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Application of multiple NIRS imaging device to the exercising muscle metabolism

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Abstract. Near infrared spectroscopy (NIRS) is a developing technique that measures the balance between muscle oxygen consumption and oxygen supply that is noninvasive and potentially portable. Differential absorption of light in the 600–900 nm region detects the changes in small vessel hemoglobin oxygen saturation and blood volume. Recent developments include the combining of multiple light sources and photodetectors to provide "images" of oxygen saturation and blood volume of wide regions of muscle. Using multiple NIRS imaging device, we monitored localized muscle metabolism during various exercises in the field as well as in the laboratory. In healthy subjects, the regional differences in oxygen saturation and blood volume were detected in the medial head of the gastrocnemius muscle during a standing plantar flexion exercise, consistent with differences in intramuscular pressure. Patients with peripheral arterial disease (PAD) showed slower recovery for both oxygenation and blood volume after exercise. Treatment for PAD resulted in improvements in NIRS-measured recovery times. In summary, NIRS devices have the ability to detect and monitor impaired muscle circulation. In addition, NIRS devices with multiple channels have the potential to evaluate the regional differences in oxygen status. Multiple NIRS imaging devices have the potential to play an important role in monitoring exercise prescription and clinical uses.

1. Introduction

Pulmonary ventilation supplies the alveoli with fresh air, which contains a high concentration of oxygen. The oxygen, which is combined with hemoglobin (Hb), is transported to the tissues via circulation, and then, it is consumed within the tissues (e.g., muscle). In order to evaluate this process in humans, the noninvasive evaluation of oxidative metabolism is required. Currently, the most powerful noninvasive method for monitoring oxidative metabolism is nuclear magnetic resonance spectroscopy (NMRS). This method measures the concentrations of phosphorus atoms to monitor phosphocreatine, phosphate, ATP, and hydrogen ion concentrations [1,2]. In addition it uses proton concentration to monitor myoglobin oxygen saturation [3]. The disadvantage of the NMRS method is that it is very expensive and very difficult to perform, and is limited to a few locations around the world.

Near infrared spectroscopy (NIRS) appears to be emerging as the preferred technique for measuring muscle metabolism [1,2]. NIRS monitors the tissue oxygen level by measuring optical absorption changes in oxygenated and deoxygenated hemoglobin and it allows the noninvasive measurement of the balance between oxygen consumption and oxygen supply. The key advantages of NIRS are that it is relatively inexpensive and easy to use. In addition, current devices can be small and portable. This review

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will evaluate the use of NIRS to study muscle metabolism, and focus on recent developments in NIRS technology to monitor multiple locations at the same time.

2. Principle of NIRS technology

Early applications of NIRS to measure oxygen status in various human tissues were made by Jöbsis [4] and Chance [5]. The methodology of NIRS involves the detection of differences in light absorption from tissues. NIRS has a number of different approaches, which include: (1) continuous-wavelength spectroscopy [6], (2) spatially-resolved spectroscopy [7], (3) time-resolved spectroscopy [8], and (4) phase-modulation spectroscopy [9]. In this review, we describe the essential aspects of continuous-wavelength spectroscopy, which is most commonly used. Near infrared light in the range of 700 to 900 nm is used in the NIRS device because of its ability to penetrate into the tissue. In a simple case, two wavelengths, 760 and 850 nm, are used (Fig. 1). At around 760 nm, deoxygenated hemoglobin has a higher absorbency, and at around 850 nm, oxygenated hemoglobin has a higher absorbency. Changes in tissue hemoglobin oxygen saturation will change the relative absorption of light at these two wavelengths. Changes in total hemoglobin concentration (blood volume) will change absorption at both wavelengths. Values obtained by NIRS are presented in units of optical density (o.d.). The o.d. is calculated as follows:

$$\text{o.d. for 760 and 850 nm} = \log 10(\text{mV for base line}/\text{mV for reference condition}).$$

The signals of 760 and 850 nm were subtracted to estimate the change of oxygen saturation and added for estimation of the change of blood volume. These parameters are calculated as follows:

$$\text{oxygen saturation} = A \times \text{o.d.760 nm} - B \times \text{o.d.850 nm},$$

$$\text{blood volume} = K(\text{o.d.760 nm} + \text{o.d.850 nm}),$$

where A and B are constants determined by the absorption coefficient of oxygenated and deoxygenated Hb and the optical path length of both 760 and 850 nm; K is a constant assuming that the mean value of the oxygenated and deoxygenated Hb absorption coefficient at two wavelengths is nearly equal to the absorption coefficient of the isosbestic point.

