ACTA ODONTOLOGICA SCANDINAVICA
2020, VOL. 78, NO. 1, 31–37
https://doi.org/10.1080/00016357.2019.1645353

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ORIGINAL ARTICLE

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Determination of baseline alveolar mucosa perfusion parameters using laser Doppler flowmetry and tissue spectrophotometry in healthy adults

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ABSTRACT

Objectives: To determine the baseline perfusion parameters of the alveolar mucosa using laser Doppler flowmetry and tissue spectrophotometry (LDF-TS) in healthy adults.

Material and methods: Forty-two healthy adult subjects of either sex were tested. The perfusion of the alveolar mucosa was evaluated using a laser Doppler flowmetry and tissue spectrophotometry using O2C 'oxygen to see' device. The measurements encompassed the maxillary and mandibular mucosa at 20 different points.

Results: The O2C device is a reliable method for noninvasive measurement of different perfusion parameters of the oral mucosa. The hemoglobin saturation values (So2 in %), as well as relative amount of hemoglobin in arbitrary units (AU) of the maxillary mucosa demonstrated lower values of that in the mandible. The flow value (AU) exhibited a significant difference in the posterior molar region only, while the velocity value (AU) showed a significant difference across all points except for the anterior region.

Conclusion: the present study provides a set of brand-new perfusion parameters of the microcirculation of the alveolar mucosa using LDF-TS. The study suggests a variation of the perfusion parameters between the maxilla and the mandible. Differences in the anatomy of the blood supply, the thickness of the mucosa and the cortical bone, may be attributed to this variation. Further studies using different probes and a combination of ultrasonic measurements and SDF imaging will aid in giving a better overview of the perfusion in the oral mucosa.

ARTICLE HISTORY
Received 15 January 2019
Revised 18 June 2019
Accepted 15 July 2019

KEYWORDS
Laser-Doppler flowmetry; tissue spectrophotometry; oxygenation; perfusion; baseline

Introduction

Adequate perfusion of tissues is an essential requirement to maintain the regular functions of every organ. The bloodstream carries oxygen to all organs and transports toxic metabolic byproducts to different excretion sites [1,2].

Multiple techniques to monitor the perfusion directly such as pulse oximetry and indirectly like with Doppler ultrasonography and angiography have been developed and are being used clinically on a daily basis [3–5]. Other costly and time-consuming methods like positron emission tomography (PET) and single photon emission computed tomography (SPECT) can also be used to assess the perfusion of tissue [6,7].

A technique combining white light spectrometry and laser Doppler spectroscopy using the O2C 'oxygen to see' device (LEA-Medizintechnik, Gießen, Germany) enables noninvasive assessment of postcapillary microcirculation. The device produces a continuous white light ranging from 500 to 800 nm and a white laser light of 830 nm simultaneously [8].

White light is used for the detection of hemoglobin parameters;

1. Postcapillary oxygen saturation (So2): this value shows the lowest oxygen saturation of the tissue. Venous oxygenation is an excellent indicator of venous hypoxias, thus, making this value critical.
2. Relative amount of hemoglobin (rHb) in the microvessels which is a measurement of relative filling of blood vessels with hemoglobin.

The movement of red blood cells within the vessels causes a Doppler shift, which can be detected with the probe and converted to arbitrary numerical values:

3. The flow of blood in the microcirculation shows how many erythrocytes move and at which velocity.
4. The velocity of the blood in microcirculation is a parameter that delivers no information on the quantity of transported blood and is rather the measurement of the average velocity of the blood in the microcirculation.

The O2C device has been used as a diagnostic tool mostly with organ transplantation and wound healing monitoring. The O2C device has also been deployed in the field of maxillofacial surgery, particularly as monitoring for soft and hard tissue reconstruction of the oral cavity and control of flap reperfusion [9,10].

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This study was conducted to determine the baseline perfusion parameters of the alveolar mucosa using laser Doppler flowmetry and tissue spectrophotometry (LDF-TS) in healthy adults. These parameters can be helpful in the future to compare the perfusion after surgical and reconstruction procedures in the alveolar cavity.

Material and methods

The study was carried out in 42 healthy adult subjects of either sex. The age range was 21–51 years, with a mean age of 28.1 ± 5.9 years. Convenience sampling was used to select test subjects. The perfusion of the alveolar mucosa was evaluated at 20 different points encompassing the overlying oral mucosa of the maxilla and the mandible approximately 5 mm from the mucogingival junction using laser Doppler flowmetry and tissue spectrophotometry as a noninvasive diagnostic tool.

