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Contents (INHALTSVERZEICHNIS)

Che gelida manina - What a cold tiny hand

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When in Puccini´s opera "La Boheme" Rudolfo met Mimi for the very first time and touched her hand accidental, he stated "Che gelida manina- what a cold little hand" From a thermological point of view, the question arises that Mimi might suffer from Raynaud´s phenomenon as she complaint about cold hands throughout the whole opera. In fact, publications on thermographic diagnosis of vasospastic finger disease have suggested that low finger temperature are diagnostic for Raynaud´s phenomenon.

This issue of Thermology international puts a focus on Raynaud´s phenomenon, described by Marcel Raynaud in 1862 (figure 1). Raynaud reported the typical colour changes of this disease and he also stated that touching the affected fingers revealed that they are frozen cold [1]. Raynaud emphasized also that appearance and colour of affected body parts such as fingers, toes, occasionally the nose and the chin, fully recovers after the vasospastic attack has resolved. Interestingly, in 2007 Richard Harding has reported a high occurrence of cold noses in patients with thermographically diagnosed Raynaud´s phenomenon [2].

There are a number of arguments against the suspect that Mimi in La Boheme suffered from Raynaud´s phenomenon or why one should not rely only on baseline temperature readings for diagnosing patients with suspected Raynaud´s phenomenon.

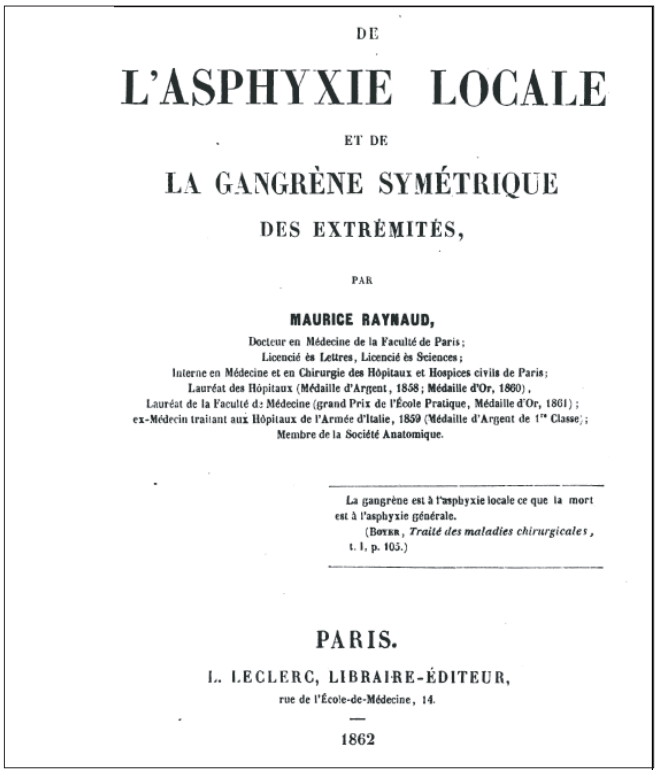
1.) Hand and finger temperatures are highly dependent on the room temperature [3, 4]. Clark et al reported greater longitudinal temperature gradients of hands at a room temperature of 23° C than of 30° in patients with primary and secondary Raynaud´s phenomenon [5]. Remarkable changes in face temperature have been reported after lowering the room temperature by 2° C [6].

2.) Even under controlled conditions (same time of the day, same person, same preparation procedure, same room temperature) the finger temperatures vary roughly by ± 1.0°C from day to day. [7].

3.) Some subjects with cold fingers at start recover normally after cold challenge [8]. Bosmansky et al. used dynamic thermography as outcome measure in a drug trial of patients with secondary Raynaud´s phenomenon caused by systemic sclerosis and observed both increase and reduction of numbers of fingers with pathological temperature gradients after a cold challenge [9].

4.) Patients with normal finger temperature prior to a cold challenge may not recover within 20 minutes after the cold stress test [8, 9].

5.) Raynaud´s phenomenon is the result of an transient disturbance of perfusion and not a permanent reduction of blood supply in fingers. Therefore, cold fingers may be



DE

L'ASPHYXIE LOCALE

ET DE

LA GANGRÈNE SYMÉTRIQUE

DES EXTRÉMITÉS,

PAR

MAURICE RAYNAUD,

Docteur en Médecine de la Faculté de Paris;
Licencié ès Lettres, Licencié ès Sciences;
Interne en Médecine et en Chirurgie des Hôpitaux et Hospices civils de Paris;
Lauréat des Hôpitaux (Médaille d'Argent, 1858; Médaille d'Or, 1860),
Lauréat de la Faculté de Médecine (grand Prix de l'École Pratique, Médaille d'Or, 1861);
ex-Médecin traitant aux Hôpitaux de l'Armée d'Italie, 1859 (Médaille d'Argent de 1re Classe);
Membre de la Société Anatomique.

La gangrène est à l'asphyxie locale ce que la mort est à l'asphyxie générale.
(Bouvier, *Traité des maladies chirurgicales*, t. I, p. 105.)

PARIS.

L. LECLERC, LIBRAIRE-ÉDITEUR,
rue de l'École-de-Médecine, 14.

1862

Figure 1
Front page of Maurice Raynaud´s doctoral thesis

caused by loss of perfusion due to various reasons such as centralisation of blood distribution [10]. The effect of toxins such as in ergotism may result in both severe vasospasm [11] or vascular obstruction caused by thrombi formation[12]. Tobacco smoking leads also to reduced finger perfusion and consecutive cold fingers [4, 13,14]. Morphological established obstruction of blood vessels results in permanent cold fingers.[15].

Three papers in this issue of Thermology international address various aspects of thermographically assisted diagnosis of Raynaud´s phenomenon.

Pauling and McHugh discuss in a review paper the contribution of a cold challenge for the diagnosis of vasospastic finger disease and conclude that the cold challenge unquestionably provides useful information on vascular reactivity that can not be derived from static assessment alone [15].

Nielsen and Mercer applied convective cooling as cold challenge and stated that the temperature changes of the rewarming period were more informative than was the primary temperature decline during fan cooling [16].

The third paper reports a retrospective study of thermal images from patients with suspected Raynaud´s phenome-

non who all underwent a diagnostic cold challenge [16]. Combined temperature gradients i.e. the temperature of the finger tip minus the temperature over the metacarpal bone prior and 20 minutes after cold challenge were used for the thermographically assisted diagnosis of Raynaud´s phenomenon. Differences of these gradients with respect to gender, age and finger involvement are reported.

All three papers recommend dynamic thermography i.e. application of a temperature related challenge for the investigation of patients with suspected Raynaud´s phenomenon.

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Does incorporation of a cold challenge provide additional diagnostic information in thermographic assessment of Raynaud's phenomenon?

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SUMMARY

Infrared thermography (IRT) provides a safe, non-invasive, indirect measure of vascular function. In addition to its many other clinical applications, IRT has developed an important place in the assessment of patients with Raynaud's phenomenon (RP), particularly those with underlying disease such as systemic sclerosis (SSc). Several studies have attempted to establish the best thermographic parameter by which to diagnose Raynaud's phenomenon. Many of these studies have incorporated a local cold challenge to allow dynamic assessment whilst attempting to recreate the conditions of an attack of Raynaud's phenomenon "in vivo". Recent studies suggest that baseline thermographic assessment alone may be sufficient to differentiate between healthy controls, primary RP and SSc. In this paper we shall explore the various thermographic parameters devised for the assessment of RP and question the contribution of the cold challenge.

KEY WORDS: Infrared thermography, Raynaud's phenomenon, cold challenge

BIETET DIE EINBEZIEHUNG EINES KÄLTEPROVOKATIONS-TESTS ZUSÄTZLICHE DIAGNOSTISCHE INFORMATIONEN BEI DER THERMOGRAPHISCHEN BEWERTUNG DES RAYNAUD'S PHÄNOMENS?

Infrarotthermographie (IRT) stellt eine sichere, nicht-invasive, indirekte Beurteilung der Gefässfunktion dar. Zusätzlich zu seinen vielen anderen klinische Anwendungen, hat IRTeinen wichtigen Platz in der Bewertung der Patienten mit Raynaudphänomen, besonders bei solchen mit einer zugrundeliegende Erkrankung wie eine systemische Sklerose (SSc). Mehrere Studien haben versucht, die besten Parameter für die Diagnose Raynaud's Phänomen zu finden. Viele von diesen Studien haben mit einer lokalen Kälteprovokation versucht, die Bedingungen für die Auslösung eines Raynaudphänomens zu rekonstruieren und eine dynamische Beurteilung des vasospastischen Geschehens zu ermöglichen. Jüngste Studien haben vorgeschlagen, dass bereits die Ausgangswerte der thermographischen Untersuchung ausreichen, um zwischen gesunden Kontrollen und Patienten mit primären RP oder SSc zu unterscheiden. In dieser Übersicht wird untersucht, welche verschiedenen thermographischen Parameter für die Bewertung der RP entwickelt wurden und welchen Beitrag der Kälteprovokations-Tests liefert.

SCHLÜSSELWörter: Infrarot-Thermographie, Raynaudphänomen, Kälteprovokation

Thermology international 2010, 20(3) 87-92

Introduction

Raynaud's phenomenon (RP) describes the abnormal reactivity of the digital circulation to cold exposure or emotional stress. It typically affects the fingers and toes and is characterised by intermittent episodes of digital cooling with associated colour changes (pallor, cyanosis, and rubor), pain and paraesthesia. RP is common (4-15%), particularly in females. For the majority of sufferers, the condition is benign with no associated features and is termed primary RP., However, for a minority of individuals, the emergence of RP can herald the onset of more widespread organ involvement most notably systemic sclerosis (SSc) and is termed secondary RP. Patients with SSc tend to have more significant vascular dysfunction and the associated ischaemia can progress to digital ulceration and gangrene. In addition, patients with SSc are at risk of vascular complications in other vascular beds such as the kidneys and lungs [1,2].

Diagnosis of RP is largely clinical however, due to its episodic nature, the majority of patients do not have evidence of an attack during clinical assessment. For this reason, patient reported questionnaires have been developed, although they carry all the inherent problems associated with self report clinical assessment tools, including potential for false negative and false positive results. For this reason, use of objective non-invasive microvascular imaging assessment tools by which to assess RP are recommended for the classification of both primary RP and early systemic sclerosis [3,4].

The two most important questions we ask of such clinical assessment tools when investigating patients with possible RP are: 1) Is this RP? And if so: 2) Is this primary or RP? Several vascular assessment tools have been studied in RP, however for the purpose of this review, we shall be concentrating on infrared thermography.

Infrared thermography

Infrared radiation is one of the principle mechanisms of heat transfer occurring in the human body. Essential to temperature homeostasis is the ability of the body to control core temperature through the regulation of the cutaneous circulation. Heat exchange increases with vasodilatation and is conserved through vasoconstriction. Using this principle, infrared thermographic (IRT) evaluation of cutaneous surface temperature can be used to provide a safe, non-invasive, indirect measure of vascular function [5]. Amongst its many clinical applications has been the role of IRT in the assessment of vascular dysfunction in

patients with RP. Thermal images of the hands at baseline provides significant information on vascular function, although many thermographic protocols additionally incorporate a cold challenge to allow dynamic assessment of vascular function whilst attempting to recreate the conditions of an attack of RP in vivo.

In this paper we explore the different thermographic parameters available for the assessment of RP, addressing the strengths and weaknesses of the available methods described. We shall review the contribution of the cold challenge and attempt to better define its role in the thermographic assessment of RP. To allow further discussion on the various thermographic parameters used, we must first devote some attention to vascular physiology in health and RP.

Digital cutaneous circulation

All areas of skin have an arcade of arterioles at the interface between the dermis and the deeper structures. Arterioles arise from this arcade and ascend into the superficial dermis. Capillary loops arising from this second network of arterioles extend into the sub-papillary plexus at the dermal-epidermal interface. The capillaries drain into venules and deeper veins that accompany the arteriolar supply within the dermis [6].

It has long been noted that normal cutaneous circulation is not uniform across the body with distinct regions of relative hyperperfusion in relation to the rest of the body. The advent of modern non-invasive measures of micro-va scular function allowed, for the first time, the assessment of the variability of cutaneous blood flow across the body. Tur et al used photopulse plethysmography and laser Doppler velicometry to measure basal skin blood flow at 52 anatomical sites, identifying regions in the hands and face for which cutaneous perfusion is much higher [7]. Regions of skin can be broadly separated into glabrous (from Latin = bald, hairless) and non-glabrous areas. Glabrous skin differs anatomically due to the presence of multiple arteriovenous anastamoses (AVAs). These thick walled, low resistance vessels allow blood to pass directly from arterioles to venules. Alteration of vascular tone within these AVAs can have substantial effects on cutaneous blood flow. Non-glabrous skin has few, if any, AVAs [8]. In a warm environment dilated AVAs can provide the pathway for 80% of digital blood flow, making a crucial contribution to thermoregulation. The remaining 20% of blood passes through the capillary bed where metabolic exchange can take place. This is usually described as the nutritional blood supply. In response to cold, these AVAs can virtually close following alpha-2 adrenoceptor stimulation, diverting much of the cutaneous blood flow away from the dermis. The nutritional capillary vascular bed remains patent in all but the most extreme cold exposure to prevent cutaneous ischaemic necrosis [6, 8-10]. The fingertips are densely populated with AVAs providing an important role in thermoregulation. In ambient temperatures, these AVAs remain dilated to allow heat transfer. The dorsum of the hand meanwhile is less densely populated with AVAs (non-glabrous). This can be visualised thermographically through the identification of a proximal (dorsum of hand, cooler) to distal (fingers, warmer) temperature gradient: sometimes referred to as a distal dorsal difference (DDD) [Figure 1A).

