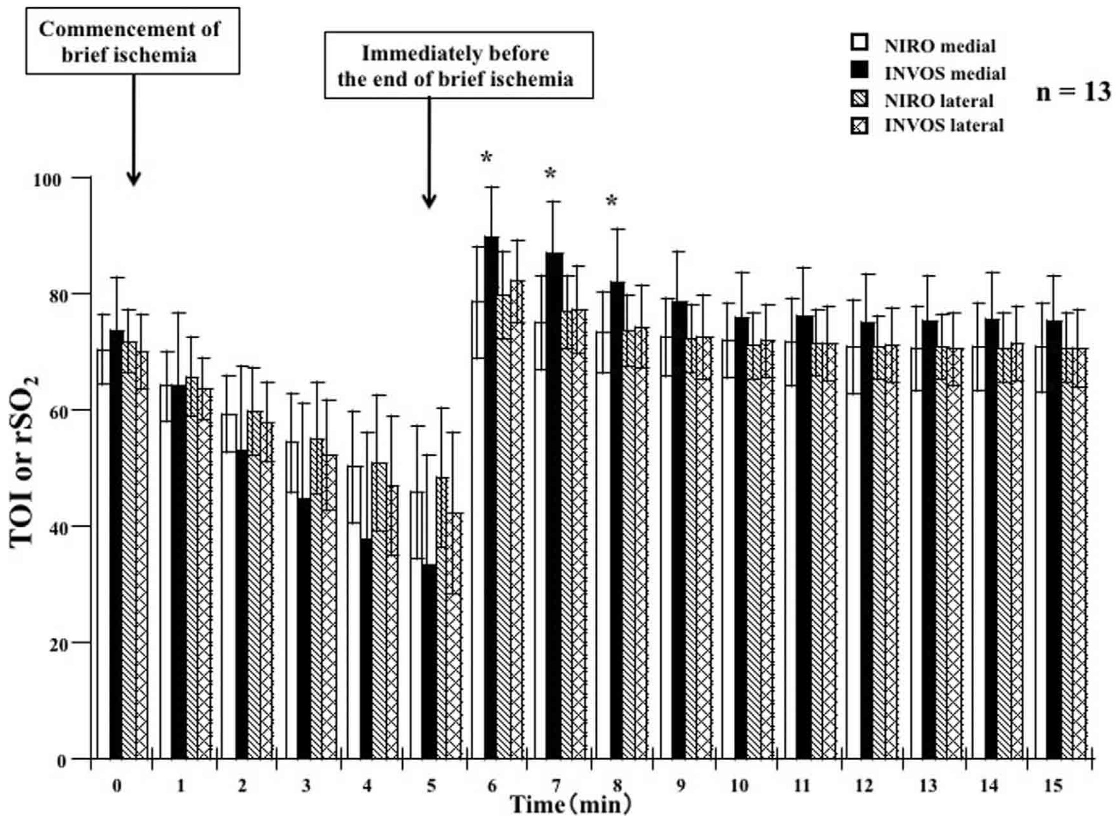

Figure 1 Changes in medial and lateral TOI (%) as well as rSO_2 (%) values in the trials 1 and 2 (n = 13 each) from the before brief ischemia to 10 minutes after the reperfusion. * : $P < 0.05$ vs. lateral rSO_2 and respective TOI values.

