Study Group Name: **Microcirculation Study Group**

Topic: **Investigation of gingival microcirculation**

Members of study group:

- Principal Investigator: Prof. Dr. Vág János
- Supervisors: Dr. Mikecs Barbara, Dr. Fazekas Réka, Dr. Molnár Eszter, Dr. Gánti Bernadett (maternity leave)
- PhD fellow: Dr. Nagy Tamás László
- Coworkers: Dr. Molnár Bálint, Dr. Bartha Ferenc, Dr. Dobos Andrea, Dr. Sólyom Eleonóra

Study title: **Investigation of gingival microcirculation**

Over the past nine years, our study group has carried out a number of studies monitoring the microcirculation of the gingiva, performing physiological tests or following the healing of oral/periodontal surgery. Several such studies are currently being carried out, some of them in collaboration with the Department of Prosthodontics and the Department of Periodontology.

1. Effect of age and sex on blood flow

Our team used the Post Occlusive Reactive Hyperemia (PORH) test to map local and temporal changes in blood flow in healthy gingiva. In case of natural teeth, ischemia was observed in the marginal gingiva during the horizontal PORH test for up to 5 seconds during the occlusion and hyperemia for up to 5 minutes after the release. This test is currently used in patients over 50 years of age to investigate the effect of age and gender in different age groups.

A parallel study, also mapping age groups and sexes, is investigating endothelium-dependent vasodilation using acetylcholine solution. In this study, participants will also undergo blood

sampling and different sex hormone levels will be analysed.

2. Effect of different 3D implant head configurations on peri-implant soft and hard tissue healing in the aesthetic zone and long-term follow-up - a randomized controlled trial

The examination is carried out in cooperation with the Clinic of Prosthodontics. The aim of this randomised controlled clinical trial is to investigate the hard and soft tissue volume changes around custom CAD/CAM made vs factory made zirconia healing abutments 4 months after their fixation, in case of immediate implantation (conventional loading). Our team performs blood flow measurements before surgery and also during follow-up for both types of implant abutments, and we also perform ultrasound gingival thickness measurements in our clinic to assess soft tissue volume.

3. Investigation of gingival blood flow after periodontal plastic surgery

Our team is carrying out this study in collaboration with the Periodontology Clinic. The aim of our working group is to monitor the wound healing of patients who have undergone gum recession surgery in the case of xenograft application. Recently, more and more studies have been using Laser Speckle Contrast Imager (LSCI); a non-invasive, two-dimensional, real-time imaging method to assess tissue microcirculation. Our previous clinical studies suggest that this technique may be a useful tool to assess adequate circulation during surgical procedures and to evaluate wound healing. We further aim to optimise the use of this tool for human oral mucosal examination.

4. Kinetics of gingival blood flow after alveolar bone grafting using LSCI

The examination is carried out in cooperation with the Periodontology Clinic. In periodontal surgery, different incisions, flaps, grafts and wound closure techniques are used, resulting in varying degrees and duration of ischemia. However, post-operative wound healing is significantly influenced by the preservation of the gingival microvasculature and the revascularisation of the surgical site. Our group aims to study the influence of different types of surgery on regeneration. In our studies, we use a Laser Speckle Contrast Imager (LSCI) device (Fazekas, Molnar et al. 2019), which can measure capillary blood flow non-invasively and reproducibly (Molnar, Fazekas et al. 2018), even covering the entire surgical site, thus providing an opportunity for objective, comparative evaluation of the effect of surgical factors on healing.

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Winning grants:

- Semmelweis Egyetem Fogorvostudományi Kari Pályázat 2017. Gánti Bernadett, Vág János: Az íny microcirculatiojának és vastagságának a vizsgálata.
- Semmelweis Egyetem Fogorvostudományi Kari Pályázat 2018. Gánti Bernadett, Vág János. Spreading vasodilatatio jelenlétének vizsgálata humán gingiván a nemek függvényében
- KFI_16-1-2017-0409, szakmai vezető, Élettani kutatásokon és méréseken alapuló új ínyformázási eljárás és prototípus elemek kifejlesztése fogászati implantációhoz 2018.01.01.-2019.12.31.
- Semmelweis Egyetem Fogorvostudományi Kari Pályázat 2019. Mikecs Barabara, Vág János Implantátumok és fogak körüli ínyszövet vasodilatációs reaktivitásának vizsgálata.
- Semmelweis Egyetem Fogorvostudományi Kari Pályázat 2020. Mikecs Barabara, Gánti Bernadett, Vág János Vasodilatatio vizsgálata a humán gingivában acetilkolin és nitrogén-monoxid alkalmazása során.
- Semmelweis Egyetem Fogorvostudományi Kari Pályázat 2021. Mikecs Barbara, Nagy Tamás László, Vág János: Nemek közti különbségek vizsgálata a véráramlás tekintetében.
- OTKA FK_2020 – 135348, témavezető: Dr. Molnár Bálint
- Semmelweis Egyetem Fogorvostudományi Kari Pályázat 2023. Nagy Tamás László, Mikecs Barbara, Vág János: A nemi hormonok keringést befolyásoló hatása a humán gingiva véráramlásában.

