ARTIGO

EVALUATION OF SURFACE TEMPERATURE OF TONGUE FOR SCREENING OF PATIENTS WITH SUSPECTED ORAL CANCER¹

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ABSTRACT

Oral cancer has become one of the most critical types of cancer today due to its late diagnosis in Brazil. The early detection is mandatory for more favorable prognosis but it depends on patient's information, specialized infrastructure and trained professionals not always available. The use of thermographic imaging becomes a viable alternative for patient screening and triage in different areas. This is a non-invasive and low-cost procedure, especially when compared to the main imaging tests such as magnetic resonance imaging and computed tomography. Thus, the aim of this work was to develop a computational model capable of representing the thermal behavior on the surface of the tongue tissue in the presence or absence of malignant neoplasms. The obtained results did not show changes in the temperature profile of the tissue when a small tumor (up to 2 mm in radius) is present. It can be concluded that it is not possible to detect a tumor in the tongue through a thermal analysis on the surface with thermographic images, due to the low differences obtained. However, other conditions for the model and also tumors in other locations should be studied in order to obtain more general conclusions.

Keywords: Oral cancer. Thermography. Screening. Infrared images.

1 INTRODUCTION

In Brazil, only 20% of tumors are detected in early stages and the other 80% are diagnosed in more advanced stages (CAMARGO, 2017). This contrasts with the concept that the earlier the diagnosis, the greater the chances of cure and better is the patient's quality of life (MINISTÉRIO DE SAÚDE, 2006). Particularly, according to the National Cancer Institute, oral cancer is often diagnosed late. More than 14.000 new cases of oral cancer are

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registered in Brazil, being the majority among men, which makes it a relevant public health problem with reported more than 4 thousand deaths/year (CRO-GO, 2017). This type of cancer is also reported among the three most common in developing countries (CAMARGO, 2017).

Some important factors associated with this disease are the patient's life habits, such as alcohol and tobacco consumption, and individual social issues, such as the lack of information about the disease. The sites with the highest incidence of oral cancer are tongue (26%), lips (23%), especially on the lower-lip, sublingual region (16%) and minor salivary glands (11%). The rest are found in the gums and other locations. These cancers may occur in all age groups but are rare in children. Approximately two-thirds of the patients are older than 55 years old (MADEIRA; LEITE; RIZZOLO, 2016; CAMARGO, 2017). Clinical examination itself is not enough to detect the extent of the tumor and the presence of cervical metastases. Computed tomography (CT) and magnetic resonance imaging (MRI) are the main tests used for diagnosis. However, both are high-cost techniques, and during CT the patient is submitted to ionizing radiation (PAIVA, 2009). The most accurate diagnosis of oral cancer is a biopsy, which is an invasive procedure that can generate false negatives if the tissue collected is not that of the cancerous region (CHAKRABORTY, 2016).

Thus, it is evident a deficiency on tools for the early detection of the disease (CHAKRABORTY, 2016). This difficulty could be overcome with the use of thermographic images, an alternative to assist by screening patients with suspected cancer. Thermography is a technique that uses specialized cameras to visualize and measure the temperature of a surface. The technique has been used in medicine as it is able of detecting, in real time, changes in temperature patterns related to inflammatory processes as well as endocrine and oncological conditions (SCHWARTZ *et al.*, 2006; FERNÁNDEZ-CUEVAS *et al.*, 2015; HADDAD, 2016).

Tumors arise from the uncontrolled development of malignant cells in the body, resulting in increased blood perfusion in the affected region, which causes an increase in local temperature. This temperature increase has the potential to be detected in thermographic images produced by the thermography technique (SILVA, 2015). In addition, changes in tumor temperature over time may support the definition of treatment strategies (COHEN, 2013).

In this context, the aim of this work is to develop a computational model to represent the temperature behavior on the surface of the tongue in the presence of tumors of different sizes. This research intends to verify if the presence of a tumor, in its early stages, can be detected through thermographic images.

2 DEVELOPMENT

2.1 BIOHEAT TRANSFER MODELS

In the presence of a temperature difference between medias or within a medium, the transfer of energy occurs in the form of heat. This transfer can occur by different means: conduction, convection and radiation. Conduction occurs due to the existence of a temperature gradient in solids or fluids in stationary medium. Convection occurs when there is a temperature difference between a surface and a moving fluid. Finally, the thermal radiation is the emission of energy in the form of electromagnetic waves (INCROPERA; DE WITT, 2008; MOREIRA, 2012).

