Multiple Source Phototherapy in Breast Cancer: A Viability Study

A. Lopes[1,2], A. Gabriel[1,2], J. Machado[1,2], P. Ribeiro[1,3], R. Gomes[4,5], João M. P. Coelho[4,5], C. O. Silva[6], C. P. Reis[5,6], J. P. Santos[1,2] and P. Vieira[1,2]

[1]*Department of Physics, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, R. Quinta da Torre, Monte da Caparica, Portugal*

[2]*LIBPhys, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, Monte da Caparica, Portugal*

[3]*CEFITEC, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, Monte da Caparica, Portugal*

[4]*Laboratório de Óptica, Lasers e Sistemas, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal*

[5]*Instituto de Biofísica e Engenharia Biomédica, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal*

[6]*CBiOS - Centre for Research in Biosciences & Health Technologies, Lusófona University, Lisboa, Portugal*

Keywords: Near Infrared, Spectroscopy, GAMOS, Monte Carlo, Phototerapy, Breast Cancer.

Abstract: Radiation therapy is one of many common treatments applied to breast cancer. Most usual radiation sources applied are ionizing radiation, such as γ-rays and X-rays, and non-ionizing radiation such as ultraviolet radiation. The possibility of using near infrared light to photoactivate a drug inside an 8 cm diameter biological object is discussed in this work via Monte Carlo simulations. Two simulation setups performed in the Geant4/GAMOS framework are presented in order to study the viability of photoactivating a drug by using several near infrared light sources. The overall objective of this technique is to minimize energy concentrated at objects surface and maximize it in a predefined region of interest. Results show an increase energy absorption in the desired region of interest inside a 8 cm object, when a higher absorption particle is present. With the use of multiple sources it is possible to photoactivate the drug while causing minimal damage to the surface of the radiated object.

1 INTRODUCTION

Radiation therapy, or radiotherapy, is one of the standard treatments for patients with breast cancer. Conventional ionizing radiotherapy is performed using X-rays and γ-rays combined with chemotherapy. This method is usually employed after surgery to improve cancer treatment (Sarkar et al., 2013). On the other hand non-ionizing ultraviolet (UV) radiation, which utilizes phototherapy techniques, is employed to treat skin cancer diseases which can develop from ionizing radiation therapies(Costa et al., 2014). There are several advantages and disadvantages to either of these types of ionizing and non-ionizing radiations. In the first case radiation will penetrate the biological tissue but it is known to cause serious side effects that one must take into account. In the latter case effective low light penetration into subcutaneous tissue is the biggest disadvantage (Sarkar et al., 2013).

To study the possibility of using near infrared (NIR) radiation is one of the aims of this work. NIR light is a non-ionizing radiation that produce even less undesired side effects and has greater effective penetration than UV radiation. NIR light sources would be applied in treatment of breast tissue and other melanoma beyond the subcutaneous surface by photoactivating gold nanoparticles with drug carrying capabilities and biocompatible coatings. The use of multiple radiation sources to minimize skin lesions and optimize energy in a specific region is the main idea behind this work and was also discussed in (Gabriel et al., 2015). By adding multiple sources our intention is to optimize the energy ratio between biological tissue surface and a predefined region of interest. Monte Carlo simulations were carried on to study this possibility as they are the reference in the realm of simulations of light interactions with biological tissues (Zhu and Liu, 2013). To perform this simulation it is used the Geant4/GAMOS framework which has already been validated by other authors as shown in (Glaser et al., 2013; Morhard et al., 2014). Geant4 is a powerful simulation tool that was developed for nuclear and particle physics experiments. GAMOS framework offers the necessary extension of

Lopes, A., Gabriel, A., Machado, J., Ribeiro, P., Gomes, R., Coelho, J., Silva, C., Reis, C., Santos, J. and Vieira, P.
Multiple Source Phototherapy in Breast Cancer: A Viability Study.
DOI: 10.5220/0005794902470250
In *Proceedings of the 9th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2016) - Volume 1: BIODEVICES*, pages 247-250
ISBN: 978-989-758-170-0

Geant4 to perform Monte Carlo simulations for Medical Physics applications. Its tissue optics plug-in was also used because it offers the possibility of simulating photons interacting with biological tissue and in the NIR range of the spectrum.

