1 Title: Magnetic soft micro-fiberbots for robotic embolization

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- 32 Abstract: Cerebral aneurysms and brain tumors are leading life-threatening diseases worldwide. 33 By deliberately occluding the target lesion to reduce the blood supply, embolization has 34 been widely used clinically to treat cerebral aneurysms and brain tumors. Conventional 35 embolization is usually performed by threading a catheter through blood vessels to the target 36 lesion, which is often limited by the poor steerability of the catheter in complex 37 neurovascular networks, especially in submillimeter regions. Here we propose magnetic 38 soft micro-fiberbots with high steerability, reliable maneuverability, and multi-modal shape 39 reconfigurability to perform robotic embolization in submillimeter regions via a remote, 40 untethered, and magnetically controllable manner. Magnetic soft micro-fiberbots are 41 fabricated by thermal drawing magnetic soft composite (i.e., hard-magnetic particles 42 dispersed in thermoplastic matrices) into micro-fibers, followed by magnetizing and 43 molding procedures to endow a helical magnetic polarity. By controlling magnetic fields, 44 magnetic soft micro-fiberbots exhibit reversible elongated/aggregated shape-morphing and 45 helical propulsion in flow conditions, allowing for controllable navigation through complex 46 vasculature and robotic embolization in submillimeter regions. We performed 1) in vitro 47 embolization of aneurysm and tumor in neurovascular phantoms and 2) in vivo embolization 48 of a rabbit femoral artery model under real-time fluoroscopy. They demonstrate the 49

- 50 potential clinical value of our work, paving the way for a new embolization scheme in 51 robotic settings.
- 52 **One-Sentence Summary:** We present magnetic soft micro-fiberbots that can perform robotic 53 embolization in blood vessels in vivo in a remote, untethered, and magnetically controllable 54 manner.

56 Main Text:

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58 INTRODUCTION

59 Cerebral aneurysms and brain tumors are leading causes of mortality, killing more than 750,000 people annually worldwide (1-2). Before an open surgery is administered, 60 embolization recently has become a prevailing minimally invasive treatment for cerebral 61 aneurysms and brain tumors (3-4). In a typical embolization, a surgeon inserts a slender 62 guidewire/catheter into the femoral artery of the patient and manually pushes/twists it to the 63 target lesion in the brain through the blood vessels, followed by the delivery of embolic 64 agents to block the target lesion (5-7). For example, a surgeon delivers metallic coils (e.g., 65 soft platinum) through the catheter to seal off the cerebral aneurysm, which stabilizes the 66 aneurysm and minimizes the risk of rupture. Particulate (e.g., polyvinyl alcohol beads) is 67 another common embolic agent in tumor embolization. As the catheter is pushed into the 68 feeding vessels of a tumor, particles are delivered to cut off the blood supply to the tumor, 69 starving the tumor for accelerated tumor removal (8-15). However, current embolization by 70 pushing/twisting a passive guidewire/catheter with a preshaped tip is often limited by its 71 low steerability through complex vascular networks, i.e., the guidewire/catheter has a great 72 challenge in turning to bifurcation branches of blood vessels. As a result, embolic agents 73 may not be accurately delivered to the target lesion, leading to safety complications such as 74 blockage of normal vessels. In addition, the surgeon suffers from the accumulated radiation 75 when manually pushing/twisting the guidewire/catheter under the X-ray imaging. Therefore, 76 there has been a high demand for a next-generation embolization technique with high 77 steerability for targeted delivery of embolic agents and a remotely controllable operation for 78 a radiation-free workplace. 79

Recently, active robots that can be remotely steered in the blood vessel have shown great 80 promise in robotic embolization (16-27). One widely used strategy is designing 81 guidewire/catheter robots with an active tip that can bend in response to external stimuli 82 such as hydraulic pressure (19), electricity (20), and magnetic fields (21-25). For example, 83 Kim *et al.* have developed a guidewire robot with a ferromagnetic tip that can bend by 84 remotely applying magnetic fields (22). Such an active guidewire robot has shown enhanced 85 steerability in blood vessels and the capability of delivering embolic agents to an aneurysm 86 (23). However, maneuvering guidewires/catheters (regardless of passive and active tips) 87 intrinsically requires tethered operation (e.g., pushing for advancement), which is of great 88 difficulty when the slender guidewires/catheters are highly distorted, buckled, and looped 89 in confined and tortuous blood vessels. This difficulty gets even more pronounced when the 90 target lesion locates in the submillimeter regions. To address this issue, another strategy is 91 to develop small-scale untethered robots that can navigate blood vessels as a substitute for 92 guidewires/catheters. For example, flow-driven magnetic swarm (28), magnetic particles 93 (29), and magnetic anchors (30) have been reported for potential application of tumor 94 embolization in submillimeter regions. However, being passively carried by blood flow, 95 these untethered robots lack reliable maneuverability for navigation in flow conditions, 96 97 which may lead to severe complications of nontargeted embolization (31-32). Although many other unterhered robots (e.g., sheet-shaped magnetic robots and magnetic stents) have 98

- shown improved navigation capability (e.g., adaptive locomotion) in flow conditions (3334), they have not been demonstrated for robotic embolization due to the limited shapemorphing ability at the target lesion. Therefore, to the best of our knowledge, there is no
 systematic study of active robots that demonstrates high steerability in tortuous blood
 vessels (especially in submillimeter regions), reliable maneuverability in flow conditions,
 and shape-morphing capability at target lesions (see Table S1).
- 105 Here, we present magnetic soft micro-fiber robots (hereafter referred to as micro-fiberbot) with enhanced steerability, reliable maneuverability, and shape reconfigurability to perform 106 robotic embolization in a remotely controllable manner (Fig. 1A and Movie S1). Magnetic 107 soft micro-fiberbots are in a helical geometry with a customizable diameter (denoted as D 108 in Fig. 1B) that can be compatible with existing catheters to maximize their clinical 109 effectiveness. A standard catheterization can be first performed by threading a commercial 110 catheter through blood vessels until the intravascular advancement is stopped. Thereafter, 111 the micro-fiberbots can be deployed into blood vessels through the catheter. Enabled by the 112 contact friction, the micro-fiberbot can anchor to the blood vessel after deployment, without 113 being flushed away by blood flow. By remotely applying magnetic fields, the micro-fiberbot 114 can be actively steered in the blood flow (both upstream and downstream) via helical 115 propulsion. The micro-fiberbots can be elongated for passing narrow regions and aggregated 116 at the target lesion. The aggerated micro-fiberbot can either block the blood flow to the 117 target aneurysm/tumor or protect the normal blood vessel, allowing for three embolization 118 applications: aneurysm coil embolization, tumor coil embolization, and tumor particle 119 embolization (Fig. 1A). We demonstrate both in vitro embolization of aneurysm and tumor 120 in neurovascular phantoms and in vivo embolization of a rabbit femoral artery model under 121 real-time fluoroscopy. As a supplement to conventional catheter-based embolization, our 122 work presents a significant advancement for the minimally invasive treatment of cerebral 123 aneurysms and brain tumors in a robotic setting. 124

125 **RESULTS**

126 Shape-morphing capability

The magnetic composite is first prepared by uniformly dispersing neodymium-iron-boron 127 (NdFeB) microparticles in a thermoplastic matrix (poly (styrene-b-(ethylene-co-butylene)-128 b-styrene), SEBS)). The volume fraction of NdFeB is 20%. Using a thermal drawing 129 technique (Fig. 1B and Fig. S1), straight magnetic micro-fibers with various diameters 130 (denoted as d in Fig. 1C) are fabricated. By applying an impulse magnetic field (2.5T), the 131 straight magnetic micro-fiber can be fully magnetized along the fiber direction. Thereafter, 132 by coiling around a cylindrical mold and demolding after curing, the straight micro-fiber 133 can be transformed into a magnetic soft micro-fiberbot with a helical magnetization **M** along 134 its body. By changing the geometry of the cylindrical mold, the helical pitch p (Fig. 1B), 135 and helical diameter D (Fig. 1D) of micro-fiberbots can be readily tuned. A representative 136 micro-fiberbot with $d=60 \ \mu\text{m}$, $p=800 \ \mu\text{m}$, and $D=800 \ \mu\text{m}$ is selected for demonstrating 137 embolization in submillimeter regions in this work (Fig. 1E). 138

When the micro-fiberbot reaches a vessel segment that has an inner diameter (denoted as H) slightly smaller than that of the micro-fiberbot, it will anchor to the blood vessel due to the contact friction, without being flushed away by the blood flow (Fig. 2A). Finite element simulation validates the total contact friction is larger than the fluidic drag force (Supplementary Text, Fig. S2). Despite the sufficient friction force, the maximum contact pressure with the vessel wall is as low as 4.3 kPa, which is much smaller than the threshold pressure for rupturing the blood vessel (12 kPa (*35-36*)). The helical magnetization profile

