Hydrogenated Nanodiamonds as Radiosensitizers for the Treatment of Radioresistant Medulloblastoma: Impact of Nanoparticle Properties and Radiation Energy

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Abstract

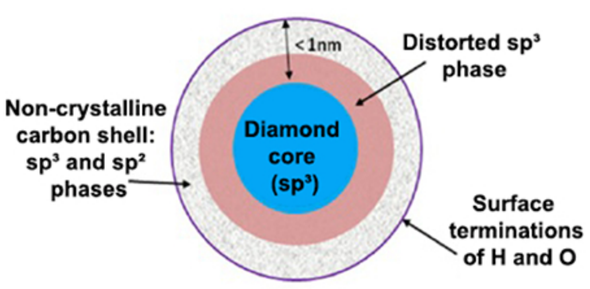
Nanotechnologies are emerging as powerful tools to enhance the effectiveness of conventional cancer therapies, offering new opportunities for precision medicine. In this work, we investigate the potential of nanodiamonds (NDs) as radio-sensitizing agents for the treatment of radio-resistant medulloblastoma. Owing to their biocompatibility, chemical stability, low toxicity, and versatile surface functionalization, NDs represent a promising nanomaterial for integration with advanced radiotherapy approaches, a key enabling technology in modern oncology.

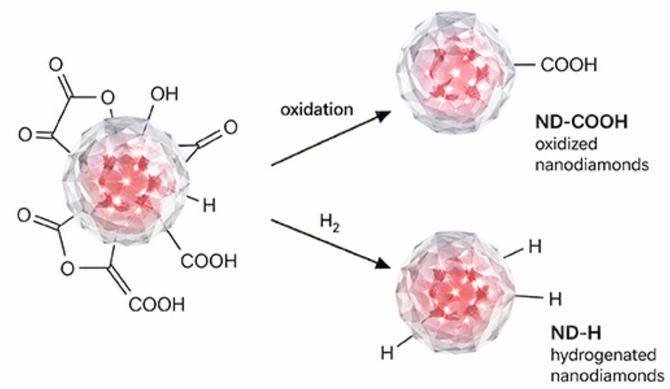
Human DAOY medulloblastoma cells were exposed to NDs characterized by different surface chemistries (hydrogenated, H-NDs, and oxidized, OX-NDs), particle sizes, and concentrations, followed by irradiation with photon beams of different energies. The study evaluated ND cellular uptake and intracellular localization, clonogenic survival after combined ND-radiation treatment, and the biological mechanisms underlying radio-sensitization through analyses of DNA damage and apoptosis.

Results demonstrate that the physicochemical properties of NDs play a crucial role in determining their biological activity. H-NDs exhibited a significant radio-sensitizing effect, reducing cellular survival in a size- and concentration-dependent manner, whereas OX-NDs showed minimal impact on both cell viability and radiation response. Furthermore, the combination of H-NDs with high-energy γ-rays (1.25 MeV) produced a stronger radio-sensitizing effect than irradiation with lower-energy X-rays (250 kVp). Mechanistic investigations revealed that enhanced cell killing is associated with the activation of Caspase-3-dependent apoptosis and occurs independently of increased DNA damage.

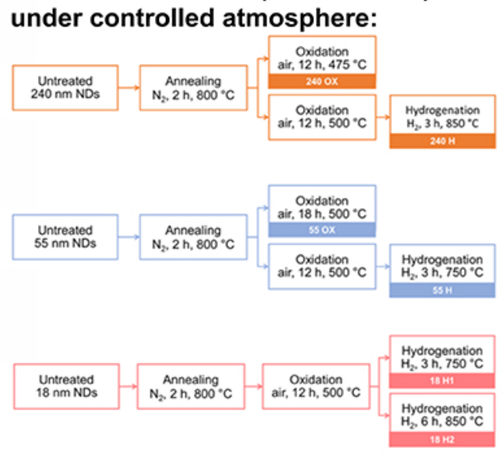
These findings highlight the importance of tailoring nanoparticle surface chemistry and selecting appropriate radiation energies to maximize therapeutic efficacy. The integration of engineered nanodiamonds with advanced radiotherapy technologies represents a promising strategy for overcoming tumor radio-resistance and improving cancer treatment outcomes. This research contributes to the development of innovative nanomedicine-based approaches for precision oncology and supports the translation of nanotechnology-enabled radiosensitizers toward clinical applications.

