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Magnetic microrobots: A paradigm shift toward clinical translation in targeted drug delivery

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INTRODUCTION

Conventional systemic administration is often limited by off-target effects and dose-limiting toxicities, contributing to the nearly 30% of drug failures in clinical trials. Magnetically guided micro- and nanorobots have garnered substantial attention for their capabilities in targeted drug delivery directly to disease sites, thereby enhancing treatment efficacy and minimizing side effects. Nevertheless, clinical translation remains challenging. First, microrobot materials must be biocompatible and biodegradable, yet these requirements constrain the magnetic properties achievable for actuation. Another barrier lies in the control platform, which is required to overcome the rapid spatial decay of magnetic fields to generate sufficient force for navigation across human-scale anatomical distances. Together, these limitations have formed the main barriers to clinical translation.

In a recent study published in *Science*,[1] Landers et al. reported the first clinically compatible magnetic microrobotic platform, named "Navion" (Figure 1) that capable of achieving precise navigation, real-time imaging and controlled drug release under physiological conditions. By masterfully integrating an electromagnetic navigation system (eMNS), a custom-designed delivery catheter, and a dissolvable capsule, the authors demonstrate targeted therapy in large-animal models. This work represents a critical step toward the clinical realization of microrobotic technology.

TECHNICAL PLATFORM DEVELOPMENT AND PRECLINICAL VALIDATION

Landers et al. address key barriers in magnetic microrobots by coupling materials engineering with system-level integration, enabling reliable operation at clinically relevant scales. The platform represents a shift from laboratory demonstrations to a configuration that could function in interventional settings.

The authors designed a 1.7-mm gelatin-based, degradable drug capsule suitable for intravascular use Zn-doped Fe_3O_4 nanocubes (18.4 ± 1.3 nm) embedded in the capsule serve as the magnetic and heating core. Lattice-level Zn doping markedly enhances magnetic actuation and heating, yielding a saturation magnetization of 96.9 emu/g—substantially higher than conventional degradable magnetic materials.[2] This enables propulsion under a 30 mT static field and capsule dissolution within 40 s under magnetic heating. Ta nanoparticles provide X-ray contrast under a clinical C-arm, avoiding reliance on MRI or fluorescence imaging. The capsule can load diverse drugs (e.g., rtPA, doxorubicin, ciprofloxacin), and all material components have prior FDA clearance for intravascular applications, easing potential regulatory translation.

To achieve human-scale control, the team developed a dual-Navion electromagnetic navigation system producing a 1 T/m gradient and a 30 mT background field within a 20 × 20 × 20 cm^3 workspace compatible with standard angiography suites. The system supports three propulsion modes: rotating-field–induced rolling along a wall interface for low-flow environments, magnetic gradient–based pulling that can propel the capsule against flows up to 21.2 cm/s, and in-flow navigation in which physiological flow transports the capsule while magnetic gradients steer it into the desired branch under higher-flow regimes (Figure 1). Compared with ultrasound-powered microswarms[3] or torque-focusing steering strategies,[4] the Landers platform provides more consistent cross-scale operation.

Preclinical validation further demonstrates the translation potential of microrobots. In patient-specific, MRI-derived silicone vascular models, the microrobots were successfully navigated from the internal carotid artery into ACA, MCA, and M2 branches under physiological flow. In an MCA clot model, rtPA-loaded microrobots dissolved within 40 s after magnetic triggering, reperfusion occurred at

