UV-C Emitting Pr^{3+} and Nd^{3+} Co-doped $LuPO_4$ Nanoparticles for Enhanced Effectiveness of X-Rays onto 3D Lung Cancer Spheroids

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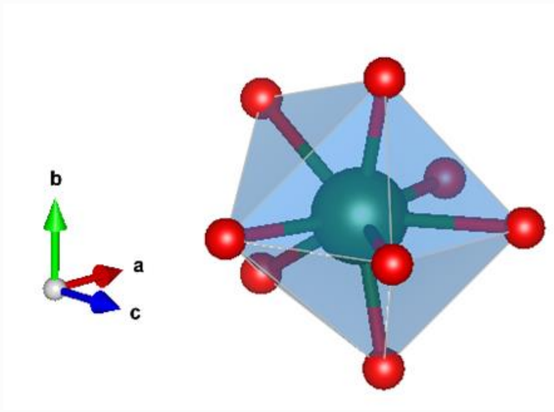
Background

About half of all cancer patients receive therapy [1], usually combined with surgery, and chemotherapy [2]. Ionizing radiation induces oxygen-dependent DNA damages in tumor cells, but can also affect the surrounding healthy tissue. Local delivery of nanoscintillators can cause increased radiation dose within the tumor tissue, increasing the therapeutic window.
This study concerns a novel nanoscale radiosensitizer, viz. $LuPO_4$ co-doped with Pr^{3+} and Nd^{3+}. Under X-ray excitation, these nanoparticles emit efficiently UV-C radiation (230-280 nm), resulting in increased tumor cell death (oxygen-independent UV-C induced damages). Over a three-week period using a 3D A549 lung cancer cells shown no specific toxicity during incubation with the nanoscintillators. In contrast, there was significant growth inhibition of cell spheres treated with 2.5 mg/ml $LuPO_4$: Pr^{3+}, Nd^{3+} in combination with ionizing radiation (4 or 8 Gy X-rays) compared with radiation alone.

Lutetiumorthophosphate ($LuPO_4$)

- Crystal structure: Tetragonal
- Space group: D_{4h} (#141)
- High density: 6.53 g/cm^3 (Z_{eff} = 63.7)
- Band gap: 8.85 eV
- Biocompatible and FDA approved (Lutathera®)



