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Dynamic infrared imaging for skin cancer screening

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HIGHLIGHTS

- We discussed and proposed a standardized analysis method for dynamic thermal imaging of actual patient data.
- We observed that selecting pixels with the same initial temperature is the key enabling tool in the analysis of the data.
- We extensively tested the methodology on more than 100 human subjects (ClinicalTrials ID number NCT02154451).
- We achieved a sensitivity of 95%, (95% CI: [87.8% 100.0%]), and a specificity of 83%, (95% CI: [73.4% 92.5%]).

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ABSTRACT

Dynamic thermal imaging (DTI) with infrared cameras is a non-invasive technique with the ability to detect the most common types of skin cancer. We discuss and propose a standardized analysis method for DTI of actual patient data, which achieves high levels of sensitivity and specificity by judiciously selecting pixels with the same initial temperature. This process compensates the intrinsic limitations of the cooling unit and is the key enabling tool in the DTI data analysis. We have extensively tested the methodology on human subjects using thermal infrared image sequences from a pilot study conducted jointly with the University of New Mexico Dermatology Clinic in Albuquerque, New Mexico (ClinicalTrials ID number NCT02154451). All individuals were adult subjects who were scheduled for biopsy or adult volunteers with clinically diagnosed benign condition. The sample size was 102 subjects for the present study. Statistically significant results were obtained that allowed us to distinguish between benign and malignant skin conditions. The sensitivity and specificity was 95% (with a 95% confidence interval of [87.8% 100.0%]) and 83% (with a 95% confidence interval of [73.4% 92.5%]), respectively, and with an area under the curve of 95%. Our results lead us to conclude that the DTI approach in conjunction with the judicious selection of pixels has the potential to provide a fast, accurate, non-contact, and non-invasive way to screen for common types of skin cancer. As such, it has the potential to significantly reduce the number of biopsies performed on suspicious lesions.

1. Introduction

Skin cancer is the most common form of cancer in the United States with over 3.5 million cases of skin cancer reported annually [1]. There is a higher incidence of skin cancer than the combined occurrence of breast, prostate, lung and colon cancers [2]. Melanoma, which accounts for an estimated 4% of skin cancer cases, is responsible for approximately 75% of all deaths from skin cancer. The total deaths in the United States due to melanomas and other types of skin cancer are estimated to be more than 12,000 for 2014 [1].

Currently, the detection of melanoma relies on a subjective ABCDE (Asymmetry, Border, Color, Diameter and Evolution) test performed visually by dermatologists, general practitioners (GP) or primary care physicians (PCP) [3]. However, the ABCDE test

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provides a qualitative guideline and it requires a trained specialist to actually distinguish malignant lesions from benign nevi. Moreover, the ABCDE approach has a relatively low specificity (56–65%) and moderate sensitivity (47–89%) [3–5]. Since a false negative could lead to metastatic cancer and death, excisional biopsies are routinely performed even on lesions that are non-cancerous. For example, the number of biopsies undertaken in nine geographical areas of the US between 1986 and 2001 is close to 60 for every melanoma detected [6].

Since biopsies are intrusive and can be painful, different non-invasive techniques are being researched in order to minimize the number of excess biopsies performed [7,8]. Some of these techniques include multispectral (MS) imaging [9–11], digital dermatoscopy and videodermatoscopy (sequential digital dermatoscopy) [12,13], reflectance-mode confocal microscopy [14], ultrasound [15,16], laser Doppler perfusion imaging [17], and optical coherence tomography (OCT) [18,19], to name a few. Currently, there are two FDA-approved non-invasive imaging devices MelaFind™ and Vivosight Multi-Beam System™, which are based on MS imaging and OCT, respectively. On one hand, the MelaFind technology only works with pigmented melanomas and the specificity is as low as 9.5% [20]. On the other hand, Vivosight presents sensitivity between 79% and 94% and specificity between 85% and 96% for non-melanoma skin cancer lesions [21] but the suspicious lesion must be probed several times, which makes the acquisition time prohibitively high.

In order to address this problem, different groups have investigated the utilization of dynamic thermal imaging (DTI) for skin cancer screening and diagnosis [22]. For example, Anbar [23] described how changes in human skin temperature convey valuable physiological and pathophysiological information. Buzug et al. [24] and Cetingul and Herman [25] studied the diagnosis of BCC and MM lesions, respectively. Both used similar techniques, requiring the cooling of the lesion to observe the warm-up pattern. Their work established that the difference in the thermal recovery may contain useful information that has the potential to non-invasively differentiate malignant lesions from benign. Nevertheless, there is not a standardized protocol to analyze the subject data such that malignant lesions are identified with high sensitivity while at the same time ensuring that benign lesions are identified with high specificity.

