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Authors:	Benoit Rosa, UNISTRA Michalina Gora, UNISTRA Jorge Lazo, POLIMI Florent Nageotte, UNISTRA Emmanuel Vander Poorten, KU Leuven Fabian Trauzettel, TU DELFT
Peer review:	Diego Dall'Alba, UNIVR Arianna Menciassi, SSSA

Abstract

This deliverable presents the workflow analysis of the different clinical scenarios for the ATLAS project. Three clinical scenarios are being studied by the different ESRs from the project: Colonoscopy, Urology, and Vascular Catheterization. For each clinical scenario, one or two operations are being analyzed. We highlight the different steps, the instruments used, and the challenges associated with those procedures.

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1 Introduction

Within the scope of the ATLAS project, ESRs will work on one or several of the clinical targets, developing key technologies to raise the level of autonomy of the robotic devices, and improve surgical gestures and outcomes. The ATLAS project is structured in 3 clinical targets: gastrointestinal operations (C1), urology and especially ureteroscopy (C2), and endovascular catheterization (C3). The three clinical targets have in common the fact that endoluminal operations play a key role in the surgery or treatment. C1 and C2 are natural orifice endoluminal procedures, while C3 is a minimally invasive surgical approach.

In this document, we will detail the workflow of some selected surgical procedures for each of the clinical targets. Through this analysis, we will see that many procedures are similar, and why and how the developments proposed by ATLAS ESR projects can answer to many of the clinical needs. The gained insights may support cross-fertilization and transfer of technology from one field to the other. At the end of the project (PrM.40), relevant demonstrator platforms (reported in deliverables D5.2 to D5.4) for each of the three domains will be able to benefit from technology developed in the neighbouring scenarios.

This deliverable document is structured as follows: sections 2 to 4 present workflow analyses for a selection of procedures in the 3 clinical scenarios of the ATLAS project. Each time a short overview of common and challenges is provided. The document concludes with Section 5 which draws general conclusions and links the identified technical challenges, making the bridge with the ESR projects within ATLAS.

2 C1 - Gastrointestinal operations

Gastrointestinal endoluminal procedures are typically carried out using a flexible endoscope. The endoscope can be inserted through the upper digestive tract to reach the esophagus or the stomach, or through the lower digestive tract to reach the colon. In both cases, the surgeon will use the endoscope as a flexible platform to reach the clinical target while *seeing* the clinical environment. Once there, the clinical gesture must be performed.

In the following of this chapter we will use two examples of common, but challenging, clinical procedures, in order to highlight the challenges associated with endoluminal surgical operations.

2.1 Endoscopic Submucosal Dissection

Endoscopic Submucosal Dissection (ESD) is an intraluminal procedure used for treating many superficial cancers in the digestive tract (esophagus, stomach, colon) with no lymph node involvement (T1 stage in the TNM classification[1]). It can replace full thickness resection when tumors are limited to the mucosa and upper third part of the submucosa (SM1), which is advantageous for the patient because it is a minimally invasive, no scar approach. An alternative endoscopic procedure is EMR (Endoscopic Mucosal Resection), but for large lesions ($>$ T1a, typically more than 2cm diameter) ESD allows en bloc resection, which is difficult with EMR. When realized correctly for the mentioned indications, ESD is generally a curative treatment with low local recurrence rates (only 1% reported in [44]). It can be complemented by endoscopic ablation of the precursor gastrointestinal diseases. ESD was originally developed for colorectal tumors [9] and was then extended to stomach [26] and esophagus [27].

2.1.1 Conventional procedure description

The procedure is generally performed by two persons: a skilled user (surgeon, endoscopist or interventional gastroenterologist depending on the countries) and an assistant. The skilled user controls a flexible endoscope (gastroscope for esophagus and stomach, colonoscope for rectum and colon) equipped with a transparent distal cap. The instruments are passed through the channel of the endoscope and are manipulated by the assistant. In normal conditions (no complications) effectors are electric knives (which can have different shapes and can be changed during the procedure) [2]. The activation of electrosurgery tools is realized by the skilled user by using pedals.

The procedure is realized with the feedback of the monocular endoscopic camera attached at the distal tip of the flexible endoscope, displayed on a 2D screen. It can be decomposed in seven steps:

1. Navigating the endoscope and locating the tumor. Usually the tumors have been detected during a previous examination and they may have been marked, when needed, with an electrosurgery tool. The longitudinal location in the organ has also been recorded by the physician for simple recognition.
2. Delineation and marking of the tumor with healthy margins by realizing several cautery burns at the periphery of the tumor. These markings will have to be present on the dissected specimen at the end of the procedure.
3. Injection of a solution for lifting up the mucosa and easing separation from the underlying muscular layer. The solution can for instance be based on Glycerol [13, 1] and is usually mixed with Methylene blue for providing a visual feedback. Further injections can be required afterwards during the dissection depending on the duration of the procedure and leaking of the solution. The injection is realized with an injection needle.
4. Creation of an access to the submucosa. Depending on the procedure, it can be done by either creating a pocket, a tunnel, or peripheral complete continuous incision of the mucosa around the markings. This is realized with an electrosurgery knife.
5. Dissection through the submucosa in order to separate it from the muscular layer of the esophagus / stomach or colon. A cautery device is used as end-effector.