Following cold exposure, these AVAs constrict to conserve heat and the positive DDD is nullified, or even transiently reversed. On removal of the cold stimulus, providing the core body temperature has not been threatened, these AVAs rapidly re-open allowing rapid reperfusion and re-w arming of the digit. This process can be witnessed thermographically beginning at the fingertips and developing proximally. In Raynaud's phenomenon, basal sympathetic tone is higher with relative vasoconstriction of the AVAs. This leads to a neutral or negative DDD (Figure 1B). During cold stress this pattern is exaggerated further and persists despite removal of the cold stimulus preventing rewarming. Gradual rewarming occurs proximally (in regions less reliant on AVAs) primarily due to conductive heat gain

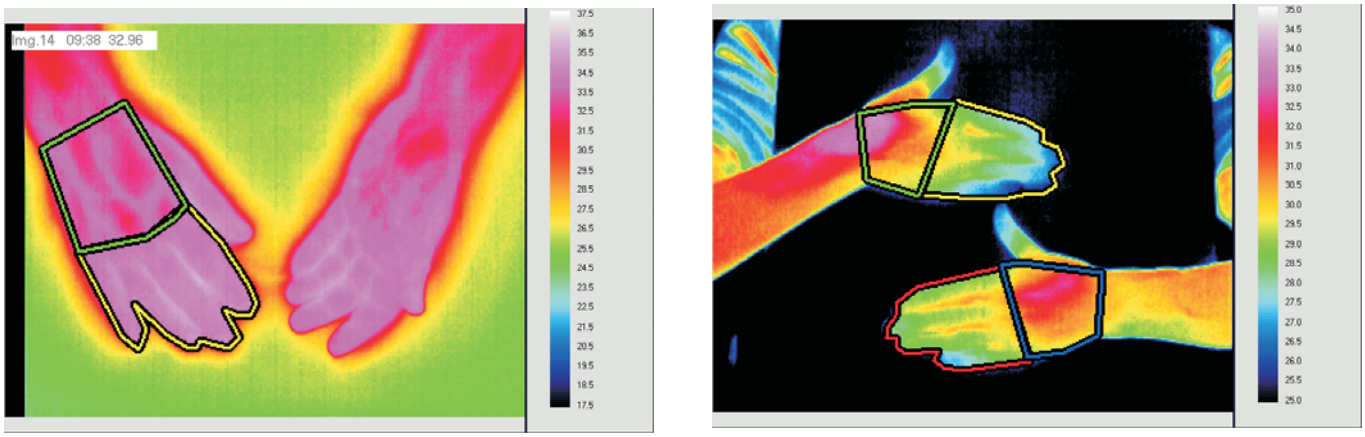

Figure 1.
Baseline thermal images with proximal and distal regions of interest are marked (adapted from Ring et al method).
A) Healthy control (right proximal mean surface temperature 33.23°C, right distal mean temperature 34.05°C, gradient +0.82°C).
B) Systemic sclerosis (right proximal mean surface temperature 30.87°C, right distal mean temperature 28.07°C, gradient -2.8°C).

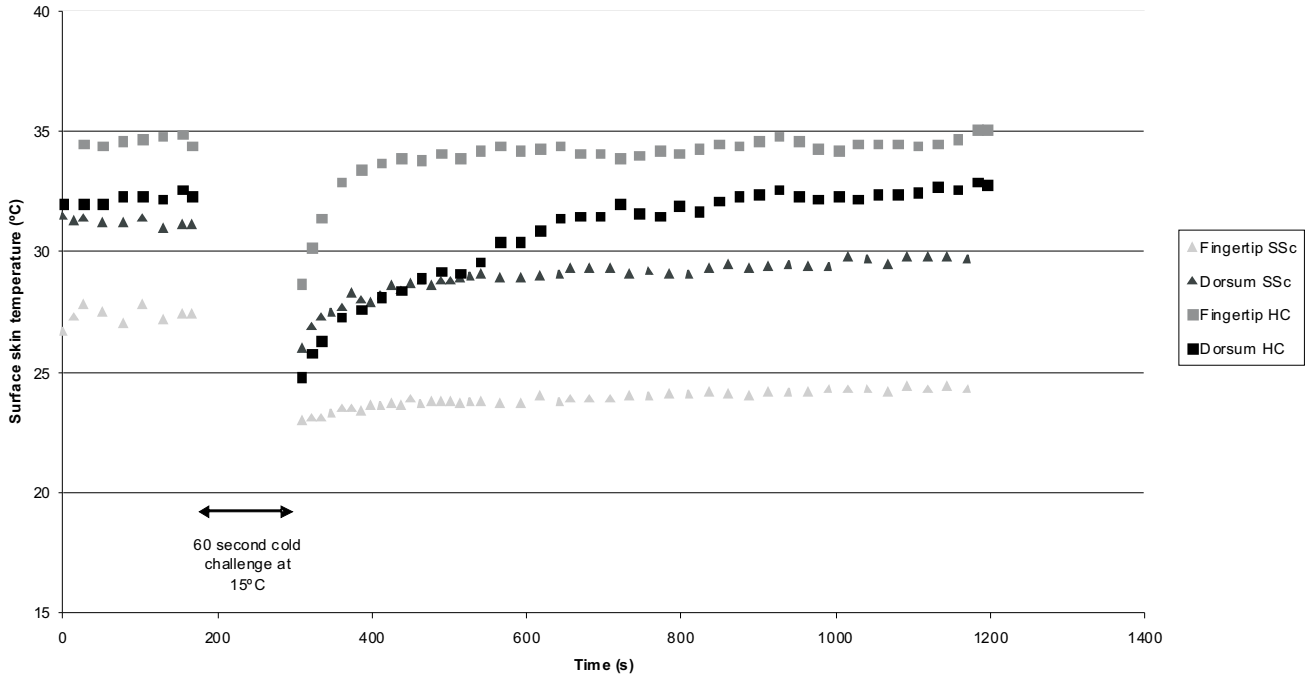

Figure 2.
Example of IRT skin temperature measurements before and after cold challenge in a healthy control (HC) and a patient with systemic sclerosis (SSc). Note the positive DDD at baseline with fingertip rapid rewarming in healthy controls in comparison with negative DDD at baseline and sluggish rewarming of fingertips in systemic sclerosis. Baseline skin temperature and response to cold challenge over the dorsum of the hands is similar for both HC and SSc reflecting the smaller contribution of thermoregulatory AVAs.

from the deeper tissues, further exaggerating the negative distal dorsal gradient (Figure 2).

Figure 2 graphically demonstrates typical thermographic assessment of glabrous (fingertip) versus non-glabrous (dorsum of hand) in healthy controls and subjects with systemic sclerosis following cold challenge. The characteristic differences observed at baseline and during rewarming (e.g. maximum gradient of rewarming and maximum temperature recovery) have been adopted as endpoints in many of the studies in this field which we shall now discuss in more detail.

Thermographic parameters in the assessment of Raynaud's phenomenon

Francis Ring and colleagues in Bath were amongst the first to describe the use of thermographic imaging in the assessment of RP. In 1980 Ring published a description of a standardised thermal stress test incorporating thermal imaging to act as an objective assessment in the assessment of upper limb ischaemia [11]. Following acclimatisation for 15 minutes in a draught free room at 22°C, baseline thermal assessments are performed of the dorsal aspect of the hands before, at 4 minutes and 10 minutes after submersion of gloved hands in a water bath at 20°C. The mean temperature of 2 distinct regions of interest is calculated: the dorsum of the hand (radiocarpal joint to MCP joint) and the dorsal aspect of the index to little fingers. The distal-dorsal difference (finger temperature – dorsal hand temperature) is calculated before and after cold stress, with combination of the 2 results to form a Combined Thermal Gradient (CTG) [12,13]. This protocol was tested on healthy controls, primary Raynaud's and Scleroderma and a CTG of -4ºC was considered an appropriate threshold for the thermographic diagnosis of RP [14] (table 1).

Table1
Differences in the Combined Thermal Gradient in healthy controls, primary RP and SSc. Adapted from Ring et al. [12].

Patient group	Combined Thermal Gradient (SD)
Healthy Controls (n=150)	+ 0.25 (1.9)
Primary Raynaud's phenomenon (n=144)	- 6.9 (2.4)
Scleroderma (n=20)	- 11 (1.8)

The CTG could differentiate between healthy controls and those with RP, but failed to distinguish primary from secondary RP. No data was reported regarding the discriminatory capacity of the DDD pre-test alone to support the value of the cold challenge. Furthermore, it is possible that some of the subjects labelled as primary RP in 1980 may now have been reclassified as SSc spectrum disease which may have influenced the discriminatory capacity of the CTG.

Kyle et al also identified the temperature gradient as a potential discriminating factor in differentiating controls from RP, but unlike Ring et al, calculated the temperature gradi-

ent longitudinally within the index finger alone. Based on a similar principle to that proposed by Ring they combined the temperature gradient 10 minutes post cold stress (20°C for 60sec) and the mean temperature change 10 minutes following cold stress to calculate a discriminant function value in an attempt to quantify vascular dysfunction [15]. Neither of these early studies addressed whether the thermal gradient at baseline provided similar discriminatory capacity, and possibly due to the challenges related to capturing infrared thermal images at that time, neither reported on differences in the rewarming curve characteristics. This latter issue was addressed by O'Reilly *et al.* who investigated response to a standardised cold stress test (15ºC for 1 minute) using IRT assessment of the dorsal aspect of the distal interphalangeal joint in healthy controls, PRP and SSc [16]. Several thermographic parameters allowed differentiation between primary and secondary RP and healthy controls including temperature at baseline (T_{pre}), temperature immediately post cold stress (T_0), gradient of recovery (G_{max}), maximum rewarming percentage ($R_{\%}$), and lag time to commencement of rewarming (T_{lag}). None of these indices allowed distinction between PRP and SSc. Discriminate analysis of the 5 parameters found that the dynamic assessments (G_{max}, $R_{\%}$ and T_{lag}) were the most effective discriminates between groups, supporting the incorporation of a cold challenge [16]. Only distal regions of interest were used in this study preventing comparison between rewarming curve characteristics and the temperature gradients proposed by Ring.

Subsequent work by Schuhfried *et al.* is notable as being one of the few studies that investigated whether a thermographic test could accurately classify patients according to the Brennan clinical criteria [17]. They investigated 87 consecutive patients referred for thermographic assessment for possible secondary RP. After 20 minutes initial acclimatisation at 24C, baseline thermographic images were taken of the dorsum of the hands. A cold challenge at 16ºC for 1 minute was undertaken. Distal measurements were taken overlying the dorsal aspects of the fingertips of the index, middle and ring fingers bilaterally. A proximal region of interest was chosen overlying the radial carpometacarpal joint of both hands. This is one of earliest studies to directly compare DDDs with characteristics of the re-w arming curve (absolute temperatures at 0, 10, and 20 minutes, maximum gradient of rewarming, area under rewarming curve and percentage recovery). Of all the endpoints assessed, the longitudinal temperature difference at baseline (LTDpre) was found to be the most effective parameter at correctly classifying patients according to clinical evidence of RP with a sensitivity and specificity of 77% and 73% respectively. The LTDpre was effective at accurately classifying those patients in whom RP was clinically absent (sensitivity 96%, specificity 62%). It was not felt the cold challenge provided significant additional information in comparison with baseline assessments alone [17]. This possibly reflected the wide inter-individual responses to cold challenge and the irreversible morphological microvascular changes present in SSc-spectrum disease preventing accurate functional dynamic assessment. They did not report whether a composite index of longitudinal gradients at baseline and following cold stress (similar to that proposed by Ring) improved the overall classification of RP. Furthermore, no attempt was made to use the LTDpre in an effort to differentiate between primary and secondary RP.

A separate study also compared thermographic endpoints in patients from a population setting characterised as healthy or RP according to clinical criteria [18] set out to define the best thermographic parameters to diagnose RP in a. The study investigated a large number of subjects (n=175 RP and n=404 healthy controls) identified by a questionnaire survey of over 3600 women in a separate study. After 15 minutes acclimatisation at 23C, the surface temperature of the palmer aspect of the 8 fingertips was measured using portable radiometry. Subjects underwent CST at 15°C for 60s. Repeat measurements were undertaken immediately post CST and again at 10 minutes. The data generated was insufficient to map rewarming curves and no proximal thermographic data was collected preventing analysis of the longitudinal gradients. Patients with RP had significantly lower temperature at baseline (28.30°C vs 29.97°C) and lower absolute rates of rewarming at 10 minutes (4.56°C vs 5.29°C). The absolute fall in temperature did not differ significantly between the two groups. Logistic regression analysis did not identify any improvement in fit on addition of any combination of fall in temperature and rewarm at 10 minutes when compared to use of baseline assessment alone. The presence of a baseline temperature of <24°C had a high positive predictive value and specificity for RP (96%) (likelihood ration 2.89), which decreased as the baseline temperature threshold increased to <30°C. The sensitivity of relying on a low baseline temperature such as <24°C is poor (11.43%), reflecting the fact that the majority of subjects fulfilling clinical criteria for RP had higher baseline temperatures [18]. The authors concluded that the CST provided little additional information with regards the classification of RP in comparison with baseline assessment alone although it may be argued that insufficient measurements were taken to allow accurate mapping and assessment of the rewarming curve following cold challenge.

None of the above studies have identified a thermographic parameter capable of distinguishing between patients with primary and secondary RP (primarily SSc) which is of key importance to clinicians. This issue was first addressed in a pilot study of 9 patients with PRP and 20 with SSc undertaken by Clark *et al* [19]. After an initial acclimatisation of 20 minutes at 23C, baseline images of the dorsal aspect of both hands were recorded. The distal-dorsal difference was calculated at baseline (mean temperature of dorsum of hand minus mean temperature of region between nail fold and distal interphalangeal joint of all 8 fingers) providing a positive gradient in possible cases of vascular dysfunction (in contrast to Ring's negative CTG). Patients then underwent a cold challenge (15ºC for 60s). The rewarming response was recorded over 15 minutes with calculation of lag time, maximum gradient of rewarming, and percentage recovery at 2, 5, 10 and 15 minutes. Subjects in whom a 1ºC

DDD was identified at baseline had an additional thermal image taken after further 20 minutes acclimatisation at 30ºC. The mean maximum DDD (3.3 vs 1.4, p=0.02) and proportion of patients with any finger DDD >1°C (90% vs 56%, p=0.05) were both statistically higher in SSc compared to PRP at 23C. At 30ºC the differences in the proportions of patients with any digit DDD of >1C between the 2 groups was greater (60% vs 11%, p=0.005) suggesting greater specificity, albeit at the expense of sensitivity which fell from 90% to 60%. None of the rewarming characteristics allowed differentiation between patients with PRP and SSc suggesting limited contribution from the cold challenge [19].

