Transcutaneous measurements of oxygen tension at edges of leg ulcers: preliminary communication

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Summary

Using skin-surface sensors, transcutaneous oxygen tension ($TcPo_2$) has been measured at the edges of ulcers and at control sites proximal to wounds on the same legs. $TcPo_2$ at 43°C at the edges of venous ulcers was found to be significantly different ($P<0.003$) from that of arterial and mixed arteriovenous ulcers ($P<0.05$) respectively. $TcPo_2$ on healed skin was higher than at any wound edge. At this temperature $TcPo_2$ was also found to be significantly different ($P<0.001$) on the intact skin of patients with venous disease when compared with measurements at identical sites on healthy controls. In the same group, these $TcPo_2$ values increased with dependency. By contrast, at 37°C $TcPo_2$ was no different between groups ($P<0.10$), nor did it alter with position. This protocol adopted for investigating ulcers enables a quantitative distinction to be made between ulcers of different aetiologies. The differences in $TcPo_2$ between different ulcers and healed skin support the fibrin cuff mechanism which has been suggested as the cause of venous ulceration.

Introduction

Skin surface sensors offer an easy, noninvasive method of measuring oxygen tension transcutaneously. These sensors use the modified Clarke electrode and were developed for paediatric use by Huch and colleagues[1]. The sensors work on the principle of detecting current generated at the cathode consequent to the breakdown of free oxygen molecules during chemical interaction with hydroxyl ions in an aqueous electrolyte, as described by Daneel in 1897[2]. Many workers, notably Silver[3], have discussed and described the principles of oxygen measurement as well as their medical and biological applications. Transcutaneous oxygen sensors heat skin locally to preset temperatures between 37°C and 45°C, causing the cutaneous vasculature to dilate. The resultant increase in blood flow in the volume of cutaneous tissue influenced by the sensor would be accompanied by increased local oxygen availability. At 45°C, this increase in oxygen due to a seven-fold increase in blood flow is said to be greater than the metabolic requirements of local tissue[4]. Oxygen diffuses out of the cutaneous vessels and, after overcoming the diffusional resistances of the dermis and epidermis, passes into the sensor. Eberhard designed a transcutaneous oxygen sensor (Roche Dual Oximeter 632) after considering diffusional distances, permeability of the intervening layers namely, dermis, epidermis, and the membrane covering the sensor and electrolyte[4]. Most of the work described in this paper has been done using this sensor.

Oxygen measured transcutaneously ($TcPo_2$) using such sensors on the skin on the chests of infants is known to bear close relationship to arterial oxygen pressures (Pao_2)[4]. In adults, however, $TcPo_2$ is reported to be less well correlated with Pao_2[1,4]. $TcPo_2$ is also reported to decrease as the measurement site moves distally from the chest[5]. There appears to be no relationship, however, with age[6]. The most widely reported use of $TcPo_2$ monitoring is to determine levels of amputation[5-8]. Its potential use in investigating the cutaneous perfusion around leg ulcers has been reported[9], and in order to investigate this potential, a full protocol to document both the macro- and the microcirculation around ulcers of different aetiologies was designed. This report discusses the protocol and preliminary results obtained.

The problems in interpreting $TcPo_2$ measured on adults appear to be related to cathode size as well as the temperatures to which the sensors are preset. Spence *et al.*[10] have reported that the Radiometer $TcPo_2$ sensor with a 20 micron diameter cathode reads skin oxygen levels more closely than the Draeger sensor with its cathode that has an area of 45 microns. In this report the Roche, the Radiometer and Hewlett-Packard (Draeger) sensors have been compared in resting and under exercise conditions.

Dodd and colleagues[11] measured $TcPo_2$ at 37°C on the skin of patients with venous disease and stated that the decrease observed with dependency is evidence of the loss of the vasoconstrictor reflex. They further argued that stasis rather than precapillary deposits of fibrin is the cause of ulceration, thus disputing the fibrin cuff hypothesis of Browse and Burnand[12]. This claim is also investigated in the present paper.

