Spatial Mapping of Blood Flow and Oxygen Consumption in the Human Calf Muscle Using Near-Infrared Spectroscopy

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ABSTRACT

We have designed a new optical probe to perform spatially resolved measurements of blood flow and oxygen consumption over an area of about 4×4 cm^2 of the lateral gastrocnemius muscle (calf muscle) of human subjects. The blood flow and the oxygen consumption were measured non-invasively with frequency-domain, near-infrared spectroscopy from the maximum rate of increase of the oxy- and deoxy-hemoglobin concentrations in the muscle during venous occlusion. In a preliminary test on one subject, involving measurements at rest and after exercise, we have found that the spatial variability of the measured blood flow and oxygen consumption is significantly greater than the variability of repeated measurements at a given tissue location. We have also observed a strong spatial dependence of the exercise-induced increase in blood flow and oxygen consumption.

Keywords: Skeletal muscle, blood flow, oxygen consumption, hemoglobin concentration, frequency-domain spectroscopy, near-infrared.

1. INTRODUCTION

Near-infrared spectroscopy is a non-invasive technique that is highly sensitive to the hemoglobin concentration and oxygen saturation in tissues. For this reason, it has the potential of measuring the local blood flow and oxygen consumption in tissues, provided that one induces an appropriate perturbation to the tissue hemodynamics. For example, a suitable perturbation is a blood-flow-dependent increase in the hemoglobin concentration in the tissue induced by either venous occlusion[1-4] or by a tilt-table approach.[5] An alternative perturbation for blood flow measurements is a change in the arterial oxy-hemoglobin concentration caused by a change in the fraction of inspired oxygen.[6]

In this work, we have exploited the fact that near-infrared spectroscopy is sensitive to a tissue volume in the order of a few cubic centimeters. As a result, near-infrared spectroscopy measures local values of blood flow and oxygen consumption, as opposed to the blood flow over the whole limb measured by plethysmography, or the systemic oxygen consumption measured by respiratory gas analysis. Therefore, near-infrared spectroscopy lends itself to spatially-resolved measurements in tissues. We report our results of spatially resolved measurements of blood flow and oxygen consumption in the human gastrocnemius muscle.

2. METHODS

We used two synchronized frequency-domain tissue spectrometers (ISS, Inc., Champaign, IL Model No. 96208) operating at a modulation frequency of 110 MHz, and at two near-infrared wavelengths of 690 and 830 nm. These instruments have a total of thirty-two light sources (sixteen for each wavelength) that are multiplexed at a rate of 50 Hz (20 ms on-time per light source), and four parallel acquisition channels. The light sources (laser diodes) and the optical detectors (photomultiplier tubes) are all coupled to fiber optics for guiding light to and from the tissue. The illuminating and

the collecting optical fibers were arranged according to the scheme of Fig. 1, which was specifically designed to perform spatially resolved measurements of blood flow and oxygen consumption in skeletal muscle. For each detector location (labeled A-D in Fig. 1), there are two pairs of sources above it, and two pairs below it, which are aligned with the detector and separated by 2.5 cm and 4.0 cm, respectively. Each source pair is made of one fiber emitting at 690 nm, and one fiber emitting at 830 nm. The two pairs of sources above (below) detector A are indicated with the symbol $A^{\uparrow}$ ($A^{\downarrow}$). A similar notation is used for the source pairs above and below detectors B-D. The two source-detector distances (2.5 and 4.0 cm) are used to implement the multi-distance scheme for quantitative measurements of hemoglobin concentration in tissues.[7] As a result, one obtains measurements of hemoglobin concentration at eight locations over a tissue area of about 4×4 cm^2. The acquisition time for the eight-pixel map of hemoglobin concentration is 20 ms/diode × 4 diodes/pixel × 8 pixels × 2 integration cycles = 1.28 s.