2 MATERIALS AND METHODS

2.1 Geometry and Optical Properties

The input parameters as well as the scattering theory used in GAMOS were firstly defined in order to begin the simulation. The use of literature values to perform this study was our first approach. However several parameters for the same variables in different references were found (van Veen et al., 2004; Jacques, 2013) which produced distinct simulations results. The output results from these parameters were not consistent with other groups' experimental results (Gibson et al., 2005) because photons were not penetrating deep enough into the tissue. To overcome these difficulties, we conducted an experiment in which the optical properties of a piece of pig lard were measured, and determined the best simulation parameters fitted to experimental results. These results will be published elsewhere and were based on (Gaigalas et al., 2009). In the present work it is assumed the simulated photons' interaction with the pig lard produce similar results as photons' interaction in breast tissue. The Mie Henyey-Greenstein scattering theory model was chosen because it has been proven by other groups to be the best to perform these kind of simulations (Jacques, 2013). To determine the Mie and anisotropy scattering coefficients we use a MATLAB script based on the work described in (Bohren and Huffman, 2007) and developed by Scott Prahl and Christian Maetzler in (Jacques and Maetzler, 2002). This software calculates both coefficients given average sphere dimensions, fractional volume and refractive indexes of tissue. The selected simulations input values were the ones which matched our pig lard experimental results and were chosen from a wide range of values taken from several referenced articles (Jacques, 2013; Wang et al., 2005; Jacques, 1996). The refractive index of the simulated object was taken from (Bashkatov et al., 2005). Two different setups were simulated and are described in the next paragraphs.

2.1.1 Setup #1

To minimize geometry dependences, we performed a simulation in a homogeneous cylinder with 8 cm diameter and 4 cm height as a first approach for modelling a section of the tumour site. Future work will comprise the study of the geometry contribution to the simulation results, namely the dependence on the angle between the beam axis and the solid surface and when one considers different solid geometries.

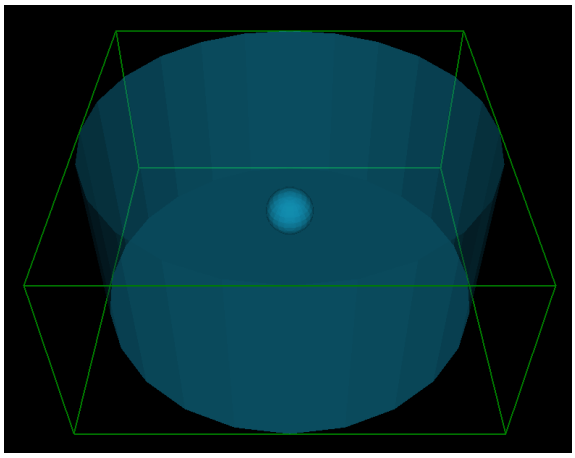

Figure 1: System geometry for setup #2.

2.1.2 Setup #2

A sphere was included in the centre of the volume of setup #1 with 1 cm diameter and higher absorption. It intents to mimic the optical properties of the photoactivated drug that its supposed to be aggregated around the tumour. Gold nanoparticles to be activated in the NIR range were developed by other members of this project. They also measured their optical properties so the spheres absorption coefficient was estimated based on their studies. These studies will be published elsewhere. A picture of this setup is displayed in Fig.1.

Both simulation setups consider 16 sources with a wavelength of 810 nm each aimed to the centre of the cylinder, equally spaced out around the object and equidistant from its lateral surface.

Input values of the GAMOS simulations are shown below:

- Wavelength: 810 nm
- Refractive Index: 1.44
- Mie scattering coefficient: 221.69 cm^{-1}
- Scattering anisotropy: 0.97
- Cylinders absorption coefficient: 0.01 cm^{-1}
- Spheres absorption coefficient: 1.00 cm^{-1}

For each setup 2 million events were generated. Each source has 1 ps pulse with Gaussian distribution

in wavelength and position of $\sigma^{\lambda} = 3$ nm and $\sigma^{p} = 0.5$ mm, respectively.