Study design

Patient recruitment took place at the Department of Oral Surgery of Bonn University Dental Clinic. Patients who matched the inclusion and exclusion criteria were approached. Inclusion criteria were adults of either sex, age of 18 years and older, nonsmoker, no previous dental treatment (conservative, prosthodontic, endodontic treatments or previous trauma), no known medical history. Exclusion criteria were tobacco smoking, patients with known systemic diseases, pregnancy, history of chemotherapy or radiotherapy in head and neck region.

Measurements

Measurements were performed using a noninvasive LDF-TS system (O2C 'oxygen to see' device, LEA-Medizintechnik, Gießen, Germany) to assess oxygen saturation So2 (%), relative amount of hemoglobin rHb in arbitrary units (AU), blood flow (AU) and velocity (AU) of the oral alveolar mucosa at depth up to 3 mm. The location of the measurement's position was in the oral mucosa 5 mm away from the mucogingival junction in an apical direction. Twenty measurement sites were selected in the maxilla and the mandible of each patient.

Previous examinations showed that results obtained with the O2C device are reproducible and accurate [11–13]. However, these studies were conducted using the O2C device in an extraoral environment. Probes were fixed to the examined tissues using a special tape in these studies [11,12]. The challenging anatomy in the oral cavity in addition to the saliva's effect meant that fixing the probe to the oral mucosa using tape was not possible and an alternative method of application was required. Thus, the measurements were conducted using a modified pressure sensitive dental probe (Figure 1). The results were consistent using the modified probe while a direct application with the finger showed great discrepancies.

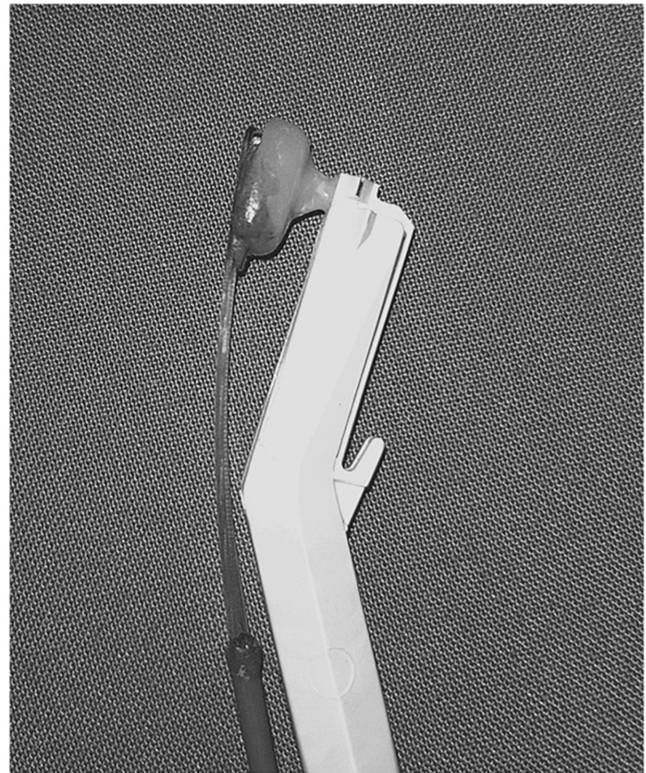

Figure 1. Modified pressure sensitive dental probe used as the carrier for the O2C sensor.

The O2C probe cannot be sterilized and, therefore, was attached to the dental instrument and covered with a transparent endoscopic protection cover (Ultracover, Microtek, Wertheim, Germany) as recommended by the manufacturer of the O2C device. Different covers have been used in the pre-studies to determine the effect of the cover material on the results of the measurement. The cover used in this study showed consistent results, whereas other covers were not reliable.

All measurements were performed using the LFX-2 probe (LEA-Medizintechnik, Gießen, Germany) that has a dimension of 5×5 mm. The measurement depth was predefined from the manufacturer at 3 mm. Conditions such as supine position, temperature-controlled room (22 °C), a dark environment to minimize interference from external light sources such as sun or fluorescent lamps were standardized. Each patient and examiner wore laser safety goggles. All measurements were performed by two experienced surgeons. Basic parameter such as age, height, weight and blood pressure (mmHg) were also recorded.

Measurements were performed for each quadrant starting from the anterior region going through to the posterior, tuber or retromolar region and ending at the palatal or lingual region of the premolars. The sites were allocated according to the diagram in Figure 2.

