INVITED PAPER

Magnetically Actuated Medical Robots: An *in vivo* Perspective

This article describes magnetically guided medical robots, both tethered and untethered, working at different scales and it analyses the in vivo *translation with increased control and safety.*

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ABSTRACT | The use of magnetic fields and field gradients to move magnetic material and devices within the human body has a surprisingly long history. Over the past two decades, there has been renewed interest in this area with the growth of magnetic medical microrobots. In this article, we focus on the state-of-the-art and future directions for magnetically actuated medical robots from an *in vivo* perspective. We initially review the history and relevant physics followed by a discussion on the limited *in vivo* research efforts that investigate magnetically guided devices. Our focus is on magnetically guided tethered probes, untethered devices (microrobots and nanorobots), and magnetic navigation systems that have been or could be utilized *in vivo* to provide increased control and safety for the physician and patient.

KEYWORDS | Catheters; endoscopes; magnetic guidance; magnetism; microrobots.

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I. INTRODUCTION

Microrobotics and magnetically actuated robots are two disciplines of robotics that are closely intertwined. Magnetically tipped endocardial ablation catheters guided by externally generated magnetic fields have been used to treat cardiac arrhythmias since 2003. The field of microrobotics has a more recent history although impressive strides have been made over the past decade as researchers have created a variety of small devices capable of locomotion within tissue and in liquid environments. Recent studies testing these small-scale devices *in vivo* offer hope for near-term clinical trials. The commonality between microrobots and magnetically actuated robots is that nearly all clinically relevant microrobots use externally generated magnetic fields for locomotion. This article summarizes the impact of magnetic actuation on surgical and interventional robotics. After a brief historical overview, we focus on magnetically steered catheters and endoscopes, untethered large-scale devices, and magnetically guided microrobots, discussing selected articles that focus on *in vivo* results or that present a clear path to *in vivo* applications. Following a short discussion, some of the limitations of translating current *in vitro* and *ex vivo* research to *in vivo*, and in particular clinical, procedures are presented.

A. Magnetics in Surgery Throughout History

The first account of using magnetism in a medical setting was reported in 600 BC. The Sushtra Samhita, an ancient Hindu medical and surgical text, describes the use of magnetite stones to remove iron fragments from wounded soldiers' bodies [1]. The text describes the ideal condition of the lesion in which the extraction can be performed and what kind of stone should be used. Other reports describing the use of magnetic stones for medical applications appeared throughout continental Europe. Their usage became somewhat commonplace even though the actual physical principles were not yet fully understood, resulting in some dubious applications of the technology [2]. In 1290 AD, Peter Peregrinus presented the first work investigating the mechanisms and properties of magnetized materials including magnetic needles and magnetic stones [1], [3]. In his "Epistola de magnete," Peregrinus investigated phenomena such as magnetization of different materials and the decay of magnetic force with distance. Peregrinus also hypothesized the existence of the North and South poles on magnets and their implication with respect to the Earth's poles.

The next milestone in the study of magnetism came 300 years later with "De Magnete" from William Gilbert. In his scientific treatise, Gilbert presented one of the first rigorous explanations of magnetism. Gilbert was also the first to introduce the modern definition of Earth's magnetic poles based on Peregrinus's previous observations. The definitive generalization of classic electromagnetism comes in 1861 with James Maxwell and his eponymous equations.

The first modern use of magnetism in a medical setting was presented by Dr. Julius Hirschberg in 1880 [1], [5], with his design of a handheld electromagnet for removing iron fragments from the human eye.

Following the experience of Dr. Hirschberg, many other ophthalmologists around the world adopted this technique and developed their own custom electromagnets for this purpose (see Fig. 1). It is only from the second half of the 20th century that the use of magnetism transcended the niche of ophthalmic use to broader clinical use. Tillander [6] was the first to demonstrate the advantages and opportunities offered by magnetic guidance in a broader clinical sense. In his 1951 work, Tillander demonstrated the use of magnetic fields to guide a surgical catheter inside the human body. Tillander pioneered the adoption of magnetic catheters as a possible alternative to traditional surgical tools. Following Tillander's work, magnetic catheters were tested for a number of procedures in different areas of the human body.

In 2003, Stereotaxis brought the first clinically approved magnetic navigation system (MNS) for steering magnetic catheters to market. Stereotaxis's MNS was used to treat the cardiac arrhythmia by steering a magnetic endocardial catheter to the heart to perform ablations on the heart wall [7]. To date, more than 140 000 cardiac ablation cases have been completed using the Stereotaxis systems [8]. A few years later, Sylvain Martel demonstrated the navigation of untethered robots *in vivo* in a porcine model. In his 2007 work, Martel navigated 1.5-mm-diameter iron beads inside the carotid artery of a living swine using a commercial magnetic resonance imaging (MRI) system [9].

