

# A NEW COMBINED DEEP-BODY-TEMPERATURE/NIRS PROBE FOR NON-INVASIVE METABOLIC MEASUREMENTS ON HUMAN SKELETAL MUSCLE

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## 1. INTRODUCTION

Temperature modulates tissue metabolism through thermodynamic phenomena, e.g. changes in enzymatic activities, pH variations, etc. In humans, temperature changes may be induced by stressful environmental conditions (e.g. immersion in cold water, etc.) or, artificially, during therapeutic procedures (extracorporeal circulation, cancer treatment using hyperthermia, etc.). Moreover, temperature distribution is not uniform in the body. In a forearm immersed in cold water at 20°C, it is possible to observe radial gradient values reaching 2°C/cm (Ducharme et al., 1991). Thus, the measurement of total tissue metabolism often results from the contribution of several subsets of tissue exposed to different temperatures, making the interpretation of the data sometimes difficult. In this context, the aim of the present study was to develop a non-invasive probe allowing one to simultaneously: 1) establish in a human skeletal muscle a region of uniform temperature; 2) measure the temperature; 3) measure the oxidative metabolism in the corresponding region.

## 2. METHODS

The probe was built using a modified Deep Body Temperature (DBT) sensor (Deep Body Thermometers Ltd., Little Eversden, Cambridge, UK). This sensor (shown in Figure 1), is attached to the surface of the tissue, and contains two temperature sensors and a heating element via which it is possible to establish zero heat flux through the underlying tissue. When this zero heat flux is established, the surface and the tissue core temperature are equal (Solman *et al.*, 1973). The probe was modified to include two slots in the silicone rubber body moulding into which two optical fibres with end mounted prisms could be mounted (fibre separation 3 cm). These fibres were attached to a white light source (Oriel 77501, Stratford CT, USA) and a CCD based spectrophotometer (Cope *et al.*, 1989) from which it was possible to measure the near infrared (NIR) spectrum of the tissue under the probe. An appropriate heat insulator was installed on the back of the DBT probe to permit its use when both it and the tissue were immersed in cold water.

This combined DBT/NIR probe enabled a uniform temperature region of approximately  $3 \times 3 \times 1.5$  (depth) cm to be established and changes in oxyhaemoglobin [ $\text{HbO}_2$ ] and deoxyhaemoglobin [ $\text{Hb}$ ] concentration in the tissue measured using an optical path-length derived from the tissue water spectrum measured at the start of the study and assuming a tissue water content of 62% (Matcher *et al.*, 1993). Preliminary measurements were performed with the probe fixed on the forearm of a subject (over the hand flexors). Muscle temperature was changed using a thermostated bath, and [ $\text{Hb}$ ] and [ $\text{HbO}_2$ ] changes were followed with a time resolution of 2 s *i.e.*, 1.5 s for the acquisition of one