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[1] From `https://en.wikipedia.org/wiki/TNM_staging_system`. The TNM Classification of Malignant Tumors [41] is a globally recognised standard for classifying the extent of spread of cancer. T describes the size of the original (primary) tumor and whether it has invaded nearby tissue; N describes nearby (regional) lymph nodes that are involved; M describes distant metastasis (spread of cancer from one part of the body to another).

6. Inspection of the dissection area for searching for perforation of the muscular layer, residual adenoma, and cauterization of damaged vessels.
7. Retrieval of the specimen for its visual inspection and afterwards histology analysis. This is realized by inserting a snare in the accessory channel to grab the specimen, and removing it together with the endoscope.

Figure 2.1 shows an illustration of the critical steps in an ESD procedure.

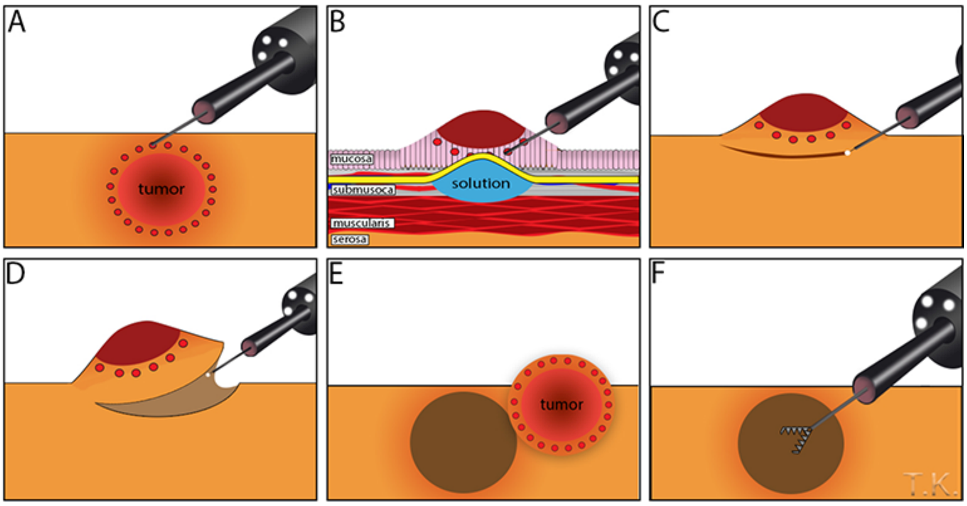


Figure 2.1: Critical steps in an ESD procedure. A: tumor delineation; B: Solution injection; C: Access creation; D: Dissection; E and F: inspection and removal. Source [11].

A typical ESD takes between 30 minutes and 2 hours when done by experts [34]. Step 5 (dissection) usually takes more than 50% of the total time.

The main complications following ESD are perforation, peritonitis and bleeding. The complication rates were reported to be 3.5% for gastric ESD, 3.3% for esophageal ESD, and 4.6% for colorectal ESD in [25]. The two main adverse events occurring during ESD are excessive bleeding and the perforation of the muscular layer. In this case the perforation has to be closed, conventionally by using clips [29]. This significantly extends the duration of the procedure. A perforation which is not detected might lead to surgical treatments for avoiding a critical outcome [37]. Another adverse event is the unwanted piecemeal resection. This makes assessment of the complete resection difficult. Incomplete resection may lead to an increased risk of local recurrence of the tumor [28].

In addition to these issues directly linked to the ESD procedure, there are other difficulties in the pre-operative and follow-up steps. The interest of ESD is the minimally invasiveness with respect to full thickness resection. The success of ESD is linked to the validity of the estimated stage of the tumor and to the completeness of the resection. Tumor staging is generally realized both visually and using an endoscopic pre-operative biopsy and confirmed afterwards by the histological analysis of the retrieved specimen. CT scans are used to evaluate the loco-regional spreading of the cancer, possibly coupled with PET. In case of early cancer, endoscopic ultrasounds (with high-frequency) can be used to assess the T stages. In this case the complete tumor must be scanned in order to assess the depth of the tumor [38].

2.1.2 Problems with ESD procedures

The ESD procedure as described is very challenging for physicians, and few training programs exists. As a result, only a few specialists perform it in daily routine in Europe. The difficulty of the surgical gesture can be attributed to the difficulty of manipulation of the instruments (flexible endoscope), and to the difficulty to evaluate the current state of the procedure from the endoscopic images.

