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# Lock-in thermal imaging for the early-stage detection of cutaneous melanoma: A feasibility study

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ABSTRACT

This paper theoretically evaluates lock-in thermal imaging for the early-stage detection of cutaneous melanoma. Lock-in thermal imaging is based on the periodic thermal excitation of the specimen under test. Resulting surface temperature oscillations are recorded with an infrared camera and allow the detection of variations of the sample's thermophysical properties under the surface. In this paper, the steady-state and transient skin surface temperatures are numerically derived for a different stage of development of the melanoma lesion using a two-dimensional axisymmetric multilayer heat-transfer model. The transient skin surface temperature signals are demodulated according to the digital lock-in principle to compute both a phase and an amplitude image of the lesions. The phase image can be advantageously used to accurately detect cutaneous melanoma at an early stage of development while the maximal phase shift can give precious information about the lesion invasion depth. The ability of lock-in thermal imaging to suppress disturbing subcutaneous thermal signals is demonstrated. The method is compared with the previously proposed pulse-based approaches, and the influence of the modulation frequency is further discussed.



## 1. Background

Cutaneous melanoma is considered to be the most serious form of skin cancer due to its ability to metastasize. The occurrence of melanoma is about 7.5 new cases per 100,000 inhabitants per year for Europe (17.9 for Switzerland), and has been drastically rising over the last decades [1,2]. Melanomas are responsible for more than 80% of all skin cancer related deaths. In this context, early diagnosis is of crucial importance.

The current standard procedure for the detection of melanoma is a clinical examination followed by excision of suspect lesions and histopathology to confirm the diagnosis. The use of epiluminescence microscopy (also referred as dermoscopy) greatly increases the diagnostic accuracy [3,4]. Dermoscopy is a non-invasive, in-vivo examination with a microscope, that uses incident light and liquid immersion to make subsurface structures of the skin accessible to visual examination. Dermoscopy allows a more detailed inspection of cutaneous lesions, nonetheless, its accuracy relies on the level of expertise and training of the physician. As a result, a large number of benign lesions are unnecessarily excised [5]. To avoid needless excision, but also to initiate the appropriate treatment at an early stage, in the case of malignant lesions, an objective and non-invasive diagnostic tool is highly needed.

Various new techniques to detect melanomas are being investigated in different laboratories worldwide. Without being exhaustive we can cite: multi-spectral imaging, laser-based systems like optical coherence tomography (OCT), laser doppler perfusion imaging, magnetic resonance imaging (MRI), PET scan, Raman spectroscopy, fluorescence spectroscopy and ultrasound imaging (see [6] for a review). Despite intensive research, and promising results from techniques like high-definition laser doppler imaging [7], or multi-spectral imaging [8], dermoscopy remains the standard for the screening of cutaneous melanoma.

Among the different techniques proposed, the past few years have seen a revival of interest for thermal-imaging based methods. It had already been noticed in the 1960's that melanoma lesions are warmer than the surrounding healthy tissue [9]. This higher temperature can be explained by two phenomena. First, the metabolism is higher at the location of the lesion. Second, the "warm" blood supply is also increased to support the growth of the tumour. In this circumstances, monitoring the surface temperature should allow detecting suspicious warmer regions. This monitoring can be easily achieved remotely, using infrared imaging often also called thermal imaging. In thermal imaging, an infrared camera measures and images the emitted infrared radiation of an object. This radiation depicts the object temperature via the Stefan–Boltzmann law. The potential of thermal imaging in the medical field has already been successfully exploited. Thermal imaging is for example very promising for the detection of breast

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cancer [10]. Other applications include skeletal and neuromuscular system, complex regional pain syndrome, dentistry, and surgery [11]. Unfortunately, early thermographic studies devoted to the detection of cutaneous melanoma showed poor results with a high percentage of false-negative [12]. Those disappointing results can be explained by several factors. First, the temperature differences involved are small and highly sensitive infrared imaging devices were not available at the time of the first studies. Second, under normal conditions steady-state infrared images of the skin are a mosaic of hyper- and hypothermic areas reflecting local circulatory, metabolic, and other general factors. A way to overcome this last difficulty is to perform a transient temperature measurement. For example, the skin surface is thermally stimulated (cooled or heated) for a defined period of time, and the way it retrieves its equilibrium temperature after removal of the stimulation is monitored. By selecting the infrared images at a specific time after the stimulation, it is possible to "reject" the effect of local circulatory and metabolic variations, taking place much deeper in the tissue and exhibiting a different time constant [13]. The use of an imposed external heat-flow to the sample while monitoring its surface temperature is referred to as active thermal imaging or active thermography in the literature [14]. The external thermal stimulus provides a non-stationary temperature gradient inside the structure under test which affects the surface temperature distribution. This surface temperature is monitored as a function of time. Regions under the surface exhibiting different thermophysical properties compared to the surrounding tissue will cause transient anomalies to appear in the surface temperature distribution. Active thermal imaging has been successfully used for decades in the field of non-destructive testing of materials [15]. Different modalities can be implemented: The sample can be heated either by conduction, convection or radiation absorption. It can also be cooled by convective or conductive heat transfer.