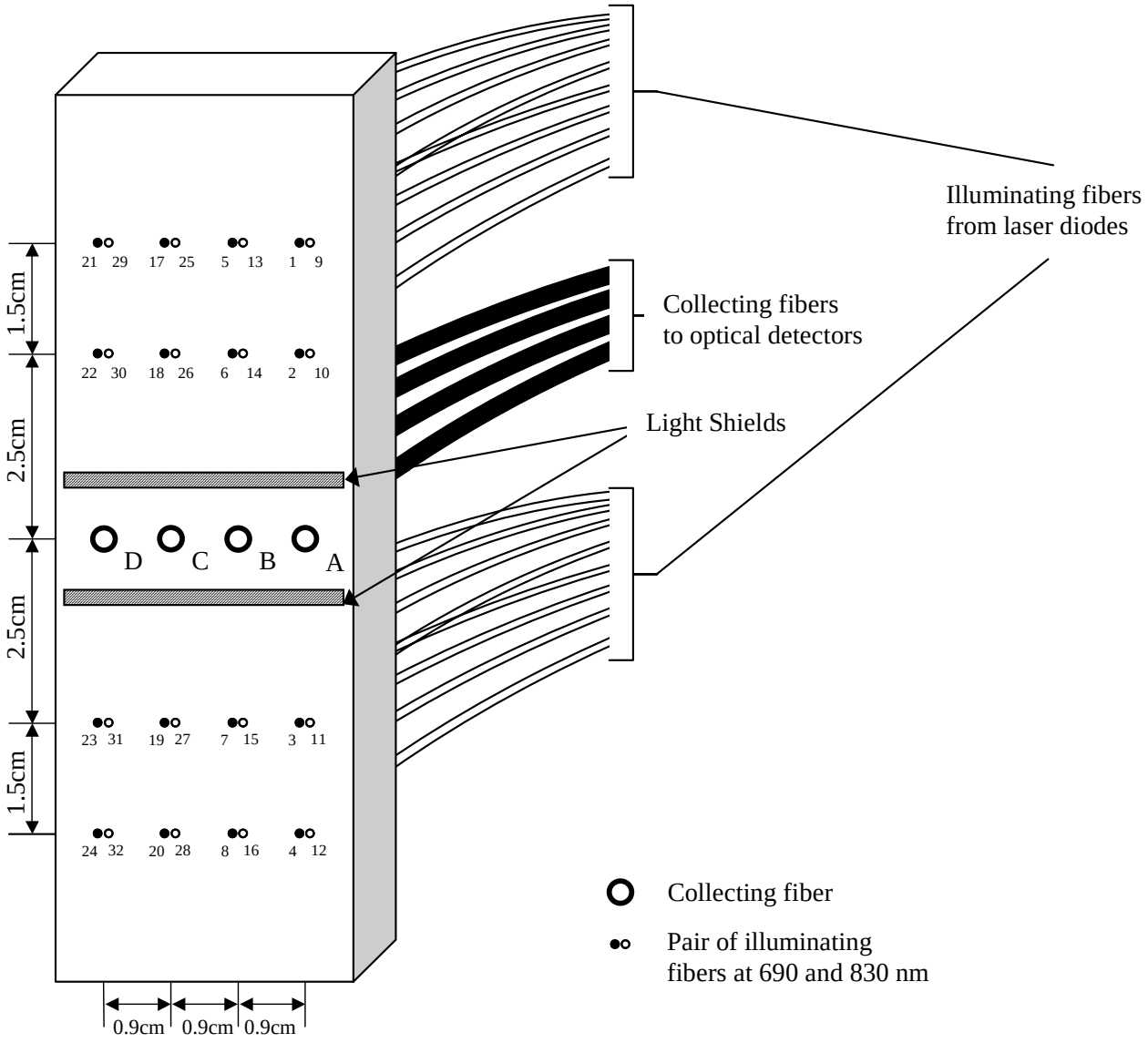

Fig. 1. Optical probe used for the spatial mapping of the blood flow and the oxygen consumption in skeletal muscle. This figure shows the geometrical arrangement of the tips of the illuminating optical fibers (numbered from 1 to 32) and the collecting fibers (labeled A-D) on the side of the optical probe to be placed on the tissue. The sequence of illumination of the

source fibers follows the numbering order 1-32. The four detectors operate in parallel. The light blocks prevent light that has not traveled through the tissue from reaching the collecting fibers.

