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Preliminary Results of Severity of Illness Measures of Rheumatoid Arthritis Using Infrared Imaging

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***Abstract*— For the first phase of a large project, we used an infrared imaging camera (thermograph) to obtain accurate measurements of body temperature in joints of twelve human normal subjects (control group) and for thirteen patients who had been diagnosed with rheumatoid arthritis (RA) by a rheumatologist. The ultimate goal is to create a low cost effective method to diagnose early synovitis. Temperature measurements of hands were analyzed with first order statistics. Results show significant temperature differences between control subjects and patients for every joint and hand portion measured. Future work will complete the analysis of knees, elbows, ankles, combine infrared (IR) imaging and intra-optical (IO) imaging, and incorporate feature extraction and classification approaches to stratify patients into severity of illness prior to, and after receiving treatment.**

***Keywords- infrared imaging; measuring temperatures; rheumatoid arthritis patients; normal subjects*.**

I. Introduction

Over 300,000 Canadians, 2.1 million Americans, and around 260,000 French are currently diagnosed with rheumatoid arthritis (RA), involving inflammation and symptoms like redness, swelling, heat, and pain. Within 10 years of diagnosis, 50% of patients have severe disability and life expectancy reduction from 3 to 18 years. With the aging of the population, the prevalence of chronic diseases and conditions is expected to increase even more over the next decades. Early diagnosis and treatment of RA could help postpone or prevent serious disability. Currently, diagnosis relies mainly on qualitative evaluation, medical history, examination, and laboratory tests. MRI (Magnetic Resonance Imaging) and HRUS (High-Resolution Ultra-Sound) have been used with some patients to detect early synovitis. However these tests are not readily available to everyone and waiting lists in many countries are very long. Less expensive technologies providing quantitative assessment to diagnose and monitor therapy in joint debilitating diseases would be a major innovation in Canada and in the world. This explains the motivation to develop more accessible approaches for active prevention.

Visual marker-based monitoring systems still remain expensive and complex to operate. As a result, they are found mainly in particular cases in rehabilitation and for research. More tractable non-invasive approaches that simultaneously combine infrared imaging with movement extension measurement should be made available in large clinics and all hospitals to provide access to a major part of the population. Replacing expensive MRI or HRUS by the proposed technology would also have a major impact on the Health Care System; the current tests (MRI and HRUS) required for early diagnosis of RA could be replaced by the new imaging technique, thus releasing the expensive tests for other applications, likely leading to a reduction of waiting times for these tests. It is anticipated that the system will aid physicians in making earlier diagnoses and delay progression of the disease to advanced stages of deformity or disability, keeping Canadian and French citizens more active, at work and in their personal lives.

Inflammation and limitation of motion are two important parameters to monitor RA, along with pain assessment. The integration of heat distribution on the skin surface along with movement capabilities to be found in one diagnostic tool is innovative and seen as a reliable, quantitative and reproducible means of assessment of RA. This aspect is innovative and promising given that injury to bones, joints and muscles are known to recover slowly. Calibration of the automated measurement with disease level estimated by medical experts will also be possible providing that the correlation is sufficiently high with other clinical assessment tools. The resulting technology will support the translation of knowledge to physicians and other health personnel to help to improve or restore musculoskeletal health with quantitative measurements that can be classified, clustered and analyzed in order to observe tendencies and general trends to be compared with real clinical investigations. The ultimate goal is the integration of the multi-spectral approach into clinical application to become a diagnosis-aid that is affordable, efficient and easy to operate, and that can be widely used over existing health services networks.

From a clinical point of view, the technique of infrared photography may provide utility in several areas of care of patients with RA. a) Early diagnosis; currently, the diagnosis of RA is based on the clinical evaluation, specifically the demonstration of joint swelling by palpation. This method is at best crude and noted for substantial inter-observer and intra-observer variation. Refinement is provided by MRI and power Doppler. However, both of these methods are labor intensive, time consuming, expensive and also subject to the expertise of the individual performing the evaluation. Infrared photography may provide an alternate approach that could detect active inflammation at a time when the joints may simply be stiff and/or tender but not detectably swollen.

b) Prognosis; currently, the identification of biomarkers of disease severity and predictors of outcome is an area of active research. No single marker has been found to predict outcome well, perhaps with the exception of the persistent elevation of CRP despite therapy. The intensity of the infrared signal may be useful as measure of inflammatory load and a predictor of outcome.

c) Achievement of remission; the ability to suppress the intensity of the infrared signal may speak to adequacy of treatment. Currently, the goal of RA therapy is to induce the lowest possible level of disease activity. Measurements of disease activity rely on clinical parameters; however future goals are not simply to attain clinical remission, but radiographic remission defined as no progression of joint damage. Methods to demonstrate radiographic remission will rely on MRI, which noted above is an expensive approach. Infrared photography may provide an alternative to MRI in defining radiographic remission

Therefore, developing a less costly, non-invasive technology to provide a quantitative assessment of RA and to monitor therapy effectiveness in joint debilitating diseases has been the main motivation behind this work.