In 2008, Kummer *et al.* [10] presented their work on an electromagnetic steering system for intraocular microrobot navigation for retinal procedures, 130 years after Dr. Hirschberg's work on electromagnets for eye surgery.

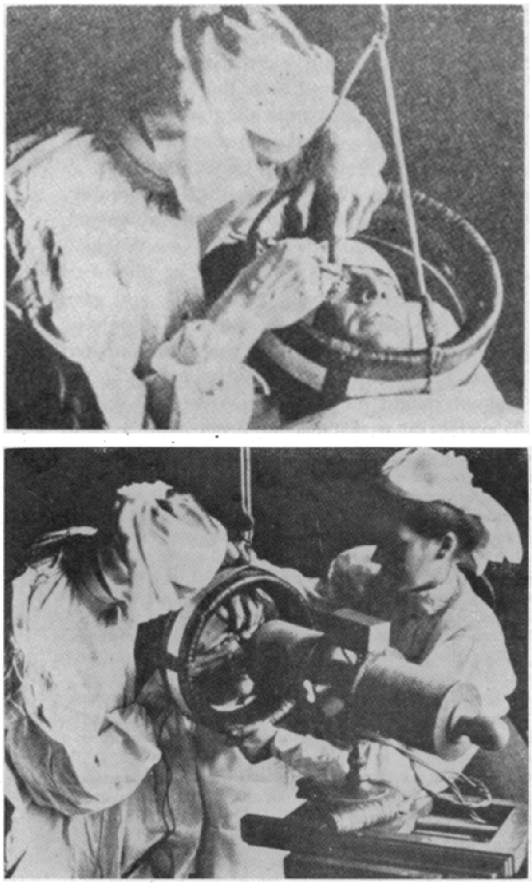

Fig. 1. ***Electromagnets used in ophthalmic surgery circa 1880. Top: Gifford's design using focusing magnetic cores. Bottom: Gifford ring magnet combined with a Haab magnet [4].***

Following Kummer *et al.*, Gang *et al.* [11] demonstrated the navigation of RF-ablation catheters inside ten pigs in 2011, establishing the capability of magnetic guidance *in vivo* for treating cardiac arrhythmias. In the same year, Carpi *et al.* [7] demonstrated the magnetic steering of an endoscopic capsule *in vivo* using magnetic control to improve upon original capsule-based endoscopy [12], [13]. In the subsequent year, Keller *et al.* [14] successfully demonstrated the guidance of a magnetic endoscopy capsule in 53 humans using a modified MRI. In their work, they demonstrated that magnetic steering greatly increases the effectiveness of endoscopic capsules. An interesting demonstration of *in vivo* microrobots was presented by Niedert *et al.* [15] in 2020, where a magnetically actuated tumbling strategy was used to guide a drug-loaded cylindrical robot in a rodent. Moving in a tumbling motion, the robot was capable of traversing the colon of the animal [15]. In 2021, Zhou *et al.* [16] demonstrated a bioprinting procedure *in vivo* using a magnetically controlled catheter in which 3-D silicone structures were printed inside a mouse while undergoing magnetic steering.

II. MAGNETICS FOR ROBOTICS

Magnetic fields are generally biocompatible and can freely transmit through the human body, making them excellent candidates for actuating catheters and microrobots for medical robotics applications [17]. The magnetic fields used for steering are commonly generated by an external machine called an MNS. MNSs are divided into two different schools of thought with respect to the generation of the magnetic fields. Historically, permanent magnets were used as external field generators, for example, for extracting iron shards from human eyes. The Niobe from Stereotaxis falls into this category and uses two large permanent magnets as field generators. The second category of MNS uses a fixed configuration of electromagnets to generate the external magnetic field. An example of this category is the system presented by Kummer *et al.* [10]. An MRI can also be used as an MNS, exploiting its strong dc fields and biasing fields, as demonstrated by the work of Martel *et al.* [9]. As magnetic manipulation using an MRI is quite different from other MNSs, we refer the interested reader to [18] and [19]. More recently, systems that use electromagnets mounted on robot manipulators have also been proposed [20]–[23].

For guiding magnetic catheters and magnetic microrobots, two reference quantities must be considered. The first quantity is the magnetic torque, defined by [24], [25]

$$\tau_{\mathbf{m}} = V_m \mathbf{M_m} \times \mathbf{B} \tag{1}$$

where τ_m is the vector representing the torques acting on the magnetic structure, V_m is the volume of the magnetic material embedded in the catheter or microrobot, $\mathbf{M_m}$ is the magnetization vector of the magnetic material, $\mathbf{B}$ is the magnetic flux density generated by the MNS, and $\times$ is the cross product. The torque generated can be used for steering the tip of a catheter in a specific direction or navigating the microrobots using helical motion. The second quantity is the magnetic force defined as

