PRINCIPLES AND CONTEXTS OF TISSUE OXYGENATION IMAGING (HSI TECHNOLOGY) AND TRANSCUTANEOUS OXYGEN MEASUREMENT IN TISSUE ($TcPO_2$)

Dr. Axel Kulcke

Diaspective Vision GmbH, Strandstraße 15
18233 Am Salzhaff, OT Pepelow, Germany
axel.kulcke@diaspective-vision.com,

1 INTRODUCTION

Tissue oxygenation measurement (tissue oximetry or NIRS / VLS technology) is mainly performed with multispectral optical sensors or spectrometer systems directly on the tissue (e.g. skin). There, the light enters the tissue through the skin, is specifically absorbed, and then analysed after leaving the tissue. The parameter tissue oxygen saturation is called StO_2, SmO_2, or SrO_2. The unit in % represents the proportion of hemoglobin molecules saturated with oxygen. Another measurement parameter of this technology is the tissue hemoglobin concentration, called THI or THb.
A non-contact and imaging version of the technology is Hyperspectral Imaging (HSI), in which the spectrometer technology is integrated into special camera systems.
Transcutaneous O_2 gas measurement can be performed using a chemical Clark electrode or an optical fluorescence quenching method. In medical technology, the parameter is called $tcpO_2$ and is measured in mmHg.
With this technology, the molecular oxygen present in the tissue must actually pass through the skin to the sensor. In order to allow the oxygen to pass through the skin, the sensor is usually heated to 44°C. The sensors can only be mounted on intact skin.

2 PHYSIOLOGICAL BASICS

There is a scientifically very well established relationship between the two measurement methods. The basis is the oxygen binding curve of hemoglobin (Figure 1). The oxygen binding curve of the blood is strongly dependent on temperature (see Figure 2). The oxygen for the cells is transported via hemoglobin from the lungs to the cells. Under standard conditions in arterial blood, about 97% of the oxygen molecules are bound to the hemoglobin and only the rest of them are dissolved as gas in the plasma.

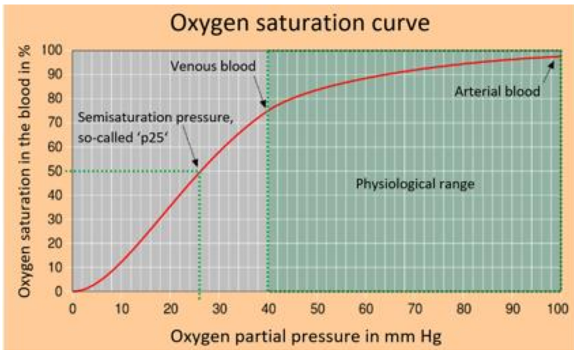

Figure 1: Oxygen binding curve of hemoglobin

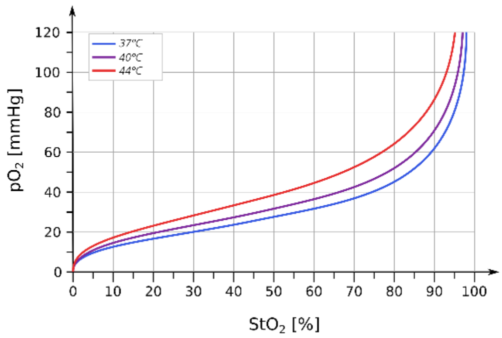

Figure 2: Oxygen binding curve of hemoglobin shown for different temperatures, according to [1].

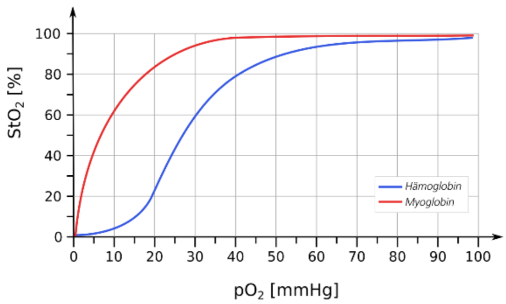

Figure 3: Oxygen binding curves for hemoglobin and myoglobin

A possibility to convert the values under standard conditions in the body (37°C and pH = 7.4) is given in Table 1.