The maximum rates of increase of the oxy- and deoxy-hemoglobin concentrations (measured as the slope of a linear fit over 12.8 s) during the first 25.6 s of venous occlusion are converted into blood flow (BF) and oxygen consumption ($\dot{V}O_2$) by the following equations:

$$BF = \frac{1}{C}\frac{d}{dt}\left([Hb]+[HbO_2]\right)\Big|_{max}, \quad (1)$$

$$\dot{V}O_2 = 4\frac{d}{dt}\left\{SaO_2[Hb]-(1-SaO_2)[HbO_2]\right\}\Big|_{max}, \quad (2)$$

where [Hb] and [HbO_2] indicate the concentrations of deoxy-hemoglobin and oxy-hemoglobin, respectively, in the tissue, C is the hemoglobin concentration in the blood, and SaO_2 is the arterial saturation. The factor 4 in Eq. (2) accounts for the fact that each molecule of hemoglobin has four binding sites for O_2. Ideally, C and SaO_2 should be measured independently for each subject. In this work, we have assumed values of C = 2.3 mM (or 14.7 g/dL) and SaO_2 = 0.98. We observe that Eqs. (1) and (2) use the maximum time derivatives (during the first 25.6 s of venous occlusion) associated with [Hb] and [HbO_2] (as in Ref. 2) rather than the initial time derivatives following the onset of venous occlusion (used in Refs. 1, 3, 4). We found the approach based on the maximum rate of increase of hemoglobin concentration to be more robust than the one based on the initial rate of increase, because of the significant time lag sometimes observed between the onset of venous occlusion and the hemoglobin concentration response.[4] The approach to spatial mapping of the blood flow and oxygen consumption in tissue based on the probe of Fig. 1 differs from the method previously reported in Ref. 4 in that it affords simultaneous, rather than sequential, measurements at all pixels.

The optical probe illustrated in Fig. 1 was positioned on the right lateral gastrocnemius muscle of a healthy 24 year-old female subjects. The probe was secured by wide elastic bands wrapped around the calf of the subject (not too tight to avoid blockage of blood flow). Venous occlusion was performed on the thigh by inflating a pneumatic cuff to a pressure of 60 mmHg. We first measured the blood flow and oxygen consumption maps at rest while the subject was comfortably lying on a bed. To study the reproducibility of the measurement, we performed five one-minute venous occlusions separated by one-minute intervals. Following the measurement at rest, the subject exercised on a stationary bicycle until exhaustion. Then the subject lay down on the bed again, and ten more one-minute venous occlusions (separated by one-minute intervals) were performed.

3. RESULTS

Figures 2(a) and 2(b) show the temporal traces of oxy-hemoglobin concentration and deoxy-hemoglobin concentration, respectively, measured at the eight locations of the lateral gastrocnemius muscle. Arbitrary offsets (indicated in Figs. 2(a) and 2(b)) are added to individual traces for clarity. The maximum rates of increase in the oxy- and deoxy-hemoglobin concentrations during venous occlusion are used to quantify the local blood flow and oxygen consumption according to Eqs. (1) and (2). Figures 3(a) and 3(b) report the values of the blood flow calculated from the traces of Fig. 2. As expected, the exercise causes an increase in the measured blood flow and oxygen consumption at each location. During the measured 23 min after exercise, we have not observed a significant recovery of the blood flow and oxygen consumption values toward the baseline readings. By averaging the five blood flow (oxygen consumption) values measured at rest, and the ten blood flow (oxygen consumption) values measured after exercise, respectively, we have obtained the eight-pixel blood flow (oxygen consumption) maps shown in Figs. 4 and 5. These maps quantify the spatial variability of the blood flow and oxygen consumption, as well as the increased blood flow and oxygen consumption induced by exercise at each pixel.

