Thermal imaging as a method to study the effect of induced ischemia on vasomotion activity

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Abstract

Vasomotion is an auto-regulation mechanism that optimizes blood distribution within the microcirculatory system. Thermal imaging is an interesting approach to measure this phenomena. Previous studies have detected that vasomotric blood flow is quantifiable as temperature micro oscillations in the frequency range of 0,005 - 0,15 Hz. Four healthy subject was recruited to investigate the possibilities of measuring changes in vasomotric blood flow caused by partial occlusion of blood supply by using thermal imaging. The temperature oscillations in the skin were measured with an infrared camera. Measurement were done under normal conditions and with 50% restriction of hands blood supply by brachial cuff. Data processing involved correction of artifacts seen in the temperature recording. An investigation seeking reasons for these artifacts led to findings of limitations in the thermal camera used for recording. Morlet continuous wavelet transform was used on the corrected temperature recording to find the frequency content in the micro temperature oscillations. Statistical analysis of the mean amplitude values within the frequency bands showed no significant difference between the magnitudes of uncuffed and cuffed. Results show thermal imaging might not be sensitive enough to detect vasomotion and clear limitations in the experimental setup.

I. Introduction

The use of thermal imaging to study the phenomena of vasomotion might present a new biomaker for the treatment of patients going into shock.[1,2] Vasomotion is the phenomena of oscillating changes in the capillary vessel diameter enforced by smooth muscle cells. This phenomena occurs in the microcirculatory system as an autoregulatory mechanism that optimizes blood distribution within the microcirculatory system.[3-6] Micro temperature oscillating changes are the source of thermal waves, from the blood flow, propagating from microvessels toward the skin surface. [7] Although there have been several studies, which have investigated the occurrences of vasomotion within the capillary network, only few have used thermal imaging as approach.[8-10] With a better knowledge of vasomotion it might be possible to add new parameters in the monitoring of intensive care patients. Particularly patients in danger of developing hypoxia due to shock as this affects alterations in the microcirculatory system and interfere with the perfusion.[1,2] New methods for studying vasomotric activity arise and thermal imaging presents advantages in larger sample area and by being non invasive. Previous studies detected that the vasomotric blood flow is quantifiable as temperature micro oscillations within three frequency bands of endothelial $(0,005 - 0,02Hz)$, neurogenic $(0,02 - 0,05Hz)$ and myogenic $(0,05 - 0,15Hz)$ origin. [3,7-9] The significance of these frequency band during disease are example vise shown in a decrease in amplitude of endothelial blood flow oscillations which assumed to be a biomaker for endothelial dysfunction, that indicates cardiovascular disorders such as arterial hyper-

tension and cardiac ischemia.[7] Therefore the interest of this study is to investigate thermal imaging's ability to detect, if there are vasomotric changes in the micro temperature oscillations of skin depending on hypoxia in the microcirculatory system.

II. Methodology

i. Subjects

Four healthy subjects, 3 males and 1 female, average age 30.5 ± 12.5 years were recruited. Subjects were recruited within the project group. Two subject were right handed and two left handed. No subjects consumed caffeine, alcoholic beverages, or medicine before the experiment. All subjects were aware of experiment procedure and were willing to participate. Subjects showed no signs of cardiac disease or tremors.

ii. Test setting

Subjects were placed in an upholstered adjustable chair for a comfortable sitting position. The hand was stabilized by a vacuum pillow covered with microfiber tissue, which was attached on the armrest. Xenics Gobi 640 $17\mu m$ GigE, sensitivity $0.005°$, resolution 480 x 640, infrared camera (Xenics NV, Belgium) was positioned with a tripod $37,5 \pm 1,0$ cm over subjects dominant hand and connected via Ethernet cable with a computer. The setup is shown in figure 1.