$$\mathbf{F_m} = V_m \cdot (\mathbf{M_m} \nabla)\, \mathbf{B}. \tag{2}$$

The magnetic force depends directly on the gradient ∇ of $\mathbf{B}$ and not the magnetic flux density itself. Equations (1) and (2) also demonstrate that both quantities are volume-dependent. Smaller magnetic volumes require higher fields and gradients to obtain the same magnetic torques and forces. The magnetic flux density $\mathbf{B}$ can be correlated with the magnetic field generated by the MNS following

$$\mathbf{B} = \mu_0 \mu_r \mathbf{H} \tag{3}$$

where μ_0 represents the permeability of free space, μ_r is the permeability of the media, and $\mathbf{H}$ is the magnetic field generated by the MNS. Equation (3) can be rewritten as

$$\mu_0 \mu_r \mathbf{H} = \mu_0 \left(1 + \chi\right) \mathbf{H}. \tag{4}$$

With the magnetic susceptibility expressed as $\chi = (\mathbf{M}/\mathbf{H})$, the magnetization vector $\mathbf{M}$ can, therefore, be rewritten as

$$\mathbf{M} = \chi \mathbf{H}. \tag{5}$$

From (5), it is beneficial to introduce the concept of hard and soft magnetic materials (see Fig. 2). Hard magnetic materials maintain their magnetization once exposed to an external magnetic field greater than the material's coercive field. The magnetization is retained unless a magnetic field stronger than the coercive field is applied in a different direction. Hard magnets are differentiated by their saturation magnetization, magnetic remanence, and magnetic coercitivity. NdFeB[1] alloys have the highest magnetic remanence of all hard magnetic materials. Since high magnetic remanence is fundamental for obtaining high magnetic torques (1), NdFeB alloys are currently the preferred choice for magnetic catheters. Given the biocompatibility requirements for magnetic microrobots, iron–platinum alloys have been recently proposed as a potential hard magnetic alloy [26]. Soft magnetic materi-

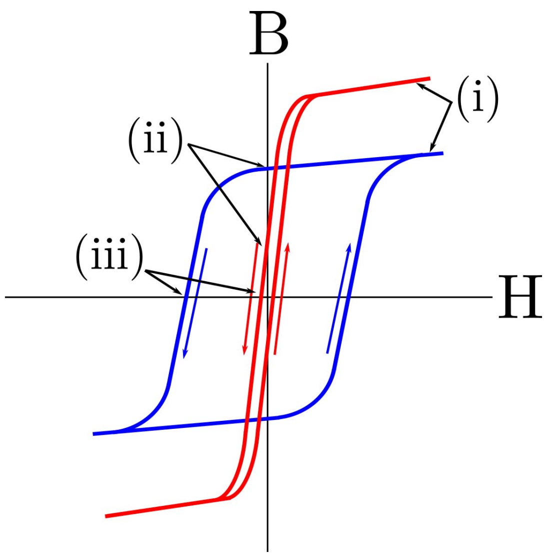

Fig. 2. *Hysteresis loop for magnetic materials. The red loop represents the hysteresis loop of a soft magnetic material with the characteristic high saturation (i) and small coercitivity (iii). The blue loop represents the standard behavior of hard magnetic material with high remanence (ii) and high coercitivity (iii). To obtain the highest possible M, it is necessary to reach the saturation magnetization of the material.*

[1] Neodymium–iron–boron.

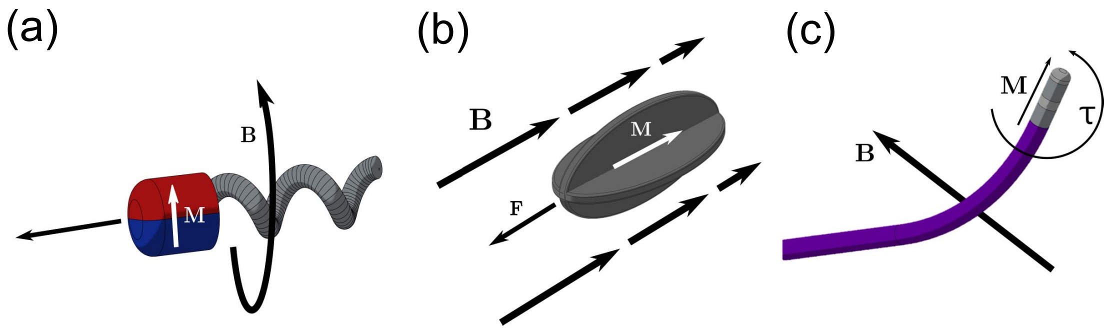

Fig. 3. ***(a) Corkscrew motion of a microrobot, the external magnetic field rotates the microrobot's tail, which translates the rotating motion to forward motion, (b) magnetic gradient-based movement, the forces generated by the magnetic gradient pull the microrobot in the direction of the applied gradient, and (c) deflection of a magnetic catheter tip under external dc magnetic field.***

als are mostly encountered in magnetic microrobot design and are defined by small coercitivity and high saturation magnetization. The current state of the art is based on iron and iron oxides as the magnetic material, given their high saturation magnetization and favorable biocompatibility features [27].