3 RESULTS

The simulation results for setup # 1 are presented in Fig.2 which shows a top-view of the absorption interactions of photons with the tissue inside the cylinder. The *X*-*Y* plane is measured in mm while the *Z*-axis represents the number of counts in each *X*-*Y* bin and is integrated in height. As expected from an homogeneous tissue the results show equivalent number of interactions when considering the same radius. The exception lies at the edge of the object where photon beams enter the tissue, where one can see a higher number of counts. This behaviour is expected because of the higher density of photons present in where the photon beams are aimed.

The simulation results for setup # 2 are also displayed in Fig.2. A top view of the absorption interactions inside the cylinder setup is presented. Besides demonstrating the same radius dependency on absorbed photons and the same higher density on the number of counts where the photon beams are aimed, this result also show a higher density on the number of counts inside the object where the higher absorption sphere lies.

Energy densities present in the region of interest were computed with and without the sphere, considering the number of photons that are absorbed in the predefined region of interest. When one does not consider the absorber sphere in the centre of the object the energy density is 1.2×10^{-27} J/cm^3. When the absorber sphere is present the energy density is 40×10^{-27} J/cm^3.

4 DISCUSSION

Scattering and absorption simulation studies of photons interaction with biological tissues were studied in (Gabriel et al., 2015). Absorption interactions with the tissue are studied in this work. There are two reasons for presenting only absorption studies. Firstly, when considering a same volume, there is more than 1 absorption interaction per each 10000 scattering interactions in average. This can be showed with the ratio between the scattering and absorption coefficients. If we proceeded with scattering and absorption interaction plots the results would be masked as fluctuations.

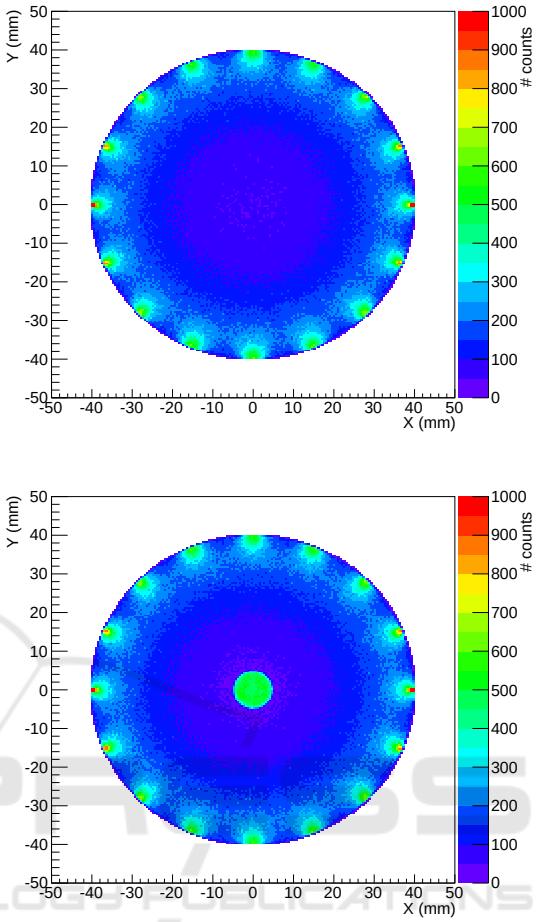

Figure 2: Absorption interactions inside the object of setup #1 on top and setup # 2 below.

Also only when photons are absorbed the drug is photoactivated by the deposited energy. The most important remark on the results of setup #2 when compared to setup #1: there is a greater number of absorption interactions in the centre of the object due to higher absorption of the drug supposedly aggregated to the tumour.

The results present in this paper also give a notion of what kind of energy ratio is expected between the location of the beam entrance and the region of interest where the drug is located. Enhancement of this ratio allow prevention of skin lesions when trying to photoactivate the drug. Another possible way of increasing this ratio is using multiple sources offset in time in order to create constructive interferences in the interest region within the tissue.

Since we are considering the same generated events between the two setups, one can compare the energy density among the two setups, and it is approximately 30 times higher. This is also an indicator of

the viability of this radiation technique.

