APARATURA
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Safety conditions in dynamic IT examinations of rheumatoid arthritis lesions

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Keywords: infrared thermography, cooling, ice water

ABSTRACT:

Purpose of the article: Human skin temperature distribution is a source of clinically relevant information about tissue pathological process and can be observed with the use of non-contact ad non-invasive measuring technique named infrared thermography (IT). The aim of the study is to establish dynamic IT measurement safety conditions in RA examination in order to prepare the refined study protocol which provides for extracting the most reliable diagnostic thermal data.
Experimental part: Thirty participants (20% of males) with diagnosed RA were included in this study. The protocol consisted in registration of thermal recovery processes after immersing left and right foot separately in ice water of less than 0 Celsius degrees. Cooling procedure included immersing left and right foot separately in ice water for 5 seconds. Separate recordings of left and right foot temperature changes were performed for 3 minute periods. The following joint temperatures were measured: ankle joint and 5 metatarsophalangeal joints.
Conclusions: Difference between the moment right after immersion and the moment after 3-minute recovery appeared to be the lowest in two different patients' ankle joints. These results suggest that the slowest rewarming rate occurs in the area of ankle joint.

Warunki BHP w badaniach zmian w reumatoidalnym zapaleniu stawów za pomocą termografii dynamicznej

Słowa kluczowe: termografia w podczerwieni, chłodzenie, woda z lodem

STRESZCZENIE:

Cel artykułu: Rozkład temperatury skóry ludzkiej stanowi źródło istotnej klinicznie informacji o patologicznym procesie toczącym się w tkance i można go obserwować za pomocą bezkontaktowej oraz nieinwazyjnej techniki pomiarowej zwanej termografią w podczerwieni (IT). Celem artykułu jest ustanowienie warunków bezpieczeństwa pomiaru za pomocą termografii dynamicznej w badaniach reumatoidalnego zapalenia stawów w celu przygotowania udoskonalonego protokołu badawczego, który zapewnia wydobycie najbardziej istotnych diagnostycznych danych termicznych.
Część eksperymentalna: Trzydziestu uczestników (20% mężczyzn) ze zdiagnozowanym RZS zostało włączonych do badania. Protokół uwzględniał rejestrację termicznego powrotu do stanu wyjściowego po zanurzeniu oddzielnie lewej i prawej stopy w wodzie z lodem o temperaturze mniejszej niż 0°C . Procedura chłodzenia polegała na oddzielnym zanurzeniu lewej i prawej stopy w wodzie z lodem na 5 sekund. Wykonano oddzielne 3-minutowe nagrania zmian temperatur lewej i prawej stopy. Zmierzono temperatury następujących stawów: stawu skokowo-goleniowego oraz stawów śródstopno-paliczkowych.
Wnioski: Różnica pomiędzy momentem bezpośrednio po zanurzeniu a momentem po 3-minutowej rejestracji okazała się być najniższa w stawach skokowo-goleniowych u dwóch pacjentów. Te wyniki sugerują, że najwolniejsze tempo ponownego nagrzewania występuje w obszarze stawu skokowego.