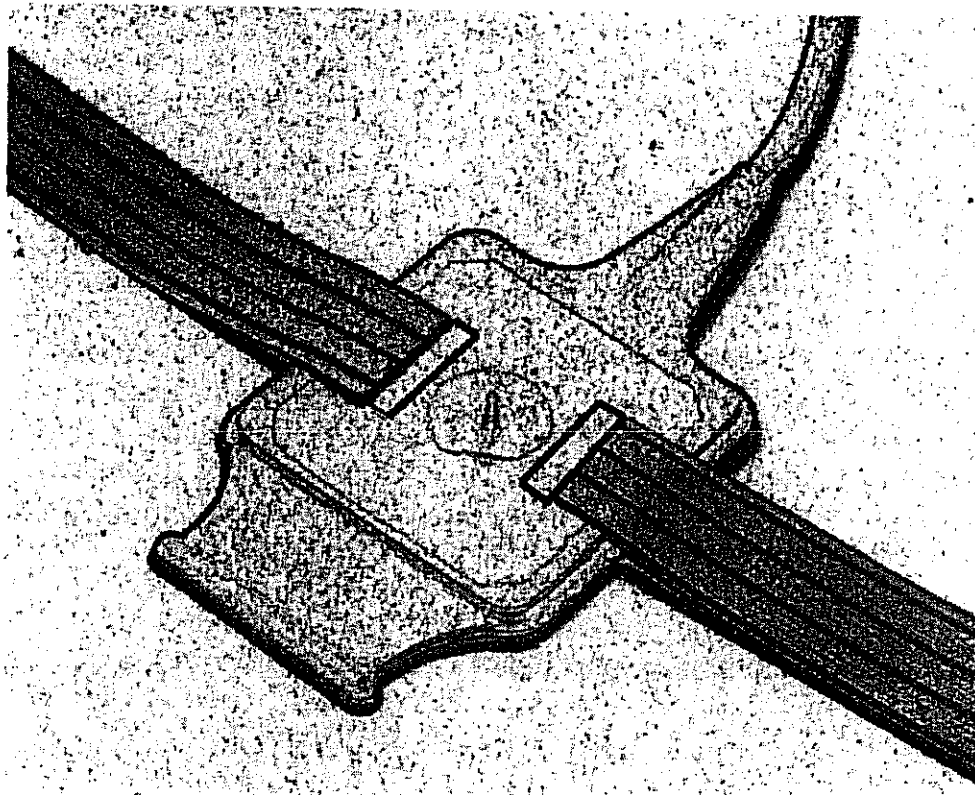


Figure 1. A schematic diagram of the combined DBT/NIRS probe.

spectrum and 0.5 s delay.  $O_2$  consumption was calculated by measuring the slope of [Hb] changes, during 3 minutes of arterial occlusion (Cheatle et al., 1991, De Blasi et al., 1993). Measurements were made at 26.0, 28.2, 30.5, 33.3, 34.8, 35.9, 37.0 and 37.8°C.

### 3. RESULTS

The 8 curves appearing in Figure 2a each represent the mean of 10 baseline spectra (sample intensity = I), acquired before the start of the ischaemia, at the different temperatures defined in the METHODS section. The curves are shifted toward the bottom of the graph with decreasing temperature. For a given wavelength,  $-\log_{10}(I/I_{air})$  varies linearly ( $p < 0.01$ ) as a function of temperature when fitted to an expression of the form  $-\log_{10}(I/I_{air}) = aT + b$ . Figure 2b shows the correlation coefficient ( $r$ ) of the linear regressions over the wavelength range studied.

Figure 3 shows the slope of the regression lines. Note that the slope increases with wavelength and exhibits an abrupt change near 840 nm.

Figure 4 shows the intramuscular oxygen consumption of the forearm at rest as a function of temperature, derived from NIRS measurements made during the arterial occlusion.

