Soft robotic systems for endoscopic interventions

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ABSTRACT

The field of soft robotics has established itself as an important research topic within robotics, offering several advantages over traditional rigid robots. This paradigm shift introduced by advances in material science and manufacturing methods has enabled new capabilities. These emerging soft robotic systems can squeeze and move through narrow openings, elongate, navigate around obstacles, and are considered inherently safe. In particular, the healthcare domain has been identified as one of the areas that might benefit from applying soft robotic systems.
This chapter focuses on the application of soft robotic systems for endoscopic interventions. At the outset, we provide an overview of endoscopic procedures and commercially available technologies and tools highlighting current challenges and how soft robotics might benefit. As soft robotic systems for healthcare application are a relatively young research area, we compiled a list of recommendations for creating soft robotic medical devices. Relevant topics include dimension requirements, bio-compatibility of materials as well as reliability, durability specification and ergonomics. Finally, a discussion of current soft robotic medical devices concerning the aforementioned endoscopic procedures will identify shortcomings and future research challenges.

1. Introduction

Open surgery has been the traditional way to obtain direct access to internal organs via a large incision for many years. Intra-operative palpation can be performed by the clinician's finger(tip)s to differentiate tumorous and unhealthy tissue from healthy tissue. This facilitates the surgeon to completely resect identified tissue, i.e. to perform a surgical excision, using surgical instruments such as scalpels, forceps, or curettes [1], or remove small tissue samples (biopsies) for histology examination. However, open surgery is associated with slow patients' recovery time, postoperative pain, increased rate and severity of postoperative complications, blood loss, and immunological stress response of the tissue resulting in less invasive surgery techniques becoming more preferred [2, 3].

With the invention of the endoscope in the early 19th century for visualisation of the oesophagus and stomach [4], medical procedures have been transformed into minimally invasive interventions for diagnosis (cystoscope, 1878) and therapy (polypectomy, 1969). This concept was adapted to surgery when laparoscopic instruments were introduced into the organism: In Minimally Invasive Surgery (MIS), also called laparoscopic or keyhole surgery, miniature video cameras and tools mounted at the end of long rigid rods are inserted through small incisions ranging from 3 to 12 mm [5, 6]. These miniature cameras provide visual feedback to the clinician of the internal organs of the patient. At the same time, surgical instruments/tools can be used to probe tissue surface (through rigid tool-soft tissue interaction) or to provide treatment such as cutting and cauterisation. From the mid-1980s, MIS has become increasingly popular worldwide. Surgery became even less invasive when the use of natural orifice was demonstrated in so called Natural Orifice Transluminal Endoscopic Surgery (NOTES).

Compared to open surgery, MIS offers several benefits including shortened postoperative recovery; better therapeutic outcome; reduced tissue trauma, postoperative pain, and scarring; and, less immunological stress response of the tissue [2]. However, compared to open surgery, MIS is more demanding because the clinicians' skills may be

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affected by the limited vision of the operative site, and motion constraints, resulting in the reduction of intuitiveness and unnatural repetitive movements [4].

In the last decade, surgical robots have been introduced into the operating theatre to provide the surgeon with advanced dexterity by using teleoperated laparoscopic tools with increased Degrees of Freedom (DoFs) compared to manually operated laparoscopic instruments. This implies controlling the robotic surgical system through a master console that can be located nearby the patient or in a remote location.Surgeons can perform remote precise surgical procedures due to 3-D high definition endoscopic vision systems and control systems that can scale surgical instruments' motion and reduce tremor of the hand.

With the introduction of wireless capsule endoscopes, flexible endoscopes, laparoscopic tools and robotic systems, examinations, biopsies, and treatments can be delivered in a minimally invasive way. Some of these systems have associated risks such as tissue/organ perforation, bleeding, or incomplete resection of adenomas in endoscopic procedures. These are mainly caused by the instruments' rigidity and the limited touch feedback of surgeons during MIS [7].

Recently, soft robots for minimally invasive surgery have been proposed. Properties such as flexibility, squeezability, and bio-compatibility of their materials make them suitable to avoid damaging tissues inside the body while navigating through a narrow opening with obstacles [7]. Moreover, their variable stiffness control allows the tool holder to become stiff to have better transmission of the force while a less stiff state allows reorienting the tools [8, 9, 10, 11]. This makes soft robotic systems more ergonomic for the surgeon and easier for navigating inside the patient [12].

Soft robots are also less prone to fulcrum effect problems and absence of triangulation that are commonly observed in laparoscopic MIS [3]. The mechanical constraints of the laparoscope at the incision point cause fulcrum effect; this effect includes scaling, and inversion of both the motion of the laparoscope and the environment-endoscope interaction forces [13]. On the other hand, triangulation refers to the triangle arrangement of the endoscope and two surgical instruments that maximises the view, and the operation of the instruments in the area of interest [14]. This convergence is achieved by having the endoscope at the top and one surgical instrument at each of the lower points of the triangle minimising the interference between instruments and the endoscope.

This chapter focuses on the application of soft robotic systems for endoscopic procedures. To understand the challenges associated to endoscopic procedures, the analysis starts by discussing common endoscopic interventions, their implications on the patient, and possible complications. Then, commercially available endoscopic tools are examined to determine their limitations and how their mechanical properties contribute to elevating potential risks or complications during endoscopic procedures. This analysis is used as the foundation to discuss how soft robotics research has proposed solutions to overcome these aforementioned challenges over the last decade. In the end, this leads to the identification of shortcoming and future research challenges in soft robotics for endoscopic applications.

2. Overview of endoscopic procedures

Medical procedures deploying endoscopic instruments involve three categories, i.e. examination, confirmation of a diagnosis and treatment. This section provides an overview and context of the differences and similarities in the requirements, risks, and limitations of these endoscopic procedures.

2.1. Visual examination and diagnose procedures

Visual information is of paramount importance to understand the preliminary health condition of soft tissue and organs. This is confirmed by the World Health Organization (WHO). In 2000, WHO proposed a classification of tumours of the digestive system that takes into account visual characteristics [15]. Table 1 summarises the colour, presence of vessels, and surface pattern of colorectal lesions characteristics of the tissue for the invasion states from 1 to 3; while, Fig. 1 contains narrow-band imaging examples that highlight the corresponding characteristics described in the table [16, 17, 18]. For instance, the figure in the third-row first column of Fig. 1 illustrates the highest invasion state (Type 3 - Carcinoma) where the colour of the tissue has changed to dark brown in certain areas.

An examination procedure is commonly carried out through natural orifices while the patient is awake to investigate the cause of symptoms. Local anaesthesia may be given to numb a specific area such as the throat or the anus. Depending on the procedure, a sedative may also be used to relax the patient and reduce awareness.

On the other hand, a biopsy is a procedure where a small sample of organ or tissue is taken to examine, i.e. the sample cell's type, internal activity, and shape. A flexible endoscope is inserted through an incision or a natural orifice such as the throat or anus. Once the distal end of the endoscope has reached the desired location, the surgeon will take the sample using small cutting tools. The anaesthesia depends on the endoscope insertion point and the investigated area inside the body. Biopsies allow assessing the severity of a condition that has already been diagnosed. These imply defining the degree of inflammation or the invasion state of cancer [18]; this information is profoundly important for the decision making of future treatment [19].

It is worth noting that surgeons have used artificial intelligence and a visual examination to provide a diagnosis in the last years. This approach has been proved to be as useful and reliable as biopsy [20]. Last year, the Food and Drug Administration designated machine learning algorithms of AI Medical Service Inc. (Tokyo, Japan) as *breakthrough devices* analysing thoroughly and rapidly images from an endoscopic examination of the entire digestive tract [21]. It provides support to clinicians in the diagnosis of conditions such as gastric cancer. Another commercially available AI algorithm is Lunit INSIGHT MMG (Lunit, Seoul, Korea) [22]. This CE certified algorithm can improve breast cancer detection using mammography images. For lung cancer detection, this algorithm has shown a higher sensitivity than radiologists [23]. In future years, AI applied to medical imaging is likely to replace biopsy when lesions are visible.

Common endoscopic examination procedures include:

- **Esophagogastroduodenoscopy (EGD)** or upper endoscopy is the examination of the oesophagus, stomach and duodenum using an endoscope that is inserted through the mouth. An endoscope comprises lenses and light to obtain visual feedback via an external monitor. It requires patient sedation. By using other tools, it can also be employed for biopsies, performing cell tests (which requires a small brush), or for treating abnormalities such as polyps, strictures, and bleeding ulcers [24]. Complications may include bleeding or gastrointestinal tract tearing.

