Scintillating Nanoparticles for X-Ray–Activated Photodynamic Radiosensitization

M.M. Isikawa[1], E. J. Guidelli[1]
[1]Departamento de Física - FFCLRP- Universidade de São Paulo, Ribeirão Preto, SP, Brasil

Corresponding Author Email: mileni.isikawa@usp.br

Scintillating nanoparticles capable of converting X-rays into visible emission provide a versatile platform for X-ray–activated photodynamic radiosensitization. In this work, we investigate nanosystems composed of scintillating nanoparticles—specifically lanthanide-based materials (europium-doped gadolinium fluoride), which are well-established scintillators, and semiconductor-based nanoparticles (bismuth selenide) explored as potential X-ray–responsive emitters—conjugated with a molecular photosensitizer and designed to enable singlet oxygen ($^1O_2$) generation under clinically relevant X-ray irradiation [1,2].

The nanosystems were engineered to promote strong interfacial coupling between the inorganic core and the photosensitizer, ensuring efficient resonant energy transfer from radiation-induced emissive states to the molecular acceptor. Time-resolved photoluminescence measurements performed on the lanthanide-based nanoparticles revealed that direct surface conjugation of the photosensitizer is essential for activating the energy transfer pathway, yielding energy transfer efficiencies exceeding 97%. Upon X-ray exposure, this process leads to dose- and energy-dependent $^1O_2$ production, confirming the effective conversion of ionizing radiation into photodynamic action.

Biological evaluation of lanthanide-based materials demonstrated limited cytotoxicity in the absence of irradiation, whereas clonogenic survival assays showed a pronounced reduction in long-term cancer cell survival only when X-ray irradiation was applied. Analysis of survival curves using the linear–quadratic formalism, together with sensitization enhancement and dose enhancement factors, indicates that the observed radiosensitization arises from the synergistic combination of radiation interactions at the inorganic core and radiation-activated photodynamic effects.

These results highlight scintillation- and emission-mediated energy transfer as robust mechanisms for achieving deep-tissue reactive oxygen species generation using X-rays, overcoming the penetration limitations of conventional photodynamic therapy. The proposed approach provides a general framework for the design of multifunctional radiation-activated nanoplatforms aimed at enhancing radiotherapy efficacy while remaining compatible with advanced radiation treatment modalities.

1. Kamkaew, A., Chen, F., Zhan, Y., Majewski, R. L. & Cai, W. Scintillating Nanoparticles as Energy Mediators for Enhanced Photodynamic Therapy. *ACS Nano* 10, 3918–3935 (2016).
2. Zhang, T. *et al.* "Rare-earth scintillating nanoparticles for X-ray induced photodynamic therapy". *J Lumin* 261, 119862 (2023).