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Functional Infrared Imaging in Medicine: A Quantitative Diagnostic Approach

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Abstract**. The role and the potentialities of high-resolution infrared thermography, combined to bio-heat modelling, have been largely described in the last years in a wide variety of biomedical applications. Quantitative assessment over time of the cutaneous temperature and/or of other biomedical parameters related to the temperature (e.g., cutaneous blood flow, thermal inertia, sympathetic skin response) allows for a better and more complete understanding and description of functional processes involved and/or altered in presence of ailment and interfering with the regular cutaneous thermoregulation. Such an approach to thermal medical imaging requires both new methodologies and tools, like diagnostic paradigms, appropriate software for data analysis and, even, a completely new way to look at data processing. In this paper, some of the studies recently made in our laboratory are presented and described, with the general intent of introducing the reader to these innovative methods to obtain quantitative diagnostic tools based on thermal imaging.**

I. Introduction

Infrared (IR) imaging allows the representation of the skin temperature distribution of the human body. The physiological fundament for using IR thermal imagery in medicine resides in the fact that the skin temperature distribution of the human body depends on the complex relationships defining the heat exchange processes between skin tissue, inner tissues, local vasculature, metabolic activity, and the regulating of the sympathetic and parasympathetic activity to maintain the homeostasis. The presence of a disease, then, locally interferes with the heat balance resulting in an increase or in a decrease of the skin temperature, both with respect to the surrounding regions or the unaffected contra lateral region. Qualitative searching for hyperthermal or hypothermal spots and/or asymmetric thermal patterns in contra lateral regions has constituted for long time the only diagnostic approach based on thermal imagery [1].

It is reasonable to suppose that the presence of the disease could influence the dynamics of the local control of the skin temperature as well Therefore, it is possible to obtain quantitative diagnostic parameters from those parameters that describe and model the activity, both spontaneous and induced, of the skin thermoregulatory system [1]. The advent around the middle ‘90s of high-resolution and high sensitive Focal Plane Array (FPA) based thermal imaging systems has literally revolutionized the way the diagnostic procedures are applied and the processing needs associate to them [2]–[4].

The “dynamic” approach has been then started and widely used in a variety of modalities reported in literature as dynamic thermography, dynamic telethermography, dynamic area thermometry (DAT), active thermography and functional infrared imaging. Successful applications of diagnostic procedures obtained through these approaches need to be supported by several important elements:

i. diagnostic protocols and paradigms effectively designed;
ii. accurate control and standardization of the experimental conditions;
iii. appropriate data analysis and image processing;
iv. multimodal approach, whenever possible.

All of the above listed items are equally fundamental for quantitative and effective medical IR imaging. While the advancement and the development of the technology are mostly pursued by private companies, a strong and continuous research about biomedical applications - involving multidisciplinary approach - is in process in clinical and medical research centres. In fact, combined efforts of physicians, physicists, physiologists, and computer scientists are carried on to face and to solve - in an integrated fashion - the “diagnostic problem” as seen through the functional and dynamic approach.

Henceforth, we will refer to functional infrared (fIR) imaging as the study for diagnostic purposes, based on the modelling of the bio-heat exchange processes, of the functional properties and alterations of the local human thermoregulatory system. In this paper, we shortly present some quantitative diagnostic applications so far developed and nowadays routinely in use in clinical settings.

II. Discriminating Secondary to Scleroderma from Idiopathic Finger Thermoregulatory Incompetence by Means of Functional IR Imaging

Raynaud’s phenomenon (RP) is defined as a painful vasoconstriction - that may follow cold or emotional stress - of small arteries and arterioles of extremities, like fingers and toes. RP can be primary (PRP) or secondary (SSc) to scleroderma. The latter is usually associated with a connective tissues disease. RP precedes the systemic autoimmune

disorders development, particularly scleroderma, by many years and it can evolve into secondary RP. The evaluation of vascular disease is therefore crucial in order to distinguish between PRP and SSc [9] and to set up proper therapies. We have demonstrated in a series of papers that the evaluation of the capability of the patient hands to re-warm after a controlled mild cold stress can effectively differentiate healthy subjects from PRP or SSc Raynaud's patients [5], [8].We proposed to model the response of the fingertips to exposure to a cold environment to get a diagnostic parameter derived by the physiology of such a response. The thermal recovery following a cold stress is driven by thermal exchange with the environment, transport by the incoming blood flow, conduction from adjacent tissue layers, and metabolic processes. The finger temperature is determined by the net balance of the energy input/output. The more significant contributes come from the input power due to blood perfusion and the power lost to the environment.

$$\frac{dQ}{dt} = -\frac{dQ_{env}}{dt} + \frac{dQ_{ctr}}{dt} \qquad (1)$$

Normal finger recovery after a cold stress is reported in Figure 1.

