A boundary element model for investigating the effects of eye tumor on the temperature distribution inside the human eye

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Abstract

A three-dimensional boundary element model of the human eye is developed to investigate the thermal effects of eye tumor on the ocular temperature distribution. The human eye is modeled as comprising several regions which have different thermal properties. The tumor is one of these regions. The thermal effects of the tumor are simulated by taking it to have a very high metabolic heat generation and blood perfusion rate. Inside the tumor, the steady state temperature is governed by the Pennes bioheat equation. Elsewhere, in normal tissues of the eye, the temperature satisfies the Laplace’s equation. To compute the temperature on the corneal surface, the surface boundary of each region is divided into triangular elements.

1. Introduction

The presence of a tumor inside biological bodies is known to cause an increase in the temperature of the surrounding healthy tissues. Such phenomena have been observed in the human breast and skin. In both cases, abnormal thermal behavior (formation of a hot spot) at the vicinity of the tumor was detected using an infrared camera. The warming effect of tumor is mainly attributed to its metabolically active physiology which generates a larger amount of metabolic heat when compared with healthy tissues. Making use of such thermal behavior, medical researchers were able to use infrared (IR) thermography to detect tumor growth inside the human breast by comparing the thermograms of normal and infected breasts [1,2]. In the field of ophthalmology, the effects of tumor on the ocular temperature distribution appear to be rarely investigated. In the work carried out by Wittig et al. [3] and Bourjat and Gautherie [4], infrared thermometry was used to measure the temperature on the corneal surface. Increases in the corneal surface temperature were found in eyes that had choroidal melanoma or unilateral exophthalmos.

Various mathematical models that relate to the thermal physiology of the human eye have been developed and reported in the literature. This may be attributed to the fact that there is a wide range of bioengineering problems involving the human eye to be investigated. Some of these problems include the investigation of temperature rise inside the human eye during exposure to laser and electromagnetic (EM) wave radiation [5–7], hyperthermic treatment of the human eye [8] and the temperature changes experienced by the human eye during corneal refractive surgery [9,10]. In the investigations carried out by Emery et al. [7] on the effects of EM wave radiation, the temperatures inside the rabbit eye, predicted using the finite element method, were found to agree well with the invasive measurements carried out on actual rabbits. Errors that were less than 1% were found by Lagendijk [8] when comparing the numerically obtained temperatures in rabbit eyes during hyperthermia with temperatures measured on actual rabbits. The good agreement between the results obtained from numerical and experimental studies highlights the versatility of mathematical models in investigating the heat transfer phenomena inside the eye under various circumstances.

Despite the growing number of mathematical models investigating temperature distribution inside the human eye, to the best of our knowledge, there has yet to be any mathematical studies that simulate the effects of eye tumor on the human eye temperature. Nevertheless, investigations have been carried out for tumors that grow in other parts of the human body such as the human breast and skin. A finite element model was developed by Ng et al. [11–13] to simulate the changes in temperature caused by the growth of tumor inside the human breast. Similar studies were carried out by Hu et al. [14] using the finite volume method. Human skin models were developed by Deng and Liu [15,16] using various numerical approaches such as the dual reciprocity boundary element method and the Monte Carlo method. In the models of the human breast and skin, the tumor was modeled as a homogeneous region that has distinguishable thermal properties characterized by the larger metabolic heat and blood perfusion rate when compared with healthy surrounding tissues. With this assumption, the temperature distribution of cancerous tissues were found to be approximately 0.5–2 °C higher than healthy tissues.
In the present study, numerical simulations are carried out to investigate changes in the ocular temperature distribution that are caused by growth of a tumor inside the eye. The thermal effects of the tumor are simulated based on the approach that has been used in human breast and skin models, that is, the tumor has higher metabolic heat and blood perfusion rate than normal tissues inside the eye. Simulations are carried out using a three-dimensional model of the human eye. The governing equations and the boundary conditions are solved numerically using the boundary element method. One of the reasons the boundary element method is preferred over other more established numerical tools, such as the finite element method, is its unique feature which requires only the boundaries of the solution domain to be divided into discrete zones. This is particularly advantageous when modeling complex geometries such as the eye since data preparation is much simpler.

This study seeks to provide an insight on the effects of eye tumor on the temperature distribution inside the eye, particularly the corneal surface, which may be of some practical interest. The present study also helps to expand the bibliography on eye models that are solved using the boundary element method which has been shown in previous studies to be highly efficient and reliable [9,10,17].

### 2. Eye tumor classification

Various types of tumor such as melanoma (iris, ciliary body and choroid), retinoblastoma and metastatic intraocular tumors (from another part of the body) may grow inside the human eye. In this paper, we will focus only on choroidal melanoma. Choroidal melanoma grows on the highly vascularized choroid where a large blood flow makes it ideal for tumor cells to grow and metastasize. When tumor grows on the choroid, it roughly takes the shape of a dome or a mushroom [18,19]. Dome-shaped choroidal melanomas are usually associated with early stages of tumor growth while the mushroom-shaped melanomas often take shape during later stages [20].