1. INTRODUCTION

Human skin is the organ which protects human body against environmental unfavourable conditions. Additionally, it plays one of the key roles in thermoregulation, in other words, it is enrolled in maintaining constant body temperature over time which is crucial for human survival. Physiological responses to heat and cold stress include: vasodilation and vasoconstriction, sweating, nonshivering thermogenesis, piloerection, shivering, and altered behaviour [1]. Skin temperature distribution as well as its abnormal patterns are a source of clinically relevant information about tissue pathological process and can be observed with the use of non-contact ad non-invasive measuring technique named infrared thermography (IT). Its low price and easy access are the great advantages over admittedly more accurate, but not neutral for human health diagnostic methods including magnetic resonance imaging and radiography. In order to provide patient's safety it is necessary to look for not harmful, easy to use for medical staff medical device and provide the best possible measurement quality. Apart from clinical diagnostics and veterinary medicine, there is a wide scope of IT applications: e.g. building construction, environmental engineering, metallurgy, food industry etc. Recent studies have also proved its usefulness in ergonomics and confirmed its usability for evaluating muscle activity and upright working posture [21]. Among IT measurement methods, two different approaches can be distinguished: passive method, where single thermogram of analysed object is taken, and active method, where temperature registration over time is performed following stimulus application. The great advantage of active thermography over passive thermography is that it is to a lesser extent dependent on environmental factors and it gives information about temperature value in selected, arbitrary time point. However, providing proper measurement conditions, adjusting study protocol and excluding unfavourable external and internal factors is crucial for extracting most exact examination results. Agents that affect thermovisual examinations can be divided into environmental, individual and technical factors [2]. The most significant environmental factor is ambient temperature. There are two kinds of individual factors: intrinsic factors that like age, gender, genetics that we are not able to manipulate, and extrinsic factors that are adjustable [20]. The influence of age on joint temperature distribution in RA have already been described e.g. between two age groups, below and over 65 years old. The last group: technical factors are dependent on protocol plan and there is an obvious influence of the researcher on its features and study procedure associated with them. Awareness of confounding factors can aid to exclude them and construct well prepared examination procedure. Applications of dynamic thermography has been widely described in literature. Herman [3] noted its beneficiary properties in melanoma diagnosis, House et al. described its use as a diagnostic test of hands and feet of hand-arm vibration syndrome (HAVS) cases and controls [4]. Local hyperthermia can also be observed in rheumatoid lesions. Rheumatoid arthritis is chronic, inflammatory disease which manifests itself in joint pain, swelling and hyperthermia and may lead to bone erosions in more advanced stages. Changes of thermophysical properties of tissue covered by inflammation can be thus observed with the use of thermovision camera. According to this, the aim of the study is to establish dynamic IT measurement safety conditions in RA examination in order to prepare the refined study protocol which provides for extracting the most reliable diagnostic thermal data.

2. EXPERIMENTAL PART

2.1 Subjects

Thirty participants (20% of males) with diagnosed RA were included in this study. Inclusion criteria for patients recruited for the study included: age above 18 years old, the duration of treatment above 1 year. Patients were excluded if they were under the age of 18 years, the duration of treatment under 1 year, rheumatoid factor below 50 IU/mL. Subject's body weight was measured using a scale with resolution of 100 g. The subject's height was measured by stadiometer. All subjects were examined by a medical doctor prior to beginning the thermovision measurements. According to declaration of Helsinki, all volunteers signed informed consent for participation in the study. Procedures were approved by Bioethical Committee of Medical University of Bialystok.

2.2 Measurement protocol

Study procedure was based on dynamic thermography method with the use of ice water as stimulus and included two approaches: first, establishment of the most convenient cooling period was performed. The protocol consisted in registration of thermal recovery processes after immersing left and right foot separately in ice water of less than 0 Celsius degrees. RA patients were examined with the use of newly adjusted cooling procedure, which included immersing left and right foot separately in ice water for 5 seconds. Separate recordings of left and right foot temperature changes were performed for 3 minute periods. The following joint temperatures were measured: ankle joint and 5 metatarsophalangeal joints. Thermovision camera FLIR E40 at a distance of 1.0 m from the subject was used for skin temperature evaluation (FLIR, Estonia). The real integrated resolution of the camera was 160×120 pixel, the temperatures ranging from –20 Celsius degrees to +120 Celsius degrees, thermal sensitivity <0.07 Celsius degrees at +30°, accuracy ±1 Celsius degree. The camera had a valid certificate. It was calibrated for reproducibility and accuracy of readings according to the Glamorgan's guidelines [18]. Thermograms and active thermography recordings were taken in participant's sitting position, ambient temperature 23 Celsius degrees. Camera was placed perpendicularly to the scanned surface. To minimize the influence of physiological factors on the measurement outcome, the participants were told to stay in seated position for 10 minutes in the examination room before the registration began. For registering thermal recordings and generating temporal plots FLIR ResearchIR Software (Belgium) was used.

