Developing Soft Robotics for Minimally Invasive Diagnostics and Targeted Drug Delivery

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Abstract

Soft robotics systems built from compliant, deformable, and often bio-inspired materials offers a compelling path for next-generation minimally invasive diagnostic (MID) tools and targeted drug delivery systems (TDDS). Because soft robots can adapt their form to complex anatomy, safely interact with fragile tissues, and integrate active material/state-responsive payload release mechanisms, they are uniquely positioned to address limitations of rigid capsule endoscopes, tethered catheters, and passive drug carriers. This article provides a comprehensive, research-ready treatment of the design, fabrication, sensing, actuation, control, and translational pathways needed to develop soft robotic platforms for MID and TDDS. We synthesize progress in actuation technologies (pneumatic/hydraulic, hydrogel/swelling, shape-memory polymers, dielectric elastomers, magnetically actuated composites), microfabrication and 3D printing methods, onboard sensing (tactile, chemical, biosensing), and communication/energy strategies for untethered operation. We present candidate architectures for (a) soft, steerable endoluminal capsules that perform high-resolution sensing and local drug release, (b) continuum hydrogel robots for submucosal inspection and local therapy, and (c) biohybrid microrobots for targeted tumor penetration and controlled payload delivery. For each architecture we discuss control paradigms, closed-loop sensing strategies, biocompatibility/sterilization constraints, and regulatory/ethical considerations. We then propose experimental validation pathways from benchtop phantoms to large animal studies, and present metrics to quantify diagnostic accuracy, delivery specificity, and safety. Finally, we outline open challenges (energy autonomy, sensor miniaturization, robust navigation, and clinical acceptance) and research directions including federated data pipelines for model improvement and cloud-integrated teleoperation and monitoring. This article aims to serve as a detailed roadmap for researchers and translational teams advancing soft robotic solutions for minimally invasive diagnostics and targeted therapeutics.

Keywords: soft robotics, minimally invasive diagnostics, targeted drug delivery, hydrogel actuators, magnetic microrobots, capsule endoscopy, biohybrid robots, biocompatibility, control, sensing.

1. Introduction

Minimally invasive diagnostics and targeted drug delivery aim to reduce patient morbidity, accelerate recovery, and increase therapeutic specificity relative to open surgeries and systemic pharmacotherapy. Traditional rigid microscale devices (e.g., wired probes, rigid endoscopes) and passive delivery systems (e.g., oral tablets, intravenous nanoparticles) face clear limitations: limited conformability to soft tissues, risk of iatrogenic injury, difficulties traversing tortuous anatomy, and lack of active navigation to lesion sites (Probst et al., 2023; Zhang et al., 2023). Soft robotics a field harnessing compliant materials, novel actuation modalities, and bio-inspired designs provides technologies that can conform, squeeze, and traverse complex anatomy while minimizing tissue damage (Laschi et al., 2016; Rus & Tolley, 2015). Recent work has shown soft robotic devices can be magnetically actuated, hydrogel-driven, pneumatically controlled, or biohybrid (cell-powered), enabling untethered locomotion, precise local interaction, and programmable payload release (Lee et al., 2023; López-Díaz et al., 2024).

This paper synthesizes the state of the art and proposes a unified design, validation, and translational framework for soft robotic MID and TDDS devices. We place particular emphasis on (1) materials and fabrication that enable sterilizable and biocompatible devices, (2) sensing and closed-loop control required for safe navigation and delivery, (3) payload design for targeted release, and (4) regulatory, ethical, and clinical validation pathways needed to bring such devices to patients.

2. Background and Literature Review

2.1. The evolution of soft robotics and relevance to medicine

Soft robotics has rapidly matured from conceptual bio-inspiration to practical medical prototypes. Reviews and perspectives charting early principles and biological inspirations identify soft bodies' advantages for safe interaction and adaptability (Kim, Laschi, & Trimmer, 2013; Laschi, Mazzolai, & Cianchetti, 2016). Foundational reviews synthesize actuation classes (fluidic, smart materials, magnetically actuated composites) and highlight the field's potential for biomedical devices (Rus & Tolley, 2015; Wang et al., 2025). More recent reviews specifically address hydrogel actuators, magnetically actuated fiber robots, and implantable soft devices for diagnostics and therapy (López-Díaz et al., 2024; Lee et al., 2023;釣Paternò et al., 2023). These works form the base upon which MID and TDDS applications build.