In absence of thermoregulatory control, fingers exchange heat only with the environment: in this case, their temperature T_{exp} follows an exponential pattern with time constant τ given by

$$\tau = \frac{\rho \cdot c \cdot V}{h \cdot A} \qquad (2)$$

Where ρ is the mass density, c the specific heat, V the finger volume, h is the combined heat transfer coefficient between the finger and the environment and A is the finger surface area. Thanks to the thermoregulatory control, the finger maintains its temperature T greater than T_{exp}. For a Δt time, the area of the trapezoid $ABCF$ times $h \cdot A$ in Figure 1 computes the heat provided by the thermoregulatory system, namely ΔQ_{ctrl}. This amount summed to ΔQ_{env} yields Q, the global amount of heat stored in the finger.

Then, the area of the trapezoid $ABDE$ is proportional to the amount Q of heat stored in the finger during a Δt interval. Therefore, Q can be computed integrating the area surrounded by the temperature curve T and the constant straight line To:

$$Q = -h \cdot A \cdot \int_{t_1}^{t_2} (T_0 - T(\varsigma))\, d\varsigma \qquad (3)$$

Where the minus sign takes into account that the heat stored by the finger is counted as positive. Q is intrinsically related to the finger thermal capacity. Under the hypothesis of constant To, the numerical integration in (2) can be used to characterize the re-warming exhibited by a healthy or a suffering finger.

The Q parameter has been used in [5], [8] to discriminate and classify PRP, SSc and healthy subjects on a set of 40 (20 PRP, 20 SSc) and 18 healthy volunteers. Single values obtained for each finger of all of the subjects are reported in Figure 2.

The results highlight that the PRP group features low intra-individual and inter-individual variability whereas the SSc group displays a large variability between healthy and unhealthy fingers. Q values for SSc finger are generally greater than PRP ones. The sensitivity of the method in order to distinguish patients from normal is 100%. The specificity in distinguishing SSc from PRP is 95%. Q clearly highlights the difference between PRP, SSc, and between and normal subjects. It provides useful information about the abnormalities of their thermoregulatory finger properties. As calculated from the re-warming curves, Q parameter seems to be particularly effective to describe the thermal recovery capabilities of the finger. The method clearly highlighted the difference between PRP and SSc patients and provides useful information about the abnormalities of their thermal and thermoregulatory finger properties.

III. TIME RECOVERY IMAGING METHOD

To capitalize on the functional and structural content of the thermal IR imaging, we proposed a new imaging technique, based on the local recovery properties of regions of interest after a controlled thermal test [6]. Starting from a general energy balance equation, it is straightforward to demonstrate that the recovery time from any kind of thermal stress for a given region of interest depends from the region thermal parameters. A given disease may alter the normal heat capacity and the tissue/blood ratio mass density of a region.

At the simplest level, the most important terms involved in the energy balance during the recovery are the heat storage in the tissue, heat clearance by blood perfusion and convective heat exchange with the environment, as described by the following equation:

$$\frac{\partial T}{\partial t} \rho \cdot c \cdot V = hA(T_o - T) + \rho_{bl} \cdot c_{bl} \cdot w_{bl}(t) \cdot (T_{bl} - T) \qquad (4)$$

where subscripts o and bl designate the properties of the environment and blood, respectively, while ρ is the density, c is the specific heat, V is the volume, T is the temperature, t is the time, h is the combined heat transfer coefficient between the skin and the environment, A is the surface area and w is the blood perfusion rate. Under the assumption of constant blood perfusion rate w_{bl} and blood temperature T_{bl}, and appropriate boundary conditions, equation (4) can be easily integrated yielding:

$$T(t) = \frac{W \cdot (T_{bl} - T_o)}{W + H} + \left(T_i - T_o - \frac{W \cdot (T_{bl} - T_o)}{W + H} \right) \cdot e^{-(W+H)t} + T_o \qquad (5)$$