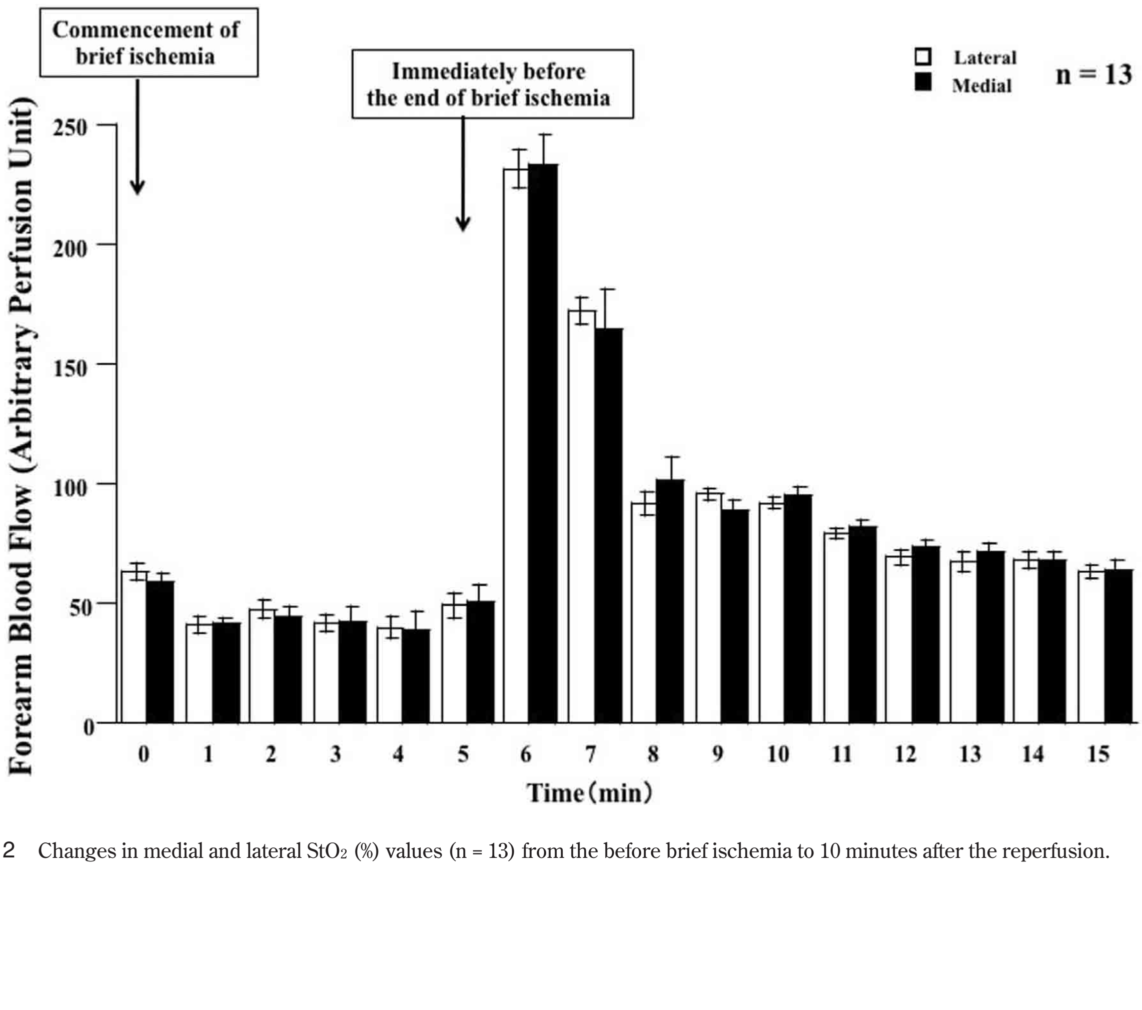

Figure 2 Changes in medial and lateral StO_2 (%) values (n = 13) from the before brief ischemia to 10 minutes after the reperfusion.