For moving the electrosurgery instrument, the main user has to move the distal head of the endoscope in 3D by: a) actuating two knobs at the proximal handle, which control the bending of the distal head in two orthogonal directions, b) by pushing / pulling the shaft of the endoscope and by c) rotating the shaft. The effect of the knobs actuation is constant in the image (left / right and up / down) but its impact on the position with respect to the environment depends on the situation. The effects of translation and rotation depend on the interactions between the shaft of the endoscope and the digestive tract, which is variable and not known by the physician. The displacement of the effector in the endoscope channel, on the other hand, only provides limited dexterity enhancement, as the instrument is not articulated. The coordination of movements for realizing precise displacements is therefore complex. The position of the physician is also uncomfortable and the rotation of the endoscope requires ample rolling of the endoscope handle. In case of badly controlled motions, the electrosurgery tool can penetrate the muscular layer and create a perforation. It can also create holes in the dissected specimen, resulting in piecemeal resection, which is undesirable. Recent developments have shown that using a teleoperated endoscopy system helps performing ESDs in a safer and faster way [18].

During the submucosa dissection (step 5), the endoscope must be slipped under the submucosa. The images of the endoscopic camera therefore only provide very local information (the typical field of view is then about 1cm wide). The user has to go backwards with the endoscope at regular time intervals in order to judge the correct proceeding of the procedure and to examine and manipulate the tissue currently resected. This implies switching between two working configurations, which is both difficult and time consuming. Depending on the location of the tumor, the specimen can also fall onto the endoscopic camera and decrease visibility.

2.2 Diagnostic and staging of colorectal cancer

Colorectal cancer (CRC) is the third most common type of cancer in the world and in Europe 432 000 new cases are reported every year [6]. Even though, when detected early, colorectal cancer is one of the most curable forms of the disease, only 40% are detected at stage I. CRC it is still one of the leading causes of cancer related death in Europe because the 5-year survival rate decreases from 74% at stage I down to 6% at stage IV. It is thus of paramount importance to diagnose the disease as early as possible [35]. Additionally, early stage cancer can be treated endoscopically in a minimally invasive way, however correct staging of the cancer is crucial to choose an optimal treatment.

While differences exist in local screening programs worldwide [35], colonoscopy is a major element of cancer screening programs. Although the overall efficiency of colonoscopy is similar to less invasive tests such as Fecal Immunochemical Testing [30], it exhibits a higher detection rate for advanced neoplasia and adenomas [30, 35]. Endoscopy has significantly improved management of gastro-intestinal (GI) tract diseases by providing access to internal organs otherwise not accessible in a noninvasive way.

2.2.1 Description of the conventional procedure

Colonoscopy procedures follow a well-established procedure plan. A typical colonoscopy takes between 20 and 30 minutes. It includes:

Colonic cleansing - A day before the procedure the subject has to undergo colonic cleansing, which requires a special diet and self-administered laxative for removing colonic contents to optimize the safety and quality of the procedure.

Preparation and sedation - Depending on the clinical guidelines and the country where the procedure is conducted the subject may or may not be sedated. In the majority of the cases the patient lays down on the examination table on the left side and sedatives of various strength are injected intravenously to improve patient tolerance of the procedure.

Intubation - The colonoscope is inserted through the rectum and is navigated towards the proximal (here distal = anal side) end of the colon using feedback from the endoscopic camera. Two knobs of the endoscope handle allow bending the distal tip of the colonoscope while inserting and rotating the whole device to navigate to the desired area. During the process the doctor can use insufflation using air or carbon dioxide delivered by the endoscope insufflation channel to improve visualization of the colon and to limit friction between the scope and the tissue.

Examination and withdrawal - once the cecum is reached the doctor slowly withdraws the endoscope and examines the tissue for presence of polyps or lesions using a white light endoscopic camera. If a suspicious lesion is observed, more advanced imaging like NBI can be used to add additional contrast. To collect a biopsy a biopsy forceps is inserted and moved forward through a working channel of the endoscope. A small sample of tissue is removed and placed in a collection jar with information about biopsy location corresponding to position marks on the endoscope. The withdrawal time is linked to the efficiency of adenoma detection rate. Slow withdrawal allows for finding more lesions.

2.2.2 Problems associated with the procedure

Problems associated with colonic screening belong to two main families. On the one hand, navigation problems associated with manipulation of the device limit the navigation performance. On the other hand, visualization problems occur, especially since inspection and effective staging of the cancerous lesions (if any) can be difficult using a simple video imaging modality.

Manipulation and navigation: endoscopic intubation requires practical skills obtained by extensive training in order to avoid looping [17]. The endoscope flexiblity is limited, the surgeon has no direct feedback showing the endoscope shape within the surrounding anatomy, and its manipulation requires several coordinated movements including pushing and turning the endoscope body, manipulation the knobs for bending the tip, shaking the endoscope, applying torque in chosen directions, as well as using the insufflation. Passing from the rectum to the sigmoid colon and then to the ascending colon is the most challenging. Only if achieved with a minimal loop formation (see Fig. 2.2 for various illustrations of colonoscope loops in the cecum) the examination of the full colon is feasible. Fine manipulation skills are also required when performing advanced diagnostic gestures at the clinical site. In fact, with the increasing number of endoscopic accessories (that include catheters that bring in advanced imaging and tools for tissue manipulation) there is a problem with positioning and/or stabilization of tools over time. This is for example the case for endomicroscopy tools where full contact at correct orientation is needed to obtain high resolution images [22]. Precise and controlled positioning is also beneficial for increasing the field of view of the microscopic technologies and to obtain e.g. a larger field of view by using mosaicking techniques [43]. Precise information about the position of the tools is also needed for co-registration of various imaging technologies, as well as to localize the biopsies. This information can be made available during a follow up imaging or minimally invasive treatment.