The same group undertook a larger retrospective analysis of all subjects attending for IRT with cold challenge over a 2 year period to further investigate the discriminatory potential of a DDD of >1°C [20]. The patients (n=161) included patients with PRP, SSc, uCTD, and SRP related to other CTD and RA. The protocol and analysis was similar to their previous pilot work. At 23ºC (even when adjusted for age, sex and smoking) all DDD parameters were significantly lower within the PRP than in those subjects with SSc allowing potential differentiation between the two groups. The differences between the groups was more pronounced when evaluating DDD parameters at 30ºC as a greater proportion of the PRP subjects exhibited more normal digital perfusion characteristics at the higher baseline temperature. In this study, the maximum rewarming gradient and the lag time to rewarming, both endpoints generated from the rewarming curve characteristics were found to allow differentiation of primary from secondary RP. The percentage of maximum rewarming recovery however was non-discriminatory, and the percentage recovery at 15 minutes only just achieved statistical significance (p=0.044). Both DDD parameters and rewarming characteristics lacked statistical significance when attempting to distinguish between PRP and other forms of secondary RP (undifferentiated connective tissue disease) [20].

In a more recent study, IRT with cold challenge was performed in healthy controls, PRP and SSc before and after cold challenge. Consistent with previous work, baseline skin temperature (mean of dorsal aspect of all 8 fingers), area under rewarming curve, maximum temperature recovery and maximum gradient of rewarming were all able to discriminate between healthy controls and patients with RP (but not differentiate between primary and secondary RP). No data on DDD was reported in this study for comparison [21].

Only one previous study has specifically compared results of baseline assessment using a longitudinal gradient with those following cold challenge in patients with suspected RP [22]. This retrospective review included 71 subjects (62 women) referred for thermography as part of the assessment of possible RP. The group was heterogeneous and at least 10 (14.1%) subjects had underlying peripheral nerve entrapment listed as a cause of their vascular dysfunction. Only five subjects were described who were known to have an underlying connective tissue disease, none of whom had SSc (3 rheumatoid arthritis, 1 Sjorgren's syndrome, 1 systemic lupus erythematosis). Ammer compared baseline thermograms (following 15 minute acclimatisation at 24C) with the results from a subsequent cold stress test (submersion of gloved hands in water bath at 20C for 60s). A distal-dorsal gradient was derived from assessment of regions of interest overlying the dorsal aspect of the meta carpophalangeal (MCP) joints and the dorsal aspects of the finger tips. A gradient of -0.5C (distal cooler than proximal) was considered suggestive of RP. The combined mean sensitivity of using the pre-CST DDD was 78.4% with a specificity of 72.4%. Anecdotal examples of a negative gradient at baseline which normalised following cold stress were described but no specific comparison between the 2 parameters and their ability to accurately characterise RP was reported. The study assumed the results following cold challenge as the gold standard and no comparison with clinical assessment tools, such as those proposed by Brennen e*t al*., was made [22].

Additional issues relating to utilisation of the cold stress test

Proponents of the cold challenge often argue that the true value of the test is to unmask subjects with abnormal vascular function who appear to have normal thermographic measurements at baseline and vice versa. Whilst we also can offer such anecdotal evidence to support this theory, no studies have systematically assessed the proportion of subjects for whom these observations relate and the subsequent impact on the overall sensitivity and specificity of the test. It is certainly our experience that the majority of patients with thermographic evidence of RP have evidence of vascular dysfunction at baseline assessment. There are additional issues surrounding the inclusion of a cold challenge that warrant discussion. Firstly, the assumption that the inclusion of a cold challenge recreates the physiological conditions responsible for an attack of RP is flawed as total body cooling is known to be of greater importance than local cooling in precipitating attacks of RP. This is attested in widely recognised observations that the cold challenge is seldom sufficient to cause an attack of RP. Therefore, the CST more accurately provides information regarding local vascular reactivity to cold stimulus. This remains valid when addressing primary RP (a true condition of vascular reactivity) but it's value is less certain in secondary Raynaud's were irreversible morphological changes affecting the microvasculature will materially influence any attempt at dynamic assessment of vascular function. Secondly, a major challenge when interpreting the results of any study incorporating a cold challenge has been the diversity in the standardised conditions of the test as highlighted in a recent systematic review [23]. Specific variables known to influence results include ambient room temperature, clothing worn by subjects, device used, body part assessed (e.g. dorsal vs palmer aspect of hands), and most importantly the conditions of cold challenge (e.g. temperature, mode of delivery, and duration of cold exposure). In the absence of

internationally agreed standards, assessment at baseline would significantly reduce the variability of future studies. Finally, there have also been concerns raised regarding the reproducibility of the technique [24]. Of the few studies to address this issue, one demonstrated higher levels of reproducibility at baseline compared with following cold challenge [25].

Conclusions

The cold challenge unquestionably provides useful information on vascular reactivity that can not be derived from static assessment alone, and at this stage there is insufficient evidence to support removal of the cold challenge from the standard thermographic assessment of RP. Nonetheless, there are valid concerns regarding the validity of the cold challenge and a growing body of evidence to suggest that baseline IRT images may be sufficient to accurately characterise vascular function in health, and disease. The additional time considerations of a well conducted cold challenge (between 30 and 60 minutes depending on protocol) and the historical high cost of thermal imaging equipment has previously restricted use of IRT to within specialist centres. In recent years, the cost of thermal imaging cameras has fallen considerably in real terms, and should information from baseline thermal images be shown to provide sufficient discriminatory capacity, there would be the potential to allow more widespread use of IRT in the assessment of RP in clinical practice. That is not to say that static thermal images would no longer require highly controlled standardised conditions (e.g. appropriate acclimatisation, avoidance of stimulants, draught free environment). The next step is to undertake carefully conducted retrospective and prospective studies that compare the discriminatory capacity of some of the thermographic parameters discussed above at baseline with those made following a standardised cold challenge in large groups of patients with primary and secondary Raynaud's, and healthy controls. Until these studies have been performed, the cold challenge should remain an integral part of the thermographic assessment of RP.

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Dynamic Thermography In Vascular Finger Disease. A Methodological Study of Arteriovenous Anastomoses

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SUMMARY

We present a non-invasive method employing infrared thermography for the continuous measurement of finger skin temperatures during fan cooling followed by spontaneous rewarming, using a FLIR ThermaCam®P695HS, infrared camera. The experiments consisted of a standardized convective (fan) skin cooling and recovery protocol. Finger tip and dorsum hand skin temperatures were continuously measured before, during and for 5 minutes after a 2 minute period of fan cooling. In some patients the hands were pre-warmed with a water filtered infrared heating lamp prior to the cooling and recovery protocol.

We hypothesized that rewarming after finger cooling begins at the arteriovenous anastomoses(AVA) of the fingertips, and that it might be an important feature of Raynaud's phenomenon, that the AVA are highly sensitive to cooling, and therefore slow to open after rewarming. This was demonstrated in a series of thirty-three patients referred for Raynaud's phenomenon, compared to three normal subjects.

Three reaction patterns were identified:

1) Normals (no history of disease): Almost instantaneous rewarming after cessation of cooling;

2) Cold intolerant (a history of cold fingers when exposed to low temperatures, but with no other signs or symptoms of disease): delayed rewarming, where the AVA opened later than in normals;

3) Secondary Raynaud's phenomenon (a history of cold fingers and connective tissue disease such as scleroderma), characterised by low peripheral blood pressure (strain-gauge measurements), low basal fingertip temperatures, and no rewarming after cessation of fan cooling.

It appeared that the temperature changes of the rewarming period were more informative than was the primary temperature decline during fan cooling.

KEY WORDS: arteriovenous anastomoses, dynamic thermography, Raynaud`s Phenomenon

DYNAMISCHE THERMOGRAPHIE BEI FINGERGEFÄSSERKRANKUNGEN: EINE METHODOLOGISCHE STUDIE ZU ARTERIOVENÖSEN ANASTOMOSEN

Es wird der Einsatz einer FLIR Therma Cam®P695HS Infrarot-Kamera zur kontinuierlichen Registrierung der Fingertemperatur während der Kühlung mit einem Ventilator und der darauf folgenden Wiedererwärmung berichtet. Die Untersuchung bestand aus einer standardisierten konvektiven Hautkühlung mit einem Ventilator und der Beobachtung der Wiedererwärmung. Dazu wurden die Hauttemperatur der Fingerspitzen und des Handrückens vor, während und 5 Minuten nach der 2 Minuten dauernden Kühlung kontinuierlich gemessen. Bei einigen Patienten wurden die Hände vor dem Abkühlen und der beobachteten Wiedererwärmung mit einer Wasser gefiltert Infrarot-Wärme-Lampe vorgewärmt.

Wir postulierten, dass die Wiedererwärmung nach Abkühlung der Finger von den arteriovenösen Anastomosen (AVA) der Fingerspitzen ausgeht, und es könnte ein wichtiges Merkmal des Raynaud Phänomens sein, dass die AVA sehr empfindlich auf Kühlung reagieren und sich zur Wiedererwärmung nur langsam öffnen. Dies zeigte sich an 33 Patienten mit Raynaudphänomen im Vergleich zu drei gesunden Personen.

Es wurden drei Reaktionsmuster gefunden:

1) Gesunde (ohne Hinweis auf Erkrankung): Fast unmittelbare Wiedererwärmung nach Abschluss der Kühlung

2) Kälteempfindlichkeit (anamnestisch kalte Fingers bei Kältexposition, aber ohne andere Krankheitszeichen oder Symptome): verzögerte Wiedererwärmung, wobei sich die AVA später öffneten als bei Gesunden.

3) Sekundäres Raynaud's Phänomen (anamnestisch kalte Finger plus Bindegewebserkrankung wie z.B. Sklerodermie), war gekennzeichnet durch niedrigen peripheren Blutdruck (Dehnungsstreifen-Plethysmographie), niedrige Ausgangstemperatur der Fingerspitzen, und fehlende Erwärmung nach Beendigung der konvektiven Kühlung.

Es zeigten sich die Temperaturänderungen während der Wiedererwärmung als Aussage kräftiger als der primäre Temperaturabfall während der konvektiven Kühlung.

SCHLÜSSELWÖRTER: arteriovenöse Anastomoses, dynamische Thermographie, Raynaudphänomen

Thermology international 2010, 20 (3) 93-99

Introduction

It is a common clinical problem how to distinguish between Raynaud's phenomenon (RP) and other types of cold intolerance in patients with cold fingers. The distinction is important, since the treatment regimens are different. Literature on thermography and RP is abundant, but suffers from lack of systematic, accurate observations of changes of skin temperature during induced cooling over time (dynamic thermography). Results of temperature measurements have so far been based on imaging made at different times after cooling has started (static thermography). No internationally recognized thermographic method for diagnosis and quantification of RP is available. Our goal was to develop a thermographic diagnostic method that is fast, non-traumatic and conclusive.

We hypothesized that it would be possible to distinguish between primary RP and other forms of cold intolerance using dynamic finger thermography. During the study it soon became apparent that re-warming after fan cooling often was preceded by opening of the arterio-venous anastomoses (AVA) of the finger tips. We decided to study whether it could be stated that RP was a manifestation of high sensitivity to low temperatures by the AVA's of the fingertips.

Methods

IR thermography:

The thermographic images of the hands were taken using a FLIR ThermaCAM®PM695 (Flir Systems Inc, Portland, USA) infrared camera (IR), with a thermal sensitivity of 0.1ºC. The infrared camera was connected to a portable computer via a firewire interface. All images were stored on the computer for later analysis using the image analysis software ThermaCAM researcher software version 2.1 (Flir Systems, Inc., Portland, USA). The latter enabled temperatures measurements within pre-defined circular regions of interest (ROI), as well as time course temperature curves to be created. Maximum, minimum and average temperatures could be determined for each ROI. In the data presented in Figures 2-6 the finger tip temperatures are maximum temperatures within each of the small circular ROI's, while the temperature presented for the dorsum of the hand is the average temperature within the larger circular ROI (Fig.1).

Fan cooling

We used fan cooling at room temperature (20-22 °C). Two standard desk top fans were used to cool the hands simultaneously, one for each hand. Each fan was positioned by an individual operator at approximately the same distance (ca. 40 cm) at an angle of ca. 50 degrees to the dorsal hand surface. During the fanning process the fans were moved to and fro over the hands to try and ensure an as even a distribution of the cooling effect as possible over the dorsal surface of the hand. Fan cooling is a moderate cooling compared to immersion in water at 10 °C, and has the advantage that temperature measurements (IR imaging) can take place during the cooling procedure. While seated, the hands of the subject rested palm-side down on a grid made of thin nylon netting that was strung across the top of a 6 cm deep flat plastic vessel (60 cm x 40 cm). The latter was placed on the subject's lap. In order to produce a background temperature that was different from the temperature to be measured, the vessel was filled with cold tap water to a depth of about 3 cm, the temperature of which was significantly lower than any finger temperature. The lower background temperature could be digitally removed in the thermal images, leaving a clear thermal image of the dorsal aspect of both hands.

The IR camera was placed on a tripod 50 cm above the hands of the patient. Dynamic changes in temperature were recorded using multiple image sequencing at 2-second intervals. Following a ten minute equilibration period thermal images were continually recorded for two minutes prior to hand cooling, during the cooling and for a five minute recovery period following the cooling.

In some patients preheating up to 15 minutes before fan cooling was necessary, namely in cases of basal finger temperatures around 20°C. The preheating was carried out using two Hydrosun®radiator's (Hydrosun® Medizintechnik, Müllheim, Germany), emitting visible light VIS and water-filtered infrared-A (wIRA). The unique principle of operation involves the use of a hermetically sealed water-filter in the radiation path that absorbs or decreases those infrared wavelengths emitted by conventional infra- red lamps that would otherwise harm the skin (especially infrared-B and -C and so-called water absorption bands within infrared-A). With wIRA high radiation intensities are perceived as pleasant and heating of deeper tissue layers over longer periods of time can be achieved. The Hydrosun®-radiator, used was the model 501, with 10 mm water cuvette, and standard orange filter. The water-filtered spectrum of 550-1400 nm had approximately 185 mW/cm² total irradiance intensity (VIS+wIRA) of which approximately 45 mW/cm² was visible light (VIS) and approxi- mately 140 mW/cm² water-filtered infrared-A (wIRA.)[1, 2].

During the hand warming procedure, the Hydrosun®-radiators were placed at a distance of 25 cm from and at an angle of 90º to the skin surface, one for of each hand. The heating procedure ended when the skin temperature of all fingers had reached at least 36ºC. The time taken to reach this level varied from patient to patient, but usually was not more than 15 minutes. The heating commenced after a 10 minute stabilization period.