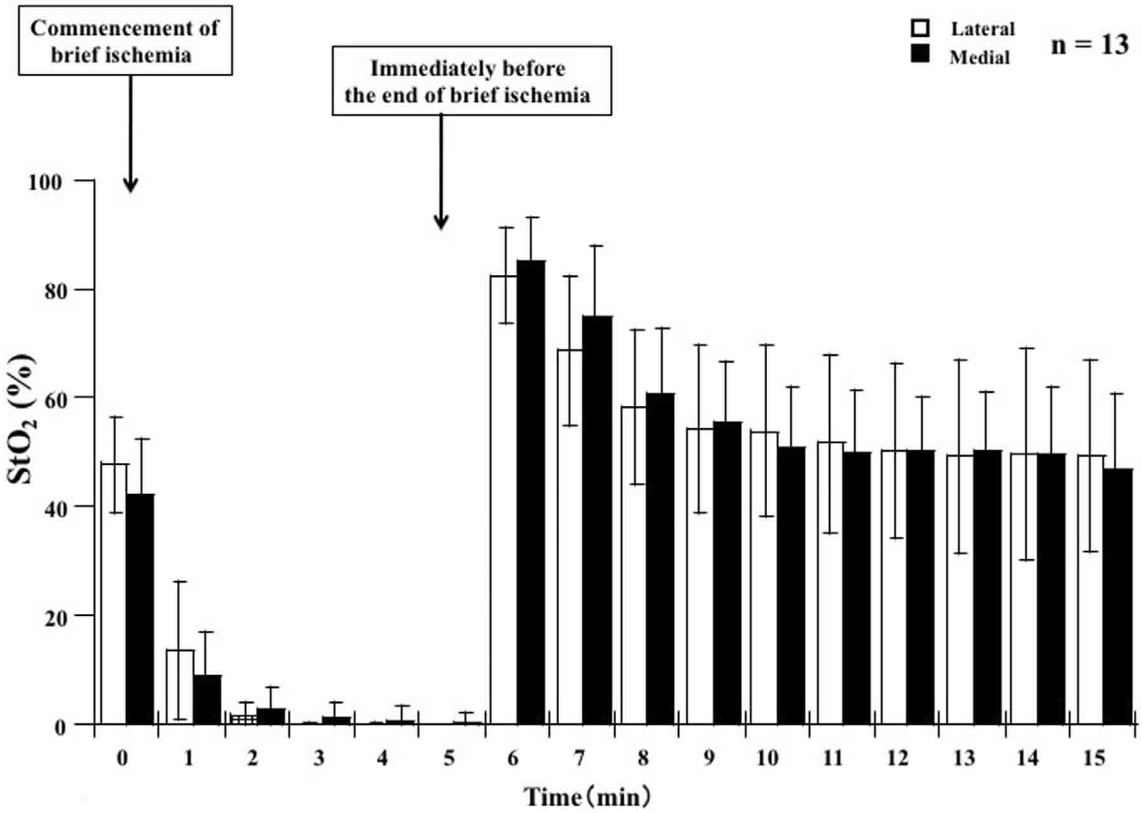

Figure 3 Changes in medial and lateral FBF (Arbitrary Perfusion Unit) values (n = 13) from the before brief ischemia to 10 minutes after the reperfusion.

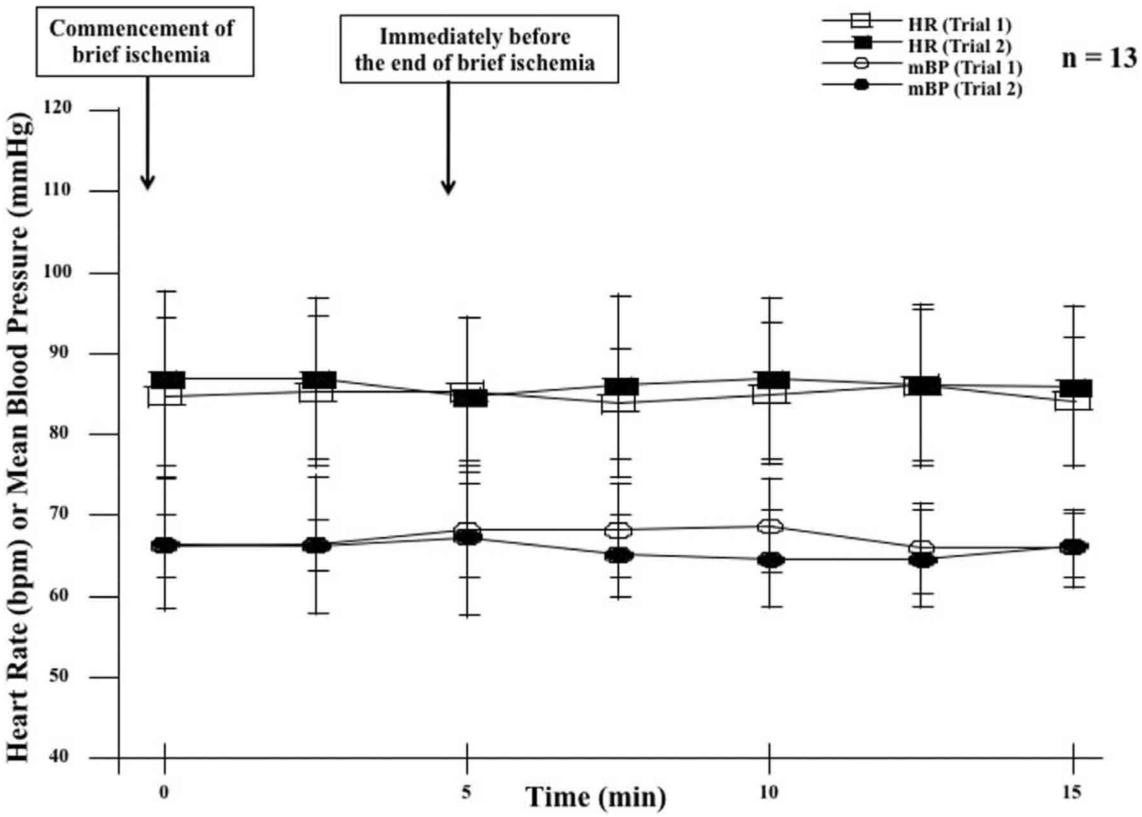

Figure 4 Levels of mean blood pressure (left) and heart rate (right) during the study including the trials of 1 and 2 (n = 13).