2.3 Statistical analysis

Means and standard deviations were calculated for the demographic data of all participants. All of the dependent variables were statistically analyzed using an independent t-test to detect any differences between the left and right foot. Temperature differences pre- and post-cooling were evaluated by Wilcoxon test. A value of $p < .05$ was considered significant. Computer software Statistica 21.0 (StatSoft, Tulsa, OK, USA) was used for analysis.

3. RESULTS AND DISCUSSION

Thirty RA patients (mean age 51.9 (11.95) years old) were recruited in this study. The mean Body Mass Index (BMI) was 25.3 (3.95) kg/m^2. Before ice water immersion thermal image acquisition of participants' both feet was performed. As a result of the procedure, 60 thermal image of 30 participants were accomplished. Figure 1 presents examples of thermograms for participant's left foot pre-cooling and post-cooling (measured right after 5-second cooling). Foot areas marked as cursors correspond to human joints; cursor 1 – ankle joint, cursors: 2-6 – metatarsophalangeal joints.

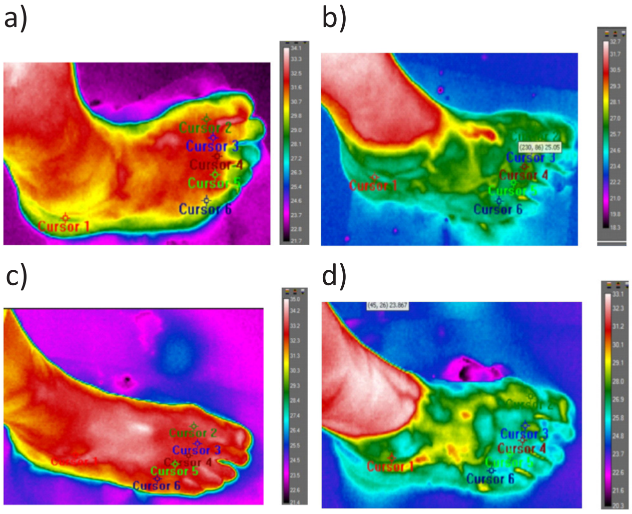

Figure 1 1 Comparison of the right foot: a), c) pre-cooling; b), d) post-cooling for exemplary RA patient

Firstly, comparison of pre-cooling temperatures, post-cooling temperatures and the temperatures after 3-minute recovery between left and right foot temperature was performed. The calculations revealed no pre-cooling neither post-cooling significant differences (p> .05). Significant between--feet differences were found for ankle joint in temperatures after 3-minute thermal recovery (p< .05). Thus, the analysis of pre- and post-cooling differences was performed for left feet only. Thermal differences between post-cooling and the temperatures after thermal recovery were accomplished for both feet. The analysis of temperature differences between pre- and post-cooling directly was performed for RA patients. Table 1 presents that between pre- and post-cooling statistically significant differences were observed for all measured regions (p< .05). The results suggest that the lowest temperature difference occurred in MTP1 in left foot of one of the participants (like previously mentioned, all participants were examined for the same, established immersion period). Surprisingly, in this area the temperature increased by 0.6 Celsius degrees. The greatest difference occurred in MTP4 of participant's left foot (the temperature fell by 8.90 Celsius degrees).

