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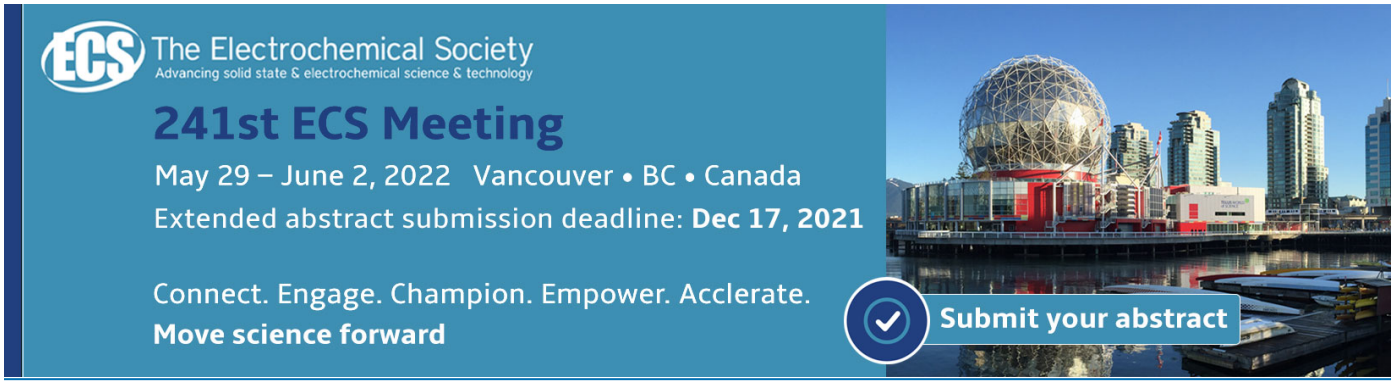

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Preliminary Monte Carlo simulation of non-laser light sources for photodynamic therapy

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Abstract. In photodynamic therapy (PDT), a photosensitizing agent is administered following irradiation on the target volume. The wavelength beam to activate the photosensitizer is ranging from 400 nm to 800 nm. Such wavelengths are generated by laser and non-laser light sources. However, the use of x-ray induced in photodynamic therapy has been investigated as a combination of radiotherapy and PDT. Moreover, x-rays are used for deeper penetration into tissue, extending the use of this therapy for tumours that would not be reachable by conventional PDT. In general, x-rays with keV to MeV energies are used for X-PDT. The aim of the present work is to investigate the use of monochromatic, low-energy beams for photodynamic therapy applications. Monte Carlo simulations are performed for distinct target volumes irradiated by a non-laser (low-energy x-rays). Models of soft tissue and a mixture some photosensitizer plus soft tissue were considered. For each case, the energy fluence distribution at a given depth was calculated. A higher percentage difference of ~20% was found when comparing the beam profile between soft tissue and the mixing Hpd, Photofrin, ALA, PpIX with soft tissue for low energy x-ray. Preliminary results showed that simulated x-ray beams could work for PDT.

Keywords. Photodynamic therapy, x-ray, PENELOPE Monte Carlo

1. Introduction

Photodynamic therapy (PDT) is a therapeutic modality recommended for treating tumour cells [1]. Dermatological, cardiovascular, and ophthalmic diseases [2-5] are among the possible PDT applications. PDT can be used for neoplastic cells with the advantage of being minimally invasive if compared to other treatments. In PDT, a photoactive drug or photosensitizer is delivered into a target volume, which is then irradiated by a light source with a selected wavelength, chosen to activate the photosensitizer. This activation is explained as it follows. When cells interact with irradiated light, the


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intracellular oxygen molecules rise to a singlet state, which has a short half-life. After that, they either decay to their rest state, emitting fluorescent energy, or advance in a chain of reactions until reaching a triple state, with a longer half-life. These triplet state molecules transfer their energy straight to intracellular oxygen, forming radical oxidizing species such as the singlet oxygen. Singlet oxygen causes oxidative injury within the cells that received the photosensitising agent [6, 7]. Since the photosensitizer is only activated upon photoexcitation, PDT has a reduced number of side effects when compared to other therapies [8]. In the last decades, several photosensitizers have been developed, tested, and approved for treating a number of distinct cancers with PDT. Each of these drugs are activated by specific wavelengths, ranging from 400 nm to 800 nm[9]. Such wavelengths are generated by laser and non-laser (lamps) light sources [10] in the so-called conventional PDT. However, the use of x-ray induced PDT (X-PDT) has been investigated as a combination of radiotherapy and PDT [11]. Moreover, x-rays are used for deeper penetration into tissue [12], extending the use of this therapy for tumours that would not be reachable by conventional PDT. In general, x-rays with keV to MeV energies are used for X-PDT.