PO$_2$(mmHg)	% S	PO$_2$(mmHg)	% S	PO$_2$(mmHg)	% S
1	0.6	34	65.16	80	95.84
2	1,19	36	68,63	85	96,42
4	2,56	38	71,94	90	96,88
6	4,37	40	74,69	95	97,25
8	6,68	42	77,29	100	97,49
10	9,58	44	79,55	110	97,91
12	12,96	46	81,71	120	98,21
14	16,89	48	83,52	130	98,44
16	21,40	50	85,08	140	98,62
18	26,50	52	86,59	150	98,77
20	32,12	54	87,70	175	99,03
22	37,60	56	88,93	200	99,20
24	43,14	58	89,95	225	99,32
26	48,27	60	90,85	250	99,41
28	53,16	65	92,73	300	99,53
30	57,54	70	94,06	400	99,65
32	61,69	75	95,10	500	99,72

Table 1: Conversion of pO_2 [mmHg] to blood saturation values in % [2].

A general transferability of the measured values has been clinically proven in many studies and is well illustrated, for example, in [3, 4]. On closer inspection, however, further details have to be considered for the respective clinical application. In Figure 3, the different binding curves of hemoglobin and myoglobin are showcased. The course of the curve shows that for high partial pressures, transcutaneous gas measurement is more advantageous and for low partial pressures, tissue oxygenation is more advantageous.

The information on how much oxygen is present in the tissue for cell respiration is very important for the physician, as under- or oversupply can lead to severe damage or generate further problems.

If there is an undersupply of oxygen (hypoxia), e.g. with diabetic feet, problems with wound healing or hypoxia in the brain, severe damage up to total tissue loss can be expected.

In case of oversupply (hyperoxia), damage to the eyes has been proven in neonatology and brain damage is also assumed.

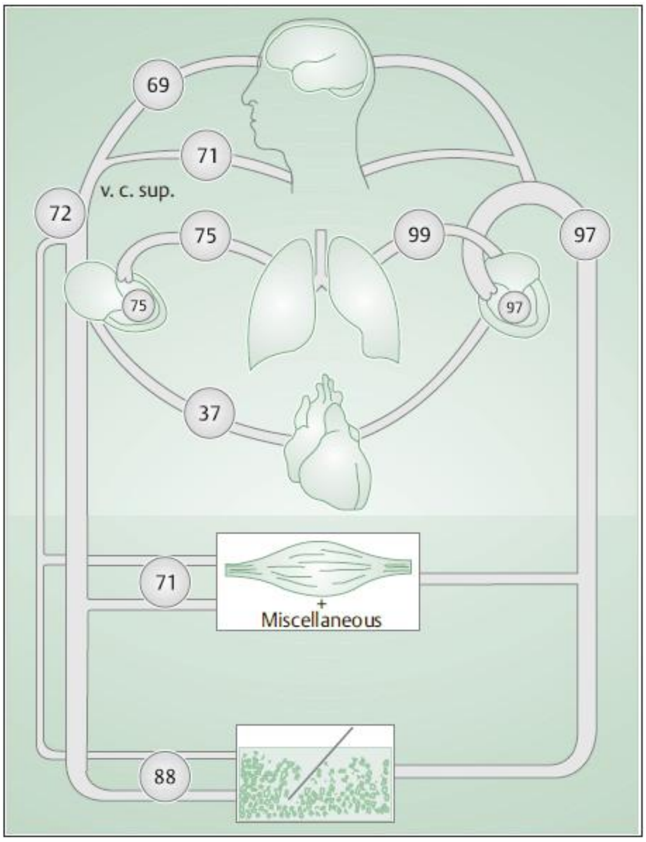

Figure 4: Typical oxygen saturation values in different areas of the body (modified according to [6]).

3 Comparison of Technologies

The properties and special features of the different measurement technologies (electrochemical gas measurement with Clark electrode, optical fluorescence measurement, and imaging tissue spectroscopy) are listed in Table 2 for comparison purposes.