The interaction between the external magnetic field and the magnetic structure is dictated by the magnetization and geometry of the magnetic structure. Varying the geometry and magnetization can lead to different types of motion for the magnetic microrobot or catheter tip. The motion of a magnetic microrobot can be classified into two categories: magnetic field driven [see Fig. 3(a)] and magnetic field gradient driven [see Fig. 3(b)]. In gradient-driven actuation, the magnetic microrobot is directly accelerated by the force exerted through the magnetic field gradient, as defined by (2). This type of actuation is usually consigned to high-power systems as it is challenging to generate large magnetic gradients over long distances. Magnetic field-driven actuation is mainly based on alternating magnetic fields and rotating magnetic fields [28], [29]. Under these conditions, the magnetic field vector direction changes continuously, creating a constant torque on the microrobot. A common magnetic field actuation strategy uses a rotating field to induce a corkscrew motion on a magnetic microrobot of appropriate shape [30]. The corkscrew action allows motion in extremely low Reynolds numbers, enabling motion of a microrobot even in a creeping fluid regime. With respect to catheter motion, the main control challenges revolve around the minimum achievable bending radius of the catheter tip under an external field and the movement of the catheter itself. The movement of the catheter is primarily accomplished using a mechanical advancer since magnetic field gradient forces are insufficient [31], [32]. Maximum tip deflection is mainly dominated by the relation between the torque generated at the tip and the stiffness of the catheter body. Careful design of the catheter tip and catheter body is necessary to reach the desired deflections [33]–[36].

III. MAGNETIC NAVIGATION SYSTEMS

As described by (1) and (2), the magnitude of the magnetic field is a key parameter in the actuation of magnetically steered catheters [see Fig. 3(c)] and microrobots. The cubic decay of magnetic fields with distance makes the scaling up of *in vitro* experiments to *in vivo* procedures challenging with respect to the magnetic field generator, limiting the number of *in vivo* demonstrations using magnetic steering [17], [37], [38].

Tillander's work in 1951 was the first to propose the use of an electromagnet to generate the necessary magnetic torques [6]. Recently, the focus has been on the development of modern clinical MNSs with workspaces adequate for human clinical use [11], [17], [20], [22], [23], [39], [40]. In the 1990s, Stereotaxis Inc. was the first to focus on the development of MNSs for clinical use [41], [42]. Although their initial goal of steering thermal ablation seeds into brain tumors was not possible with their six-coil superconducting magnet design [43], [44], they were able to demonstrate successful steering of magnetically tipped microcatheters into the brain for biopsies [45]. The experiments were performed *in vivo* in pigs and used a magnetic field to control the orientation of the catheter tip, while the advancement was controlled mechanically. This system was subsequently redesigned into the current two-permanent-magnet configuration commercialized by Stereotaxis, which was first demonstrated for cardiac ablation in 2003. The system uses uniform magnetic fields to apply torque to the tip of the catheter, abandoning magnetic force completely [see Fig. 4(a)] [46]. Another *in vivo* commercial effort in magnetic navigation was established by Magnetecs. In 2011, they introduced their certified magnetic manipulation system based on eight electromagnets in a cubical arrangement. Similar to Stereotaxis, the magnetic field sources of the Magnetecs system are distributed around the surgical bed in a symmetrical fashion. The Magnetecs surgical bed can be moved in and out of the system to allow fluoroscopy. The Magnetecs system demonstrated electrophysiology (EP) procedures inside the human heart to address cardiac arrhythmia [11], [17].

Following Stereotaxis and Magnetecs developments, Aeon Scientific marketed a magnetic catheter steering system, the Aeon Phocus, for clinical use in 2015 [17]. The design is illustrated in [see Fig. 4(b)]. The two halves of the system can be moved away from the patient table to allow the physician access to the patient and the freedom to use an angiography system during the preparatory catheterization phase, as well as other types of procedures that are conducted in a typical EP laboratory. The magnetic field in the torso of the patient can be controlled from an X-ray-protected control room. Steering is conducted through a user interface that has a joystick and monitors. After manually inserting the catheters into the heart, the physician controls the ablation catheter from the control room, which permits remote continuation of the procedure. One of the key benefits of this method is the degree of maneuverability that can be achieved, as the catheter can be bent in the direction of the magnetic field with a small radius of curvature. With enhanced control, the catheter tip can be precisely positioned during the ablation phase of the procedure so that continuous ablation lines are achieved. This is illustrated in Fig. 4(c) for the case of pulmonary vein isolation, which is commonly applied for the treatment of atrial fibrillation. Another interesting approach was taken by Rahmer *et al.* [47] with their preclinical 16-coil magnetic particle imaging field generator system [see Fig. 4(d)]. While they have yet to demonstrate their system *in vivo*, their procedure and system are unique, as they can provide magnetic steering and imaging feedback simultaneously [47].