2.1.1 Pennes' Model

The most widely used equation for describing heat transfer in living tissues was developed by Harry H. Pennes (1948) known as the Bioheat Transfer or Pennes Equation. The Pennes equation describes the temporal and spatial distribution of temperature in living beings and, although it carries some limitations, this model is very useful for this type of heat transfer analysis (SILVA, 2012).

The arrangement of this equation was made from the energy balance, considering the rate of internal energy storage, heat exchange by conduction and convection, the local generation of heat and neglecting the chemical, physical, nuclear and electrical effects. The solid, linear, homogeneous biological medium with isotropic thermal properties is considered to obtain the temperature field. The convective heat exchange will only occur in the capillary system. It is assumed, for the energy balance, that the blood flow inside the tissue is non-directional to the capillary level. Therefore, it will be adopted that the capillaries are oriented according to their arteriolar and venular connections (BEZERRA, 2007). The Equation (1) is the result of energy balance on a tissue with blood flow, metabolic heat generation and an external heat source (SILVA, 2012).

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$$\rho_t c_t \frac{\partial T_t}{\partial t} = \nabla (k_t \nabla T_t) + Q_m + Q_p + Q_e, \qquad (1)$$

Where ρ_t is the tissue density (kgm⁻³), c_t is the tissue specific heat (Jkg⁻¹ K⁻¹), T_t is the tissue temperature (K), t is the time (s), k_t the thermal conductivity of the tissue (Wm⁻¹K⁻¹), Q_m is the rate of metabolic heat generation per unit of volume (Wm⁻³), Q_p is the rate of heat generation or withdraw per unit of volume due to blood perfusion (Wm⁻³) and Q_e is the rate of heat generation per unit of volume due to external sources (Wm⁻³).

Pennes' theory proposes that the heat transfer caused by the blood flow can be described by a blood perfusion rate as a scalar heat source or sink (SILVA, 2012). This heat source or sink can be described according Equation (2):

$$Q_p = \omega \rho_b c_b (T_a - T_v), \tag{2}$$

where ω is the blood perfusion rate (s⁻¹), ρ_b is the blood density (kgm⁻³), c_b is the specific heat of the blood (Jkg⁻¹K⁻¹), T_a is the arterial blood temperature entering the tissue (K) and T_v is the venous blood temperature entering the tissue (K).

If the thermal equilibrium between the blood and local tissue is considered, $T_v=T_t$, also it is often considered that the venous blood leaves the tissue with the temperature of the arterial blood, thus $T_v=T_a$ (BEZERRA, 2007).

2.1.2 Limited keff model

In the limited keff model, the blood flow of smaller vessels is described using the tissue conductivity keff in the first term of the right hand side of Equation (3), which represents the tissue conduction and convection (CREZEE, 1994; PARK; ALONSO; NUNES, 1999).

$$\rho_t c_t \frac{\partial T_t}{\partial t} = k_{eff} \nabla^2 T_t + Q_p + Q_m + Q_e \tag{3}$$

The effective tissue conductivity coefficient k_{eff} depends on vessel size, velocity of flow and vascular structure, and reduces to a scalar for isotropic flow. The limitation of this model is that it only applies to vessels with a diameter smaller than 500 µm (CREZEE, 1994).

2.1.3 Mixed Model

The mixed model is suggested when there is the presence of thermally unbalanced vessels larger than 500 μ m. The model has the advantage of being applied in situations where there is no information about the actual vascular anatomy (CREZEE, 1994). The mixed model is the combination of the Pennes' model and the limited k_{eff} with the addition of the modifying factor *f* in the term Q_p:

$$Q_p = f \omega \rho_b c_b (T_a - T_v), \tag{4}$$

the modifying factor *f* of the heat source/sink term, depends on the local vessel network. For a closed vessel system $0 \le f \le 1$ (CREZEE, 1994). Since the mixed model improves on previous models while keeping its simplicity, it will be adopted in this study.