The probe was calibrated before each measurement session according to the instructions of the manufacturer. Each measurement consisted of a preliminary 5 seconds period. The additional period was included in the measurement protocol to give the examiner adequate time to place the probe accurately without compressing the area with more

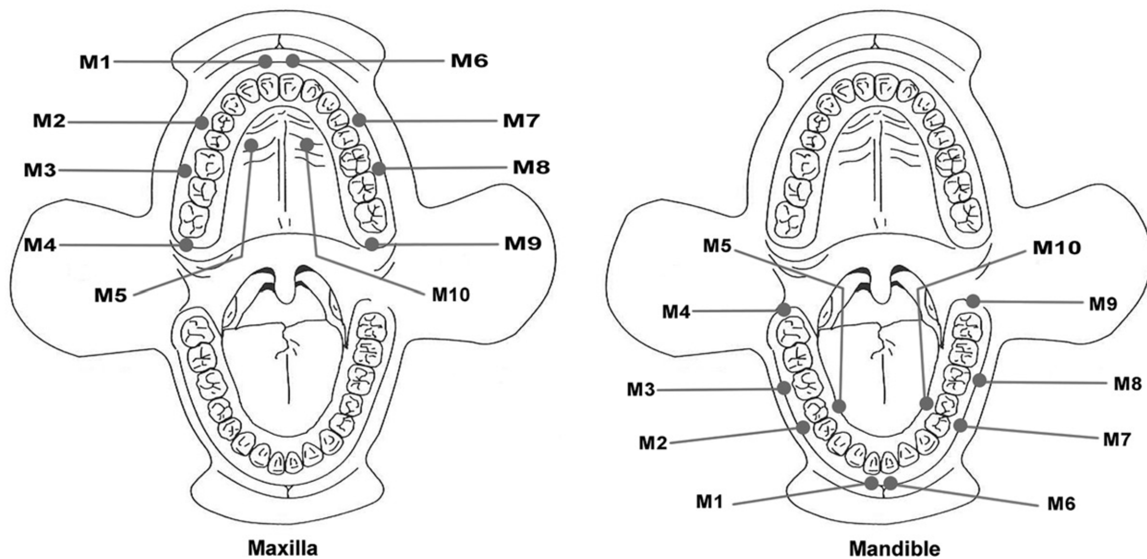

Figure 2. Diagram of measurement points in the maxillary and mandibular mucosa.

than 0.25 N force. The duration of the measurement was set at 15 s. During this period, measurements recorded with the O2C device were averaged and saved as mean number automatically. The period was set to more than 10 seconds to compensate for fluctuations caused by minimal bodily movements such as swallowing and breathing of the patient.

Different measurement points were clustered into the following zones to take the average values:

1. Maxillary or mandibular anterior region: measuring points M1 and M6;
2. Maxillary or mandibular posterior region: measuring points M2, M3, M7 and M8;
3. Tuber or retromolar region: measuring points M4 and M9;
4. Palatal or lingual region of the premolars: measuring points M5 and M10.

Statistical analysis

A Kolmogorov–Smirnov test was used to analyze the distribution of the values. Subsequently, the *t* test (Welch-test) was used to compare the heteroscedastic values. Statistical significance was set at 5% ($p \leq .05$). In the cases of multiple tests, a Bonferroni correction was performed to neutralize the alpha adjustment for multiple comparisons. The analysis was performed with SPSS software version 21 (IBM Corp., Armonk, NY, USA).

Results

Hemoglobin oxygenation (So2)

The average hemoglobin oxygenation for the entire maxilla was 75.6 ± 9 [%] while the mandibular counterpart had a significantly higher value at 77.2 ± 7.9 [%] ($p = .007$). The average value of the anterior region of the maxilla at 73.8 ± 8.2 showed a significant statistical lower oxygenation to the value of the anterior region of the mandible at 76.9 ± 8.9 [%] ($p = .02$). Measurements of the tuber region also demonstrated lower values with a statistically significant difference at 72.7 ± 7.1 [%] compared to the retromolar region at a higher value of 77.7 ± 7.2 [%] ($p < .001$). Measurements of the posterior region of the maxilla and the mandible, as well as the palatal and lingual areas of the premolars, showed no statistical differences (Table 1 and Figure 3(A)).

Table 1. Hemoglobin oxygenation (So2 values) and relative amount of hemoglobin (rHb) of different areas of the maxilla and the mandible.

