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Microfluidic Synthesis of Europium-doped Gadolinium Fluoride Nanoparticles: Developing Theranostic Nanodevices with Dosimetric Properties

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Introduction: According to the National Institute of Cancer José Alencar Gomes da Silva (INCA), in 2018, world estimation indicated that 18 million new cases of cancer and 9.6 million deaths occurred worldwide [1]. Nanodevices, i.e., devices manufactured with one or more dimensions on the nanoscale, have been used to improve the efficiency of cancer treatment [2]. Europium-doped gadolinium fluoride nanoparticles combine luminescent and magnetic properties in a single nanoparticle, besides presenting excellent scintillation emission [3]. In medical physics, these theranostic nanoparticles have potential applications in X-ray activated photodynamic therapy (X-PDT) when combined with a photosensitizer [4]. Furtheremore, due to their near infrared emission, they could be employed a radiation dosimeters for real time in vivo dosimetry. In this work, we developed a scintillating europium-doped gadolinium fluoride (GdF_3:Eu) using microfluidic reactors.

Material and method: Europium-doped gadolinium fluoride (GdF_3:Eu) nanoparticle was chose for this work and synthesis was made microfluidic reactor technique. Samples were characterized,transmission electronic microscopy (TEM), dynamic light scattering (DLS), photoluminescence (PL), radioluminescence (RL), and magnetization. All data analyses were performed by using Origin software (OriginPro 8). For dosimetric characterization, the LnNP was irradiating with an equipment GE-Isovolt Titan E-160M-2, operating at 80-160kVp and variating tube current (2 – 10mA). The attenuation of light was collected with two material in different thickness. The emitted light was collected using a fiber-optic with several integration time and detected with ocean optics (USB4000) and processed with the SpectraSuite software. The therapeutic action of GdF_3:Eu was investigated with mixture solution of the spin trap, solution of GdF_3:Eu and photosensitizer (Methylene Blue- MB). One part was sustained in the dark and the other part was irradiated 48kVp delivering a dose of 50 Gy. Electron spin resonance (ESR) spectra were recorded at room temperature, on a JEOL-JES-FA 200 (9.5 GHz).

Results and conclusion: The morphological and structural characterizations were performed and revealed particles with a mesoporous structure and 100 nm in size. The GdF3:Eu nanoparticle presented intense emission in the region between 590-700 nm, which is in the range of the therapeutic window. Dosimetric characterization reveled excellent linear dose-rate response, a crucial characteristic for a good dosimeter. Furthermore, emission light at 694 nm could be detected for a skin phantom layer of up 150 mm, suggesting a good material for in vivo dosimetry application, once light can pass through the skin and be detected externally. Applications in X-PDT with the nanoparticle conjugated to methylene blue (MB) in a core-shell structure resulted in enhanced singlet oxygen generation under x-ray irradiation. Irradiated and non-irradiated nanoparticles presented low cytotoxicity. However when irradiated with x-rays, the GdF/MB conjugates presented high toxicity. These results undoubtably reveals the GdF_3:Eu as a theranostic nanodevice for combining radiotherapy and photodynamic therapy cancers treatments and for advancing radiation dosimetry towards next-generation in vivo dosimetry

References:

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