Presentations on Congresses:

- Nagy T, Mikecs B, Vág J, Dose-related effect of acetylcholine on human gingival blood flow, Semmelweis Symposium Budapest, 2024
- Nagy T, Mikecs B, Vág J: A nemi hormonok keringést befolyásoló hatása a humán gingiva véráramlásában. Kari Pályázat, Semmelweis Egyetem, Budapest 2023.
- Nagy T, Mikecs B, Vág J, Sex-related differences in vasodilation after application of acetylcholine compared to nitrogen-monoxide in human gingiva, Semmelweis Symposium Budapest, poster presentation, 2023.
- Nagy T, Mikecs B, Vág J, Endothelium-Dependent and Non-Dependent Vasodilation in Human Gingiva, CED/IADR-NOF Oral Health Research Congress, Brussels,

Belgium, virtual oral presentation, 2021. szeptember 16-18.

- R. Fazekas, B. Molnár, F. Bartha, F. Veress, K. Weninger: Blood flow kinetics after alveolar ridge augmentation assessed by Laser Speckle Contrast Imaging. EAO Digital Days 2021
- Mikecs B, Nagy T, Fazekas R, Vág J, Age and Gender-Related Differences in Human Gingival Blood Flow, CED/IADR-NOF Oral Health Research Congress, Brussels, Belgium, virtual oral presentation, 2021. szeptember 16-18.
- Mikecs B, Nagy T, Vág J, Investigation of Vasodilatation Induced by Different Solutions in Human Gingiva, Integrating Vascular Biology & Medicine, European Society of Microcirculation, Online Conference, 2021.
- Mikecs B, Nagy T, Vág J, Nemek közti különbségek vizsgálata a gingiva véráramlásának tekintetében, Kari Pályázat, Semmelweis Egyetem, Budapest 2021.
- Mikecs B, Gánti B, Vág J, Vasodilatatio vizsgálata a humán gingivában acetilkolin és nitrogén-monoxid alkalmazása során, Kari Pályázat, Semmelweis Egyetem, Budapest, 2020
- Mikecs B, Fazekas R, Molnár E, Gánti B, Lohinai Zs, Veress G, Vág J, Gingival Blood Flow at Teeth Versus Dental Implants, CED/IADR-NOF Oral Health Research Congress, Madrid, Spain, 2019 szeptember 19-21.
- Gánti B, Mikecs B, Fekete Á, Heródek P, Makk R, Lohinai Zs, Vág J, Regional Effect of Epinephrine on the Microcirculation of Human Gingiva, CED/IADR-NOF Oral Health Research Congress, Madrid, Spain, 2019 szeptember 19-21.
- Mikecs B, Molnár E, Fazekas R, Gánti B, Vág J, Post-occlusive blood flow measurement of the oral gingiva surrounding natural teeth and dental implants, PhD tudományos napok, Semmelweis Egyetem, Budapest, 2019. április 25-26.
- Mikecs B, Veress G, Vág J, Implantátumok és fogak körüli ínyszövet vasodilatációs reaktivitásának vizsgálata, Kari pályázat, Semmelweis Egyetem, Budapest 2019.
- Mikecs B, Vág J, Molnár E, Fazekas R, Gánti B, Post-occlusive blood flow measurement of the oral gingiva surrounding natural teeth and dental implants, EFOP-3.6.2-16-2017-00006 Translational interactive hands-on training and conference on epithelial ion transport including two symposia „natibacterial and mucolytic therapy in cystic fibrosis" and „Research in oeal cavity-from basic science to clinical use", Budapest, 2018.
- Gánti B, Molnár E, Fazekas R, Mikecs B, Lohinai Z, Vág J, Investigation of the

spreading vasodilatation on human gingiva, EFOP-3.6.2-16-2017-00006 Translational interactive hands-on training and conference on epithelial ion transport including two symposia antibacterial and mucolytic therapy in cystic fibrosis" and „Research in oeal cavity-from basic science to clinical use", Budapest, 2018