M endows the micro-fiberbot with a net magnetization (denoted as M_{net} in Fig. 2A) along 146 its central axis. By applying an actuation magnetic field **B** that has the same direction as 147 M_{net}, the micro-fiberbot is elongated. The helical diameter gradually reduces as the 148 magnetic field strength increases (Fig. S3). Conversely, when **B** is opposite to \mathbf{M}_{net} , the 149 micro-fiberbot is aggregated (Fig. 2A and Movie S2) and its length gradually reduces as the 150 magnetic field strength increases (Fig. S3). Such an aggregation/elongation shape-morphing 151 is fully reversible even after 1000 cycles as validated by three micro-fiberbots with different 152 153 pitches (Fig. S4). More impressively, the micro-fiber can still recover its helical shape even after a compression test under a rigid punch, manifesting a high elasticity and robustness 154 (Fig. S5). 155

156 Magnetic maneuverability in flow conditions

- Fig. 2B illustrates the strategy for magnetically maneuvering the micro-fiberbot in flow 157 conditions. A cubic magnet (5×5×5 cm, residual magnetic flux density $\mathbf{B}_{\mathbf{r}} = 1.38$ T) is 158 adopted as an actuation source (Fig. S6-S7). The magnet is manipulated by a 6-DoF robotic 159 arm that can precisely control its current position denoted as (x, y) in the xyz coordinate 160 system, axial rotation (rotating axis parallel with x-axis), and in-plane rotation (in xy 161 plane)(Fig. S8). The rotating magnetic fields allow for high flexibility for manipulating 162 untethered magnetic soft micro-fiberbot (37). By axially rotating while moving the magnet 163 leftward, we can maneuver the micro-fiberbot to the left via helical propulsion. Aside from 164 high flexibility of control, such a helical propulsion motion is different from direct pulling 165 mode by magnetic body force $\mathbf{f} = (\mathbf{M} \cdot \nabla)\mathbf{B}$ where a large magnetic field gradient $\nabla \mathbf{B} =$ 166 $[\partial \mathbf{B}/\partial \mathbf{x}, \partial \mathbf{B}/\partial \mathbf{y}, \partial \mathbf{B}/\partial \mathbf{z}]^{\mathrm{T}}$ is required (38-40). When the micro-fiberbot reaches the target 167 lesion, by rotation of 90° in the xy plane, we can generate a local actuation magnetic field **B** 168 opposite to \mathbf{M}_{net} , leading to the aggregation shape morphing. If further magnetic pulling 169 operation is needed, we can further rotate the magnet in the xy plane by 45° to generate a 170 field gradient $\nabla \mathbf{B}$ as shown in Fig. S7. Therefore, the body force **f** will pull the micro-171 fiberbot to move with the magnet (38). This magnetic pulling maneuvering will finally allow 172 us to pull the aggregated micro-fiberbot to fill the aneurysm for embolization application. 173 Corresponding actuation magnetic fields in each maneuvering process are shown in Fig. S6 174 and detailed magnetic maneuvering processes by the robotic arm equipped with a rotating 175 permanent magnet are presented in Movie S3. 176
- To validate the shape-morphing and magnetic maneuvering of the micro-fiberbot in flow 177 conditions, we prepare a vessel phantom with an inner diameter H=800 μ m and fill it with 178 simulated blood (50% glycerol solution, viscosity 4 mPa·s). The flow rate is set as 100 mm/s 179 via a pump system to mimic the typical blood flow in submillimeter regions of 180 neurovascular networks (41). We first show that the micro-fiberbot can stably anchor to the 181 vessel in the absence of magnetic fields (Fig. 2C). By tuning the strength and the frequency 182 of the rotating magnetic field, the helical propulsion velocity can be adjusted (Fig. S3C). If 183 the simulated blood is not flowing, the helical propulsion velocity of the micro-fiberbot can 184 reach up to 1.6 mm/s under a rotating magnetic field B=40 mT at a frequency of 5 Hz. When 185 the flow rate is 100 mm/s, the upstream and downstream helical propulsion velocities of the 186 micro-fiberbot change to 0.32 mm/s and 1.75 mm/s, respectively. It is also worth noting that 187 the aggregated micro-fiberbot can also anchor to the blood vessel when the magnetic field 188 is removed due to friction. This anchoring capability at the aggregated state allows the 189 micro-fiberbot to be further pulled by applying a magnetic field gradient $\nabla \mathbf{B}$ that generates 190 magnetic body force f. For example, by tuning the magnet's orientation of 45° in the xy 191 plane, the aggregated micro-fiberbot can be further pulled inside the vessel (Fig. 2C). The 192 helical shape of the micro-fiberbot is recovered when aligning the magnetic field **B** with a 193

194net magnetization M_{net} . It is also worth noting that such shape-morphing and propulsion195capabilities may not be seriously affected by the size of the micro-fiberbot. We show that a196micro-fiberbot with a 500 µm diameter still preserves comparable upstream propulsion197velocity with that of the 800 µm micro-fiberbot in flow conditions up to 200 mm/s flow rate198(Fig. S9, Movie S4).

199 Catheter-assisted deployment

200 Considering that there is a long way from the incision (usually at the femoral arteries) to the target lesion in the brain, our micro-fiberbot can be combined with existing medical 201 catheters to reduce the operation time while increasing the embolization safety. Here, a 202 representative medical catheter (MicroVention Terumo, tip inner diameter ID=0.027 inch 203 (685 μm), distal outer diameter OD=2.6 F (866 μm), Fig. 1E) is selected for demonstrating 204 the catheter-assisted deployment (Fig. 3). We show that the micro-fiberbot ($D=800 \mu m$) can 205 be easily injected into the catheter via a 200 µm-needle syringe (Fig. 3A). Due to the elastic 206 nature and high robustness, the highly coiled micro-fiberbot can quickly recover its helical 207 shape after injection (less than 1s). In the absence of magnetic fields, perfusing saline into 208 the catheter will push the micro-fiber to travel inside the catheter (since the diameter of the 209 micro-fiberbot D is smaller than the inner diameter of the catheter H). When traveling inside 210 the catheter, the micro-fiberbot can be readily tracked by X-ray imaging (Fig. 3B). Although 211 the catheter cannot directly reach the target lesion, it still paves a safe way for the micro-212 fiberbot to approach the target lesion as close as possible. Thereafter, the micro-fiberbot 213 will be remotely maneuvered by magnetic fields to complete the rest journey to the target 214 lesion. 215

A blood vessel phantom with bifurcation branches (fabricated using a sacrificial template 217 method, Fig. S10) is selected as an example (Fig. 3C, D). The mechanical properties 218 (Young's modulus 2 MPa) and contact friction coefficient (0.1) are carefully tuned to mimic 219 that of human blood vessels. Assume that the catheter can only reach the main blood vessel 220 and two target lesions located on the bifurcation branches. To reach target 1, the micro-221 222 fiberbot can be released at the first bifurcation in the main vessel. Thereafter, the microfiberbot can be magnetically maneuvered to target 1 by helical propulsion, followed by on-223 demand aggregation. Similarly, to reach target 2, the catheter can be first threaded to the 224 second bifurcation, and the micro-fiberbot is then released, magnetically steered, and 225 aggregated at target 2. Detailed catheter-assisted deployment is shown in Movie S5. By 226 combing with existing medical catheters, the clinical effectiveness of the micro-fiber can be 227 maximized by reducing magnetic maneuvering, especially when multiple micro-fiberbots 228 need to be deployed. In comparison, we show that without the micro-fiberbot, the catheter 229 can only reach the second bifurcation. If coils are directly delivered at the second bifurcation, 230 targeted embolization cannot be ensured (Fig. S11). 231

High steerability in submillimeter regions

The steerability of soft robots in blood vessels is often characterized by the angle of 234 bifurcation branches and the diameter of the accessible blood vessel (see Table S1). To 235 demonstrate the high steerability in submillimeter regions, we fabricate two phantoms of 236 blood vessels (Fig. 4) with uniform diameter $D=800 \ \mu m$. The first phantom has two 237 bifurcation branches with angles of 30° and 60° (Fig. 4A), respectively, and the second 238 phantom has two bifurcation branches with angles of 90° and 120° (Fig. 4B), respectively. 239 It clearly shows that the micro-fiberbot can easily turn to the bifurcation branches of 30° via 240 downstream helical propulsion. By reversely rotating the magnet, the micro-fiberbot can 241 return via upstream helical propulsion. This reverse maneuvering implies that, if the micro-242