In this work, our goal is to conduct a preliminary investigation of the use of a low-energy x-ray source for PDT. This is done by simulating the irradiation of phantoms, modelled to represent soft tissue, and a mixture of the later with specific PDT drugs.

2. Methods and materials

PENELOPE Monte Carlo code [13-14] was used to simulate a low-energy source irradiating a target phantom filled with distinct materials. Although the beam is non-laser source, the beam is chosen to be monochromatic of 50 keV due can be experimentally obtained by a low-energy x-ray source. Regarding the simulation geometry, was simulated a cylindrical phantom with a 15 cm diameter and a 22 cm length. The punctual source simulated was placed at 40 cm above it is a flat circle, opening the size of the cylindrical of 2 cm, parallel to the top of the cylinder. Were used of 1×10^{10} particles for each simulation and $0.8 mm^2$ pixel size of spatial resolution. The penmain file of the code generates an output number of simulated primary showers, secondary-particle generation probabilities, average deposited energies, and statistical error, etc.

After being emitted by the source, the monoenergetic beam was directed perpendicularly to the cylinder bases. Monte Carlo simulations were performed for phantoms filled with Hpd, photofrin, ALA, PpIX and soft tissue materials, modelled in PENELOPE [15-17]. First, the phantom is filled with soft, normal tissue, which is part of the PENELOPE database. Second, it is filled with materials created as photosensitizing agents: Hematoporphyrin Derivative (Hpd) [18], photofrin [19] aminolevulinic acid (ALA) [20], Protoporphyrin IX (PpIX) [21]. The chemical compositions of the agents were obtained through the PubChem database [22]. Table 1 shows the components for each material used in this work.

Table 1: Compounds and weight fraction form different materials created by PENELOPE code.

		Soft tissue*	Hpd	Photofrin	ALA	PpIX
Density (mg/cm^3)		1 x10^3	[1 - 5]	[0.00103 - 0.01545]	[0.00103 - 0.10300]	[0.000309 - 0.01545]
Element	**z**					
Hydrogen	1	0.6305	0.0634	0.0627	0.0687	0.0604
Carbon	6	0.1176	0.6811	0.6733	0.4580	0.7247
Nitrogen	7	0.0108	0.0935	0.0924	0.1068	0.0995
Oxygen	8	0.2396	0.1620	0.1336	0.3665	0.1154
Sodium	11	0.0003	-	0.0380	-	-
Magnesium	12	0.0003	-	-	-	-
Phosphorous	15	0.0002	-	-	-	-
Sulfur	16	0.0004	-	-	-	-
Chlorine	17	0.0003	-	-	-	-
Potassium	19	0.0004	-	-	-	-
Calcium	20	0.0003E-01	-	-	-	-
Iron	26	0.0005E-01	-	-	-	-
Zinc	30	0.0002E-02	-	-	-	-

* This material is disposal in PENELOPE code based on the ICRP

3. Results and discussion

From simulated conditions proposed through PENELOPE code were plotted dose profiles on the superifice of the phantom and at a 5 mm depth from the cylinder face, as shown in figure 1, that shows the energy deposited in terms of eV/g. All photosensitizing materials showed a plateau-like at central region, with a diameter slightly larger than the light source, followed by an exponential decay as the radius increases. It is interesting to compare the energy fluence distribution in the plateau-like region for all materials.