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- Mikecs B., Molnár B., Fazekas R., Molnár E., Tóth Zs., Vág J.: A humán palatinalis nyálkahártya gyógyulásának vizsgálata Laser Speckle Contrast Imager segítségével műtéti sebzést követően. Magyar Haemorheologiai Társaság XXV., a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság és a Magyar Szabadgyök-Kutató Társaság VI. Közös Kongresszusa, Balatonkenese, 2018.
- Gánti B., Mikecs B., Mikó S., Lohinai Zs., Vág J.: Spreading vazodilatáció jelenlétének vizsgálata humán fogínyben. Magyar Haemorheologiai Társaság XXV., a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság és a Magyar Szabadgyök-Kutató Társaság VI. Közös Kongresszusa, Balatonkenese, 2018.

Publications:

- 2022: Vag J, Nagy T, Mikecs B. „Sex-related differences in endothelium-dependent vasodilation of human gingiva" BMC Oral Health. 2022, DOI 10.1186/s12903-022-02186-2. PMID: PMC9107103 https://pubmed.ncbi.nlm.nih.gov/35562729/
- 2021: Mikecs B, Vág J, Gerber G, Molnár B, Feigl G, Shahbazi A. „Revisiting the vascularity of the keratinized gingiva in the maxillary esthetic zone." BMC Oral Health. 2021, DOI: 10.1186/s12903-021-01445-y.PMID: 33766000 https://pubmed.ncbi.nlm.nih.gov/33766000/
- 2021: Mikecs B, Molnár E, Fazekas R, Vág J. „Microvascular reactivity of peri-implant mucosa in humans: effect of abutment material." Int J Periodontics Restorative Dent. 2021 Sep-Oct; 41(5):761-768. doi:10.11607/prd.5343. PMID:34547080 https://pubmed.ncbi.nlm.nih.gov/34547080/
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- 2019: Fazekas, R., B. Molnar, L. Kohidai, O. Lang, E. Molnar, B. Ganti, G. Michailovits, P. Windisch and J. Vag (2019). "Blood flow kinetics of a xenogeneic collagen matrix following a vestibuloplasty procedure in the human gingiva-An explorative study." Oral Dis **25**(7): 1780-1788.https://www.ncbi.nlm.nih.gov/pubmed/31336001. DOI: 10.1111/odi.13163.
- 2019: Fazekas, R., E. Molnar, B. Mikecs, Z. Lohinai and J. Vag (2019). "A Novel Approach to Monitoring Graft Neovascularization in the Human Gingiva." J Vis Exp(143): e58535.https://www.ncbi.nlm.nih.gov/pubmed/30688301. DOI: 10.3791/58535.
- 2019: Molnar, B., E. Molnar, R. Fazekas, B. Ganti, B. Mikecs and J. Vag (2019). "Assessment of Palatal Mucosal Wound Healing Following Connective-Tissue Harvesting by Laser Speckle Contrast Imaging: An Observational Case Series Study." Int J Periodontics Restorative Dent **39**(2): e64-e70. https://www.ncbi.nlm.nih.gov/pubmed/30794263. DOI: 10.11607/prd.3878.
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- 2018: Fazekas, R., E. Molnar, P. Nagy, B. Mikecs, P. Windisch and J. Vag (2018). "A Proposed Method for Assessing the Appropriate Timing of Early Implant Placements: A Case Report." J Oral Implantol **44**(5): 378383.https://www.ncbi.nlm.nih.gov/pubmed/29870305. DOI: 10.1563/aaid-joi-D-

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- 2018: Molnar, E., R. Fazekas, Z. Lohinai, Z. Toth and J. Vag (2018). "Assessment of the testretest reliability of human gingival blood flow measurements by Laser Speckle Contrast Imaging in a healthy cohort." Microcirculation **25**(2).https://www.ncbi.nlm.nih.gov/pubmed/28976050. DOI: 10.1111/micc.12420.
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