II. Literature review

Over the past 50 years, infrared imaging has been applied to many fields. The major limitations encountered in early work were the lower resolution, large size of sensors, and the limited power of computers for the image analysis [1]. A few clinical studies demonstrate that heat distribution provides a quantitative measure of disease activity and especially of inflammation in knee joints of patients [2], [3], [4]. Correlation has been observed between heat distribution measurement and physicians' assessment based on degree of swelling, warmth, limitation of motion, grip strength, morning stiffness and pain score. Early studies mainly focused on knees and ankles to assess the effect of various treatments on RA patients. In this study, we analysed the temperatures of various joints in the hands, wrist, back of the hand, palm, thumb shaft, for both controls and patients. Our intent was to indentify how clearly we could separate patients from controls and to examine which joints are the most indicative of an RA condition in patients.

Anomaly detection in infrared images is a challenging task. Often the key element of an automated anomaly detection system is the segmentation of relevant information from noise and background. Numerous algorithms are available in the literature for the segmentation of visible images, but these differ significantly from infrared images. The intensities of the latter depend on object temperature, object surface properties, surface orientation, wavelength, and are not necessarily uniform across an object, even if the temperature of that object is uniform. The environmental conditions at the time of imaging also influence the resulting images. Moreover, the range of intensities of infrared images is typically much less than for visible images, leading to low contrast, poor resolution, and less texture information. Key features that are successfully used in the processing of visible images cannot be used reliably when dealing with infrared images, thus the segmentation of the latter presents unique challenges and depends greatly on the application considered. Methods developed for automated tracking of military targets [5] or for predictive maintenance [6] do not perform well when translated to applications in medicine. Our group introduced a method based on morphological processing of edge maps using both strong and weak edges to recover the contour of faint parts of the object in low contrast and high noise situations [7, 8, 9]. Promising results were obtained for synthetic images of hands on three types of real backgrounds. The segmentation approach is part of a larger framework for automated identification of abnormal regions in infrared images of the human body and will be integrated into this project at a later stage. To date, our framework was applied to the assessment of pain [10], of musculoskeletal disorders in the arms and hands of computer users, and to capture the evolution of the temperature distribution on pianists' hands and arms during practice. We intend to incorporate this approach to the measurement of joints for diagnosing RA, once the first phase of the study described here is completed.

A second long-term goal is to develop a multi-spectral quantitative sensing approach to assess the severity of RA, combining infrared imaging (IR) and intra-optical imaging (IO). Building on previous work of our team to reconstruct the 3D position of human limbs from a segmented set of synchronized video captures without markers [11], precise gesture estimation can be achieved to evaluate the range of motion of a subject. It also provides a recording mechanism for temporal comparisons of the subject's capability of movement and dexterity. Our hypothesis is that this combination of infrared and passive intra-optical imaging will help in the early diagnosis of (RA) and to measure the effectiveness of therapy for patients treated for RA. The current paper addresses the first part of the work: measuring and analysing the temperature distribution in various joints of the hands and of other parts such as wrist, palm, and back of the hand. In subsequent work, the analysis will be completed on the other views taken of patients and normal subjects such as elbows, knees, ankles, and feet. Following this step, the superposition of the two imaging techniques will be developed.