Materials and methods

Protocol for investigating ulcers

On the first visit following clinical examination, the lower limb circulation was investigated with Doppler ultrasound. Both 8 and 4 MHz Doppler probes Sonicaid BV380 were used to test the arterial and venous flow respectively in the legs. The test of the arterial tree comprised recording the blood flow at the femoral, popliteal and posterior tibial arterial testing sites and measuring the ankle systolic pressure. The ankle systolic pressure measurement was used to determine the resting pressure index (RPI). RPI is equal to ankle systolic pressure divided by brachial systolic pressure. The test of the venous

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Table 1. Patients with frank ulceration investigated during the study (healed ulcer group included ulcers of all 3 groups)

Type of ulcer	*No. of patients*	*Age range (mean) in years*	*Sex*
Venous	7	37–80 (65.6)	5F, 2M
Arterial	6	60–86 (79.8)	3F, 3M
Mixed arteriovenous	6	66–93 (77.5)	3F, 3M

system was to document the presence or absence of incompetence in the valves of the deep veins of the legs. The investigations were always carried out with patients supine in hospital environments where room temperature was maintained between 21 and 24°C.

Prior to investigating the microcirculation, ulcerated legs were thoroughly cleaned with 0.9% saline and dried. Legs were then degreased using isopropyl alcohol swabs (Scherring-Pebbles). $TcPo_2$ sensors (Roche Dual Oximeter 632) were positioned using double-sided adhesive discs at wound edges and at control sites at least 15 cm proximal to ulcers on the same legs. Electrode temperatures were preset to 43°C and at least 15 minutes allowed for the cutaneous vasculature to dilate, after which $TcPo_2$ was recorded. On subsequent investigations on the same patient, one of the sensors was always positioned at the wound edge while the other was repositioned on the same site as far as practicable. A photoreflectance plethysmograph described previously[9] was used to record cutaneous pulsatility on four sites around ulcers. Contours of ulcers were mapped on tough but pliable clear polyvinyl sheets with a felt-tip pen, and the area enclosed by the contour was then calculated from these. The procedure with oxygen sensors, photoreflectance probes and contour mapping was repeated on every patient at approximately four-weekly intervals.

Twenty-eight patients referred to the Leg Dressing Clinic, Department of Dermatology, were investigated with this protocol. Nineteen of this group had frank ulceration during the course of this work. As no specific treatment modality was under test, patients were assigned to different regimens depending upon the clinical assessment of their condition. None of these treatment regimens incorporated any mechanism known to increase local tissue oxygenation. Table 1 shows the age and sex distribution as well as other relevant details.

The Mann-Whitney test was used for significance testing between groups. The best fit when comparing sensors was obtained on performing linear regression of Hewlett-Packard versus Roche and Radiometer versus Roche $TcPo_2$ respectively.

Comparison between Roche, Hewlett-Packard and Radiometer oxygen sensors

These tests were conducted because cathode construction for oxygen sensors is not standard. This could cause disagreement in the absolute values measured by different systems. The tests were conducted on young, normal volunteers ($n=11$, age range 18–40). Oxygen sensors were positioned on clean and degreased skin on the volar surface of forearms. Electrode temperatures were preset to 43°C on all occasions and at least 15 minutes were allowed for cutaneous vasodilatation. At the start, subjects were seated with their test arm supported at the level of the heart. After taking initial readings over three minutes at rest, subjects were asked to raise their arms vertically and maintain this position for five minutes. During the last two minutes in this position, a sphygmomanometer cuff was inflated to occlude arterial inflow to the raised arm. $TcPo_2$ was recorded during arterial occlusion of two minutes as well as during release and recovery in the horizontal position.

Effect of electrode temperature on $TcPo_2$

To investigate the effect of electrode temperature on $TcPo_2$, two oxygen sensors were positioned adjacently on clean, degreased skin on the legs of both control volunteers ($n=11$) and patients ($n=5$) with venous ulcers. The heated electrode temperature was set to 43°C, while the other was left to measure at skin temperature. Measurements were made on unbroken skin in both patients and controls. After allowing 15 minutes for stabilization, readings were taken with the patient/control supine. Following this, the patient/control was asked to stand and $TcPo_2$ was recorded after at least two minutes in this position. A final reading of $TcPo_2$ was made in the initial supine position.

Table 2. $TcPo_2$ (mmHg) on leg ulcers (mean ± 1 s.d.)

