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Evaluation of hyperbaric oxygen therapy for free flaps using planar optical oxygen sensors. Preliminary results

S. Gehmert[a], S. Geis[a], P. Lamby[a], C. Roll[a], U. Braumandl[b], M. Hidayat[a], M. Sultan[a], B. Fuechtmeier[a], E.M. Jung[a] and L. Prantl[a,*]

[a]*Center of Plastic, Hand and Reconstructive Surgery, Department of Trauma Surgery, University Hospital Regensburg, Regensburg, Germany*
[b]*Institute of Hyperbaric Medicine, Regensburg, Germany*

Abstract. *Objectives*: This study was designed to determine if a) hyperbaric oxygen increases the tissue oxygenation of free flaps and b) verification of this effect is possible by using a recently validated and innovative method for two-dimensional pO_2 measurement (Luminescence lifetime imaging = LLI).

Methods: Six patients with a free parascapular flap transplanted to the lower limb received hyperbaric oxygen (HBOT) therapy. The HBOT regimen consisted of treatment over 90 minutes with 100% O_2 (FiO_2 1.0) at 240 kPa (Marx-Schema). The transcutaneous oxygen partial pressure ($p_{tc}O_2$) was measured over the entire flap with the use of luminescence lifetime imaging (LLI) before and 30, 60, 120 minutes after treatment. The LLI is based on the oxygen dependent quenching of phosphorescence of the indicator dye platinum (II)-octaethyl-porphyrin implemented in a polystyrene sensor foil.

Results: In all six free flaps we could find a significant increase of tissue oxygen over the entire flap in form of increased *R*-values as well as subsequently calculated absolute $p_{tc}O_2$ values over a period of 120 min after hyperbaric therapy. The $p_{tc}O_2$ values increased significantly from 42.59 ± 1.11 Torr before to 81.14 ± 5.95 Torr after hyperbaric treatment ($p < 0.001$). Even after 2 hours the $p_{tc}O_2$ values were significantly higher (83.45 ± 13.80 Torr) compared with values prior to HBOT ($p < 0.006$).

Conclusions: The findings of this study demonstrated an increase of oxygen supply over the entire flap after hyperbaric oxygen therapy.

1. Introduction

Improving the survival rate of tissue flaps as random-pattern skin flaps, composite flaps, and free flaps, is of general interest in medicine [3, 6, 11, 13, 14, 18, 19]. To date, only 2 studies investigated the efficacy of hyperbaric oxygen with respect to flap survival [4, 21]. Although some animal studies could show an improvement of skin flap survival, the mechanisms remain unclear [12, 21]. The purpose of the present study was to show $p_{tc}O_2$ changes in free flaps before and after hyperbaric therapy. For the first time Luminescence Lifetime Imaging (LLI) was used to evaluate the oxygen supply over the entire flap surface. In our previous experiments LLI was proven to be a precise and non-invasive monitoring system for transcutaneous oxygen measurement [2, 8, 16] The major advantage of LLI is the lack of oxygen consumption during measurement allowing both a more realistic estimation of $p_{tc}O_2$ compared to the gold standard (polarographic electrode technique) as well as the permanent use in regions with critically low

*Corresponding author: Prof. Dr. Lukas Prantl, Center of Plastic, Hand and Reconstructive Surgery, University Hospital Regensburg, Franz-Josef-Strauß-Allee 11, 93053 Regensburg, Germany. E-mail: lukas.prantl@klinik.uni-regensburg.de.

oxygen supply. Other disadvantages of the polarographic electrode technique are the required calibration time prior to measurement and the lacking spatial resolution.

2. Patients and methods

Six patients with free parascapular flaps were included in this prospective clinical trial. Each patient was given verbal and written information with regard to the nature of the study; signed informed consent was obtained before treatment. The study was performed according to the ethical guidelines of Clinical Hemorheology and Microcirulation [1].

Age of the patients (5 male, 1 female) ranged from 19 to 65 years (40.1 ± 6.6). Flap transplantation was performed to cover tissue defects of the lower limb caused by trauma in all six patients. The first day after surgery the patients underwent hyperbaric oxygen therapy (HBOT). The HBOT regimen consisted of treatment over 90 minutes with 100% O_2 (FiO_2 1.0) at 240 kPa (Marx-Schema).

$p_{tc}O_2$ of the six free parascapular flaps was detected before and 30, 60, 120 min after the hyperbaric therapy with the use of luminescence lifetime imaging (LLI). This new method for two-dimensional pO_2 measurements is based on the oxygen-dependent quenching of phosphorescence of the indicator platinum (II)-octaethyl-porphyrin (Pt-OEP). The indicator is immobilized in a polystyrene matrix as a transparent planar sensor. The chemical and electronic aspects of this method and the in vivo evaluation have already been published by our group [2, 8, 16].

