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3D optimal light distribution in brain tumors for Photodynamic Therapy

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ABSTRACT

Photodynamic therapy is a treatment technique that takes advantage of the effects induced by the body itself, together with a photosensitizer, to destroy unwanted tumor volumes with high accuracy and low invasiveness. This study analyzes treatment volume by 3D optical distributions in a realistic way from MRI images. First of all a volumetric model of a real head is built from MRI images. Optical distributions generated by the source over the tissue are considered at different brain tumor stages, and with multitude of processes that occur within the volume to be treated. By means of Monte Carlo we can estimate the photonic density that is absorbed by the tissues, whose optical properties are previously collected. This application considers that a reasonable time has passed for the photosensitizer to have reached the area under study, and that there is a minimum concentration in adjoining areas during radiation exposure. With this approach it is possible to estimate the level of radiation exposure and the affected volume. This is very relevant due to the fact that, as the radiation increases, different areas with different energy densities appear. This makes it much more complicated to apply a certain known optimal radiation on the treatment volume. A non-optimal high radiation density would damage healthy tissue, while, on the contrary, a non-optimal low radiation would not bring unwanted tissue to necrosis or apoptosis for tumor destruction, generating recurrence. This tool could be of great interest in treatment planning.

Keywords: 3D light propagation, turbid biological tissues, photodynamic therapy, optical properties, brain tumors

1. INTRODUCTION

Several clinical areas employ Photodynamic Therapy (PDT). The aim of this optical technique is malignant tissue destruction. It is based on the administration of a photosensitive substance, which is activated by the subsequent irradiation of the tumoral area. Reactive oxygen species are produced and destroy the cancerous cells [1]. Despite its many advantages, the development of dosimetry for PDT remains a challenge due to the high variability of the treatment outcome on the basis of complex photophysical and photochemical processes [2]. As long as the limited penetration of optical radiation into the biological tissues, several shortcomings are associated with the photosensitizers such as the hydrophobic nature of most of them or their poor selectivity, among others. Emerging strategies to overcome these problems and provide an effective delivery of the photosensitizer to the target tissue include the use of nanoparticles as an alternative to conventional molecular dye type photosensitizers, taking into account their ease of synthesis, biocompatibility and their optical properties dependence with size and shape [3], or even temperature [4].

One of the most relevant issues in the evaluation of the outcome of PDT is optical propagation, as an insufficient penetration depth could lead to tumor recurrence. Light propagation in a biological tissue implies dealing with an heterogeneous medium. In this type of medium, the scattering is dominant over absorption and therefore both the Radiation Transport Theory (RTT) and the Diffusion Equation can be employed for this purpose [1]. The Monte Carlo method has demonstrated its applicability and accuracy for the numerical analysis of the radiation transport equation compared with the exact solutions. The implementation of the Monte Carlo model can be multi-layered and three-dimensional. The optical characteristics and dimensions of each tissue are required to get a proper definition of the model. The optical parameters needed are the index of refraction n, the absorption and scattering coefficients and the anisotropy of scattering g.

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Regarding the photochemical interaction, it can be modeled by means of a differential equations system, based on the Jablonski diagram for the generation of singlet oxygen in a type II reaction. It usually takes into account the electronic transitions of the molecular components involved in the photodynamic procedure such as the photosensitizer or the oxygen, and its solutions may allow to analyze the temporal evolution of the main molecular components concentrations [5,6]. These models can be clinically relevant when they are considered in relationship with the photodynamic dose [7], for instance by means of parameters such as the photodynamic treatment depth, d_{TFD}. Although there are several options to be considered, photodynamic depth is usually assumed to be approximately two times the effective penetration depth. These tools help to adequately plan PDT treatment on a particular patient and on a particular lesion with a particular geometry, and has been applied to dermatological diseases [8].

Brain cancer presents an incidence of 9.8 and a mortality rate of 7.8. In the USA, the incidence rate of malignant tumors is 7.08 cases, with a survival rate of 36% after 5 years. Brain tumors are particularly complex to treat, due to the high risk of collateral damage and neural functionality impairments. Although surgical resection is the main treatment strategy, together with fractionated radiation plus chemotherapy, they encompass important drawbacks such as the lack of specificity and incomplete resection [9]. Most of these tumors are fatal, and even benign brain tumors can interfere with brain functions that are essential for daily life. Due to extremely high mortality, especially among patients diagnosed with glioblastomas, and significant morbidity due to brain tumors, there is an increasingly intense interest in understanding the basis of their causes to diagnose and treat them appropriately.

In this work, an approach for estimating optical distribution in brain tumors in presented, in connection to the desired treatment area for PDT. The morphological volumetric information is extracted from MRI images, as stated in the next section. Section three contains the three-dimensional optical propagation approach, and the results on tumors at different stages. Finally the main conclusions of the work are presented and discussed.