Where

$$H = \frac{h \cdot A}{\rho \cdot c \cdot V}; \qquad W = \frac{\rho_{bl} \cdot c_{bl} \cdot w_{bl}}{\rho \cdot c \cdot V} \qquad (6)$$

The time $t_{f\,to}$ reach a certain pre-set (final) temperature T_f is then given by:

$$t_f = -\frac{1}{W+H}\ln\left(\frac{\left(1+\frac{H}{W}\right)\cdot(T_f - T_o) - W(T_{bl} - T_o)}{\left(1+\frac{H}{W}\right)\cdot(T_i - T_o) - W(T_{bl} - T_o)}\right) \quad (7)$$

The exponential solution described in (4) suggests to use the time constant τ as a characterizing parameter for the description of the recovery process after any kind of controlled thermal stress, with τ mainly determined by the local blood flow and thermal capacity of the tissue.

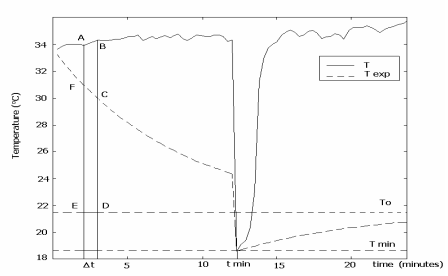


Fig. 1. Experimental re-warming curves after cold stress in normal subjects. The continuous curve represents the recorded temperature finger. The outlined curve represents the exponential temperature pattern exhibited by the finger in absence of thermoregulatory control. In this case, the only heat source for the finger is the environment.

Functional IR imaging permits an easy evaluation of τ, which can be regarded as a parameter able to discriminate areas interested by the specific disease from healthy ones. Rather than a static imaging of the skin thermal distribution to pictorially describe the effect of the given disease, an image reporting pixel to pixel the τ recovery time can be used to characterize that disease [6].

The method is actually used in a variety of diagnostic applications. The interested reader can refer to [1], [6] for further description. Just as an example, we report here time recovery image of scleroderma patient's hand. The method properly individuates areas where the tissue degeneration is in progress (Figure 3).

IV. Evaluation of Postural Disorders by Means of Total Body Infrared Imaging

Control of posture and movements involves proprioceptive mechanisms throughout muscular, articular, and cutaneous afferents. Differentiation of the muscular tone and volume between homologous contra lateral and agonist-antagonist muscles can be caused by postural disorders, such as for example leg length discrepancy. Consequently, asymmetrical activity of some muscles of one hemi soma with respect to the other one may be observed [11]. Activity, in turn, influences the metabolic needs of the muscles and of the tissues, from which the local control of the haematic flux depends. The result is a local vasodilatation of small arteries for feeding active muscles [10], with effects on skin temperature distribution, and this effect is appreciable even in the simple situation of maintaining the orthostatic position. IR imaging can be used to assess whether or not skin temperature distribution may be associated with postural disorders [11].

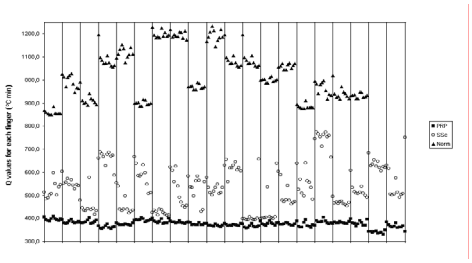


Fig. 2. Q values calculated for each finger of each subjects. Vertical grid lines are placed to discriminate the ten fingers. PRP fingers are characterized by a strong intra and inter individual homogeneity. Greater mean Q values and greater intra and inter individual variations characterizes the SSc fingers.

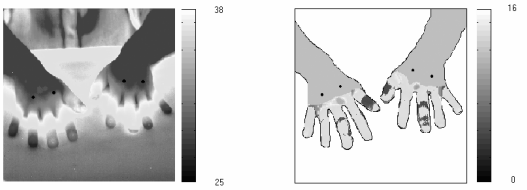


Fig. 3. Raynaud's Phenomenon Secondary to Scleroderma. Left) Thermal image. The colorbar shows the pixel temperature colour mapping. Right) recovery time image after mild cold stress. The colorbar illustrates the recovery time, in minutes, for each pixel. The regions associated with longer recovery times identify the more damaged finger regions.