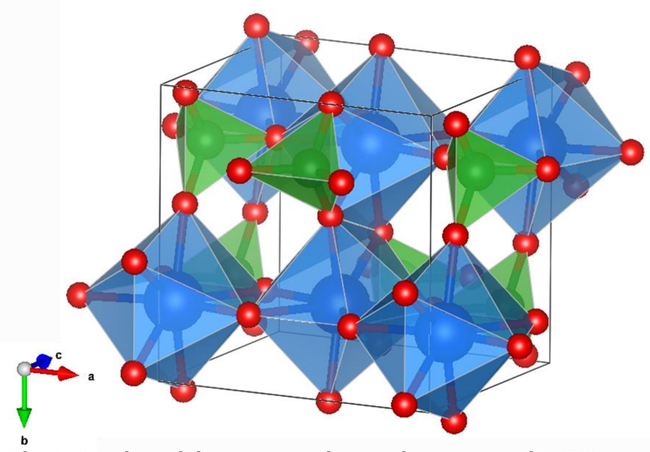


Fig. 1: Section of the tetragonal crystal structure of $LuPO_4$

Results / Measurements

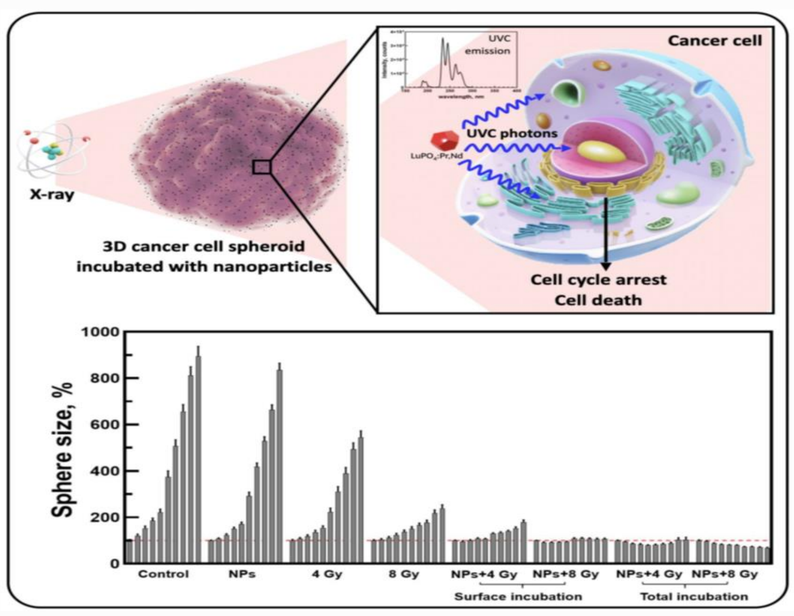


Fig. 2: Schematic description of the way and the results in which the $LuPO_4$:Pr^{3+}(1%), Nd^{3+}(2.5%) nanoparticles interact

- Nanoparticles penetrate the 3D structure of A549 lung cancer cells (37 °C, 99 °F in 5% CO_2 atmosphere)
- Particles are not toxic to cells when incubated 2.5 mg/ml for up to 7 days
- Nanoscintillator + irradiation (4 and 8 Gy/min) leads to significantly inhibited growth of 3D cell cultures

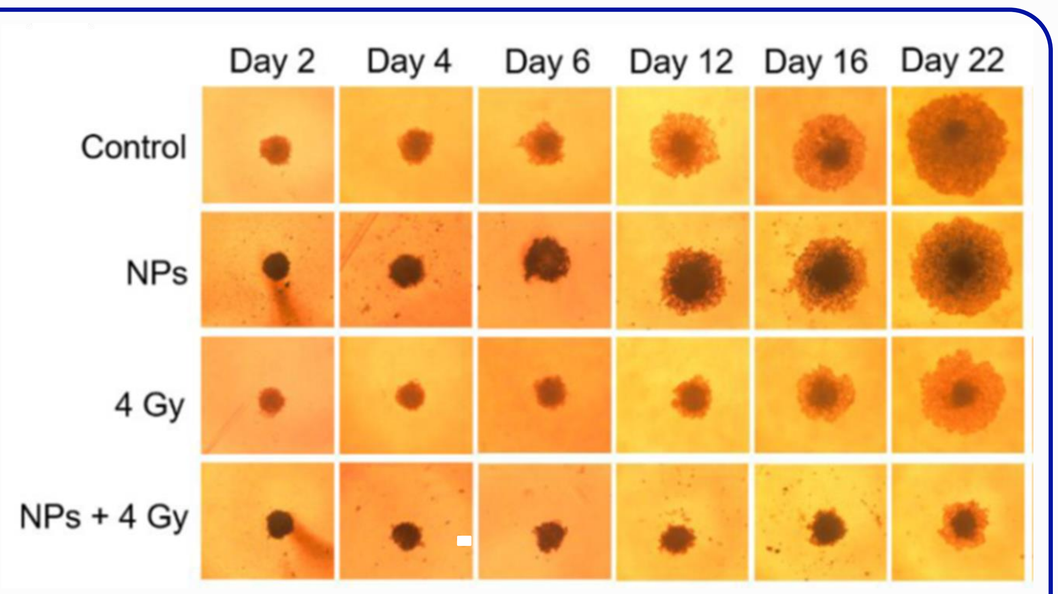


Fig. 3: Brightfield microscopy images show spheroid morphology and size changes after treatment

- Four strong emission bands between 230 and 280 nm due to interconfigurational $[Xe]4f^15d^1 \rightarrow [Xe]4f^2$ transitions of Pr^{3+}
- Overlap of the emission integrals between germicidal efficacy of E. coli and $Pr^{3+}$and Nd^{3+} doped $LuPO_4$ nanoparticles is 76 %
- Particle size distribution with a D_{50} value of around 100 nm (Crystallite size of around 20 nm)