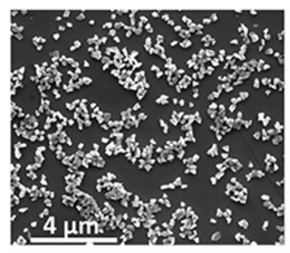
Nanodiamond characteristics:

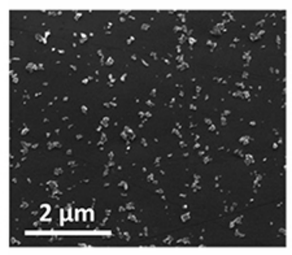


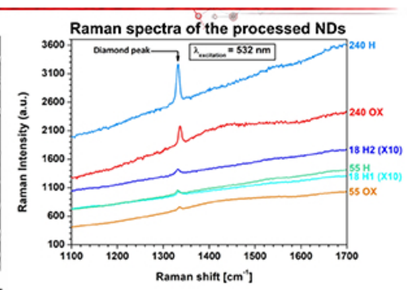


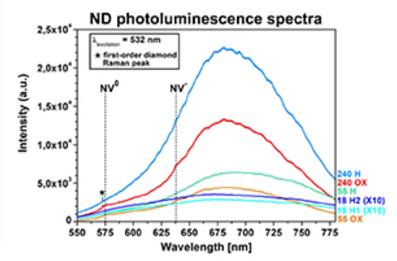
Thermal treatments (tube furnace) under controlled atmosphere:



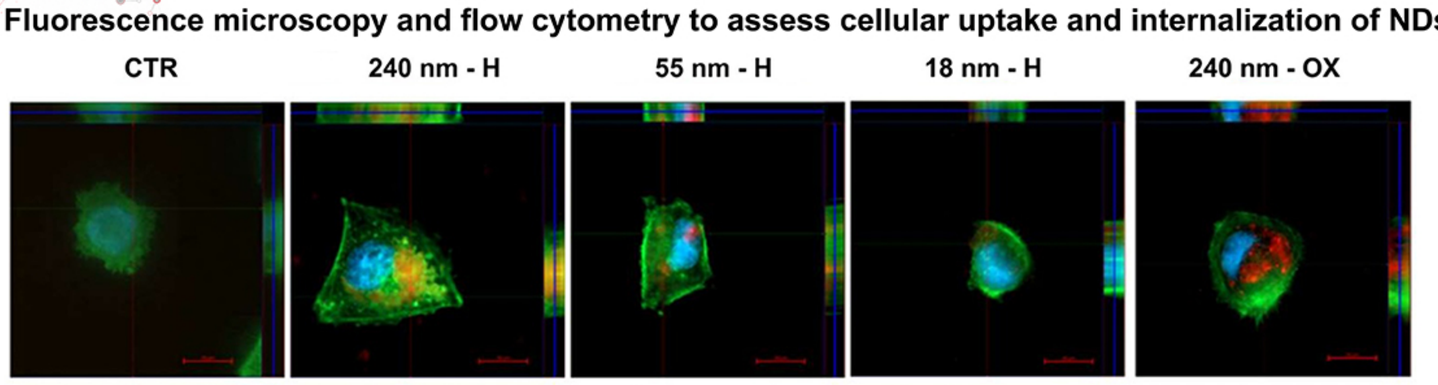






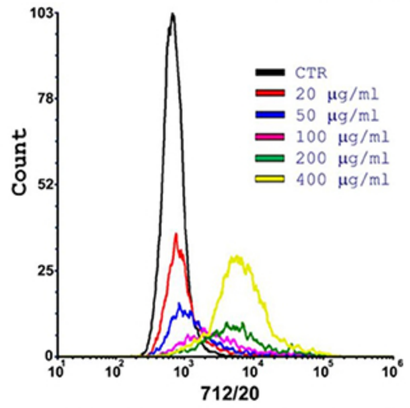


Fluorescence microscopy and flow cytometry to assess cellular uptake and internalization of NDs:

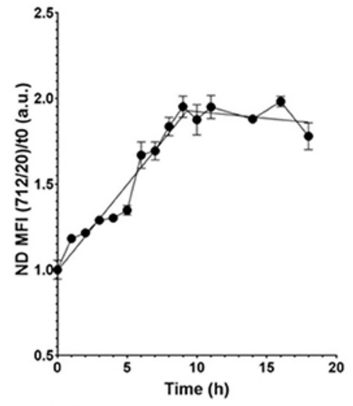


Comparison of DAOY cells after 13 h incubation: the images show the natural fluorescence signal of NDs in red overlapped with the stained nuclei in blue (DAPI) and cell cytoplasm in green (Phalloidin).
Nanoparticle concentration of 20 µg/ml.

Flow Cytometry Analysis

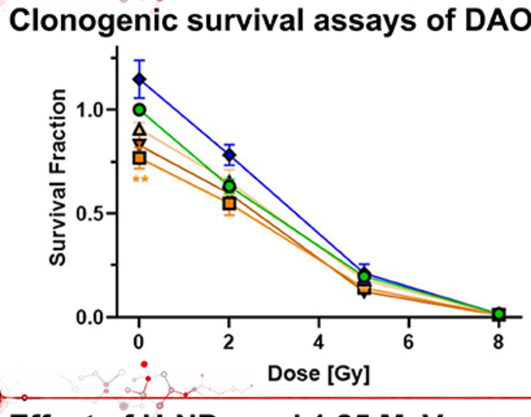


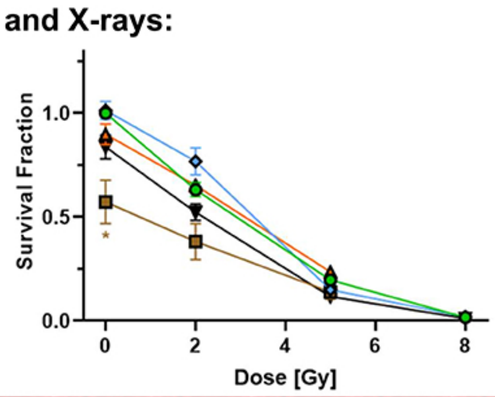
MB cells treated with different concentration of 55 nm H-NDs

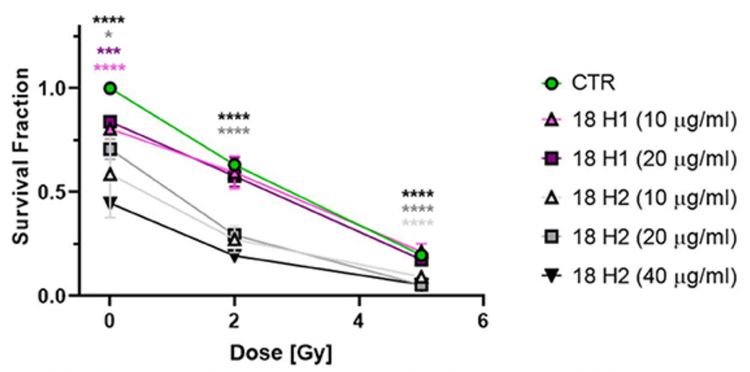


Uptake curve for 20 µg/ml 240 nm H-NDs

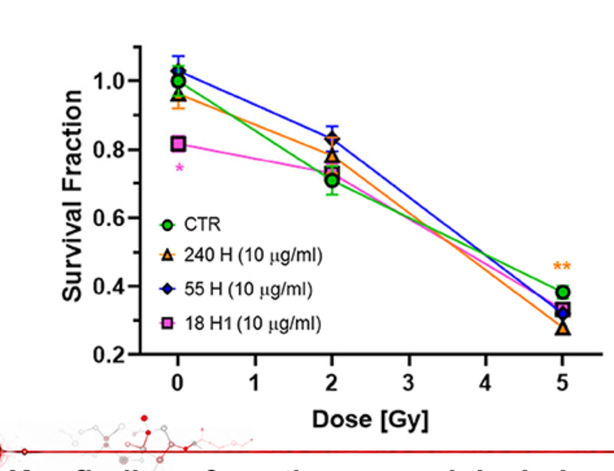
Clonogenic survival assays of DAOY cells exposed to NDs and X-rays:

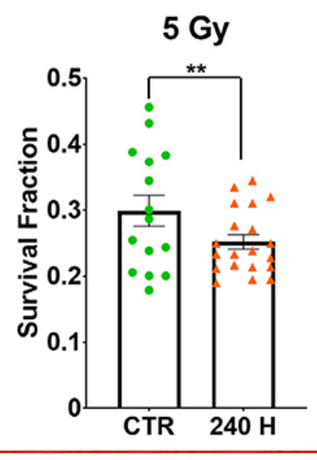


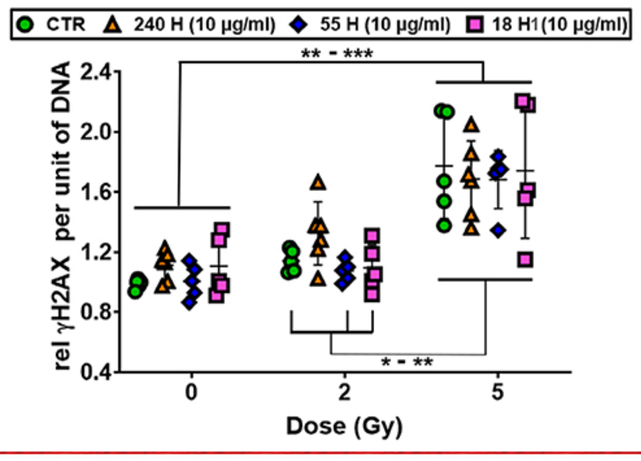


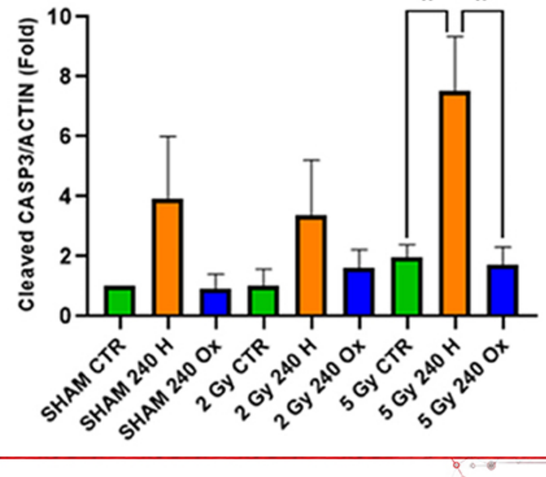


Effect of H-NDs and 1.25 MeV γ-rays combined treatment on DAOY cells:









Key findings from the research include:

* Hydrogenated nanodiamonds (H-NDs) were identified as the most effective radiosensitizers among the ND types tested.
* Their radiosensitizing performance could potentially be enhanced further through optimized surface modification techniques.
* Unlike metallic nanoparticles, which typically exhibit maximum radiosensitization under kilovoltage photons H-NDs show stronger radiosensitizing effects when combined with megavoltage (MV) radiation.
* This is particularly relevant because 1-25 MV photon beams are routinely used in clinical practice to treat deep-seated tumors, including brain cancers.
* As summarized in the figure on the right, the radiosensitizing action of H-NDs appears to occur through a caspase-3-dependent apoptotic pathway and is independent of direct DNA damage. However, the precise molecular mechanisms underlying ND-biological interactions remain incompletely understood and require further investigation.

Conclusion

The study suggests that optimizing the combination of nanodiamond surface properties and radiation energy could provide an effective strategy to improve radiotherapy outcomes, particularly for radioresistant tumors. Hydrogenated nanodiamonds, used alongside high-energy radiation, represent a promising avenue for future cancer treatment research.