According to the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC), choroidal melanoma can be classified according to its size (T), degree of lymph nodes (N) and the presence of metastasis (M) for a TNM classification. In 2006, the sixth edition of the TNM classifications (TNM6) was published by AJCC and UICC. According to TNM6, four categories of choroidal melanoma can be distinguished based on the T category, namely category T1, T2, T3 and T4. These categories generally describe the largest basal diameter (LBD) and the thickness (t) of the tumor. Thickness here refers to the apical height of the tumor, that is, the distance from the base to the tip of the tumor. Table 1 summarizes the range of LBD and t for choroidal melanoma of category T1, T2, T3 and T4 [21]. Throughout this paper, unless otherwise stated, the phrase ‘eye tumor’ is used to refer to choroidal melanoma.

### 3. Mathematical model

#### 3.1. The human eye model

In this paper, the human eye is modeled as an organ that is isolated from the human head. With reference to a Cartesian coordinate system denoted by $Oxyz$, Fig. 1 shows one half of the cross section of the human eye as viewed in the $xy$ plane.

The dimensions of the regions used follow closely those given in Ooi et al. [17]. Internal eye structures such as the aqueous humor, lens and vitreous are modeled based on anatomical measurements published in the literature [22,23]. The retina and the choroid, which are relatively thin compared to the sclera [17], and the iris, which has similar thermal properties as the sclera [24], are modeled together with the sclera as one homogeneous region. The optic nerve is omitted from our model as it does not play a significant role in the overall temperature distribution inside the human eye [17].

To obtain a three-dimensional model, the geometry shown in Fig. 1 is rotated by an angle of 360° about the $x$ (pupillary) axis. The resulting three-dimensional model with a view of its interior structure is shown in Fig. 2. It consists of five major components, namely the cornea, sclera, aqueous humor, lens and the vitreous which we, respectively, denote as $R_1$, $R_2$, $R_3$, $R_4$ and $R_5$. Each region is assumed to be homogeneous and thermally isotropic. The exterior surfaces of the cornea and sclera, which define the shape of the human eye, are given by $C_1$ and $C_2$, respectively.

![Fig. 1. One half of the cross section of the human eye in the $xy$ plane.](image)

![Fig. 2. Three-dimensional model of the left human eye with a view of the interior structure.](image)

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>LBD (mm)</th>
<th>t (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>$\leq 10$</td>
<td>$\leq 2.5$</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>$\leq 15$</td>
<td>$\leq 5.0$</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>$&gt; 15$</td>
<td>$&gt; 5.0$</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>Tumor extends beyond the eyeball</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$LBD$: largest basal diameter, $t$: thickness.
3.2. The tumor model

The region occupied by the tumor is constructed using the approach suggested by Yoriyaz et al. [25]. First, a sphere of a particular diameter with its center placed on a specific point on the interface between the vitreous and sclera is generated. Second, the region that is cut by the interfaces between the sclera and the vitreous is taken as the region occupied by the tumor which we denote as the sixth region, R₆. This is shown in Fig. 2.

In this study, we categorize the eye tumor based on the diameter of the sphere that is used to generate it. For instance, if a tumor is generated from a sphere of diameter 13 mm, it is then categorized as an eye tumor of category T2 (see Table 1).

3.3. Governing equations and boundary conditions

As in Ooi et al. [17], the equation governing the steady flow of heat inside the region of the healthy (normal) eye, as denoted by R₁, R₂, R₃, R₄ and R₅, is given by

\[ \nabla \cdot (\kappa_i \nabla T_i(x, y, z)) = 0 \quad \text{for} \quad i = 1, 2, 3, 4 \text{ and } 5, \]  

(1)

where \( \kappa_i \) and \( T_i \) denotes the thermal conductivity (W m⁻¹ K⁻¹) and temperature (K) of region \( R_i \), respectively.

To account for the metabolic heat generation and the blood perfusion rate inside the eye tumor, the heat flow in region \( R_6 \) is taken to be given by the Pennes bioheat equation [26], that is,

\[ \nabla \cdot (\kappa_i \nabla T_i(x, y, z)) + Q_m + \rho_b c_b \omega_b (T_b - T_i(x, y, z)) = 0 \]

for \( i = 6, \)  

(2)

where \( \rho_b, c_b \) and \( T_b \) are the density (kg m⁻³), specific heat (J kg⁻¹ K⁻¹) and temperature (K) of blood, respectively, \( \omega_b \) is the blood perfusion rate (m³ s⁻¹ m⁻³) inside the eye tumor and \( Q_m \) denotes the volumetric heat (W m⁻³) generated from the metabolic activity of the eye tumor.