The comparison in temperature differences (Celsius degrees) between the post-cooling and after 3-minute recovery in RA patients is presented in Table 2-3. In left foot statistically significant differences were found for 5 out of 6 measured regions (all MTP joints), p< .05. Similar results were obtained for right foot: all regions except

Table 1 Temperature differences (Celsius degrees) between pre- and post-cooling directly in RA patients' particular regions of left foot

Region of the left foot	Pre-cooling			Post-cooling			p
	Min [°C]	Max [°C]	Mean [°C] (SD)	Min [°C]	Max [°C]	Mean [°C] (SD)	
Ankle joint	28.1	33.1	30.24 (1.47)	23.9	30.1	26.49 (1.99)	< .05
MTP1 joint	26.1	33.9	29.33 (2.61)	22.2	28.2	24.60 (2.23)	< .05
MTP2 joint	27.3	34.1	29.66 (2.42)	21.3	28.7	24.11 (2.26)	< .05
MTP3 joint	27.4	33.7	29.47 (2.37)	22.4	27.5	24.49 (1.67)	< .05
MTP4 joint	28.1	33.4	29.67 (2.00)	22.5	27.5	24.23 (1.66)	< .05
MTP5 joint	27.3	32.7	29.44 (1.69)	21.3	28.0	24.17 (1.97)	< .05

ankle joints exhibited between post-cooling and after 3-minute recording statistically significant differences ($p< .05$). The results shows that the lowest difference prevailed in ankle joint of participant's left foot and also ankle joint of participant's right foot: 0 Celsius degrees in both cases. However this was noted not for the same patient. Interestingly, in few cases the temperature after 3-minute recovery fell. This situation occurred for the following joints: MTP1 of left foot and ankle joint of right foot (in case of two participants). The greatest difference was observed two times. In both cases the increase of 4.9 Celsius degrees was observed and it affected the following joints of two different participants: MTP3 and MTP5.

Table 2 Temperature differences (Celsius degrees) between post-cooling and after 3-minute recovery in RA patients' particular regions of left foot

Region of the left foot	Post-cooling			After 3 minutes of recovery			p
	Min [°C]	Max [°C]	Mean [°C] (SD)	Min [°C]	Max [°C]	Mean [°C] (SD)	
Ankle joint	23.9	30.1	26.49 (1.99)	26.3	31.2	28.36 (1.65)	< .05
MTP1 joint	22.2	28.2	24.60 (2.23)	24.4	30.6	27.00 (2.21)	< .05
MTP2 joint	21.3	28.7	24.11 (2.26)	25.3	31.2	27.54 (1.93)	< .05
MTP3 joint	22.4	27.5	24.49 (1.67)	25.9	30.7	28.04 (1.63)	< .05
MTP4 joint	22.5	27.5	24.23 (1.66)	26.5	30.9	28.21 (1.27)	< .05
MTP5 joint	21.3	28.0	24.17 (1.97)	26.1	30.3	27.67 (1.34)	< .05

Table 3 Temperature differences (Celsius degrees) between the post-cooling and after 3-minute recovery in RA patients' particular regions of right foot

Region of the right foot	Post-cooling			After 3 minutes of recovery			p
	Min [°C]	Max [°C]	Mean [°C] (SD)	Min [°C]	Max [°C]	Mean [°C] (SD)	
Ankle joint	22.7	29.2	26.23 (1.71)	24.0	28.1	26.70 (1.36)	0.214
MTP1 join	22.7	28.1	24.74 (1.88)	24.9	30.5	27.38 (1.99)	< .05 < .05
MTP2 joint	23.4	27.9	24.73 (1.63)	24.9	30.8	28.09 (1.79)	< .05 < .05
MTP3 joint	23.2	27.5	24.67 (1.35)	23.4	30.4	28.10 (1.98)	< .05 < .05
MTP4 joint	22.8	26.5	24.50 (1.35)	26.6	29.7	28.22 (1.15)	< .05 < .05
MTP5 joint	23.3	27.0	24.96 (1.22)	25.1	29.0	27.58 (1.38)	< .05

Finally, 60 graphs of foot 3-minute thermal recovery to steady-state were plotted with the use of ResearchIR programme. The exemplary plot accomplished for the exemplary study participant is shown in Figure 2. Each of the coloured curves correspond to certain foot joint of the participant.