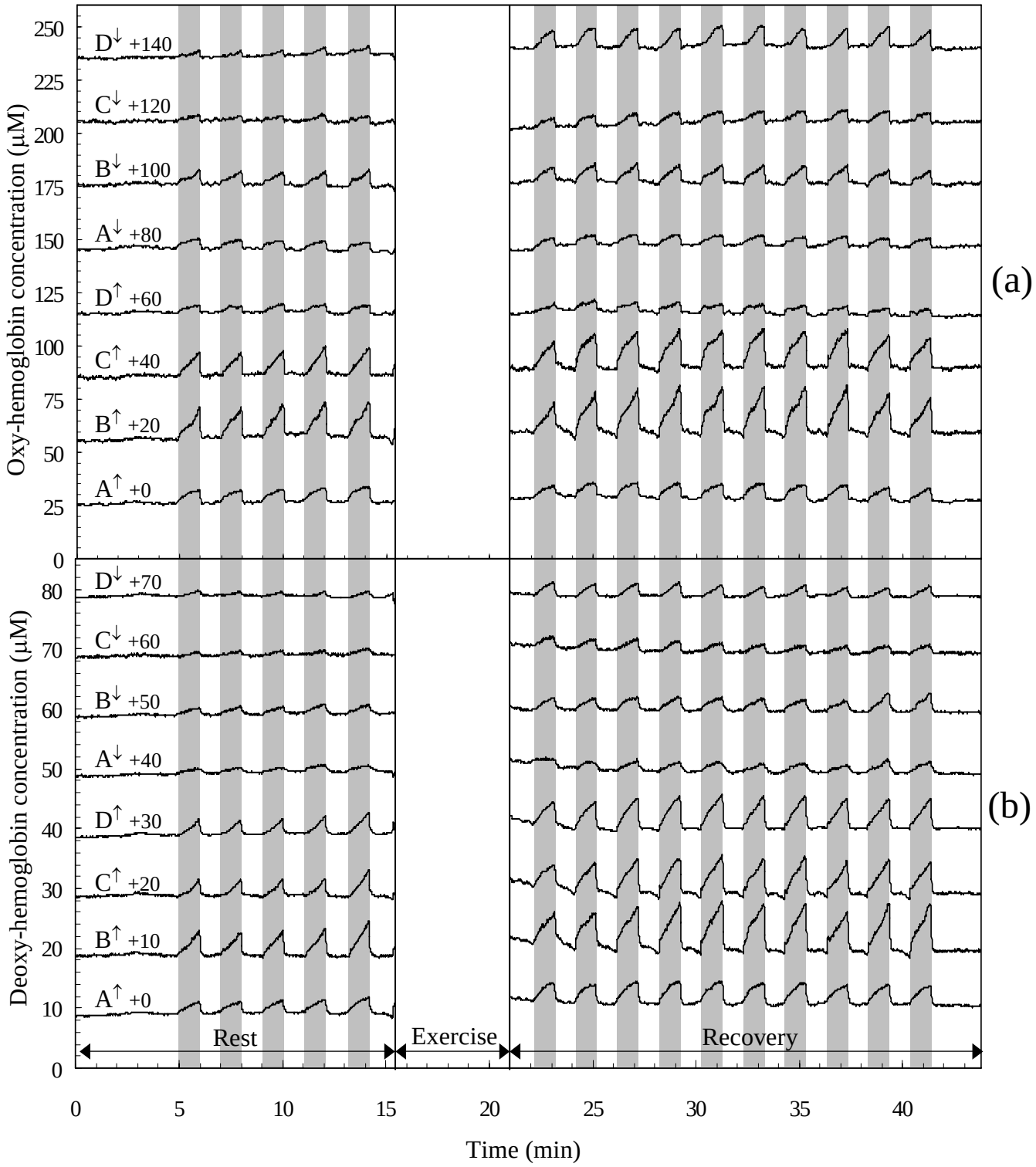

Fig. 2. Temporal traces of (a) oxy-hemoglobin concentration and (b) deoxy-hemoglobin concentration measured at eight locations in the lateral gastrocnemius muscle during the experimental protocol. The eight locations are represented by the detector letter (A, B, C, or D; see Fig. 1) and an arrow indicating the region above (↑) or below (↓) the detector location. Individual offsets (indicated next to each trace) are added for clarity. The temporary increases in oxy- and deoxy-hemoglobin concentration are caused by venous occlusions (five at rest, and ten after exercise), which are indicated by the shaded bars.