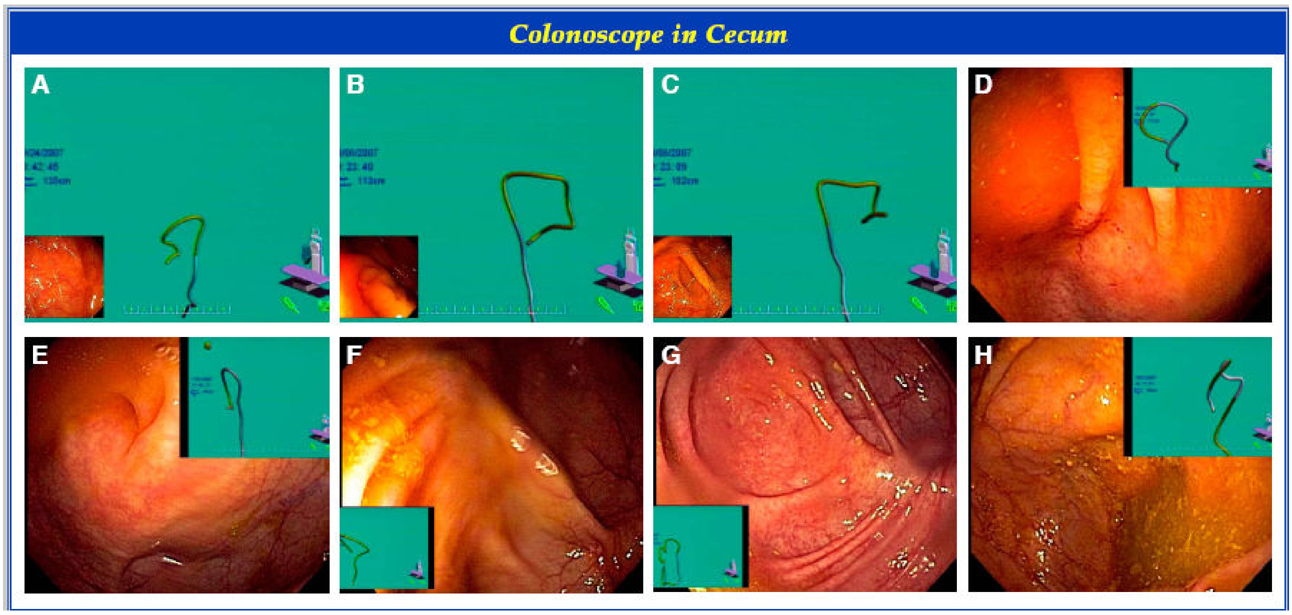


Figure 2.2: Illustration of colonoscope looping in the cecum of different patients. Source [10]

Visualization and characterization: Large efforts are placed on the development of advanced endoscopic imaging methods to improve sensitivity and specificity in diagnosing lesions detected during withdrawal. These developments include for example:

- Digital chromoendoscopy: based on the enhancement of the image by either spectral processing of color images (e.g. Fujinon FICE and Pentax i-SCAN) or by employing filtered visible illumination (e.g. Olympus NBI), which results in an increase in contrast of the vasculature and mucosal changes.
- Cellular imaging: because standard of care histopathology is based on the microscopic examination of tissue samples, combining optical microscopy with endoscopy has received significant attention. Magnification endoscopy, microendoscopy, and confocal laser endoscopy allow for imaging microscopic details of the mucosa, revealing cellular changes, with magnifications ranging from 150x for magnification endoscopy and 1000x for microendoscopy. However, while displaying exquisite details of the intestinal mucosa, all of these technologies require contact with the mucosa and provide information only about superficial mucosa from a small field of view.
- Optical Coherence Tomography (OCT), which relies on an interferometer approach to provide depth-sensitive scattering contrast within tissues at very high resolution and very high acquisition speed. Recent studies revealed that results from OCT correlated with those from histopathology, suggesting its potential for assisting gastroenterologists in their diagnosis.

Abovementioned advanced imaging technologies can be used for better staging of the cancer. Correct staging is necessary to choose between minimally invasive endoscopic treatment in early stage cancer and open / laparoscopic surgery in more advanced stages. Cancer stage depends on cancer size and its invasion in the wall of the colon or rectum. In general if cancer invasion has not reached the muscle layer and is contained to mucosa and submucosa, it is a stage I cancer that can be treated endoscopically. Tissue biopsies provide only partial representations of the lesion and thus other methods are needed in order to obtain a global representation co-registered with local information. Co-registration of imaging modalities with the endoscopic images [46] as well as advanced map construction methods [42] are promising research developments in this field.