iii. Software setting

Xeneth 2.6 software (Xenics NV, Belgium) installed on computer was used for data acquisition. The sampling rate was set to $6,25$ Hz, the file format to a raw data $.xvi\ file$ and both, room and ambient temperature, to $25°C$ and emissivity of observed object to 1.

iv. Experimental procedure

The experiment involved 2 x 20 min data acquisition periods. One under normal conditions without the presence of hypoxia in the targeted hand, and another where blood flow restriction enforces hypoxia. The camera was set to warm up for at least 15 min. Meanwhile systolic blood pressure was measured to determine total occlusion pressure (TOP) of subjects dominant arm. Needed brachial cuff pressure (p_{cuff}) for restricting 50% blood flow is 30% of the TOP. TOP was calculated with $p_{cuff} = TOP \times 0.3$.[11] The subjects had at least 30 minutes to adjust to the room temperature.

Figure 1: *Test setting at Region Hospital Nordjylland showing setup of chair, thermal camera and computer.*

The brachial cuff for enforcing blood flow restriction in the second acquisition period was affixed on subjects dominant arm without tightening it. Subject is placed in the chair and its dominant hand is stabled with the vacuum pillow. Lens focus was adjusted for a sharp image of the hand.

After the first measurement under normal conditions, pressure in the cuff was set to enforce 50 % blood flow restriction. The subject did not move the hand while cuff tightening. To minimize any possible movement bias the subject was not allowed to move or speak during the whole procedure.

v. Data processing

v.1 Preparation of data

The acquired xvi. files were read and processed in MATLAB R2017b. The header in the beginning of each file and frame was removed. Af-

terwards the raw uint 16 pixel intensities was divided into frames.

v.2 Regions of interest

Regions of interest (ROIs) were selected on behalf of getting full representation of the hand. As shown in figure 2 originating from the fingertips elongating down the hand to the beginning of the wrist. 28 ROIs were chosen. Each region represent one pixel intensity in the 480 x 640 image matrix.

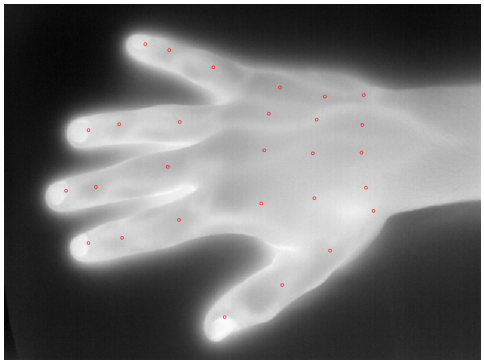

Figure 2: *Frame from thermal image of subject 1. Red dots showing the 28 ROIs.*

This pixel represents an area of the hand with a diameter of $417\mu m$.

v.3 Artifacts

Under visual inspection of the temperature trace over time, some unexplainable jumps were present. These jumps were characterized as artifacts made by the camera. From the raw data of all regions four types of artifacts were characterized. A noise component is observed during the whole recording. Adjustments of the shutter from non-uniformity correction due to the internal temperature. The intervals between two jumps contain a drift component. An overall drift component can also be observed. Figure 3 shows the signal of one ROI to present the occurring artifacts.

The artifacts is assumed to occurs because each microbolometer in the focal plane array has a different response to the same infrared excitation. This leads the camera to perform a non-uniformity correction, where all microbolometers are re calibrated, resulting in an offset.[12,13]

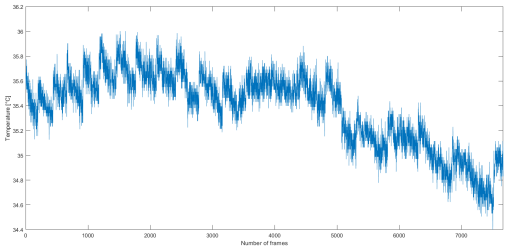

Figure 3: *The original data of region 15 in the uncuffed recording of subject 1 used as an example to outline the artifacts. The intensity is shown over time.*

v.4 Correction method

The shutter adjustments and the drift between these adjustments seen in figure 3 corrupted the original the most. Therefore a correction method based on linear regression was implemented. A linear regression is made on each drift between shutter adjustments. As shown in figure 4, the found regression lines er are put together at the middle point of an adjustment forming a new temperature recording base. Figure 5 show how the residual are projected on to the newly corrected base forming a new temperature trace.