2. VOLUMETRIC BRAIN MODEL

Brain tumors of the type astrocytic or gliomas encompass a wide range of neoplasms that differ according to morphological characteristics, location within the central nervous system, growth potential, degree of invasiveness, tendency to progression, and distribution by age and sex [10]. Gliomas are generated from glial cells that surround the brain and spinal nervous system. Evidences suggest that differences in the tumors reflect the type and sequence of genetic alterations originated by carcinogenesis.

The presented approach needs a volumetric model of the brain. Volumetric information is extracted from Magnetic Resonance Imaging (MRI) images, as those shown in Figure 1. From these MRI scans a segmentation process is carried out. In this way, it is possible to move from the plane of the images to images in three dimensions with good resolution [11]. This process generates a 3D volume composed of tetrahedra with different optical properties, on which a Monte Carlo approach can be implemented.

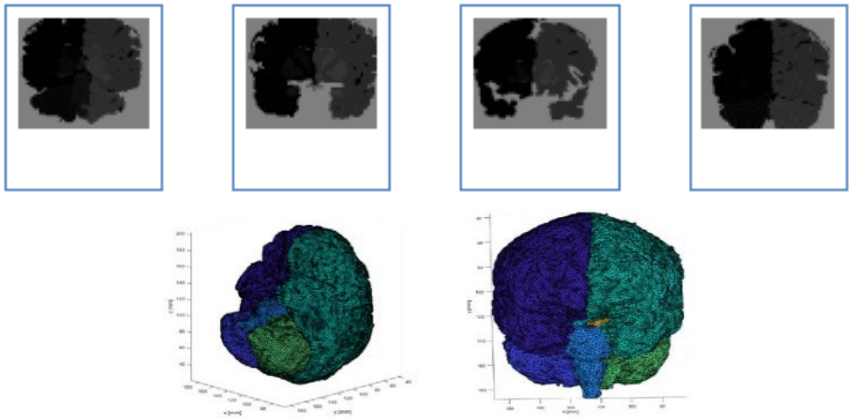

Figure 1. Brain images of brain glioma patient renderized and sectioned from magnetic resonance imaging; 2D slices (top), segmented volume (bottom).

3. IMPLEMENTATION AND RESULTS

Three different structures are analyzed, which reflect the progression of the tumor over time as the stage increases. These three structures are called phase 1 for the smallest volume, phase 2 for the intermediate one, and phase 3 for the most grown one, with the largest tumor volume. Once the concentration of the photosensitizer is known to be sufficient for the process to continue optimally [7], the optical distribution generated by radiating the tumor is estimated [12]. The implementation of the process relies on the optical characteristics of each of the tissues [13], and particularly their absorption properties that could facilitate the photochemical process. This process is critical in eliminating the tumor structure. The system works on the peak absorption of this type of tissue at 630 nm, and radiation is carried through an optical fiber, so as to reach the affected area. External radiation testing has been carried out, but stored energy levels were insufficient for the photochemical effect. This fiber will be strategically located in the center of the tumor according to the already known exact position of the tumoral structure, shortening the fiber path in the brain as much as possible, avoiding critical areas. The amount of energy absorbed by the tissue in steady state (with a reference time of 50 ns), is monitored, and the influence of increasing the energy of the optical source is analyzed. Higher energy levels (1J, 4J, 7J, 10J) area applied by varying the optical source, and the influence on the tumor structures is shown. The analysis distinguishes subsequently different energy regions. The analysis is focused on the most extreme phases (1 and 3).

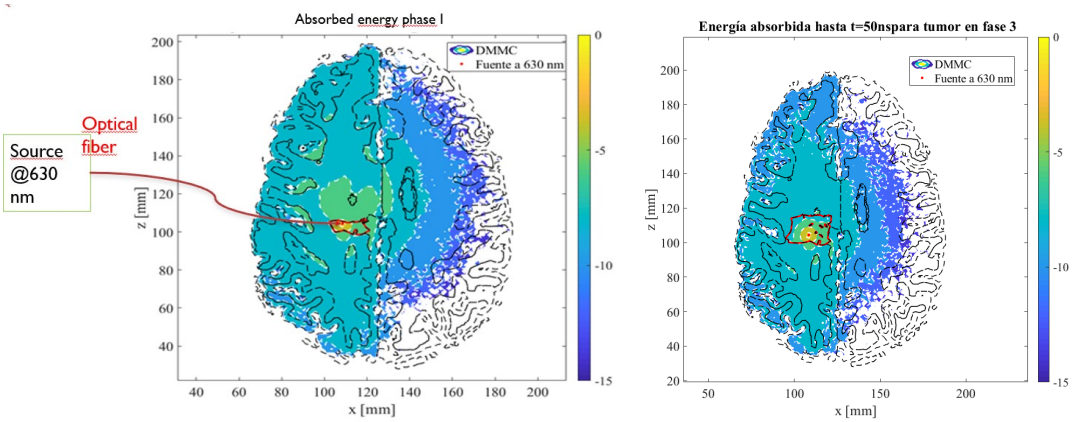

Figure 2. Section of the tumor structure evaluated for each one of the energy levels for sources with 1J, 4J, 7J and 10J for phase 1(left) and phase 3(right).