For obtaining a reflected-light signal from skeletal muscle, the light source and the photodetector (PD) are typically separated by 2.5 to 3.0 cm. As shown in Fig. 2, the near infrared light penetrates in a shallow arc with a banana shape. The penetration depth is one-half of the separation between the light source and the PD (approximately 1.25 to 1.5 cm). This means that longer separation distances result in deeper penetrations, but also result in less light reaching the detector. The actual penetration depth is very difficult to measure, and varies with hemoglobin concentration and with the thickness of tissue (skin and fat) [10,11] between the light source and detectors and the muscle. This is the primary difference between the use of NIRS with reflected light and the use of NIRS in transmitted light (such as pulse oximeters where the light pathlength is known).

3. Important notice for measurement

The inability to accurately measure pathlength with reflected NIRS means that this method is not able to provide the absolute oxygen saturation in the tissue [12]. A number of studies have reported absolute

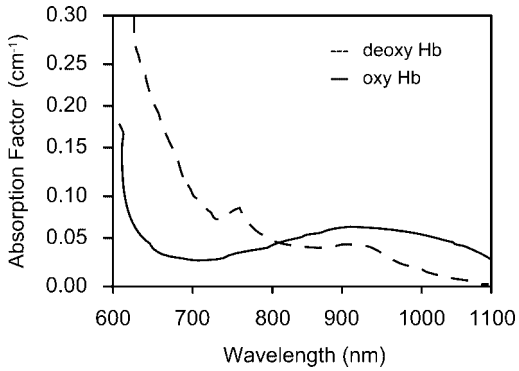

Fig. 1. Absorption curves for oxygenated hemoglobin (solid line) and deoxygenated hemoglobin (dotted line). NIRS devices typically use wavelengths in the 700–900 nm regions. Note that the absorption curves for oxygenated and deoxygenated hemoglobin cross at 805 nm and are opposite in intensity at 760 and 850 nm.

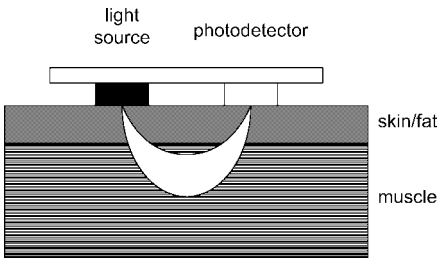

Fig. 2. Typical arrangement of the NIRS device. The light is scattered by the tissue, with some of the light being reflected back to a photodetector in a rough banana shaped light path. The shape of the reflected light depends of the size of the skin/fat layer and the amount of hemoglobin in the small vessels in the muscle.

values, by using multiple pathlengths, 3–4 wavelengths, and with phasemodulated NIRS. However, these approaches have not been completely successful in human studies [11]. Therefore, it is hard to compare the raw data (o.d.) among various subjects. In order to compensate for them, some studies have used "physiological calibrations" [13]. The muscle oxygen level was determined by the resting value as 100% and then inducing arterial occlusion (200–300 mmHg) to obtain the lowest value (0%). Though arterial occlusion can be uncomfortable and inappropriate for some subjects, this method is typical and allows comparison among subjects.

The approach of calculating a time constant of recovery or a half-time of recovery is also useful because recovery kinetics doesn't require knowing the absolute signal intensity [10,14]. The rate of recovery of oxygen saturation after exercise or ischemia indicates the capacity of oxygen utilization and oxygen delivery.

4. Studies in muscle metabolism using NIRS

Oxygen uptake estimated from pulmonary gas exchange parameters has been used as an indirect index for muscle metabolism. NIRS has made it possible to directly and noninvasively measure the localized muscle metabolism. A number of studies have used NIRS to measure the muscle oxygen status of working muscles. Figure 3 shows the typical changes in oxygen saturation during cycling at five constant