Region	So2 (%)	SD	*p* value	rHb (AU)	SD	*p* Value
entire maxilla	75.6	9.0	.007	82.5	13.9	<.001
entire mandible	77.2	7.9		87.4	9.9	
anterior region - maxilla	73.8	8.2	.02	85.9	9.2	<.001
anterior region - mandible	76.9	8.9		90.6	6.7	
posterior region - maxilla	77.0	8.9	.782	89.6	11.9	.715
posterior region - mandible	76.8	7.6		89.2	8.7	
tuber region	72.7	7.1	<.001	80.6	10.6	.016
retromolar region	77.7	7.2		84.3	9.1	
palatal region of the premolars	72.2	10.6	.764	66.8	10.8	<.001
lingual region of the premolars	77.7	8.3		83.4	13.1	

SD: Standard deviation. (AU = arbitrary unit).

Relative amount of hemoglobin

The relative amount of the hemoglobin value of the entire mandible also demonstrated a significant difference 87.4 ± 9.9 [AU] compared to the maxilla with 82.5 ± 13.9 [AU] ($p < .001$). The anterior region of the maxilla had a value of 85.9 ± 9.2 [AU] significantly different compared to the anterior region of the mandible at 90.6 ± 6.7 [AU] ($p < .001$). Measurements of the lower retromolar region demonstrated a higher value at 84.3 ± 9.1 [AU] in comparison to the tuber region at 80.6 ± 10.6 [AU] ($p = .02$). In contrast to the results of So2, the relative amount of hemoglobin in the palatal and lingual area of the premolars was significantly different at 66.8 ± 10.8 [AU] and 83.4 ± 13.1 [AU] respectively ($p < .001$).

Measurements of the posterior region of the maxilla and the mandible (M2, M3, M7 and M8) exhibited no statistical differences (Table 1 and Figure 3(A)).

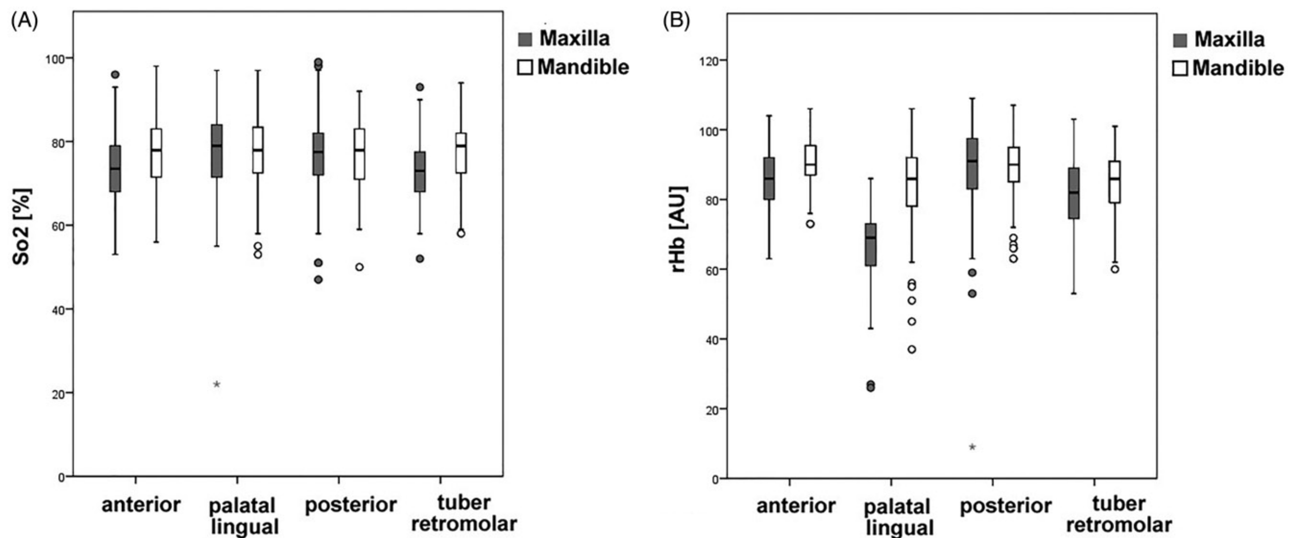

Figure 3. (A) Box plot diagrams indicating results of the comparison of hemoglobin oxygenation (So2 values in %) measured in the maxilla and the mandible. (B) Box plot diagrams indicating results of the comparison of the relative amount of hemoglobin (rHb values) measured in the maxilla and the mandible (AU = arbitrary unit).

Table 2. Blood flow and velocity values of different areas of the maxilla and the mandible.