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fiberbot goes into a wrong branch vessel, it can be readily re-oriented to the right track. 243 244 After that, the micro-fiberbot can be further maneuvered to a bifurcation branch vessel with 60° . In the second phantom, since the bifurcation angles are large, the micro-fiberbot needs 245 to first turn its "head" into the branch vessel under a rotating magnetic field. Thereafter, a 246 magnetic field **B** parallel to \mathbf{M}_{net} is applied to stretch the micro-fiberbot, dragging it into the 247 branch vessel. Once the whole body is steered to the bifurcation branches, the stretched 248 micro-fiberbot quickly recovers its helical shape, continuing the helical propulsion in the 249 250 branch vessel (Movie S6). In addition to the high steerability in large-angle bifurcation vessels, we further demonstrate that the micro-fiberbot can simply pass through a narrowing 251 vessel with a minimum diameter of 100 µm in Fig. 4C and Movie S7. The micro-fiber is 252 stretched by applying a parallel magnetic field so that it can pass the narrowing vessel with 253 the flow. Considering that real blood vessels are three-dimensional (3D), we further present 254 the steerability of the micro-fiberbot in an S-shaped (Movie S8) and 3D blood vessel 255 phantom (Movie S9) in Fig. 4D and E, respectively. Both results show that the micro-256 fiberbot can be quickly steered through the blood vessel phantom. In contrast, we 257 demonstrate that the commercial catheter cannot be directed to the bifurcation and 258 narrowing branches as shown in Fig. S12. 259

In vitro demonstration of robotic embolization

To demonstrate the potential for treating cerebral aneurysms and brain tumors, we first 262 perform robotic embolization demonstrations in submillimeter neurovascular vessel 263 phantoms, which include aneurysm coil embolization (Fig. 5A, B), tumor coil embolization 264 (Fig. 5C, D), and tumor particle embolization protection (Fig.5E-H). The first blood vessel 265 phantom (H =800 μ m) has a dilated aneurysm (Fig. 5A) and the second blood vessel 266 phantom has three bifurcation branches with thinner diameters (H = 500μ m) that are labeled 267 as branch 1, branch 2, and branch 3, respectively (Fig. 5C-H). In aneurysm coil embolization, 268 the micro-fiberbot is first helically propelled to the aneurysm and then transformed into the 269 aggregated state. Via magnetic pulling, the aggregated micro-fiberbot can be pulled to fill 270 the aneurysm (Fig. 5A and Movie S10). It is evident that the flow to the dilated aneurysm 271 is significantly reduced after the aneurysm is filled (Fig. 5B). In tumor coil embolization, 272 branch 2 is assumed to be tumor vessel while branch 1 and branch 3 are healthy blood 273 vessels (Fig. 5C). A micro-fiberbot is first magnetically steered to branch 2 and aggregated. 274 But it is found that only one aggregated micro-fiberbot cannot completely occlude branch 2 275 (Movie S11). Therefore, a second micro-fiberbot is deployed for a dual aggregation in 276 branch 2. Compared with one aggregated micro-fiberbot, two aggregated micro-fiberbots 277 significantly increase the blocking ratio (defined as the cross-sectional area of the micro-278 fiberbots divided by the blood vessel, Fig. S13) that almost blocks flow in branch 2 after 279 embolization (Fig. 5D). Here, the dual aggregation is enabled by the independent actuation 280 of each micro-fiberbot in sequence. As shown in Fig. S6, the rotating magnetic field for 281 helical propulsion is zero along the M_{net} direction (i.e., Bx=0 in the x-direction), while 282 elongation/aggregation requires $Bx \neq 0$. Therefore, when one micro-fiberbot is already 283 aggregated at the target lesion, the magnetic field for helical propulsion of subsequent 284 micro-fiberbots will not affect the already aggregated one, allowing for even quadruple-285 aggregation at the same target (Fig. S14) and occlusion at multiple blood vessel branches 286 (Fig. S15 and Movie S12). In tumor particle embolization protection, branch 2 and branch 287 3 are assumed as tumor vessels while branch 1 is a healthy vessel (Fig. 5E). To prevent the 288 embolic particles from flowing into healthy branch 1, a micro-fiberbot is first magnetically 289 steered to branch 1 and aggregated. Then embolic particles (average diameter 250 µm) are 290 291 released into the flow to selectively occlude branch 2 and branch 3 (Fig. 5F). Note that few particles may still be able to pass through the occluded area with one aggregated micro-292

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fiberbot. To achieve a large blocking ratio, dual aggregation can be performed, and the block
ratio can reach up to 90% (Fig. S13). After the particle embolization is completed, the
aggregated micro-fiberbot can be recovered and safely retrieved (Fig. 5G and Movie S13).
It is confirmed that the tumor vessels (branch 2 and branch 3) are successfully occluded
while the healthy vessel (branch 1) is perfectly protected (Fig. 5H).

298 In vivo demonstration of robotic embolization in a rabbit

299 We further demonstrate in vivo robotic embolization of a rabbit blood vessel on the right hind leg (diameter is from 500 µm to 800 µm) under real-time fluoroscopy (Fig. 6A). The 300 micro-fiberbot is first injected into the femoral artery through a Terumo 2.6Fr catheter (Fig. 301 6B). The tortuous vessel is marked with 4 sites (Fig. 6C). Guided by fluoroscopic imaging 302 (X-ray), the micro-fiberbot is helically propelled from site 1 to site 4 (Fig. 6D) and then 303 returned to site 2 and eventually aggregated at site 2 (Fig. 6E and Movie S14). To validate 304 the completed embolization, we then obtain the angiography of the femoral artery by 305 injecting iodinated contrast media (Fig. 6F). Before embolization, we can see iodinated 306 contrast media throughout the femoral artery, suggesting a normal flow in the artery. After 307 embolization, no contrast media is observed due to the blockage of the flow by the 308 aggregated micro-fiberbot (Fig. 6G and S16). The presence of the aggregated micro-fiberbot 309 blocks the blood flow from the proximal to the distal end of the vessel, which leads to the 310 formation of thrombosis inside the artery, as validated by the histological analysis two 311 weeks after embolization (Fig. 6G, H). It is worth noting that no inflammation or 312 pathological abnormalities are observed from the hematoxylin-eosin (H&E) staining results 313 of the main organs including the lung, liver, spleen, kidney, and heart after two weeks (Fig. 314 S17) and compared with an untreated control group, the levels of numbers of blood cells 315 (RBCs, white blood cells, platelets, and lymphocytes) of robotic embolization procedure 316 remained at normal levels after three weeks (Fig. S18), suggesting that the proposed robotic 317 embolization by magnetically steering micro-fiberbots is safe. 318

319 **DISCUSSION**

320 Conventional embolization surgery by threading passive catheters to the target lesion is largely limited by the low steerability in complex blood vessels (especially in submillimeter 321 regions) and accumulated radiation risk by manual operation. As a significant advancement, 322 we develop magnetic soft micro-fiberbots that can perform embolization with high 323 steerability by remotely controlling a 6-DoF robotic arm. With a helical magnetization along 324 its body, the micro-fiberbot can be magnetically steered via helical propulsion in blood 325 vessels and perform on-demand aggregation at the target lesion to occlude the blood flow. 326 Using demonstration in submillimeter neurovascular vessel phantoms and in vivo rabbit 327 femoral artery, we validate the potential for performing robotic embolization. 328

Our micro-fiberbots are still in their infancy, and we provide the following considerations 329 for their clinical translation in the future. First, we have only demonstrated a micro-fiberbot 330 with $D = 800 \mu m$ for embolization in submillimeter blood vessels in this work. Actually, 331 332 the helical diameter D of the micro-fiber can be effectively tuned by changing the geometry of the cylinder mold (Fig. 1B). If large aneurysms or blood vessels are encountered, micro-333 fiberbots with higher diameters may be selected. Also, we have shown that two aggregated 334 micro-fiberbots can significantly enhance the blocking rate (Fig. S13), thus multiple micro-335 fiberbots can be deployed to the target lesion, if needed. Second, although the soft matrix 336 of SEBS has been approved by U.S. Food and Drug Administration (FDA) for intravascular 337 applications (42), the ferromagnetic NdFeB particles may induce safety concerns for long-338 term implantation. In this regard, we can first coat a protective layer of pure SEBS shell by 339