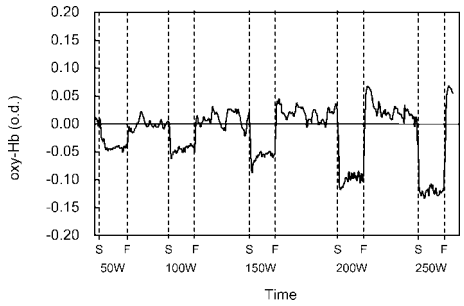

Fig. 3. Continuous recording of the oxygenated hemoglobin trace of the vastus lateralis muscle during cycling. The symbol S means start point for each exercise and F means the finish point for each exercise [15]. Note the progressively decreasing signal (hemoglobin desaturation) with increasing work level.

work rates [15]. With increasing work rate, oxygen saturation at vastus lateralis muscle decreased progressively. In the beginning of exercise, oxygenated Hb increased due to the increments of cardiac output and muscle blood flow. Thereafter, with increasing exercise intensity, oxygenated Hb decreased due to the increments of oxygen consumption and oxygen extraction in the working muscle. During recovery, oxygenated Hb increased rapidly due to the greater oxygen supply to muscle (hyperemia). Previous studies have measured oxygen status in the thigh or calf muscles during cycling [15–17], rowing [14], skating [18], knee extension [19], ankle plantar flexion [10,20], and in the arm muscles during arm cranking [21], elbow flexion [22], or finger flexion/hand grip exercise [13,23]. These measurements have been conducted in the field as well as in the laboratory.

NIRS measures the muscle oxygen status in the small blood vessels, capillaries, and intracellular sites. Muscle oxygen status has been correlated to localized muscle activity such as myoelectric activity and change in blood lactate concentration [15]. NIRS measurements have also been correlated with phosphocreatine measurements with NMRS [24].

5. Multiple NIRS imaging device

A recent development with NIRS is the combining of multiple light sources (tungsten flashlight bulb) and photodetectors, and it allows the 2-dimentional imaging of oxygen status [25–27]. While similar in principal to previous single channel NIRS, the multiple NIRS imaging device can measure the oxygen status in several different areas at the same time. This is a big advantage over previous NIRS. This device has been produced for measuring brain and muscle metabolism. In one of these NIRS imaging devices, dual wavelength spectroscopy (760 and 850 nm) was adopted [25–27]. The sensor included three rows of three light sources and two pairs of photodetectors (Fig. 4). The size was 7×12 cm and the measurement area was 4×10 cm. The nine light sources illuminates the nearest photodetector pair consequently for a short interval, with 3 to 8 sec required for a complete cycle of data acquisition (12 photodetector pair combinations). The separation between light source and photodetector was 2.5 cm. The outputs of the optical sensor were connected to a 12-bit AD converter, set to have a minimum step of 0.304 mV, and it was considered to be within the noise level of the photodetector/amplifier. The absorbance values during a task were computed and subtracted from the baseline value. These values were processed by a direct back projection algorithm and presented as a 64-pixel image based on all possible combinations of light source/photodetector. For display purposes, the 64-pixel images were color coded, using a continuous

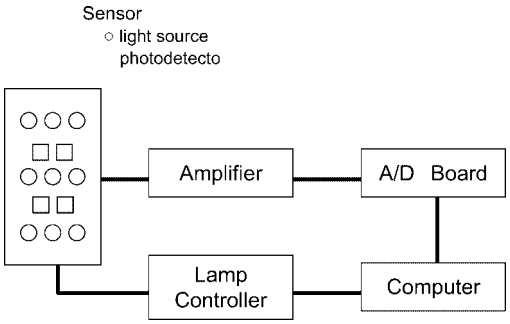

Fig. 4. Diagram for multiple NIRS imaging device (modified from [25,28]). This imaging device has 9 light sources and two sets of photodetector pairs. It produces signals from 12 different areas.

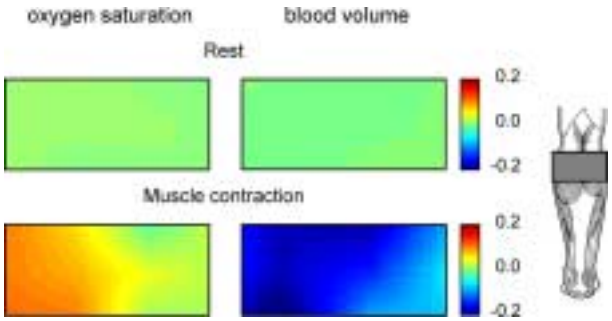

Fig. 5. Typical image of changes for oxygen saturation and blood volume during rest and exercise. Scale shows the optical density (modified from [28]). These results were obtained with the imaging device shown in Fig. 4. Note the uniform signal at rest and the difference in signal with exercise (lateral versus medial heads). The location of the imaging device is shown on the right of the figure.

color scale, from red to blue. A positive number represented deoxygenation or increased blood volume, while a negative number represented oxygenation or decreased blood volume.