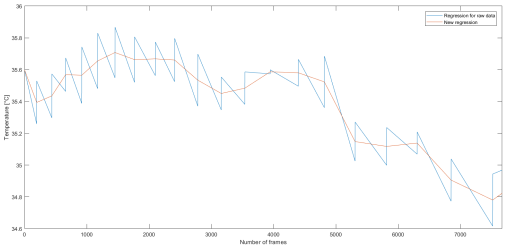

Figure 4: *Connected regression line of the original data of region 15 in the uncuffed recording of subject 1 in blue. New created orientation line of the same recording in the same region shown in red.*

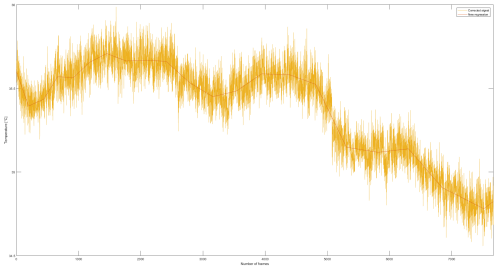

Figure 5: *Orientation line based on the data of the uncuffed recording of subject 1 in region 15 shown in red. Corrected signal of the same data in yellow.*

v.5 Time-frequency analysis

Analysis of the corrected data is done in the time frequency domain by the use of Morlet continues wavelet transform (CWT). The CWT present higher resolution of frequency content in low frequency signals, compared the Fourier transformation, why this method is used to look for the low frequency content of the temperature micro oscillations.[5,6]

In the CWT, the signal is convoluted with the Morlet wavelet in equation 1:

$$W(\tau, s) = \int_{-\infty}^{\infty} x(\tau) \frac{1}{\sqrt{\mid s \mid}} \psi * (\frac{\tau - t}{s}) dt \quad (1)$$

A scalogram showing the time-frequency content of the uncorrected signal given as output of the CWT can be seen in figure 6.

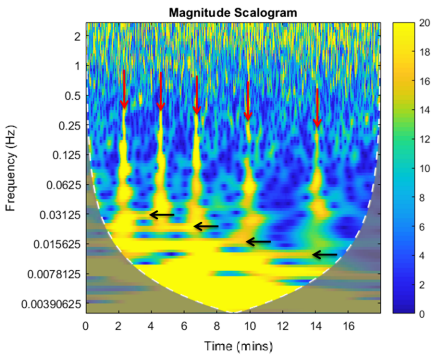

Figure 6: *Scalogram from subject 3, uncorrected uncuffed recording in ROI 8.*

The jump artifacts within the signal are clearly shown as high magnitude spikes in the scalogram. In figure 6 those spikes are marked with red arrows. The black arrows mark the drift that is contained in between each jump artifact, as seen the the frequency of the drift is not uniform.

After application of the correction method, each signal trace and its corresponding scalogram was submitted a manual control. During this control it was noticed that some signals still contained jump artifacts which hampers correct data analysis for those signals traces. Five RIOs have been chosen valid for further data analysis. The criterion for this selection was, that those ROIs showed good response to the correction method and no jump artifacts was visible in the scalogram. The five selected ROIs are 10, 14, 20, 21 and 22, these can be seen in figure 2.

The corrected signal from 6 is shown in 7 also showing the frequency bands of interest.