thermal drawing technique (Fig. 1) and then dip coat a thin layer of hydrogel (15 μ m) on 340 the whole body of the micro-fiberbot to enhance biocompatibility and hemocompatibility 341 (Fig. S19). This protection layers coating technique has been widely adopted to reduce the 342 toxicity of the NdFeB-embedded composites (22,23,34,43-45). According to the cell 343 viability test and hemolysis assay, we show that the hydrogel skin can significantly reduce 344 toxicity (cell viability 96%, Fig. S20) and hemolytic effect (hemolysis 1%, Fig. S21). Third, 345 to realize the precise control of micro-fiberbots in tortuous blood vessels, an advanced 346 347 positioning system is required. In addition to the fluoroscopy, we show that our microfiberbot can also be tracked using ultrasound imaging. An ex vivo demonstration in a 348 porcine blood vessel is provided to validate the tracking capability under ultrasound imaging 349 (Fig. S22). Other approaches such as photoacoustic computed tomography may also be 350 helpful to obtain higher spatiotemporal resolution (46). Last but not least, a faster thrombus 351 formation is always desired for occluding the blood flow, leading to a successful 352 embolization. In this regard, we present two potential solutions that have been reported in 353 the literature for enhancing embolization efficiency. The first solution is to coat the micro-354 fiberbot with thrombin (47) such that blood cells can be absorbed onto the micro-fiberbot. 355 as validated by the reduced blood clotting index and scanning electron microscope images 356 in Fig. S22. The formed thrombus can resist a pressure of up to 22 kPa, which is large 357 enough for blocking the blood flow in vivo (Fig. S23). The second solution is to further coat 358 the micro-fiberbot with a thin functional layer (20 µm) of iron oxide (Fe₃O₄) nanoparticles 359 that can generate heat upon radiofrequency (RF) stimulation (Fig. S19). By remotely heating 360 the aggregated micro-fiberbot at the target lesion via RF coil (200 kHz), we can generate 361 local hyperthermia that promotes thrombus formation. In vitro demonstration in the blood 362 vessel phantom shows that a thrombus can be formed within 5 min (Fig. S24). The 363 mechanism of local hyperthermia-induced thrombus formation lies in the activation and 364 aggregation of platelets. When the temperature increases to about 41 °C, platelets are 365 activated in vivo and aggregated to form a thrombus. This mechanism has been widely 366 reported in the literature (48-51) and is also validated by our experiments in which the 367 activated coagulation time of the porcine blood decreases as the temperature rises from 37 368 to 50°C (Fig. S26). In summary, we envisage that our magnetic soft micro-fiberbots will 369 pave the way for the unterhered robotic embolization of cerebral aneurysms and brain 370 tumors in the future. 371

372 MATERIALS AND METHODS

Fabrication of magnetic soft micro-fiberbots. In the experiment, the ferromagnetic 373 Neodymium Iron (NdFeB) particles with an average diameter of 5 µm were purchased from 374 Guangzhou XND Co., Ltd., the soft elastomeric matrix styrene-ethylene-butylene-styrene 375 (SEBS) materials (Kraton G1657) were purchased from KRATON Co., Ltd., the supporting 376 polycarbonate (PC) pellets (Makrolon ET3113) was purchased from Covestro AG Co., Ltd. 377 All materials were used as received. The ferromagnetic NdFeB particles were mixed in a 378 pre-dissolved SEBS/Hexane solution (14.3 vol.%) with a volume ratio of 1:4 between 379 NdFeB and SEBS. After mechanical stirring for 30 min and ultrasonic dispersing for 1 hr, 380 381 the NdFeB/SEBS/Hexane suspensions were poured and doctor-bladed on PTFE films and dried in a fume hood for 10 hr. After fully dried, the resulting NdFeB/SEBS thin films were 382 pealed from PTFE and cut into small slices of magnetic SEBS (M-SEBS). For M-SEBS 383 core fabrication, the yielded M-SEBS slices were loaded in mold between a 384 thermocompressor (Qien, Wuhan Qien Sci. & Tech. Co., Ltd.) and thermally pressed at 180°C 385 into M-SEBS cylinders. For supporting PC cladding fabrication, the fully dried PC pellets 386 387 were loaded in mold between the thermocompressor and thermal pressed at 230°C into cuboids. The PC cuboids were latterly lathed and drilled into PC tubes with an inner 388

diameter slightly larger than M-SEBS cylinders. The yielded M-SEBS cylinders were 389 390 inserted into PC tubes for a monolithic preforms. The magnetic composites were prepared through the dispersion of unmagnetized magnetic microparticles (e.g., neodymium-iron-391 boron, NdFeB) in soft elastomeric matrix (e.g., poly (styrene-b-(ethylene-co-butylene)-b-392 styrene), SEBS) through chemical solution. Due to the limited drawability of the soft 393 magnetic elastomer composite, we induced thermoplastic polycarbonate (PC) as sacrificial 394 cladding for co-drawing. After thermal consolidation in a LEGO-like way, the preforms 395 consisting of a magnetic soft core and sacrificial cladding were later thermally drawn into 396 magnetic microfibers with different diameters (Fig. 1C) at 230°C in a custom thermal draw 397 tower. 398

Thermal drawing of magnetic microfibers. The resulting preforms consisted of M-SEBS 400 core and PC cladding were thermally drawn into M-SEBS/PC fibers, referred to as magnetic 401 fibers, at 230°C in a custom thermal drawing tower. With a drawing ratio between 100 to 402 200, the diameter of magnetic fibers can be tuned between 20-90 μ m. To enhance the 403 functionality of micro-fiberbot, the functional layer was induced to the soft core perform. 404 The performs consisting of a magnetic soft core (M-SEBs) and a functional layer (Fig. S19). 405 The functional layer can be chosen according to different situations. For example, to 406 enhance biocompatibility and hemocompatibility, a pure polymer protect layer can prevent 407 corrosion of ferromagnetic particles (e.g. NdFeB). In addition, to enhance the embolization 408 efficiency, a functional layer containing iron oxide (Fe₃O₄) nanoparticle can promote 409 thrombus formation via RF heating. 410

412 **Mechanical testing.** The $80 \times 80 \times 2$ mm M-SEBS thin film was cut into dumbbell test 413 specimens using a standard part cutter. The mechanical testing was subjected to standard 414 test methods (ASTM D412) on a mechanical testing machine at a displacement rate of 5 415 mm/s (width: 8 mm; gauge length: 60 mm).

Fabrication of magnetic soft micro-fiberbots. The magnetic microfibers were first 417 magnetized by a 2.5 T impulse magnetic field generated by a digital pulse magnetizer 418 419 (Beijing Eusci Technology Ltd). The fibers with PC cladding were then wrapped with identity helical parameters on a high thermal conductivity rod by tweezers. Adhesive tape 420 was applied to ensure that the fiber was tightly contacted with the rod. The rod around with 421 microfibers was then placed on a hot plate at 90°C for 30 min. After the magnetic microfiber 422 was molded into helical-shaped structure, the robots were detached from the rods. sacrificial 423 PC cladding was chemically selectively removed by N, N-Dimethylacetamide (Sinopharm 424 425 Chemical Reagent Co., Ltd) until the cladding was completely dissolved. Finally, the robot was cut into desired structure parameters. 426

Ex vivo experiments under real-time ultrasound imaging. The medical imaging system 428 compatibility of magnetic soft micro-fiberbot was demonstrated in a porcine coronary artery 429 ex vivo under real-time ultrasound imaging. The porcine hearts were obtained from 430 Shenzhen Advanced Medical Services Co. Ltd. A solution of glycerol (Sigma-Aldrich) in 431 deionized water was used as a blood analog (Viscosity is 4 mPa·s) and the arteries were 432 connected to a programmable pump (Longer Pump) to create the bloodstream (100 mm/s). 433 The wireless portable ultrasound probe (SonoStar) with a maximum of 14 MHz was used 434 for real-time guidance of the magnetic soft micro-fiberbot. After injection into the artery, 435 the magnetic soft micro-fiberbot is magnetically actuated to swim with the flow to the 436 437 targeted site. When the magnetic field was removed, the magnetic soft micro-fiberbot is anchored to the target blood vessel wall while withstanding the flow. The ultrasound 438

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imaging in pulse repetition frequency mode verified the anchoring of the robot in dynamic
flow. The magnetic soft micro-fiberbot is also magnetically actuated to swim against the
flow and retrieved by a catheter inside the artery vessels.

