Letter to the Editor

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Nanorobots crossing the blood–brain barrier for targeted chemotherapy: the next frontier

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Abstract

The impermeability of the blood–brain barrier (BBB) remains one of the greatest challenges in neuro-oncology, limiting the effectiveness of chemotherapeutic delivery to malignant brain tumors. Programmable nanorobots, nanoscale devices with autonomous or guided motion have emerged as a transformative technology capable of actively crossing the BBB and releasing cytotoxic drugs directly at tumor sites. By integrating biomimetic coatings, enzymatic propulsion, and PH-responsive targeting, these systems achieve selective tumor accumulation while minimizing systemic toxicity. Preclinical studies from China, the United States, and Europe demonstrate significant advances in nanorobot-assisted chemotherapy, heralding a paradigm shift in glioblastoma management. Despite promising results, clinical translation requires careful attention to safety, biocompatibility, and regulatory oversight. This letter outlines current progress, key technical strategies, and future directions in nanorobotic chemotherapy. The approach holds profound implications for precision medicine and offers renewed hope for patients with intractable brain malignancies.

Keywords: blood–brain barrier, cancer, chemotherapy, nanorobots, oncology

To the Editor,

Glioblastoma multiforme remains one of the most lethal cancers, with median survival under 2 years despite maximal therapy. The principal barrier to therapeutic success is the blood–brain barrier (BBB), which excludes most systemic chemotherapeutic agents[1]. Conventional drug delivery achieves poor tumor penetration, prompting an urgent need for novel, precise delivery methods.

Nanorobots, engineered nanoscale devices combining sensing, propulsion, and targeting, offer a potential breakthrough. These intelligent systems can actively traverse the BBB, guided by magnetic or enzymatic propulsion, and release drugs in response to tumor-specific cues such as acidic pH or enzymatic activity. In China, natural killer cell membrane-coated nanorobots have been shown to transiently open endothelial junctions and deliver chemotherapeutics directly to glioma tissue[2]. In the United States, DNA-origami nanorobots capable of exposing cytotoxic ligands in acidic microenvironments demonstrated tumor-specific apoptosis and minimal off-target toxicity[3]. Similarly, enzyme-driven nanomotors developed in Germany and Japan enhance penetration through brain vasculature, highlighting rapid global progress[4].

Clinically, nanorobotic delivery systems promise higher drug concentration at tumor sites with reduced systemic exposure. The "Trojanbot" platform from China- neutrophil-carried nanomotors crossing the BBB via chemokine gradients achieved remarkable tumor regression in murine glioblastoma models[5]. Integration with imaging agents may soon enable real-time tracking of drug release, while artificial intelligence (AI) could coordinate nanorobot swarms for autonomous precision targeting. Nonetheless, challenges remain: ensuring biodegradability, preventing immune clearance, and establishing ethical transparency for AI-guided nanotherapeutics are essential steps toward clinical use. Our work is in line with the TITAN Guidelines on the need for transparency in AI use in healthcare[6].

In summary, BBB-penetrant nanorobots represent a pivotal advancement in targeted chemotherapy. Through international collaboration and responsible innovation, this technology could redefine therapeutic strategies for brain cancers and transform outcomes for patients with currently untreatable disease.

Ethical approval

Not applicable.

Consent

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Author contributions

M.K. contributed to the study concept, framework, and initial drafting. M.Z. assisted in literature review, literature search,

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