The problem is an objective and quantitative assessment of symmetrical/asymmetrical temperature distribution. In this section we present a simple solution to this problem, based on first-order statistics algorithm. As a first step, it is important to refer measurements to objective and reliable reference landmarks. We use small cutaneous paper markers located on anatomical palpable landmarks. Based on the spatial distribution of such markers, regions of interest are selected by the operator. Then, the algorithm detects and recognizes homologous contra lateral regions and computes parameters of similarity for the temperature distributions. Among those measurements, particularly effective are the histogram asymmetry factor ρ and the spatial correlation factor (CF), respectively defined as:

A. Histogram asymmetry factor ρ

This parameter determines the asymmetry factor between two calculated frequency tables of the temperature distributions of the considered regions of interest (left side and right side on contra lateral regions), through the following equation:

$$\rho(L,R) = \frac{N\sum_{i=1}^{\max(i)} L_i R_i - \left(\sum_{i=1}^{\max(i)} L_i\right)\left(\sum_{i=1}^{\max(i)} R_i\right)}{\sqrt{N\sum_{i=1}^{\max(i)} L_i^2 - \left(\sum_{i=1}^{\max(i)} L_i\right)^2}\sqrt{N\sum_{i=1}^{\max(i)} R_i^2 - \left(\sum_{i=1}^{\max(i)} R_i\right)^2}} \quad (10)$$

where ρ is the asymmetry factor ($0< \rho<1$, where 0 is for regions with perfectly symmetric histograms), L_i represents class values (temperature) for the left side region (number of pixels), R_i represents class values (temperature) for the right side region (number of pixels), i is the total number of classes and N is the total number of pixels in the region.

The ρ factor measures how differently the two temperature distributions are, but it ignores any structural analysis about spatial temperature patterns [12].

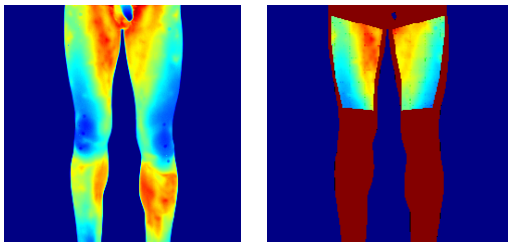
B. Correlation Factor

It may happen that two contra lateral regions may have the same histograms of temperature distribution, but with a completely different spatial distribution of the temperature values. The correlation factor compares homologues contra lateral regions through a cross correlation method [14]:

$$CC(i,j) = \frac{\sum_{i,j}(L_{i,j} - E(L))(R_{i,j} - E(R))}{\sqrt{\sum_{i,j}(L_{i,j} - E(L))^2}\sqrt{\sum_{i,j}(R_{i,j} - E(R))^2}} \quad (11)$$

Where $E(\ )$ is the expect operator.

This measure of similarity is computed for window pairs from the left and right sides of the subject, having the second one reversed with reference to the chosen asymmetry axis.



(a) (b)

Fig. 4. Total body IR imaging for assessing postural disorder. Frontal view of lower limbs taken in orthostatic position. a) Thermal image. b) Contra lateral regions of interest. The subject hereby considered suffers for lower limbs different lengths (the right one about 1.5 cm higher than the left). The measurement parameters are, respectively: ρ = 0.19 (very similar histograms); CF = 0.43 (poorly correlated thermal patterns); t-test ($\alpha < 0.05$) p-value < 0.01).

A combined comparison of the relative changes of the mentioned parameters allows the quantitative assessment of regional variations of the temperature distributions, thus permitting identification of functional asymmetries related to the posture (Figure 4). As a complementary technique, total body IR imaging may be advantageously combined to more structural investigations like 3D posturography, to assess functional consequences of postural disorders.. Moreover, IR imaging may be also used to evaluate the effectiveness of corrective therapy of postural disorders.

V. Conclusions

Functional IR imaging is a biomedical imaging technique that relies on high resolution infrared imaging and on the modelling of the heat exchange and control processes at the skin layer. It is aimed to provide quantitative diagnostic parameters through the functional investigation of the thermoregulatory processes. It is also aimed to provide further information about the studied disease to the physicians, like explanation of the possible physics reasons of some thermal behaviour and their relationships with the physiology of the involved processes. fIR is not invasive and it is a touch less imaging technique. Possible fIR applications are numerous, ranging from those described into this paper, to psychometrics, cutaneous blood flow modelling, peripheral nervous system activity, and some angiopathies. The applications described in this paper show that fIR imaging provides highly effective diagnostic parameters. The method is highly sensitive, but also highly specific into discriminating different conditions of the same disease.

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