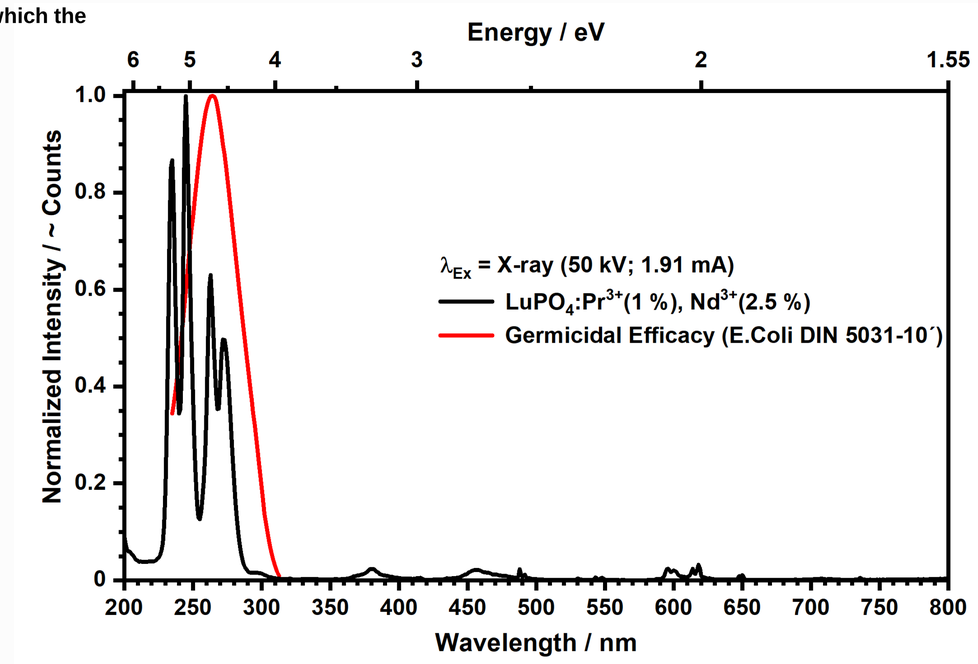


Fig. 4: X-ray excited emission spectra of $LuPO_4$:Pr^{3+}(1%), Nd^{3+}(2.5%) compared to the GAC absorption curve of E. Coli

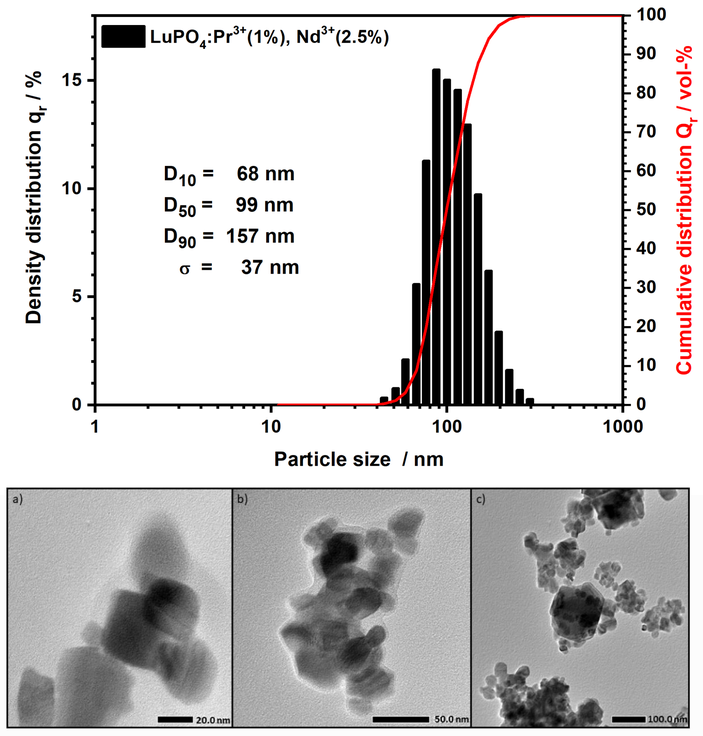


Fig. 5: Particle size distribution and TEM images of $LuPO_4$:Pr^{3+}(1%), Nd^{3+}(2.5%)

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