- **Colonoscopy** comprises examining the inside of the colon from the rectum until the cecum (where the small bowel attaches to the large bowel) using a specific endoscope called colonoscope. It may require patient sedation. Similarly to upper endoscopy, a colonoscope provides visual feedback and can be used to obtain a biopsy. Sometimes, this procedure can be used for treating abnormalities such as polyps, strictures, or bleeding. This method is commonly used to evaluate the colon of patients with conditions such as iron deficiency anaemia, colorectal cancer (CRC), post-polypectomy and post-cancer resection surveillance; complications may imply colon perforation, post-polypectomy bleeding, and missed or incomplete resected adenomas [25]. Colonoscopy is more sensitive but has less patient acceptance than sigmoidoscopy [26].

- **Enteroscopy** allows visualising the small bowel. Enteroscopy can be performed using *a*) a longer conventional endoscope to examine the upper part of the small bowel; or, *b*) a swallowable capsule endoscopy that comprises a wireless camera sending information to a recording device worn by the patient; after finishing, the data is downloaded for a clinician's analysis; patient sedation is not required; this approach is only for exploration. Depending on the approach, the complications may imply bleeding, perforation, or pancreatitis.

- **Endoscopic Retrograde Cholangiopancreatography (ERCP)** uses a technique in the treatment and examination of the ducts involving the liver, pancreas, and gallbladder. A specialised endoscope together with a side-mounted camera that facilitates passing a catheter into the bile and pancreatic ducts is deployed. The catheter inserted through the endoscope allows injecting a contrast material (dye) that outlines those ducts when x-rays are taken. This endoscopic examination's complexity and length require patient sedation and significant training and experience of the clinician. ERCP is used to detect blockages that may be caused by cancerous tissue, narrowing of the ducts, or other alterations. This endoscopic procedure helps to treat conditions such as pancreatic cancer, pancreatitis, and biliary strictures. Adverse conditions related to this procedure are cholangitis, bleeding, pancreatitis, or perforation [27].

- During **bronchoscopy**, a thin endoscope, called bronchoscope, is inserted through the mouth or nose allowing the examination of breathing passages in the lungs. This procedure requires fasting prior to the procedure, local anaesthesia, patient sedation and may include taking a biopsy. Cause of symptoms such as noisy breathing, persistent cough, or coughing up blood can be investigated. It has therapeutic applications such as tracheal intubation, retrieving an inhaled foreign body, or suction of sputum [28]. Complications such as bleeding can occur depending on the level of comorbid diseases [29]. Between 6 and 12 hours after the procedure, one in three patients may develop fever or sweat. Approximately one in ten patients, who required a transbronchial biopsy, suffer from lung wall perforation caused by the bronchoscope [30].

- **Laryngoscopy** is an examination of the larynx and vocal cord movement using an endoscope, which might require the patient to receive local anaesthesia. The clinician can choose between a flexible endoscope, called

Table 1
Narrow-band image (NBI) colorectal endoscopic classification [18].

	Colour	Vessels	Surface patterns
Type 1 Hyperplastic	Lighter or similar than surrounding tissue.	None or isolated lacy vessels.	Absence of patterns or homogenoeus dark or white spots.
Type 2 Adenoma	Browner than surrounding tissue.	White structures surrounded by brown vessels.	Branched white, tubular or oval structures surrounded by brown vessels.
Type 3 Carcinoma	Brown to dark brown.	Missing vessels.	Amorphous or absent pattern.

fibreoptic laryngoscope, or a rigid optical instrument, called direct laryngoscope. Laryngoscopy allows for performing biopsies, microsurgical procedures such as removing polyps in the vocal cord or urgent endotracheal intubation. Laryngoscopy is used for investigating hoarseness [31], trouble breathing or swallowing, persistent earache or sore throat, or a symptom related to cancer. Rare complications including pain, infection, bleeding, and hoarseness can occur. Because of comorbidities, variability on the operators' expertise, and the uncontrolled events during an urgency, urgent endotracheal intubation by direct laryngoscopy might require multiple attempts in urgent endotracheal intubation [32].

- During **cystoscopy**, clinicians reach the bladder through the urethra to examine its internal volume and lining using a thin endoscope, called the cystoscope. Similarly to laryngoscopy, cystoscopy can be performed using a flexible or rigid endoscope. Depending on the necessity of treatment and, hence, type of the optical instrument, the patient may need anaesthesia, e.g., a spinal or general anaesthesia. Cystoscopy is used to investigate the cause of problems such as frequent tract infections, blood in the urine, or persistent pelvic pain; to take a biopsy; or provide treatments, i.e. injecting a medicine, removing or inserting a stent, or removing bladder stones. Cystoscopy is considered a safe procedure; however, risks can include urinary tract infections, not being able to urinate after the procedure, and potential damage to the bladder caused by the cystoscope [33].
- **Hysteroscopy** is the gold standard for examining the inside of the uterus [34] inserting a narrow rigid small endoscope, called hysteroscope, into the vagina and through the cervix to reach the uterus. This procedure is used to investigate the cause of health issues related to miscarriages, heavy periods, or pelvic pain; to diagnose conditions, i.e. polyps and fibroids; and to provide treatment such as removal of polyps, fibroids, or scar tissue. The patient may need local or general anaesthesia (in particular, when treatment is provided). Although uncommon, the main complications might be uterus or cervix damage, excessive bleeding, or uterus infection [35].
- **Endoscopic Ultrasound (EUS)** examination requires a special endoscope fitted with a small ultrasound device on the distal end. This endoscope is inserted through the mouth or anus. Patient sedation is required. This examination allows visualising layers of the gastrointestinal tract wall and surrounding organs such as the spleen, liver, pancreas, gallbladder, and adrenal glands. The clinician can gain more understanding about cancer stages or diseases of the bile duct, pancreas, and gallbladder [36]. Complications may comprise bleeding, throat or intestinal wall perforation, or pancreatitis.

2.2. Endoscopic treatments

After a diagnosis is confirmed, the clinician will understand and suggest the treatment for the patient. This may imply invasive, open interventions such as *operative procedures* that would comprise manual tissue manipulation with one hand or *surgical procedures* that would require tissue handling with both hands. Endoscopes can offer the opportunity to deliver treatments in a minimally invasive way. During Minimally Invasive Surgery (MIS), direct treatment such as removing polyps, cauterising a bleeding vessel, or removing an inflamed organ can be delivered.

MIS has become the preferred method over open surgery because of smaller incisions needed to introduce surgical tools, less postoperative pain for the patient, lower risk of infection, shorter hospital stay and recovery time, and reduced scarring and blood loss [2]. Here, endoscopes can be inserted through small incisions or natural orifices using either rigid laparoscopic optical instruments or flexible endoscopes.

Laparoscopic MIS is performed using long thin instruments inserted through small 3 to 15 mm incisions (i.e. trocar ports) in the abdominal area [1, 6]. Prior to the procedure, the patient will receive anaesthesia. On the one hand, single-port MIS comprises using an endoscope with the surgical instruments being passed through its working channel. On the other hand, several small incisions are required for multi-port MIS to introduce a single laparoscopic instrument through each trocar port. Whereas single-port MIS is considered to be less invasive, challenges in triangulation [38] in combination with the fulcrum effect might occur. In comparison, multi-port surgery offers enhanced manoeuvrability and less physical interference between the laparoscopic instruments.

Another minimally invasive procedure is Natural Orifice Transluminal Endoscopic Surgery (NOTES). Here, a flexible endoscope can be navigated to reach other organs or tissues with reduced postoperative pain, minimal or little skin scarring, and faster recovery time. Furthermore, among the procedures through the various natural orifices, transvaginal NOTES is the preferred [39] access point operating on female patients because of its safe entry, simple closure, and lower risks for decontamination [40].

There are two types of NOTES: On the one hand, pure NOTES uses a flexible endoscope passed through a natural orifice (i.e. urethra, rectum, vagina, or mouth) [41] to perform a surgical intervention. Therefore, the surgery could be performed without any incision in the abdomen [39]. On the other hand, surgeons use flexible or rigid endoscopes that are passed through trocars and natural orifices simultaneously during hybrid NOTES [42]. A common procedure is transvaginal gallbladder removal, in which an endoscope introduced through an umbilical port provides visual feedback.