Prior to the thermographic examination measurements of finger blood pressure (FBP) were made using a standard strain gauge system (Digimatic DM2000, Medimatic, Denmark). These measurements were carried out in a separate laboratory at Hillerød Hospital by a trained nurse using standardized technique that involved pre-warming with a heating blanket. The FBP measurements were made at room temperature (20-22°C). The following blood pres-

sure values were regarded as normal: 1st finger blood pressure values equal or higher than systolic arm blood pressure, 2nd to 5th finger blood pressure values equal to or higher than systolic arm pressure – 15 mm Hg. Values less than these are regarded as being pathological. IR thermography was performed not less than 1 hour after the FBP measurements. FBP during cooling was not attempted due to lag time problems.

Patients

Thirty-three consecutive patients, thirty-two females and one male, aged 40 to 80 years, referred for FBP measurements under the tentative diagnosis RP were investigated. They all complained of cold fingers, especially in cold weather. For comparison three normal women were investigated.

Analysis

The images were analyzed as follows: Circular ROI were placed distally on each finger inclusive of the nail beds. For comparison a circular, larger ROI was placed on the dorsum of the hands (Fig. 1). Time-temperature curves were generated for each ROI and compared to IR images at different time points.

Results

The inter-individual variability of the responses to fan cooling is so pronounced that mean values for groups of patients cannot be given (different fingers involved with different degrees of disease), but characteristic patterns are described. Accordingly, the results shown here are illustrations of the possibilities of IR thermography during fan cooling rather than description of a clinical method ready for differential diagnosis in any clinical situation. Below we present three typical patterns of cooling and rewarming of fingers, which seem to be helpful in classifying patients with cold fingers.

Healthy subjects

The three healthy women, aged 29-45 years, all had normal FBP and high basal finger temperatures (around 30°C), and fan cooling induced a reduction of about 6°C with complete spontaneous rewarming after a few minutes. None of the normal subjects were smokers. Fig. 2 shows a typical finding in a normal subject, without symptoms or signs of cold-induced disease (29 year old woman). It can be seen:
1) that the temperatures of the fingertips prior to fan cooling vary between 35-36.5°C, and drop about 6°C during cooling;
2) that rewarming starts immediately after cessation of fan cooling and the resulting rate of increase in skin temperature is rapid and identical for all fingers (ca. 6°C/min in normal subjects) and
3) that the variability of the temperature response of the fingers is small. (note: already mentioned above). It can be seen that rewarming begins at the fingertips and that warm dorsal hand veins can be identified 60 seconds after cessation of cooling. Note that rewarming taking place from the fingertips first and later at the dorsum of the hands. This is presumably due to the openings of arterio-venous ana-

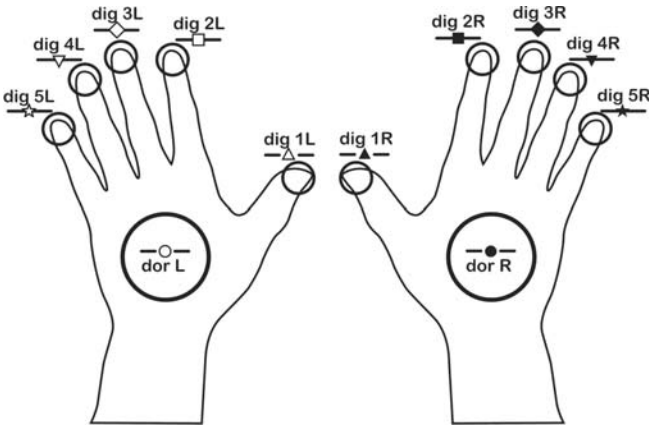


Figure 1
Schematic diagram of the dorsal aspect of the hands showing the location of the 12 temperature measuring sites used in the experiments. (one site on each finger tip [small circles] and one site on the back of the hand [large circle]). Each measuring site is depicted as a circle with a corresponding symbol that is used in the curves presented in Figures 2-6. In the data presented in Figures 2-6 the maximum measured temperature within the respective small circles on the finger tips and the respective average temperature within the larger circles on the back of the hands (dorsum) are presented.
dor = dorsum of hand; dig = digit; L = left; R = right.

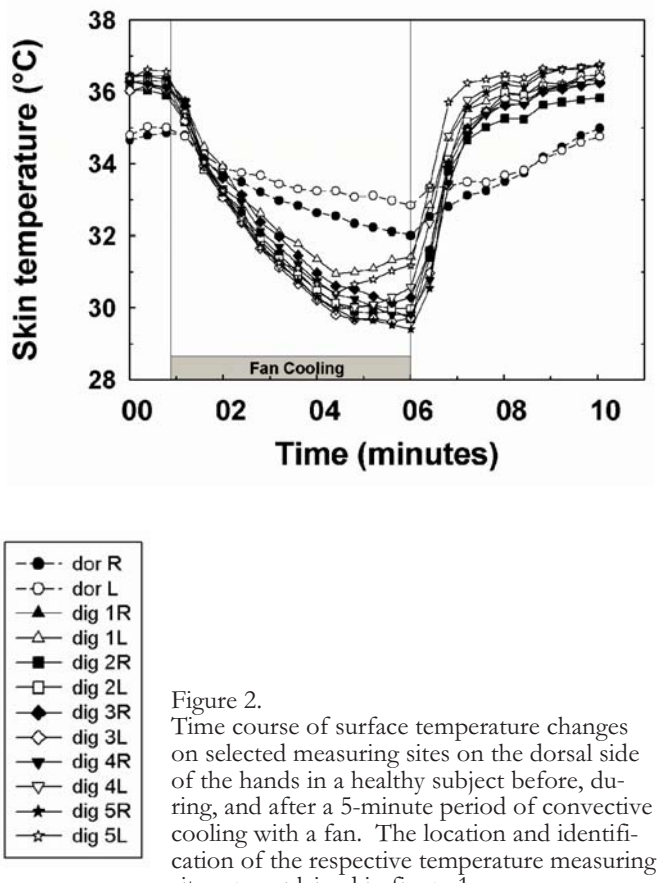


Figure 2.
Time course of surface temperature changes on selected measuring sites on the dorsal side of the hands in a healthy subject before, during, and after a 5-minute period of convective cooling with a fan. The location and identification of the respective temperature measuring sites are explained in figure 1.

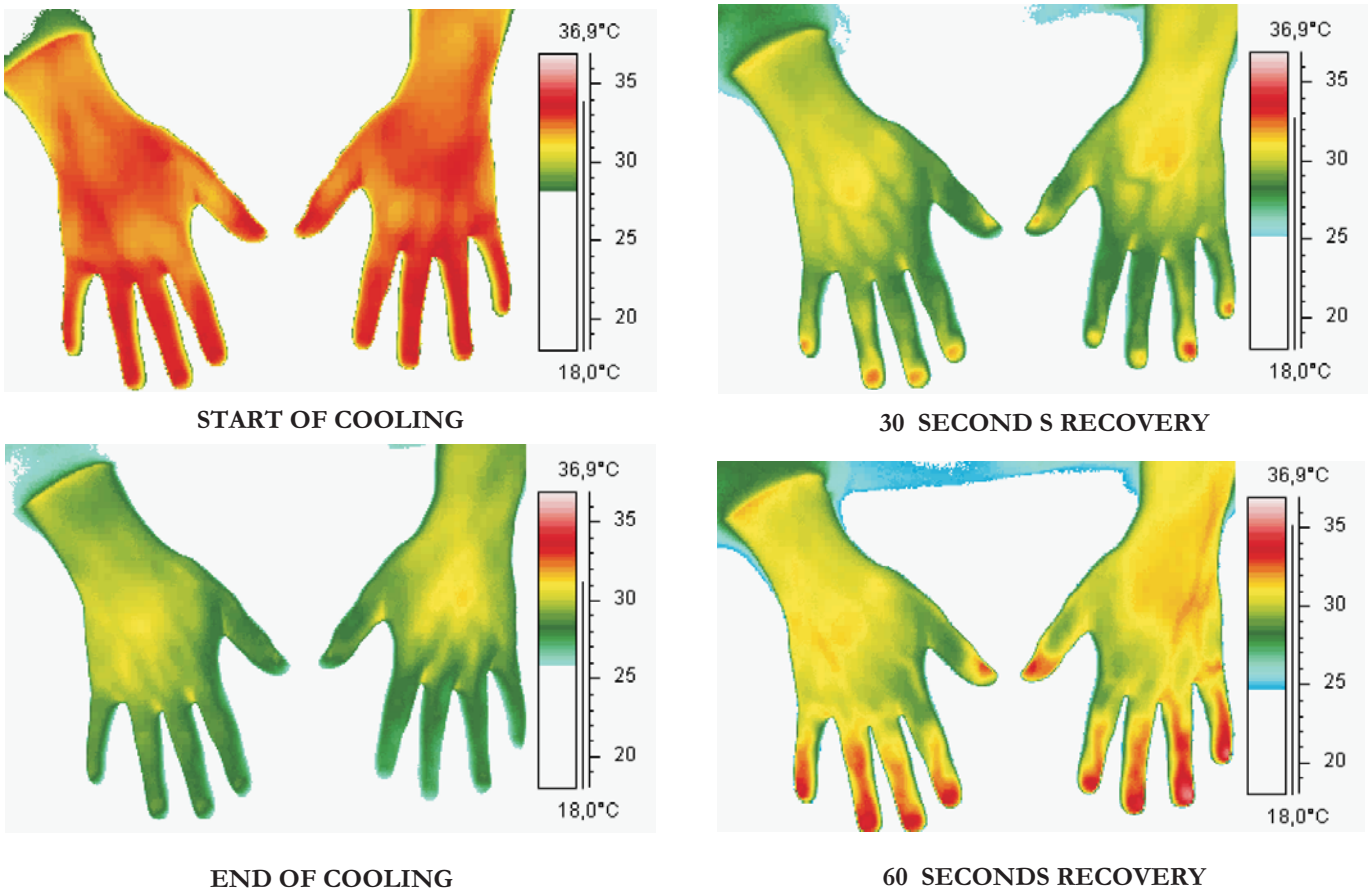


Figure 3.
Infrared thermal images of the dorsal surface of the hands of the healthy subject shown in Fig.1 prior to and immediately after and during recovery from a 5 minute period of fan cooling. The thermograms illustrate 1) opening of the arteriovenous anastomoses at the fingertips during recovery; 2) subcutaneous warm

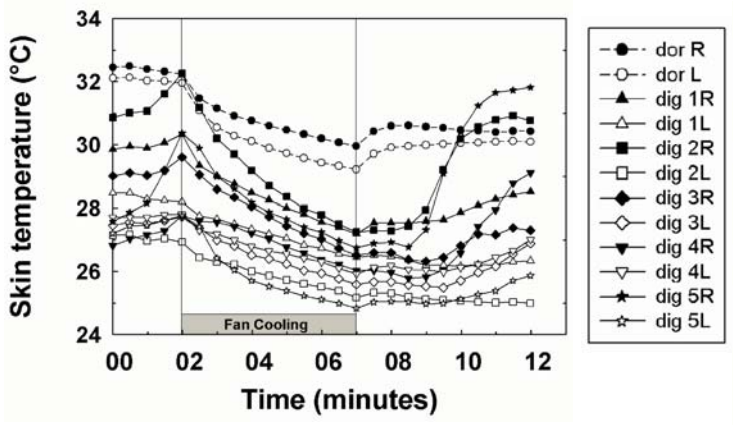


Figure 4.
Time course of surface temperature changes on selected measuring sites on the dorsal side of the hands in a patient with apparent primary Raynaud's phenomenon, during, and after a 5-minute period of convective cooling with a fan. Rewarming takes place at some of the fingertips.
The location and identification of the respective temperature measuring sites are explained in figure 1.
dor = dorsum of hand; dig = digit; L = left; R = right.

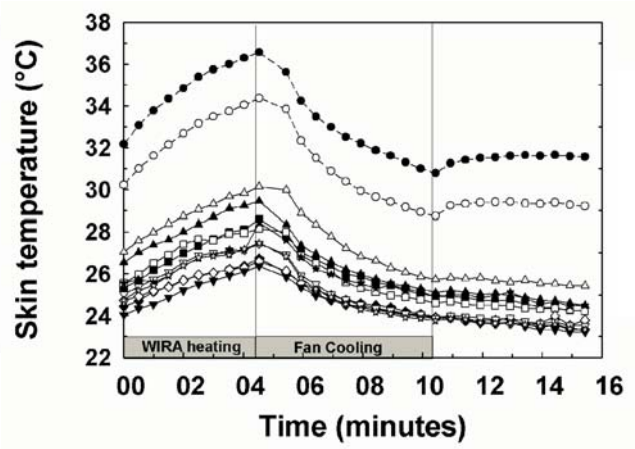


Figure 5.
Time course of surface temperature changes on selected measuring sites on the dorsal side of the hands and finger tips in a patient with known scleroderma (secondary Raynaud's phenomenon), before ,during, and after a 5-minute period of convective cooling with a fan. Note low basal temperatures, and no rewarming after cooling. Preheating due to low basal skin temperatures. Advanced case. The location and identification of the respective temperature measuring sites are explained in figure 1.
dor = dorsum of hand; dig = digit; L = left; R = right.

stomoses (AVA's). The tips of the fingers are particularly rich in these shunts which diminish gradually along the fingers [3]. Infrared thermograms illustrating these points can be seen in Fig. 3.