Hydrogel skin fabrication. The dip-coating methods were used to create a hydrogel laver 443 on the magnetic soft micro-fiberbot. The monomer of the hydrogel layer was acrylamide 444 (AAm) (Sigma-Aldrich, A8887). The silane coupling agent was 3-(trimethoxysilvl) propyl 445 methacrylate (TMSPMA). For 1 mL solution of AAm (2 moles per a liter of DI water, 2 mol 446 L^{-1}), 1 µL of CTA (10% volume ratio in THF), 10 µL of acetic acid (0.1 moles per a liter 447 of DI water, 0.1 mol L^{-1}), and 5.7 µL of TMSPMA are added, followed by vortex mixing 448 for 60 s, and then 50 mg of Thrombin (2000 u/mg, Shanghai Yuanye Bio-Technology Co., 449 Ltd.) was added. The bare magnetic fiber was treated with plasma within the 60 s to form 450 the network of hydrophilic groups. The treated magnetic fiber was fixed to a home-made 451 machine and immersed in the pre-gel solution (Fig. S23). Lastly, the hydrogel-coated 452 microfiber is sealed in a bottle with saturated humidity and stored in an oven at room 453 temperature for 24 h. 454

Cell toxicity assay. Human cardiac microvascular endothelial cell line was cultured and 456 removed from the flask using enzymatic digestion (trypsin/EDTA). The cell suspension was 457 centrifuged at 1000 rpm for 5 min. Resuspend the cell suspension in medium to adjust the 458 density to 1×10^5 cells/ml. Use a multi-channel pipette to add 100 µL of medium to the 459 peripheral wells of a 96-well tissue culture microtiter plate, and add 100 µL of cell 460 suspension at a density of 1×10^5 cells/ml to the remaining. Cells were incubated for 24 h (5%) 461 CO₂ at 37°C, >90% humidity) to exponential growth. The medium was aspirated after 24 h 462 of incubation. To evaluate the cell toxicity of M-SEBS composites, 100 µL of the 100% of 463 sample leaching solution including negative control, positive control, bare magnetic fiber, 464 and hydrogel-coated magnetic fiber were added for treatment. Cells were incubated for 465 another 48h (5% CO₂ at 37°C, >90% humidity). After removing the co-cultured material 466 and replacing the medium, 10 µL CCK-8 solution (AR1199, Boster, China) was added to 467 each wall, and the plate was placed on a microtiter plate photometer (Multiskan FC, Thermo 468 Scientific) equipped with a 450 nm filter to measure the absorbance. The cell viability was 469 calculated according to the following equation 470

Cell viability (%) =
$$\frac{C_{\text{sample}} - C_{\text{blank}}}{C_{\text{control}} - C_{\text{blank}}} \times 100\%$$

Where C_{sample} is the absorbance of sample, C_{sample} is the absorbance of control (without sample), C_{blank} is the absorbance of blank group.

Live/dead assay. Human cardiac microvascular endothelial cell line was cultured and 475 removed from the flask using enzymatic digestion (trypsin/EDTA). The cell suspension was 476 centrifuged at 1000 rpm for 5 min. 5 x 10⁵ cells were inoculated in each well of a 6-well 477 plate and incubated in a CO₂ incubator (5% CO₂ at 37°C, >90% humidity) for 24 hours to 478 allow the cells to adhere to the wall. Subsequently, the medium was removed and 2 mL of 479 the sample leaching solution from each group was added to the 6-well plate and incubation 480 was continued for 48 hours. After washing the cells twice with PBS buffer, 0.5 mL of 481 staining solution (KTA1001, Abbkine, China) was added to each well and incubated for 15 482 min at 37°C protected from light. After washing 2 more times with PBS, the cells were 483 placed under a fluorescent microscope and photographed. 484

Hemolysis rate assay. 20 mL of newly collected immune blood (Shenzhen Advanced
Medical Services Co. Ltd.) was added with 1 mL of 20 g/L potassium oxalate to prepare
fresh anticoagulated immune blood. Take 8 mL of fresh anticoagulated rabbit blood and

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dilute it with 10 mL of normal saline. Weigh 3 samples of 5 g each. After rinsing with tap 489 490 water, rinse with distilled water, absorb the water with filter paper and put it in a test tube, add 10 mL of normal saline to each tube; for the negative control, add 10 mL of normal 491 saline of the same batch number to each tube; for positive control, add 10 mL of distilled 492 water to each tube. To evaluate the Hemolysis rate of M-SEBS composites, two groups 493 including bare magnetic fiber and hydrogel-coated magnetic fiber were added 0.2 mL of 494 diluted rabbit blood for treatment and placed in a 37°C water bath and continue to incubate 495 for 60 min. Pour out the liquid in each tube and centrifuge for 5 min (2500 r/min). and the 496 absorbance was measured with a spectrophotometer at a wavelength of 545 nm. The 497 hemolysis rate was calculated according the following equation 498

Hemolysis rate (%) =
$$\frac{H_{sample} - H_{neg}}{H_{pos}} \times 100 \%$$

500 Where H_{sample} is the absorbance at 545 nm of the sample, H_{neg} is the absorbance of negative 501 group, and H_{pos} is the absorbance of positive group.

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504 **Blood clotting index test:** First, 10 mg of pure hydrogel coating and thrombin hydrogel coating micro-fiberbot, was placed into the polypropylene dish, and pre-warmed at 37°C for 505 5min. Second, 4.5 mL of fresh anti-coagulated porcine blood was added with 0.5 mL of 0.1 506 mol/L solution of Calcium Chloride to prepare fresh blood samples. Third, 100 μ L of the 507 blood was coated onto the materials immediately for 10 s. Then, 10 mL of deionized water 508 was added to the dish and shaken at 50 rpm for 10 min to lyse RBCs that were not stuck in 509 510 the clot. The absorbance of the resulting hemoglobin solution (sample) was measured at 540 nm by a MultiSkan microplate reader (Multiskan GO, Thermofisher scientific), and 511 absorbance of 100 uL of clotted whole blood in 10 mL of deionized water was used as the 512 control Finally, the Blood clotting index of different materials was calculated using the 513 following equation: 514

Blood clotting index (%) = $\frac{S_{sample}}{S_{control}} \times 100 \%$

Preparation of RBC solution: A volume of 5 mL of fresh anti-coagulated porcine blood was taken into a blood centrifuge tube. RBCs were centrifuged at 200 g for 20 min at room temperature and the supernatant was gently removed. RBCs were washed three times with 500µl 1× PBS solution and finally resuspended with 500µl 1× PBS.

523 In vivo animal experiment setup.

The 8- to 10-week-old male New Zealand rabbits, weighing 1.5 to 2.0 kg, were obtained 524 from Shenzhen Advanced Medical Services Co. Ltd. The ethical approval from the 525 Institutional Animal Care and Use Committee was obtained prior to the research (AMS 526 C2305004 R). The rabbit was anesthetized before the embolization procedure. The femoral 527 artery is exposed through a small incision, and then the femoral artery is accessed using a 528 standard 22-gauge needle and a 4-Fr sheath (Glidesheath, Terumo). Under fluoroscopic 529 guidance (DSA, CGO-2100, Wandong), the iodinated contrast media is released to obtain 530 the blood vessel frame and the magnetic soft micro-fiberbotwas gently injected into the 531 artery through a 2.6-Fr catheter (Headway 27TM microcatheter, Terumo). The rotating 532 magnetic field was generated by a cubic NdFeB magnet (50 mm in diameter and 50 mm in 533 height). The magnetic soft micro-fiberbots were reliable steered and navigated in a helical 534 propulsion manner in the blood vessel. After the robot contracted into an aggregation state, 535

the magnetic field was removed and iodinated contrast media is gently released to obtain
the angiography (See Fig.6). Then, the catheter and sheath were removed, and the wound
was sutured. After two-week of post-surgery, tissue sections in embolization regions were
prepared and stained with H&E for histological examinations.

Analysis and simulation. Magnetic fields around a cubic magnet are calculated using 541 commercial software COMSOL Multiphysics 6.0. Finite element simulations of shape 542 543 morphing of micro-fiberbot were conducted using commercial software ABAQUS/Standard 2017. The NdFeB embedded magnetic composite was modeled as the 544 ideal hard-magnetic soft material with shear modulus 1 MPa and residual magnetization 545 M = 120 kA/m. To account for the interaction between magnetic composite with embedded 546 NdFeB particles and the external magnetic field **B**, we adopted a user element (UEL) 547 subroutine based on the continuum framework (52,53). The magnetic torque density τ can 548 be implemented by computing the magnetic Cauchy stress $\sigma^{\text{magnetic}} = -B \otimes FM$ where F is 549 the deformation gradient and operator \otimes represents a dyadic product that takes two vectors 550 to yield a second-order tensor. The blood vessel is simplified as a rigid tube. The contact 551 between the micro-fiberbot and the blood vessel is modeled as "Hard contact, No 552 penetration" with a friction coefficient of 0.1. All simulations are checked with convergence. 553