3 C2 - Urology and ureteroscopy

Urology is the branch of medicine that focuses on medical and surgical treatment of the urinary tract and the male reproductive organs. Organs typically concerned are the adrenal glands, the bladder, the kidneys, the prostate and the seminal vesicles. Minimally invasive approaches typically follow the retrograde approach, entering the urinary tract through the ureter. This approach has the advantage to be incision free since the entry point is a natural orifice in the body. For this reason, in ATLAS, we focus on clinical and surgical procedures using ureteroscopic approach.

3.1 Kidney stone removal

Kidney stones, or urolithiasis, can be described as an accumulation of mineral material (calcium oxalate, uric acid, struvite or cystine) inside the kidney in a solid form. Although risk factors depend on many factors such as the age, sex, BMI, or ethnicity of the patient, it is estimated that 1 in 15 persons may be affected at some point in their lives, with a recurrence rate of about 50% [3, 19]. Calculi may appear anywhere in the urinary tract but are more common in the kidneys.

Small kidney stones may be evacuated with urine. When the size of a stone is larger than 5 mm, it can block the urinary tract, leading to what is called an acute renal colic. Three approaches exist: shock wave lithotripsy, percutaneous nephroloithotomy, and ureteroscopy. Those three treatment options (together with the more radical open surgery) are complementary. For patients with large, resistant kidney stones, or patients who are pregnant, morbidly obese, or with specific conditions such as coagulopathy, the ureteroscopic approach is preferred [19, 4]. In the following we will describe the ureteroscopic approach for the management of stones located inside the kidney.

3.1.1 Ureteroscopic management of kidney stones

Ureteroscopy is a procedure generally performed by one surgeon and one assistant. After exploring the bladder with a cystoscope to identify the ureteral orifices, a flexible ureteroscope is inserted. A guidewire is then passed through the ureter up to the kidney calices. This guidewire insertion is made under x-ray guidance (fluoroscopy). Once its position is confirmed, the ureteroscope is guided through the ureter by the guidewire, still under fluoroscopy guidance. The surgeon inserts the endoscope while the assistant holds the handle to make sure that the bendable tip keeps a straight shape.

Once the endoscope is inside the kidney, connections for the video cable and light are made, and the surgeon can start seeing the endoscopic images. Exploration of the renal pelvis is carried out in order to identify all stones (in fact, ureteroscopy may be carried out after an unsuccessful shockwave lithotripsy, with several stone fragments remaining).

Once stones are identified, several options can be used. If the stones or fragments are small enough, they can be retrieved using a nitinol stone retrieval basket passed through the endoscope working channel. This operation requires removing and reinserting the whole ureteroscope for each stone. If stones are too big, they must be destroyed *in situ*.

A fiber connected to a Holmium:YAG pulsed laser source (2100 nm) is used to destroy the stones. The surgeon first collects the stone using a nitinol basket to bring it inside the main cavity of the renal pelvis. The laser is then aimed at the stone in order to destroy it layer by layer. Small fragments will be evacuated by normal urine flow, while larger fragments must be either destroyed again with laser or collected with a nitinol basket.

3.1.2 Challenges associated with the procedure

The first problem which occurs during these type of procedures is the access difficulty. Even though advances have been made to access the upper urinary tract, sometimes complications are present when introducing the ureteroscope into the ureteral orifice, negotiating the intramural ureter, or progressing up the ureter or around the calyces. The underlying reasons which could lead to these situations are: unusual patient anatomy ureteral narrowing which could be caused by stricture or extrinsic compression; obstruction from an edema. As reported in [36] this kind of problems are present in around 1.6% of a study of 322 procedures. As suggested in [12] the use of a flexible rather than a semirigid ureteroscope can facilitate safer and more reliable access to the mid-and upper ureter and collecting system.

Visualizing both the anatomy and the endoscope at the same time is also challenging. This is due to the fact that the surgeon typically has two forms of feedback (see Figure 3.1). On the one hand, the endoscopic camera at the tip of the

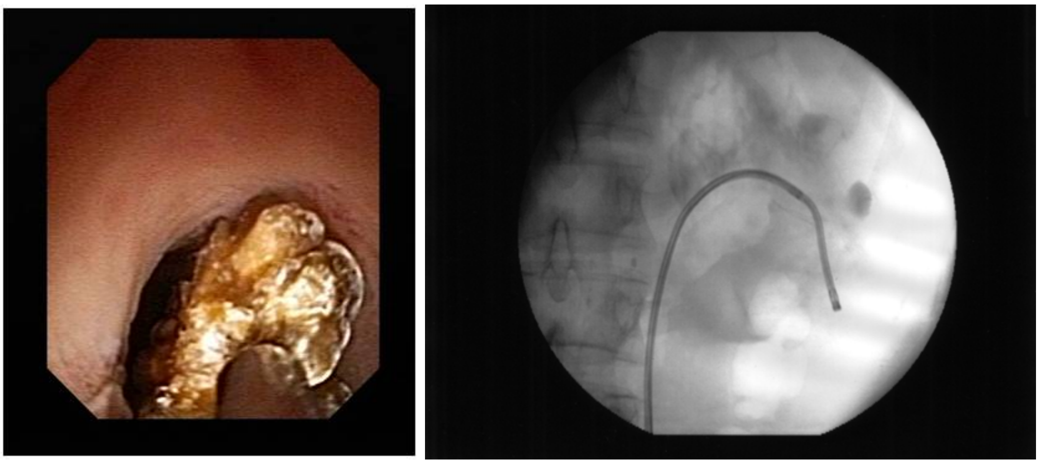


Figure 3.1: Visual feedback in ureteroscopy through the endoscopic camera (left) and the fluoroscopy images (right). Source [7]