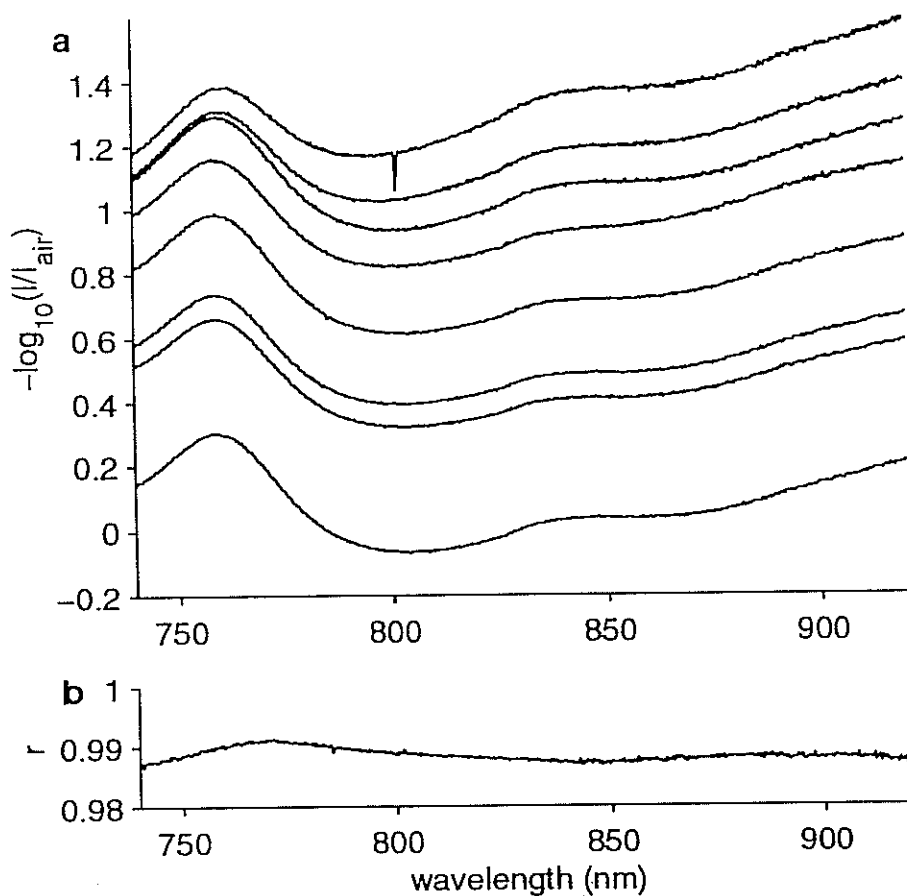


Figure 2. a) Baseline spectra at  $T = 26.0$  (bottom curve), 28.2, 30.5, 33.3, 34.8, 35.9, 37.0 and 37.8 (top curve) °C. b) Correlation coefficient ( $r$ ) as a function of the wavelength of the linear regression:  $-\log_{10}(I/I_{ref}) = aT + b$ .

