

Radiotherapeutic Impact of Nanoscintillators: Interplay of Physical Dose Effects and Biological Radiosensitization

Sarah Stelse-Masson¹, Xenie Lytvynenko², Frédéric Chaput³, Frédéric Lerouge³, Kristel Bedregal-Portugal¹, Matéo Lavaud¹, Malika Kadri¹, Eva Mihóková^{2,4}, Václav Čuba², Hélène Elleaume⁵, Anne-Laure Bulin¹

¹University Grenoble Alpes, Inserm, CNRS, Institute for Advanced Biosciences, Grenoble, France

²Faculty of Nuclear Sciences and Physical Engineering, Czech Technical University in Prague, Prague, Czech Republic

³Chemistry Department, École Normale Supérieure de Lyon, University of Lyon, CNRS, Lyon, France

⁴Institute of Physics, Czech Academy of Sciences, Prague, Czech Republic

⁵Synchrotron Radiation for Biomedicine, University Grenoble Alpes, Inserm, Grenoble, France

Corresponding Author Email: anne-laure.bulin@inserm.fr

Nanoscintillators have rapidly gained attention as innovative agents for improving radiation therapy for cancer treatment, via several distinct mechanisms [1,2]. Our recent work has focused on unraveling the specific mechanisms by which nanoscintillators alone can potentiate radiation therapy. We have demonstrated their capacity to enhance radiotherapy efficacy in aggressive cancer models, such as glioblastoma and pancreatic tumors, primarily through a physical radiation dose enhancement effect [3,4]. Our latest results demonstrated the existence of a newly identified effect: nanoscintillators not only increase the physical dose of radiation, but also induce a biological radiosensitization effect. This effect appears to be linked to the disruption of double-strand breaks repair mechanisms, the most common DNA damage caused by radiotherapy, thereby amplifying the overall therapeutic impact.

In this presentation, we will share results obtained using two distinct types of nanoscintillators. The first are Lu₃Al₅O₁₂:Pr nanoparticles, synthesized by the team of Prof. Václav Čuba, with results recently published [5]. The second are GdF₃:Tb nanoparticles, developed by the group of Dr Frédéric Chaput and Frédéric Lerouge. Our latest data confirm the existence of this biological radiosensitization effect with both types of nanoscintillators. Identifying this novel biological pathway offers new opportunities to improve the overall effectiveness of radiotherapy using nanoscintillators. By harnessing both physical and biological effects, these nanoscintillators may pave the way for more potent and targeted cancer treatments.

References

1. K. Bedregal-Portugal et al., “Nanoscintillators as Next-Generation Radiotherapeutics: Bridging Physics, Chemistry, and Oncology,” *Bioconjugate Chemistry*, **36**, 1919-1932 (2025).
2. C. Dujardin et al., “Inorganic Nanoscintillators: Current trends and future perspectives”, *Advance Optical Material*, **2402739** (2025).
3. Bulin et al, “Radiation dose enhancement is a potent radiotherapeutic effect of rare-earth composite nanoscintillators in preclinical models of glioblastoma” *Advanced Science*, **7**, 2001675 (2020).
4. Aubrun et al. “Nanoscintillator Coating: A key parameter that strongly impacts internalization, biocompatibility, and therapeutic efficacy in pancreatic cancer models”, *Small Science*, **2400041** (2024).
5. Stelse-Masson et al., “Combined Physical and biological contributions to radiotherapy enhancement by Lu-based nanoscintillators in pancreatic cancer models”, *Nanotheranostics*, **9**, 199-215 (2025).

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