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555	55 Supplementary Materials								
556	Supplementary Text								
557	Fig. S1. Fabrication and characterization of magnetic soft micro-fiberbots.								
558	Fig. S2. Analysis of the anchored state of micro-fiberbot in flow conditions.								
559	Fig. S3. Characterization of micro-fiberbots with a helical diameter of 800µm under varying								
560	magnetic parameters.								
561	Fig. S4. Reversibility test of the shape morphing of the micro-fiberbot.								
562	Fig. S5. High elasticity and mechanical robustness of the micro-fiberbot.								
563	Fig. S6. Control strategy of micro-fiberbot using a cubic magnet.								
564	Fig. S7. Spatial magnetic gradient distribution of a cubic magnet with a width of 50 mm.								
565	Fig. S8. Magnetic maneuvering system.								
566	Fig. S9 Demonstration of shape-morphing capability and in-flow maneuverability of micro-								
567	fiberbot with 500 µm diameter.								
568	Fig. S10. Fabrication of blood vessel phantoms.								
569	Fig. S11. Demonstration of nontarget coil embolization using a commercial catheter.								
570	Fig. S12. Demonstration of the low steerability of a commercial catheter.								
571	Fig. S13. Comparison of the blocking ratio between one micro-fiberbot aggregation and dual								
572	aggregation by two micro-fiberbots.								
573	Fig. S14. Demonstration of four micro-fiberbot achieve quadruple-aggregation at the same								
574	target site in a vessel phantom.								
575	Fig. S15. Demonstration of micro-fiberbots achieve aggregation in different vessel branches.								
576	Fig. S16. Angiography of the rabbit blood vessels after 21 days embolization.								
577	Fig. S17. Histology analysis of main organs of rabbits after two-week embolization surgery.								
578	Fig. S18. Comprehensive blood cell counts taken from a rabbit before and after embolization								
579	(24h, 72h, 21 days).								
580	Fig. S19. Fabrication of coating hydrogel skin.								
581	Fig. S20. Cell viability tests of magnetic composites with different coatings.								
582	Fig. 521. Analysis of blood cell hemolysis of positive control, negative control, dare micro-								
583	Fig. S22. Ex vive demonstration of real time ultracound treaking conshility of micro fiberbot.								
584 595	Fig. S22. EX vivo demonstration of real-time utilasound tracking capability of micro-inderdot.								
303 506	Fig. S24. Pressure assessment of the micro-fiberbot within a vessel phontom								
200 587	Fig. S24. Flessure assessment of the filero-fiberbot within a vessel phantom.								
588	thrombus formation								
589	Fig. S26. Thrombus formation when incubated in different temperatures								
590	Table S1 Comparison between this work and existing embolization procedure								
591	Movie S1. Overview movie of magnetic soft micro-fiberbots for robotic embolization								
592	Movie S2. Shape morphing capability of micro-fiberbots under magnetic fields.								
593	Movie S3. Magnetic maneuvering of micro-fiberbot in flow condition.								
594	Movie S4 Demonstration of shape-morphing capability and in-flow maneuverability of								
595	micro-fiberbot with 500 um diameter.								
596	Movie S5. Catheter-assisted deployment of micro-fiberbots.								
597	Movie S6. Demonstration of micro-fiberbots steering in bifurcation branches of blood vessel								
598	phantom.								
599	Movie S7. Demonstration of micro-fiberbots steering in a narrowing blood vessel phantom.								
600	Movie S8. Demonstration of micro-fiberbots steering in an S-shaped blood vessel phantom.								
601	Movie S9. Demonstration of micro-fiberbots steering in a 3D blood vessel phantom.								
602	Movie S10. In vitro demonstration of aneurysm embolization								
603	Movie S11. In vitro demonstration of tumor coil embolization.								
604	Movie S12. Dual-aggregation of micro-fiberbots								

- 605 Movie S13. In vitro demonstration of particle embolization protection and retrieval. 606 Movie S14. In vivo demonstration of robotic embolization in a rabbit.
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- Author contribution: J.Z., G.T., G.-Z.Y., and X.L. conceived the idea and designed the research.
 X.L. and Y.X. performed the thermal drawing experiments. X.L. and F.L constructed the
 experimental platform. X.L., F.L, N.L., performed other experiments and analyzed the data. L.W.

and X.L. performed the theoretical analysis and numerical calculations. X.L., L.W, Y.X., G.-Z.Y.,
G.T. and J.Z. wrote the manuscript with input from all authors. All authors participated in drafting
the manuscript, discussing, and interpreting the data.

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Competing interesting: J.Z. and X.L. have a provisional patent application on the fundamental
 principles and designs of transforming untethered magnetic soft micro-fiberbot for endovascular
 intervention. The other authors declare that they have no competing financial interests.

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Data and materials availability: All data are available in the main text or the supplementary
 materials.



Fig. 1. Magnetic soft micro-fiberbots for robotic embolization. A, Schematic illustration of 768 functionalities and potential applications of magnetic soft micro-fiberbots. The micro-fiberbot can 769 770 anchor to a blood vessel after being released, navigate inside the blood flow via helical propulsion, pass through narrow regions by elongation, and block the blood flow by aggregation. The 771 aggregated micro-fiberbots can be used as embolic agents for coil embolization of aneurysms and 772 tumors, as well as a protection device for selective particle embolization of tumors. **B**, Fabrication 773 process of magnetic soft micro-fiberbots: thermal drawing of magnetic soft micro-fiber, 774 magnetizing by a strong impulse magnetic field (2.5 T), and molding/demolding into a helix shape. 775 C, Optical imaging of magnetic soft micro-fibers with different fiber diameters denoted as d. D, 776 Optical images of magnetic soft micro-fiberbots with different helical diameters denoted as D. Scale 777 bar, 1mm. E, An image of magnetic soft micro-fiberbots deployed via Terumo 2.6Fr catheter to the 778 surface of the brain phantom. Scale bar, 5 mm. 779



Fig. 2. Shape-morphing capability and magnetic maneuverability in flow conditions. A, The 781 micro-fiberbot can anchor to the vessel in the absence of magnetic fields. By further applying static 782 magnetic field **B** parallel to its net magnetization (denoted as M_{net}), the magnetic soft micro-fiberbot 783 can have reversible elongated and aggregated states. Scale bar, 1 mm. B, Schematic illustration of 784 manipulating the micro-fiberbot by controlling a cubic magnet with a 6-DoF robotic arm. The 785 786 helical propulsion is enabled by axially rotating the magnet (rotating axis is parallel with x-axis), while magnetic pulling is enabled by rotating magnet in the xy plane. C, Experimental pictures 787 show that the micro-fiberbot (d = 60 um, p = 800 um, and D = 800 um) can steadily anchor to a 788 vessel phantom (inner diameter $H = 800 \mu m$) in the absence of magnetic fields, 789 upstream/downstream helical propulsion under rotating magnetic fields (B = 40 mT, frequency 5 790 Hz), and magnetic pulling under magnetic field gradient and recover to the helical shape. 791



Fig. 3. Catheter-assisted deployment of the micro-fiberbot. A, The micro-fiberbot can be injected into a commercial catheter with a micro-needle syringe. The micro-fiberbot quickly recovers its helical shape after injection. **B**, The micro-fiberbot travels inside the catheter by perfusing saline under X-ray imaging guidance. **C-D**, Catheter-assisted deployment of the micro-fiberbot for embolization at target 1 (C) and target 2 (D) in a blood vessel phantom with bifurcation branches.



Fig. 4. Steerability of the micro-fiberbot in submillimeter regions. A, Schematic illustration 801 (left) and experimental demonstration (right) of the micro-fiberbot navigating in a blood vessel 802 phantom with bifurcation branches of 30° and 60°. **B**, Schematic illustration (left) and experimental 803 pictures (right) of the micro-fiberbot navigating in a blood vessel phantom with bifurcation 804 branches of 90° and 120°. C, Experimental demonstrations of the micro-fiberbot navigating in a 805 vessel phantom with a narrowing diameter (1 mm to 100 µm). Scale bar, 2 mm. D, Demonstration 806 of the micro-fiberbot navigating a S-shaped vessel phantom. E, Demonstrations of the micro-807 fiberbot navigating a 3D vessel phantom. Scale bar in D-E, 1 mm. 808

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Fig. 5. In vitro robotic embolization in neurovascular vessel phantoms. A, Demonstration of 812 aneurysm coil embolization by magnetic soft micro-fiberbot. B, Validation of the embolization 813 results under X-ray fluoroscopy. The flow into the aneurysm is significantly reduced after coil 814 embolization. C, Demonstration of tumor coil embolization in which branch 2 is assumed to be 815 tumor vessel. Two micro-fiberbots are steered subsequently to completely occlude branch 2. D, The 816 contrast agent is released to validate the occluded branch 2. E, Demonstration of tumor particle 817 embolization protection in which branch 1 is assumed to be a healthy vessel. F, After the micro-818 fiberbot block the healthy branch 1, the embolic particles are released to occlude tumor vessels 819

- 820 (branch 2 and 3). G, The micro-fiberbot can be safely retrieved after particle embolization is
- completed. **H**, The contrast agent is released to validate the occluded vessel branch 2 and 3. Scale
- bar in A-H is 1 mm.