Patients with cold intolerance

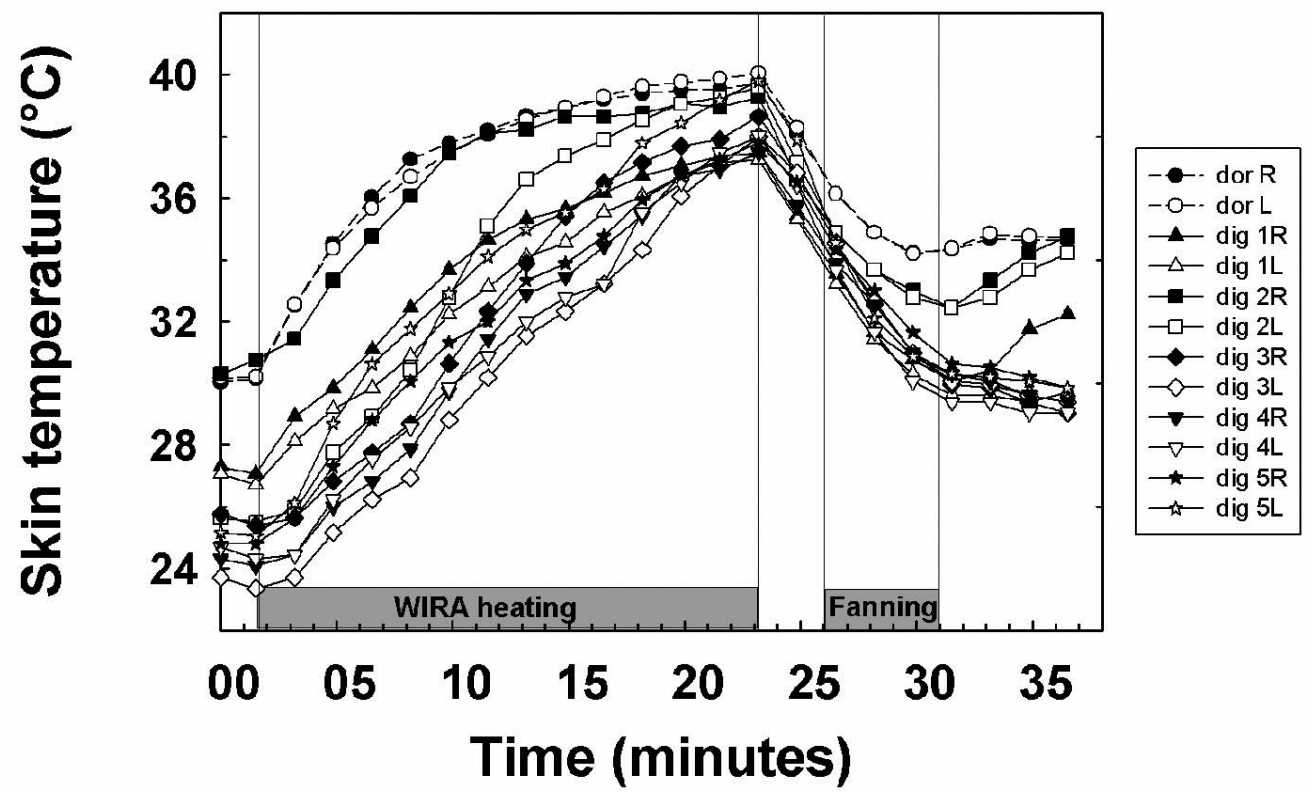
Nine patients, all women had symptoms and signs of classical RP based on preliminary clinical observations, no signs of other disease, and they received no treatment. They all complained of cold fingers at low outdoor temperatures. Their fingers looked normal at room temperature. All these patients had normal finger FBP at room temperature. Since no other disease was present they were classified as primary RP. The main feature of the patients was that rewarming was slow, the more severe the disease the slower and more variable the rewarming, which also in these patients began at the fingertips (opening of AVA) and their decline in finger temperature during fan cooling was not significantly greater than in normal subjects. None of the patients were smokers. Fig. 4 shows the thermography results in a 40-year-old woman with primary RP. During the rewarming period the temperature of all fingers, except the 2nd digit on the left hand, began to rise within a few minutes of each other (opening of AVA).

Patients with secondary RP

Twenty-four patients who had long-lasting, often permanent symptoms and objective changes of the skin of the fingers (oedema, redness, pallor) were classified, based on preliminary clinical observations, as secondary RP. Many had sub-normal FBP's in the most affected fingers at room temperature. This group was very heterogeneous. Seven of the patients were smokers. Fig 5 shows dynamic thermography results in a 75 year old women with known scleroderma. The cooling from intermediate basal values was intermediate after preheating, and there was no rewarming. All FBP values were subnormal Fig. 6 shows results in a 68-year-old man with symptoms of RP over many years, mainly from the three ulnar fingers. Very low basal finger temperatures. Heating by with the Hydrosun WIRA irradiator induced a rise in fingertip to around 36°C. There was a spontaneous decline in temperature after fan cooling, followed by a spontaneous rewarming period. Note: The symptomatic ulnar fingers showed no rewarming, but the non-symptomatic fingers did. FBP's were normal.

Discussion

We here present a method of dynamic infrared thermography with fan cooling for the study of patients with cold fingers. Patterns of skin temperature changes are presented in normal subjects, patients with clinical primary RP, and patients with finger vasculitis. The results suggest that by a standardised procedure of fan cooling followed by spontaneous rewarming it is possible to obtain important clinical information. In particular the temperature changes



of the fingertips during the rewarming period seem to be of importance. The results are in accordance the hypothesis that RP might be a heterogeneous disease of the AVA, being characterized by a high sensitivity to low temperatures.

IR thermography has unfortunately been introduced for clinical work without proper studies of normal subjects. International standards for performance and accepted reference materials are scarce. So, the clinical thermographer often does not know whether an observation is pathological or whether he/she observes a phenomenon within normality. The present paper basically does not change that situation, but presents certain patterns of finger temperatures during fan cooling and rewarming which might help classifying patients, and introduces dynamic thermography in a clinical setting.

RP has been widely studied by IR thermography, without significantly improving knowledge of the pathogenesis and differential diagnosis. Little is known about rewarming after finger cooling in normal subjects. However, a recent publication showed that rewarming is slower in elderly normal persons than in young ones [4] a finding that should be taken into account when evaluating studies in patients. They found that rewarming of fingers occurred most rapidly at the finger tips, suggesting that rewarming begins by opening of the AVA.

RP is a common clinical disorder consisting of recurrent, long lasting or episodic vasospasm of fingers and toes, often associated with exposure to cold. The classical progression consists of triphasic colour changes: well- demarked pallor of fingers leading to cyanosis, pain, numbness, and finally red flush upon rewarming [5]. Objective criteria for the diagnosis are not at hand, and it is often difficult to distinguish the classical RP from vasculitis, which can be secondary to auto-immune diseases e.g. scleroderma or smoking (previously termed Buergers disease). Using data from the Framingham Heart Study it was demonstrated in 717 women and 641 men that the incidence of RP was 2.2% in women 1.5 % in men i.e. a rather rare phenomenon. RP remitted in more than half of the patients [6]. It has been suggested that RP can be 1) an idiopathic condition; 2) part of scleroderma and other connective tissue disease; 3) and secondary to hand-arm vibration syndrome [7]. The distinction is important, since treatment regimes differ.

It is difficult to predict whether a case classified as primary RP later will develop into a manifestation of scleroderma. For a small group of patients RP can be the first symptom of scleroderma. RP is often seen at an early stage in patients with mixed connective tissue disease. FBP measurements in patients with systemic scleroderma showed low finger blood pressures, suggesting an increased flow resistance in the palmar arch and digital arteries, since sympathetic blockade did not influence those low blood pressures [8]. This would concur with our finding that patients which we did not classify as primary RP had low finger tem- peratures and low FBP at room temperature.

Bornmyr et al. [9] in a careful study using FBP measurements during cooling of the cuff and laser Doppler scanning concluded that there is no correlation between the decrease of finger blood flow and systolic blood pressure during local cold provocation, and that the ideal clinical method for demonstrating increased cold-induced vasospasm is still lacking. We suggest that IR thermography might be developed to a stage where it can be used as a simple, accurate and precise diagnostic test.

In this study it was obvious from visual inspection and inspection of skin temperature curves that rewarming in normal subjects and patients with primary RP started from the fingertips and moved proximally. AVA are plentiful in the tip of fingers and toes and scarce in the dorsum of hand and feet [3]. In contrast to the fingers there was little if any effect of cooling or rewarming on skin temperature of the dorsum of the hands. This would suggest that PR might be a condition affecting the AVA.

The AVA are important for thermoregulation during whole body cooling or heating. An AVA is a vessel that connects an artery and a vein, acting as a shunt to by-pass the capillary bed. It has been shown by pharmacological inhibition of nitric oxide (NO) generation in man that blood flow in finger pulp becomes reduced, whilst that of the dorsum of the hand is unaffected [10]. Another study of AVA showed that NO inhibition of microvasculature was not abolished by cervical ganglionectomy, suggesting a non-neural mechanism [11]. This is consistent with a physiological role of NO by direct action on the vascular wall. Physiological studies in normal subject using ultrasound Doppler measurements of finger arteries suggest that there is a local thermal level below which there is an abrupt, sustained closure of AVA. This level is between 23-20 degrees C [12]. It therefore seemed relevant when patients in our study presented with finger temperatures between 20 and 23 degrees that we preheated their fingers before fan cooling, since further significant cooling is unlikely to take place when the AVA are already closed. Other studies point to a crucial role of the AVA of the fingers in RP, hypersensitivity to cold being essential for the symptoms [13, 14, 15]. The latter authors used a labelled microspheres technique, demonstra- ting a low patency rate of AVA during finger cooling in RP.

IR thermography is presently the only imaging technique that can rapidly and non-invasively depict the location and opening of AVA simultaneously over a large area. The present study confirms the investigation of Rasmussen and Mercer [4], showing that rewarming after cooling always takes place from the fingertips when AVA open. IR thermography clearly showed that the rewarming of the finger tips is delayed or even absent in RP patients compared to normals. This would suggest that RP is mainly a disease of the AVA in primary and secondary RP, where AVAs are particularly sensitive to low temperatures.

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Temperature gradients in Raynaud´s Phenomenon. Comparison by gender, age class and finger involvement

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SUMMARY

BACKGROUND: Temperature gradients from the fingertip to the dorsum of the hand have been used for the differential diagnosis between primary and secondary Raynaud´s phenomenon. A combined temperature gradient (CTG), summing up temperature gradients before and after a cold challenge, may have additional discriminative power.

OBJECTIVE. What is the difference in magnitude of the CGT between females and males and does the magnitude of CTG differ in Raynaud patients of different age? Does the magnitude of CGT vary in patients presenting with Raynaud´s phenomenon in all fingers or in individual fingers?

METHOD: Thermal images from 240 consecutive patients referred for dynamic thermography due to suspected Raynau´ds phenomenon were re-evaluated retrospectively. Data were allocated to three age classes: 14 to 30 years, 31 to60 years and older than 60 years. A negative CTG greater than 1 degree was defined to be diagnostic for Raynaud´s phenomenon. In case of pathological CTG in 1 to 7 long fingers, the patients were diagnosed as Raynaud´s phenomenon in individual fingers. Diagnostic CTGs in all fingers, but thumbs excluded, were diagnosed as Raynaud´s phenomenon in all fingers. CTGs were compared by gender, age class and finger involvement.

RESULTS: More women than men presented with thermographic signs of vasospastic disease, but males showed more often Raynaud´s phenomenon of individual fingers than females. No difference in the magnitude of CTG with respect to gender or age classes was detected. The majority of patients with vasospastic finger disease were 31 to 60 years old. Subjects with normal or pathological findings were distributed in similar percentage to the younger and elderly age class. The magnitude of CGT was significantly greater in patients with Raynaud´s phenomenon in all fingers than in patients with vasospastic disease in individual fingers.

CONCLUSION: Dynamic thermography can clearly identify finger temperatures unable to recover after a mild cold challenge, but cannot identify the cause of vasospastic finger disease.

KEY WORDS: Combined temperature gradient, Raynaud´s phenomenon, age classes, gender, finger involvement

TEMPERATURGRADIENTEN BEI RAYNAUDPHÄNOMEN - VERGLEICH IN ABHÄNGIGKEIT VON GESCHLECHT, ALTERKLASSE UND FINGERBETEILIGUNG

HINTERGRUND: Temperaturgradienten von der Fingerspitze zum Handrücken wurden zur Differentialdiagnose zwischen primären und sekundären Raynaudphänomen verwendet. Ein kombinierter Temperaturgradient (KTG), der aus den Gradienten vor und nach einem Kaltwassertest gebildet wird, könnte verbesserte Differentialdiagnose erlauben.

ZIEL DER STUDIE: Ist der Wert des KGT bei Frauen und Männern unterschiedlich groß bzw. unterscheidet sich das Ausmaß des KTG Alters abhängig ? Differiert die Größe de KTG zwischen Patienten, bei denen alle Finger oder nur einzelne Finger ein Raynaudphänomen zeigen.

METHODE: Wärmebilder von 240 aufeinander folgenden Patienten, die wegen des Verdachts auf Raynaudphänomen zu einer dynamischen Thermographie zugewiesen worden waren, wurden retrospektiv neuerlich ausgewertet. Die Daten wurden drei Altersklassen 14 bis 30 Jahre, 31 bis 60 Jahre und älter als 60 Jahre zugeordnet. Ein negativer KTG größer als 1 Grad wurde als beweisend für ein Raynaudphänomen definiert. Patienten, die an 1 bis 7 Langfingern pathologische KTGs zeigten, wurden als Raynaudphänomen einzelner Finger diagnostiziert. Pathologische Gradienten an allen Fingern mit Ausnahme der Daumen wurden als Raynaudphänomen aller Finger bezeichnet. KTGs wurden abhängig von Geschlecht, Altersklassen und Fingerbeteiligung verglichen.

ERGEBNISSE: Es zeigten mehr Frauen als Männer thermographische Zeichen eines Raynaudphänomen, jedoch zeigten Männer häufiger als Frauen Raynaudphänomene einzelner Finger. In Abhängigkeit von Geschlecht und Alterklasse unterschied sich die Größe des KTG statistisch nicht. Die Mehrzahl der Patienten mit vasospastischer Erkrankung war 31 bis 60 Jahre alt. Ähnliche Prozentsätze von Personen mit unauffälligen und pathologischen Befunden fanden sich der jungen und alten Altersklasse. Bei Patienten mit Raynaudphänomen aller Finger zeigten sich die Werte der KGT signifikant größer als bei Patienten mit Raynaudphänomen einzelner Finger..

SCHLUSSFOLGERUNG: Dynamische Thermographie kann eindeutig jene Finger entdecken, deren Temperatur sich nach einem milden Kaltreiz nicht wiederherstellt, aber sie kann die Ursache des Vasospasmus nicht identifizieren.

SCHLÜSSELWÖRTER: kombinierter Temperaturgradient, Raynaudphänomen, Altersklassen, Geschlecht, Fingerbeteiligung

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Introduction

Francis Ring proposed in 1980 a temperature gradient from the dorsal hand to the finger tip for the thermographic evaluation of suspected Raynaud´s phenomenon [1]. He also suggested. a combined temperature gradient which includes recovery time if computed from temperature gradients prior to and 10 or 20 minutes after cold challenge. Various regions of interest have been proposed for the determination of temperature gradients [2, 3]. As the thumb is less severe affected by vasospasm [4], measurement areas have often excluded the first finger in thermographic assessment of Raynaud´s phenomenon. [1, 3].

