Peripheral blood perfusion controlled by auricular vagus nerve stimulation

J.C. Széles¹, S. Kampusch², E. Kaniušas²

¹University Clinic for Surgery, Vienna General Hospital, Medical University Vienna, Austria
²Institute of Electrodynamics, Microwave and Circuit Engineering, Vienna University of Technology, Austria
¹E-mail: jozsef.szeles@meduniwien.ac.at

Introduction. Electrical stimulation of vagal nerve fibers comprises an effective treatment in therapy refractory epilepsy, major depression, chronic pain, and congestive heart failure [1], [2]. There is recent evidence for vagus nerve stimulation effects on a range of other diseases, including neuropsychiatric, movement, or cardiovascular disorders [1]-[3].

Various methods are used to modulate vagus nerve activity. These include stimulation of the vagus cervical trunk as well as stimulation of the auricular branch of the vagus nerve (ABVN) [1]-[4]; both modulate specific brain regions involved in autonomous nervous control (Fig. 1) [5]. Our group has shown that (afferent) ABVN stimulation modulates (efferent) sympathetic control of vascular tone, which is highly beneficial in the treatment of vascular disorders [2], [6], [7]. An increase in the blood perfusion index was reported, i.e. a reduction in vascular resistance and corresponding increase in blood perfusion.

This short paper focuses on favourable effects of percutaneous ABVN stimulation on peripheral blood perfusion in the foot of patients, with advantages of minimal-invasiveness, selective stimulation of Aβ-fibers, low risk, and reduced side effects [3].

Method. Percutaneous ABVN stimulation was performed to investigate effects of external (parasympathetic) nervous system control on peripheral blood perfusion (Fig. 1). Three needle electrodes for stimulation were inserted at vagally innervated regions of the auricle. The stimulation device (P-Stim; Biegler GmbH) delivered monophasic pulses with changing polarity [3]. Blood perfusion was estimated by skin temperature using infrared imaging (VarioCAM; InfraTec GmbH).

The stimulation was applied on two patients, suffering from peripheral arterial disease and a chronic diabetic wound, respectively. The stimulation protocol included phases of acclimatization, stimulation and pause (Fig. 2 a and b).

![Fig. 1: Experimental setup with potential signal transduction pathways](image-url)
Fig. 3 a). Specific regions of interest (ROI in Fig. 2b and Fig. 3b) were analysed using histograms to compile changes of the skin and wound temperature. Temperature counts were normalized to their maximum at the given protocol steps (Fig. 2 a and Fig. 3 a). The attained normalized counts were subtracted from each other to derive temporal changes in ROI-temperature.

**Results.** Stimulation effects on blood perfusion considering peripheral arterial disease are summarized in Fig. 2 c, d. The normalized difference E-D in

![Stimulation protocol](attachment://stimulation_protocol.png)

![Temperature distribution](attachment://temperature_distribution.png)

**Fig. 2.** (a) External control by percutaneous auricular vagus nerve stimulation and (b) monitoring of forefoot skin temperature in a female patient (with peripheral arterial disease). (c) Exemplary relative probabilities $p$ of temperature in the region of interest (ROI) at time instances C, D, and E. (d) Normalized differences $d$ of temperature counts in the ROI for paused stimulation (D-C) versus active stimulation (E-D).
Fig. 2 d shows a corresponding increase in higher temperatures as well as a decrease in lower temperatures during stimulation, and an opposite effect during paused stimulation (D-C). The initial phases of acclimatization (B-A) and stimulation (C-B) are not shown due to extensive cooling in the first 60 minutes of measurement (26.2°C to 22.4°C, mean over ROI), which strongly overlapped with expected stimulation effects. Histograms of time instances D and E (Fig. 2 c) indicate favourable effects of stimulation with a shift to higher temperatures in the ROI. Distinct maxima in the normalized differences (Fig. 2 d) are due to significantly lower mean temperature in the toe than in the rest of the ROI.

Fig. 3: (a) External control by percutaneous auricular vagus nerve stimulation and (b) monitoring of wound temperature in a male (diabetic) patient. (c) Normalized differences $d$ of temperature counts in the region of interest (ROI) during acclimatization (B-A), active stimulation (C-B, E-D), and paused stimulation (D-C).
Fig. 3c shows analogous results of a diabetic chronic wound. Heating effects can be observed during acclimatization and first stimulation phase (32.7 °C to 33°C, mean over ROI), with the particular stimulation effects being hidden. However, the second stimulation cycle yields obvious stimulation effects, i.e. an increase in higher temperatures and a decrease in medium temperatures (around 33 °C), with a favourable out-of-phase behaviour in the differences D-C and E-D. The heterogeneous temperature distribution and a slight increase in lowest temperatures during stimulation (E-D) can be expected due to a better reperfusion of non-necrotic tissue in the ROI. Stimulation effects are less pronounced compared to Fig. 2d, which could be due to the already higher mean temperature in the wound region (32.7 °C versus 26.2 °C).

**Discussion.** Percutaneous electrical stimulation of the auricular branch of the vagus nerve seems to yield favourable effects on peripheral skin temperature and thus on peripheral blood perfusion. Since only two cases with peripheral arterial disease and a chronic diabetic wound were included, further studies are required to validate the observed effects. The severity of symptoms seems to be an important factor to be considered in future patient selection. The presented study was limited by relatively low ambient temperature (25 °C), which impaired the results, i.e. the acclimatization phases appeared to be too short. No adverse or aggravating effects of stimulation were observed.

Clinical applications of the auricular stimulation include the treatment of peripheral arterial disease (e.g., prolongation of pain free walking distance [8]), or of chronic diabetic wounds (e.g., conversion into active wounds, improved local oxygenation, metabolism, and anti-inflammatory effects [2], [7]).

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**References**


7. Kaniusas E., Gbaoui L., Széles J.C. et al. Validation of auricular electrostimulation by heart rate variability and blood perfusion: possibilities and
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¹University Clinic for Surgery, Vienna General Hospital, Medical University Vienna, Austria
²Institute of Electrodynamics, Microwave and Circuit Engineering, Vienna University of Technology, Austria

Percutaneous auricular vagus nerve stimulation was performed to investigate effects of external nervous system control on peripheral blood perfusion. Blood perfusion was monitored by temperature changes using infrared imaging. Favourable effects of the stimulation were shown in two patients suffering from peripheral arterial disease and chronic diabetic wound, respectively. Besides an absolute increase in mean temperature, the stimulation evoked widening of higher temperature and shrinkage of lower temperature regions.