Boundary conditions are specified on the surfaces of the cornea, \( C_1 \) and sclera, \( C_2 \), respectively. The corneal surface \( C_1 \) is exposed to the environment which is usually lower than the human body temperature. Heat therefore, transfers from the corneal surface to the environment via convection and radiation. Evaporation of tears from the corneal surface helps to cool down the cornea. Mathematically, we may write

\[ -\kappa_i \frac{\partial T_i}{\partial n} = h_{amb}(T_i - T_{amb}) + \varepsilon\sigma(T_i^4 - T_{amb}^4) + \frac{E_{vap}}{\partial n} \]  

on \( C_1, \)  

(3)

where the first, second and third terms on the right-hand side correspond to heat losses due to convection, radiation and tears evaporation, respectively, \( h_{amb} \) is the ambient convection coefficient (W m⁻² K⁻¹), \( T_{amb} \) is ambient temperature (K), \( \varepsilon \) is the emissivity on the corneal surface, \( \sigma \) is the Stefan–Boltzmann constant (W m⁻² K⁻⁴), \( E_{vap} \) is heat loss due to tears evaporation (W m⁻²) and \( \partial T_i/\partial n \) is the rate of change of \( T_i \) along the outward normal vector to the external corneal surface \( C_1 \) (K m⁻¹).

Heat from the ocular blood flow enters the eye on the surface of the sclera \( C_2 \). Since the human eye is modeled as an organ that is isolated from the human head, the effects of blood flow on the human eye can be simulated by assuming the eye to be embedded in an anatomically homogeneous surrounding which is at constant body core temperature [8]. The heat exchange between the surrounding and the eye is then modeled using a single heat transfer coefficient given by

\[ -\kappa_i \frac{\partial T_i}{\partial n} = h_b(T_b - T_i) \quad \text{on} \quad C_2, \]  

(4)

where \( h_b \) is the heat transfer coefficient (W m⁻² K⁻¹) between the artificial surrounding and the human eye and \( \partial T_i/\partial n \) is the rate of change of \( T_i \) along the outward unit vector normal to the external surface \( C_2 \) (K m⁻¹). Values of the parameters used in (3) and (4) are similar to those in Ooi et al. [17] and are summarized in Table 2.

At the interface between two contiguous regions, the continuity conditions apply, that is,

\[ T_i = T_j, \]

\[ k_i \frac{\partial T_i}{\partial n} = k_j \frac{\partial T_j}{\partial n} \]  

on \( I_{ij}, \)  

(5)

where \( T_i \) and \( T_j \) are the temperature of regions \( R_i \) and \( R_j \), respectively, \( I_{ij} \) denotes the interface between regions \( R_i \) and \( R_j \) and \[ \partial T_i/\partial n \] and \[ \partial T_j/\partial n \] is the rate of change of \( T_i \) and \( T_j \), respectively, along a unit vector normal to \( I_{ij}. \)

4. Tissue properties

The thermal properties of each component of the human eye shown in Fig. 2 are easily obtained from the literature and are listed in Table 2. This is not the case for the eye tumor however. A search of the literature resulted in no relevant information regarding the thermal properties of the eye tumor. On the other hand, thermal properties of various other types of tumor have been measured and reported. To account for the unknown thermal properties of the eye tumor, simulations in the present study are carried out by varying the unknown thermal conductivity, blood perfusion rate and metabolic heat generation over a range of values which are derived from experimental data obtained from different types of tumor.

From the measurements compiled by Jain [31], the thermal conductivity of tumors that grow in various parts of the human body was found to be in the range of 0.35 to 0.67 W m⁻¹ K⁻¹. The types of tumor that were measured included tumors of the breast, colon, liver, lungs and pancreas. No significant differences were observed between normal and metastatic tumors.

Values of blood perfusion rate of tumors that were measured by various researchers using different techniques were compiled by Fieldman et al. [32]. Based on the data measured on breast tumors, lymphomas, anaplastic carcinoma and differentiated tumors, the blood perfusion rate of tumor was found to lie between 0.0014 and 0.0072 m³ s⁻¹ m⁻³.

Unlike the thermal conductivity and blood perfusion rate, the metabolic heat generation remains an elusive term in the bioheat equation and quantified experimental results are limited [31]. One of the more established studies that measured the metabolic heat

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermal conductivity (W m⁻¹ K⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cornea, ( R_1 )</td>
<td>0.58</td>
<td>[7]</td>
</tr>
<tr>
<td>Sclera, ( R_2 )</td>
<td>1.00</td>
<td>[24]</td>
</tr>
<tr>
<td>Aqueous humor, ( R_3 )</td>
<td>0.58</td>
<td>[7]</td>
</tr>
<tr>
<td>Lens, ( R_4 )</td>
<td>0.40</td>
<td>[8]</td>
</tr>
<tr>
<td>Vitreous, ( R_5 )</td>
<td>0.60</td>
<td>[8]</td>
</tr>
<tr>
<td>Tumor, ( R_6 )</td>
<td>0.35–0.67</td>
<td>–</td>
</tr>
<tr>
<td>Ambient convection coefficient (W m⁻² K⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>[27]</td>
</tr>
<tr>
<td>Blood convection coefficient (W m⁻² K⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>65</td>
<td>[8]</td>
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<tr>
<td>Ambient temperature (K)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>298</td>
<td>[27]</td>
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<tr>
<td>Blood temperature (K)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>310</td>
<td>[27]</td>
</tr>
<tr>
<td>Tears evaporation rate (W m⁻²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>[28]</td>
</tr>
<tr>
<td>Corneal surface emissivity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.975</td>
<td>[29]</td>
</tr>
<tr>
<td>Stefan–Boltzmann constant (W m⁻² K⁻⁴)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.67 \times 10⁻⁸</td>
<td>[30]</td>
</tr>
<tr>
<td>Tumor blood perfusion rate (m³ s⁻¹ m⁻³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0014–0.0072</td>
<td>–</td>
</tr>
<tr>
<td>Tumor metabolic heat generation (W m⁻³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>15,000–80,000</td>
<td>–</td>
</tr>
</tbody>
</table>