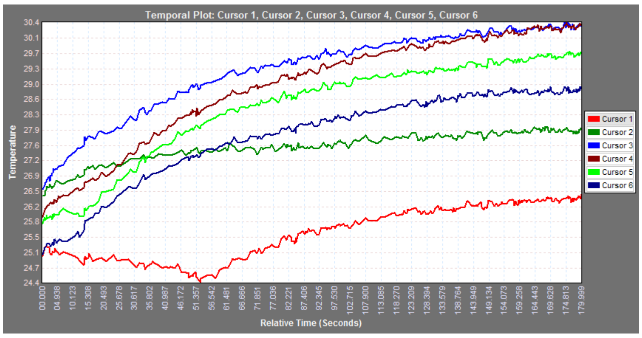

Figure 2 The right foot of exemplary patient during 3-minute thermal recovery to steady-state

Adjusting measurement conditions and excluding factors that could possibly affect results of the measurement is one of the inseparable parts of refined examination protocol in every meaningful study. As presented before, agents that affect thermovisual examinations can be divided into environmental, individual and technical factors [2]. Among environmental factors, the most important is ambient temperature. Cuevas et al. describe that extremities have the tendency to present lower temperature in low ambient temperature and recommend room temperature of 22-24 Celsius degrees for thermovisual examinations. When adjusting room temperature, it is important to know features characteristic for the disease which the study aims to diagnose. Rheumatoid arthritis is the disease which manifests itself in inflammatory lesions localized mostly in joints of hands and feet. According to et al. these are easily localised in cool conditions below 20 Celsius degrees [5]. In our study we propose different approach. We suggest applying cold stimulus (which is ice water of temperature below 0 Celsius degrees) to highlight the difference between inflammatory and healthy tissue, and then observing temperature changes standard room temperature of 23 Celsius degrees. This approach is reasonable as Herman [3] reported that dynamic thermography is much less dependent on ambient temperatures and conditions and noted that after cooling in active method during thermal recovery, the difference in tissue properties result in temperature differences between the lesion and healthy tissue.

According to Cuevas et al. [2], the next important group of factors are individual factors: intrinsic factors and extrinsic factors. Firstly the analysis of intrinsic factors will be provided. Few authors reported the impact of gender difference on skin thermal patterns in humans. Karki et al. [6] explained that due to higher fat percentages women are able to maintain warmer temperatures following cold stimulation. In our study, it is discernible that female temperature evolutions following cold stimulation exhibit less rapid leap and are more constant compared to rewarming period of male representative. Haas et al. [7] have indicated that males exhibit a more quick rewarming in hand after cold stimulation. These results are in accordance with the results obtained in current paper, as among the group of RA patient the highest temperature at the endpoint of rewarming period was achieved by male participant (31.1 Celsius degrees for metatarsophalangeal joint in left foot).

Among intrinsic factors, age is not less important. Rasmussen and Mercer [8] described a slower rewarming process in elderly individuals after local cooling of the hands and feet. These results are in accordance with our study. Comparison of rewarming pattern between 5-second cooling period in RA patients revealed that none of RA participants (mean age, standard deviation) exhibited as high temperature at the endpoint of rewarming period as 24-year old male. However, not great difference was observed (31.1 Celsius degrees for metatarsophalangeal joint number 3 for 55 year old man versus 31.3 Celsius degrees for metatarsophalangeal joint number 5 in 24 year old male).

According to the region of the body chosen for the examination, the next worth considering agent is circadian rhythm. Due to the fact that certain parts of the body exhibit temperature differences over the course of a day, it is necessary to perform examination of particular body region in the same time of a day. Krauchi and Wirz-Justice [9] reported that hand and feet temperature exhibited different pattern when compared to infraclavicular region, the thigh, and the forehead. Ring [10] informed that the most stable time for measuring skin temperature time is before 12 pm. In current paper, thermovisual examinations were performed between 8:30 and 11:30 am, thus our time range matches well to requirements suggested by Ring.