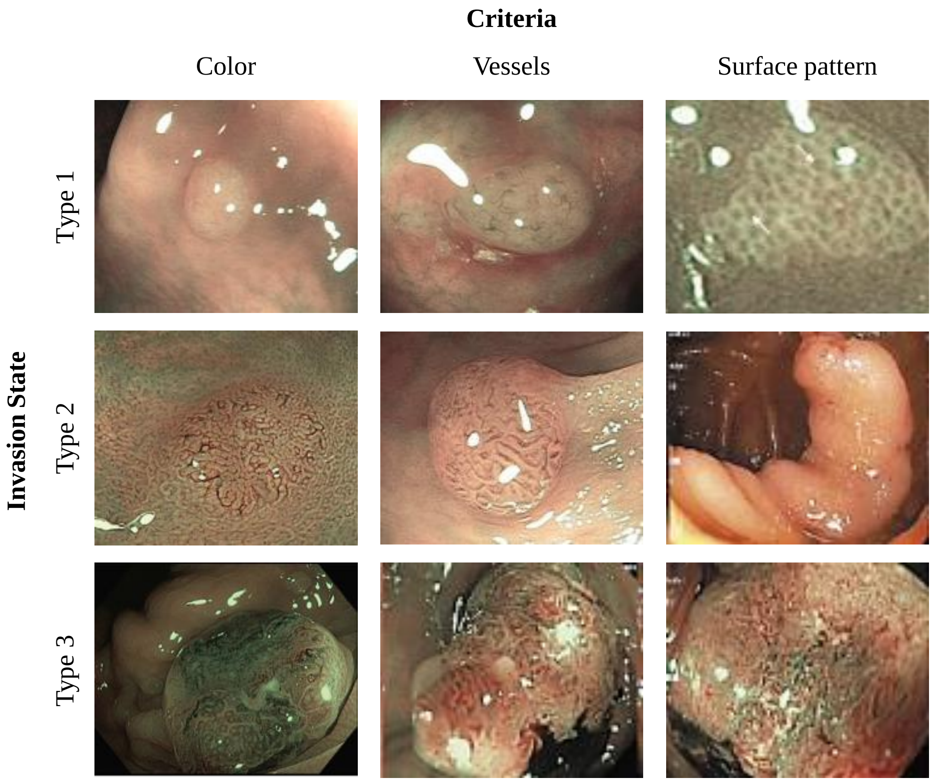

Figure 1: Narrow-band image (NBI) colorectal endoscopic classification (presented in Table 1) considering visual information that can be provided by an endoscope. The criteria are based on the colour, amount of vessels, and surface patterns that can be observed in the examined tissue. (These figure samples are taken from [16, 18, 37]. The final, published version of [16] is available via `https://doi.org/10.1053/j.gastro.2012.05.006` and [18] is available via `http://www.karger.com/?doi=10.1159/000487470`).

Common minimally invasive endoscopic (laparoscopic, NOTES, or hybrid) procedures for treatment include the following:

- **Peroral Endoscopic Myotomy (POEM)** is performed to treat Achalasia which is a condition where the lower oesophagal sphincter (LES, muscular ring that closes the oesophagus from the stomach) becomes bulky, eventually fails to open during swallowing, and food does not reach the stomach. During POEM, an endoscope incises the muscle fibres of the LES to decrease LES' resting pressure unblocking the pass of food from the oesophagus to the stomach. POEM is considered pure NOTES, in which the patient receives general anaesthesia [43]. This procedure is generally safe. However, some complications might include perforation of the oesophagus, bleeding during the procedure, and infection.

- In **Percutaneous Endoscopic Gastrostomy (PEG)**, an endoscope assists in placing a flexible feeding tube into the stomach through a small incision in the abdominal wall. This requires patient sedation. Patients with insufficient oral intake or swallowing problems might benefit from PEG. Complications such as bowel perforation or haemorrhage may occur [44].

- **Endoscopic Laser Ablation (ELA)** requires an endoscope with a therapeutic laser. It is used in cases such as twin to twin transfusion syndrome (TTTS) [45], prostate problems [46], or lung cancer[47]. According to [48], TTTS risks such as tissue damage and premature rupture of the membrane are mainly caused by the poor adaptability of the semi-rigid or rigid instruments employed.

- **Transanal Endoscopic Microsurgery (TEM)** requires a specific microscope and instruments. Incisions are not needed because the rectum is reached through the anus. It is widely applied in procedures such as removing benign polyps, repairing complex rectovisceral fistulas or excision of rectal neoplasms [49]. TEM risks are lower than using open surgery, but some of the complications include bleeding, infection, or pelvis inflammation. **Transanal Minimally Invasive Surgery (TAMIS)** is an alternative for removing benign polyps and early-stage rectal cancers [50]. The difference between TAMIS and TEM is the former uses a disposable port while the latter employs an resterilised reusable port. TAMIS is a more accessible and cost-effective than TEM [51].

3. Review of commercially available solutions for endoscopic procedures

Endoscopes deployed for minimally invasive procedures that allow examining and/or provide visual feedback during treatments of, e.g., the brain, joints, lungs, or bladder, must meet strict requirements with regards to: material biocompatibility for avoiding adverse reactions of the body, stability of the distal tip for avoiding any overshooting or problem related to inertia, manoeuvrability for navigating through the soft tissue and organs, reliability and durability, depth perception, and localisation of the distal tip.

As stated in Section 2, endoscopes are used for examination, diagnostic confirmation (by taking biopsies), and treatment. An examination can be performed using optical tools, while biopsies and treatments use minimally invasive tools (in particular, laparoscopic tools, flexible endoscopes, or even robotic platforms). Therefore, this review of commercially available endoscopic instruments is divided into optical tools and instruments for therapeutic endoscopy.

3.1. Instruments for optical examination

A wireless capsule endoscope can provide visual feedback of the internal tissues or organs for investigating the cause of a problem such as stomach ulcers, or abdominal pain. This untethered single-use approach is a less invasive alternative to standard endoscopy. Before swallowing the capsule, the patient needs to fast and take purgatives and liquids for bowel preparation. Then, the capsule moves passively through the digestive system using peristalsis. The sensors placed on the patient's body allow the wireless recorder to collect video data transmitted from the capsule. The information can be downloaded onto a computer and analysed by medical personnel. In the end, the capsule is excreted naturally from the body.

Capsule endoscopes do not require patient sedation (though the patient might experience minimal discomfort). This is one reason why capsule endoscope has become standard for diagnosing Crohn's disease [52].

The commercially available PillCam™ capsule (Medtronic, Dublin, Ireland) is used for monitoring lesions that may be related to Crohn's disease, iron deficiency anaemia, or obscure bleeding. It can also be used for visualising the small bowel. EndoCapsule 10 (Olympus, Tokyo, Japan) can provide a 160 ° view angle and has a battery life of

Table 2
Requirements of a flexible endoscope used for an examination (camera) and operative (tools) procedures for single-port and multi-port surgery: here, Total Mesorectal Excision (TME).

Requirements	Single-port surgery		Multi-port surgery	
	Camera	Tools	Camera	Tools
Tube stiffness	Variable for organ or tissue adaptability			
Degrees of Freedom (DoFs)	At least 2 DoFs for bending + 1 DoF for elongation (tip navigation)			
Tip diameter	Acceptable: 10 mm Ideally: 8 mm			
Max. Trocar diameter	40 mm		Acceptable: 15 mm Ideally: $\leq$ 10 mm	
Overall length	350 mm		300 mm	Acceptable: 350 mm Ideally: $\geq$ 400 mm
Force at the tip	Low holding force	Acceptable: 3 N Ideally: 4 to 5 N	Low holding force	Acceptable: 3 N Ideally: 4 to 5 N

up to 12 hours [53]. This allows monitoring the entire gastrointestinal tract with minimal disruption to the patient and endoscopist.

Nevertheless, the absence of control for, e.g., orientating, navigating, and manoeuvring, discards this method for investigating specific areas [54]. To overcome this limitation, the C-Scan® endocapsule (Check-Cap Ltd., Isfiya, Israel) employs x-ray to construct 2-D and 3-D maps of the inside of the colon [55]. On the other hand, MiroCam® (Intromedic, South Korea) and NaviCam (Ankon Medical Technologies, Wuhan, China) improved the manoeuvrability and controllability of the capsule endoscope system using external magnetic fields. NaviCam can advance and change the viewing angle in steps of 2 mm and 3°, respectively. Additionally, the ANKON ESNavi software provides dimensions of visualised lesions [56].

Flexible endoscopes can also provide visual feedback of the internal organs or tissues for investigating the causes of problems. They commonly comprise a working channel where surgical instruments are introduced to provide a treatment or confirm a diagnosis while performing an examination. Therefore, flexible endoscopes can also be employed for therapeutic endoscopy, so they are presented in Section 3.2.1.

3.2. Instruments for therapeutic endoscopy

In therapeutic endoscopy, an instrument is used to confirm a diagnosis or provide treatment such as removing polyps, a failing organ, or cauterising bleeding vessels. After the patient has been sedated, small operative instruments are inserted through the working channel of an endoscope (single-port surgery) or through several incisions (multi-port surgery). Simultaneously, visual information is provided to the clinician on a monitor.