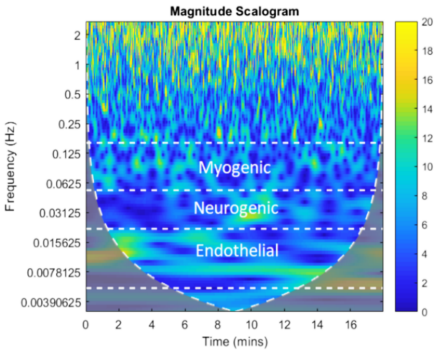

Figure 7: *Scalogram from subject 3, corrected uncuffed recording from ROI 8. Frequency band of endothelial, neurogenic and myogenic are shown*

The combination of a valid corrected signal across all subjects corresponding to the same ROI is needed for equally comparison between subjects, why only five regions could be used for further data analysis.

vi. Statistical approach

The magnitude within the scalograms of both conditions was compared for each subject. This comparison is conducted for the five ROI within the endothelial, neurogenic and myogenic frequency band. Therefore the magni-

tude values a scalogram provides in the frequency range $0.005 - 0.15\ Hz$ have been allocated to the corresponding frequency band. In every recording one mean value was computed for each frequency band. Those mean magnitudes for engothelial, neurogenic and myogenic band are visualized by boxplots. To test the statistical significance of the difference between the mean magnitudes a paired t-test has been applied.

III. Results

The box plots shown in figure 8 display the mean magnitude for each subject ordered by color in both conditions. A box plot is made for each region and frequency band. The line connecting uncuffed and cuffed condition indicates if the magnitude increased or decreased.

Throughout the combination of frequency band and regions no clear pattern are created by the four subjects. In each frequency band the mean magnitude both increase and decrease for each subject. Only subject two shows a clear pattern before and after the intervention were mean magnitude seem to decrease in every frequency band and region.