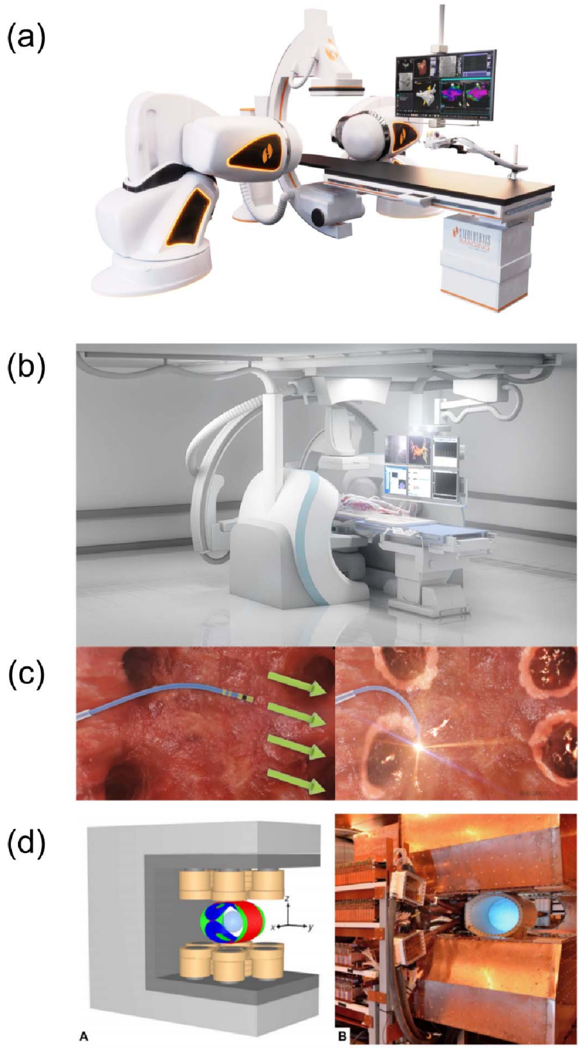

Fig. 4. ***(a) Stereotaxis' Genesis system based on two permanent magnets [48], (b) Aeon Phocus electroMNS, (c) pulmonary vein isolation for the treatment of atrial fibrillation using the Aeon Phocus, and (d) 16-coil MPI magnetic field generator, as described in [47].***

IV. MAGNETIC TOOLS

Historically, magnetic tools have been subdivided into two classes: tethered and untethered devices. Tethered devices are those tools that have a section of their body inside the patient's body but are not completely embedded in the body [17]. This refers to magnetic catheters, magnetic endoscopes, and magnetic probes. Untethered devices are those that are fully immersed in the human body during a procedure. Microrobots and nanorobots belong to this category, as well as magnetic particles and powders [29]. Magnetic catheters are typically designed based on traditional catheters. Recently, the focus has been on extending the capability of magnetic catheters by introducing new functionalities. In 2019, Kim *et al.* [49] demonstrated a novel method for producing self-lubricating soft magnetic catheters at the submillimeter scale. The magnetic catheter body was based on a soft PDMS body embedded with hard magnetic particles [49]. A hydrogel coating was applied to the catheter to promote slipping inside the vasculature. The soft magnetic catheter was navigated using an external permanent magnet. Using this configuration, they were able to navigate the soft magnetic catheter inside a brain vasculature model. Another approach was presented by Lussi *et al.* [50], who demonstrated a magnetic catheter for minimally invasive surgery that could change its stiffness on command. The magnetic catheter incorporated low-melting-point alloys in its structure [50], which featured phase changes at room temperature. The magnetic catheter employed a set of microcoils embedded in the section containing the low-melting-point alloys. The microcoils were used as heaters to phase change the LMPA and change the linear stiffness of the catheter. Using this capability, they demonstrated minimally invasive epiretinal membrane peeling, where the catheter was precisely guided above the retina using a custom MNS. An interesting combination of capabilities combined with an *in vivo* demonstration was performed by Zhou *et al.* [16] in 2021. In their work, they combined a magnetically guided catheter with a 3-D printing nozzle to print soft structures under magnetic control *in vivo*. Compared to other bioprinting methods, their proposed magnetic catheter featured a soft printing tip based on a polymeric body

(a)

(b)

(c)