Characteristics and requirements for an endoscope depend on the medical procedure and the number of ports and the tools employed. For instance, Table 2 summarises the requirements of a therapeutic endoscope for single-port and multi-port surgery such as Total Mesorectal Excision (TME). The maximum trocar diameter increases from 15 mm (multi-port surgery) to 40 mm (single-port surgery). Since the camera has a lower interaction with the environment than a tool, the camera requires a low holding force while the tool needs 3-5 N.

3.2.1. Flexible endoscopes

Fundamental control interfaces and components of flexible endoscopes are illustrated in Fig. 2. Endoscopists use one hand to operate the controls such as suction valves or angulation of the distal end. The other hand manages torquing, pushing or removal of the insertion tube.

The insertion tube is part of the endoscope that mainly changes across procedures. The insertion tube comprises a bending section at the distal end to facilitate the orientation of the camera. As Fig. 2 - C shows, this tube contains:

1. a working channel which is fundamental for many reasons including flushing, gas distention, suction, injection, bleeding control (energy or clipping) and eventually taking biopsies which can be done by forceps or by needle cutting or aspiration.

2. channels for water and air feeding and water jet.

3. a bending mechanism including four wires to control the angulation of the distal tip of the endoscope.

4. a visualisation system that refers to the camera (image sensor) and cables for transmitting the video signal.

5. a lighting system for the distal end of the endoscope.

6. spiral metallic bands to provide flexibility to the tube, transmit the torques and subtle movements from the wrist of the endoscopist, and protects the internal components from external forces.

7. a cover made of polymer is bio-compatible. The cover provides watertight capability, and its smoothness provides negligible damage to tissues when the endoscope is inserted.

8. mechanical features that enhance the comfort of the patient and endoscopist and the ease and speed of its insertion in the patient.

The dimensions of an endoscope, such as length and external diameter, depend on the medical procedure. For instance, the dimensions of an endoscope for examining the stomach and the lungs (bronchoscope) are different due to the characteristics of the examined tissues.

Advantages of flexible endoscopes, compared to their stiff, rigid counterpart, are that flexible endoscopes do not present the fulcrum effect and there may be a lower risk of loss of triangulation. Furthermore, flexibility can improve the adaptability of the insertion tube to the organs and tissues. The risk of damaging the interior of the body during navigation is lower than that of the rigid endoscope. This adaptability facilitates reaching organs that are far from the incision or entry point. The tools needed for the interventional procedure are inserted through the working channel, which minimises any damage caused to surrounding tissue or organs.

Flexible endoscopes can be employed for NOTES. While laparoscopic surgery may require up to five incisions [57], pure NOTES may not require any incision. This shortens the recovery time, trauma, and pain to the patient. Moreover, these instruments can be used for hybrid NOTES; where they work together with laparoscopic instruments.

Nevertheless, the flexibility affects the precision, stability of the tip and the force that can be applied. For instance, when pulling soft tissue, flexible endoscopes may bend; this dissipates the pulling force applied to the tissue [58]. In addition, there might be a risk of looping, and the reduced haptic feedback would not provide an accurate judgment of the force applied. These drawbacks increase the risk of tissue or organ damage.

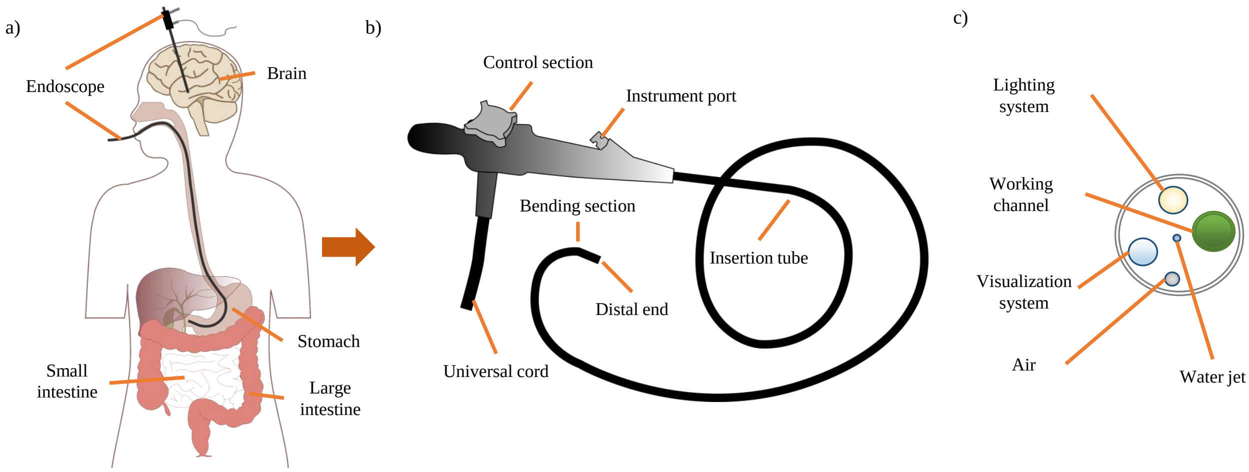

Figure 2: Endoscope. a) Endoscopes can be used for performing in medical procedures in different parts of the body, such as the brain, stomach, intestines, and joints. Endoscopes can be inserted through incisions or natural orifices. b) Fundamental components of a standard flexible endoscope, and c) the distal end of the insertion tube. Endoscopes contain a working channel to increment its usability. Surgical instruments inserted through the instrument port allow using endoscopes to examine tissues or organs, confirm a diagnosis (by taking a biopsy), or provide treatment.

3.2.2. Laparoscopic instruments

As illustrated in Fig. 3, a laparoscope is a long rigid variation of an endoscope presented in Section 3.2.1. It is made of a small stiff tube, which is inserted through a small incision, with a light source and camera at its tip to retrieve visual feedback. Clinicians insert a laparoscope to access the internal abdominal area and pelvis. Small surgical tools and a tube to inflate the abdomen with carbon dioxide are inserted through the endoscope's working channel or additional trocars. These so-called laparoscopic instruments allow the clinician to manipulate soft tissue and have various functionalities, including a needle driver for suturing, trocar, bowel grasper, and surgical mesh, for instance. After the procedure, the gas is evacuated, the small incision is sewed, and a dressing is applied. A similar procedure is also conducted for removing tissues samples (biopsy) or damaged organs.

Conventional laparoscopic surgery has several advantages over open surgeries (e.g., smaller incision, fewer tissues damage, and less blood loss). However, *a*) stiff endoscopes make it challenging to navigate through the internal anatomy increasing the risk of injury to soft tissue or organs; *b*) the motion range and dexterity is limited by the DoF provided by the joints of the laparoscopic tools making it challenging for clinicians to work in small spaces; *c*) 2D visual feedback provides a poor depth perception; *d*) rigid tools can affect the judgment of the force applied to organs or tissues; *e*) reduced tactile feedback makes delicate tasks such as tying sutures more challenging; *f*) laparoscopic surgery is not ergonomic for clinicians because unnatural movements have to be performed repetitively; and, *g*) the fulcrum effect requires developing a non-intuitive motor skill as tool endpoints move in the opposite direction to the surgeon's hands.

These limitations leave room for complications that may not be common. However, there are still risks, such as organ or major artery damage, gas bubbles entering into arteries or veins; or vein thrombosis that lead to pulmonary embolism, limiting the applicability of laparoscopic surgeries. Furthermore, to treat most of the complications, further surgical intervention might be required [59].

Robotic-assisted Minimally Invasive Surgery (RMIS) comprises a robotic surgical system that has been designed to improve surgeons' predictability, accuracy, repeatability [57], and ergonomics. Before surgery, specialised nurses need to dedicate time to set up the slave side of the surgical robot inserting the instruments through trocars and connecting these to each robotic arm. During the procedure, the surgeon controls the robotic system on the slave side through a master console allowing the surgeon to navigate a 3D high-definition endoscopic camera as well as a number of robotic arms simultaneously. Robotic surgical systems are more ergonomic for the clinician as they maintain an upright position and can navigate and control the robotic surgical instruments with high dexterity intuitively [60]. Another advantage is that simulators can be employed for training and enhancing the surgeon's skills.

Current commercially available, robotic-assisted surgical platforms provide a 3D magnified high-definition image to the master console. These optical tools give a more detailed vision during interventions. The master-slave robotic system allows the clinicians to execute more precise movements filtering any vibrations/physiological tremor. Therefore, surgeons can perform procedures with higher precision.