Region	Flow (AU)	SD	*p* Value	Velocity (AU)	SD	*p* Value
entire maxilla	218.1	78.2	.556	30.5	8.4	.019
entire mandible	214.1	113.0		29.2	7.7	
anterior region - maxilla	219.1	75.0	.546	30.0	7.8	.326
anterior region - mandible	233.5	204.5		28.8	7.7	
posterior region - maxilla	246.5	86.1	.019	32.9	9.4	.015
posterior region - mandible	225.7	76.7		30.7	7.5	
tuber region	186.6	63.2	.168	25.7	6.0	.031
retromolar region	199.9	62.0		27.7	6.1	
palatal region of the premolars	191.7	61.5	.574	31.1	6.8	.021
lingual region of the premolars	185.8	72.7		28.2	8.9	

SD: Standard deviation (AU = arbitrary unit).

Blood flow and velocity

Comparing the values of the blood flow demonstrated a significant difference only in the posterior regions of the maxilla and mandible at 246.5 ± 86.1 [AU] and 225.7 ± 76.7 [AU] respectively ($p = .019$). Other regions had similar comparable values. The blood velocity, on the other hand, exhibited significant differences in all regions except in the anterior maxilla and mandible (Table 2 and Figure 4).

Discussion

Sufficient perfusion is essential for all cells to function correctly. Diseases, traumas, surgeries as well radiotherapy and chemotherapy have a considerable impact on the circulation of the affected organ. Noninvasive monitoring of the circulation is of great importance to minimize intervention time as well as trauma caused by invasive procedures. Laser Doppler flowmetry and tissue spectrophotometry (LDF-TS) measurements using the O2C device offers noninvasive, real-time monitoring capabilities of all perfusion parameter. The device has been extensively used in various fields of medicine such as angiogenesis research [14], neurosurgery [15–17], gastrointestinal reconstruction [18] wound healing [19,20] and vascular disease research [13,21].

The number of studies encompassing tissues of the oral cavity up to now has been limited. Hölzle and coworkers [9] performed monitoring of free flaps to detect early perfusion problems using the O2C device. The measurements were able to detect vascular complications in real time and decide over surgical revisions. A sudden reduction in blood flow and So2 values indicated an arterial occlusion, while a swift rise in hemoglobin concentration of more than 30% indicated venous congestion in transplant sites [10].

A pilot study at the Department of Oral Surgery in Bonn University Dental Clinic used the O2C device to compare the perfusion parameters of 20 healthy Han Chinese adult to those of 20 Caucasian adults. The measurements were performed at 8 different points (upper and lower vestibular mucosa of the incisors, palatal mucosa and cheek mucosa). The study showed a significant difference in perfusion values of Caucasian and the Han Chinese adults [22].

Another study was also performed to measure the perfusion parameters in different patient categories (healthy vs. with periodontal disease, with or without nicotine consumption or diabetes mellitus) after tooth extraction. Four measurements were performed at different dates (pre-extraction, on extraction day, seven days and fourteen days later). The study showed a significant statistical difference in oxygen saturation in smokers and diabetic patients compared to the control group. The flow value (AU) was significantly higher in periodontally affected teeth compared to those in the healthy group with no periodontal disease. [23].

Our current study was able to provide a set of brand-new baseline values of all perfusion parameters of the maxillary and mandibular mucosa at 20 different points using the O2C device in healthy adults. The measurement procedure should be coupled with a pressure sensitive dental probe to reduce unwanted pressure on the examination area influencing the microcirculation.