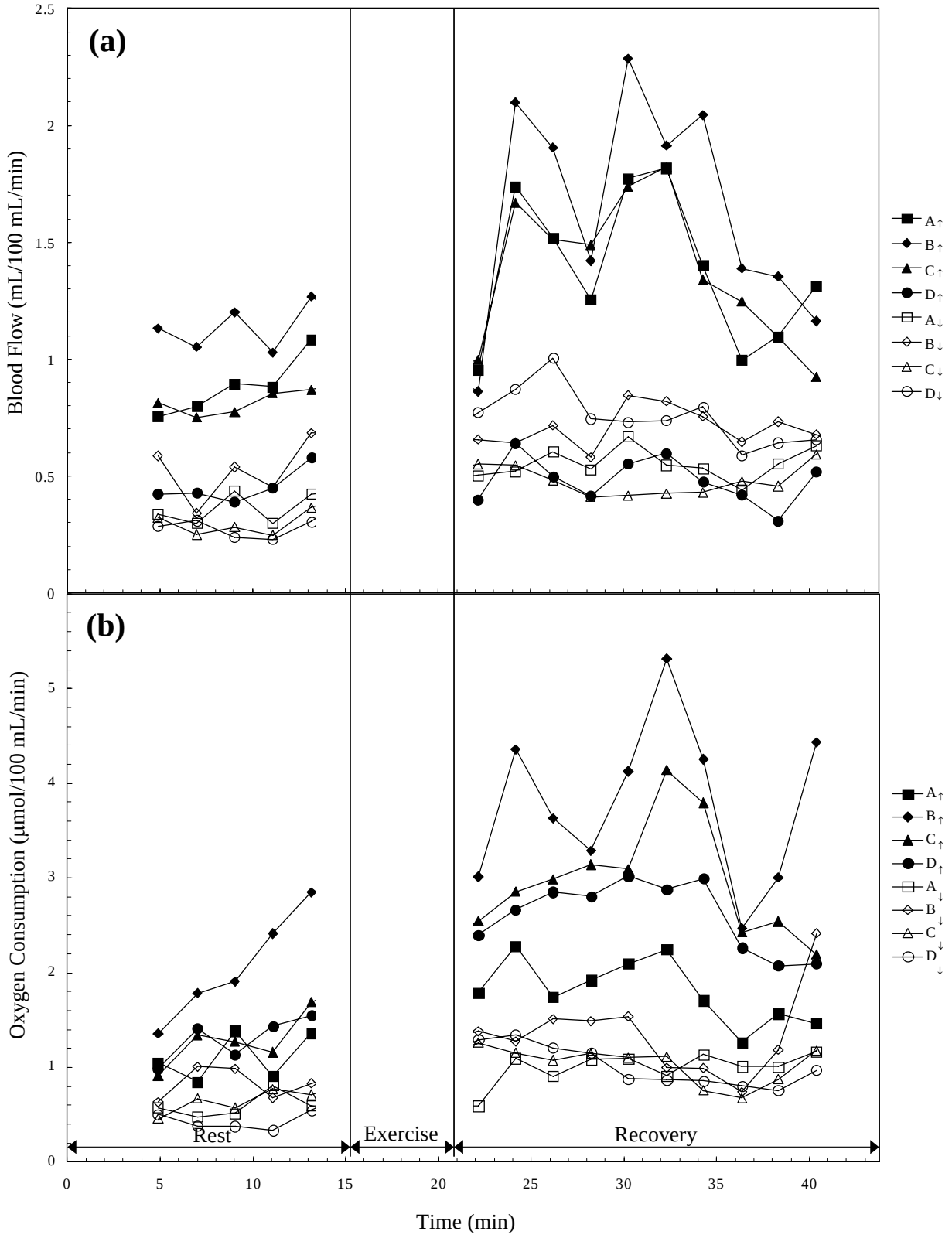

Fig. 3. Values of (a) blood flow and (b) oxygen consumption calculated from the traces in Fig. 2 for the eight measured locations of the lateral gastrocnemius muscle. The bicycle exercise induces an increase in the blood flow and in the oxygen consumption at all locations.

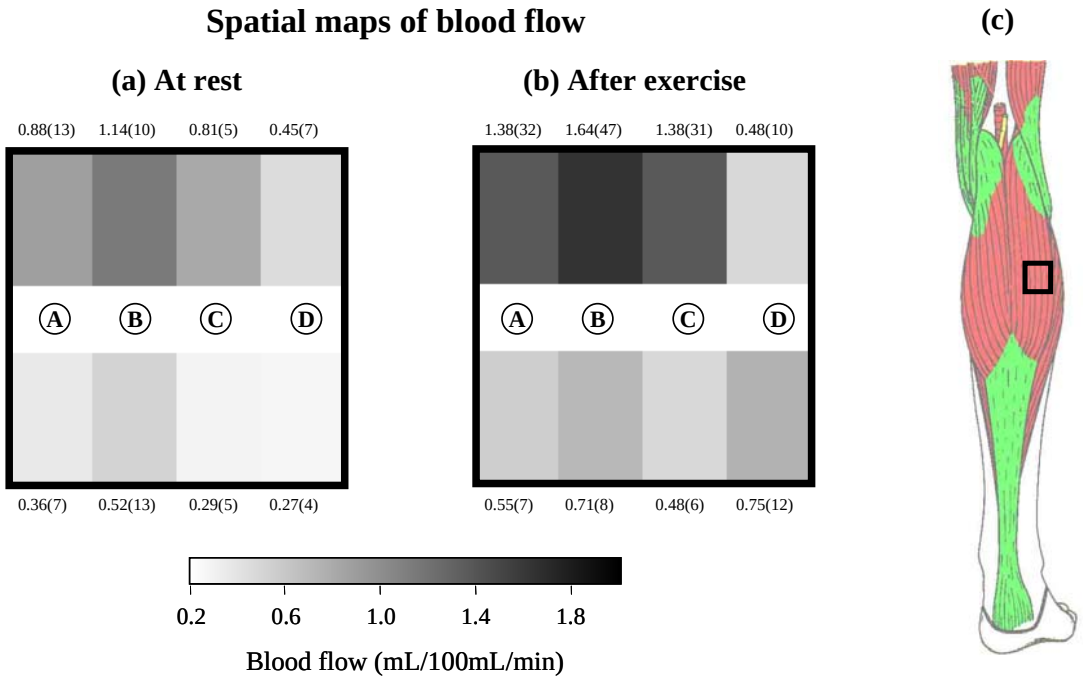

Fig. 4. Spatial maps of blood flow (a) at rest, and (b) after exercise of the area of the lateral gastrocnemius muscle indicated in panel (c). The gray scale is the same for panels (a) and (b). The measured values of blood flow are indicated next to each pixel, together with the corresponding standard deviation (in parentheses, referring to the last one or two digits of the measured values). By comparison, the standard deviations of the eight pixel values are 0.32 mL/100mL/min (at rest), and 0.47 mL/100mL/min (after exercise).