	Wound site	*Control site*	*Resting pressure index●*
Ulcers of venous aetiology ($n=7$, no. of observations = 48)	22.3 ± 3.8	46.5 ± 8.7	>1
Ulcers of arterial origin ($n=6$, no. of observations = 22)	15.3 ± 7.2	45 ± 13.8	0.33–0.65
Ulcers of mixed origin ($n=6$, no. of observations = 32)	13.9 ± 10.7	52.6 ± 7.2	0.33–0.9
Healed ulcers ($n=9$, no. of observations = 15)	27.2 ± 8.9	49.8 ± 5.6	—

● Resting pressure index = $\frac{\text{ankle systolic pressure}}{\text{brachial systolic pressure}}$

The differences in wound site $TcPo_2$ between venous and arterial as well as between venous and mixed ulcer groups are significant ($P<0.003$ and $P<0.05$ respectively, Mann–Whitney test). The differences between $TCPo_2$ at wound sites and their respective controls in all groups are also highly significant ($P<0.001$)

Results

The differences in $TcPO_2$ between the three types of ulcer at wound sites and their respective controls are statistically significant (Table 2). The values shown are the mean of the mean value for each patient. All control site $TcPO_2$ values fall within the normal range determined by both the authors[13] and Dowd[6], while those at wound sites are clearly outside these. $TcPO_2$ on healed ulcers is closer to the healthy skin values than any measured at the edges of wounds.

Figure 1 is a typical example of cutaneous pulsatility detected with a photoreflectance probe around ulcers that healed. The waveforms are read from left to right and show rhythmic changes in cutaneous blood volumes. The swift upstroke has been shown by Roberts[14] to be synchronous with systolic events.

Figure 2 shows that $TcPO_2$ measured with heated (43°C) electrodes is clearly and significantly ($P<0.001$) different for healthy skin and that of patients with venous disease. It is also evident that these values increase as controls/patients stand. The ranges also agree with previously determined values. By contrast, neither patient nor control groups showed changes in $TcPO_2$ measured with unheated (37°C) sensors with position (NS, $P<0.10$). The range of these values agrees with Evans and Naylor[15].

Comparison between the different oxygen systems as shown in Figure 3 shows that despite constructional differences, the Roche and the Radiometer sensors are closely matched, $r^2=0.91$, while the Hewlett-Packard sensor is clearly different, $r^2=0.22$. Spence *et al.*[10] have reported the differences between

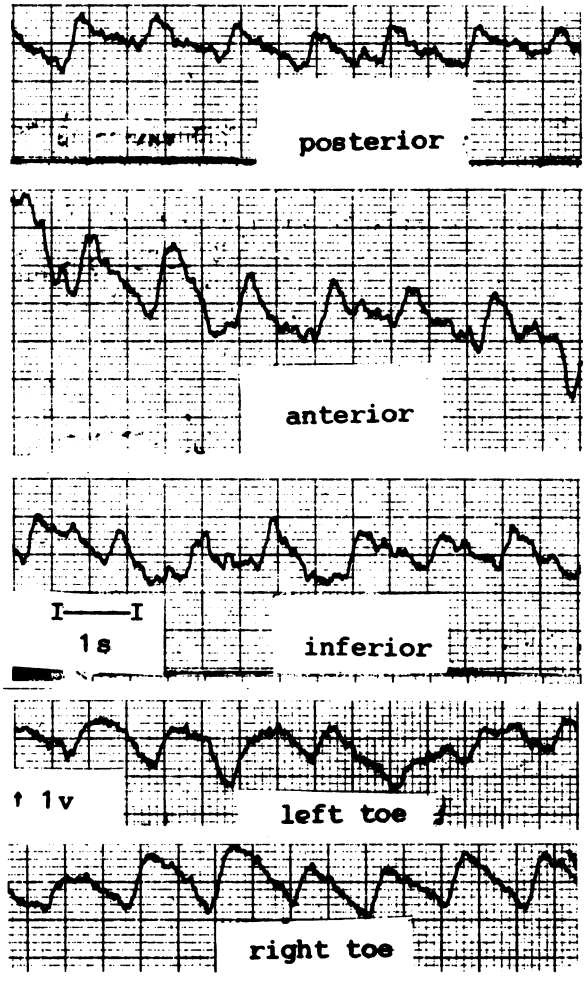

Figure 1. Cutaneous pulsatility detected with a photoreflectance probe around ulcers