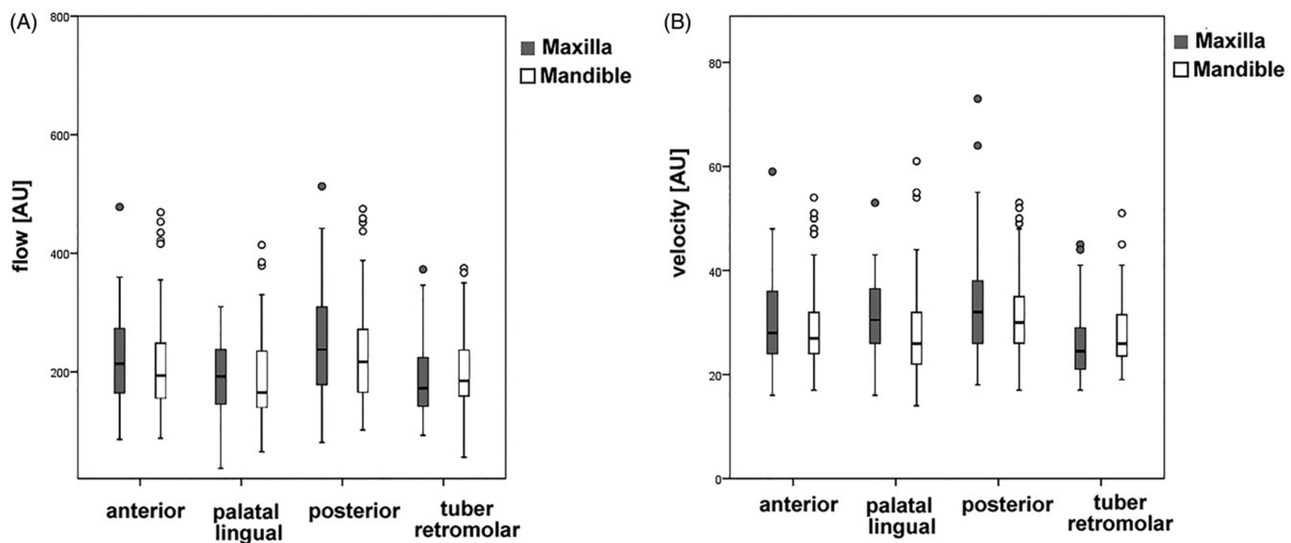

Figure 4. (A) Box plot diagrams indicating results of blood flow values measured in the maxilla and the mandible (AU = arbitrary unit). (B) Box plot diagrams comparing blood velocity values measured in the maxilla and the mandible (AU = arbitrary unit).

The measurement depth in this study was 3 mm and is predefined by the so-called separation in the probe. Other probes can perform measurements up to 8 mm in 2 separate channels. The gingiva was excluded in this study as the biotype of patients and the thickness of the tissues can vary greatly and accurate measurements with the 5×5 mm probe were not physically possible.

According to the results of the study, the hemoglobin saturation values (So2 in %), as well as the relative amount of hemoglobin (in AU) of the maxillary mucosa, demonstrated lower values compared to the mandible. The flow value (in AU) exhibited a significant difference in the posterior molar region only, while the velocity values (in AU) showed differences across all points except for the anterior region. These differences could be attributed to the variation of the oral mucosa thickness, neurovascular regulations, or environmental factors as well as the anatomical variation. We speculate that the thickness of the cortical bone in the mandible plays a role when comparing the results to the maxilla. The measurements of the O2C device are a representation of postcapillary circulation, up to a depth of 3 mm in this study. A thick cortex limits the amount of vascular communication with the bone marrow; this consequently leaves more oxygenated blood in the microcirculation and increases the values. Since the measurement of the flow value is a representation of the number of erythrocytes moving in the microcirculation, the value can be affected similarly in the posterior maxilla because the probe may be able to penetrate beyond the thin cortical bone giving higher values. A difference between the maxilla and the mandible regarding the velocity value can be expected due to differences in the diameter of the nutrient blood vessel as well as the number of primary branches. The anastomoses in the anterior region can be attributed to neutralizing such difference between the maxilla and the mandible. The effects of the environment and neurovascular changes should be minimal in this study since the measurements were standardized as described earlier in the article.

The thickness of the tissue can be assessed with an ultrasonic scan. A B-scan ultrasonic analysis of the maxillary gingiva showed that male subjects had thicker maxillary gingiva in comparison to females [24]. A newer A-scan measurement technique has been developed to achieve more precise results (measurement range: 0.25–6 mm with an axial resolution of 0.01 mm). This method has been used so far in implant-related research [25]. The technique can be combined in future studies with LDF-TS to get more information on the blood supply and perfusion of examined tissues while taking into consideration the thickness of the mucosa and the anatomical well-described concept of angiosomes [26].

Capillary microcirculation has also been studied using optical spectroscopic based microvascular imaging techniques. Orthogonal polarization spectral imaging and more recently sidestream dark-field (SDF) imaging, have demonstrated reproducible measurements of the capillary density of the gingiva [27,28]. Milstein and coworkers conducted measurements of microcirculation parameters to assess the differences between normal and alveolar cleft gingiva using the O2C device in addition to sidestream dark-field imaging [29]. The measurements showed significant differences in blood flow and velocity in areas of previous surgery. The SDF of the alveolar cleft gingiva demonstrated altered angiomorphology with notable large avascular zones [30] similar to the alveolar crest mucosa of edentulous jaws [26].