The first attempt to use active thermal imaging for the detection of cutaneous melanoma was achieved by Di Carlo [13]. With the help of a setup where the thermal stimulation is achieved by a balloon filled with a thermostatic alcohol solution, Di Carlo investigated qualitatively the thermal signature of melanomas subject to heating or cooling. A few seconds after the removal of the stimulation, melanoma lesions exhibit drastic temperature differences compared to the surrounding healthy skin and are therefore easily detectable. Very recently, Çetingül and Hermann have redone this experiment trying to extract quantitative information from the transient thermal signal [16,17]. The transient skin surface temperature is recorded and compared with the outcome of a computational multilayer heat transfer model. Çetingül and Hermann demonstrated that the average thermal signature of melanomas, even at an early stage, is very different from healthy skin or benign melanocytic nevi [16]. According to the results of their computational model, blood perfusion is the main thermophysical parameter influencing the melanoma thermal response [17].

The different experimental setups demonstrated so far in the literature are all based on a non-periodic thermal stimulation: the tissue is either cooled or warmed for a defined period of time and the skin surface transient temperature is monitored after the removal of the stimulation. We believe that the accuracy of the above-mentioned methods can be drastically increased if a periodic thermal modulation is used. For this reason, we propose to use lock-in thermal imaging (LIT), a technique developed by Busse and co-workers in the early 90s for the non-destructive control of materials [18,19]. LIT works as follows: the sample is thermally stimulated at a determined frequency and the simultaneously recorded infrared images of the sample surface are processed digitally according to the lock-in principle. The result of this demodulation is a phase and an amplitude image. The phase image is a map of the phase angles between the periodic thermal stimulation and the harmonic temperature response of the skin surface. The amplitude image is proportional to the dissipated power at the skin surface. LIT has been used for decades in the field of non-destructive testing of materials [15] and in the photovoltaic industry, but to our knowledge, it has never been applied to the detection of cutaneous lesion.

The direct advantage of lock-in thermal imaging compared to the main methods proposed in the previous studies lies in the averaging nature of the technique. LIT allows detecting very small temperature gradients even "buried" in a noisy background. The high sensitivity of LIT can be advantageously used to reduce the amplitude of the thermal modulation applied to the skin. Large temperature gradients may influence the skin's thermophysical parameters like the blood perfusion. In addition, if the thermal modulation frequency is chosen high enough, lock-in thermal imaging has the ability to "suppress" lateral heat spreading from the infrared images [20]. In our case, LIT should allow a more precise determination of the lesion margins. One of the strong points of LIT is the phase image, which is relatively independent of experimental artefacts and infrared surface features. For example, experimental artefacts refers to non-uniform heating/cooling or bad infrared camera calibration as infrared surface features may concern variability in the surface emissivity [20].

In this paper, we aim to investigate theoretically the feasibility of lock-in thermal imaging for the detection of cutaneous melanomas. Hence, we present in the next section the computational model used to derive the transient temperature of the skin surface, subject to periodic convective heat transfer. We developed in our laboratory a lock-in thermal imaging setup especially dedicated to dermatological applications [21]. In this apparatus, the skin surface temperature is periodically modulated by convective heat transfer using an airflow. The temperature-modulated airflow can be achieved using a cold air device in series with a resistive wire whose voltage is periodically modulated. A microbolometer infrared camera synchronized with the airflow modulation records the thermal emission of the skin surface. Both the IR camera and the air-flow modulation can be incorporated into a compact hand-held pistol-like housing that can be brought into contact with the patient skin during the measurement. The processing of the infrared images is achieved in real-time by a personal computer. The apparatus is currently evaluated in a clinical environment.

## 2. Methods

### 2.1. Steady-state skin surface temperature

Many publications have been devoted to the development of biological heat-transfer models for the thermographic assessment of cutaneous diseases [22–27], or skin burns [28]. In those studies, the bio-heat equation from Pennes [29] is used to model the temperature distribution in the different tissue layers. Pennes' model describes the influence of blood perfusion on temperature distribution in terms of volumetrically distributed heat sources or sinks. The generalized Pennes bio-heat equation can be written as

$$\rho C\frac{\partial T}{\partial t}+\rho_b C_b \omega (T-T_b)-Q=k\nabla^2 T \quad (1)$$

where $C$, $k$, $\rho$, $\omega$, and $Q$ are respectively the specific heat, heat conductivity, density, blood perfusion rate and metabolic heat generation. $C_b$, $\rho_b$, and $T_b$ denote the blood specific heat, the blood density, and the blood temperature. $T$ represents the local tissue temperature, $t$ denotes the time variable and $\nabla^2$ is the Laplace operator (see Table 1).

Eq. (1) states that the rate of change of thermal energy contained in a unit volume is equal to the sum of the rates at