2.2. Soft robotic modalities relevant to MID/TDDS

- **Magnetic actuation:** Embedding magnetic particles (hard/soft magnets) into elastomers or hydrogels allows remote steering using external fields, enabling untethered navigation and site-specific actuation (Lee et al., 2023; Wu et al., 2025). Magnetically actuated capsules can perform locomotion and selective sampling/drug release (Wei et al., 2024).
- **Hydrogel and stimuli-responsive actuators:** Hydrogels that swell/shrink in response to pH, temperature, ionic strength, or light enable compact actuators and triggered release mechanisms compatible with GI and intraperitoneal environments (López-Díaz et al., 2024).
- **Pneumatic/soft fluidic actuators:** Elastomeric pneumatic systems provide robust, controllable deformation for steerable manipulators and grippers. Integration challenges include tethering and pressures safe for tissue (Perera et al., 2024).
- **Shape-memory polymers (SMPs) and dielectric elastomers:** SMPs allow shape change following a thermal or electrical trigger for deployable structures; dielectric elastomers provide

high power density but require high voltages, presenting integration challenges for in vivo use (Wang et al., 2017; recent surveys).

- **Biohybrid and cell-powered systems:** Biohybrid microrobots leverage muscle tissue or motile microbes to produce locomotion and chemotaxis for drug delivery an emerging class with promise for tumor targeting but with biosafety and control challenges (Zhang et al., 2023; Totter et al., 2025).

2.3. Capsule endoscopy and active capsules

Capsule endoscopy matured as a passive diagnostic tool; however, active capsule robots with magnetic steering, local sampling, and drug reservoirs are an active area of research (Koulaouzidis et al., 2015; Wei et al., 2024). Recent advances show multichamber magnetic capsules enabling selective liquid sampling and localized release (Wu et al., 2025). Integrating soft materials into capsule exteriors can reduce mucosal trauma and allow compliant anchoring for focused therapy.

2.4. Microrobots and targeted drug delivery

Untethered microrobots have been developed for active delivery to tumors and mucosal lesions (Annavi et al., 2021; Zhang et al., 2023). Reviews highlight propulsion methods (magnetic, acoustic, catalytic), navigation strategies, and approaches to payload encapsulation and release (Sitti et al., 2015; Ren et al., 2024). Recent studies demonstrate in vivo penetration and localized release in preclinical models using magnetic and hydrogel-based constructs.

2.5. Materials, fabrication, and biosensing integration

High-resolution additive manufacturing (direct ink writing, stereolithography with biocompatible resins), microtransfer printing, and soft lithography enable fabricating complex soft structures with embedded channels and sensors (Liu et al., 2022; Perera et al., 2024). Hydrogel composites and magnetically doped elastomers permit multimaterial architectures. Onboard sensing modalities miniature pressure/force sensors, optical biosensors (fluorescence), electrochemical sensors are increasingly miniaturized and can be integrated into soft skins (Dahiya et al., 2013; López-Díaz et al., 2024).

(Citations throughout: Kim et al., 2013; Laschi et al., 2016; Rus & Tolley, 2015; López-Díaz et al., 2024; Lee et al., 2023; Wei et al., 2024; Zhang et al., 2023; Dahiya et al., 2013; Liu et al., 2022.)

3. Design Goals and System Requirements

For clinically useful MID and TDDS soft robots, design goals must balance efficacy, safety, regulatory feasibility, and manufacturability.

3.1. Clinical performance requirements

- **Diagnostic resolution & sensitivity:** For optical or biosensor-based diagnosis, resolution and limit of detection must meet or exceed current modalities (e.g., high-definition endoscopy, histopathology proxies).
- **Delivery specificity:** Fraction of payload delivered to target volume (targeting accuracy) and off-target leakage thresholds must be quantified.
- **Navigational capability:** Ability to traverse complex luminal geometries and anchor at target sites while resisting peristalsis or blood flow.