A well-known surgical robot is the multi-port da Vinci® Surgical System, illustrated in Fig. 4-A, and the single-

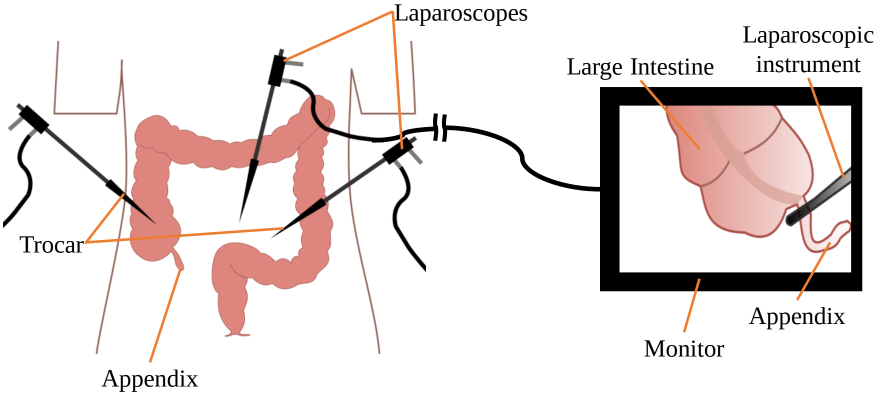

Figure 3: Laparoscopic appendix removal surgery with three incisions (trocars). The laparoscope is inserted through the trocar in the umbilicus providing the surgical site's visual feedback to the clinician. The trocars on the left and right hand side are used to insert rigid laparoscopic instruments and, hence, maintain triangulation. Any clashing between instruments is minimal. The endoscope provides a clear view of the instruments and the surgical site.

port surgical robot da Vinci SP® (Intuitive Surgical®, Sunnyvale, CA, USA) . The da Vinci® is commonly used in procedures such as cardiac, colorectal and general surgery [65]. It is composed of the surgeon console (master side), the vision and patient cart (slave side). The surgeon console contains the controls of the surgical instruments and provides 3D visual feedback to the clinician. The vision cart provides image processing capability, information systems, power generation, and visual feedback to the operating team through a screen. The patient cart comprises four robotic arms that the surgeon can teleoperate via the console. The rigid straight laparoscopic instruments with articulated tips are cable-driven and/or actuated through traditional mechanical couplings enabling the clinician to deliver an intervention with high precision and stability [57]. On the other hand, the patient cart of the da Vinci SP® contains a single robotic arm. This single-port surgical system includes three wristed elbowed instruments and a wristed elbowed da Vinci endoscope that are inserted through a 2.5 cm cannula. Da Vinci SP® can be used for urological procedures and removing benign and T1 and T2 tumours by transoral otolaryngology surgical procedures in the oropharynx. This robotic system is not intended for general laparoscopic surgery procedures, yet [65]. Thus, due to the rigidity of the tools, these laparoscopic solutions are useful when the organ is close to the incision location.

The Versius® Surgical Robotic System (CMR Surgical Ltd, CAM, UK) is a laparoscopic robot with a master-slave configuration similar to the da Vinci® Surgical System. The major differences compared to the da Vinci® are that the clinician operates the console in an upright position while standing or sitting (rather than looking slightly downwards through the console binoculars) wearing 3D glasses and each robotic arm is installed on an individual cart [66]. Hence, repositioning of the robotic arms is simplified.

The Senhance® Surgical System (TransEnterix Inc, NC, USA) is a laparoscopic platform as shown in Fig. 4-B. The clinician teleoperates rigid tools mounted on individual carts in an upright position while sitting. 3D High Definition (HD) visualisation is provided on the screen of the master console. Also, the Senhance® Surgical System provides kinesthetic feedback to the clinician (pressure and tension between the instruments and the environment) [67].

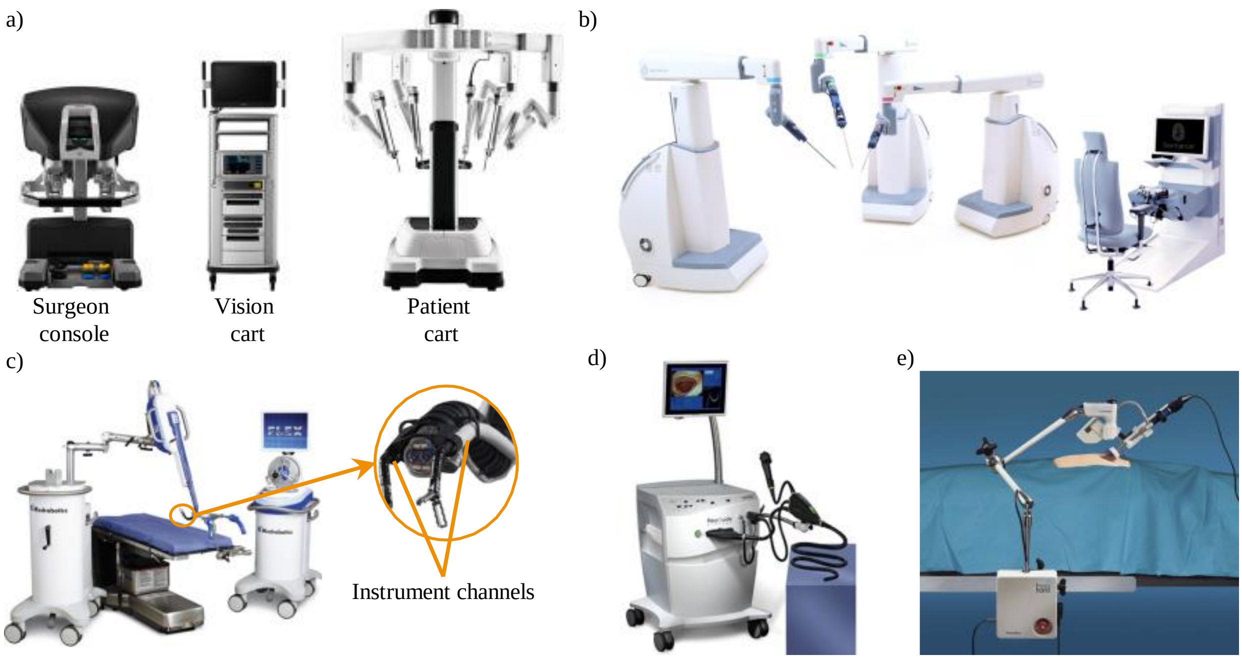

Figure 4: Endoscopic robotic-assisted technologies that are commercially available and have FDA approval and/or CE certification. a) the da Vinci® Surgical System is the most successful robotic platform for laparoscopic procedures (taken from [61]), b) the Senhance® Surgical System uses rigid instruments, measures tool interaction with the environment and provides kinesthetic feedback to the clinician (taken from [62]), c) Flex® Robotic System for single point medical procedures comprises a compliant endoscope with two instrument channels (taken from [61, 63]), d) the NeoGuide™ Endoscopy System is a computer-assisted colonoscope providing 3D real-time maps (taken from [64]), and e) the FreeHand Assisted Surgery supports standard-laparoscopic surgeons by holding the laparoscopic camera steadily and, hence, providing comfort to the clinician (taken from [64]).

The Monarch® Platform (Auris Health, Inc., CA, USA) comprises a flexible robotic endoscope that allows entering the body through natural orifices. Once it reaches the desired location, a needle can take soft tissue samples. The console is fundamentally different from the laparoscopic surgical robotic systems as the controller interface is held with both hands allowing clinicians to navigate the endoscope and reach peripheral nodules in the lung. Lung cancer diagnosis and treatment are the main medical applications [68].

Flex® Robotic System (Medrobotics, MA, USA), presented in Fig. 4-C, is a compliant flexible endoscope surgical system with gravity compensation for single-port MIS [69]. It has an onboard HD visualisation system. Compliance is achieved by its concentric mechanism together with its multiple linkages. Two working channels allow inserting flexible surgical instruments. The tip of the robot is steered via a parallel robotic joystick.

The NeoGuide™ Endoscopy System (NeoGuide Endoscopy System Inc, Los Gatos, CA, USA), illustrated in Fig. 4-D, presents a modular compliant structure. It is made of 16 equally sized electro-mechanically actuated modules. The distal tip provides a wide range of movements in all directions. Its mapping approach to navigate through the natural curves of the colon and its looping reduction system [70] decrease any forces applied to the colon wall [71]. The system employs an external position sensor for localisation measurements. In the system's passive mode, the endoscope is stiff to take a biopsy or deliver therapy. In the active mode, the system follows the commands of the surgeon given through the controller interface.

The InvendoScope (Invendo Medical GmbH, Germany - acquired by Ambu®, Denmark, in 2017) is a single-use flexible colonoscope. The system is made of a colonoscope, a reusable handheld controller, and processing unit. After the instrument is introduced into the rectum, the distal end advances using its propulsion mechanism based on an inverted sleeve mechanism with eight drive wheels gripping into the inner side of this sleeve; the rotation of this wheels allows growth or reduction at the tip [72]. Its DoFs provide a 180° rotation in all directions; the maximum insertion length is 170 cm; its bending radius is 35 mm for retroflexion colon visualisation; and, the radius of its working channels is 3.1 cm [73].