6. Studies in muscle metabolism using multiple NIRS imaging device

Some studies have reported heterogeneity for muscle metabolism determined by the multiple NIRS imaging devices [27,28]. Figure 5 shows the typical two-dimensional displays of time-related changes in oxygen saturation and blood volume during rest and standing plantar flexion. When comparing between the medial and lateral heads, the medial head had greater deoxygenation during standing plantar flexion. Within the medial head of the gastrocnemius muscle, oxygen was not uniformly distributed throughout the muscle, but instead was consistently different in the proximal and distal areas; the distal portion had greater deoxygenation and decrement of blood volume during exercise, and it had greater oxygenation and increment of blood volume compared with the proximal portion (Fig. 6). Regional differences in oxygen status within one muscle are consistent with regional variations in pressure or stress distribution caused by complex muscle architecture [28]. Reduced blood flow to the distal portion of the gastrocnemius muscle as the result of greater intramuscular pressure would increase oxygen extraction and result in greater deoxygenation.

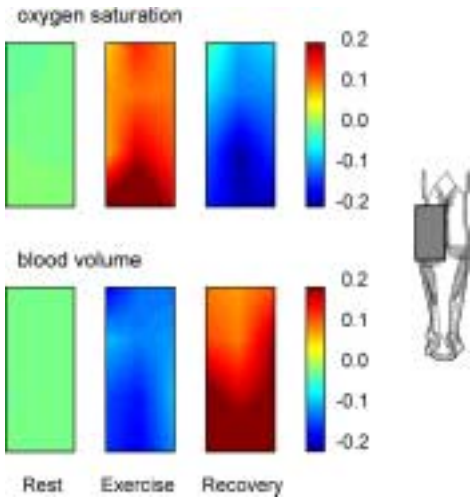

Fig. 6. Typical changes for oxygen saturation and blood volume during rest, exercise, and recovery. Scale shows the optical density (modified from [27]). Note the differences in oxygen saturation and blood volume between the proximal and distal portions of the medial head of gastrocnemius muscle.

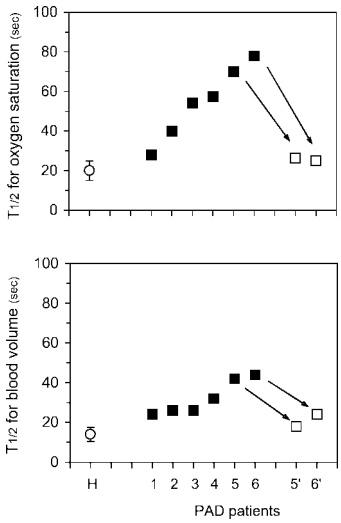

Fig. 7. $T_{1/2}$ for oxygen saturation and blood volume in PAD (opened and closed square) and healthy subjects (opened circle). The larger number indicates greater severity of PAD. No. 5′ and 6′ indicate the data after taking medication (modified from [31]).

Magnetic resonance imaging (MRI) and NMRS have been used to examine the heterogeneity in muscle recruitment and metabolism in individual muscle [1,2,29,30]. The resolution of MRI is excellent, although it is limited to the providing information on muscle activation levels. Localized NMRS provides excellent exercise information on metabolic intensity, but it has limited signal time resolution. Furthermore, both methodologies require the use of a huge bore magnet. The advantage of the multiple NIRS imaging device is that it is much less expensive, simpler and portable.

This multiple NIRS imaging device can be applied not only to muscle research, but also to rehabilitation [31]. People with peripheral arterial disease (PAD) have larger decrements of oxygenation and

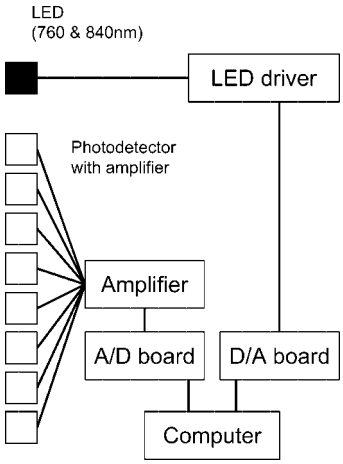

Fig. 8. New diagram for multiple NIRS imaging device which we developed (personal data). Note the circular arrangement of source and detectors. This device has a faster time resolution compared with the previous imaging devices.