III. METHODOLOGY

A. Data collection

Thirteen patients (nine females and four males) diagnosed with rheumatoid arthritis and eighteen control subjects were recruited after receiving the ethical clearance certificate from the hospital and the Universities. Six control subjects were eliminated from the total of eighteen volunteers for this preliminary analysis to maintain a database of subjects who were 50 years old or less; the six were between 60 and 70 years old. In the future, an in-depth analysis will be done with respect to the effect of age on mean temperatures of joints, but a quick observation was that persons over 50 had higher temperatures than younger subjects. All subjects (five females and seven males) and patients followed the protocol: not to use talcum powder, lotion, drug or deodorant on the skin on the day of the session; not to consume alcoholic beverages 12 hours prior to the session; not to consume hot beverages at least 1 hour prior to the session; not to use procedures such as acupuncture, transcutaneous electrical nerve stimulation (TENS), hot or cold patches, or any other form of physiotherapy at least 24 hours prior to the session. They were asked not to do intense physical exercises at least 4 hours prior to the tests, avoid prolonged sun exposure for at least one week, not smoke for at least 2 hours prior to the testing, and not wear any rings, necklaces, and bracelets during the session.

The room had a controlled temperature of around 20 degrees C, with no windows. All test subjects wore light clothing (short-sleeved T-shirt and shorts); they removed their shoes and socks and were seated in the room without any of their limbs touching the other for a fifteen minute period before images were taken. This is to cool the parts of the body that were covered by clothing and have everyone in the same condition prior to the imaging session. The IR camera uses a solid state uncooled microbolometer focal plane array of 320×420 pixels, operating in the window 7.5μm−13μm of the far IR range of the electromagnetic spectrum. It has a 24mm germanium lens with an anti-reflective coating. This gives a 24°x18° field of view with a minimum focus distance of 30 cm. Its spatial resolution is 1.3mrad. The thermal resolution is 0.05°C at 30°C. The camera was connected to a laptop via a Firewire interface, thereby capturing sequences of 14bit digital thermal images at a set speed of 30 frames per seconds. Images were taken of the hands (dorsal and palm), arms, knees, feet (top and palm).

The preliminary analysis consisted of three steps:

(i) Calculating the mean temperature, the median, and the standard deviation for the twelve control subjects and thirteen patients for the following: Metacarpal Phalangeal (MCP) joints (all of the four joints together enclosed in a quadrilateral); Metacarpal Phalangeal joint of the third finger (MCP3); the third proximal interphalangeal joint (PIP3); the third distal interphalangeal joint (DIP3); the Mid Phalange (MP), the wrist, the back of the hand, and the palm; for the palms, the standard diameter was 120 pixels, which corresponded to approximately 4 cm in diameter. See Figure 1 for a drawing of the hand with the name of each joint. The mean temperatures for each view are presented in Table I with the first column reporting the results for the control group, the second column presenting the results for the patients, and the third column reporting the difference between the former two columns.

(ii) For the patient group, the joint temperatures are reported, as well as the mean temperature of all patients for each of the joints and parts of the hand. This is intended to see if a patient's joint temperatures are higher than, lower than, or equal to the mean temperature for each joint or part of all patients; it is our belief that patients whose joints are at higher temperatures than the mean temperature for all patients would have more serious inflammation and vice versa for those under the mean temperature. These results are presented in Table II. Of course, in the long run, it is the comparison of a patient's own temperature measures which will be important to determine if the disease if progressing or regressing at each visit.

(iii) The difference of the mean temperature between patients and participants for the right hand and the left hand were calculated for: MCP, MCP3, the wrist, and the back of the hand. The results are presented in Table III.

Since there are between fifty and seventy-five images for each view, for each patient or subject, it was decided that for this preliminary analysis, the twentieth image for each view would be analyzed. The region of interest is indentified in the same way for each test and the mean and median is calculated for each. In the future, when the automation of the analysis has been completed, then it will be possible to average the data from all the images taken of each particular view.

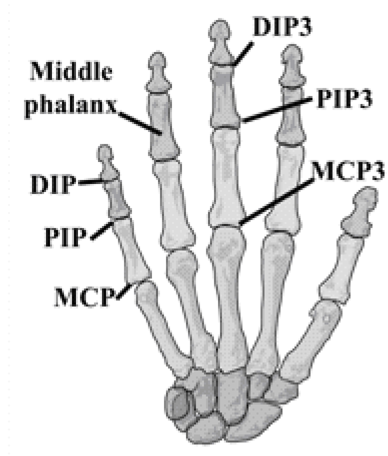

Figure 1: Joints of the left hand

During these imaging sessions, measurements were also taken of the following: Inside and outside of the left and right arms in a straight position, then inside and outside the right and left elbows in a bent position; the back as well as a front view of the bent right and left elbows. Similarly, the knee was imaged with the following positions: Back view of left knee and of the right knee, then a front view of these two joints; then inside and outside views of each knee. Finally, each foot was imaged with top view followed by a view of the sole. However the focus of this paper is mainly the hands; the analysis of all the other measurements will be part of future paper.

