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SCINTILLATING NANOPARTICLES FOR X-RAY-ACTIVATED PHOTODYNAMIC THERAPY AND NEXT-GENERATION IN VIVO DOSIMETRY

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Objective: The aim of this study was to develop scintillating nanoparticles to simultaneously monitor the x-ray dose delivered to tumors during treatments with x-ray-activated photodynamic therapy (X-PDT). **Methods:** A microfluidic synthesis was developed to grow GdF3:Eu theranostic scintillating nanoparticles (ScNPs). The flow reaction was optimized to enhance scintillation emission from the Eu+3 ions. **Results:** The as-prepared ~15 nm rhombohedral-shaped nanoparticles self-assembled into ~100 nm mesoporous flower-like nanostructures, but the rhombohedral units remained intact and the scintillation spectra were unaltered. The conjugation of the ScNPs with multilayers of methylene blue (MB) in a core-shell structure (GdF@MB) resulted in enhanced singlet oxygen ($1O_2$) generation under x-ray irradiation, with maximum $1O_2$ production for nanoparticles with 4 MB layers (GdF@4MB). High $1O_2$ yield was further evidenced in cytotoxicity assays, demonstrating complete cell death only for the association of ScNPs with MB and x-rays. Because the scintillating Eu+3 emission at 694 nm was within the therapeutic window and was only partially absorbed by the MB molecules, it was explored for getting in vivo dosimetric information. Using porcine skin and fat to simulate the optical and radiological properties of human tissues, we showed that the scintillation light can be detected for a tissue layer of ~16 mm, thick enough to be employed in radiotherapy treatments of breast cancers, for instance. **Conclusion:** The GdF3:Eu ScNPs and the GdF@4MB nanoconjugates are strong candidates for treating cancer with X-PDT while monitoring the treatment and the radiation dose delivered, opening new avenues to develop a next-generation modality of real-time in vivo dosimetry.

Keywords: Nanoparticles. Luminescence. Lanthanides. Microfluidic. Radiotherapy. Dosimetry.