blood volume with exercise and they have slower recovery following exercise. Figure 7 shows the half time of recovery ($T_{1/2}$) for oxygen saturation and blood volume. $T_{1/2}$ for both oxygen saturation and blood volume was slower in PAD patients compared with healthy subjects. However, two PAD patients had faster $T_{1/2}$ values after taking medication to improve their circulation. These patients reported reduced symptoms of PAD including greater ability to walk without pain as determined by the subjective judgment of a medical doctor. While clinical assessment of PAD severity is less precise than numerical indices such as ankle branch index or arterial blood flow using Doppler measurements, the agreement with changes in clinical symptoms of PAD suggests that a multiple NIRS imaging device is a valuable tool for screening the presence or severity of peripheral vascular disease during the rehabilitation period.

7. New approach in multiple NIRS imaging device

Previous NIRS imaging devices, however, had some problems: (1) the light sources did not cycle fast enough, reducing time resolution, (2) the distance from the light source to photodetectors were fixed. In order to eliminate for these problems, we developed a new NIRS imaging device. A block diagram of this device is shown in Fig. 8. The optical sensor has one light emitting diode (LED) source module (15 mm diameter) and eight photodetectors modules (15 mm diameter). The reflected light from human tissue is received by the photodetectors. The detected signal is amplified by cascading amplifiers, one of which is mounted in each photodetector. The amplified signals are stored in a personal computer through an A/D converter board. Each of the LED with drive circuit module and the photodetectors with amplifier module is molded into a cylindrical shape. The diameter of each cylindrical module is 15 mm. The detector modules are connected via the source module to the second amplifier array and the computer with wires.

One of the interesting points is that the light source module and the photodetector modules are adaptable for arbitrary arrangement according to the muscle size or placement. The use of one LED light source provides a faster time resolution (signal from eight regions in less than 0.5 sec). Another point is that this upgraded device can allow various displays of oxygen status such as oxygenation, deoxygena-

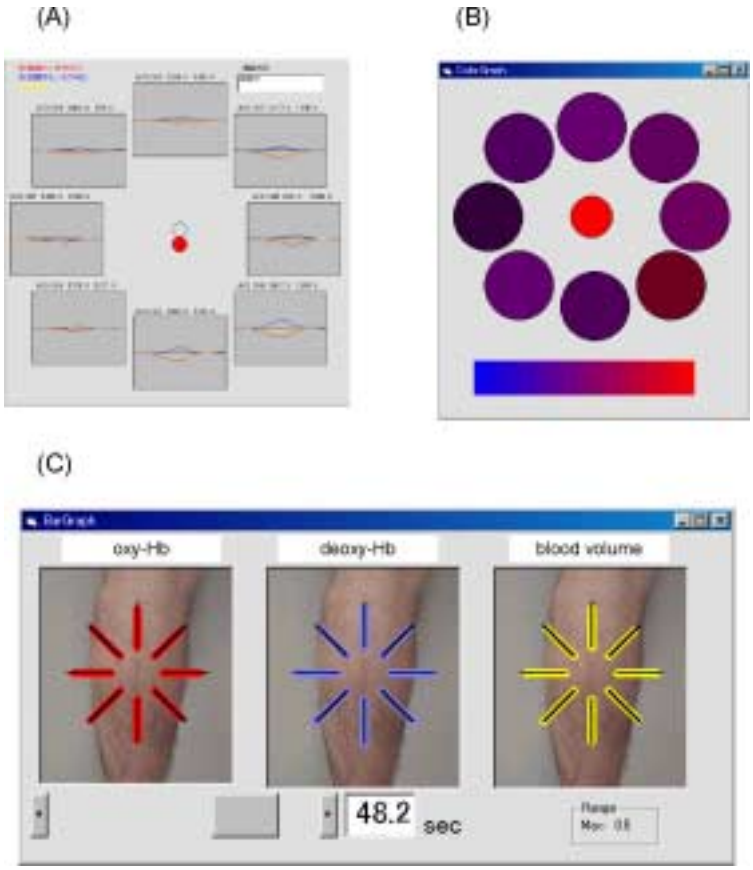

Fig. 9. Various displays using new multiple NIRS imaging device shown in Fig. 8 (personal data). (A) shows dynamic changes in tissue oxygenation and blood volume in the different regions. (B) shows a color coded image from the different regions at one time point. (C) shows color coded changes in oxygen saturation superimposed on images of the lower leg.

tion or blood volume via line graph (A), bar graph (B), or color coded graph (C) (Fig. 9). We believe that it is easy for subjects to recognize how much and which area oxygen is utilized.