To make thermovisual analysis more reliable, emissivity value of analysed object has to be considered. Thermovision is based on measurement of electromagnetic waves emitted by the body and depending on its roughness, emissivity value ranges between 0 and 1. Human skin emissivity reaches very high values almost like a black body. Few authors reported that it ranges between 0.97 and 0.99 [11, 12]. Rusowicz et al. [13] suggested establish the value of 0.98. Thus, in our study we also assumed this value for skin thermal measurements.

The intrinsic factor of a great importance which differs among study groups is medical history. Every medical condition results in changes of thermophysical properties of tissue covered by the disease which is discernible in thermovision camera. In current paper we mainly consider skin temperature reaction to inflammatory lesions in rheumatoid disease. Firstly, inflammatory process results in higher vascularization of affected tissue and higher blood flow in this area which leads to skin hyperthermia in the area of such process [2]. Secondly, not properly treated RA may result in joint and bone erosions and, in contrast to inflammation, these changes appear in thermal images as hypothermia [8]. Thirdly, as previously mentioned, Herman [3] reported that after cold stimulation pathological changes are visual and easier to diagnose. In current paper we decided to apply cold stimulus (ice water immersion of feet), thus it is also necessary to also consider the impact of autonomous nervous system as it controls vasodilatation and vasoconstriction of blood vessels following rapid ambient temperature change in order to maintain homeostasis. Among intrinsic factors genetics is not of a lesser importance, however in current paper all of examined participants have polish origins, thus we haven't analysed it in the impact of this factor.

Second group of individual factors are extrinsic factors. Among these it is necessary to include intake factors, basically medications. With reference to current study, the most important pharmacological group involves all the preparations against inflammation: non-steroidal anti-inflammatory drugs (NSAIDs, glucocorticosteroids, disease modifying anti-rheumatic drugs (DMARDs) and biological disease anti-rheumatic drugs (bDMARDs). These drugs act against inflammatory mediators and any change in the level of these substances triggers skin temperature alterations discernible in thermovision camera. Duration of anti-rheumatic treatment can also impact temperature distribution in the area of rheumatoid lesions [19]. Thus, none of examined participants in current paper received any medicinal product at least 24 hours before the examination procedure began. Intake factors also cover alcohol, tobacco and hydration [2]. In terms of extrinsic factors application factors should also be discussed. Before thermovisual measurement the use of ointments, cosmetics and sunlight exposition has to be excluded as it may also impact the results. In terms of the topic covered by current paper, cold and hot external stimulus in the form of e.g. cold and hot water application, ice pads, physical therapies based on high or low temperature et cetera are of a great importance as well. In current paper, application of ice cold water on feet up to ankle was performed.

Last but not least group of factors are technical factors, among which its necessary to include camera distance from the measured object. This agent should be mainly considered due to its impact on reliability of obtained results. However, camera distance does not impact participant's safety, as infrared radiation is not any harmful for human organism. Part of emitted and reflected by the environment infrared radiation is always lost as the atmosphere absorbs a small portion of it [14]. Few authors reported a small difference of 0.2 Celsius degrees between the distance of Cuevas [2] suggested using a short distance if the target is a fixed body area in order to increase the number of pixels thus improving the quality of thermal image. According to both recommendations we decided to perform measurements at a distance of 1 m from the examined object. Selection of region of interest (ROI) is not of a lesser importance either, Cuevas et al. suggest automatic procedure for ROI selection, however it is not possible in many cases. Different shapes and sizes of participants' hands and feet hinder the automation of ROI selection. Thus, in current paper ROI selection was performed manually. Final worth mentioning technical factor is statistical analysis. Cuevas et al. [2] reported that despite average temperature values of ROIs are used in majority of studies, they may exhibit errors especially when selection of ROI is performed manually. Thus, in current paper we extend our statistics to minimal and maximal temperature of the analysed area.