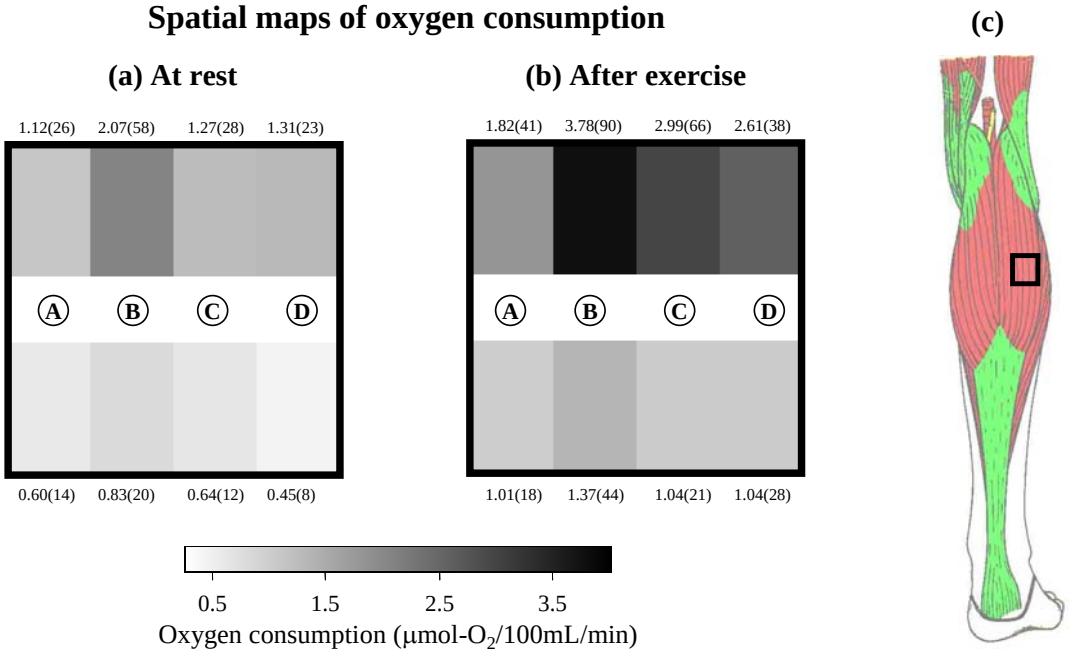

Fig. 5. Spatial maps of oxygen consumption (a) at rest, and (b) after exercise of the area of the lateral gastrocnemius muscle indicated in panel (c). The gray scale is the same for panels (a) and (b). The measured values of oxygen consumption are indicated next to each pixel, together with the corresponding standard deviation (in parentheses, referring to the last one or two digits of the measured values). By comparison, the standard deviations of the eight pixel values are 0.53 μmol-O_2/100mL/min (at rest), and 1.0 μmol-O_2/100mL/min (after exercise).

4. DISCUSSION

Figure 3 shows that the spatial variability of the blood flow and oxygen consumption is greater than the variability observed in repeated measurements at the same location. In fact, the average relative standard deviation of the blood flow measurements (standard deviation divided by the average value) describing the spatial variability at rest (for the same venous occlusion) is 54%, while the one describing the reproducibility (at a fixed location) is 15%. After exercise, these two values are 51% and 18%, respectively. For the oxygen consumption measurements at rest, the average relative standard deviation of the measurements over the eight locations is 52%, while the one for the repeated measurements at the same location is 22%. After exercise, these values become 55% and 23%, respectively. These results are summarized in Table I. This finding indicates the potential importance of spatially resolved, as opposed to single-point, optical measurements of blood flow and oxygen consumption. On one hand, the spatial distribution of blood flow and oxygen consumption may be physiologically and diagnostically relevant *per se* for its capability of detecting under-perfused or non-viable tissue areas. On the other hand, the relatively large spatial variability of the optical measurement of the blood flow and oxygen consumption suggests that the probe location is critical. Consequently, an average reading over multiple locations may yield more meaningful measurements of muscle blood flow and oxygen consumption with respect to a single-point measurement.