2.2 MATHEMATICAL MODELING

A three-dimensional model was performed to determine the distribution of temperature in a human tongue in the presence of a tumor. Tongue dimensions were collected from the authors of this study. The simplified geometry of the model was based on the shape of the tongue (SANDERS; MU, 2013) and built in the software COMSOL Multiphysics[®] 5.1 and is shown in Figure 1. The tumor was positioned in the lateral border of the tongue, near its base, which is the region of higher incidence of this type of cancer (HIROTA; MIGLIARI; SUGAYA, 2006; MADEIRA *et al.*, 2016). The tumor was represented as a sphere of different diameters, all located at 0.5 mm from the lateral surface of the tongue.



Figure 1 - Geometry of the tongue used in the computational model Source: Own author.

The temperature distribution in the tongue and tumor were modeled according Equation (5) which consider the mixed model without external heat sources and with f=1.

$$\rho_t c_t \frac{\partial T_t}{\partial t} = k_{eff} \nabla^2 T_t - f \omega \rho_s c_s (T_t - T_a) + Q_m$$
(5)

2.2.1 Boundary conditions

To establish the boundary conditions, it was considered that the tongue is initially at rest inside the oral cavity and the mouth of the patient is closed for such a period of time that the temperatures on the surface of the tongue were stable. Additionally, the images of the thermographic camera were obtained immediately after the tongue is placed out of the mouth, so no considerable heat exchanges between the organ and the environment.

In order to reproduce the environment of the oral cavity, boundary conditions of constant temperature and heat flux were set to the surfaces of the tongue. The body temperature of 37°C were considered on the surface of the base of the tongue. On the sublingual region, the sublingual temperature of 36.6 °C were considered (LÓPEZ; LAURENTYS-MEDEIROS, 2004). For the rest of the tongue surfaces, a conduction heat flux trough a saliva film was considered between the lateral and the top surfaces of the tongue and the air inside the oral cavity. The heat flux is described by the Equation (6):

$$q = U(T_{oral} - T) \tag{6}$$

where $U=k_{saliva}/L$ is the global coefficient of heat transfer, k_{saliva} (W/mK) is the thermal conductivity of the saliva, L (m) is the thickness of the saliva film, T_{oral} (K) is the temperature of the air inside the oral cavity and T (K) is the temperature of the surface of the tongue. The thickness of the saliva film was considered as L=0.085 mm (COLLINS; DAWES, 1987).

2.2.2 Physical properties and model parameters

There is a lack of data in the literature regarding the physical properties of tongue tumors, thus properties of the breast tumor were used during the simulations that are widely reported in the literature. The rate of metabolic heat generation on an early stage tumor is much higher than on advanced stages due to the large amount of blood vessels formed in the ABREU, Amanda Isabella; LIMA, Thiago Parente; MEIRELES, Agnes Batista; SOUZA, Bárbara 7 Emanuella; TORRES, Libardo Andrés Gonzáles. Evaluation of surface temperature of tongue for screening of patients with suspected oral cancer

region (COIMBRA *et al.*, 2011). This rate decreases as the tumor grows. Tumors up to 10 mm and 30 mm have a metabolic heat rate of 65400 Wm^{-3} and 5740 Wm^{-3} , respectively (BEZERRA, 2007). As the study aims to reproduce a diagnosis on an early stage, the rate of heat generation was considered constant at 65400 Wm^{-3} .

Table 1 shows the physical properties considered in the model. The properties of the saliva were approximate to the water due to its high content of water, 99% (DE MOURA *et al.*, 2007). The remaining properties are k_{eff} =1.8 (W°C⁻¹m⁻¹) (CREZEE, 1994), T_a=37 (°C) and T_{oral}=34.4 °C as measured by the authors.

Table 1 - Physical properties					
Property	Tongue	Blood ^(a)	Saliva ^(a)	Tumor ^(b)	
Heat generation rate, Q (Wm ⁻³)	1.21x10 ³ (a)	-	-	65400	
Density, ρ (kgm ⁻³)	1090 ^(a)	1050	994	1080	
Specific heat, $c_t (J kg^{-1}K^{-1})$	3421 ^(a)	3617	4178	3500	
Thermal conductivity, $k_t (Wm^{-1}K^{-1})$	0.49 ^(a)	0.52	0.6	0.48	
Blood perfusion rate, ω (s ⁻¹)	0.0018 ^(c)	-	-	0.009	

Source: (a) It is Foundation (2018), (b) Bezerra (2007) and (c) Crezee et al. (1994).