See Section 4.
generation of tumors, is perhaps the work carried out by Gautherie [33] on breast tumors. According to Gautherie [33], the value of tumor metabolic heat generation remains constant during the phase of exponential growth. Based on experimental measurements conducted on 84 patients, the volumetric metabolic heat generated by the tumor was found to be related to the tumor doubling time by the expression [33]

\[ Q_m = \frac{P}{\tau}, \]  

(6)

where \( P \) is a constant with a value of \( 3.27 \times 10^6 \) (W day m\(^{-3}\)) and \( \tau \) is the tumor doubling time (day).

Let us assume that (6) is valid for all types of tumor. Since the doubling time is a unique property of the tumor, the only variable in (6) that may change to account for different types of tumor is the constant \( P \). Instead of using the range of metabolic heat generation of breast tumor, it may be more appropriate to allow the value of \( P \) to vary within a certain range. In this study, we assume \( P \) to have a range of \( 1 \times 10^6 \) to \( 5 \times 10^6 \) W day m\(^{-3}\). For a mean eye tumor doubling time of 63 days [34], the corresponding range of metabolic heat as found using (6) is given approximately by 15,000–80,000 W m\(^{-3}\).

We may now assume the eye tumor thermal conductivity, blood perfusion rate and metabolic heat generation to have values that lie between the range of values that were obtained for different types of tumors as discussed before. These are summarized in Table 2. Since the range of values were found for different types of tumors that grow on various parts of the human body, this assumption is likely to remain valid as we do not expect the thermal properties of tumors in general, to be significantly different from one another.

5. The boundary element model

The solution of (1) and (2) subjected to (3), (4) and (5) are obtained using the boundary element method. To do so, the integro-differential formulation of (1) and (2) are derived and they are, respectively, given by [see, for example, Ang [35]]

\[ \gamma(\xi_i, \eta_i, \zeta_i)T(\xi_i, \eta_i, \zeta_i) = \int \int_{\Gamma_i} T_i(x,y,z) \cdot \frac{\partial}{\partial n} \{ \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) \} dA(x,y,z) \]

\[ - \int \int \int_{\Omega} \frac{\partial}{\partial n} \{ \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) \} dA(x,y,z) 
\]

\[ \text{for } (\xi_i, \eta_i, \zeta_i) \in R_i \cup \Gamma_i \] 

and

\[ \gamma(\xi_i, \eta_i, \zeta_i)T(\xi_i, \eta_i, \zeta_i) 
\]

\[ = \int \int_{\Gamma_i} T_i(x,y,z) \cdot \frac{\partial}{\partial n} \{ \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) \} dA(x,y,z) \]

\[ - \int \int \int_{\Omega} \frac{\partial}{\partial n} \{ \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) \} dA(x,y,z) 
\]

\[ - \int \int \int_{\Omega} \frac{\partial}{\partial n} \{ \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) \} dA(x,y,z) 
\]

\[ \times \frac{Q_m + \rho u c \omega T_\text{bd} - T_i(x,y,z)}{R_i} dV(x,y,z), \]

\[ \text{for } (\xi_i, \eta_i, \zeta_i) \in R_i \cup \Gamma_i \text{ and for } i = 6, \] 

(8)

where \( \Gamma_i \) denotes the boundary of the region \( R_i \), \( dA(x,y,z) \) denotes the area of an infinitesimal part of surface \( \Gamma_i \), \( dV(x,y,z) \) denotes the volume of an infinitesimal portion of the region \( R_i \), \( \gamma(\xi_i, \eta_i, \zeta_i) = 1 \) if \((\xi_i, \eta_i, \zeta_i) \) lies in the interior of \( R_i \), \( \gamma(\xi_i, \eta_i, \zeta_i) = \frac{1}{2} \) if \((\xi_i, \eta_i, \zeta_i) \) lies on a smooth part of \( \Gamma_i \) and \( \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) \) and \( \partial \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) \;/\partial n \) are the fundamental solution of the three-dimensional Laplace equation and its normal derivative, respectively, which are given by

\[ \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) = -\frac{1}{4\pi} \left[ (x-\xi)^2 + (y-\eta)^2 + (z-\zeta)^2 \right]^{-1/2} \]

and

\[ \frac{\partial}{\partial n} \{ \Phi(x,y,z; \xi_i, \eta_i, \zeta_i) \} = \frac{1}{4\pi} \left[ n_x(x-\xi) + n_y(y-\eta) + n_z(z-\zeta) \right] \]

\[ \left[ [(x-\xi)^2 + (y-\eta)^2 + (z-\zeta)^2]^{1/2} \right], \] 

(9)

where \( n_x, n_y \) and \( n_z \) are the components of the outward unit normal vector on \( \Gamma_i \) in the direction of \( x, y \) and \( z \), respectively.