Table I. Relative standard deviations of the measurements of blood flow and oxygen consumption at different locations (for the same venous occlusion), and at the same location (for different venous occlusions) under rest and post-exercise conditions.

		Relative standard deviation (std/avg)	
Condition of subject	Tested parameter	Blood flow (BF)	Oxygen consumption ($\dot{V}O_2$)
At rest	Spatial variability	54%	52%
	Reproducibility at one location	15%	22%
After Exercise	Spatial variability	51%	55%
	Reproducibility at one location	18%	23%

The measurement of the blood flow is based on the rate of increase of the total (oxy- plus deoxy-) hemoglobin concentration during venous occlusion. The fact that there is no need to separately determine the oxy- and deoxy-hemoglobin concentrations renders the measurements at two wavelengths redundant. In fact, a single wavelength measurement at the isosbestic point for hemoglobin (~800 nm) is sufficient to determine the blood flow. However, the additional measurement of deoxy-hemoglobin concentration is necessary to quantify the local oxygen consumption in tissue.

5. CONCLUSIONS

We have reported a non-invasive optical approach for the spatial mapping of the skeletal muscle blood flow and oxygen consumption. We have found that the spatial variability in the measurements of blood flow and oxygen consumption is significantly greater than the variability of repeated measurements at a given location. This result, which awaits validation on a statistically significant number of subjects, indicates that spatially resolved optical measurements of blood flow and oxygen consumption may be more meaningful than a single-point measurement.

6. ACKNOWLEDGMENTS

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7. REFERENCES

1. R. A. de Blasi, M. Ferrari, A. Natali, G. Conti, A. Mega, and A. Gasparetto, "NonInvasive Measurement of Forearm Blood Flow and Oxygen Consumption by Near-Infrared Spectroscopy," J. Appl. Physiol. **76**, 1388-1393 (1994).

2. S. Homma, H. Eda, S. Ogasawara, and A. Kagaya, "Near-Infrared Estimation of O_2 Supply and Consumption in Forearm Muscles Working at Varying Intensity," J. Appl. Physiol. **80**, 1279-1284 (1996).

3. M. C. P. van Beekvelt, W. N. J. M. Colier, B. G. M. van Engelen, M. T. E. Hopman, R. A. Wevers, and B. Oeseburg, "Validation of Measurement Protocols to Assess Oxygen Consumption and Blood Flow in the Human Forearm by Near-Infrared Spectroscopy," Proc. SPIE **3194**, 133-144 (1998).

4. C. Casavola, L. A. Paunescu, S. Fantini, and E. Gratton, "Blood Flow and Oxygen Consumption with Near-Infrared Spectroscopy and Venous Occlusion: Spatial Maps and the Effect of Time and Pressure of Inflation," J. Biomed. Opt. **5**, 269-276 (2000).

5. C. Casavola, L. A. Paunescu, M. A. Franceschini, S. Fantini, L. Winter, J. Kim, D. Wood, and E. Gratton, "Near-infrared spectroscopy and tilting table protocol: a novel method to study the blood flow and the oxygen consumption in tissue," Proc. SPIE **3597**, 685-692 (1999).

6. A. D. Edwards, C. Richardson, P. Van der Zee, C. Elwell, J. S. Wyatt, M. Cope, D. T. Delpy, and E. O. R. Reynolds, "Measurement of Hemoglobin Flow and Blood Flow by Near-Infrared Spectroscopy," J. Appl. Physiol. **75**, 1884-1889 (1993).

7. S. Fantini, M. A. Franceschini, J. S. Maier, S. A. Walker, B. Barbieri, and E. Gratton, "Frequency-Domain Multichannel Optical Detector for non-Invasive Tissue Spectroscopy and Oximetry," Opt. Eng. **34**, 32-42 (1995).