COMPUTER METHODS AND PROGRAMS IN BIOMEDICINE 122 (2015) 199–206

journal homepage: www.intl.elsevierhealth.com/journals/cmpb

Tuberculine reaction measured by infrared thermography

José Antonio Fiz[a,c], Manuel Lozano[b], Enrique Monte-Moreno[c], Adela Gonzalez-Martinez[a], Marcos Faundez-Zanuy[d,*], Caroline Becker[a], Laura Pons-Rodriguez[a], Juan Ruiz Manzano[a]

[a] Pulmonology Department, Germans Trias I Pujol Universitary Hospital, 8th, Carretera del Canyet s/n, 08916 Badalona, Spain
[b] Innovation Group, Health Sciences Research Institute of Germans Trias i Pujol Fundation(IGTIP), Ctra, de Can Ruti/Camí de les escoles s/n, 08916, Badalona, Spain
[c] Center for Language and Speech Technologies and Applications (TALP), Technical University of Catalunya (UPC), Jordi Girona, 1-3, S112, Campus Nord, Barcelona, Spain
[d] Pompeu Fabra University, Escola Superior Politècnica Tecnocampus, Avda. Ernest Lluch 32, 08302 Mataró, Spain

ARTICLE INFO

Article history:
Received 25 February 2015
Received in revised form
13 August 2015
Accepted 17 August 2015

Keywords:
Tuberculine test
Infrared thermography
Image processing

ABSTRACT

Setting: The infection with *Mycobacterium tuberculosis* gives a delayed immune response, measured by the tuberculine skin test. We present a new technique for evaluation based on automatic detection and measurement of skin temperature due to infrared emission.
Design: 34 subjects (46.8 ± 16.9 years) (12/22, M/F) with suspected tuberculosis disease were examined with an IR thermal camera, 48 h after tuberculin skin injection.
Results: In 20 subjects, IR analysis was positive for tuberculine test. Mean temperature of injection area was higher, around 1 °C, for the positive group (36.2 ± 1.1 °C positive group; 35.1 ± 1.6 °C negative group, $p < 0.02$ T test for unpaired groups).
Conclusion: IR image analysis achieves similar estimation of tuberculin reaction as the visual evaluation, based on higher temperature due to increased heat radiation from the skin lesion.

1. Introduction

According to the World Health Organization, two billion people are infected with the tuberculosis (TB) bacilli [1], and it is estimated that every year eight million new cases appear. TB is a contagious disease not totally under control with great differences between rich and poor countries [2]. The diagnosis of TB is based on the interpretation of a skin immunologic reaction. The infection with *Mycobacterium tuberculosis* gives a delayed immune response, measured by the tuberculin skin test (TST) [3]. This consists of the intradermal injection of tuberculin purified protein derivative (PPD) and measurement of the resulting reaction. The induration size, measured in millimeters, indicates if the test result is negative or positive. Palpation and pen methods have been typically applied to measure the PPD reaction, but the measurement depends on the subjective interpretation of the reaction area [4,5]. New

* *Corresponding author*. Tel.: +34 93 169 65 01.
E-mail addresses: jafiz@msn.com (J.A. Fiz), mlozanogar@gmail.com (M. Lozano), enric.monte@upc.edu (E. Monte-Moreno), agonzalezm.germanstrias@gencat.cat (A. Gonzalez-Martinez), faundez@tecnocampus.cat (M. Faundez-Zanuy), arialcb@gmail.com (C. Becker), laurarodriguezpons@gmail.com (L. Pons-Rodriguez), jruizmanzano.germanstrias@gencat.cat (J. Ruiz Manzano).

http://dx.doi.org/10.1016/j.cmpb.2015.08.009
0169-2607/

technologies are currently being developed to improve the sensitivity and specificity of the TB diagnosis [6].

In this study, we present a new technique for the evaluation of the tuberculine reaction based on the automatic detection and measurement of infrared (IR) emission of inflammatory effects produced by tuberculine immune response. IR thermal imaging is a noninvasive technique for monitoring temperatures and is widely applied in medicine [7,8]. The IR radiation increases due to inflammatory processes, such as that in the tuberculine reaction. An increased IR radiation is most likely caused by elevated blood flow, metabolic activity, and inflammatory reactions [9]. Therefore IR thermal imaging can be used to measure the rise in temperature due to an inflammatory process, which causes the increase of the blood flow with vascular dilatation, blood proteins and cellular extravasations [10]. PPD inflammatory response is characterized by edema, leukocyte lymphocyte-mononuclear infiltration, and erythrocyte extravasation in the dermis and epidermis [11]. Our hypothesis in the present work was that intradermal inflammatory PPD reaction produced an increase in the temperature of the injected area, which can be measured by IR thermal imaging, and the features extracted from the resulting IR images after applying digital image processing techniques helped to improve the reliability in the TB diagnosis.