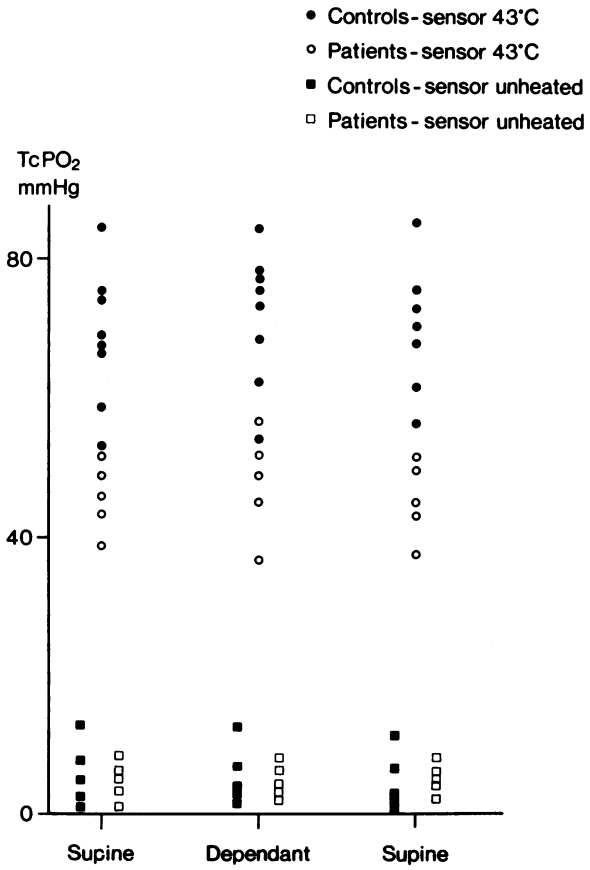

Figure 2. Changes in $TcPO_2$ with position using Roche Dual Oximeter. The unheated (37°C) $TcPO_2$ values have been plotted separately for clarity

the Radiometer and the Draeger systems and argued that the former provides the best estimate of tissue oxygen levels. The Hewlett-Packard system in this report uses the Draeger sensor. The similarity evidenced between the Radiometer and the Roche sensors permits the extrapolation that the $TcPO_2$ values in Table 2 must be closely representative of tissue oxygen levels.

Figure 4 demonstrates the differences in the response times between the Roche and Hewlett-Packard sensors during passive exercise, the latter being clearly the slower.

Discussion

Previous work has produced conflicting evidence on the oxygen content of venous blood in patients with venous disease. While the original findings of De Takats *et al.*[16] suggested lower venous oxygen content, other workers have found the opposite[17–19]. All the data in these reports have been on venepuncture samples. Sampling venous blood from varicose veins may be influenced by different variables[20]. The skin surface sensors used here are noninvasive and reproducible while being easy to use. $TcPO_2$ measured at the edges of pure venous ulcers is the highest, while the lowest is in the mixed ulcer group. When $TcPO_2$ is used to interpret arterial flow, as is the case with measurements at arterial ulcer sites, there are fewer variables to contend with than in the case of venous or mixed ulcers where there could be oedema, chronic shunting or venous stasis. While oedema and chronic shunting would lower skin tension and tissue oxygen pressures respectively, venous stasis would have the opposite effect. None of these effects has been precisely determined. The presence of fibrin cuffs in