The data collected in this study is a representation of baseline values of postcapillary microcirculation in healthy adults. Our aim is to give a reference for future real-time measurements. A change in the parameters should be expected after surgical procedures; an increase in the flow and velocity values after surgery should indicate good healing due to the increased angiogenesis and proper utilization of the oxygen. A fall in the relative amount of hemoglobin, for instance, should indicate arterial congestion, whereas an increase in the value can be attributed to more venous congestion and edema formation.

Further clinical studies are needed to assess the pattern of changes in blood perfusion related to pathologies and following dentoalveolar surgery to obtain better values during healing stages. The clinical advantages of using the O2C device include providing detailed information about the perfusion parameters prior to surgical procedures such as soft or hard tissue augmentation or other reconstruction procedures, as well as consequent postoperative monitoring during the healing period.

Some limitations of this method are acknowledged, such as requiring proper training and standardized measurement conditions. Anatomical microvascular changes associated with tissue healing can be detected using the O2C device. However, the data cannot be linked to a certain microvascular network. Additional measurements using ultrasonic measurements and SDF imaging could be of great value in relation to the individual soft tissue thickness. The effects of the environment and neurovascular regulation should be taken into consideration when performing the measurements in a nonstandardized setting. Further studies with different probes are also required to assess the perfusion of the bone and mucosa after various surgical procedures.

Ethical Approval

The study was carried out according to the Declaration of Helsinki, and the study protocol was approved as a part of a general project in this field by the Ethics Committee of the Medical Faculty of the University of Bonn. (Ethikvotum Nr. 086/11).

Informed consent

Informed consent was obtained from all individual participants included in the study.

Disclosure statement

The authors declare that they have no conflict of interest.

Funding

This work was supported by the Department of Oral Surgery of Bonn University Clinic in Bonn, Germany.

References

[1] Treacher DF, Leach RM. Oxygen transport-1. Basic principles. BMJ. 1998;317:1302–1306.

[2] Doenecke D, Koolmann J, Fuchs G, et al. Die Zellatmung: Energetik und Prinzip der Atmungskette [Cell respiration: energetics and the principle of the respiratory chain]. In: Doenecke D, Koolmann J, Fuchs G, Gerok W, editors. Hrsg. Karlsons biochemie und pathobiochemie. Stuttgart: Thieme Verlag; 2005. p. 404–406.

[3] Stern MD. In vivo evaluation of microcirculation by coherent light scattering. Nature. 1975;254:56–58.

[4] Ruengsakulrach P, Brooks M, Hare DL, et al. Preoperative assessment of hand circulation by means of Doppler ultrasonography and the modified Allen test. J Thorac Cardiovasc Surg. 2001;121:526–531.

[5] Hui FK, Bain M, Obuchowski NA, et al. Mycotic aneurysm detection rates with cerebral angiography in patients with infective endocarditis. J NeuroIntervent Surg. 2015;7:449–452.

[6] Anderson H, Yap JT, Wells P, et al. Measurement of renal tumour and normal tissue perfusion using positron emission tomography in a phase II clinical trial of razoxane. Br J Cancer. 2003;89:262–267.

[7] Henneman MM, Chen J, Ypenburg C, et al. Phase analysis of gated myocardial perfusion single-photon emission computed tomography compared with tissue Doppler imaging for the assessment of left ventricular dyssynchrony. J Am Coll Cardiol. 2007;49:1708–1714.

[8] Krug A. Mikrozirkulation und Sauerstoffversorgung des Gewebes: Methode des so genannten O2C (oxygentosee) [Microcirculation and tissue oxygenation: method of the so-called O2C (oxygentosee)]. Phlebologie. 2006;35:300–312. German.

[9] Wang F, Loeffelbein DJ, Nolte D, et al. Free flap monitoring using simultaneous noninvasive laser Doppler flowmetry and tissue spectrophotometry. J Craniomaxillofac Surg. 2006;34:25–33.

[10] Hölzle F, Rau A, Loeffelbein DJ, et al. Results of monitoring fasciocutaneous, myocutaneous, osteocutaneous and perforator flaps: 4-year experience with 166 cases. Int J Oral Maxillofac Surg. 2010;39:21–28.

[11] Ghazanfari M, Vogt L, Banzer W, et al. Reproduzierbarkeit nichtinvasiver Durchblutungsmessung mit der Laser-Doppler-Spektroskopie [Reproducibility of non-invasive blood flow measurement with laser Doppler spectroscopy]. Phys Rehab Kur Med. 2002;12:330–336.