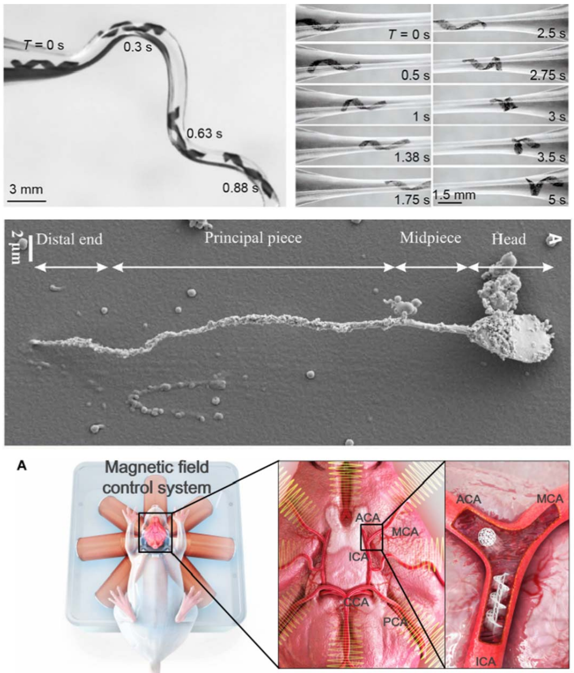

Fig. 5. ***Magnetic microrobots for targeted therapies: (a) adaptive locomotion of artificial soft magnetic microswimmers [52], (b) magnetite coated sperm cells [53], and (c) magnetic actuation of microrobots for stem cell transplantation in an ex vivo rat brain [54].***

embedded with magnetic particles. An inner lumen was utilized to pass different customized functional inks. Magnetic control was performed using four moving permanent magnets to induce translation and rotation of the 3-D printing magnetic catheter tip, in which a conductive hydrogel was bioprinted on a rat liver.

Compared to their tethered counterparts, untethered magnetically actuated devices are small, motile devices that utilize external magnetic fields for motion (see Fig. 5) and have the potential to enable minimally invasive treatment and high-precision targeted drug/cell delivery. For active drug delivery strategies, these machines can locally concentrate therapeutic payloads around pathological sites to reduce the dose of administered drugs and their systemic side effects [51]. As shown in Fig. 5, microrobots have numerous other applications for healthcare, particularly for localized diagnostics and treatment in areas filled with bodily fluids.

Over the past decade, a broad range of drug delivery systems based on nanomaterials, including liposomes, dendrimers, nanoparticles, polymer micelles, polymer–drug conjugates, and metal organic frameworks [55], [56], have been studied, and these materials have been incorporated into magnetic microrobots [29], [57]. Due to their small size and controllable mobility, they can be steered inside the human body to perform biomedical tasks, such as minimally invasive surgery, biomaterial extraction, and drug delivery [51], [58]. For targeted drug delivery, swimming microrobots can act as an active carrier for therapeutic agents and transport them directly and precisely to diseased tissue, thereby improving therapeutic efficacy and reducing the side effects.

More recently, the concept of deformable, shape-changing microrobots has emerged. Smart materials are designed to change their physical or chemical properties upon the application of an external stimulus, such as heat, mechanical stress, the concentration of certain chemical species, light, ultrasound, or magnetic and electric fields. Examples of materials that fall into the "smart" category include shape-memory alloys [59] and polymers, magnetostrictive [60] and piezoelectric compounds [61], hydrogels [62], and chromogenic materials [63]. Stimuli-responsive hydrogels [64]–[68] are promising material candidates for soft magnetic microrobots. These materials are usually biocompatible, mechanically deformable, and sensitive to environmental changes [69]–[71].

V. EXPERIMENTATION *in vivo*

Recent work on magnetic catheters and magnetic soft microrobots has comprehensively investigated characteristics such as biodegradability, biocompatibility, dexterity, and usability, and has been either *in vitro* or *ex vivo* [29], [51], [57], [58]. However, these types of demonstrations can, at best, be considered a proof of concept and lack the complexity of long-term *in vivo* testing. For example, the interaction of a magnetic catheter or microrobot with human blood and human vasculature, or the substantial differences between young and old tissue, is difficult to capture *in vitro* or *ex vivo* but can significantly impact the translation of the *in vitro* procedure to clinical use [40], [72], [73]. Currently, there remains a substantial lack of *in vivo* procedures using magnetic guidance. Only a few recent efforts attempt to provide *in vivo* demonstration [11], [15]–[17], often relying on testing in small rodents. Although these animal models can offer valuable insight into *in vivo* issues, they are quite different from a human patient, particularly with respect to scale. Large porcine models offer a more realistic experience for the human counterpart in certain procedures, such as in cardiology, but have associated disadvantages, including high cost and intensive infrastructure requirements [74]–[76]. Often, only specialized centers have the equipment and personnel necessary for *in vivo* porcine testing. The shift from *in vivo* rodent testing to larger mammals, such as pigs or sheep, further limits MNSs with limited working space. Due to the scaling nature of magnetic fields with distance [24], [25], it is challenging to generate large magnetic fields over a large work space in a practical manner. For this reason, demonstrations conducted with MNSs with limited work spaces can become infeasible when considering translation to human use, as it may not be possible to generate the required magnetic fields or field gradients. Based on these considerations, we believe that widespread adoption of magnetic navigation as a clinical tool requires that the following points should be addressed to form a bridge between *in vitro* lab testing and *in vivo* clinical use:

1) demonstrations *in vivo* at the same scale as clinical applications using magnetic instrumentation, while considering the limitations imposed from surgery in an actual operating room on a human patient;
2) design and realization of smaller, higher energy density magnetic manipulation systems that are easily installed in an operating room and fully compatible with other operating room equipment.