ureteroscope provides a local information at the ureteroscope's tip. Although the image quality has improved with chip-on-tip digital cameras [47], images are sill low quality, distorted, and providing only local information at the ureteroscope's tip. On the other hand, clinicians use fluoroscopy to navigate the endoscope in the anatomy. This technique has two major drawbacks: first, it produces ionizing radiations to both the patient and the surgeon (forcing him/her to wear a heavy leaded vest, increasing fatigue). Second, it shows the endoscope and guidewires but not the anatomy (the latter can be briefly seen with contrast agent, but its use should be limited because of nephropathology risks). Advanced techniques enabling the reconstruction of both the endoscope shape and the anatomy it is progressing in, possibly registered spatially with fluoroscopic and/or endoscopic images, would greatly improve navigation and orientation during surgery. Such techniques are however not used in clinical practice and would require new developments, as well as slightly changing the clinical workflow of the procedure.

A second challenge with visualization is related to the limited degrees of freedom of ureteroscopes. Due to diameter constraints, bending is only controlled in one plane, and it should be coupled with rotation of the endoscope shaft in order to perform 3D movements. This makes spatial orientation difficult for surgeons because the line of horizon is almost never horizontal and changes orientation as the intervention evolves. It is not uncommon for surgeon to inject air bubbles through the working channel in order to know where is up (12 o'clock) and where is down, as can be seen on Fig. 3.2

Figure 3.2: Injection of bubbles to see where 12 o'clock really is in the endoscopic image (the scope is upside down). Source [8]

Finally, the last problem is related to the difficulty of handling fine gestures. As for gastroscopy, the insertion of the endoscope is directly handled by the surgeon, while bending of the tip is controlled by one knob on the handle. As said before, 1-degree of freedom bending is combined with rotations of the endoscope body to perform 3D movements. Such movements require fine coordination. The recent introduction of robotic systems with a teleoperation console improved on this point [33]. Robotization is however handled at the proximal side, and nonlinearities in the transmission mechanism prevent the user from performing fine distal movements. This is particularly critical when using laser energy for destroying kidney stones: shooting repeatedly at one point will break the stone into fragments which will later need to be retrieved one by one with a basket. On the contrary, sweeping the stone surface while shooting with the laser will vaporize it layer by layer. Actuators embedded at the tip may improve on this point, although existing research on this topic is quite preliminary [31].

The above-mentioned challenges result in intraoperative complications. A review of the most common intraoperative complications [32] cites avulsion, major and minor perforation, mucosal abrasion and stricture as typical complications. Minor perforation is the one which appears in more cases with an average of 1.99% of the analyzed procedures followed by Stricture (0.58%), and major perforation the complication the one with lower rate (0.06% of the cases). An overexposure to x-ray or increase of procedure time related with difficulties in orienting the endoscope and performing fine manipulations are not listed, since those are not intraoperative complications. They can however be associated to co-morbidities since they increase the dose of ionizing radiation received by the patient, and the time of anesthesia, respectively.

4 C3 - Endovascular Catheterization

4.1 Coronary Total Occlusion

A chronic total occlusion (CTO) is defined as the complete obstruction of a coronary artery with an occlusion duration of more than 3 months. CTOs are identified in up to one third of patients with coronary artery disease [15]. Percutaneous Coronary Intervention (PCI) is a procedure which aims to treat this condition, in which cardiologists try to (re)cannulate the coronary arteries by pushing aside the plaque. A stent is placed next to restore and maintain the blood circulation.

4.1.1 PCI procedure

Cardiologists employ multiple sorts of catheters and guidewires that are introduced in the femoral or the radial artery and moved up to the coronaries where they are employed to cannulate the occluded vessel. After the occlusion has been crossed a balloon catheter is advanced and dilated to restore the blood flow. One or multiple stents will be advanced and deployed in the affected region of the coronaries to maintain the vessel patency. A final angiography will be conducted to ensure flow has been restored before removal of all equipment and closing off of the patient. Surgeons may make use of following devices to access the vascular system and (re)cannulate the occluded vessels:

- guide catheters and guide wires
- microcatheters
- dual lumen catheters
- balloons
- stents

During the procedure, feedback is almost always indirect for the surgeon. Insertion of the catheter is done manually through a small port in the femoral or radial artery, severely limiting any haptic feedback the surgeon may feel. The visual feedback is also indirect, with ample use of fluoroscopy and angiography. Local feedback can also be used with IntraVascular UltraSound (IVUS) and Optical Coherence Tomography (OCT) to visualize the coronaries, the occlusion itself, or a stent that was put in place [5, 16].