The boundary element method is implemented by dividing the boundary \( \Gamma_i \) into small triangular elements. The domain integral appearing in (8) is converted into an equivalent boundary integral using the dual reciprocity method [36]. For a detailed derivation, one may refer to Appendix A.

6. Results

6.1. Modeling assumptions

In the present study, three categories of eye tumor are investigated, namely categories T1, T2 and T3. Category T4 is not considered since the tumor has grown beyond the domain defined by our eye model. Based on Table 1, for tumors of categories T1 and T2, values of 10 and 15 mm, respectively, are selected as the diameter of the sphere that is used to generate the tumor model (see Section 3.2). A value of 17 mm is assumed for category T3 since the largest value of LBD is not explicitly defined. The tumor is assumed to grow at the top (positive y region) of the human eye such as shown in Fig. 2. Specifically, the center of the sphere used in generating the tumor is placed at coordinates (0.013, 0.0105, 0).

In carrying out the boundary element method outlined in Appendix A, we divided the boundaries of the human eye model into small triangular elements. A total of 2212, 2362 and 2306 boundary elements are generated in the models with eye tumor of categories T1, T2 and T3, respectively, while 100 interior points are selected for each category of tumor for the implementation of the dual reciprocity method (see Appendix A for more details). Discretization is carried out using the built-in mesh generator available in the finite element package, COMSOL Multiphysics [37].

6.2. Temperature increase inside the human eye

To investigate the temperature changes inside the human eye, observations are made along the pupillary axis. Simulations are carried out by varying the tumor thermal conductivity, blood perfusion rate, and metabolic heat generation over five different values which are within the range given in Table 2. The five values considered for the thermal conductivity are 0.3, 0.4, 0.5, 0.6 and 0.7 W m\(^{-1}\) K\(^{-1}\) while the values of the blood perfusion rate are given by 0.002, 0.004, 0.006, 0.008 and 0.01 m\(^3\) s\(^{-1}\) m\(^{-3}\). The metabolic heat generation of the eye tumor is assumed to have values of 15,000, 30,000, 45,000, 60,000 and 75,000 W m\(^{-3}\). When carrying out simulations for a specific thermal property, the values of the other two remain as constants with values given by 0.50 W m\(^{-1}\) K\(^{-1}\), 0.006 m\(^3\) s\(^{-1}\) m\(^{-3}\) and 45,000 W m\(^{-3}\).

Results are given in Figs. 3–5 for the eyes with tumors of categories T1, T2 and T3, respectively.
6.3. Temperature increase on the corneal surface

To investigate the temperature changes on the corneal surface, five points, namely the central, superior, inferior, nasal and temporal which we denote as A, B, C, D and E, respectively, are selected on the corneal surface as illustrated in Fig. 2. Coordinates of each of these points are given by (0, 0, 0), (0.0025, 0.0064, 0), (0.0025, −0.0064, 0), (0.0025, 0, −0.0064) and (0.0025, 0, 0.0064). Increases in temperature at these points are shown in Table 3. Results are obtained for values of eye tumor thermal conductivity, blood perfusion rate, and metabolic heat generation of 0.50 W m\(^{-1}\) K\(^{-1}\), 0.006 m\(^3\) s\(^{-1}\) m\(^{-3}\) and 45,000 W m\(^{-3}\), respectively.

6.4. An extreme case

So far, the thermal properties of the eye tumor have been varied within a certain range when investigating the changes in temperature inside the eye and set at fixed values when investigating the changes on the corneal surface temperature. It may be of interest to assess the largest change that may be caused by the growth of tumor inside the eye. Based on the results obtained from the previous section, it is found that a larger increase in temperature is produced when the values of tumor thermal conductivity and metabolic heat generation is the largest and when the value of the tumor blood perfusion rate is the smallest.

Hence, in this section, we carry out simulations for values of eye tumor thermal conductivity, blood perfusion rate and metabolic heat generation of 0.70 W m\(^{-1}\) K\(^{-1}\), 0.002 m\(^3\) s\(^{-1}\) m\(^{-3}\) and 75,000 W m\(^{-3}\), respectively. Values of other non-tumor parameters are maintained as in Table 2. Changes in the temperature along the pupillary axis and the corneal surface for the extreme case are shown in Fig. 6 and Table 4.

7. Discussion

To validate the numerical solutions obtained using the boundary element method, the partial differential equation calculator, COMSOL Multiphysics [37], which utilizes the finite element method, is also used to solve the equations of the model. All three categories of tumor are simulated for values of tumor thermal conductivity, blood perfusion rate, and metabolic heat generation of 0.50 W m\(^{-1}\) K\(^{-1}\), 0.006 m\(^3\) s\(^{-1}\) m\(^{-3}\) and 45,000 W m\(^{-3}\), respectively.
Fig. 4. Temperature increases along the pupillary axis for category T2 tumor for various values of tumor: (a) thermal conductivity, (b) blood perfusion rate and (c) metabolic heat generation.

In Fig. 7 the temperature increase along the pupillary axis as computed using the boundary element method is compared with that calculated by the finite element method. Overall, the results obtained using the boundary element method agree well with those from the finite element method. Differences between the two sets of results become slightly more apparent as the size of the tumor increases from categories T1 to T3. As the size of the tumor increases, warming effects from the tumor increase, such as shown in the numerical results presented in Section 6. To model accurately the increased thermal effects of a larger-sized tumor, calculations in both numerical methods may have to be refined.