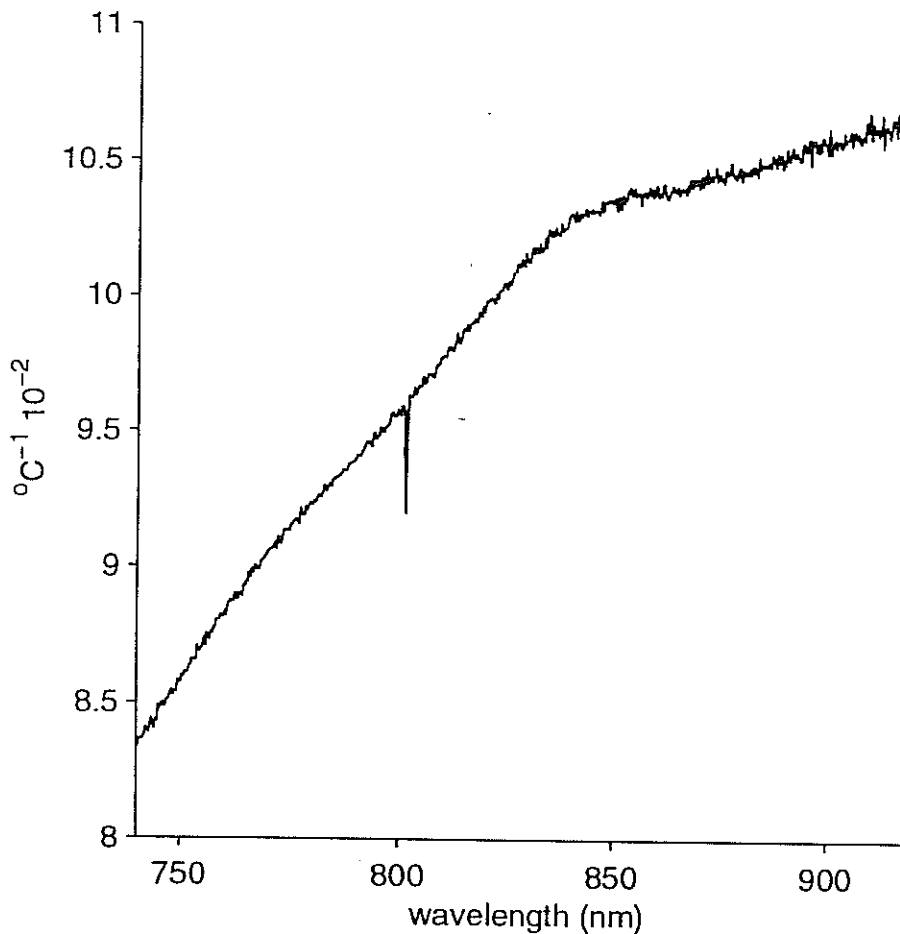


Figure 3. Slope (a) of the linear regression  $-\log_{10}(I/I_{ref}) = aT + b$  as a function of the wavelength (Note that the "spike" around 810 nm is an artifact due to a cosmic ray hitting a CCD pixel).

#### 4. DISCUSSION

If it is assumed that [Hb] and [HbO<sub>2</sub>] remain reasonably constant during intramuscular temperature changes, then the results reported in Figure 2 allow one to conclude that  $-\log_{10}(I/I_{air})$  shifts by an offset proportional to the intramuscular temperature and that the slope itself also depends on the wavelength. This means that the attenuation spectra expressed as  $-\log_{10}(I_T/I_T(0))$ , where  $I_T(0)$  is a reference spectrum acquired at the same temperature (T) as  $I_T$ , will eliminate the effect of the offset, i.e.:

$$\begin{aligned} -\log_{10}(I_{T1}/I_{T1}(0)) &= \log_{10}(I_{T1}(0)) - \log_{10}(I_{T1}) \\ &= \{\log(I_{T1}(0)) + \text{offset}\} - \{\log_{10}(I_{T2}) + \text{offset}\} \\ &= -\log_{10}(I_{T1}/I_{T2}(0)) \end{aligned}$$

where  $I_{T2}$  and  $I_{T2}(0)$  are measure at any reference temperature T<sub>2</sub>. From the practical point of view, this allows us to compare [Hb] and [HbO<sub>2</sub>] changes at different temperatures, i.e. O<sub>2</sub> consumption can reasonably be compared. Of course, the hypothesis that the [Hb] and [HbO<sub>2</sub>] remain constant is not completely true but, fortunately, this problem only seems to become noticeable in the Hb region (~760 nm) when the muscle reaches the critical temperature of ~36°C. (In Figure 2a, the third curve from the top, at 35.9°C, is not parallel to the others). In fact, it has been demonstrated that during the present pro-