Though it has already been applied to the brain metabolism and cancer detection, multiple NIRS imaging device is also useful for measuring muscle metabolism. The final goal of this approach is to assist in the exercise prescription, exercise therapy, and clinical uses.

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References

[1] T. Hamaoka, K. McCully, T. Katsumura, T. Shimomitsu and B. Chance, Non-invasive measures of muscle metabolism, in: *Handbook of Oxidants and Antioxidants in Exercise*, C. Sen, L. Packer and O. Hanninen, eds, Amsterdam, Elsevier Science, 2000, pp. 485–509.

[2] P. Cerretelli and T. Binzoni, The contribution of NMR, NIRS and their combination to the functional assessment of human muscle, *Int. J. Sports Med.* **18** (1997), S270–S279.
[3] T.K. Tran, N. Sailasuta, U. Kreutzer, R. Hurd, Y. Chung, P. Mole, S. Kuno and T. Jue, Comparative analysis of NMR and NIRS measurements of intracellular PO2 in humans skeletal muscle, *Am. J. Physiol.* **276** (1999), R1682–R1690.
[4] F.F. Jöbsis, Non-invasive infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters, *Science* **198** (1977), 1264–1267.
[5] B. Chance, S. Nioka, J. Kent, K. McCully, M. Fountain, R. Greenfeld and G. Holtom, Time resolved spectroscopy of hemoglobin and myoglobin in resting and ischemic muscle, *Anal. Biochem.* **174** (1988), 698–707.
[6] M. Cope and D.T. Delpy, A system for long-term measurement of cerebral blood and tissue oxygenation in newborn infants by near-infrared transillumination, *Med. Biol. Eng. Comp.* **26** (1988), 289–294.
[7] S. Suzuki, S. Takahashi, T. Ozaki and Y. Kobayashi, A tissue oxygenation monitor using NIR spatially resolved spectroscopy, *Proc. SPIE* **2597** (1999), 582–292.
[8] M. Miwa, Y. Ueda and B. Chance, Development of time resolved spectroscopy for quantitative non-invasive measurement, *Proc. SPIE* **2389** (1995), 142–149.
[9] A. Duncan, T.L. Whitlock, M. Cope and D.T. Delpy, A multiwavelength, wideband, intensity modulated optical spectrometer for near-infrared spectroscopy and imaging, *Proc. SPIE* (1993), 248–257.
[10] K. McCully, L. Landsberg, M. Suarez, M. Hofmann and J.D. Posner, Identification of peripheral vascular disease in elderly subjects with optical spectroscopy, *J. Gerontol. Biol. Sci.* **52A** (1997), B159–B165.
[11] M.C. van Beekvelt, B.G. van Engelen, R.A. Wevers and W.N. Colier, Near-infrared spectroscopy in chronic progressive external ophthalmoplegia: adipose tissue thickness confounds decreased muscle oxygen consumption, *Ann. Neurol.* **51** (2002), 272–273.
[12] E. Sevick, B. Chance, S. Leigh, S. Nioka and M. Maris, Quantitation of time- and frequency-resolved optical spectra for the determination of tissue oxygenation, *Anal. Biochem.* **195** (1991), 330–351.
[13] T. Hamaoka, H. Iwane, T. Shimomitsu, T. Katsumura, N. Murase, S. Nishio, T. Osada, Y. Kurosawa and B. Chance, Noninvasive measures of oxidative metabolism on working human muscle by near-infrared spectroscopy, *J. Appl. Physiol.* **81** (1996), 1410–1417.
[14] B. Chance, T.M. Dait, C. Chang, T. Hamaoka and F. Hagerman, Recovery from exercise induced desaturation in the quadriceps muscle of elite competitive rowers, *Am. J. Physiol.* **262** (1992), C766–C775.
[15] H. Miura, H. Araki, H. Matoba and K. Kitagawa, Relationship among oxygenation, myoelectric activity, and lactic acid accumulation in vastus lateralis muscle during exercise with constant work rate, *Int. J. Sports Med.* **21** (2000), 180–184.