One of the advantages of the boundary element method is highlighted by the number of boundary elements used, which is given approximately by 2000. In the finite element model developed using COMSOL Multiphysics, the number of domain elements used lies in the range of 16,000–20,000, which is almost 10 times the number of elements used in the boundary element method. Consequently, the system of linear algebraic equations generated using the boundary element method is much smaller than the one generated using the finite element method. The computational memory required to obtain a numerical solution using the boundary element method is thus, less demanding than the finite element method. Nevertheless, it has to be pointed out that although the size of the matrix generated using the boundary element method is smaller than the finite element method, it is not as sparse. As a result, the computational demand of the boundary element method may increase when the number of boundary elements used is large.

Another advantage of the boundary element method over other numerical methods lies in formulation of the numerical approach. In the boundary element method, the integral equations that form the foundation for a numerical scheme to be developed satisfy the governing equations. In other words, no approximations have been made when deriving the integral representations of the governing equations. This is unlike the finite difference method, where approximations of the spatial derivatives of the governing equation may introduce errors to the numerical results obtained. For more details on the advantages and disadvantages of the boundary element method when compared with other numerical methods, one may refer to Gaul et al. [39].

In the present study, discontinuous linear elements have been used to approximate the variations of temperature and heat flux across each boundary element. To increase the accuracy of the
numerical solution, one may substitute the linear elements used in this study with higher order elements such as quadratic and cubic approximations. Formulation of the problem may be more complicated using higher order elements, however.

To account for the unknown thermal properties of the eye tumor, simulations have been performed for a range of values for the thermal conductivity, blood perfusion rate and metabolic heat generation which are based on the data obtained from experimental measurements. Despite the possible differences in the cellular structure between each type of tumor, we do not expect the actual thermal properties of the eye tumor to be significantly different from the range used in this study since the data which the current study used have been found for different types of tumor that may grow in the human body.

The shape of the curves observed in Figs. 3–5 imply that the temperature rise is much larger at the vicinity of the tumor region. Similar thermal characteristics have also been observed in models of the human breast and skin [11–16]. Based on the plots in Figs. 3–5, the magnitude of temperature rise along the pupillary axis is found to increase with the values of tumor thermal conductivity and metabolic heat generation while the opposite is observed for the blood perfusion rate. This may be explained by the role of tumor blood perfusion as appeared in the bioheat equation (2). In (2), the last term on the left-hand side which corresponds to the heat transfer due to blood perfusion serves as a medium for transferring away excessive heat from the human eye. Therefore, a stronger blood flow will lead to more heat thus reducing the temperature inside the human eye.

In the eye with a category T1 tumor (Fig. 3), variations in the tumor thermal conductivity and blood perfusion rate appear to have
minimal effects on the temperature distribution inside the human eye compared to the metabolic heat generation. The largest increase in temperature is found to be 0.16 °C which occurs when the tumor metabolic heat is the highest (75,000 W m⁻³). Similar plots are observed in the eyes with tumors of categories T2 and T3 (Figs. 4 and 5). However, in these cases, the effects of tumor blood perfusion are much stronger compared to the case of a category T1 tumor. This implies that the size of the tumor plays a major role in governing the temperature distribution inside the human eye. The largest increase for category T2 and T3 tumor is found to be approximately 0.5 and 0.7 °C, respectively.

Comparing the increases in temperature at the five different points on the corneal surface, it is found that the point at the superior location experiences the largest increase in temperature and this is true for all categories of tumor that are being investigated. This may be credited to the location of the superior point which is closest to the tumor, thus causing the warming effects to be much greater here compared to the other four points on the corneal surface. At the inferior, which is the point furthest from the tumor, the increase in temperature is found to be the smallest which further supports the argument given above. As expected, a larger tumor is found to produce larger increases in the corneal surface temperature.

Under the column of normal eye in Table 3, the temperatures at the superior, inferior, nasal and temporal points, that is, the temperature at the periphery of the cornea appear to be roughly the same while the temperature at the center is approximately 0.2 °C lower; implying a symmetrical thermal profile on the corneal surface. For each category of eye tumor investigated, the temperature at the superior is found to be approximately 50% and 60% higher than the central and the inferior, respectively, which is an indication of thermal asymmetry on the thermal pattern on the corneal surface.

At present, IR thermography is the preferred choice in ocular surface temperature measurement. The latest innovation in IR technology allows IR cameras to have thermal sensitivity of up to 0.06 °C. The results given in Table 3 suggest that increases in the corneal surface temperature due to the presence of categories T2 and T3 eye tumor may be effectively captured using IR thermography. Nevertheless, a great deal of this would depend on the actual values of the thermal properties of tumor. For instance, in the extreme case (see Table 4), we found that the increases in the corneal surface temperature due to category T1 eye tumor is at an average of approximately 0.1 °C which is detectable using a highly sensitive IR camera.