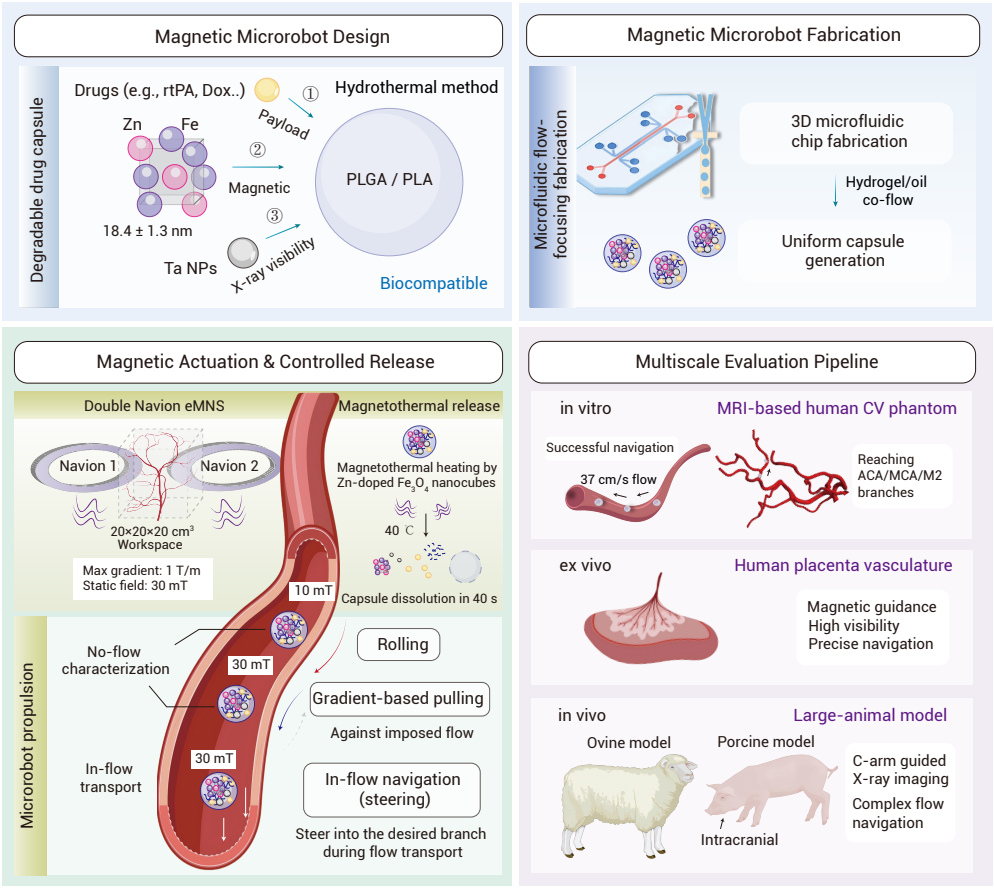

Figure 1. Design and workflow of the navion microrobotic platform and its electromagnetic navigation system (eMNS).

7.5 min, and produced substantial thrombus clearance by 19 min. Large-animal studies extend this work into sheep brain ventricles and porcine intracranial arteries, all three navigation modes were executed, with preprocedural MRI used for planning. Multiple capsules were sequentially delivered to target vessels via flow-assisted guidance, confirming reliable performance under true anatomic and hemodynamic conditions.

CORE INNOVATIONS AND MAJOR ADVANCEMENTS

Landers et al. report a major advance in magnetic microrobots by combining materials engineering with system-level integration, enabling the first demonstration of reliable operation at human- scales. Their work bridges the long-standing gap between laboratory feasibility and practical use in the human body, establishing the most clinically compatible magnetic microrobot platform to date. The core innovations can be summarized as three fundamental shifts.

First, the study presents a clinically coherent system architecture rather than incremental improvements to individual components. Previous work often focused on isolated advances in materials, actuation, imaging, or release mechanisms, without a unified platform capable of coordinated operation. In contrast, the Landers platform integrates a degradable capsule, Zn-doped magnetic nanomaterials, X-ray visibility, catheter-based delivery, and electromagnetic navigation, providing a clear technical pathway for clinical translation rather than a collection of disconnected capabilities.

Second, the study provides the first evidence that magnetic navigation can function under human-scale anatomy and physiological blood flow. Magnetic microrobots have long been constrained by rapid decay of field gradients beyond centimeter scales,[5] making most laboratory demonstrations difficult to generalize to *in vivo* conditions. Here, the authors maintain a 1 T/m gradient and 30 mT background field within a 20 × 20 × 20 cm^3 workspace and achieving rapid branch selection. (e.g., 53-100 ms at 37 cm/s ICA flow) with 95% success in an 84 cm/s Y-bifurcation model.

Third, the authors establish a cross-model validation framework aligned with clinical workflow. Beyond silicone vascular phantoms, they confirm visibility and magnetic response in human placental vessels, demonstrate fine control in the 3D sheep ventricular system, and achieve rolling, gradient pulling, and flow-assisted navigation in porcine intracranial arteries. In an MCA clot model, rtPA-loaded capsules were delivered precisely to the occlusion site, achieving magnetothermal dissolution with recanalization at 7.5 min and major thrombus clearance by 19 min—approaching clinical thrombolysis performance.