Method	Transcutaneous oxygen measurement	Tissue oximetry / NIRS
Measuring method	Clark electrode / Fluorescence Quenching	HSI technology
Measurement	Partial pressure of the gas dissolved in liquid after skin penetration	Measurement of the oxygen bound to hemoglobin in tissue
Measuring set-up	Sensor is glued gas-tight to the skin	Camera system (contact-free)
Measuring parameters	$tcpO_2$	StO_2 / THI
Spatially resolved information	No	Yes, imaging
Required sensor temperature	40 - 44°C	None
Effects	Local strong increase of the oxygen partial pressure*	None
Stable measured values after sensor application	ca. 5 - 10 min	ca. 10 sec
Limited application time at measuring point	4 -12 hours	Punctual time measurement only
Calibration before measurement	Yes	No
Drift of the measured values	Yes / No	No
Gas cylinder in system	Yes / No	No
Contact liquid required	Yes	No
Membrane change required	Yes	No
Measurement possible on damaged skin	No	Yes

Table 2: The oxygen binding curve of the blood depends strongly on the temperature.

4 SIGNIFICANCE FOR WOUND MEDICINE

Human tissue that has too little oxygen available for cell respiration can be described as critical tissue. In conventional subjective visual tissue inspection, critical tissue is not a tissue class, as it is difficult or impossible for the treating physician to recognize it with the human eye. However, based on the guidelines for wound treatment, an assessment of less perfused tissue or ischemia of the extremities should be carried out. Conventional techniques are used for this assessment [7]:

- *Patients with critical limb echemia (systolic ancle pressure of ≤ 50 mmHg or toe systolic pressure of ≤ 30 mmHg) usually have a $tcpO_2$ value of < 30 mmHg when breathing normobaric air;*
- *A $tcpO_2$ value of < 40 mmHg, obtained during breathing of normobaric, correlates with a reduced probability of healing of the amputation wound.*
- *An increase of the $tcpO_2$ value up to > 40 mmHg during normobaric air breathing after revascularization is usually connected with subsequent healing, although the increase in $tcpO_2$ might be delayed;*

A comparable assessment is given in [8]:

- *Ulceration of the foot in diabetes often heals when toe pressure is > 55 mmHg and $tcpO_2$ is > 50 mmHg.*
- *Healing is usually severely affected when toe pressure is < 30 mmHg and $tcpO_2$ is < 30 mmHg.*

It is known from scientific studies that the correlation between transcutaneous oxygen measurement ($tcpO_2$) and imaging tissue oximetry (StO_2 [%], NIR perfusion), which can be derived from the oxygen binding curve of hemoglobin, also exists in practice.
Three study results should be quoted here in extracts.
In [9], a study was made on the correlation of transcutaneous oxygen measurements with HSI imaging measurements (VIS tissue oximetry):

"A clear increase of OxyHgb of the HSI measurements with heated $tcpO_2$ sensors was observed, whereby it was observed that the $tcpO_2$, Sat and Sum measurements also increased with temperature. These measurements were influenced by heat inducing vasodilatation in the superficial skin layers. HSI measurements can be clinically useful for measuring wound healing potential as they correlate with $tcpO_2$ concentrations under normal physiological conditions"

In [10], a detailed study was performed on the correlation of transcutaneous oxygen measurements with imaging NIRS spectroscopy (tissue oximetry). An extract from the results is quoted below:

"There was a significant correlation between measurements of tissue oxygenation using tcpO₂ and NIR spectroscopy. NIR spectroscopy has the advantage of not requiring skin contact and measurements can even be performed in the wound bed. Further advantages are: Time (2 minutes vs. 90 minutes), disposable costs ($150 tcpO₂ vs. $0 NIR spectroscopy) and the ability to perform serial studies over time. Further studies are needed to specifiy, whether this information is useful in determining the response to HBOT or in predicting wound healing.