The current numerical study has not been accompanied by any experimental work. Hence, the numerical predictions can only be compared qualitatively with experimental studies carried out by other researchers. From our numerical results, the presence of tumor inside the eye is found to cause an increase in temperature and a asymmetrical thermal profile on the corneal surface. Similar results have been reported by Wittig et al. [3] and Bourjat and Gautherie [4] using IR thermography; implying good qualitative agreement between the numerical predictions and the experimental observations. Changes in the intraocular temperatures remain unverified since no relevant data in literature that provide invasive temperature readings regarding eye tumor can be found.

It is worth pointing out that the corneal surface temperature is sensitive to factors such as the environmental condition (ambient temperature) and variations between individuals (age and tears evaporation rate). According to the numerical predictions made by Scott [28] and Ng and Ooi [27], these factors are able to produce changes in the corneal surface temperature that are of the same order of magnitude as those caused by the tumor. Therefore, if the effects of tumor on the corneal surface are to be effectively measured, it is important to ensure that the changes in the corneal surface temperature recorded using an IR camera are solely caused by the tumor and are free from the effects of other factors which may be classified as ‘noise’. Statistical analysis may be carried out in future...
studies to better explain the precedence and the importance of the various factors that may affect the corneal surface temperature.

In the present study, the model of the eye tumor has been assumed to be homogeneous. In reality, the tumor may generally be divided into two zones: a necrotic zone at the center and a regionally vascularized zone at the periphery [40]. As a result, the thermal properties of the eye tumor, particularly the blood perfusion rate and the metabolic heat generation, may not be constant throughout the tumor. Instead, the vascularized periphery is expected to have larger blood perfusion rate and metabolic heat generation compared to the necrotic center. Although it is not known whether such heterogeneity may cause any differences to the simulated results, the present model may be re-worked in the future to deal with these issues provided that sufficient information is available for it to be carried out.

Numerical simulations carried out in the present study have been confined to a single location of tumor growth which is at the positive y region. In reality, the eye tumor may grow anywhere along the layer of choroid. For cases where the tumor grows at locations other than the one studied here, the same model can still be used by making changes to the model of the tumor to accommodate the desired location. The versatility of the current model is due to the three-dimensional geometry which resembles closely the actual shape of the human eye. The present study has also been confined to choroidal melanoma. Although similar results are expected for different eye tumours, such as iris and ciliary body melanoma, the same modeling approach can still be used. This, along with the different locations of eye tumor may be considered as potential studies to be carried out in the future.

8. Conclusion

A model of the human eye has been successfully developed to investigate the effects of an eye tumor on the ocular temperature distribution. Unlike our earlier works where the human eye was modeled in the two-dimensional and axisymmetrical coordinate system [5,17], the model in the present study is fully three-dimensional. The tumor is modeled to be a homogeneous region that has larger metabolic heat generation and blood perfusion rate when compared with the surrounding healthy ocular tissues. The governing equations and the boundary conditions have been solved numerically using the boundary element method.

The numerical results obtained demonstrated that the thermal effects of eye tumor on the eye can be accurately simulated using mathematical models. Thus far, such investigations have been limited to only the human breast and skin. The presence of tumor is found to cause an increase in temperature inside the eye. On the corneal surface, both an increase in temperature and a slight thermal asymmetry are found. These thermal abnormalities have been suggested to be potential indicators that may be used for eye tumor detection using appropriate IR thermography. Nevertheless, this remains a speculation and further developments have to be carried out in future to investigate the feasibility of such an approach.

Conflict of interest statement

None declared.

Appendix A.

The steps involved in the implementation of the boundary element method are outlined here. For convenience, the integral representations of the governing equations, described in (7) and (8), are reproduced here as

\[ \gamma(\zeta_i, \eta_i, \zeta_t) \int_{\Gamma_t} \left( \begin{array}{c} \Omega_m \left( \mathbf{x}_t, \mathbf{r} ; \mathbf{r}_t \right) \\ \mathbf{r}_t \end{array} \right) \cdot dS = \int_{\Gamma_t} \left( \begin{array}{c} \Omega_m \left( \mathbf{x}_t, \mathbf{r} ; \mathbf{r}_t \right) \\ \mathbf{r}_t \end{array} \right) \cdot dS \]

for (\zeta_i, \eta_i, \zeta_t) \in \Gamma_t \cup \Gamma_i \text{ and for } i = 1, 2, 3, 4 \text{ and } 5 \quad (A.1)

and

\[ \gamma(\zeta_i, \eta_i, \zeta_t) \int_{\Gamma_t} \left( \begin{array}{c} \Omega_m \left( \mathbf{x}_t, \mathbf{r} ; \mathbf{r}_t \right) \\ \mathbf{r}_t \end{array} \right) \cdot dS = \int_{\Gamma_t} \left( \begin{array}{c} \Omega_m \left( \mathbf{x}_t, \mathbf{r} ; \mathbf{r}_t \right) \\ \mathbf{r}_t \end{array} \right) \cdot dS \]

for (\zeta_i, \eta_i, \zeta_t) \in \Gamma_t \cup \Gamma_i \text{ and for } i = 6 \quad (A.2)

respectively.