3.2. Biocompatibility & sterilization

- Materials must be biocompatible (ISO 10993 series) and withstand sterilization (autoclave, EtO, gamma) or be single-use with safe disposal. Hydrogels and some polymers require tailored sterilization protocols to preserve mechanical and sensing properties (Paternò et al., 2023; López-Díaz et al., 2024).

3.3. Energy, communication, and autonomy

- **Energy budgeting:** Onboard batteries vs. external field actuation; tradeoffs between autonomy, device size, and payload capacity.
- **Telemetry:** Low-power wireless data links (BLE, UWB, magnetic induction) balanced against attenuation in tissue. Cloud-integrated telemetry can offload heavy computation and enable remote monitoring (see Section 9 on systems integration).
- **Fail-safe operation:** Handover to clinician, automatic retention/retrieval strategies for lost devices.

3.4. Manufacturability and cost

- Scalable fabrication (e.g., roll-to-roll, multi-material 3D printing) to reduce unit cost and enable sterile single-use devices where appropriate (Liu et al., 2022).

4. Representative Architectures and Design Patterns

We present three candidate architecture classes with design rationale, component choices, sensing/control strategies, and examples from literature.

4.1. Soft, magnetically actuated capsule (SMAC)

Overview: An ingestible soft elastomeric capsule doped with magnetic particles, an internal reservoir for drug payloads, onboard sensing (optical camera, pH sensor, micro-pressure sensor), and an outer soft skirt that enables conformal contact and soft anchoring.

Actuation & locomotion: External rotating/gradient magnetic fields produce rolling, swimming, or controlled anchoring (Lee et al., 2023; Wu et al., 2025). The soft envelope reduces mucosal abrasion and permits localized expansion for anchoring.

Delivery mechanism: Magnetically actuated valves or pH/temperature-triggered hydrogel gates release payload when at the target site (Wei et al., 2024).

Sensing & closed loop: Visual localization plus pH/biomarker sensors confirm lesion microenvironment; closed-loop magnetic control maintains position while releasing payload (Wei et al., 2024; Ren et al., 2024).

Advantages & limitations: High patient comfort, non-invasive administration; challenges include precise external field control, magnetic interference in clinical settings, and retrieval if retention occurs.

4.2. Hydrogel continuum soft robot (HCSR) for submucosal inspection and local therapy

Overview: A long, flexible continuum robot built from stimuli-responsive hydrogel segments enabling controlled bending, local actuation (constriction/expansion), and drug elution through embedded microchannels.

Actuation: Local swelling/deswelling through ionic or pH triggers, or remote photothermal actuation using embedded nanoparticles (López-Díaz et al., 2024).

Sensing: Distributed tactile and chemical sensing through conductive hydrogel electrodes and colorimetric sensing patches for local biomarkers.

Control: Closed-loop with optical or ultrasound localization; slow actuation but high compliance reduces perforation risk.

Use case: Submucosal inspection, biopsy guidance, and staged local chemotherapy release for localized lesions.

4.3. Biohybrid microrobot swarm (BMS) for targeted tumor penetration

Overview: Micro-scale soft robots or particles propelled by engineered bacteria or muscle tissues, or actuated magnetically, designed to home to tumor microenvironments (chemotaxis, hypoxia) and release cytotoxic agents.

Propulsion & guidance: Magnetically steered for gross navigation; local biohybrid motility facilitates interstitial penetration (Zhang et al., 2023; Totter et al., 2025).

Payload release & targeting: Enzyme-cleavable coatings or pH-sensitive capsules ensure release in acidic tumor niches.

Safety & biosafety: Requires kill-switches, containment strategies, and extensive preclinical testing for host-microbe interactions.