5 CONCLUSIONS

We have presented a study about the use of NIR light to photoactivate a drug which aggregates around the tumour site inside an object with 8 cm. We have shown by using multiple sources for irradiating an homogeneous tissue absorption interactions behave similarly on equal radius distances, while minimizing the energy absorption at its surface. When higher absorption drug particles are simulated inside the object results show they can be photoactivated thus enabling treatment in the tumour area, while minimizing the damage to the surrounding healthy tissues.

In future work it will be important to make the model more realistic by including skin and vascularisation. It will be also important to optimise the source distribution and modulation in order to maximize the power delivery in the region of interest.

ACKNOWLEDGMENTS

This work was partially supported by national funding by the Portuguese FCT - Fundação para a Ciência e Tecnologia through the projects PTDC/BBB-BMD/0611/2012, UID/BIO/00645/2013 and PD/BD/105920/2014.

REFERENCES

Bashkatov, A. N., Genina, E. A., Kochubey, V. I., and Tuchin, V. V. (2005). Optical properties of human skin, subcutaneous and mucous tissues in the wavelength range from 400 to 2000nm. *Journal of Physics D: Applied Physics*, 38(15):2543.

Bohren, C. F. and Huffman, D. R. (2007). *Appendix A: Homogeneous Sphere*, pages 477–482. Wiley-VCH Verlag GmbH.

Costa, M. M., Silva, S., and et al. (2014). Phototherapy 660 nm for the prevention of radiodermatitis in breast cancer patients receiving radiation therapy: study protocol for a randomized controlled trial. *BioMed Central*, 15.

Gabriel, A., Machado, J., Gomes, R., Coelho, J., Silva, C., Reis, C., Santos, J., and Vieira, P. (2015). Concentrated photoactivation: focusing light through scattering. In *World Congress on Medical Physics and Biomedical Engineering, June 7-12, 2015, Toronto, Canada*, volume 51, pages 1727–1730, Toronto, Canada.

Gaigalas, A. K., He, H.-J., and Wang, L. (2009). Measurement of absorption and scattering with an integrating sphere detector: Application to microalgae. *Journal of Research of the National Institute of Standards and Technology*, 114(2):69.

Gibson, A. P., Hebden, J. C., and Arridge, S. R. (2005). Recent advances in diffuse optical imaging. *Physics in Medicine and Biology*, 50(4).

Glaser, A. K., Kanick, S. C., Zhang, R., Arce, P., and Pogue, B. W. (2013). A gamos plug-in for geant4 based monte carlo simulation of radiation-induced light transport in biological media. *Optical Society of America*, 4(5):741–759.

Jacques, S. and Maetzler, C. (2002). http://omlc.org/software/mie/.

Jacques, S. L. (1996). Origins of tissue optical properties in the uva visible and nir regions.

Jacques, S. L. (2013). Optical properties of biological tissues: a review. *Physics in Medicine and Biology*, 58(11):R37.

Morhard, R., Jeffery, H., and McEwan, A. (2014). Simulation-based optimization of a near-infrared spectroscopic subcutaneous fat thickness measuring device. *Engineering in Medicine and Biology Society (EMBC), 36th Annual International Conference of the IEEE*, pages 510–513.

Sarkar, J. S., Rajput, S., Tripathi, A. K., and Mandal, M. (2013). Targeted therapy against egfr and vegfr using zd6474 enhances the therapeutic potential of uv-b phototherapy in breast cancer cells. *Molecular Cancer*, 12.

van Veen, R. L. P., Sterenborg, H., Pifferi, A., Torricelli, A., and Cubeddu, R. (2004). Determination of VIS-NIR absorption coefficients of mammalian fat, with time-and spatially resolved diffuse reflectance and transmission spectroscopy. *Proc. Biomedical Topical Meetings, on CD-ROM, Paper SF5, Optical Society of America, Washington, DC*.

Wang, X., Pogue, B. W., Jiang, S., Song, X., Paulsen, K. D., Kogel, C., Poplack, S. P., and Wells, W. A. (2005). Approximation of mie scattering parameters in near-infrared tomography of normal breast tissue in vivo. *Journal of Biomedical Optics*, 10(5):051704–051704–8.

Zhu, C. and Liu, Q. (2013). Review of monte carlo modeling of light transport in tissues. *Journal of Biomedical Optics*, 18:73–100.