A pO_2 sensor foil was applied to the free parascapular flap after acclimatization of the six patients in a laying position at room temperature of 20°C. For bubble-free adherence, a thin film of ultrasonic gel was placed between the skin and the sensor foil. A constant skin temperature (40°C) of the measurement site was achieved with the aid of a transparent heating foil (No. H 6708 R 9.6, Telemeter Electronic, Donauwörth, Germany), placed on the sensor foil. During measurement a constant temperature was controlled by a thermometer (Peak Tech Inc., Ahrensburg, Germany; absolute temperature accuracy as specified by the manufactor: ±0.5%°C). Both the decay time and the intensity of emitted luminescence depending on the oxygen concentration at the respective sensor were detected. Measurement of the decay time is independent of light intensity or tissue inhomogenities. Thus, each measurement was conducted by rapid lifetime determination (RLD). Luminescence was detected for every pixel of the CCD chip and converted into grayscale values. The grayscale picture then has been translated into a false color picture, which represents the pO_2 distribution (mapping) over the entire flap. Furthermore the absolute pO_2 values were subsequently calculated compared.

3. Results

$p_{tc}O_2$ values of the six parascapular flaps detected by LLI before hyperbaric oxygen therapy was 42.59 ± 1.11 Torr. In all cases the absolute $p_{tc}O_2$ values increased significantly after oxygen therapy over the entire flap area independent of the flap perfusion, assessed by using contrast-enhanced US ($t = 0$ min, 81.14 ± 5.9 $p < 0.001$; $t = 30$ min, 81.9 ± 8.2 $p < 0.001$; $t = 60$ min, 87.2 ± 11.2; $t = 120$ min 83.5 ± 13.8 $p < 0.006$) (Fig. 1). In one flap with compromised tissue perfusion by swelling and hematoma the $p_{tc}O_2$ values were lower after HBO therapy at all time points ($t = 0$ min, 71.91; $t = 30$ min, 65.51; $t = 60$ min, 67.64; $t = 120$ min, 61.25) than in the normal perfused flaps. However the $p_{tc}O_2$ values of low perfused tissue areas also increased significantly under hyperbaric therapy and remained high over the whole measurement period of 120 minutes (Fig. 2). 120 minutes after hyperbaric oxygen therapy was applied

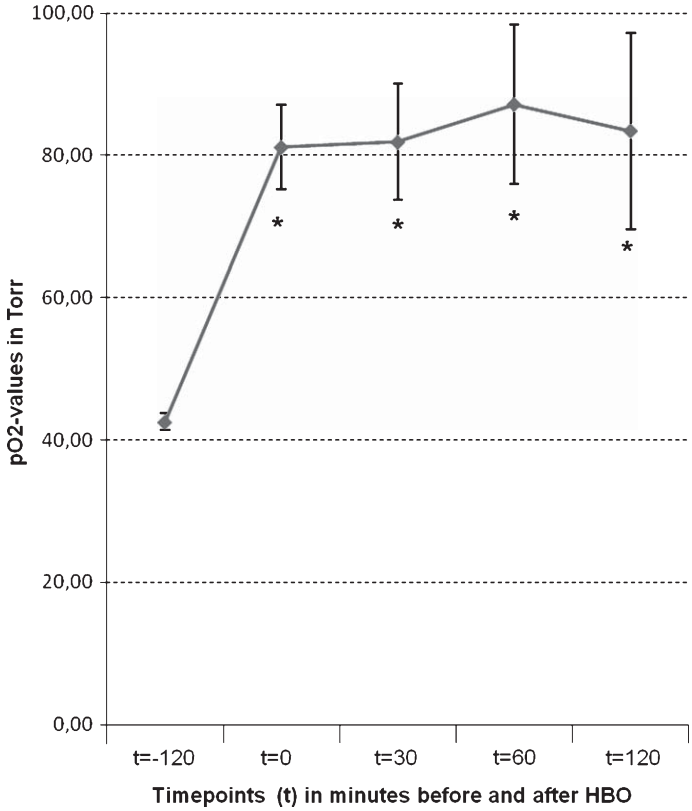

Fig. 1. $p_{tc}O_2$ before HBO therapy showed mean values of 42.59 Torr (±1.1) that were significant lower to all values at observed time points after the therapy ($t = 0$ min, 81.14 ± 5.9 $p < 0.001$; $t = 30$ min, 81.9 ± 8.2 $p < 0.001$; $t = 60$ min, 87.2 ± 11.2; $t = 120$ min 83.5 ± 13.8 $p < 0.006$). These results indicate that $p_{tc}O_2$ values increase immediately due to the HBO therapy but tend to be significant higher even after 2 hours when compared with $p_{tc}O_2$ values before the therapy; * = Significant difference.