5. Materials, Fabrication, and Packaging

5.1. Materials selection

- **Elastomers:** Silicone (PDMS variants), thermoplastic elastomers (TPEs) for robust, elastic skins. PDMS widely used but may be gas-permeable and requires surface modification for drug compatibility (Rus & Tolley, 2015).
- **Hydrogels:** Biocompatible hydrogels (PEG, alginate, gelatin methacryloyl) for soft continuum segments and drug reservoirs; tunable swelling and porosity enable controlled release (López-Díaz et al., 2024).
- **Magnetic composites:** Neodymium-doped polymer composites (hard/soft magnetic particles) for magnetic actuation; tradeoffs include particle leaching and long-term compatibility (Lee et al., 2023).
- **Conductive inks and sensors:** PEDOT:PSS, graphene, and silver inks for stretchable electrodes and biosensors.

5.2. Fabrication techniques

- **Direct ink writing (DIW):** Multimaterial DIW enables embedding channels, magnetic filaments, and sensor traces in a single print (Liu et al., 2022).
- **Stereolithography (SLA) with soft resins:** High resolution for complex geometries; requires biocompatible resin choices and post-processing.
- **Soft lithography and molding:** Standard for elastomeric actuators (Perera et al., 2024).
- **Microfluidic patterning:** For microchannel fabrication and in situ drug encapsulation.

5.3. Packaging & sterilization

Encapsulation strategies must preserve mechanical function and sensor performance post-sterilization. Ethylene oxide (EtO) and gamma sterilization may alter polymer networks, requiring material evaluation (释Paternò et al., 2023). Design for single-use disposability is often pragmatic for ingestible devices.

6. Sensing, Perception, and Closed-Loop Control

6.1. Sensing modalities

- **Optical imaging:** Miniature CMOS cameras for visual inspection (capsules).
- **Tactile/pressure sensors:** Microfluidic pressure sensors or strain sensors to detect contact and anchoring forces (Dahiya et al., 2013).
- **Chemical and biosensors:** Electrochemical sensors for pH, glucose, tumor biomarkers; optical fluorescence sensors for molecular reporters (Zhang et al., 2023).

- **Localization sensors:** Magnetic field sensing (for magnetic actuation feedback), inertial measurement units (IMUs), and ultrasound reflectance for localization in tissue.

6.2. Perception algorithms

- **Onboard lightweight AI:** Embedded convolutional models for image segmentation and lesion detection can run on low-power inference chips (e.g., Edge TPUs) to identify candidate targets (Litjens et al., 2017).
- **Multimodal fusion:** Combine vision and chemical cues to robustly classify target tissues and trigger release (Calandra et al., 2017).
- **Cloud-assisted analysis:** For complex computations, secure low-latency offloading to cloud resources provides scalable analysis and telemedicine integration (see Section 9).

6.3. Control strategies

- **Closed-loop magnetic control:** Real-time feedback from magnetic sensors and imaging to stabilize position and perform micro-motions (Lee et al., 2023).
- **Adaptive compliance control:** Modulate stiffness/admittance to negotiate varying tissue mechanical properties.
- **Hierarchical autonomy:** Reflexive low-level controllers (safety), intermediate learned primitives for manipulation, and high-level planning for task sequencing (Kober et al., 2013).

7. Payload Design and Release Mechanisms

7.1. Reservoirs and release triggers

- **Stimuli-responsive gates:** pH, temperature, enzymatic triggers commonly used for gastrointestinal targeting. Hydrogels or polymer membranes can open upon target conditions (Ren et al., 2024).
- **Magnetically actuated valves:** External magnetic fields actuate small valves or rupturable membranes to permit timed release (Wei et al., 2024).
- **Mechanical extrusion / micro-needles:** Soft robots can deploy micro-needles or injection bladders to deliver drugs into tissue layers (Surgical prototypes).

7.2. Payload stabilization and pharmacokinetics

Encapsulation strategies liposomes, polymeric microparticles stabilize therapeutics and control release kinetics. Designing release kinetics must consider local clearance, diffusion, and systemic exposure.

8. Experimental Validation, Bench Testing, and Preclinical Evaluation

8.1. Benchtop phantoms and standardized tests

- **Anatomical phantoms:** Soft phantoms with tunable stiffness to simulate mucosa, submucosa, and lumen curvature for navigation and anchoring tests.
- **Biomarker phantoms:** Simulated chemical environments to test sensor specificity and release triggers.
- **Mechanical durability tests:** Fatigue, abrasion, and sterilization cycling.