Figure 2(left) shows 3 zones with different levels of irradiance in phase 1. Ideally the energy levels should be as homogeneous as possible, because this will show which areas will be eliminated and which ones not. On the contrary, Figure 2(right) distinguishes 4 regions with different energy levels. Irradiation data from the different areas are collected. A previous model for tissue photochemical reaction is employed [8]. The results show that, in this case, almost only the tumor structure is affected. The expected necrosis entails the whole tumoral volume when employing 10 J, while 7 J are considered to be quite limited to the boundaries of the volume. Smaller energy values do not contribute to the elimination of the complete tumoral volume.

4. CONCLUSIONS

The photodynamic process has been analyzed in the case of brain tumors, particularly gliomas, which present in general a bad prognosis leading to death. The presented approach allows to estimate on one side optical radiation distribution in the tumor, by applying an optical fiber, for different tumor stages and optical source characteristics. The photochemical model indicates that all the regions with enough photodynamic dose are expected to suffer from necrosis and will therefore be eliminated. On the contrary, areas or regions below the dosage threshold will not be completely eliminated and, as a consequence, may be a possible risk for tumor recurrence. The expected relationship between tumoral phase and optical source parameters has been shown, with more unaffected regions generated for further stages and fewer optical radiation. The model is adapted to a real volumetric brain tumor structure, that makes the implementation highly

personalized. The results in this case, for this tumor and for the volumetric geometry, show that a 10 J radiation dose would be needed for the phase 3 tumor, while 7 J could be enough for phase 2. The tool is easily extendable for other tumor types and/or optical sources.

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REFERENCES

[1] Vo-Dinh, T., [Biomedical Photonics Handbook], CRC Press, Boca Raton (2015).
[2] Salas-García, I., Fanjul-Vélez, F. and Arce-Diego, J. L., "Spatial photosensitizer fluorescence emission predictive analysis for photodynamic therapy monitoring applied to a skin disease," Optics Communications 285, 1581–1588 (2012).
[3] Salas-García, I., Fanjul-Vélez, F., Ortega-Quijano, N., Lavín-Castanedo, A., Mingo-Ortega, P., López-Escobar, M. and Arce-Diego, J. L., "Effect of gold nanoparticles in the local heating of skin tumors induced by phototherapy," Proc. SPIE 8092, 8092041-8092047 (2011).
[4] Fanjul-Vélez, F. and Arce-Diego, J. L., "Modeling thermotherapy in vocal cords novel laser endoscopic treatment," Lasers in Medical Science 23, 169-177 (2008).
[5] Salas-García, I., Fanjul-Vélez, F. and Arce-Diego, J. L., "Spatial photosensitizer fluorescence emission predictive analysis for photodynamic therapy monitoring applied to a skin disease," Optics Communications 285, 1581-1588 (2012).
[6] Salas-García, I., Fanjul-Vélez, F. and Arce-Diego, J. L., "Superficial radially-resolved fluorescence and three-dimensional photochemical time-dependent model for Photodynamic Therapy," Optics Letters 39, 1845-1848 (2014).
[7] Salas-García, I., Fanjul-Vélez, F. and Arce-Diego, J. L., "Photosensitizer absorption coefficient modelling and necrosis prediction during photodynamic therapy," Journal of Photochemistry and Photobiology B: Biology 114, 79-86 (2012).
[8] Salas-García, I., Fanjul-Vélez, F. and Arce-Diego, J. L., "Influence of the human skin tumor type in Photodynamic Therapy analysed by a predictive model," International Journal of Photoenergy 2012, 759205 (2012).
[9] M. S. Eljamel, "Brain photodiagnosis (PD), fluorescence guided resection (FGR) and photodynamic therapy (PDT): past, present and future", Photodiagnosis and Photodynamic Therapy 5, 29-35, 2008.
[10] F. del Monte and M. R. Gilbert, Tumors of the brain and spine, 2015.
[11] A. Custo, "Effective scattering coefficient of the cerebral spinal fluid in adult head models for diffuse optical imaging", Applied Optics 45, 4747-55 (2006).
[12] Q. Fang, "Mesh-based Monte Carlo method using fast ray-tracing in Plücker coordinates", Biomedical Optics Express, 165-175 (2010).
[13] A. N. Yaroslavsky, P. C. Schulze, I. V. Yaroslavsky, R. Schober, F. Ulrich and H.-J. Schwarzmaier, "Optical properties of selected native and coagulated human brain tissues in vitro in the visible and near infrared spectral range", Physics in Medicine and Biology 47, 2059 (2002).