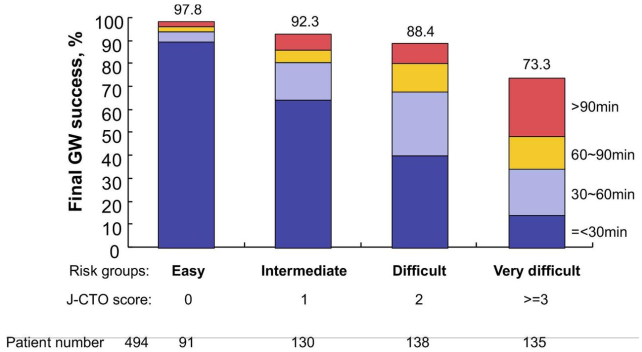


Figure 4.1: CTO procedural success as a function of the J-CTO score. Source [20]

Morino et al. reported the success-rates of CTO-PCI treatment in function of their J-CTO score (see Fig. 4.1). *Easy* lesions with a J-CTO score of 0–1 had a success rate greater than 90% (97.8% and 92.3% respectively). *Difficult* lesions with a J-CTO score of 2 had 88.4% success rate, and *Very difficult* lesions with a J-CTO score equal or greater than 3, having a 73.3% success rate and demanding a prolonged time for crossing.

4.1.2 Challenges associated with the procedure

Whereas the success-rate of CTO-PCI has increased over the last years, clinicians still face quite some problems and successful treatment is far from guaranteed. Problems can be roughly categorized in two categories:

Visualisation: Due to poor visualization the location and the extent of the occlusion is often difficult to determine. X-ray radiation and angiography are commonly used, but locating the CTO with them is not straightforward. Moreover, such imaging modalities are harmful for the patient because of radiation, and contrast agents may induce nephropathy and severely increase the overall morbidity for high-risk patients [23]. The occlusion is often located at the entry of the side-branch. Contrast agent will therefore be flushed through the non-occluded vessel given little insight in where the side branch starts. Plaque or calcifications are not visible on X-ray/angiography. As described above, IVUS or OCT can be used to observe and assess plaque or calcifications. The problem is that these patients typically have a lot of plaque and calcifications, not only at the level of the occlusion. Furthermore IVUS and OCT have difficulty to see through plaque or calcification, which makes it hard to detect whether behind some plaque or calcification a side-branch is hiding. Clinicians are reluctant to use OCT in anything else than a-posteriori validation as the OCT relies on a clear view which involves flushing a clearing agent under relatively high pressure. On the onset of the procedure this may cause the creation of a false lumen if the intima has been pierced. Finally, note that given the limitations of current visualization tools clinicians make use of their anatomic understanding of the procedure. Additionally they rely on haptic feedback which may tell them whether or not they are in contact with a somewhat stiffer occlusion or a vessel wall.

Manipulation: The occlusion consists of stenosis, lipid cores and areas of fibrosis which are typically stiffer than the vessel wall and even instruments that are used for crossing the occlusion. The success rate of the procedure is highly correlated to the configuration of the occlusion. Morino et al. introduced a lesion-related difficulty grading tool, the J-CTO score [20]. An occlusion length greater than 20 mm, the presence of a greater than 45 degrees bend within the occlusion, the presence of intralesional calcification, and the delineation of a stump at the proximal end are four angiographic parameters shown to influence the percentage and time requested for anterograde recanalisation. With the addition of a fifth non-angiographic parameter derived from the clinical history –a previous failed attempt– the J-CTO score can be calculated by attributing one point to each of these parameters [15].

Manipulation is difficult for several reasons. First, the small diameter and tortuous nature of the coronaries, making it difficult to introduce steerable catheters or guidewires. Instead, pre-bent guide-wires are often used, but the pre-bent portion may damage other parts of the fragile vasculature. Second, the rigidity of the CTO which is often more stiff than the guide-wire that is used to cross it, making the wire buckle and bent away. A number of rather exotic micro-catheters have made their appearance on the market to deal with the occlusion in other ways, e.g. by embedding a laser and ablating the occlusion, by including a pneumatic drill to cut ones way through the occlusion or by pressure waves that are directed to disintegrate the occlusion. Other approaches avoid the rigid occlusion by passing through the softer sub-intimal space.

4.2 Iliac peripheral artery disease

Peripheral artery disease (PAD) is a medical condition in which plaque -consituted of fat, cholesterol, calcium or other substrates in the blood- builds up in the arteries. In case of Iliac PAD, blood flow towards the legs is restricted or blocked. Lower extremity PAD is often asymptomatic and, consequently, is under-diagnosed. An evolving PAD condition may however lead to several complications, from limb pain during exercise, intermittent claudication, to Critical Limb Ischemia (CLI). Randomized multi-center studies have found that 25 to 30% of patients with asymptomatic PAD will develop CLI. In turn, in patients, with CLI, 1-year outcomes include amputation in 30% of the cases and death in 25% of the cases [24].