Fig.6. Robotic embolization in rabbit blood vessel in vivo. A, Schematic illustration of robotic
embolization in rabbit blood vessel on the leg under real-time fluoroscopy. B, The magnetic soft
micro- fiberbot is released into the blood vessel by a catheter. Scale bar, 5 mm. C, The angiology
of targeted blood vessel before embolization by infusing iodinated contrast media. D, Fluoroscopy
images of micro-fiberbot navigating from site 1 to site 4. E, Fluoroscopy images of micro-fiberbot
returning from site 4 to site 2 and aggregated. F, The angiology of blood vessel after embolization
by infusing iodinated contrast media. Scale bar, 1 mm. G, The blood vessel is separated for

- histological analysis two weeks after embolization. Scale bar, **D-G**, 1 mm. **H**, The H&E staining
- cross-section images of the blood vessel. Cross-section 1 and 2 show the formation of thrombus
- after embolization. Scale bar, 250 μm.

Science Robotics AAAS 1 Supplementary Materials for 2 Magnetic soft micro-fiberbots for robotic embolization 3 Xurui Liu^{1,2}[†], Liu Wang³[†], Yuanzhuo Xiang²[†], Fan Liao^{1,2}, Na Li^{1, 2}, Jiyu Li³, Jiaxin Wang⁴, Qingyang Wu¹, 4 ², Cheng Zhou^{1, 2}, Youzhou Yang^{1, 2}, Yuanshi Kou^{1, 2}, Yueying Yang^{1, 2}, Hanchuan Tang^{1, 2}, Ning Zhou⁴, Chidan 5 Wan⁵, Guang-Zhong Yang⁶*, Guangming Tao^{2, 7}*, Jianfeng Zang^{1, 2, 8}* 6 7 [†]These authors contributed equally to this work. 8 9 *Corresponding authors. Email: gzyang@sjtu.edu.cn (G.-Z.Y.); tao@hust.edu.cn (G.T.); jfzang@hust.edu.cn (J.Z.); 10 11 This PDF file includes: 12 13 Supplementary text 14 Figs. S1 to S26 15 Table S1 16 17 References Legends for Movies S1 to S14 18 19 Other Supplementary Materials for this manuscript include the following: 20 Movies S1 to S14 21 22 23

24 Supplementary Text

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²⁶ Analysis of the anchored state of micro-fiberbot in flow conditions.

- ²⁷ The flow velocity distribution inside a cylindrical vessel can be expressed(*1-3*)
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$$v_r = f(r, H)v_m$$
 Eq. S1

where *H* is the diameter of the vessel, *r* denotes the position with respect to the cylinder center O, and the mean flow velocity v_m . Considering that the diameter of the fiber ($d = 60 \mu m$) is much smaller than the vessel diameter ($H = 800 \mu m$), the position of the anchored micro-fiberbot can be estimated as

$$r = (H - d)/2.$$
 Eq. S2

³³ In a flow condition with $v_m = 100$ mm/s, Plugging Eq. S2 into Eq. S1 gives the flow velocity at the micro-³⁴ fiberbot

- $v_r = 15 \text{ mm/s}$ Eq. S3
- ³⁶ Therefore, the fluidic drag force applied on one pitch of the micro-fiberbot can be estimated as
- $F_d = \frac{1}{2}\xi\rho Sv_r$ Eq. S4

³⁸ where ξ is the drag coefficient, ρ is the flow density, *S* is the cross-section area of the micro-fiberbot. ³⁹ Substituting $\xi = 0.15(4)$, $\rho = 1.11 \times 10^3$ kg/m³, $S = 2.9 \times 10^{-6}$ mm² into Eq. S4, we obtain that

- ⁴⁰ $F_d = 5.43 \times 10^{-7}$ N. According to the FEA, the total contact friction $F_f = 2.03 \times 10^{-6}$ N.
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Strategy		Target indication	Embolic agent type	Embolic agent deployment technique	Steerability (max bifurcation angle θ , min diameter of accessible vessels H)	Maneuverability in flow conditions	Shape- morphing capability	Embolization Validation	Ref.
Commercial passive catheters		Aneurysm and tumor	Coil	Manually pushing/twisting	Low $\theta < 90^{\circ}$ $H \sim 1 \text{ mm}$	Intermediate		Commercial	Catheter: TERUMO Headway 27 TM Coil: Stryker, Target TM Nano TM
Active robots	Tethered hydraulic catheters	Aneurysm	Coil	lesions, followed by catheter delivery	Intermediate $\theta > 90^{\circ}$ $H \sim 2.5 \text{ mm}$	in tortuous blood vessels)	Bending only	In vivo (porcine)	5
	Tethered electronic catheters	Aneurysm	Coil		Low $\theta > 90^{\circ}$ $H \sim 2.5 \text{ mm}$			In vitro	6
	Tethered magnetic guidewire	Aneurysm	Coil		Intermediate $\theta > 90^{\circ}$ $H \sim 2.5 \text{ mm}$			In vitro	7
	Tethered magnetic catheter	Tumor	Liquid embolic	Catheter-directed to blood vessel & passively carried by blood flow & passively aggregate at target lesions	Intermediate $\theta < 90^{\circ}$ $H \sim 100 \ \mu m$	Intermediate (Impractical in unpredictable flow conditions)		Ex vivo	8
	Flow-driven swarms	Tumor	Particle		v blood flow & High	Low (Untraceable & passive drifted)	Particle aggregation	In vivo (porcine)	9
	Flow-driven particles	Tumor	Particle		(theoretically can steer to submillimetre			In vitro	10
	Flow-driven anchors	Tumor	Particle		regions due to the micro-size)		Radial expansion	In vivo (rabbit)	11
	Magnetic soft micro-fiberbots	Aneurysm and tumor	Coil and particle	Catheter- directed to blood vessel & active navigation in blood flow & shape-morphing at target lesions	High $ heta$ >90 \degree $H \sim 100 \ \mu m$	High (controlled by magnetic fields & visible to X- ray/ultrasound)	Elongation, contraction, aggregation	In vivo (rabbit)	This work

Table. S1. Comparison between this work and existing embolization procedure



Fig. S1. Fabrication and characterization of magnetic soft micro-fiberbots. A, Schematic of fabrication of millimeter-scale magnetic composite preform. **B**, A millimeter-scale perform is thermally drawn into a micrometer-size perform with sacrificial PC cladding and magnetic microfiber core. C, the magnetic fiber can be molded into magnetic soft micro-fiberbots with identified helical geometry parameters by employing different molds. D, Magnetic hysteresis of SEBS+NdFeB (20 vol.%) composite. Residual magnetization M=120 kA/m. E, Stress-strain curves of SEBS+NdFeB (20 vol.%) composite. F, Fitting the stress-strain curve by the incompressible neo-Hookean constitutive model (Shear modulus is 1 MPa).



Fig. S2. Analysis of the anchored state of micro-fiberbot in flow conditions. The fluidic drag force (per pitch) F_d is estimated by the drag pressure times the cross-sectional area of the micro-fiber (S =

$$\pi\left(\frac{H^2}{4}-\frac{\left(\frac{H}{2}-d\right)^2}{4}\right)).$$



Fig. S3. Characterization of micro-fiberbots with helical diameter of 800μ m under varying magnetic parameters. A, Helical diameter of micro-fiberbot as a function of actuation magnetic field strength. B, Length of the micro-fiberbot as a function of actuation magnetic field strength. C, Helical propulsion velocity as a function of magnet rotation frequency in the absence of flow (B = 40 mT). D, Helical propulsion velocity within vessels with different diameters H.



Fig. S4. Reversibility test of the shape morphing of the micro-fiberbot. After 1000 elongation-contraction cycles, the pitch of the four magnetic soft micro-fiberbots (Pitch p = 500, 800, and 1000 µm) remains almost unchanged.



Fig. S5. High elasticity and mechanical robustness of the micro-fiberbot. The magnetic soft micro-fiberbot quickly (0.1 s) recovers to the initial helical shape after being compressed by a rigid punch. Scale bar, 5 mm.



Fig. S6. Control strategy of micro-fiberbot using a cubic magnet. A, schematic of the cube magnet with a residual magnetic flux density Br = 1380 mT. **B**, the magnetic fields around the cub magnet. **C**, the magnetic actuation for micro-fiber is achieved by dynamically controlling the vertical, horizontal, and rotational movements of the cube magnet. **D**, The magnetic soft micro-fiberbots can have aggregation and elongation shape-morphing by changing the external magnetic field. The elongated state of the micro-fiberbot is achieved by controlling the magnet to generate the magnetic field along with **M**_{net}. **E**, The magnetic field strength B_x as a function of distance *s* along the centerline of the magnet. **F**, the upstream helical propulsion is achieved by rotating the magnet in a clockwise manner, and magnetic pulling is achieved by moving the magnet. **G**, The magnetic field strength B_y as a function of distance *s* along the centerline of the strength the centerline of the magnetic pulling is achieved by moving the magnet.