A. Magnetic Instrumentation Applications *in vivo*

Applications pursued *in vivo* have the intrinsic disadvantages of being expensive, time-intensive, and requiring substantial infrastructure. If the procedure is to be conducted on a large mammal, such as a pig, a full animal laboratory is often required, including the relevant medical personnel. However, the results of an *in vivo* test can often identify the limitations of the procedure and give greater credibility to the usefulness and feasibility of the proposed method when considering clinical translation. The medical research community must strive toward presenting work that is tested *in vivo* and provide frameworks that simplify this testing. Future emphasis should be placed on forming larger *in vivo* test centers that can be used and supported by a number of researchers, where the maximum number of tests is performed on individual animals, thereby reducing the number of animals required. Another possible avenue could be to systematically investigate the differences between specific procedures performed *in vitro* to their *in vivo* counterparts. For example, current studies that investigate blood-catheter-vessel wall interactions focus on *in vitro* demonstrations or simulations without fully exploring the translation to the *in vivo* case [77], [78]. The goal of such an investigation would be to create datasets containing all the pertinent characteristics of the environment of that specific procedure. Based on this data, standardized *in vitro* tests could be designed to allow objective comparison between different efforts and provide a direct correlation to similar *in vivo* procedures. While this would not substitute proper *in vivo* testing, it could help select, through objective comparison, those procedures that should move toward a full *in vivo* study and possible clinical application. In addition, this study could also lead to the discovery of unique *in vivo* related effects (e.g., flow characteristics) that could potentially be used to design better magnetic tools.

B. Next-Generation Magnetic Navigation Systems

Although most current research in magnetically actuated robotic systems is primarily focused on magnetic tools, this is only part of the problem. For successful translation to *in vivo* procedures, external magnetic manipulation systems also require additional investigation and research. Current preclinical and clinical systems tend to be bulky and complex (see Fig. 4) [7], [11], [17], [48]. Their large size requires a dedicated operating room with extensive infrastructure, limiting the use of the operating room to operations requiring the MNS. These requirements are a disincentive for hospitals in acquiring bulky MNSs.

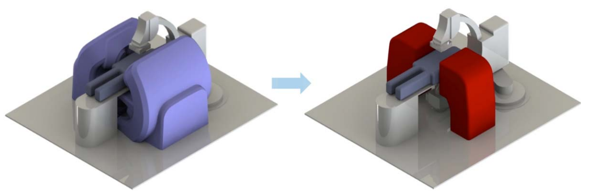

Fig. 6. ***Size comparison of a current MNS to a future MNS. Although magnetic performance is key to successful procedures, space and infrastructure requirements play an important role in the acceptance of new systems in the operating room. Future MNSs will be required to generate fields and gradients comparable to current systems but with diminished spatial and infrastructure requirements.***

For electromagnet-based MNSs, higher energy densities are required for future MNSs in order to reduce the size and footprint of future systems. These will allow a reduction of the system size, making it practical for a hospital operating room (see Fig. 6).

Another advantage of smaller systems is that they can be mobile, which allows them to be brought into an operating room without the need to alter the room layout or infrastructure, which permits seamless integration into the overall surgical workflow. Another possibility is mobile magnetic systems that can be wheeled into the outpatient clinic to adjust the position of implanted probes, e.g., for patients with pain stimulators who need to readjust the position of the stimulator. Permanent magnet MNSs would also benefit from a reduction in size and could offer a satisfactory solution when cooling for high-power-density electromagnets is not available. Strategies for safe cooperation between the medical staff and the moving permanent magnets would also have to be investigated. To reduce operating costs independent of the method used to generate the magnetic field, the simplification and user-friendliness of the infrastructure required for operating the system will also be critical for future MNS adoption.

VI. CLINICAL APPLICATIONS: FUTURE PROCEDURES

Clinical application is the ultimate goal for the technologies presented here. Cardiac ablation has paved the way for routine clinical use of MNSs [79]. Magnetically guided endoscopic procedures also encourage research and substantial *in vivo* experimentation, partly due the accessibility of the digestive system [15], [80]–[85]. Given the abundance of research in this area, the interested reader is redirected to [86]–[88]. In several other medical areas, promising advances are being made toward clinical translation although there remains a general lack of *in vivo* demonstrations. In the subsequent subsections A and B, we propose two areas that we believe could benefit from a more concentrated effort in translating *in vitro* and *ex vivo* demonstrations to *in vivo* preclinical procedures.