(iv) Three patients were retested in April 2009, nearly one year after the first imaging session done between April and June of 2008. Table IV shows the mean temperatures for MCP3, PIP3, and DIP3 taken at two different points in time (spring 2008 and spring 2009) for patient no. 1, 4, and 13.

IV. Results and Discussion

The results clearly show that the mean temperatures measured with infrared techniques were greater for all patients and all joints and hand parts than for the control subjects; see Table I. Greater temperatures were even seen at the DIPs, joints that are not often involved clinically in RA. On the day of the infrared testing, we did not examine each joint for clinical signs and symptoms of RA such as swelling or tenderness and are therefore unable to provide a correlation between clinical assessment and infrared signal. All infrared imaging tests were done at the University and in order to respect the requirements of the Ethics Review Board, these were to be separate at this time from the clinical evaluation. However, in the future, the new ethics proposal will suggest testing at the hospital facility and all patients will be assessed by a physician, by the imaging, and results compared to MRI tests (as ground truth). For this study, all patients had well established long-term RA and were being treated with disease modifying drugs. The physician's global assessment of disease activity at the time of the patient's visit was that the disease appeared to be less active in some patients (e.g. patients 1and 2) and very active in another (e.g. patient 7). However, by the time these patients participated in the imaging sessions, their RA status could have changed as indicated by the temperature measurements reported here. The preliminary analysis of the temperature measurements did not discriminate yet among patients with different degrees of clinical activity. Nevertheless, it is also known that clinical evaluation is often inadequate to evaluate joint inflammation except with approaches such as MRI testing. Other analysis approaches including classification techniques will be applied to this data in the near future to assess whether some discrimination of level of disease is possible.

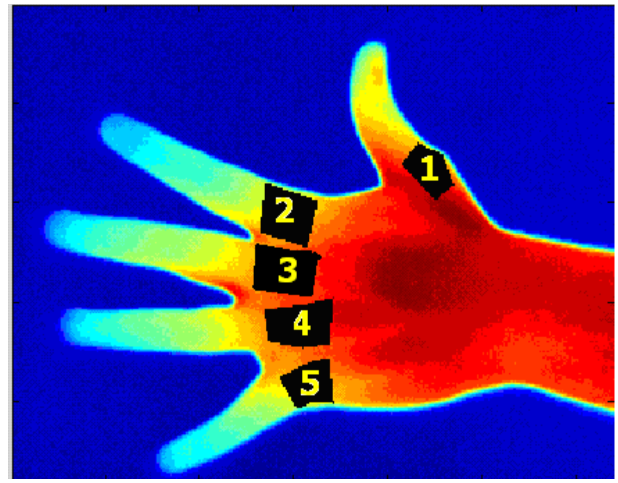

FIGURE 2: MCP LABELS ON A PARTICIPANT'S HAND

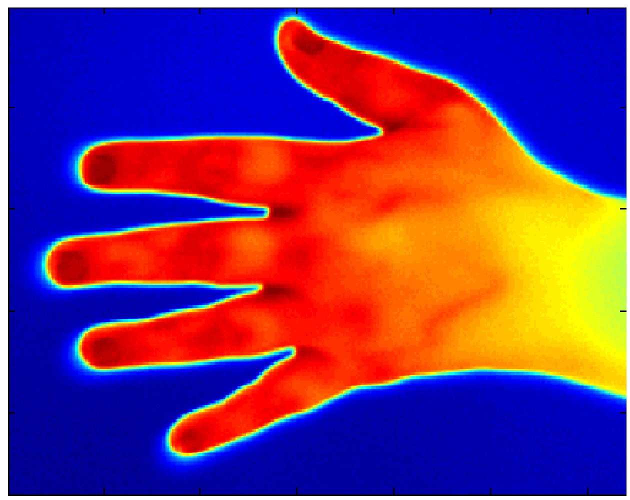

FIGURE 3: EXAMPLE OF A INFRARED IMAGE OF A PATIENT'S HAND

TABLE I. MEAN TEMPERATURE FOR CONTROLS AND PATIENTS IN VARIOUS JOINTS IN LEFT HAND (DEG. CELSIUS)