Fig. S7. Spatial magnetic gradient distribution of a cubic magnet with width of 50 mm.



Fig. S8. Magnetic maneuvering system. The magnetic maneuvering system is composed of 6-DoF robotic arm, a step motor controller and driver, and a cubic magnet.



Fig. S9. Demonstration of shape-morphing capability and in-flow maneuverability of micro-fiberbot with 500 μ m diameter. A, Image of a micro-fiberbot inside a tube with a 500 μ m diameter. B, The 500 μ m micro-fiberbot can still have shape-morphing and upstream propulsion in a flow condition with 100mm/s flow rate. C, The upstream propulsion velocity of the 500 μ m robot is comparable to that of the 800 μ m micro-fiberbot in both 100 mm/s and 200 mm/s flow. Scale bar, 1mm.



Fig. S10. Fabrication of blood vessel phantoms. The sacrificial template method was used to fabricate the vessel phantom. Melted wax was first injected into 3D-printed negative molds, and then solidified wax mold with the desired shape was carefully taken out. Next, the wax mold was immersed into uncured PDMS (mass ratio 10:1) and cured at room temperature (23° C) for 72 hours. Lastly, the phantoms were placed on a hot plate (120° C) to melt the wax and the vessel phantom with hollow lumen structure was placed in ultrasound cleaner with ethanol for 2 h. To obtain similar friction conditions to realistic blood vessels, a thin hydrogel layer (~ 10 µm) was coated in the inner surface of the hollow lumen structure (*12*). Therefore, the vessel phantoms have similar young's modulus properties (2 MPa) and friction properties with the coefficient of 0.1.



Fig. S11. Demonstration of nontarget coil embolization using commercial catheter. A, Commercial catheter can only reach the second bifurcation. B, The limited accessibility of catheter may lead nontarget coil embolization. Scale bar, 2mm.



Fig. S12. Demonstration of the low steerability of commercial catheter. A-B, Commercial catheter cannot be steered to the bifurcation vascular phantom with bifurcation angle (A) $\theta = 60^{\circ}$ and (B) 90°. C, Commercial catheter cannot access narrowing branches with diameter smaller than its tip. Scale bar, 2mm.



Fig. S13. Comparison of the blocking ratio between one micro-fiberbot aggregation and dual aggregation by two micro-fiberbots. A, the blocking ratio was calculated by cross-section area ratio between the aggregated micro-fiberbots and the blood vessels. B, Demonstration showing that particles are fully blocked with dual aggregated micro-fiberbots. Scale bar, 1 mm.



Fig. S14. Demonstration of four micro-fiberbot achieve quadruple-aggregation at the same target site in a vessel phantom. Scale bar, 1 mm.



Fig. S15. Demonstration of micro-fiberbots achieve aggregation in different vessel branches. Scale bar, 1 mm.



Fig. S16. Angiography of the rabbit blood vessels after 21 days embolization.



Fig. S17. Histology analysis of main organs of rabbits after two-week embolization surgery. A, The crosssection 3 of H&E staining cross-section images were selected from the proximal to distal blood vessels to validate the embolization results. Scale bar, 250 μ m. **B**, The H&E staining cross-section image of the rabbit femoral artery. The sample for the soft micro-fiberbot group was collected after locomotion. Scale bar, 250 μ m. **C**, no inflammation or pathological abnormalities were observed in the samples collected from the control group and embolization group of rabbits. Scale bar, 500 μ m.



Fig. S18. Comprehensive blood cell counts taken from rabbit before and after embolization (24h, 72h, 21 day).



Fig. S19. Fabrication of coating hydrogel skin. A Schematic of the steps used to fabricate millimeter-scale magnetic composite preform with embedded functional layers. **B**, Schematic of dip-coating hydrogel on a magnetic fiber in pre-gel solution (AAM). **C**, The optical imaging of bare magnetic fiber shows that the magnetic particles are exposed without hydrogel coating. **D**, After hydrogel coating, the magnetic particles were isolated and a hydrogel layer (~15 µm) was observed. Scale bar 50 µm.



Fig. S20. Cell viability tests of magnetic composites with different coatings. A, Fluorescence microscopic images of human cardiac microvascular endothelial cells incubated with the composites at the exposure times of 24 hours and 48 hours, respectively. **B** Relative cell survival rate of positive control, hydrogel-coated, SEBs-coated, SEBs-Fe₃O₄ magnetic soft micro-fiberbots.



Fig. S21. Analysis of blood cell hemolysis of positive control, negative control, bare micro-fiberbots and hydrogel-coated micro-fiberbots.



Fig. S22. Ex vivo demonstration of real-time ultrasound tracking capability of micro-fiberbot. A, Schematic of magnetic soft micro-fiberbots locomotion and retrieval for targeted drug delivery under realtime ultrasound imaging. Right: The optical images of magnetic soft micro-fiberbots navigating in a porcine coronary artery. Scale bar, 5 mm. **B**, Real-time ultrasound imaging-tracked navigation of magnetic soft microfiberbots controlled by the external magnetic manipulation system in an ex vivo porcine coronary artery under the flow. The white arrow indicates the flow directions. **C**, Downstream navigation of magnetic soft microfiberbots to a targeted site. Red arrows show the navigation directions. **D**, Magnetic soft micro-fiberbots selfretained in flow environments with dynamically changed porcine coronary artery diameters, the insets show the enlarged images of the magnetic soft micro-fiberbots. PRF: 1.0 kHz. **E**, Upstream navigation and catheter retrieval of magnetic soft micro-fiberbots. Scale bar, 2 mm (D to E).



Fig. S23. Thrombin-hydrogel coating of the micro-fiberbot promotes thrombus formation. A, Experimental image demonstrating the dip coating method used to form a thin layer of thrombin-hydrogel on the micro-fiberbot. Scale bar, 1 mm. **B**, Blood clotting index of control, pure hydrogel coating, and thrombin-hydrogel coating groups. **C**, Scanning electron microscope (SEM) image displaying red blood cell (RBC) absorption on the micro-fiberbot. **D**, Injection of blood to stimulate thrombus formation within the aneurysm phantom. Scale bar, 1 mm.



Fig. S24. Pressure assessment of the micro-fiberbot within a vessel phantom. A, Schematic of the in vitro occlusion setup employing a syringe pump and a pressure gauge to measure the pressure needed to drive blood through the tube. **B,** Pressure as a function of time for control (blood alone), pure hydrogel coating, and thrombin hydrogel coating.



Fig. S25. Demonstration of micro-fiberbot under RF signal for local hyperthermia and thrombus formation. A, Infrared picture shows the temperature of micro-fiberbots before RF heating. B, Infrared picture shows the temperature of micro-fiberbots after RF heating. **C,** The temperature change of micro-fiberbot in 300 seconds. **D,** Micro-fiberbot was placed on the vessel phantom with animal whole blood and then heated by RF coil. **E,** After 5 min RF heating, the thrombus formation was observed. As a comparison, without RF heating, no significant thrombus formation.



Fig. S26. Thrombus formation when incubated in different temperatures. A, Schematic illustration of platelet activation and aggregation. B, Images show the porcine whole blood incubated in four feature Temperature with different times. C, Activated coagulation time (ACT) at different incubated temperatures. D, Temporal shape variation of formed thrombus in anticoagulated porcine blood. Scale bar, 10 mm.

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Legends for Movies S1 to S14

Movie S1. Overview movie of magnetic soft micro-fiberbots for robotic embolization.

Movie S2. Shape morphing capability of micro-fiberbots under magnetic fields.

Movie S3. Magnetic maneuvering of micro-fiberbot in flow condition.

Movie S4 Demonstration of shape-morphing capability and in-flow maneuverability of micro-fiberbot with 500 µm diameter.

Movie S5. Catheter-assisted deployment of micro-fiberbots.

Movie S6. Demonstration of micro-fiberbots steering in bifurcation branches of blood vessel phantom.

Movie S7. Demonstration of micro-fiberbots steering in a narrowing blood vessel phantom.

Movie S8. Demonstration of micro-fiberbots steering in an S-shaped blood vessel phantom.

Movie S9. Demonstration of micro-fiberbots steering in a 3D blood vessel phantom.

Movie S10. In vitro demonstration of aneurysm embolization

Movie S11. In vitro demonstration of tumor coil embolization.

Movie S12. Dual-aggregation of micro-fiberbots

Movie S13. In vitro demonstration of particle embolization protection and retrieval.

Movie S14. In vivo demonstration of robotic embolization in a rabbit.