In vasospastic disease associated with connective tissue disease (labelled secondary Raynaud´s phenomenon), the gradient might be more severe than in primary Raynaud´s phenomenon without underlying disease [1]. However, secondary Raynaud´s phenomenon may be seen in individual fingers only. A previous study compared the combined temperature gradient in patients presenting with thermographic signs of Raynaud´s phenomenon in all or in individual fingers and could not find a relationship between the magnitude of the gradient and the distribution of thermographically identified Raynaud´s phenomenon in all or in individual fingers [5].

A greater proportion of women than men suffer from Raynaud´s phenomenon [6]. Vasospastic finger disease is more common in women, with a female : male ratio of approximately four : one [7]. The prevalence of Ray- naud´s phenomenon varies between 6%and 20% in wo- men and between 3% and 12.5% in men, depending on the climate [7]. Males had higher hand temperatures and recover faster than females after exposure to a water bath 3-5°C [8]. However, delayed recovery of hand temperature after cooling may also occur in males. A retrospective analysis of British male army personnel aged over 18 assessed at the Institute of Naval Medicine Cold Injury Clinic found normal temperature recovery only in 24% of 311 patients investigated by thermography [9].

Rasmussen and Mercer reported higher hand temperatures and a more rapid recovering time after cooling in young subjects than in elderly subjects [10]. A recent study comparing combined temperature gradients from patients with Raynaud´s phenomenon in age classes (14 to 30 years, 31 t0 60 years, older than 60 years) found no significant difference in the magnitude of temperature gradient in the three age classes [11]. A higher percentage with normal recovery was detected in the oldest than in the youngest age class.

Considering the wide variation of thermographic assessment of patients with suspected Raynaud´s phenomenon [12], a retrospective study was performed to answer the following questions:

1.) What is the difference in magnitude of the combined temperature gradients (CGT)between females and males presenting with thermographic signs of Raynaud´s phenomenon? Does a gender related difference exist in the frequency of vasospastic finger disease ?

2.) Is there difference in the magnitude of CTG in Raynaud patients of different age ?

3.) Does the magnitude of CGT vary in patients presenting with Raynaud´s phenomenon in all long fingers or in individual fingers?

Method

In the last 3 years, the out-patient clinics for angiology had regularly referred patients with suspected Raynaud´s phenomen for dynamic infrared Thermography to the Thermography Unit at the Institute of Physical Medicine & Rehabilitation at the Hanuschkrankenhaus. Series of thermal images from consecutive patients were retrospectively evaluated.

All images were recorded in the following way. The patient sat on a comfortable chair with bare forearms with the arms hanging freely and acclimatised in this position for 15 minutes to a room temperature of 24 degrees. After acclimatisation the hands were positioned on a table, and images in the dorsal view for both hands were recorded. Then the hands, covered with plastic gloves, were fully immersed for 1 minute in water of 20°C. Immediately after taking off the gloves, and at in interval of 10 minutes 3 other thermal images were captured].

Temperature gradients for single fingers were determined in the following way: Circular regions of interest (ROI) were defined in a way that the outline of the circle was adjacent to the outline of the fingertip of the little finger. ROIs were positioned on the tip and over the mid of metacarpal bone of each finger. Temperature gradients were calculated by subtracting the metacarpal temperature from the temperature of the finger tip. This method of evaluation was found to be the most sensitive in detecting diagnostic temperature gradients [2]. A combined temperature gradient (CTG) was calculated by summing up the temperature gradient prior to cold challenge with the gradient 20 minutes post cold challenge.

Such temperature gradients can easily interpreted a negative gradients indicate cold fingertips and positive gradients are found when the temperature of the fingertip is higher than the temperature of the dorsal hand. A negative CTG greater than 1 degree, was interpreted as diagnostic for Raynaud´s phenomenon.

With respect to the distribution of combined temperature gradients, the thermograms were allocated to the following three groups.

Healthy subjects

All fingers presented with negative CTGs greater than 1 degree (figure 1). Fingers with normal temperature gradients from the groups "Raynaud´s phenomenon in individual fingers" and "Raynaud´s phenomenon in all fingers" were added for calculation of mean values of combined temperature gradients of "healthy subjects".

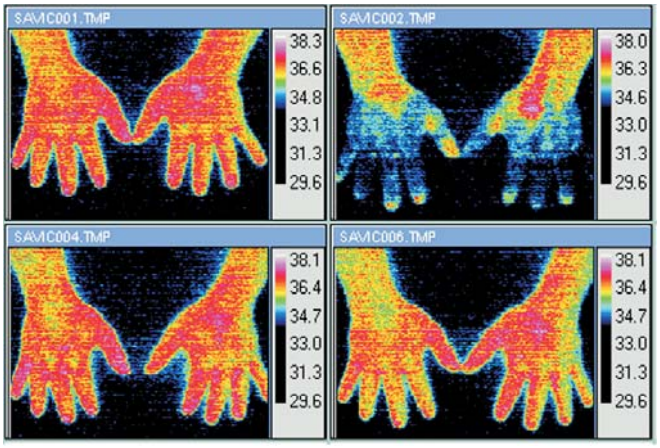

Figure 1
Healthy subject; prior, immediately, 10 and 20 minutes after cold challenge all finger showed temperature gradients greater

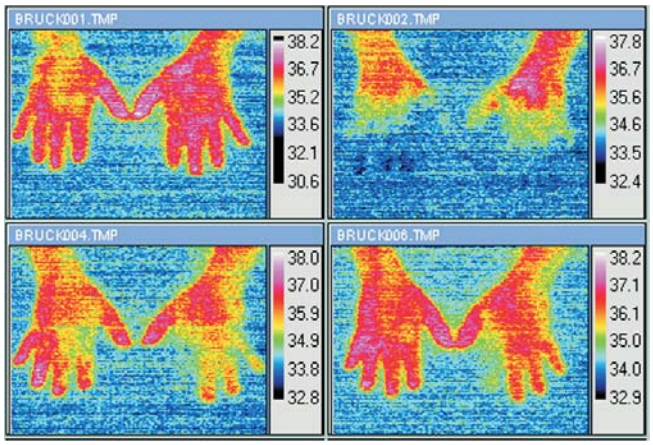

Figure 2
Normal temperature gradients prior to the cold challenge, pathological gradient of the left index 10 and 20 minutes after cold challenge indicating Raynaud´s phenomenon in individual fingers

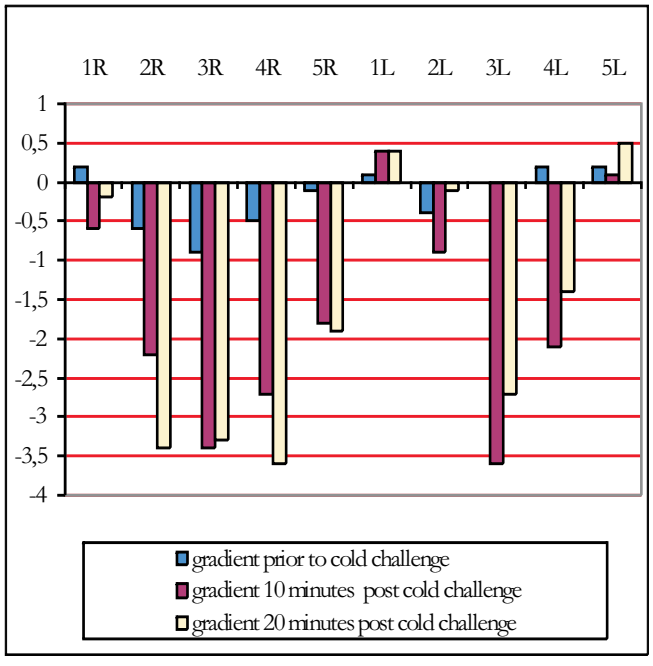

Figure 3
Temperature gradients in a patient with involvement of the 2nd to 5th finger right hand side and 3rd and 4th finger left hand side

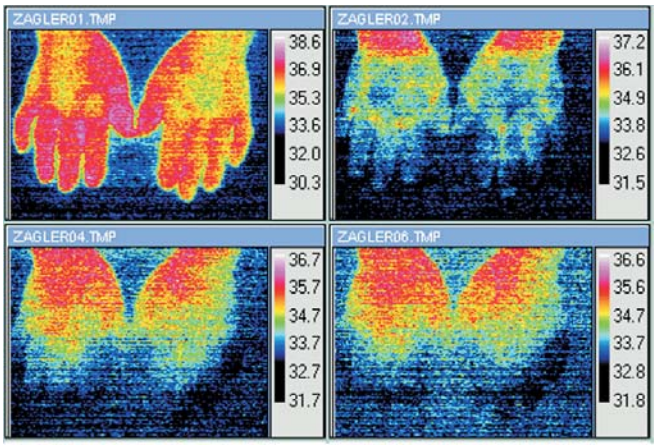

Figure 4
Normal gradients before cold challenge and the highly negative temperature gradients 10 and 20 minutes after cold challenge results in pathological combined gradients of all fingers

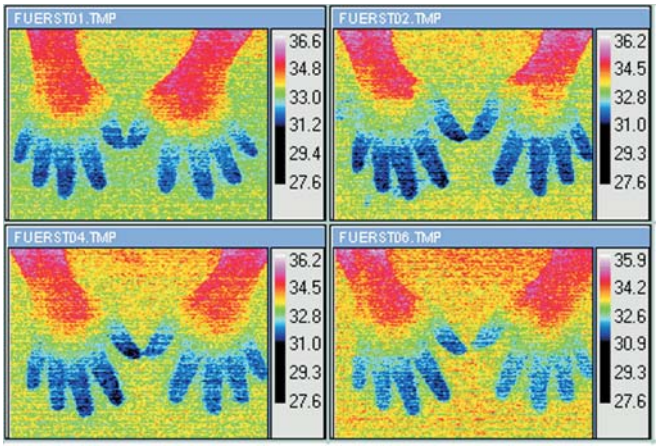

Figure 5
All fingers present with pathological temperature gradients at all time points

Individual fingers

In case of pathological CTG in 1 to 7 long fingers, the patients were diagnosed as Raynaud´s phenomenon in individual fingers (figure 2). Figure 3 shows a diagram of the magnitude of CTG in an individual patients, with normal temperature recovery of both thumbs and the 2nd and 5th finger on the left hand side. For the calculation of mean CTG, pathological temperature gradients of thumbs were added to the group" Raynaud´s phenomenon in individual fingers".

All fingers

Negative combined temperature gradients greater than 1 degree in all fingers, but thumbs excluded, were diagnosed as " Raynaud´s phenomenon in all fingers" (figure 4 and figure 5). Pathological gradients of thumbs remained for the statistical analysis in the group "Raynaud´s phenomenon in all fingers"

Age classes

Three age classes were generated: 14 to 30 years, 31 to 60 years and more than 60 years.

Statistical analysis

All calculations were performed with the software package SPSS 10.0. For descriptive statistics mean values ± standard deviation were allocated by gender, finger involvement and age group. One way ANOVA was used for comparison of mean values between age classes. Non-parametric test were used for comparing findings by gender and diagnosis.

Results

Thermal images from 240 subjects, 60 healthy subjects (38 female, 22 male) 73 patients with Raynaud´s phenomenon of individual fingers (47female, 27male) and 107 patients (88 female, 19 male) with vasospastic finger disease of all long fingers were evaluated. 106 normal findings from individual fingers of patients with Raynaud´s phenomenon were added to the group healthy subjects resulting in a total of 346 cases.

Gender

31,2 % of males showed normal temperature recovery of hand temperature after cooling, while females had a rate of 21,9% for normal recovery. A higher percentage of men (40,3%) than women (27,2%) presented with Raynaud´s phenomenon of individual fingers. About half all females showed vasospastic disease of all fingers, but only 28,4% of men presented with lack of temperature recovery in all fingers.

Cumulated data from 250 females and 96 males were analysed. Table 1 shows the mean values of combined temperature gradients in healthy females and males. Table 2 provides information of the magnitude of temperature gradients in patients with Raynaud´s phenomenon in individual fingers and table 3 shows the temperature gradients in females and males with vasospastic disease of all fingers. Comparison of gradients between men and women with the non parametric Mann Whitney-U-Test did not obtain any significant difference.

Age classes

44 patients were aged between 14 and 30 years (18,3% of the total sample). The majority (52,5%) of subjects were found in the age class "31 to 60 years" and the remaining 29.2 % of the sample were older than 60 years (table 4). 16,7% of healthy subjects were younger than 31 years and 26,7% were older than 60 years. 21,9% of patients with Raynaud´s phenomenon in individual fingers were found in the lowest age class and 30,1% of these patients were in the top age class. 16.8% of patients younger than 31 years presented with vasospastic disease of all fingers and 29.9% of these patients were older than 60 years.

Tables 5 to 7 provide information on CTG in healthy subjects, patients with Raynaud´s phenomenon of individual or all fingers in relationship to age. One-way ANOVA detected the only statistical difference between age classes for the right thumb in healthy subjects. No difference in the magnitude of CTG in patients with Raynaud´s phenomenon was observed in different age classes.

Involvement of individual versus all fingers

Comparison with respect to age classes was impossible due to low numbers of patients with Raynaud´s phenomenon in individual fingers. Analysis of CTGs with Mann- Whitney-U-Test obtained highly significant statistical differences between patients with involvement of individual fingers or affection of all fingers with thermographic signs of vaso-spastic disease (table 8).

Discussion

Several parameters have been used for the evaluation of thermal images from patients with suspected Raynaud´s phenomenon [12]. As the CTG comprises information about the temperature distribution at defined time points, temperature values prior to a cold challenge can be extracted from this measure. A negative CTG greater than 2 degrees can be interpreted in a way that cold fingertips were with high probability present prior to the cold challenge.

Although the percentage of Raynaud´s phenomenon in individual or all fingers is higher in the lowest than in the highest age class, this study based on 346 observations confirms previous findings [11], that a relationship between age and magnitude of CTG in patients with Raynaud`s phenomenon is absent. The majority of findings was obtained in middle aged subjects, and a nearly identical distribution to young and elderly subjects was detected for normal and pathological temperature gradients.

In this study, Raynaud´s phenomenon was overall more frequent in females than in males., but men had a higher percentage of thermographic signs of vasospastic disease in individual fingers than women.

Raynaud´s phenomenon in individual fingers may indicate secondary vasospastic disease, but thermographic data on Raynaud´s phenomenon in individual fingers are scarce.