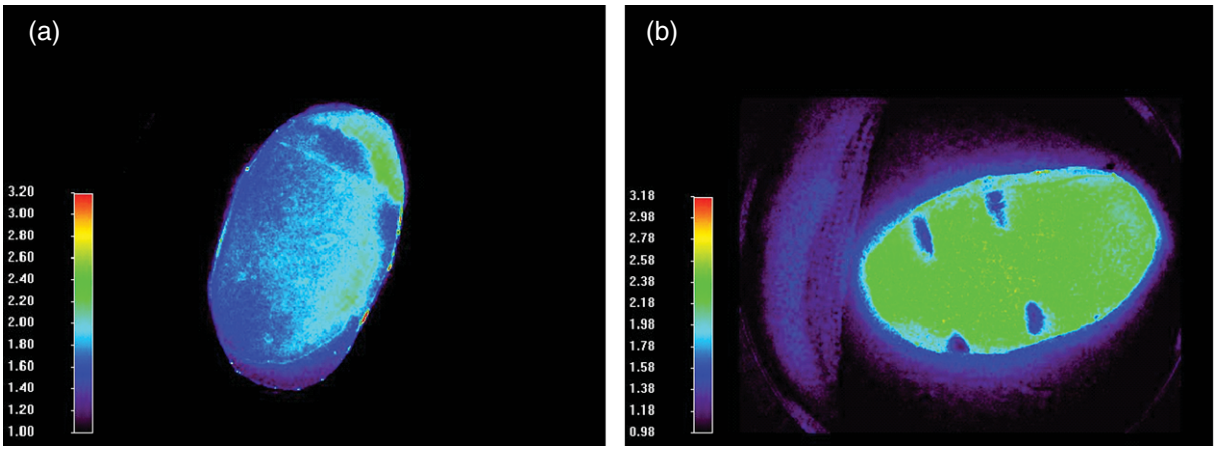

Fig. 2. False color picture before (a) and after (b) hyperbaric oxygen therapy in a normal perfused free parascapular flap. *R*-values of the entire flap were 2.30 ± 0.02 before hyperbaric oxygen therapy and 3.02 ± 0.11 after therapy.

$p_{tc}O_2$ reached stabile values of 83.5 ± 13.8. These results indicate that even after 2 hours the $p_{tc}O_2$ values were significantly higher compared to values detected before hyperbaric oxygen therapy.

4. Discussion

Hyperbaric oxygen therapy (HBOT) has been suggested to improve oxygen supply and therefore is generally used for various acute and chronic diseases e.g. gas embolism, carbon monoxide poisoning, clostridal myositis and myonecrosis, compartment syndrome, decompression sickness, diabetic retinopathy, necrotizing fasciitis, osteomyelitis, radiation injury, thermal burns, wound healing, skin graft and flap survival [4, 5, 12, 15, 17, 20]. In other clinical situations the cause of tissue hypoxia may be small vessel disease or edema, and may be overcome by a high driving pressure of oxygen in the arterial blood. This has been demonstrated in hypoxic tissue where regional perfusion is reasonably preserved, through the use of transcutaneous and implantable oxygen electrodes [5]. In wound healing, insufficient supply of oxygen may inhibit healing processes. The intermittent presentation of oxygen to those hypoxic tissues, therefore, may allow the resumption of normal healing [1, 4]. However the exact mechanisms for wound healing, limb salvage, flaps and graft survival are still unclear [20].

Partial arterial oxygen pressures greater than 1000 mmHg are routinely achieved during HBOT. Such oxygen tensions in plasma have been suggested to cause up-regulation of growth factors, down-regulation of inflammatory cytokines, increased fibroblast activation, angiogenesis, antibacterial effects and enhanced antibiotic activity [5, 9, 10, 20]. Through increasing arterial oxygen tension, the hypoxic tissues should be supplied with oxygen until adequate circulation is restored and improvement of the microvasculature is noted. Even if a number of studies have shown the efficacy of HBOT on enhancement of flap and graft survival in experimental situations a Cochrane review from 2009 summarizes that there is low to moderate level of evidence that HBOT promotes successful "take" of compromised flaps and grafts [7, 20]. By using transcutaneous pO_2 imaging with LLI we could show for the first time a significantly increased oxygen tension o all areas of the flap over period of 120 min independent of the clinical conditions of the flap, e.g. venous congestion, hematoma ore edema. Maximum $p_{tc}O_2$ values were measured in all six flaps after 60 min. After 120 min a trend to a decrease of oxygen values was observable, however the values were significantly higher as prior to hyperbaric therapy.

In conclusion this clinical study showed that luminescence lifetime imaging is a valuable tool to detect $p_{tc}O_2$ changes during hyperbaric oxygen therapy in free flaps. The new method enables a continuous and non-invasive $p_{tc}O_2$ measurement over the entire flap and can be easily handled. The fact that two-dimensional oxygen maps are generated makes this technique particularly suitable for the observation of free flaps after transplantation.

Further revaluation is needed to determine how long increased skin oxygenation can be detected in tissue transplants and especially whether there are clinically significant beneficial effects from HBOT for compromised flaps.

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