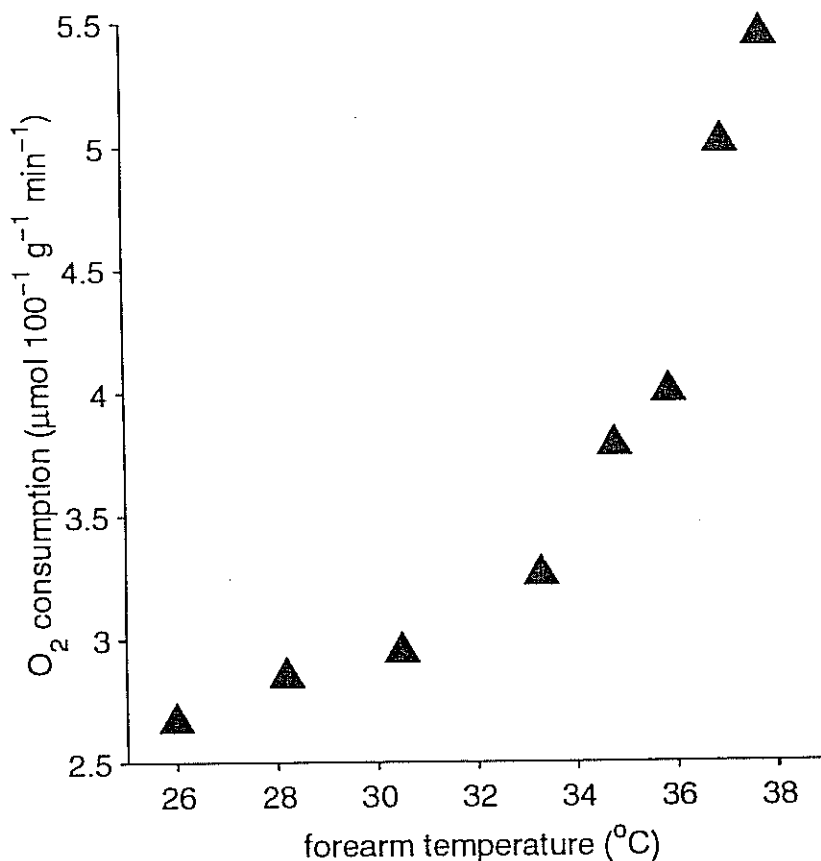


Figure 4. Forearm oxygen consumption as a function of temperature.

tolcol there is a variation in blood perfusion, heat flux and tissue blood volume when the temperature exceeds  $\sim 36^{\circ}\text{C}$  (Binzoni et al., 1995). Thus, it is likely that the observed offset is due to changes in the scattering coefficient of the tissue induced by the temperature variations. The present results are in agreement with analogous *in vitro* studies in tissue (Kelly et al., 1995). It must be noted that scattering associated changes are not observed *in vitro* when studying the spectra of pure Hb, HbO<sub>2</sub> or H<sub>2</sub>O (Kelly et al., 1995, Sfareni et al., 1997). However, there are small temperature dependent changes in the absorption spectra of these compounds, and the precision in the calculation of [Hb] and [HbO<sub>2</sub>] changes can be improved by using temperature corrected extinction coefficients.

The above results allow us to calculate and to compare intramuscular O<sub>2</sub> consumption values measured at different temperatures if care is taken to acquire  $I_T(0)$  at the same temperature as  $I_T$ . The results presented in Figure 4 seem to be in agreement with early findings on animals (Cossin and Bowler 1987). Moreover, we have previously demonstrated (Binzoni et al., 1998) that during the present protocol, the skeletal muscle metabolism remains aerobic even during the three minute ischaemic period so the O<sub>2</sub> consumption data should represent the total energy consumption of the tissue. It will be necessary to perform further experiments to define the exact mathematical function describing these data. It is however noteworthy, that a variation of  $2^{\circ}\text{C}$ , i.e. of the order of the possible intramuscular temperature gradients, are sufficient to produce measurable changes in oxygen consumption. This point shows the importance of clamping the temperature at a fixed value, by means of the DBT/NIRS probe, when measuring precise O<sub>2</sub> consumption values. To our knowledge, these are the first data

for resting human intramuscular O<sub>2</sub> consumption as a function of a well defined temperature.

The results shown in Figure 3 are not essential for the calculation of the O<sub>2</sub> consumption but it is interesting to notice the abrupt change in the slope of the regression near ~840 nm. It is difficult to explain the change in slope in this region in terms of variations in [Hb], [HbO<sub>2</sub>] or tissue water content, since changes in their absorption spectra as a function of temperature are too "smooth" in this wavelength range (Sfäreni *et al.*, 1997), and the wavelength dependence of pathlength is approximately linear (Matcher *et al.*, 1997). It would thus be interesting to use this type of analysis to study the behaviour of the scattering coefficients of the skeletal muscle in this region when changing temperature.

## 5. CONCLUSIONS

The combined DBT/NIRS probe should enable new studies of the biological effects of temperature on humans. The probe should allow one to take "temperature biopsies" in a defined muscle region in order to investigate muscle metabolism and changes in optical properties. The non-invasive character of the measurements is ideal for the follow-up of time dependent processes. Further studies are now needed to improve the algorithm for [Hb] and [HbO<sub>2</sub>] calculation in the presence of large temperature changes.

## ACKNOWLEDGMENTS

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