Tauchmannova investigated by thermography a large sample of patients with Raynaud´s phenomenon caused by various connective tissue diseases [13]. Thermographic diagnosis was based on a negative temperature gradient from the fingertip to dorsum of the hand. In systemic sclerosis, 50 of 59 patients presented with pathological temperature gradients in all fingers. In 68 patients with systemic lupus erythematosus involvement of all fingers occurred in 23 subjects (34%) and became obvious only after the cold challenge in 15 of these 23 patients. In the small subgroups with mixed connective tissue syndrome (16 patients) or with overlap syndrom (16 patients) Raynaud´s phenomenon of all fingers was observed in 3 and 7 patients respectively.

A previous study reported that diagnostic temperature gradients in all fingers occurred in 8/71 patients and patho- logical thermographic findings of individual fingers were observed in 35/71 subjects [14]. Anderson et al provided mean temperature gradients prior to cold challenge at room temperatures of 23 or 30°C in patients with primary Raynaud´s

Table 1
Mean temperature gradients in healthy subjects, grouped by gender

Healthy subjects		Combined temperatue gradient									
		Right hand side					Left hand side				
		1st finger	2nd finger	3rd finger	4th finger	5th finger	1st finger	2nd finger	3rd finger	4th finger	5th finger
female	numbers	99	55	57	58	63	98	57	57	61	62
	mean	0,57	0,41	0,38	0,64	0,31	0,51	0,50	0,44	0,73	0,54
	standard deviation	0,97	0,95	0,95	0,95	0,86	0,86	0,84	0,98	0,99	0,85
male	numbers	47	39	34	42	38	48	33	30	37	37
	mean	0,88	0,39	0,45	0,38	0,42	0,47	030	0,60	0,67	0,58
	standard deviation	1,16	0,84	0,93	0,78	0,71	0,79	0,62	0,68	0,79	0,74
all	numbers	146	94	91	100	101	146	90	87	98	99
	mean	0,67	0,40	0,41	0,53	0,35	0,49	0,43	0,49	0,71	0,56
	standard deviation	1,04	0,89	0,94	0,89	0,81	0,83	0,77	0,89	0,91	0,81

Mann-Whitney-U-Test	Right hand side					Left hand side				
	1st finger	2nd finger	3rd finger	4th finger	5th finger	1st finger	2nd finger	3rd finger	4th finger	5th finger
2-sided p-value	0,147	1,000	0,678	0,177	0,299	0,866	0,234	0,258	0,980	0,369

Table 2
Mean temperature gradients in patients with Raynaud´s phenomenon in individual fingers, grouped by gender.

Raynaud´s phenomenon in individual fingers		Combined temperatue gradient									
		Right hand side					Left hand side				
		1st finger	2nd finger	3rd finger	4th finger	5th finger	1st finger	2nd finger	3rd finger	4th finger	5th finger
female	numbers	8	29	27	26	25	6	28	29	23	23
	mean	-1,76	-2,33	-3,00	-2,52	-2,20	-1,97	-2,44	-2,18	-1,94	-2,19
	standard deviation	0,80	1,32	1,94	1,22	1,04	1,13	1,43	1,05	0,98	0,97
male	numbers	1	7	11	3	7	1	13	16	8	8
	mean	-2,80	-2,87	-2,11	-1,97	-1,53	-1,40	-3,72	-3,09	-2,75	-2,40
	standard deviation		1,83	0,96	1,06	0,58		2,04	2,26	1,47	0,93
all	numbers	9	36	38	29	32	7	41	45	31	31
	mean	-1,88	-2,45	-2,74	-2,46	-2,05	-1,89	-2,85	-2,50	-2,15	-2,25
	standard deviation	0,83	1,43	1,75	1,20	0,99	1,06	1,73	1,62	1,16	0,95

Mann-Whitney-U-Test	Right hand side					Left hand side				
	1st finger	2nd finger	3rd finger	4th finger	5th finger	1st finger	2nd finger	3rd finger	4th finger	5th finger
2-sided p-value	0,237	0,144	0,209	0,430	0,064	1,000	0,034	0,433	0,182	0.527

Table 3
Mean temperature gradients in patients with Raynaud´s phenomenon in all fingers, grouped by gender.

Raynaud´s phenomenin in all fingers		Combined temperatue gradient									
		Right hand side					Left hand side				
		1st finger	2nd finger	3rd finger	4th finger	5th finger	1st finger	2nd finger	3rd finger	4th finger	5th finger
female	numbers	66	88	88	87	87	70	88	88	88	88
	mean	-3,23	-4,93	-4,99	-4,65	-3,97	-3,45	-4,82	-5,12	-4,64	-3,79
	standard deviation	1,92	3,91	1,96	1,87	1,77	1,83	1,95	1,96	1,79	1,60
male	numbers	17	19	19	19	19	16	19	19	19	19
	mean	-3,18	-5,11	-4,70	-4,65	-3,62	-3,01	-4,85	-5,10	-4,81	-3,74
	standard deviation	1,88	2,04	1,82	1,50	1,38	1,95	1,78	1,95	1,65	1,38
all	numbers	83	107	107	106	106	86	107	107	107	107
	mean	-3,22	-4,96	-4,94	-4,65	-3,91	-3,37	-4,81	-5,12	-4,67	-3,76
	standard deviation	1,90	3,64	1,93	1,80	1,71	1,85	1,91	1,95	1,76	1,55

Mann-Whitney-U-Test	Right hand side					Left hand side				
	1st finger	2nd finger	3rd finger	4th finger	5th finger	1st finger	2nd finger	3rd finger	4th finger	5th finger
2-sided p-value	0,973	0,336	0,499	0,705	0,510	0,318	0,702	0,958	0,701	0,883

Table 4
Age classes and finger involvement

	Healthy subjects	Raynaud´s phenomenon in individual fingers	Raynaud´s phenomenon in all fingers	All subjects
14 to 30 years	10	16	18	44
31 to 60 years	34	35	57	126
Older than 60 years	16	22	32	70

Table 5
Mean temperature gradients in healthy subjects allocated to age classes

Healthy subjects		Age group	ANOVA p-values	n	mean	standard deviation	95%-Confidence interval of the mean	
							Lower limit	Upper limit
Right hand side	1st finger	14 to 30 years	0.042 *	27	0.37	0.85	0.04	0.71
		31 to 60 years		79	0.61	0.95	0.40	0.83
		older than 60 years		40	0.99	1.27	0.59	1.40
		total		146	0.67	1.04	0.50	0.84
	2nd finger	14 to 30 years	0.174	18	0.06	0.65	-0,27	0.38
		31 to 60 years		50	0.51	0.95	0.25	0.78
		older than 60 years		26	0.41	0.90	0.05	0.77
		total		94	0.40	0.89	0.22	0.58
	3rd finger	14 to 30 years	0.483	17	0.53	1.12	-0,05	1.11
		31 to 60 years		48	0.47	0.90	0.20	0.73
		older than 60 years		26	0.22	0.88	-0.13	0.58
		total		91	0.41	0.94	0.21	0.60
	4th finger	14 to 30 years	0.239	18	0.76	1.09	0.22	1.30
		31 to 60 years		53	0.39	0.85	0.16	0.63
		older than 60 years		29	0.63	0.80	0.33	0.94
		total		100	0.53	0.89	0.35	0.70
	5th finger	14 to 30 years	0.549	17	0.48	0.92	0.01	0.96
		31 to 60 years		53	0.27	0.85	0.03	0.50
		older than 60 years		31	0.42	0.66	0.18	0.66
		total		101	0.35	0.81	0.19	0.51
Left hand side	1st finger	14 to 30 years	0.128	28	0.28	0.73	0,00	0.56
		31 to 60 years		76	0.47	0.78	0.29	0.65
		older than 60 years		42	0.68	0.96	0.38	0.98
		total		146	0.49	0.83	0.36	0.63
	2nd finger	14 to 30 years	0.323	16	0.17	0.66	-0.18	0.52
		31 to 60 years		47	0.50	0.81	0.27	0.74
		older than 60 years		27	0.44	0.74	0.15	0.74
		total		90	0.43	0.77	0.27	0.59
	3rd finger	14 to 30 years	0.401	16	0.68	0.99	0.16	1.21
		31 to 60 years		45	0.53	0.89	0.26	0.80
		older than 60 years		26	0.32	0.81	-0,01	0.64
		total		87	0.49	0.89	0.31	0.68
	4th finger	14 to 30 years	0.307	17	086	1.14	0.28	1.44
		31 to 60 years		51	0.78	0.87	0.53	1.02
		older than 60 years		30	0.50	0.84	0.18	0.81
		total		98	0.71	0.91	0.52	0.89
	5th finger	14 to 30 years	0.793	17	0.49	0.83	0.06	0.92
		31 to 60 years		54	0.54	0.83	0.31	0.76
		older than 60 years		28	0.64	0.78	0.34	0.94
		total		99	0.56	0.81	0.40	0.,720

* significant 2 sided p-value at the level of 0.05

phenomenon and secondary Raynaud´s pheno- menon caused by systemic sclerosis or undifferentiated connective tissue disease [15]. The average number of fingers with a negative temperture gradient greater than 1 was 2.9.±3.4 in primary Raynaud´s phenomenon 5.7±2.8 in systemic sclerosis and 2.8 ± 3.0 in undifferentiated connective tissue disease, indicating that involvement of all fingers occurred only in secondary vasospastic disease.

Although it is known for long that the thumb is less severe affected by vasospasms, the first study related to Raynaud´s phenomenon in the first finger was published in 2008 [4]. Chikura et al. reported mean temperature gradients of each finger and found lower values in patients with systemic sclerosis than in patients with primary Raynaud´s phenomenon. The frequency of diagnostic temperature gradients in each finger was also recorded, but average values of pathological gradients of the affected fingers have not be calculated. Another previous study observed that the magnitude of temperature gradients 20 minutes after the cold challenge did not differ between involvement of individual or all fingers[5].

Table 6
Mean temperature gradients in patients with Raynaud´s phenomenon in individual fingers, allocated to age group

Raynaud´s phenomenon in individual fingers		Age group	ANOVA p-values	n	mean	standard deviation	95%-Confidence interval of the mean	
							Lower limit	Upper limit
Right hand side	1st finger	14 to 30 years	0.410	2	-1.20	0.28	-3.74	1.34
		31 to 60 years		3	-1.87	0.90	-4.11	0.37
		older than 60 years		4	-2.23	0.89	-3.63	-0.82
		total		9	-1.88	0.83	-2.51	-1.24
	2nd finger	14 to 30 years	0.984	7	-2.36	1.07	-3.34	-1.37
		31 to 60 years		17	-2.44	1.55	-3.24	-1.65
		older than 60 years		12	-2.48	1.50	-3.44	-1.53
		total		36	-2.44	1.42	-2.92	-1.96
	3rd finger	14 to 30 years	0.879	9	-2.48	1.13	-3.34	-1.61
		31 to 60 years		18	-2.84	1.66	-3.66	-2.02
		older than 60 years		11	-2.80	2.36	-4.39	-1.21
		total		38	-2.74	1.75	-3.32	-2.17
	4th finger	14 to 30 years	0.605	7	-2.14	0.93	-3.01	-1.28
		31 to 60 years		14	-2.69	1.52	-3.56	-1.81
		older than 60 years		8	-2.34	0.74	-2.96	-1.72
		total		29	-2.46	1.20	-2.92	-2.00
	5th finger	14 to 30 years	0.180	8	-1.50	0.36	-1.80	-1.20
		31 to 60 years		17	-2.29	1.15	-2.88	-1.70
		older than 60 years		7	-2.11	0.91	-2.96	-1.27
		total		32	-2.05	0.99	-2.41	-1.70
Left hand side	1st finger	14 to 30 years	0.744	1	-1.00	.	.	.
		31 to 60 years		3	-2.00	1.06	-4.63	0.63
		older than 60 years		3	-2.07	1.33	-5.38	1.24
		total		7	-1.89	1.06	-2.86	-0.91
	2nd finger	14 to 30 years	0.427	10	-2.52	1.35	-3.49	-1.55
		31 to 60 years		21	-2.71	1.40	-3.35	-2.07
		older than 60 years		10	-3.46	2.55	-5.29	-1.63
		total		41	-2.85	1.73	-3.39	-2.30
	3rd finger	14 to 30 years	0.525	10	-2.43	1.52	-3.52	-1.35
		31 to 60 years		23	-2.30	1.31	-2.87	-1.74
		older than 60 years		12	-2.96	2.21	-4.36	-1.55
		total		45	-2.50	1.62	-2.99	-2.02
	4th finger	14 to 30 years	0.318	8	-1.73	1.16	-2.69	-0.76
		31 to 60 years		16	-2.15	1.07	-2.72	-1.58
		older than 60 years		7	-2.64	1.32	-3.87	-1.42
		total		31	-2.15	1.16	-2.58	-1.73
	5th finger	14 to 30 years	0.346	8	-2.18	0.95	-2.97	-1.38
		31 to 60 years		14	-2.50	0.96	-3.05	-1.95
		older than 60 years		9	-1.91	0.91	-2.61	-1.21
		total		31	-2.25	0.95	-2.59	-1.90

Table 7

Mean temperature gradients in patients with Raynaud´s phenomenon in all fingers, allocated to age groups