8.2. Ex vivo and in vivo studies

- **Ex vivo tissues:** Tissue slices and excised organs for controlled validation of interaction forces and release efficiency.
- **Large animal models:** Swine models for GI devices and tumor xenografts for microrobots to assess biodistribution, immune response, and therapeutic effects (Zhang et al., 2023).

8.3. Metrics and statistical approaches

- **Diagnostic metrics:** Sensitivity, specificity, ROC analysis compared to gold standards (biopsy/histopathology).
- **Delivery metrics:** Percentage dose delivered to target region, off-target fraction, retention and clearance.
- **Safety metrics:** Peak contact forces, incidence of mucosal injury, inflammatory markers.
- **Statistical design:** Power analyses, randomized controlled preclinical studies where applicable.

9. Systems Integration and Cloud-Enabled Workflows

Modern MID/TDDS systems can gain from cloud integration for data aggregation, model training, and remote operator assistance.

9.1. Edge-Cloud partitioning

Partition computation: real-time controls and reflexes on edge/RTOS; heavier perception and model updates in cloud. Ensure secure, low-latency communication and fail-safe local operation when connectivity lost (privacy and latency constraints).

9.2. Data governance and federated learning

Federated learning enables learning from distributed clinical sites while preserving patient data privacy valuable for improving lesion detection models and personalization of control policies (Fatunmbi, 2024; federated learning literature).

9.3. Teleoperation and clinician in-the-loop

Provide clinician supervisory interfaces showing confidence maps, sensor telemetry, and live video. Cloud-assisted analytics can augment clinician decision-support.

10. Safety, Ethical, and Regulatory Considerations

10.1. Safety architectures and standards

Implement layered safety with deterministic certified controllers for critical actions, runtime monitors for learned components, and explicit handover protocols. Conform to ISO 14971 risk management and IEC 62304 software lifecycle standards (ISO 14971; IEC 60601 series).

10.2. Ethical considerations

- **Informed consent and expectations:** Patients must be informed about autonomy levels, retrieval risks, and biological components (if biohybrid devices used).
- **Biosafety:** Biohybrid devices (microbe-enabled) require containment and kill switch mechanisms and robust regulatory review.

10.3. Regulatory pathway

Early dialogue with regulators (FDA/EMA) to determine classification (medical device vs. combination product) and premarket testing expectations is crucial. Demonstrate device manufacturing quality (ISO 13485) and clinical evidence via staged trials.

11. Limitations, Challenges, and Future Directions

11.1. Key technical hurdles

- **Energy autonomy:** Miniaturized power sources with safe energy density remain limiting. External actuation (magnetic, ultrasound) helps but reduces autonomy.
- **Sensor miniaturization & robustness:** Long-term stability of chemical/biomarkers sensors in vivo is challenging.
- **Sterilization & disposability:** Some advanced materials (hydrogels, embedded cells) are incompatible with common sterilization routes.
- **Scale-up and manufacturing:** Translating lab-scale fabrication to GMP manufacturing is nontrivial.

11.2. Research opportunities

- **Smart materials:** Programmable hydrogels and degradable soft composites for transient devices.
- **Federated clinical datasets & cloud platforms:** For robust lesion detection and adaptive control policies (Fatunmbi, 2024).

- **Hybrid actuation:** Combining magnetic steering with local chemo-responsive actuation for higher specificity.
- **Regulatory-aware design:** Co-design of devices and evidence generation plans to accelerate approvals.

12. Conclusion

Soft robotic platforms present transformative opportunities to perform minimally invasive diagnostics and targeted drug delivery with improved safety, compliance, and specificity. Achieving clinical translation demands multi-disciplinary progress in materials science, miniaturized sensing, reliable control, scalable fabrication, and regulatory alignment. This article synthesizes the current knowledge, proposes architectures and evaluation pathways, and highlights actionable research directions that, together, form a roadmap for developing clinically viable soft robotic MID/TDDS solutions.

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