A robotic approach occupying minimal footprint has been realised by the FreeHand Assisted Surgery, shown in Fig. 4-E. This commercially available system gives the surgeon a "third" hand to stabilise the laparoscopic camera. Visual feedback is improved as the clinician can control the camera with head movements only and without the need to unhand any laparoscopic tools [74].

As mentioned earlier, robotic surgical systems can provide a number of benefits, including the surgeon's predictability, accuracy, repeatability [57], and ergonomics. Though a wide range of interventional applications may be suggested for these systems (leveraging the economic justification for healthcare providers), their deployment might not always be the ideal option when delivering treatment, and some clinicians would prefer open surgery [75].

3.3. Challenges in current endoscopic interventions

Technology has rapidly advanced over the last decades with many available and emerging surgical robotic platforms entering the market in the near future. Nevertheless, some challenges make open surgery the only option to complete or perform certain surgeries. Taking into account the various endoscopic procedures, the risks faced by clinicians and patients, and the current commercially available technologies discussed in previous sections, it can be stated that there are common challenges across endoscopic procedures.

Clinicians can understand the location and orientation of laparoscopic cameras once they have been inserted into the body through trocar ports as these are non-flexible, rigid rods. However, challenges occur when navigating these optical tools and additional laparoscopic instruments around organs to the point of interest. In some cases, new incisions have to be made to allow easier access.

When deploying flexible endoscopes, manoeuvring and navigating the tip of these devices, which have multiple DoFs, in 3D space becomes challenging. In addition, endoscopes are usually advanced through natural orifices by pushing the tail. On the one hand, the insertion process can lead to undesired rubbing motions between the endoscope's body and surrounding soft tissue. On the other hand, poor navigation capability can result in incorrect pathways and trajectories. During colonoscopy for instance, lateral pressure of a bowed loop of the colonoscope against a stretched loop of the colon can cause substantial intestinal ruptures [4]. These cannot only lead to tissue damage (traumatic contact inside the lumen), but experienced endoscopists might also miss locations of polyps. Furthermore, the loss of dexterity might become critical in neurosurgical operations such as tumour extraction [76].

From the ergonomics point of view, colonoscopists commonly suffer hand, wrist, forearm and shoulder injuries. These may be caused by the repetitive pinching, excessive use of upper limbs, torquing and gripping forces, and unnatural neck and body posturing [77] that are required when conducting endoscopic interventions (in particular, in operations when a rigid endoscope is deployed). It is of paramount importance to solve these ergonomic challenges because these procedures are a significant part of the endoscopist's workload.

It is worth highlighting that it is essential to maintain healthy ergonomics and comfort of endoscopists and patients for endoscopic examination and confirmation of diagnostic procedures. Improving ergonomics can increase efficiency in the examination (polyp detection), and an increasing number of patients may be keen to undergo an endoscopic procedure. Therefore, clinicians may be able to give an earlier and accurate diagnose together with their corresponding treatment.

Endoscopic systems with haptic (tactile and kinesthetic) feedback could also enhance the skills of clinicians. Compared to open surgeries, touch information is lost during robotic-assisted surgical procedures due to most master-slave configurations not having embedded haptic feedback solutions. In fact, the Senhance® Surgical System provides force feedback, but training is required to accurately judge the received feedback. In procedures such as neurosurgical operations, an accurate judgment of the forces is essential to avoid damaging healthy tissue [2]. Therefore, haptic feedback systems should be intuitive to have a transparent interpretation of the information. Having feedback of the tissue stiffness is likely to improve precision, effectiveness, safety, and reliability of surgical procedures such as tumour excision [2]. In these medical interventions, there is a risk of requiring recurrent surgeries due to incomplete removal of the affected tissue.

Despite these challenges, lower tissue trauma, immunological stress response, postoperative pain, and patient recovery time make surgeons prefer minimally invasive approaches. During the last decade, research in soft robotics has resulted in promising solutions to overcome some of the aforementioned limitations. In fact, researchers have been successful in combining the accessibility of flexible endoscopes, the controllability of rigid robots, and safety and environmental adaptability of soft materials mechanisms [78].

4. Soft robotic systems for endoscopic procedures: state-of-the-art in research

With ongoing discussion about the definition of *soft robots*, the term *soft* is commonly referred to the inherent material and structural compliance [79]. In this chapter, we use this term to denote robots that are made of soft materials and might include mechanisms that change their body stiffness and shape [80].

Soft materials can include colloids, polymers, liquids, gels, foams, granular materials, and most soft biological materials [81]. According to [82], *soft robotics* comprises all the active and reactive compliant systems ranging from soft actuators and sensors, artificial muscles (i.e. electro-active polymers) up to soft electronics and soft energy harvesting.

Soft robotics offer characteristics that make them suitable for healthcare application, including endoscopic interventions. A number of soft materials that soft robots are made of have different levels of bio-compatibility. For instance, silicone elastomers (NuSil Technology, CA, US) are safe to work inside the body for a limited period of time [83, 84]. On-demand stiffness of soft robotic structures (e.g., to manipulate soft tissue) can be controlled using external stimulus, for instance, such as electric current [11, 85], light, or injection or extraction of fluids [86, 87]. This controllable stiffness capability, together with the inherent softness, squeezability, and flexibility of the materials, facilitates inherently safe navigation and manoeuvrability inside the body with a low risk of damaging tissue or organs. Moreover, soft robotic interaction with the environment and their elongation capabilities [87, 88], which can be used for locomotion, can simplify the process for reaching distant organs. Commonly, the properties of the soft robot are defined by the soft actuator and sensors, that the system is made of.

Soft actuators are usually driven by fluids [89, 90], material jamming [91], tendons [92] or smart materials [85]. Flexible fluidic actuators are made of shrinkable and soft materials that are non-ferromagnetic and, hence, Magnetic Resonance (MR)-compatible. Many flexible actuator structures have embedded hollow chambers that can produce active locomotion when inflated and/or deflated [88]. Inflation also increases the contact area with the environment and, therefore, can increase friction between the soft actuator and environment. Soft actuators are commonly lightweight because they are pneumatically actuated by an external source. Granular jamming actuators comprise an external membrane filled with granules. The stiffness of these type of actuators varies based on different levels of applied negative pressure, "jamming" the internal material affecting the relative speed of the particles of the filling material and its density inside the membrane. Therefore, the rigidity of these actuators will incrementally increase [93]. Other approaches include cable-driven actuators that can be lightweight and scalable if the electric components (motors) are externally located [8]. Smart materials such as shape memory alloys present a high energy density, corrosion resistance, MR-compatible (non-magnetic behaviour), and scalable [57].

Sensors provide feedback for controlling soft actuators and understanding physical interactions with the environment. Apart from application-driven requirements with regards to the sensing range, resolution, durability and repeatability, sensing systems for soft actuators should be flexible and, in some cases, stretchable. Soft robotic applications can employ capacitive, resistive [94, 95], magnetic, optoelectronic, or light intensity [96] sensing. Capacitive, resistive, miniature magnetic elements or waveguides, respectively, are embedded inside the soft robotic body returning a variation of the sensed parameter depending on the applied strain. In optoelectronic sensing, electrical signals that vary with the applied strain as the distance the light has to travel changes are measured. Embedding these materials in elastomers of soft robotic bodies without affecting the overall stiffness is possible due to the use of nanomaterials or conductive elastomer composites, deterministic and ultrathin structures, liquid metals or conductive gels.

Based on this overview of principles of soft actuators and sensors, the following section will present the state-of-the-art of current soft robotic systems for endoscopic applications that have been validated in *ex vivo* phantom and cadaver environments. *In vivo* animal or human clinical tests involving soft robotic systems for endoscopic applications have not been reported up to the time of writing this publication to the best of the authors' knowledge.

It has to be highlighted that this review comprises entirely soft and hybrid (including soft and rigid parts) robots for endoscopic applications. Following the structure of previous sections, this review is divided into optical examination tools and instruments for therapeutic endoscopy.

4.1. Soft robotic instruments for optical examination

When performing visual examinations, endoscopic capsules are the least invasive, as mentioned in Section 3.1. Commercially available capsule endoscopes move through peristalsis inside the body. This approach is less invasive than conventional endoscopy. However, the lack of the capsule's orientation and navigation control hinders the diagnostic efficacy, especially in the stomach [97]. Additionally, frequent production of obstructed images and the inability to perform therapeutic procedures or biopsy decrease the usability of capsule endoscopes [98, 99].