Ongoing topic of analysis is the ultimate cooling time for providing safety conditions and extracting the greatest part of relevant thermal data. Dębiec-Bąk et al. [15] performed cryotherapy on healthy subjects and afterwards observed thermal reaction of participants' body surface. They noted that directly after the cooling procedure mean temperature of the body surface dropped, however the decrease was dependent on the body region. They observed that longer duration of exposure for cryotherapy (3 min) as well as the lowest temperature used for cooling (120 and -140 Celsius degrees) triggered the most intensive response of the body. Lower limbs exhibited the highest temperature decrease along with the slowest return to baseline, the weakest response was observed for trunk. In current paper, in the area of human feet the slowest return to baseline was observed for the ankle joint.

House et al. [16] performed the analysis of feet temperatures of persons with hands and feet of hand-arm vibration syndrome (HAVS). They performed the comparison of foot temperatures between patients with HAVS and healthy subjects prior and after cold water immersion, during re-warming period using repeated measures analysis. Before applying cold stimulus the average temperatures in the toes were slightly lower in the cases than the controls and the differences were statistically significant for toes 1, 4, 5 and the average of all five toes. Re-warming curves were similar for each toe. After completing cold water immersion, healthy participants re-warmed slightly faster than patients with HAVS and the difference was rising with increasing duration of re-warming course. These results are in accordance with the data provided in current study, as in ankle joint of RA patient's left foot and also ankle joint of other RA patient's right foot, no temperature change during thermal recovery process occurred, thus suggesting that in these joints the thermal recovery did not appear at all. Additionally, after the rewarming period, two different RA patients exhibited the decrease of the temperature of these joints.

Stathopolous et al. [17] examined blood flow patterns on five distinct points of the lower limp after cooling by means of an ice cube. Skin temperature was measured every 30 seconds as the temperature was locally reduced and then restored to baseline value. The measurements were performed in relation to two foot positions: vertical and horizontal. The author observed that re-warming process after initial cooling followed approximately the same pattern for all points of measurement. Horizontal foot position exhibited faster return to baseline than vertical position. Thus, the position during thermal recovery process of human feet should also be considered.

4. CONCLUSIONS

In presented study, between pre- and post-cooling statistically significant differences were observed for all measured regions ($p < .05$). The greatest difference occurred in MTP4 of participant's left foot (the temperature fell by 8.90 Celsius degrees). It can be concluded that 5 second cold water immersion is a proper stimulus for exposing temperature differences during thermal recovery process in human hand joints.

In the group of RA patients the difference between the moment right after immersion and the moment after 3-minute recovery appeared to be the lowest in two different patients' ankle joints. These results suggest that the slowest rewarming rate occurs in the area of ankle joint. Also, after the rewarming period, two different RA patients exhibited the decrease of the temperature of these joints. In terms RA pathology and joint termophysical properties in the course of RA disease it may be concluded that erosive process that encompass RA foot joints leads to the decrease of the temperature of these joints.

The greatest difference after thermal recovery was observed two times. In both cases the increase of 4.9 Celsius degrees was observed and it affected the following joints of two different participants: MTP3 and MTP5. These changes can be explained by intensive inflammatory process in the area of aforementioned joints, which manifests itself in increased vascularity and, by extension, higher temperature in the area of affected joints.

To provide safety conditions for RA patients analysis, maximal reduction of immersion time concomitantly with providing proper study protocol for extracting reliable diagnostic thermal data was accomplished. Affirmed differences between pre-cooling moment versus the moment right after cooling as well as between the moment right after cooling versus the moment after returning to steady-state after 5-second cooling period suggest that there is no need to perform longer cold application as it provides discernible effects and safety examination conditions.

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