Boron Neutron Capture Therapy (BNCT) is a highly selective binary radiotherapy approach, yet its clinical translation remains limited by a major bottleneck: the difficulty in achieving sufficient 10B concentrations in tumor cells while sparing healthy tissue. Overcoming this delivery challenge is therefore central to unlocking the full therapeutic potential of BNCT.

Here we report the development of hybrid core–shell nanoarchitectures (BAuNAs) designed to simultaneously enhance boron delivery and radiation potential. These nanocarriers consist of a biodegradable silica shell encapsulating ultrasmall gold nanoparticles (~3 nm) and functionalized hexagonal boron nitride nanostructures (~5 nm), enabling the co-delivery of 10B and a radiosensitizing metallic agent within a single platform.

The synthesis proved highly reproducible and scalable, producing stable nanoarchitectures with an average diameter of ~115 nm and excellent colloidal stability. Elemental mapping by TEM–EDX confirmed the successful co-localization of B, N, Au, and Si within individual carriers.

In vitro validation demonstrated high biocompatibility and negligible cytotoxicity in both tumor (SCC25) and healthy epithelial (16HBEo14) cells. BAuNAs achieved an 16-fold increase in intracellular boron uptake compared with free boron nanostructures, exceeding the therapeutic concentration and tumor-to-normal (T/N) boron ratio thresholds required for effective BNCT. Validation in an in ovo CAM-based SCC25 tumor model supported efficient penetration into complex tumor microenvironments.

A key advantage of the ultrasmall-in-nano design is the time-controlled degradation of the silica shell (24–48 h), releasing sub-10 nm components that are compatible with renal clearance and therefore mitigate long-term accumulation of inorganic materials. By combining high boron loading with the radiosensitizing potential of gold nanoparticles, BAuNAs emerge as a promising multifunctional platform capable of significantly improving the therapeutic index of BNCT. Overall, this work highlights a nanotechnology-driven strategy to address one of the central limitations of BNCT, opening new opportunities for the development of advanced boron delivery systems.