Part imaged	**Controls**	**Patients**	**Difference**
MCP	28.2	31.5	3.3
MCP3	28.1	31.4	3.3
Wrist	29.7	31.9	2.2
Back hand	29.5	31.6	2.1
PIP	27.2	30.9	3.7
PIP3	27.5	31.0	3.5
DIP	27.0	30.5	3.5
DIP3	27.3	30.6	3.3
MP	27.3	31.0	3.7
Thumb	27.7	31.7	4.0
Palm	30.5	32.5	2.0

TABLE II TEMP. PATIENTS LEFT HAND (DEG. CELSIUS)

Patient	Test date	MCP	MCP3	PIP3	DIP3	Wrist	Back	MP	Palm
1	Apr. 29	32.9	32.8	32.6	32.8	32.8	33.2	33.6	33.3
2	Apr. 25	32.9	32.9	32.9	32.7	32.5	32.8	33.4	34.3
3	May 8	33.3	33.5	32.3	32.1	33.1	33.4	33.1	33.7
4	Jun. 12	29.8	29.7	29.7	29.2	29.0	30.0	30.0	30.6
5	Jun. 12	28.8	29.0	27.2	25.8	29.9	29.8	28.0	30.0
6	Jun. 13	28.0	28.4	25.5	24.8	29.5	29.4	27.8	29.9
7	Jun. 13	33.1	33.1	31.0	30.2	33.5	33.5	32.2	32.8
8	Jun. 16	32.1	32.2	32.6	32.1	29.2	31.1	32.6	31.8
9	Jun. 17	30.7	30.1	31.6	31.9	30.0	30.8	32.3	31.9
10	Jun. 17	33.1	32.4	33.6	33.3	33.0	33.3	33.7	33.5
11	Jun. 19	32.9	32.6	33.0	32.8	33.0	33.3	33.4	33.4
12	Jun. 21	32.1	31.9	32.3	32.2	32.2	32.5	32.8	32.9
13	Jun. 24	28.9	28.9	28.5	27.8	31.4	30.2	29.1	31.3
Mean		**31.4**	**31.3**	**30.9**	**30.5**	**31.4**	**31.7**	**31.6**	**32.2**
SD		**1.93**	**1.83**	**2.51**	**2.84**	**1.70**	**1.59**	**2.17**	**1.46**

TABLE III DIFFERENCE OF THE MEAN TEMPERATURE OF TWO HANDS FOR CONTROLS AND PATIENTS (DEGREES CELSIUS)

Part imaged	Control Left	Control Right	Patient Left	Patient Right	Diff. Control	Diff. Patients
MCP	28.2	28.2	31.5	31.6	0.0	0.1
MCP3	28.3	28.1	31.4	31.5	0.2	0.1
Wrist	29.6	29.7	31.6	32.0	0.1	0.6
Back hand	29.4	29.5	31.9	32.0	0.1	0.1

TABLE IV. MEAN TEMPERATURE OF LEFT HAND OF THREE PATIENTS IMAGED AT TWO DIFFERENT TIMES (PATIENTS 1, 4, AND 13): SPRING 2008 (A) and SPRING 2009 (B)

Part imaged	A patient 1	B	A patient 4	B	A patient 13	B
MCP3	32.8	33.3	29.7	27.5	28.9	32.4
PIP3	32.6	33.1	29.7	25.9	28.5	33.4
DIP3	32.8	33.5	29.2	26.8	27.8	33.3

Again, although the physician could not be present at these second tests for patients 1, 4 and 13, it is evident from the tests results that patient 1 suffers from slightly more inflammation from the hand joint temperatures reported in Table IV. Patient 4 seems to be better and patient 13 seems worse.

V. CONCLUSION AND FUTURE WORK

The first phase of this research project enabled us to conclude that there are measurable differences in temperatures of hands in patients versus control subjects, establishing a proof of concept and leading to future work. Moreover it is interesting to note that subjects do not show much temperature difference between the right and the left hand joints or other hand parts (palm and back of hand), which is expected since they are not suspected of having any abnormality in either hand. For the next phase of the project, physician assessment, infrared imaging, visual imaging, and MRI studies will be collected and compared. Also, building upon C. Herry's work [7], future developments will include feature extraction processed through a pattern recognition system to optimize the classification of outcomes in terms of severity of RA and degree of changes at each visit. An index will be established, independent from the acquisition setup, to classify thermographic measurements into categories of RA diseases that correspond to currently used RA levels, as diagnosed by medical experts. A database will be created over this phase of research on patients already diagnosed with RA.

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