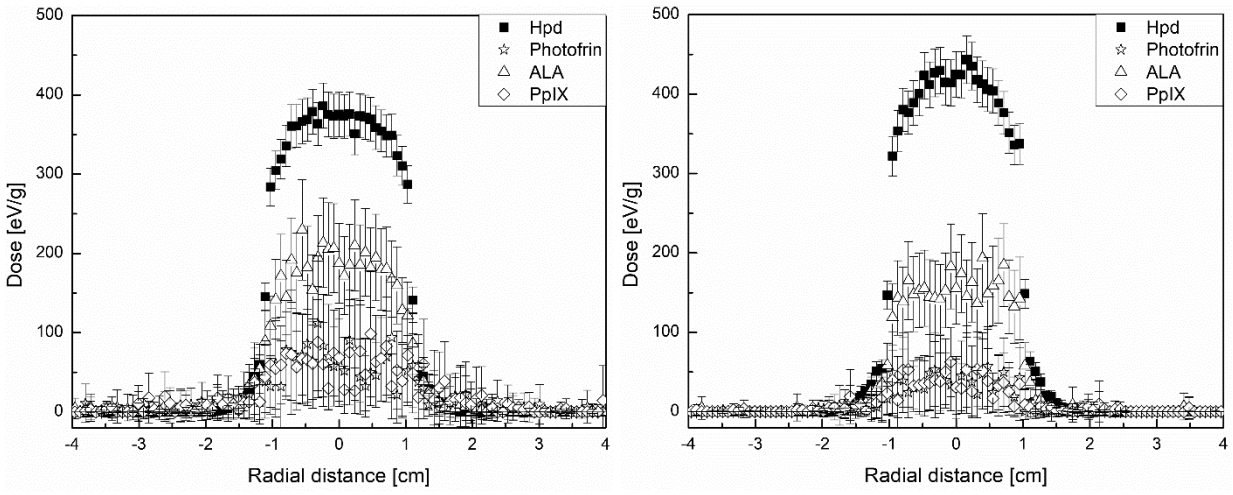
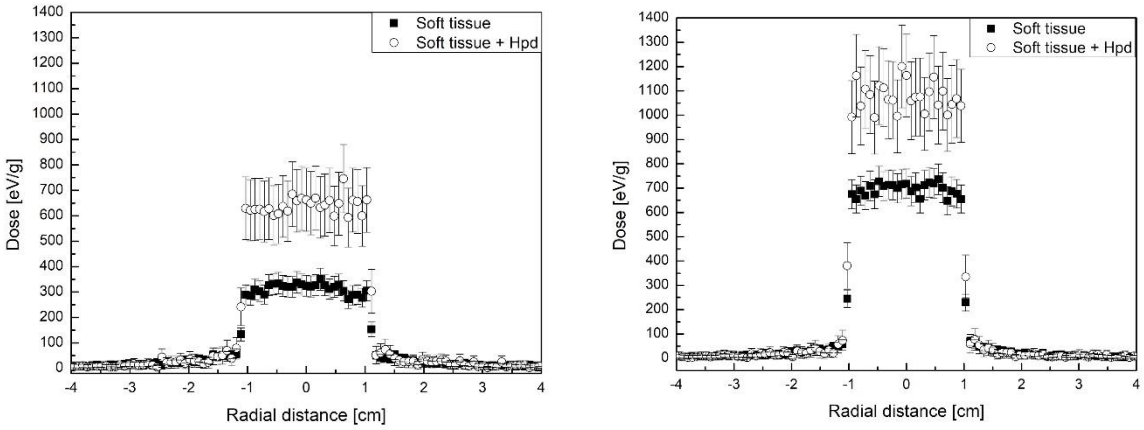


Figure 1. Dose profile for Hpd, photofrin, ALA, PpIX materials for the monoenergetic photon beam. a) at the superficie and b) at 5mm depth

The Hpd agent showed more dose values for the conditions studied than the other agents, due this have more density. Also was shown a uniformity the plateau-like at the central region. Comparing the doses for Hpd, from figure 1a and 1b, was obtained a 13% higher dose at 5 mm.

As the Hpd showed with higher dose compared with the other agents this was added to soft tissue with data from table 1 and were determinate the dose profile shows in figure 2.



a) b)

Figure 2. Dose profile for Hpd plus soft tissue and soft tissue for the monoenergetic photon beam. a) at the superficie and b) at 5mm depth

A difference of 20 % was found when comparing the dose profile from the soft tissue and Hdp plus soft tissue.

The mix material (Hdp plus soft tissue) evidences the greater probability of the cross section due to more interaction of the photons with the combination than without it. Thus, increasing the energy deposited, and consequently can guarantee the production of free radicals with greater energy and more range to injure the cell organelles in a more radii relative to the origin of the free radical.

4. Conclusion

The increase of ~20% in the dose distribution when mixing Hpd with soft tissue suggests that a low energy x-ray light source could work for PDT. Moreover, by optimizing the chosen parameters, it could be possible to obtain even higher values for the energy fluence distribution of the tumour and Hpd mix. However, more simulations with a broader range of parameters, non-laser light sources [23, 24], and other photosensitizers should be performed. Also, it would be interesting to investigate how the addition of nanoparticles [25] would affect the obtained results.

Finally, comparison of simulation results and experimental data would allow one to verify the reliability of the adopted models for the evaluated materials and the obtained results.

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