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The use of Design of Experiments for steady-state and transient inverse melanoma detection problems

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ABSTRACT

Melanoma is one of the most fatal skin cancers; for this reason, there is a need for the development of new safe, non-invasive and efficient diagnostic techniques. Dynamic thermography is showing to be a promising technique for the early detection of skin cancers. Therefore, this paper investigates two different inverse bioheat problems using steady-state and transient skin temperature measurements. Both problems are investigated numerically to estimate how accurate blood perfusion rate, metabolic heat generation, diameter and thickness of the tumour can be estimated simultaneously under exact and noisy measurement data, based on a complex numerical model describing multilayer tissue. The inverse problems have been tested using different melanoma size, Clark II and Clark IV. The Design of Experiments (DOE) technique has been used to solve and analyse the inverse problems. A substantial number of numerical model evaluations, totalling 2,306,486 simulations, had to be undertaken as part of the full factorial DOE. The results show that it is always possible to obtain tumour parameters using exact static or dynamic measurement data. However, for noisy temperature data, the use of a dynamic approach showed an advantage over the steady-state one, which failed because of the very small temperature differences between the healthy skin and the tumour. The dynamic thermography can retrieve blood perfusion rate, thickness and diameter of the tumour as well as the metabolic heat generation despite the low sensitivity for low and high levels of measurement error; however, to detect melanoma lesions at an early stage, the measurement and model errors should be kept as low as possible.

1. Introduction

Skin cancer can be generally categorized into melanoma and non-melanoma, and further divided into pigmented and non-pigmented lesions. Among all types of skin cancer, melanoma is the most fatal because it metastases rapidly and can spread to soft tissues like lung and liver [1]. According to Clark et al. [2]. and Breslow [3], the survival rate of patients with malignant melanoma is directly correlated with its thickness or level of invasion. The deeper the invasion, the lower the survival rate. For this reason, it is important to detect skin cancer in its early stage and it is essential to develop accurate and sensitive diagnostic techniques in order to enable early detection and diagnosis.

Nowadays the most frequently used diagnostic technique is visual inspection based on the ABCDE (Asymmetry, Border, Colour, Diameter, Evolution) criteria and dermatoscopes. As it is known, the ABCDE criteria uses only qualitative guidelines for melanoma identification and can therefore produces high rates of false positives or false negative identification. To avoid the risk of missing an early stage melanoma, excisional biopsies are performed for further pathological investigation [4–7]. Therefore, new techniques for skin cancer detection are being developed like digital photography, multispectral imaging systems, confocal scanning laser microscopy (CSLM), laser Doppler perfusion imaging (LDPI) optical coherence tomography (OCT), ultrasound and magnetic resonance imaging (MRI) [8–16]. Usually, they are a compromise between certain aspects like effectiveness, accuracy, cost and invasiveness.

Thermography or thermal tomography is offering a new non-invasive diagnostic technique for medicine in different fields, based on the bioheat transfer of the observed tissue. This is nowadays possible due to the development of infrared (IR) thermal cameras, computers and numerical modeling. Bioheat transfer is mainly governed by blood perfusion and metabolic heat generation, which affect the temperature difference between the normal and abnormal tissues. There have been many studies of thermography in the field of breast cancer, skin cancer, vascular diseases, thyroid gland disease, eye diseases as well as therapeutic assessment [17–30]. Thermography can be done passively

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(static) or actively (dynamic). Static thermography involves recording the skin temperature under steady-state conditions, which is time consuming because the patient has to acclimatise to the environment in the temperature controlled room [31]. On the other hand, active thermography involves introducing external thermo-stimulation like heating or cooling to induce thermal contrast between the healthy and investigated tissue. Thermal contrast is the effect of different thermal and physiological properties of tissues. Based on the thermography measurement data a mathematical or numerical model can then provide some information about the tissue state under investigation. The general advantage of dynamic thermography is that it is faster than the static one and can reveal more information about the tissue or tumour under investigation [19,20,22,26,30,32].

In order to estimate the physiological parameters of the tumour, its size and position, based on static or dynamic thermo-graphic measurements, we have to solve an inverse bioheat problem based on the appropriate numerical model of the corresponding system. In this paper, we focus on the detection of melanoma lesion based only on the skin surface temperature measurements; however, the numerical techniques could be generally applied to other similar applications like breast tumour detection. Most research work to determine the tumour characteristics in general are based on steady-state temperature measurements (static thermography) for 2D and 3D using evolutionary algorithms [33–37]. They show that if the thermal properties, blood perfusion and metabolic heat generation of the tumour and surrounding tissue are predetermined, the size and location of the tumour can be found fairly successfully even for noisy measurement data. For the case of skin tumour identification, Luna et al. [36] tried to estimate the size of the tumour and its blood perfusion rate for steady-state surface temperature measurements using a simulated annealing (SA) algorithm. The results are promising even with noisy measurement data for the case of two searched parameters, diameter and blood perfusion of the tumour or thickness and blood perfusion.