Raynaud´s phenomenon in all fingers		Age group	ANOVA p-values	n	mean	standard deviation	95%-Confidence interval of the mean	
							Lower limit	Upper limit
Right hand side	1st finger	14 to 30 years	0.942	14	-3.11	1.84	-4.17	-2.05
		31 to 60 years		43	-3.19	1.94	-3.79	-2.60
		older than 60 years		26	-3.32	1.94	-4.10	-2.53
		total		83	-3.28	1.90	-3.63	-2.80
	2nd finger	14 to 30 years	0.641	18	-4.54	1.72	-5.39	-3.69
		31 to 60 years		57	-5.28	4.70	-6.52	-4.03
		older than 60 years		32	-4.65	1.85	-5.32	-3.98
		total		107	-4.96	3.64	-5.66	-4.27
	3rd finger	14 to 30 years	0.590	18	-4.86	1.69	-5.70	-4.02
		31 to 60 years		57	-5.11	2.09	-5.67	-4.56
		older than 60 years		32	-4.68	1.77	-5.37	-4.04
		total		107	-4.94	1.93	-5.31	-4.57
	4th finger	14 to 30 years	0.827	18	-4.47	1.64	-5.28	-3.65
		31 to 60 years		56	-4.75	1.99	-5.28	-4.21
		older than 60 years		32	-4.59	1.55	-5.15	-4.03
		total		106	-4.65	1.80	-5.00	-4.31
	5th finger	14 to 30 years	0.588	18	-3.87	1.40	-4.56	-3.17
		31 to 60 years		56	-4.06	1.88	-4.56	-3.56
		older than 60 years		32	-3.70	1.57	-4.23	-3.10
		total		106	-3.91	1.71	-4.24	-3.58
Left hand side	1st finger	14 to 30 years	0.865	14	-3.61	2.11	-4.82	-2.39
		31 to 60 years		47	-3.35	1.74	-3.86	-2.84
		older than 60 years		25	-3.28	1.97	-4.09	-2.47
		total		86	-3.37	1.85	-3.77	-2.97
	2nd finger	14 to 30 years	0.632	18	-4.42	1.69	-5.26	-3.58
		31 to 60 years		57	-4.90	2.07	-5.45	-4.35
		older than 60 years		32	-4.88	1.77	-5.52	-4.25
		total		107	-4.81	1.91	-5.18	-4.45
	3rd finger	14 to 30 years	0.596	18	-4.79	1.76	-5.67	-3.92
		31 to 60 years		57	-5.28	2.04	-5.82	-4.77
		older than 60 years		32	-4.98	1.89	-5.66	-4.30
		total		107	-5.10	1.95	-5.48	-4.74
	4th finger	14 to 30 years	0.836	18	-4.47	1.58	-5.26	-3.69
		31 to 60 years		57	-4.75	1.88	-5.25	-4.25
		older than 60 years		32	-4.64	1.67	-5.24	-4.04
		total		107	-4.67	1.76	-5.01	-4.33
	5th finger	14 to 30 years	0.871	18	-3.64	1.29	-4.29	-3.02
		31 to 60 years		57	-3.84	1.66	-4.28	-3.40
		older than 60 years		32	-3.70	1.54	-4.25	-3.15
		total		107	-3.76	1.55	-4.06	-3.47

Table 8

Temperature gradients (mean ± standard deviation) in patients with individual fingers affected compared to patients presenting with Raynaud´s phenomenon of all fingers

Mann-Whitney-U-Test	Right hand side					Left hand side				
	1st finger	2nd finger	3rd finger	4th finger	5th finger	1st finger	2nd finger	3rd finger	4th finger	5th finger
2-sided p-value	0.032	0.000	0.000	0.000	0.000	0.019	0.000	0.000	0.000	0.000
Individual fingers	-1.88 ± 0.83	-2.44 ± 1.42	-2.74 ± 1.75	-2.46 ± 1.20	-2.05± 0.99	-1.89 ± 1.06	-2.85 ± 1.73	-2.50 ± 1.62	-2.15 ± 1.16	-2.25± 0.95
All fingers	-3.22 ± 1.90	-4.96 ± 3.64	-4.94 ± 1.93	-4.65± 1.80	-3.90 ± 1.71	-3.37± 1.85	-4.81 ± 1.91	-5.11 ± 1.95	-4.67 ± 1.76	-3.76± 1.55

The present study compared combined temperature gradients and found significant greater gradients in all fingers affected by vasospastic disease than in Raynaud´s phenomenon of individual fingers. This is caused by the fact, that in most patients with involvement of individual fingers the gradient was normal prior to the cold challenge (figure 3). Patients presenting with Raynaud´s phenomenon in all fingers showed very often marked negative temperature gradients prior to the cold challenge (figure 5) and although almost all patients recoverd after the mild cold stress to baseline readings, the magnitude of the combined temperature gradient becomes much greater than in patients who started with nearly normal temperature gradients (figure 4).

Coffman proposed the following modification of the criteria by Allen and Brown for the diagnosis of primary Raynaud's disease (16).

1) Vasospastic attacks induced by cold exposure.

2) Bilateral involvement of the extremities.

3) Absence of gangrene or involvement of only the skin of the fingertips.

4) History of symptoms for at least 2 years.

5) No evidence of an underlying disease including absence of antinuclear antibodies, a normal erythrocyte sedimentation rate, and normal nailfold capillaroscopy and esophageal motility studies

The clinical diagnosis of vasospastic attacks was defined by Brennan et al [17] as follows:

1) definite Raynaud´s phenomenon is comprised of repeated episodes of biphasic colour changes on cold exposure;

2) possible Raynaud´s phenomenon is defined by uniphasic colour changes plus numbness or paresthesia; and

3) no Raynaud´s phenomenon is characterised by no colour changes on cold exposure.

None of these definitions recommend temperature changes as means for diagnosis. However, the criteria for classification of early systemic sclerosis by LeRoy and Medsger [18] require for objectively documented of Raynaud´s phenomenon direct observation of any 2 of

A. Pallor (well demarcated whitening of acral skin)

B. Cyanosis (dusky blueness, which disappears on rewarming)
C. Suffusion (well demarcated redness)

or direct measurement of response to cold by

A. objective evidence of delayed recovery after cold challenge

B. Nielsen Test (19] or equivalent (such as laser Doppler ultrasound, thermography, skin thermistor measurements, thermosensitive crystals).

The number of affected fingers is not yet an established diagnostic criterium. The modified Allen criteria for primary Raynaud´s phenomenon require bilateral involvement of the extremities, but that does not necessarily mean involvment of all fingers. Secondary Raynaud´s phenomenon might be seen in individual fingers only, but the most important cause of secondary Raynaud´s phenomenon systemic sclerosis affects almost all fingers [13, 15].

Entrapment of peripheral nerves is often missed as the cause of Raynaud´s phenomenon in individual fingers [14, 20]. Significant different temperature gradients of the first, third and fourth finger between patients with pathological or normal conduction velocity of the median nerve have been described prior and after a mild cold challenge [21]. Recently, a study from Finland reported low skin temperatures at the first to third fingertip of patients with electro neurographically confirmed carpal tunnel syndrome, which rewarmed after carpal tunnel release and did not differ any longer from healthy control subjects [22] A group from Lancashire observed delayed temperature recovery after cold challenge in patients with carpal tunnel syndrome and normal recovery after surgical release of the median nerve [23]. It must also be mentioned, that the symptoms numbness and paresthesia which may indicate together with uniphasic colour changes possible Raynaud´s phenomenon [17], do not reflect disturbed vascular functions, but express a functional failure of the peripheral nerve system.

Conclusion

It is concluded from the findings of this study that

1.) More women than men showed thermographic signs of Raynaud´s phenomenon, but the magnitude of CGT did not differ between females and males, neither in healthy subjects nor in patients with Raynaud´s phenomenon. A higher percentage of men than women presented with Raynaud´s phenomenon in individual fingers.

2.) No difference in the magnitude of CTG was observed in Raynaud patients of different age. The majority of patients with vasospastic finger disease were 31 to 60 years old. Subjects with normal or pathological findings were distributed in similar percentage to the younger and elderly age class.

3.) The magnitude of CGT is significantly greater in patients with Raynaud´s phenomenon in all fingers than in patients with with vasospastic disease in individual fingers.

Evaluation of dynamic thermography by a combined temperature gradient of individual fingers provides information on the distribution of finger temperatures unable to recover after a mild cold challenge within 20 minutes, and identifies fingers with a pre-established cold finger tip at baseline of the dynamic thermographic investigation. Due to the manifold reasons for a disturbed ability to cope with cold stimuli and non established patterns of involved fingers in primary and secondary Raynaud´s phenomenon, thermography cannot identify the cause of vasospastic finger disease.

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News in Thermology

Ph.D Awards based on thermal imaging

University of Tromsø

Dr Louis de Weerd, plastic surgeon and PhD student of Prof Mercer, defended successfully his thesis on "Free Perforator Flap Surgery and Dynamic Infrared Thermography" at the North Norway University Tromsø.

After presenting his trial lecture on "Perfusion imaging in reconstructive surgery", the candidate discussed in his thesis the advantages of infrared images in preparation and monitoring breast reconstruction based on perforator flaps originating from the subcutaneous tissue of the abdomen. Louis de Weerd studies investigated infrared imaging and found this imaging method to be reliable and practical technique,. which correlates with ultrasound Doppler investigations, and helps to identify perforator vessels which can nourish abdominal flaps. Dynamic Infrared Thermography was used to map the best perforator preoperatively. Applying he same technology helped to determine the permeability of the micro-anastomoses and to detect early thrombosis intra- operatively. The information revealed in the postoperative phase provided new understanding of the function of the vascular anatomy in healing of perforator flaps

Prof Hamdi, a world authority in perforator flap surgery from the University Hospital Gent, was the first opponent. He questioned the rationale for the selection of particular perforator vessels and in which way the small rate of partial flap failures can further be reduced. The candidate defended successfully this part of his thesis.

Prof Ammer asked for thermal description of hot spots beyond vision by eye. He proposed to describe the rapid appearance of hot spots by the time lag between the end of the cold challenge and the appearance of the hot spot or by the size and temperature of the spot The temperature difference to the surrounding tissue or the temperature change of hot spots in time are other possible measurements. The candidate agreed that detailed thermal description of hot spots will increase the repeatability of the thermographic evaluation of abdominal perforator flaps. This part of the thesis was also successfully defended and

Figure 1
Successful thesis defense by Dr Louis de Weerd
From left to right: Prof Hamdi (first opponent), Dr Louis de Weed (PhD candidate), Linda de Weerd, Prof Ammer (second opponent) Mona Johannessen(examination chair), Prof Tone Nordoy (third opponent) Prof Mercer

Louis de Weerd will be awarded with the degree of Philosophiae Doctor.

University of Glamorgan

Kevin Howell clinical scientist at the Royal Free Hospital London, was awarded with the academic degree Doctor of Philosophy at the degree ceremony in July 2010. Dr Kevin Howell´s degree is based on a portfolio comprising thermographic studies related to Raynaud´s phenomenon and localised Scleroderma in children.

Standard for Specifications of Thermal imagers

An international group of metrologists, chaired by Prof Graham Machin, are currently discussing standards for "technical data specification for thermal imagers". Prof Machin emphasised that the standard is to include only the essential parameters required for specifying the imager performance. The parameters should help the purchaser of an imager decide which device best meets his particular measurement requirements.

A the following draft list of parameters should be included in the standard.

- Waveband
- Instantaneous Field of View (Spatial Resolution)
- FOV
- Temperature resolution (NETD-like)
- Temperature measurement accuracy
- Short term stability
- Temperature range
- Non-Uniformity Correction (include in image uniformity
- Image uniformity
- Display resolution (image)
- Power supply (Effect on temperature output)
- Display resolution (temperature)
- Frame Rate
- Response time
- Long term stability (linked to temperature accuracy)
- Stability (Ambient Temperature Effect)
- Emissivity setting
- Effects of ambient conditions
- SSE
- Interchange (as per spot pyro standard)
- Warm up time (ready from switch on)
- Reflection and path corrections (humidity, distance, atmospheric temperature and transmission)
- Focus range
- Number of pixels in sensor
- Storage conditions
- Operating environmental conditions
- Calibrated temperature range
- Measurement temperature range

Meetings

2010

27-30th July 2010

QIRT 2010 The 10th Quantitative Infrared Thermography Conference at Université Laval, Québec City, Canada

Topics:

• State of the art and evolution in the field of infrared scanners and imaging systems allowing quantitative measurements and related data acquisition and processing.

• Integration of thermographic systems and multispectral analysis. Related problems like calibration and characterization of infrared cameras (mono and multidetector systems), emissivity determination, absorption in media, spurious radiations, three dimensionality of observed objects, certification and standardization.

• Thermal effects induced e.g. by electromagnetic fields, elastic waves or mechanical stresses.

• Application of infrared thermography to radiometry, thermometry and physical parameters identification in all fields such as (and not limited to): industrial processes, material sciences, structure and material non destructive evaluations, medicine, and biomedical science, fluid mechanics, cultural heritage, environment, food production.

Further information

QIRT 2010 Secretariat

Electrical and Computer Engineering Dept.
Université Laval, Québec (Québec)
CANADA G1V 0A6

Http://qirt2010.gel.ulaval.ca

8th -12th November 2010

InfraMation Thermography Conference 2010
Las Vegas, Nevada

The Leading Infrared Camera Users & Applications Conference including papers on

Building Science, Weatherization/Energy Audits, Infrastructure
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Venue:: Bally's, Las Vegas, Nevada

Registration Fee: $1395

Information: www.inframation.org
Email: Inframation@flir.com

13th November 2010

23rd Thermological Symposium
of the Austrian Society of Thermology

Venue: SAS Hotel Vienna, Austria

Deadline for Abstracts: 10thOctober 2010

Speakers:

Prof Francis Ring, UK

Dr. Kevin Howell, UK

Prof. Rod Thomas, UK

Ricardo Vardasca, Portugal

Prof. Anna Jung, Poland

Prof Adriana Nica, Romania

Prof Kurt Ammer, Austria

Electronic submission is preferred and strongly suggested (Email: KAmmer 1950@aol.com)

Information
Prof K. Ammer, MD, PhD
Austrian Society of Thermology
Hernalser Hauptstr 209/14
Email: KAmmer 1950@aol.com

The Royal Photographic Society
Imaging Science Group

Thursday October 7th 10.15-5pm

at the Royal Astronomical Society, Burlington House, Piccadilly. London

Convenor: Prof. Francis Ring FRAS FRPS

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Keynote lecture: RW Wood at Johns Hopkins: A Panchromatic legacy

Prof. Paul Feldman (Johns Hopkins University, Baltimore. U.S.A.

A Century of Infrared Photography	Mr. Andy Finney
Infrared thermal imaging of the human body; from analogue to digital	Prof.Francis Ring
High-Performance Thermal Imagery from 1st and 2nd Generation Cameras.	Prof. C.T. Elliott
"Your Tiny Hand is Frozen"	Prof. Kurt Ammer (Vienna)

LUNCH

Thermal behaviour of the African Elephant	Prof. James Mercer (Univ. N. Norway)
Sleep Deprivation and Frustration - Filming Wildlife for Television using Infra-Red	Mr.Colin Jackson (BBC)
IR surveys of buildings, the energy conservation story	Mr. John Snell (Vermont USA)
Satellite and Terrestrial Thermal Imaging to Monitor Volcanoes	Mr.Talbian Barnie (CambridgeUK)
Visualising the Earth with Infrared (in a multispectral context).	Prof. G. Awcock (Brighton Univ)

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Further information

Prof Dr. Anna Jung

ajung@wim.mil.pl or a.jung@spencer.com.

6th-8th July, 2011

17th International Conference on Thermal Engineering and Thermogrammetry (THERMO)

at the Budapest University of Technology and Economics (BME), Budapest, XI .Müegyetem rkpt.3., Hungary

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Information

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