2.2.3 Numerical procedure

The steady state form of Equation (5) and its boundary conditions were implemented in the software COMSOL Multiphysics[®] 5.1 and solved through the Finite Element Method (DE SOUZA, 2003). The mesh independence study was performed with meshes of 8815, 33930 and 161833 tetrahedral elements. The temperature of three points on the external surface of the tumor were monitored for the three meshes. This region was chosen because it presents the steeper temperature gradients of the domain. The maximum temperature difference between the meshes was of $3x10^{-4}$ %, thus, the solution was considered mesh independent. Since the difference in computational time between the first and the second meshes was negligible, the second mesh of 33930 elements were chosen for this study.

2.3 RESULTS AND DISCUSSION

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The tumor was included in the region of higher incidence, which is the upper lateral border (HIROTA, 2006) and its diameter varied between 1.0 and 4.0 mm sizes, difficult to detect by visual inspection. Simulations were performed for a healthy tongue (no tumor), and with tumor to estimate the surface temperature. All tumors were located at a distance of 0.5 mm from the extremity of the upper lateral border of the tongue. For better visualization, two images were generated: one of the surfaces of the tongue and other of a transversal section passing by the center of the tumor.



Figure 2 - Healthy tongue Source: Own author.

After performing the simulations for the chosen case studies, we have extracted some relevant results. The temperature on the surface of the healthy tongue varied between 34.40°C and 37.00 °C (Figure 2) which corresponds to the body temperature previously reported in the literature (SILVA, 2012). The side edges and upper part of the tongue lose more heat because the air temperature inside the oral cavity is lower than the sublingual temperature and the body temperature. This generates a greater temperature difference between the media and a higher heat transfer flux.

Figure 3 shows the lateral views (a) and in a transversal section at the center of the tumor (b).



Figure 3 - Temperature distribution on the tongue with tumors of various sizes: 1) 1.0 mm radius 2) 1.5 mm radius 3) 2.0 mm radius Source: Own author

Temperature profile was not modified in the region where the tumor is inserted in any of the cases. Thus, there were not changes in the surface profile with the presence of a tumor up to 2.0 mm of diameter. The temperature at the center of the tumor was close to the temperatures used in the boundary conditions, 35.4 °C (air inside the mouth) and 36.6 °C (sublingual region).

In order to estimate how the temperature patterns would change if the tumor generated a much larger amount of heat, simulations were made with the heat generation rate of the tumor artificially increased by 100 times. With this increase, it is possible to detect the temperature variation in the tumor region (Figure 4), where (a) represent the surface of the tongue and (b) a cut at the center of the tumor.



Figure 4 - Temperature of the tongue with increase by 100 times in the heat generation rate of the tumor. 1) Tumor of 1.0 mm radius; 2) tumor of 1.5 mm radius; 3) tumor of 2.0 mm radius Source: Own author

The temperatures at the center of the tumor are presented in Table 3:

Table 2 - Temperature at the center of the tumor with the increase of Q_m by 100 times				
Radius of the tumor (mm)	Tumor temperature (°C)	Tumor temperature with		
		increased heat generation rate		
		by 100 times (°C)		
1.0	34.95	36.32		
1.5	35.10	37.69		
2.0	35.23	39.28		

It can be observed that the increase in the heat generation rate of the tumor does not meet the real patterns as expected. A tumor able of generating such heat would be easily noticed by the patients due to their very high temperatures present by the tissue. However, such increase demonstrated that a much higher heat generation rate would be necessary to allow the detections of a tumor by thermographic images. This higher heat generation would produce a greater difference between the temperatures of the boundary conditions and the tumor, making the temperature pronounced and facilitating the detection.

3 CONCLUSIONS

With the considerations adopted in this computational model, it was not possible to detect a tumor of up to 2.0 mm in radius, located in the tongue through a thermal analysis of its surface. This could happen because the analyzed organ is located inside the body, the temperatures of the tissue and surrounding regions are close to tumor temperatures. It can justify non-significant modification in the temperature profile.

An early diagnosis of a tumor using thermography as a screening tool would only be possible if the tumor heat generation rate was considerably higher, as it has been demonstrated in this work. Nevertheless, more studies will be needed to advance in this topic, in other conditions not studied here, variable boundary conditions, real geometries and also for different tumor locations.

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