[12] Hölzle F, Swaid S, Nolte D, et al. Nutritive perfusion at donor site after microvascular fibula transfer. Microsurgery. 2003;23:306–312.

[13] Beckert S, Witte MB, Königsrainer A, et al. The impact of the micro-lightguide O2C for the quantification of tissue ischemia in diabetic foot ulcers. Diabetes Care. 2004;27:2863–2867.

[14] Scholz D, Ziegelhoeffer T, Helisch A, et al. Contribution of arteriogenesis and angiogenesis to postocclusive hindlimb perfusion in mice. J Mol Cell Cardiol. 2002;34:775–787.

[15] Walter B, Bauer R, Krug A, et al. Simultaneous measurement of local cortical blood flow and tissue oxygen saturation by near infra-red Laser Doppler flowmetry and remission spectroscopy in the pig brain . Acta Neurochir Suppl. 2002;81:197–199.

[16] Rejmstad P, Åkesson G, Åneman O, et al. A laser Doppler system for monitoring cerebral microcirculation: implementation and evaluation during neurosurgery. Med Biol Eng Comput. 2016;54:123–131.

[17] Sommer B, Weidinger CS, Wolf D, et al. Intraoperative continuous cerebral microcirculation measurement in patients with aneurysmal subarachnoid hemorrhage: preliminary data on the early administration of magnesium sulfate. BMC Anesthesiol. 2017;17:143.

[18] Buise MP, Ince C, Tilanus HW, et al. The effect of nitroglycerin on microvascular perfusion and oxygenation during gastric tube reconstruction. Anesth Analg. 2005;100:1107–1111.

[19] Harrison DK, McCollum PT, Newton DJ, et al. Amputation level assessment using lightguide spectrophotometry. Prosthet Orthot Int. 1995;19:139–147.

[20] Held M, Medved F, Petersen W, et al. A quantitative analysis of microcirculation in skin defects covered with topical wound dressings or a newly developed collagen matrix. Adv Skin Wound Care. 2017;30:517–521.

[21] Jørgensen LP, Schroeder TV. Micro-lightguide spectrophotometry for tissue perfusion in ischemic limbs. J Vasc Surg. 2012;56:746–752.

[22] Wang Y, Barry O, Wahl G, et al. [Pilot study of laser-Doppler flowmetry measurement of oral mucosa blood flow]. Beijing Da Xue Xue Bao Yi Xue Ban. 2016;48:697–701.

[23] Ciper N. Kombinierte Gewebespektrometrie- und Laser-Doppler-Messungen bei parodontal erkrankten Zähnen sowie bei Abheilungsvorgängen nach Extraktionen [Combined Tissue Spectrometry and Laser Doppler measurements on periodontally

diseased teeth as well as on healing after extraction] [Inaugural-Dissertation]. German: Medical Faculty, University of Bonn; 2016 [urn:nbn:de:hbz:5n-42297].

[24] Tzoumpas M, Mohr B, Kurtulus-Waschulewski I, et al. The use of high-frequency ultrasound in the measurement of thickness of the maxillary attached gingiva. Int J Prosthodont. 2015;28: 374–382.

[25] Schwarz F, Claus C, Becker K. Correlation between horizontal mucosal thickness and probing depths at healthy and diseased implant sites. Clin Oral Impl Res. 2017;28:1158–1163.

[26] Kleinheinz J, Büchter A, Kruse-Lösler B, et al. Incision design in implant dentistry based on vascularization of the mucosa. Clin Oral Implants Res. 2005;16:518–523.

[27] Lindeboom JA, Mathura KR, Harkisoen S, et al. Effect of smoking on the gingival capillary density: assessment of gingival capillary density with orthogonal polarization spectral imaging. J Clin Periodontol. 2005;32:1208–1212.

[28] Lindeboom JA, Mathura KR, Ramsoekh D, et al. The assessment of the gingival capillary density with orthogonal spectral polarization (OPS) imaging. Arch Oral Biol. 2006;51:697–702.

[29] Milstein DM, Mathura KR, Lindeboom JA, et al. The temporal course of mucoperiosteal flap revascularization at guided bone regeneration-treated implant sites: a pilot study. J Clin Periodontol. 2009;36:892–897.

[30] Milstein DM, Cheung YW, Žiūkaitė L, et al. An integrative approach for comparing microcirculation between normal and alveolar cleft gingiva in children scheduled for secondary bone grafting procedures. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013;115:304–309.