Overall, the significance of this study lies not in isolated performance metrics but in establishing that magnetic microrobots can operate and deliver therapy under clinically relevant anatomical, hemodynamic, and imaging constraints. This work defines the first clinically verifiable benchmark for the field.

CLINICAL PROSPECTS AND FUTURE CHALLENGES

Magnetically guided microrobots demonstrate therapeutic potential across several clinically scenarios. In flow-controlled *in vitro* models, the platform achieved millisecond-scale branch selection under a 37 cm/s ICA flow, entering the ACA at 53 ms, the MCA at 67 ms, and more distal branches by 100 ms. These speeds significantly outperform those of manual catheter manipulation and offer distinct advantages for time-critical conditions such as acute ischemic stroke. When loaded with rtPA, capsules were accurately delivered to an MCA clot and triggered to release the drug by magnetic heating, resulting in substantial thrombus clearance within 19 min. This demonstrates the feasibility of localized, high-efficiency thrombolysis with minimal systemic exposure.

Further validation supports the platform's robustness. The microrobot maintained stable visibility and magnetic actuation in *ex vivo* human placental vessels, navigated through the architecture of the sheep ventricular system, and achieved targeted delivery into multiple branches of porcine intracranial arteries. These results indicate that minimally invasive, potentially catheter-free interventions in high-flow cerebral vessels are achievable.

Despite these advances, clinical translation faces several challenges. The controllability of microrobots in diseased vasculature remains unproven. Although patient-specific 3D vascular reconstructions and MCA occlusion models represent important progress, these settings typically involve single-lesion geometries and fail to capture the broader spectrum of clinical pathology, including atherosclerotic plaques, irregular stenosis, calcification, anatomic variants, or prior interventions. Such features can significantly alter local shear profiles and flow vortices, potentially affecting capsule stability and target accessibility. To address the variability and unpredictability of clinical vasculature, the integration of deep learning-based adaptive navigation algorithms becomes essential. Real-time, closed-loop control is particularly required to accommodate patient-specific vascular geometry, pulsatile blood flow, and lesion morphology, which require adaptive navigation beyond preprogrammed paths. Furthermore, the current 1.7-mm capsule also approaches the diameter limit of distal branches, indicating that further optimization of size and mechanical safety margins will be needed for broader indications.

Long-term biocompatibility also requires systematic evaluation. Although all component materials are FDA-cleared for intravascular use, the degradation products generated under magnetothermal activation—and the long-term distribution, clearance kinetics, and potential neuroinflammatory effects of iron and tantalum nanoparticles —remain undefined. These factors will directly influence regulatory readiness and must be addressed through extended studies prior to early-phase clinical trials.

CONCLUSION

In summary, the study represents a pivotal transition for magnetic microrobotic technology, advancing from fundamental research toward clinical translation. By systematically addressing long-standing technical barriers including material biocompatibility, millimeter-scale navigation accuracy, multi-modal imaging integration, and spatiotemporally controlled drug release, this work establishes a comprehensive technological framework that sets a new paradigm for next-generation targeted drug delivery systems. The most forward-looking value of the platform lies in its groundbreaking "clinical-ready" design philosophy—aligned from the outset with clinical workflow, device compatibility, procedural safety, and regulatory requirements, rather than with maximizing laboratory performance, establishing a new benchmark for future intelligent medical robot development. With the increasing cross-disciplinary convergence of materials science, magnetic field control, real-time imaging, and intelligent navigation algorithms, magnetic microrobotic technology is poised to play an increasingly vital role in the era of precision medicine. Future research should focus on dynamic optimization of personalized treatment protocols, development of deep learning-based adaptive navigation algorithms, and implementation of large-scale multicenter clinical trials, thereby accelerating the full transition of this transformative technology from laboratory discovery to routine clinical practice.

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AUTHOR CONTRIBUTIONS

Yuan-Ting Huang and Zhi-Jun Li: visualization, conceptualization and writing. Yu Shi and Xiao-Qian Xu: visualization, writing and Supervision. All authors contributed to and approved the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.