2. Material and methods

2.1. Ethics statement

The study was conducted in the Respiratory Function Laboratory at HUGTIP, from February–September 2014, and approved by the Hospital's Human Research and Ethics Committee. All participants came from pulmonology dept to discard tuberculosis contact and gave written informed consent, following the World Medical Association's Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects (Ref 10/00214-28/03/2014).

2.2. Mantoux tuberculin skin test

The Mantoux tuberculin skin test (TST) was performed in all subjects by intradermal injection of 0.1 ml of tuberculine purified protein derivative (PPD) (Tuberculina PPD Evans 2 UT/0.1 ml, UCB Pharma S.A., Madrid, Spain) in the anterior forearm. First, the reading of the Mantoux TST was manually performed 48 h following the skin injection [3] by inspection, palpation, and measurement of the induration. The longer distance within indurated skin was measured using a measuring tape. An induration size greater than 0.5 cm was considered to be a positive TST result. An experienced technician in TST readings made all TST tests [12].

2.3. IR thermal imaging

The size of the induration was also measured by IR thermal imaging. Subjects remained in the laboratory room for at least 15 min to achieve thermal equilibrium. Temperature, humidity and air circulation were all controlled. Laboratory temperature was maintained between $23 \pm 1\,^{\circ}$C, and humidity was around 50%. Subjects were requested not to consume hot drinks or food for at least an hour before image session, nor use any skin preparations such as creams or talcum powder. Emissivity of the skin was assumed at a value of 0.98 ± 0.01. There was no ceiling air filter. The lighting in the laboratory was maintained at wavelengths longer than 1 micron.

The IR thermal images were obtained from the anterior surface of the forearm of each subject, using a TiR32 Fluke Camera (2009 Fluke Corporation USA; 320×240 focal plane array; $0.01\,^{\circ}$C noise equivalent temperature difference; 8–14 μm spectral range). The IR thermal camera was installed on a tripod with a fluke compact photo-movie. The distance between the camera focus and the forearm was 40 cm. The forearm was placed on a black foam cushion over a wooden table, with the anterior surface facing the camera focus. To take a reference distance, we placed a 24 mm diameter coin below the area to be measured. The detection of that reference object allowed us to convert pixels to millimeters (Fig. 1). The image acquisition and storage were made with the SmartView® software. Each image was exported in JPG format. Additionally, the temperature measurements were transferred to a text file.

2.4. IR image processing

The IR image processing was performed using Matlab 2014b and following the scheme shown in Fig. 2. Each text file containing the temperature data of an IR image was imported in a 2D numerical array (*temp*). As IR images had different temperature ranges, each *temp* array was scaled, as in (1), in order to have values between 0 and 1, thus obtaining the gray scale image *temp_n* (Fig. 3a).

$$temp\_n = \frac{temp - T_{min}}{T_{max} - T_{min}} \quad (1)$$

T_{min} and T_{max} are the minimum and the maximum temperatures in *temp*, respectively. After obtaining the gray scale image *temp_n*, we detected the reference object of known size that was present in the image in order to obtain the conversion factor from pixels to millimeters. For that purpose, we first applied the Canny edge detector to the normalized image *temp_n* (Fig. 3b). Then, since the reference object was a circle, we used the circular Hough transformer to detect its position and match its edge (note that the Hough transform can be adapted to detect specific shapes in an image) [13]. As the radius in millimeters of the reference object was known, we were able to calculate the conversion factor to express measured lengths in millimeters (Fig. 3c).

The temperature in the forearm area was much higher than the surrounding temperature outside the forearm area (air). Therefore, the values of all pixels in the forearm area were in the upper range of the scaled *temp_n* image. In order to clarify the differences between the internal pixels of the forearm area, we applied an intensity transformation to *temp_n*. All pixels below 0.5 were set at 0, whereas pixels in the range 0.5–1 were expanded to the range 0–1, thus obtaining the *temp_e* image (Fig. 3d). The difference between the PPD reaction area and the rest of the forearm was more noticeable in *temp_e* than in *temp_n*.