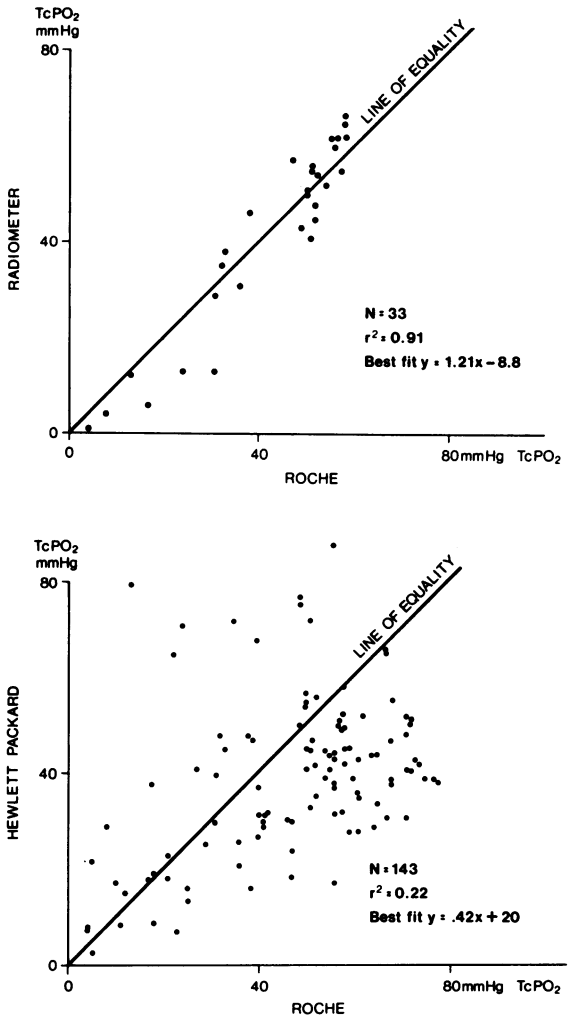

Figure 3. Comparison between Roche, Radiometer and Hewlett-Packard (Draeger) electrodes

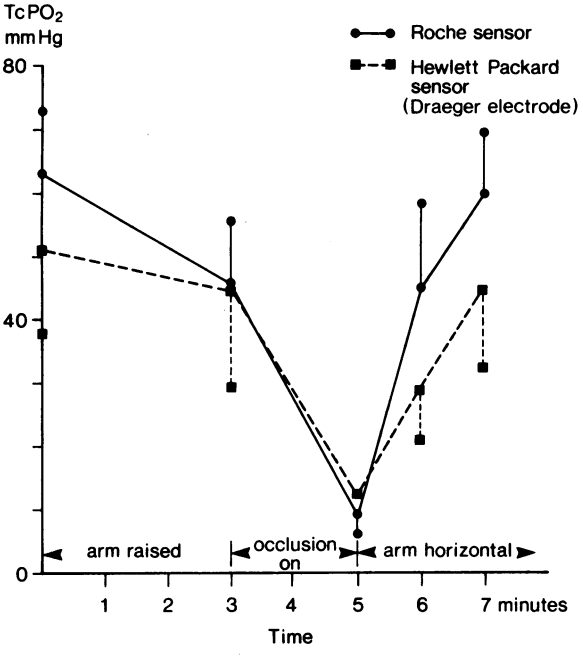

Figure 4. Changes in $TcPo_2$ with position. Comparison between Roche and Hewlett-Packard (Draeger) electrodes following positional changes

precapillary areas surrounding venous ulcers has also been reported by Browse and Burnand[12]. It is conceivable that as ulcers heal these fibrin cuffs impose less of a physical barrier to oxygen diffusing from capillaries to tissues.

$TcPo_2$ is a function of oxygen delivered and oxygen consumed. Our findings at wound edges are in agreement with Hunt and colleagues[21], who reported a range of $TcPo_2$ of 5–28 mmHg, with a mean of 15.5 mmHg is wound fluid. Measured at the edge, $TcPo_2$ must represent the advancing edge of the wound. On healed skin characterized by thin epithelium covering newly vascularized areas, there is no phagocytic activity which, if present, would sink oxygen delivered to tissues. Thus at wound edges, $TcPo_2$ must be a measure of the oxygen available for healing.

As can be seen from Figure 2, heating the electrode enables patients with venous disease to be clearly separated from normals. There is no difference between patients and controls or indeed among the respective groups with change in position when $TcPo_2$ is measured with unheated sensors. These findings thus do not support the claim made by Dodd *et al.*[11] that postural changes depress $TcPo_2$. Indeed, with the absolute values of $TcPo_2$ with unheated sensors being so small, any changes would need to be interpreted with caution. The heated sensor was not found to have any obvious effect on the adjacent unheated one. These oxygen sensors were not developed for adult use and this must be borne in mind when using them or during any appraisal. The cathodes utilize oxygen despite the optimal designs used in their manufacture. An absolute reading of 0 mmHg must not be interpreted as a total lack of blood flow beneath the sensor. The slower response of the Hewlett-Packard sensor underlines the need to make specific response studies before attempting to use the sensor to monitor induced changes in skin oxygen tension.

It has been suggested by Thune[22] that waveforms of the kind shown in Figure 1 can be characteristic of vessel reactivity. We have merely documented the presence or absence of these clearly identifiable waveforms.

The conclusions from this preliminary study are that it is possible to separate ulcers of different aetiologies on the basis of $TcPo_2$ measurements at 43°C. The results are consistent with the fibrin cuff hypothesis of Browse and Burnand.[12] More measurements in different experimental conditions need to be carried out, however, before other mechanisms – such as stasis – that have been suggested as causal factors in the development of ulcers, can be commented upon.

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