In this paper, we address this problem by presenting a standardized analysis protocol of DTI that judiciously selects pixels with the same initial temperature in order to compensate deficiencies in the cooling process, which, at the same time, is the key process that enables the classification of the lesion condition with an specificity >80% for a 95% of sensitivity. We evaluate its effectiveness by presenting results from a cross-sectional sample of 102 subjects.

2. Material and methods

2.1. Data acquisition equipment

The data acquisition equipment consists of four components. First, a cooling unit that is used to impart a temperature stimulus to the lesion and the surrounding skin tissue; the cooling unit was a Ranque–Hilsch vortex tube that generates an oil-free, moisture-free, ultra-quiet air flow. Second, an infrared marker, which is used for correction of involuntary movement of the subject (i.e., image registration); the marker is a square piece of plastic with a square opening in the middle. Third, the imaging portion of the system consists of a commercial visible camera to capture a reference image before the acquisition commences and a longwave infrared (LWIR) camera to capture the thermal recovery of the skin after the cool air is applied. The LWIR camera uses a 320 × 256 focal-plane array (FPA) of quantum-well infrared photodetectors (QWIP) operating at 60 K. The noise equivalent temperature difference (NEDT) of the FPA is 20 mK and the QWIP camera is fitted with a 50 mm, *f*/2 LWIR lens, yielding an approximate spatial resolution of 300 μm per pixel. The QWIP camera was chosen for our pilot study because it has higher array uniformity, lower NETD and high spatial resolution as compared with other IR camera technologies [22,28]. Fourth, a custom computer program developed and coded by the authors, which performs image registration and undertakes the analysis of the subject data.

2.2. Imaging procedure

After informed consent, each subject was escorted to a designated room in the UNM Dermatology Clinic to perform the imaging procedure. The temperature of the room was controlled to be between 20 °C and 22 °C to make sure that all the patients were at the same temperature before applying the cooling stimulus to the area of interest. At the beginning of the procedure, a square registration marker was placed around the lesion with the lesion centered in the opening, as shown in Fig. 1. A visible image of the lesion was then taken with the digital camera for reference purposes. After collection of the visible image, a 15 s infrared image sequence of the marked area was collected to serve as a baseline. Later, the subject's skin within the marker opening was cooled for 30 s using the cooling unit. After cooling, the exposed area was allowed to warm up naturally to ambient temperature. During the cooling and warm-up phases, thermal images of the skin were captured for a total of 2 min at a rate of 60 frames per second. All the thermal images were recorded using an uncompressed 14-bit format. The total time required to complete the imaging procedure was less than 5 min. If the subject was scheduled for a biopsy, the biopsy was performed following the data collection by the attending dermatologist and sent to pathology for diagnosis. The biopsy results were delivered to us within the next two weeks following the imaging procedure.

2.3. Data processing

2.3.1. Data registration

Since involuntary movements cannot be avoided, image registration must be performed on the sequence of IR images. Moreover,

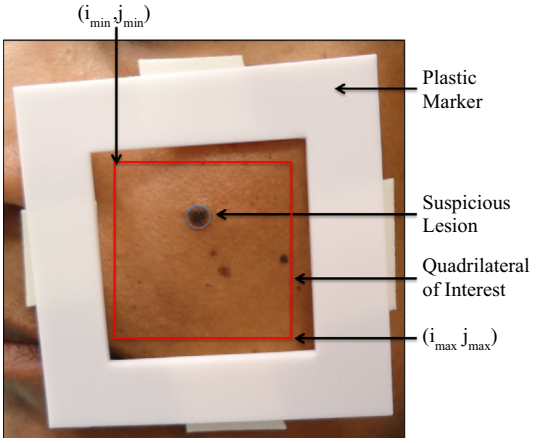

Fig. 1. Example of one square plastic marker used in the data acquisition step; the biggest rectangle that can be drawn within the opening of the marker is defined by the points (i_{min},j_{min}) and (i_{max},j_{max}), labeled in the inset. The suspicious lesion is also labeled and surrounded by the ellipse (light blue) drawn by the user. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)