To address some of these limitations, recent research proposes using magnetically actuated soft capsule endoscopes [52]. The locomotion and rotation of the capsule and, hence, the camera view can be controlled externally via an interface. These capsules can then be steered towards soft tissue areas to collect biopsy samples acquiring stomach deep tissue biopsy samples through a fine-needle biopsy technique. After taking a sample, the capsule is retrieved by a tether to avoid any contamination. Nevertheless, reorientation of the patient is required to take biopsies in various locations (anterior, posterior, and lateral stomach surfaces). The advantage of this soft capsule endoscope over its commercially available counterparts is its ability to performing needle biopsy. Its soft Sarrus linkage allows naturally aligning the needle translation to the capsule's longitudinal axis, and the collapsing motion of its soft body exposes the needle for taking the sample. Therefore, examination and collection of samples for diagnosis confirmation can be performed simultaneously [52].

In recent years, there has been an increasing interest in inchworm like soft robots for colonoscopy [87, 88, 100]. They are characterised by advancing peristaltically and being navigated through tubular structures. In [100], an 18 mm external diameter Soft Pneumatic Inchworm Double balloon (SPID) mini-robot is presented. This robot is made of Vero-Clear, a transparent photopolymer, and Ecoflex™ 00-30, a soft, stretchable silicone material. It is worth noting that the actuation pressure is significantly lower than the internal pressure of the colon when it is inflated for a surgical procedure. Anchoring is provided by two inflatable balloons linked by a three-DoF soft pneumatic actuator. Pressurising one or two of the three embedded chambers will result in bending behaviour beyond 100°, whereas simultaneous actuation of all three chambers will lead to overall elongation [100]. Bernth *et. al* proposed a three-module worm-inspired robotic endoscope illustrated in Fig. 5-A [88]. Each module is made of an elastic mesh structure driven antagonistically by tendons. The minimum dimension of the tubular environment that the robot can move through is defined by the 26 mm outer diameter of the rigid collar of its modules. The endoscopic robot can move forwards and backwards as well as anchoring itself. Controlling the bending of its flexible modules adjusts the camera's orientation. It is worth noting that this robot is designed for tubular environments; hence, robot-environment interaction has been proposed to improve sensing capabilities and force generation [101].

To minimise the risk of cross-contamination or infections, [102, 103] developed a disposable low-cost endoscope, illustrated in Fig. 5-B, for examining the stomach and oesophagus. The total cost of this 13.5 mm tip diameter endoscope is $ 25. It comprises an HD camera and three LEDs for illumination at the tip. The tip bending, elongation and retraction are produced by the pressurisation of three rubber bellows connected in parallel. Syringes control the internal pressure of these bellows. During the evaluation, novice, gastroenterology fellows, and gastroenterology attendings required less time to perform a task with the conventional endoscope than with the lows-cost endoscope. It is worth noting that attendings and fellows stated that the new endoscope is more mentally demanding than the conventional

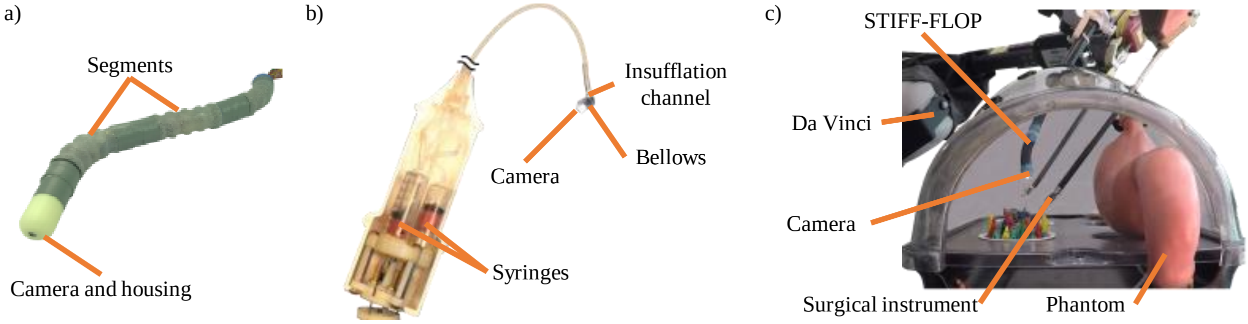

Figure 5: Soft robots for endoscopic applications: a) Worm inspired robotic endoscope (Courtesy: Julius Bernth [88]). b) Low-cost disposable endoscope for visual examination. Its high definition camera and the LEDs at the tip are connected to three rubber bellows. Retraction, elongation, and bending are controlled through the pressurisation of these bellows using Syringes (This figure is a modification from [102]). c) The STIFF-FLOP robotic manipulator for MIS is inspired by the octopus arm - the first soft robotic instrument that performed procedural steps of colorectal surgery in a human cadaver.

endoscope, but novices found it intuitive and easy to learn. This may suggest a short learning curve for the low-cost endoscope.

4.2. Soft robotic instruments for therapeutic endoscopy

Nature can provide valuable inspiration when creating soft robotic devices. For instance, the octopus arm has the ability to squeeze through narrow openings, bend and navigate around obstacles, and catch and manipulate prey through controlling the stiffness of its arm. The STIFF-FLOP project funded by the European Commission has created soft, stiffness-controllable endoscopic devices (as illustrated in Fig. 5-C) inspired by capabilities of the octopus allowing these new medical instruments to be navigated and manoeuvred inside the body with a low risk of damaging soft tissue or organs. The STIFF-FLOP manipulator has multiple embedded chambers that can be fluidically actuated. Elongation is achieved by pressurising all chambers simultaneously, while bending can be performed by activating one or two chamber(s) (pairs) only. Furthermore, squeezability is a feature of the STIFF-FLOP robot as its body is made of soft silicone. Stiffness-controllability has been achieved by integrated granular jamming chambers [104] or applying an antagonistic principle using air and tendon-driven actuation [92]. To improve the stability and transmission of forces of the robotic arm, Brancadoro *et al.* [91] proposed a fibre jamming approach to provide variable stiffness capabilities without increasing its length or external radius of 14.5 mm. The STIFF-FLOP device has been designed to have a free working channel allowing to deploy an endoscopic camera (e.g., with an integrated stiffness sensor [105, 106]) or flexible instruments [3].

Russo *et al.* proposed a multi-articulated soft pop-up robotic arm. 3D structures were created by a hybrid soft pop-up manufacturing approach based on folding multiple layers of laminated rigid-flexible, bio-compatible material. This robotic arm is integrated on the distal end of a flexible endoscope. The pitch joint of the three-DoF mechanism can actuate the end effector (a soft suction-based gripper) to manipulate soft tissue. The add-on device was evaluated inside an *ex vivo* porcine stomach, demonstrating that soft tissue can be handled without any visual obstruction in the camera image of the endoscope [83].

In [107], a manual platform for single-port surgery is proposed based on a variable stiffness mechanism using liquid metal to overcome challenges in limited payload and workspace, triangulation, and to address the fulcrum effect. The bi-directional solid-to-liquid conversion of the metal composite, activated by a variable temperature system, allows controlling the stiffness of the tubes holding the surgical instruments. In particular, effective force transmissions can be achieved in a solid state. On the other hand, reorientation of the tools can be accommodated when the metal is soft and liquid.

Using low-melting-point-alloys (LMPAs) to stiffen soft continuum devices has been investigated for various applications in MIS [11, 85, 108]. They comprise a central flexible inner pipe covered by a heating wire in contact with the LMPA. The entire structure is embedded inside a silicone body. Changing the electric current in the heating wire will change the temperature, which again varies the stiffness. A high current leads to high heat dissipation, which stimulates the solid-to-liquid transition of the LMPA.

On the other hand, Runciman *et. al* propose a soft approach to deploy flexible endoscopes and two flexible surgical instruments for performing Endoscopic Submucosal Dissection. This soft approach intends to decrease the risk associated with the interaction between the endoscope and the tissues. While navigating, the soft robot made of 120 μm thickness material surrounds the flexible endoscope. Once the surgical site is reached, the soft robot inflates to increase its volume and increase its radial stiffness. Force transmission cables connected to the variable stiffness structure hold end-effectors through which surgical instruments can pass. By controlling the length of these cables, the pose of the instruments can be controlled [109].

4.3. Soft haptic technologies for minimally invasive endoscopic procedures

Haptic refers to the sense of touch. Haptic feedback is generally defined as a combination of tactile and kinesthetic feedback. Tactile feedback refers to the mechanoreceptors' information (i.e. Pacinian, Merkel, Meissner, or Ruffini corpuscles) under the skin. They provide information about pressure distribution, stimulus location, deep static touch feature (shapes and edges), and stiffness [110]. Each mechanoreceptor is sensitive to vibrations in a particular range. Their concentration on human skin depends on the part of the human body. For instance, fingerpads are the places with the highest concentration of Meissner and Merkel corpuscles while that of the other two corpuscles is relatively low [111]. Kinesthetic feedback refers to the information given by sensors from muscles, tendons, and joints. They provide information regarding weight and joint angles of the arm, wrist, hand, and fingers. This information helps to determine an approximate weight and dimensions of objects with whom the hands are interacting. In general, haptic feedback supports clinicians on the decision-making process.