[16] H. Miura, H. Araki and H. Matoba, Relationship between oxygenation and myoelectric activity at vastus lateralis and lateral gastrocnemius muscles, *Jpn. J. Phys. Sports Med.* **48** (1999), 413–420.
[17] R. Belardinelli, T.J. Barstow, J. Porszasz and K. Wasserman, Changes in skeletal muscle oxygenation during incremental exercise measured with near infrared dpectroscopy, *Eur. J. Appl. Physiol.* **70** (1995), 487–492
[18] K.W. Rundell, S. Nioka and B. Chance, Hemoglobin/myoglobin desaturation during speed skating, *Med. Sci. Sports Exerc.* **29** (1997), 248–258.
[19] M. Shinohara, M. Kouzaki, T. Yoshihisa and T. Fukunaga, Mechanomyogram from the different heads of the quadriceps muscle during incremental knee extension, *Eur. J. Appl. Physiol.* **78** (1998), 289–295.
[20] W.N.J.M. Colier, I.B.A.E. Meeuwsen, H. Degens and B. Oeseburg, Determination of oxygen consumption in muscle during exercise using near infrared spectroscopy, *Acta Anaesthesiol. Scan.* **39** (1995), 151–155.
[21] Y. Bhambhani, R. Maikala and S. Buckley, Muscle oxygenation during incremental arm and leg exercise in men and women, *Eur. J. Appl. Physiol.* **78** (1998), 422–431.
[22] J.K. Kahn, J.C. Jouanin, J.L. Bussiere, E. Tinet, S. Avrillier, J.P. Ollivier and H. Monod, The isometric force that induces maximal surface muscle deoxygenation, *Eur. J. Appl. Physiol.* **78** (1998), 183–187.
[23] R. Boushel, F. Pott, P. Madsen, G. Radegran, M. Nowak, B. Quistorff and N. Secher, Muscle metabolism from near infrared spectroscopy during rhythmic handgrip in humans, *Eur. J. Appl. Physiol.* **79** (1998), 41–48.
[24] K. McCully, S. Iotti, K. Kendrick, Z. Wang, J. Posner, J. Leigh and B. Chance, Simultaneous in vivo measurements of HbO2 saturation and PCr kinetics after exercise in normal humans, *J. Appl. Physiol.* **77** (1994), 5–10.
[25] B. Chance, Q. Luo, S. Nioka, D.C. Alsop and J.A. Detre, Optical investigations of physiology: a study of intrinsic and extrinsic biomedical contrast, *Philos. Trans. R. Soc. Lond. B* **352** (1997), 707–716.
[26] Q. Luo, S. Nioka and B. Chance, Functional near-infrared imager, *Proc. ISPE* **2979** (1997), 84–93.
[27] H. Miura, K. MuCully, L. Hong, S. Nioka and B. Chance, Regional difference of muscle oxygen saturation and blood volume during exercise determined by near infrared imaging device, *Jpn. J. Physiol.* **51** (2001), 599–606.
[28] H. Miura, K. MuCully, S. Nioka and B. Chance, Validity for measuring skeletal muscle oxygen status using functional near infrared imaging machine, *Jpn. J. Phys. Fitness Sports Med.* **49** (2000), 211–216.
[29] J.A.L. Jeneson, S.J. Nelson, D.B. Vigneron, J.S. Taylor, J. Murphy-Boesch and T.R. Brown, Two-dimensional 31P-chemical shift imaging of intramuscular heterogeneity in exercising human forearm muscle, *Am. J. Physiol.* **263** (1992), C357–C364.

[30] J.A.L. Jeneson, J.O. van Dobbenburgh, C.J.A. van Echteld, C. Lekkerkerk, W.J.M. Janssen, L. Dorland, R. Berger and T.R. Brown, Experimental design of 31P MRS assessment of human forearm muscle function: restrictions imposed by functional anatomy, *Magn. Reson. Med.* **30** (1993), 634–640.
[31] H. Miura, K. MuCully, L. Hong, S. Nioka and B. Chance, Exercise-induced changes in oxygen status in calf muscle of elderly subjects with peripheral vascular disease using functional near infrared imaging machine, *Therap. Res.* **21** (2000), 1585–1590.