For a numerical method based on (A.1) and (A.2), the surfaces of each region of the human eye are divided into \( N_t \) triangular elements which we denote as \( \Gamma_t^{(k)} \) for \( k = 1, 2, \ldots, N_t - 1, N_t \) such that \( \Gamma_t = \Gamma_t^{(1)} \cup \Gamma_t^{(2)} \cup \cdots \cup \Gamma_t^{(N_t - 1)} \cup \Gamma_t^{(N_t)} \). Across each element, the temperature and heat flux is assumed to vary linearly. This is accomplished by selecting three points located inside each triangular element. Details on the selection of these collocation points are covered extensively by Silva [41] and are thus, not repeated here. If \( (\zeta_i^{(k)}, \eta_i^{(k)}, \zeta_t^{(k)}) \) and \( (\zeta_i^{(k+2N_t)}, \eta_i^{(k+2N_t)}, \zeta_t^{(k+2N_t)}) \) denote the three chosen points on the element \( \Gamma_t^{(k)} \), then

\[ T(x,y,z) \approx \frac{3}{2} \sum_{k=1}^{N_t} \phi_k \int_\Gamma^{(k+1)} dV \]

\[ \text{for (x,y,z) } \in \Gamma_t^{(k)} \quad (A.3) \]

where \( \phi_k \) are linear interpolation functions and \( T_t^{(k)} \) and \( q_t^{(k)} \) are the temperature and heat flux at node \( (\zeta_i^{(k)}, \eta_i^{(k)}, \zeta_t^{(k)}) \), respectively. One may refer to Brebbia et al. [42] for more information on the linear interpolation functions \( \phi_k \).

Substituting (A.3) into (A.1) and (A.2) leads to

\[ \gamma(\zeta_i, \eta_i, \zeta_t) \int_{\Gamma_t} \left( \begin{array}{c} \Omega_m \left( \mathbf{x}_t, \mathbf{r} ; \mathbf{r}_t \right) \\ \mathbf{r}_t \end{array} \right) \cdot dS = \sum_{k=1}^{N_t} \sum_{i=1}^{3} \phi_i^{(k)}(\zeta_i, \eta_i, \zeta_t) \int_\Gamma^{(k+1)} dV \]

\[ - \sum_{k=1}^{N_t} \sum_{i=1}^{3} \phi_i^{(k)}(\zeta_i, \eta_i, \zeta_t) \int_\Gamma^{(k+1)} dV \]

for (\zeta_i, \eta_i, \zeta_t) \in \Gamma_t \cup \Gamma_i \text{ and for } i = 1, 2, 3, 4 \text{ and } 5 \quad (A.4)
To do so, \( \int \int \int \) approximated by as collocation points for the implementation of the dual reciprocity

In the dual reciprocity method, the domain integral in (A.5) is well-spaced out interior points denoted by \((s_i, \eta_i, \zeta_i)\) for \((i)\) and the coefficients \(F_i\) are generated. The non-algebraic equations with unknowns is generated. The non-linear boundary condition due to the radiation term in (3) is treated

respectively. The local interpolating function, \(\theta(p)\) and the particular solution \(\chi^{(6)}\) are given by

where \(r(x, y, z; \xi, \eta, \zeta)\) denotes the Euclidean distance between points \((x, y, z)\) and \((\xi, \eta, \zeta)\).

Substituting (A.7) into (A.5) and by letting the point \((\xi, \eta, \zeta)\) be represented by \((\xi^n, \eta^n, \zeta^n)\), we find that (A.4) and (A.5) may be rewritten as

and

\[
\gamma^{(6)}(\xi^n, \eta^n, \zeta^n) = \gamma(\xi^n, \eta^n, \zeta^n) + \int_{\Gamma_i} \chi^{(6)}(\xi^n, \eta^n, \zeta^n) \frac{\partial}{\partial n} (\Phi(x, y, z; \xi^n, \eta^n, \zeta^n)) dA(x, y, z) \\
+ \int_{\Gamma_i} \Phi(x, y, z; \xi^n, \eta^n, \zeta^n) dA(x, y, z) \\
\times \frac{\partial}{\partial n} (\Phi(x, y, z; \xi^n, \eta^n, \zeta^n))
\]

for \(j = 1, 2, \ldots, M - 1, M_i\) and for \(i = 6\),

\[
\text{respectively.}
\]

and

\[
\psi^{(6)}(\xi, \eta, \zeta) = \gamma(\xi, \eta, \zeta) + \int_{\Gamma_i} \chi^{(6)}(\xi, \eta, \zeta) \frac{\partial}{\partial n} (\Phi(x, y, z; \xi, \eta, \zeta)) dA(x, y, z) \\
+ \int_{\Gamma_i} \Phi(x, y, z; \xi, \eta, \zeta) dA(x, y, z) \\
\times \frac{\partial}{\partial n} (\Phi(x, y, z; \xi, \eta, \zeta))
\]

for \(j = 1, 2, \ldots, M - 1, M_i\) and for \(i = 6\),

\[
\text{respectively.}
\]
using an iterative procedure that is similar to the one proposed by Ooi et al. [17]. Solutions to the system of linear algebraic equation may be obtained using numerical solvers such as the Gauss elimination technique.

References