Haptic technologies for remote or robotic-assisted endoscopic applications aim to reproduce the physical interaction between the soft tissue and clinician's hands or fingertips that would have been experienced if the surgery had been performed in an open way. As [110] states, tactile feedback systems intend to provide mechanical properties (i.e. surface texture, viscosity, and compliance) of soft tissue. Surgeons use this feedback to differentiate healthy from cancerous tissue or to detect arteries [112]. On the other hand, kinesthetic feedback informs about the force applied to the tissue. The clinician uses this type of feedback in tasks such as suturing and pulling tissue, which is crucial for avoiding unnecessary trauma or damage to tissues or organs.

Several haptic modalities have been investigated: visual feedback [113], haptic tactile feedback, haptic force feedback, haptic stiffness feedback as well as a combination of these. In this section, we highlight haptic stiffness feedback displays made of soft material structures. In [114], a 3D haptic display is proposed that can change its shape and stiffness. The display is made of an array of inflatable silicone pouches with embedded granular jamming material. Applying positive or negative pneumatic pressure will result in shape-change or stiffening. Medical applications include palpation training.

In [115], a multi-fingered variable stiffness tactile feedback actuator is proposed. Similarly to [114], the variable stiffness mechanism is a combination of granular jamming that is located on top of a pneumatic chamber. The pneumatic chamber's role is to enhance stiffness discrimination while the granular jamming provides the variable stiffness stimulus. This solution can be applied to the index, middle and ring finger to improve the haptic feedback of surgeons while performing robotic-assisted minimally invasive procedures [115]. The INSTINCT project funded by the Engineering and Physical Sciences Research Council (grant agreement number EP/S014039/1) aims at integrating miniaturised variable stiffness tactile feedback actuators into the master console of surgical robots for MIS. The advantage of these haptic displays is that surgeons can use their fingertips to palpate soft tissue and assess their mechanical properties.

4.4. Technical challenges for emerging soft robotic, endoscopic tools

As soft robotic systems offer promising advantages over traditional rigid (flexible) endoscopic systems, their development has often been motivated by medical applications. However, only a small number of soft robotic medical devices have actually demonstrated their capabilities in anatomical phantom or cadaver environments. In general, technical requirements for these systems are set by specific endoscopic procedures. For instance, MR-compatibility of medical devices is usually necessary for endoscopic retrograde cholangiography [116, 117]. In this section, however, we will focus on overarching challenges that occur when applying soft robotic systems to a majority of endoscopic procedures. Here, fundamental challenges remain to be investigated - some of which require multi- and interdisciplinary approaches - for successful applications in endoscopic surgery:

1. **Maintaining consistent quality in fabrication and manufacturing:** Soft robotic systems have been created using casting and 3D printing fabrication techniques, respectively. Both methods are associated with substantial limitations such as narrow material choices, low durability, and high variation in fabrication quality. In particular,

weak points of soft robotic systems might occur at interfaces between soft and rigid components that these robots are made of.

2. **Challenges in miniaturisation :** Any medical device for endoscopic interventions must meet size requirements. In particular, constraints in miniaturisation occur when embedding sensing, actuation, and variable stiffness mechanisms into a soft robotic system. These are explained by the current manufacturing processes and the limited variety of miniaturised, commercially available components such as micropumps.

3. **Need for next generation of actuators:** A large number of soft robots are fluidically actuated, but pressurised fluid and proportional valves are commonly located externally due to size requirements. In cable-driven soft actuators, non-linear friction might occur which presents challenges in the development of mathematical models; and, the transmission of forces via tendons to the distal end of a soft manipulator might affect the configuration of the soft body that the tendons are guided through. In addition, a number of smart materials require high electric current resulting in low actuation speed (compared to other fluidic actuation approaches) and complex control methods due to thermo-mechanical behaviour.

4. **Performance of soft robots:** Some soft robotic manipulators show high hysteresis looking into their position vs actuation or force vs displacement data. For instance, using granular jamming as a means to actuate can result in low repeatability performance because of challenges in maintaining the same distribution of the filling material every time the vacuum is applied.

5. **Real-time modelling:** To compensate for some of the aforementioned limitations in manufacturing and actuation as well as in the overall performance of soft robots, real-time kinematic and dynamic models that could provide valuable input for model-based controllers are still under development.

6. **New functional materials:** Depending on the application in endoscopic procedures, soft robotic systems need to be sterile and should not suffer from fatigue of any components over the duration of usage. Sterilisation of (multiple-use) medical devices can have a negative impact on soft materials [57]. To execute a surgical procedure and manipulate soft tissue requires a level of stability and the availability of on-demand stiffness. Therefore, there is a need for new materials that are unaffected by sterilisation processes and can change their stiffness over a wide range and provide effective stiffness capability even when embedded in miniaturised soft robots.

7. **Soft structured sensing elements:** Creating and integrating transducers for soft robots pose challenges as it requires embedding a conductive element inside the elastomer. As mentioned earlier, the interface between the soft robot body and sensing element might be challenging. Furthermore, the combination of different materials might lead to an increment in the structure's stiffness, artefacts in the acquired data, hysteresis, and risk of damaging soft elements of the device or soft tissue in the environment. These could affect the flexibility, durability, and repeatability of the sensor across several sensing cycles.

8. **Intuitive interfaces for multi-DoF soft flexible robotic systems:** Soft robots' continuous and elastic body provides infinite DoFs, in theory: they are able to bend, elongate, and squeeze through narrow opening. A new generation of interfaces should enable clinicians to navigate and steer the tip of these high-DoF robotic manipulators intuitively without focusing on how to position the remaining tail, which can result in additional cognitive load and distraction.

It is worth noting that regulatory bodies should establish a standard framework for benchmarking surgical robots as well as endoscopic solutions in general [118]. This framework should consider clinical evidence, economic parameters, and patient benefits in order to scrutinise and compare results among various platforms. One of these key parameters should include training required (learning curve) by surgeons and endoscopists to use these new soft robotic solutions. More intuitive solutions should be preferred as clinicians may need less intensive training to achieve and then deliver current quality, safety, and consistency expected levels across procedures.

5. Conclusions and potential opportunities for endoscopic soft robotic systems

Endoscopic procedures have become a preferred method over open surgery due to patients' shorter recovery time, shorter stay in the hospital, lower tissue damage, less blood loss, lower impact in the immune system, and lower requirement of anaesthesia. Due to these advantages, endoscopic cameras and instruments are employed in a growing variety of medical examination and treatments.

Medical devices and robotic technology aiming at improving patient's outcome and supporting the clinician during endoscopic procedures have advanced rapidly over the last decades. However, commercially available endoscopic tools such as capsule endoscopes, flexible endoscopes, laparoscopic tools, and other specific endoscopes (for instance neuroendoscopes or bronchoscopes) still require further development to improve manoeuvrability, including haptic feedback, enhance control perspectives, and increase endoscopists' and patients' ergonomics. Addressing these challenges might lead to an increase in numbers of patients who are willing to undergo an endoscopic procedure, which again might increase the early detection of illnesses such as cancer.

Soft robotic systems can provide effective solutions to overcome current limitations of endoscopic procedures as these systems are compliant, squeezable, soft and allow extensive navigation and manoeuvrability inside the body. These properties, together with variable stiffness mechanisms, can improve the ergonomics of endoscopists and patients. Soft robotic systems can reduce clinicians' unnatural repetitive postures and the need to change a patient's posture during medical procedures.

However, current emerging soft robotic technologies require further advancements focusing on how to maintain consistent high quality in the fabrication and manufacturing process; challenges in miniaturised soft robotic systems; the next generation of actuators, sensors and functional materials; real-time modelling approaches. Overcoming shortcomings in these areas will improve the performance of current systems and allow for the development of accurate real-time kinematic and dynamic models. In addition, navigating multi-DoF, soft flexible robotic manipulators through confine space inside the body can be an additional cognitive load to the clinician. As a consequence, intuitive interfaces enabling clinicians to navigate and steer the tip of these high-DoF robotic manipulators without focusing on how to position the remaining tail should be explored.

It is profoundly important, however, that new developments in the field of soft robotic endoscopic systems concentrate on improving the patient's outcome and health. The focus should be on addressing shortcomings and limitation of current procedures that negatively impact the patient and clinician to make medical procedures safer and less invasive and demanding for patients and clinicians. Hence, interdisciplinary research and collaboration between medical experts and engineers are essential to developing innovative soft robotic systems that deliver the expected positive impact in the field of endoscopic interventions.

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