A. Magnetically Steered Probes for Stereotactic and Functional Neurosurgery

Stereotactic and functional neurosurgery is the neurosurgical subspecialty that focuses on the planning of trajectories to access targets in the central nervous system. In these procedures, probes are inserted through an access point and guided to the desired location to retrieve tissue for biopsy, modulate neuronal function, or ablate tissue [89]. Currently, this is being done for the treatment of movement disorders (Parkinson's disease, essential tremor, dystonia, and so on), pain (spinal cord stimulation, peripheral nerve stimulation, and so on), epilepsy, and tumor ablation [90]. A major restriction for the functional neurosurgeon is that the preplanned trajectory can only be followed in a linear fashion. With the current technologies, curved trajectories are not permitted. This significantly reduces the surgeon's ability to: 1) plan trajectories that bypass obstacles en route to the target and 2) obtain flexibility at the target itself, e.g., the surgeon cannot rotate the probe at the target to ablate a certain aspect of an epileptogenic focus [91] or adjust the target for a deep brain stimulation procedure without having to remove the probe and reinsert a new trajectory. These limitations have encouraged the development of the first prototype of a neuromodulation electrode [92]. This initial work and subsequent proof-of-concept studies demonstrated that the development of magnetically guided neurosurgical needles and navigation strategies could lead to a significant improvement in the DBS procedure [93]–[95]. Demonstrations *in vivo* could reinforce the advantages demonstrated in the proof of concepts and attract more practitioners toward magnetically guided DBS procedures.

B. Magnetically Guided Neurovascular Catheters

Vascular neurosurgery encompasses the treatment of pathologies originating from blood vessels in the central nervous system. These pathologies include strokes, aneurysms, arteriovenous malformations, dural arteriovenous fistula, and others [96]. Treatment can be done through open neurosurgery or less invasive endovascular neurosurgery, in which the surgeon inserts a catheter into the vasculature and guides the probe to the area comprising the pathology [97]. Currently, clinicians use manual control when inserting catheters and/or performing endovascular catheter-based diagnostic and therapeutic procedures [98]. The manual approach is limited by the variability of the patient's anatomy, especially for tortuous vasculature. This is further limited by an increasing number of branching points making accurate navigation of the catheter challenging. In some instances, it becomes unachievable when a sharp radius of curvature is needed or remote distal locations are targeted [97], [99]. This shortcoming has considerable clinical consequences for the patient. In the example of a thrombectomy for stroke, it can prolong the time for clot retrieval, even up to the point that no treatment is offered to the patient due to the inability to steer the catheter to the desired site [100]. Both prolonged treatment time and the inability to treatment can result in a functional loss for the patient, worsened clinical outcomes, and an immense socioeconomic burden. Magnetic navigation is a powerful tool to address these unmet clinical needs. Compared with a surgeon's manual control, magnetic navigation of endovascular catheters not only permits the endovascular surgeon to steer the catheter through sharp curves but also permits significantly improved dexterity since the technology allows precise steering, regardless of the number of branching points or how far away the target is located from the entry point. In addition, the use of MNSs could improve patient outcomes for regions that do not have a dedicated stroke or aneurysm center by exploiting telesurgery. In this application, a surgeon stationed in a specialized center could teleoperate on a patient in a more remote hospital, providing treatment to the patient that would otherwise not be available.

VII. CONCLUSION

The field of medical robotics is experiencing a resurgent interest in magnetically guided therapeutic devices. One reason for this is because surgery is increasingly shifting toward a minimally invasive approach in which surgeons access through a small opening and operate within narrow corridors, making the benefits of magnetic guidance compelling. Magnetically guided surgical instruments have the potential to meet a critical clinical need in the era of minimally invasive surgery and could represent an extended arm to the surgeon, permitting operation at angles and curves that would otherwise be challenging for the surgeon to achieve. Recent work has demonstrated that impressive strides have been made in increasing the capabilities of tethered and untethered devices, including improved drug loading, biocompatibility, bioreabsorbility, improved dexterity, and increased safety for the patient. However, the number of *in vivo* demonstrations is limited to a few recent efforts. Due to the significant differences that can be encountered when moving from *in vitro* and *ex vivo* to a preclinical *in vivo* procedure, the translation of recent scientific work to common clinical practice must be carefully considered. In the near term, significant research efforts must be invested in investigating MNSs for human use, moving away from the smaller systems useful only in the engineering laboratory. In the long term, the medical robotic community should strive toward implementing more *in vivo* experimentation by developing frameworks and collaborations. Focusing on *in vivo* demonstrations will have the additional benefit of allowing researchers to verify their work in the most realistic conditions possible before clinical application. This also exposes medical personnel to state-of-the-art medical robotics, further aiding in the translation of the technology. This exposure will help forge better connections between engineering research and clinical needs with the end goal of improving patient outcomes. ■

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