CONCLUSIONS

In healthy volunteers, TOI and StO_2, but not rSO_2, reflected changes in FBF of both medial and lateral sides simultaneously in response to the reperfusion after brief ischemia. These results indicate that the muscle tissue oxygenation during reperfusion favors the use of TOI and StO_2, but not rSO_2 and that the NIRS monitor using the spatially resolved methodology have to be selected when physicians need to evaluate FBF non-invasively in the clinical conditions.

CONFLICT OF INTEREST

The authors have no conflict of interest.

ACKNOWLEDGEMENTS

This work was presented in part at the annual meeting of the International Anesthesia Research Society, Honolulu, HI, USA, March 21-24, 2015, and that of the American Society of Anesthesiologists, San Diego, CA, USA, October 24-28, 2015. The authors thank Hamamatsu Photonics (Hamamatsu, Japan) for the kind support offering the use of C9183™ to us.

STATEMENTS OF FUNDING

This work was supported by departmental sources.

REFERENCES

1. De Santis V, Singer M : Tissue oxygen tension monitoring of organ perfusion : rationale, methodologies, and literature review. Br J Anaesth 115 : 357-65, 2015
2. Sakudo A : Near-infrared spectroscopy for medical applications : Current status and future perspectives. Clin Chim Acta 455 : 181-8, 2016
3. Moritz S, Kasprzak P, Arlt M, Taeger K, Metz C. Accuracy of cerebral monitoring in detecting cerebral ischemia during carotid endarterectomy : A comparison of transcranial Doppler sonography, near-infrared spectroscopy, stump pressure, and somatosensory evoked potentials. Anesthesiology 107 : 563-9, 2007
4. Sørensen H, Secher NH, Siebenmann C, Nielsen HB, Kohl-Bareis M, Lundby C, Rasmussen P. Cutaneous vasoconstriction affects near-infrared spectroscopy determined cerebral oxygen saturation during administration of norepinephrine. Anesthesiology 117 : 263-70, 2012
5. Yoshitani K, Kawaguchi M, Miura N, Yoshitani K, Kawaguchi M, Miura N. Effects of hemoglobin concentration, skull thickness, and the area of the cerebrospinal fluid layer on near-infrared spectroscopy measurements. Anesthesiology 106 : 458-62, 2007
6. Messere A, Roatta S : Influence of cutaneous and muscular circulation on spatially resolved versus standard Beer-Lambert near-infrared spectroscopy. Physiol Rep 1 : e00179 (doi : 10.1002/phy2.179), 2013
7. Quaresima V, Sacco S, Totaro R, Ferrari M. Noninvasive measurement of cerebral hemoglobin saturation using two near infrared spectroscopy approaches. J Biomed Opt 5 : 201-5, 2000
8. Tange K, Kinoshita H, Minonishi T, Hatakeyama N, Matsuda N, Yamazaki M, Hatano Y. Cerebral oxygenation in the beach chair position before and during general anesthesia. Minerva Anestesiol 76 : 485-9, 2010
9. Klijn E, Hulscher HC, Balvers RK, Holland WP, Bakker J, Vincent AJ, Dirven CM, Ince C. Laser speckle imaging identification of increases in cortical microcirculatory blood flow induced by motor activity during awake craniotomy. J Neurosurg 118 : 280-6, 2013
10. Hampson NB, Piantadosi CA : Near infrared monitoring of human skeletal muscle oxygenation during forearm ischemia. J Appl Physiol 64 : 2449-57, 1998
11. Wilson JR, Mancini DM, McCully K, Ferraro N, Lanoce V, Chance B. Noninvasive detection of skeletal muscle underperfusion with near-infrared spectroscopy in patients with heart failure. Circulation 80 : 1668-74, 1989
12. Poriazi M, Kontogiorgi M, Angelopoulos E, Vasileiadis I, Tripodaki ES, Nanou V, Fassoulaki A, Nanas S, Routsi C. Changes in thenar muscle tissue oxygen saturation assessed by near-infrared spectroscopy during weaning from mechanical ventilation. Minerva Anestesiol 80 : 666-75, 2014
13. Cunniffe B, Sharma V, Cardinale M, Yellon D. Characterization of muscle oxygenation response to vascular occlusion : Implications for remote ischaemic preconditioning and physical performance. Clin Physiol Funct Imaging (doi : 10.1111/cpf.12353), 2016 (in press)