All the previous papers used simplified computational domains containing only two regions, healthy tissue and tumour or lesion. More complex numerical models using multilayer tissue structures have been developed by Hossain et al. [38], Bhowmik and Repaka [39] and Hatwar and Herman [30]. Most interesting is the work of Bhowmik and Repaka [39], who tried to identify several skin tumour parameters based on steady-state skin surface temperature measurements considering a 3D multilayer tissue. Their models used genetic algorithm (GA) and SA to compare the two different approaches. The results show that the solution of inverse problems is strongly dependent on the value of other parameters, which is not desirable for new diagnostic techniques. The recent work of Hatwar and Herman [30] presents the estimation of tumour radius, depth and blood perfusion rate of breast tumours based on a 2D numerical model including multilayer tissue, using commercially available software and the Levenberg-Marquardt optimisation algorithm. Under steady-state temperature measurement, they were able to detect tumour dimension and depth and they demonstrate numerically that the blood perfusion rate cannot be simultaneously detected. For that, transient surface temperature measurements are needed, where they took only transient measurements at the middle surface point. Herein, a better reconstruction of parameters is achieved using greater surface and time temperature measurement resolution also for deeper tumour locations. Although breast cancer parameter estimation is not the topic of this paper, there are similarities between our numerical techniques and those of [30].

This paper analyzes two different inverse bioheat problems of estimating several skin tumour parameters based on skin surface temperature measurements. The first inverse problem deals with steady-state temperature measurements (static thermography), while the second uses transient measurements (dynamic thermography) as proposed by Çetingül and Herman [26]. The number of parameters to be determined is four: diameter, thickness, blood perfusion rate and metabolic heat generation of the melanoma, from which the thickness and blood perfusion are the most important factors in reflecting the stage and progression of the skin tumour. The numerical model to estimate these parameters is based on the work of Çetingül and Herman [26], Bhowmik and Repaka [39] and Cheng and Herman [32] using a 2D computational domain and considering a multilayer tissue structure that better reflects the real problem.

The non-linear numerical model for solution of the direct problem is based on a sub-domain Boundary Element Method (BEM) solver presented in our previous paper [40], where it is shown that it can solve direct bioheat problems accurately and efficiently, which is desirable when solving inverse problems. The optimisation technique for solving inverse bioheat problems presented in this paper is the full factorial Design of Experiments (DOE) not using the surrogate model (SM). The reason for choosing the full factorial DOE is that it is possible to explore the complete design space, and to analyse and compare the differences between static and dynamic thermography. The DOE allows to plot the objective function (response surface) and to estimate the sensitivity of each parameter, which helps in analysing which parameters can be estimated easily and which parameters cannot be estimated at all. The DOE for both inverse problems required 2,306,486 evaluations of the numerical model, which is substantial, time consuming and impractical for clinical implementation. However, it is valuable in this stage of investigation due to the design space and problem exploration, which could not be done using other algorithms. The paper shows inverse problem analyses for steady-state and transient measurement approaches based on two melanoma sizes (Clark II and Clark IV) under exact as well as noisy measurement data.

The novelty of this paper can be found in the solution of steady-state and transient inverse bioheat problems to estimate four important skin tumour parameters using complex numerical models. Another novelty is the use of DOE for solving inverse problems, obtaining the solution, analysis of the design space and comparison of both problems under exact and noisy measurement data.

The paper is organized as follows. Section 2 presents the numerical model used for solving direct bioheat problems, together with the two numerical examples under investigation. Section 3 describes and discusses the steady-state and transient inverse bioheat problems, the evaluation of the objective function and the DOE approach. Section 4 discusses the results obtained for both inverse problems under exact and noisy measurement data, together with a detailed discussion of the inverse problem results. Finally, Section 5 presents the conclusions of the work with its most important results.

2. Numerical model

To investigate the inverse problem of estimating the size and material properties of skin tumour based on the skin surface temperature, we need to define the numerical model, as well as numerical examples upon which the inverse analysis will be done. The numerical model is based on the work of Bhowmik et al. [39,41], Çetingül and Herman [26] and Cheng and Herman [32] that treated the bioheat transfer problem in skin considering epidermis, papillary dermis, reticular dermis, fat and muscle tissue, where the tumour has been placed inside the papillary dermis. Therefore, the numerical model can describe heat transfer in skin containing a tumour more accurately than the simplified models considering only the lesion and uniform surrounding tissue.

Although different layers of tissue will be considered in the numerical model, there is still some room for improvement to describe thermal and pathological behaviour of the skin, malignant melanoma lesion and surrounding tissue together with some response mechanisms more realistically, especially for the cooling-rewarming process. We could include more realistic behaviour by adding the inflammation of tissue around the tumour blending the tumour boundary, temperature response of the skin (skin contraction under cooling), blood flow and water content in tissue which affects the thermal properties like tissue heat storage capacity, as well as pathological changes of the tumour in