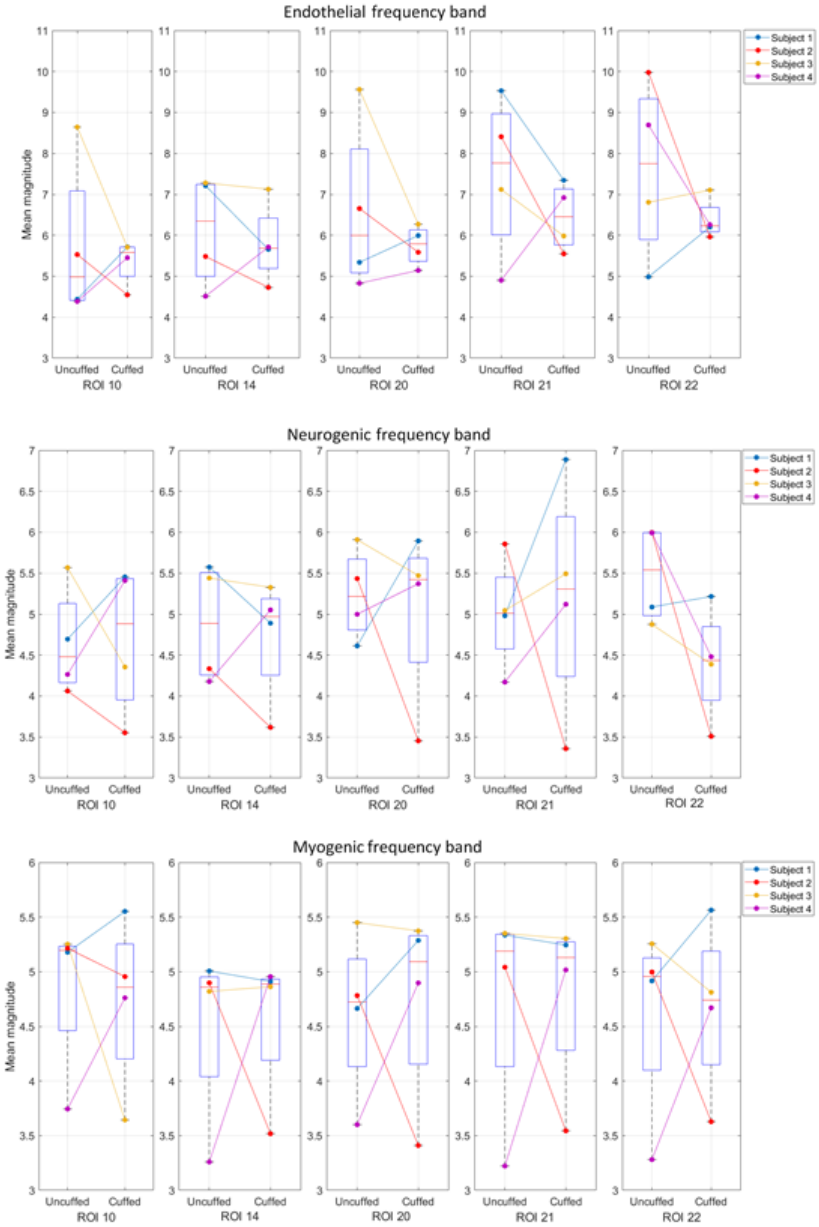

Figure 8: *Box plots showing the mean magnitudes for each subject within endothelial, neurogenic and myogenic frequency bands.*

With the values visualized by the box plots in figure a paired t-test provides the following p-values (table 1).

Table 1: *Table showing the p-values corresponding to specific ROI in correlation with frequency band.*

	p-endo	p-myo	p-neuro
ROI 10	0.7116	0.8454	0.9389
ROI 14	0.6254	0.9237	0.6955
ROI 20	0.4141	0.9237	0.8004
ROI 21	0.4062	0.9564	0.8452
ROI 22	0.3826	0.9323	0.1552

IV. Discussion

This study investigates the thesis, if thermal imaging is sensitive enough to measure the effects of vasomotion activity, and thereby investigate if changes in the microcirculatory system caused by a 50 % restriction of blood flow occur.

i. Results

The obvious assumption, based on the presented p-values, that there are no changes in the microcirculatory system or rather in vasomotion by 50% restriction of blood flow can be substantiated by two reasons. Firstly that the microcirculatory system is independent of the macrocirculatory system in terms of vasomotion activity. The reason for this is that the available amount of blood in the microcirculatory system is dependent on the amount of blood the macrocirculatory system provides. Consequently this explanation can be excluded. Another explanation for the insignificant result could be by incorrect brachial occlusion. Incorrect occlusion would yield insufficient restriction for affecting the microcirculatory system. Also the blood pressure measurements of three subjects delivered high values around 140 mmHg and 150 mmHg. Since those three subject were in different age and shape, a suspicion for incorrect values arise. Even if the blood pressure monitor delivered wrongly high values, the outcome of the second measurement would not have been influenced negatively. This would only lead to a calculated occlusion pressure higher than the one needed to reach the intended restriction, which would just lead to a larger difference between both conditions. It would be more problematic with a occlusion level to low. All blood pressure measurements were conduced and verified by a professional anesthesiologist.

The mean values that the paired t-test is based on, are extracted from the cwt data in the specific frequency bands. Though the cone of influence (COI) has not been taken into consideration. This might be preferable to exclude, because the data outside of the COI is containing areas where the edge effect is significant and these data might not be representative for the result. A way this could have been achieved was by generating a mask to collect the data inside the COI and only include these values in the calculation of the means. By excluding the data outside of COI it might have lead to different results.

The approach of the statistical test is a paired t-test to test for significance differences within the dataset. This method is mainly used because of the study design, where it is determined if there is a difference before and after two conditions, within each subject. It is assumed that the data is normal distributed by the assumption that there are a natural variance withing the population, why a parametric test is used. But with the small sample size it is unknown if the dataset is normal or non-normally distributed. In case of non-normally distribution a non-parametric test should be used. In this case a Wilcoxon signed rank test would be the approach for the statistical test. This test does not require a normal distribution in the population and is focusing on the population median value instead of the population mean like the paired t-test [14].

ii. Critique of study design

The small sample size of four subjects applied to the statistical methods are not sufficiently meaningful. With a larger amount of subjects this study would get a more meaningful result.