[…]The relationship between tcpO₂ (mmHg) and NIR spectrum (saturation in %) was defined as y = 0.93 x + 5.35 with a correlation coefficient of 0.92 and r2 = 0.84. "

Another current study on the correlation of imaging tissue oximetry to transcutaneous oxygen partial pressure measurement comes to comparable results and conclusions. [11]:

"RESULTS:
Interoperability reliability ranged from 86% to 94% for the four hyperspectral imaging devices, while intraoperator reliability ranged from 92% to 94%. The HT-Oxy, HT-Sat, TcpCO₂, and ABI of the diseased limbs correlated significantly with the severity of PVD. HT-Sat correlated significantly with tcpO₂ (R = 0.19), TcpCO₂ (R = -0.26), ABI (R = 0.42) and skin temperature (R = 0.56). HT-deoxy also correlated with TcpCO₂ (R = 0.27).

CONCLUSIONS:
This study shows the reliability of hyperspectral imaging compared to TCOM (tcpO₂ measurement), ABI, skin temperature and severity of PVD in a number of patients. Their correlation with other established modalities and the low interoperator and intraoperator variability may make this modality a useful screening tool in PVD. "

From the field of sensor-based tissue oximetry, there are a large number of studies on the correlation of the technologies "Transcutaneous oxygen measurement - NIRS tissue oximetry". The validation of the correspondence between imaging tissue oximetry and sensor-bound tissue oximetry is presented in [12,13].

Following from these results, the term critical tissue is used here as classification threshold for less perfused or ischemic tissue (in the wound). The decision to use this term results from the knowledge that this tissue does not yet show any necrotic or avital characteristics: It is known, however, that there is a high risk of tissue loss without the use of perfusion-enhancing measures.

5 Conclusion

- Transcutaneous measurement of oxygen partial pressure and imaging tissue oximetry are partially used in the same applications.
- The tcpO₂ measurement is more widespread, as these sensors were historically available for clinical use in the past and more studies exist on their application.
- The StO₂ measurement has clear advantages in the practical handling of the measurement.

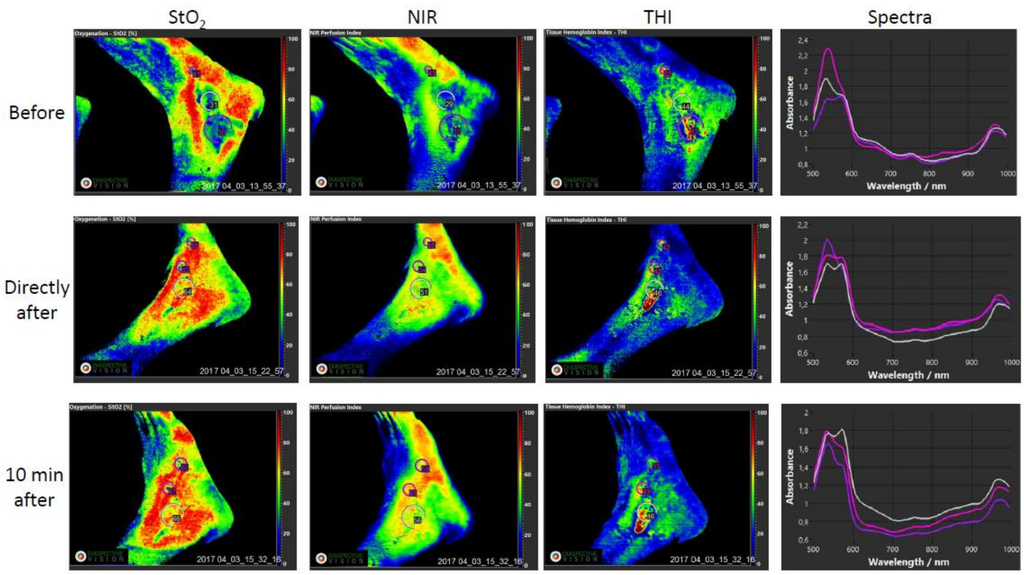

Figure 5: Measurements with the TIVITA® HSI camera before and after application of topical wound oxygen therapy (TWO₂) for 60 minutes. Comparison of tissue oxygen values measured before and after TWO₂ application:1. Significant improvement in oxygenation in superficial tissue (StO₂); 2. Significant improvement in oxygenation in deeper tissue layers (NIR); 3. Increase in total hemoglobin (THI); 4. Partially persistent effects on the entire distal lower limb and foot area.

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