A larger amount of subjects might therefore have provided a significant difference between both conditions. An even gender distribution might also have been preferable. Originally a larger amount of subjects was planned to be recruited for the experiment. However, the notice of artifacts in the signal lead to the determination of not recruiting more subjects. Instead the focus was put on finding the origin of these artifacts and find a way to bypass these. Furthermore the statistics might not have lead to any valid results with these artifacts in the signal, even with a greater amount of subjects.

Other limitations might be that the subjects hands had to be stabilized by a vacuum pillow with the assumption the subjects were still, but this does not give sufficient support to inhibit every movements of the subject. A mechanism for better stabilization of the hands should be included. An approach to compensate for instability of the hand during the experiment could have been to include image alignment in the data processing to limit the drawbacks of possible movements in the recordings. Furthermore with the used setup exact same conditions for each subject cannot be granted. For instance the room temperature should have been measured beforehand and taken into consideration before the start of each experiment to create the same conditions for all subjects. The presetting of the room temperature might have affected the data. This suspicion is enhanced by regarding subject 1*s* hand temperature which was 38°C. Also by regarding the hand temperature of 26°C of subjects 2 and 3, who had cold hands during the measurement, this suspicion is enhanced. The software settings should be verified and if necessary changed beforehand of the experiment. An optimization of the test setting would require a more controlled setup of the experiment and a thermal camera of higher quality preferable of a cooled type.

iii. Limitations in using thermal camera

Due to the corrupted temperature reading the correction method was implemented, which clearly affects parts of the signal in specific ROIs. The pixel drift increases with increasing distance to the center of the thermal image why pixel drift of ROIs located in the outer areas of the thermal image cannot be completely compensated for with the implemented correction method. The explanation for this is likely that the correction method is based on the assumption that the drift component in every interval is linear. This assumption might be wrong and a correction method that uses another regression method or combines different regression methods might adjust the artifacts in a better way. As a result the ROIs located in the outer area of the thermal image were excluded from the data analysis. Another camera might also be preferable to reduce the risks of technical artifacts like these. It should be noticed that one of the recordings, of subject 2 had no jump artifacts in the signal traces in the uncuffed recording, but two in the cuffed. This subject is the only in which there can be seen a pattern as a decrease in the mean magnitude of all the frequencies bands from the intervention, this is further illustrated on figure 8. If no jump artifacts had been present, the general tendency of the mean magnitudes from the data might have looked different, assumable with an decrease in mean magnitude like in subject 2's case.

Furthermore the smaller the observed area the closer the thermal camera has to be to this area. Thus the area represented by one pixel gets smaller. Within this study one pixel represents an area with a diameter around 417tm. Whereas previous studies observed smaller areas which means that the pixel represent a smaller area. With the use of a larger ROI, it might be that the amount of inverse dilating capillaries is equal and thereby canceling each other out. Due to inverse dilating capillaries there might be no changes over time measurable because the frequency contents are occurring alternating in the different capillaries. In addition, it is obvious that the artifacts content in the signal is significantly higher than in the temperature signals detected in previous studies. Comparing the signals the question

arises if the artifacts overlaps or suppresses the frequency content of vasomotric activity. Even though temperature changes over time in the skin were detected, it is uncertain, if this signal just represents the general skin temperature or also vasomotric activity.

V. Conclusion

The results of this study indicate that thermal imaging is not sensitive enough for detecting vasomotion activity. There have been no findings of a statistical significant difference in the dataset between the two conditions investigated, indicated by the high p-values in table 1. Despite no findings, this study provides information about key points that should be considered when with thermal imaging, for instance that the regions that is of most interest should be placed in the center of the thermal image. Further investigation in this field is needed, to show thermal imaging as a promising technique for detecting vasomotion activity.

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