Shu and Santulli estimate that worldwide, more than 200 million people suffer from some degree of PAD, with a prevalence greater than 20% among those aged over 80. [39] Furthermore, according to a 2015 article studying a cohort of 756 newly-diagnosed patients (mean age 65 ±9.8 years) by Smolderen et al [40], 51% of patients showed a single lesion, 26% presented with two, and 23% three or more. These lesions were classified as being in either:
(1) proximal locations (distal aorta, common iliac,external and internal iliac),
(2) distal locations (common femoral, deep femoral, superficial femoral, popliteal, crural, tibial and peroneal)
(3) proximal *and* distal locations, or
(4) non-significant locations.

4.2.1 Iliac artery recanalisation

In the case of suspected lower extremity PAD, it is generally preferred to first perform an angiography of the problematic vessel via the less affected (i.e. contralateral) femoral artery. Such a pathway is depicted on Fig. 4.2, and follows an initial retrograde (against blood flow) approach before travelling across the aortic arch and down the other common iliac artery

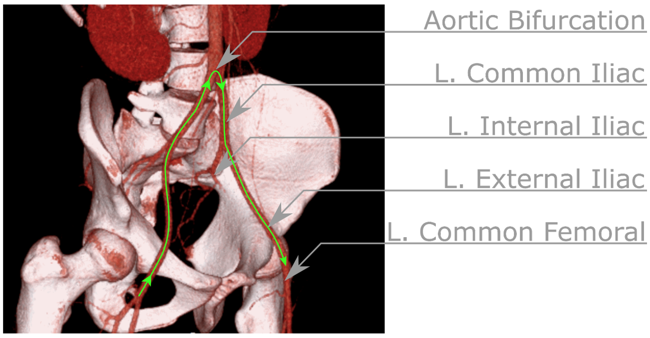


Figure 4.2: Volume rendered CT showing a contralateral retrograde access from the right common femoral artery to the left via the aortic bifurcation.

in an antegrade (with blood flow) direction. Upon angiographic analysis, if the location and size of the patient's lesions allow, the operating physician may elect to place an ipsilateral (same side) access.

Normally, Iliac artery lesions pose an exception to this rule, and are preferentially accessed ipsilaterally in retrograde as this makes for better control of intravascular instruments. However, if the lesion(s) extend into the external iliac or the common femoral artery, such an access may overlap with the lesions or obstruct blood flow and impair angiography [21], forcing a contralateral approach.

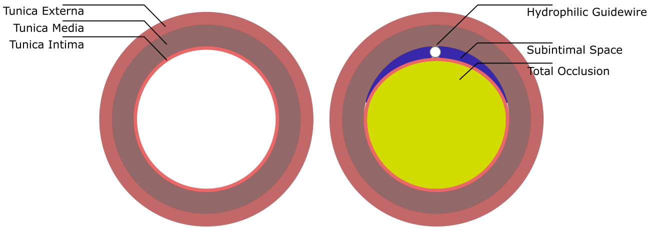


Figure 4.3: Primary layers of an artery (left) showing the subintimal space with a guidewire (not to scale) on the right

Similarly to the case of CTO, totally occluded vessels are often crossed by passing a wire subintimally (see Fig. 4.3) past an occlusion [14], and then reentering into the lumen behind it. An angioplasty balloon is then inserted over the wire and inflated, creating a replacement lumen which bypasses the blockage. This task requires a great deal of dexterity in wire manipulation, and if there are multiple occlusions or stenoses to treat in this way, controlling the wire in a second or even third lesion becomes more and more difficult, especially if the artery has to be accessed contralaterally.

4.2.2 Challenges associated with the procedure

Patients with multiple or particularly long lesions affecting the distal external iliac artery are difficult to treat with existing intravascular interventions as the surgeon has to guide wires across the aortic bifurcation before trying to cross the target lesion. Furthermore, patients showing an iliac occlusion at the level of the junction to the distal aorta are impossible to treat via a contralateral femoral approach, and need to be treated via the brachial artery (on the inside of the upper arm), further complicating these cases. Existing steerable catheters such as the Medtronic TourGuide$^{\text{TM}}$have some tip steerability capability which allows traveling in the vascular anatomy. Such catheters, however, require deflecting against the vascular walls, which may be dangerous for the patient, especially in the case of multiple PAD locations. All those challenges make the success rate of the subintimal approach quite low, with 25% of technical failure cases [45].

5 Discussion and outlook

As we have seen through the analysis of the different clinical use cases endoluminal interventions share many common points, even in different clinical scenarios such as Colonoscopy, Urology, and Endovascular Catheterization.

The main points requiring attention are manipulation, fine navigation, and visualization. Such clinical problems can take many forms, but often share an underlying technical reason. In ATLAS, we have identified four main areas where the developed technologies may improve the state of the art and bring us closer to semi-autonomous or autonomopus procedures in endoluminal surgery: Actuation, Sensing, Modeling and Control, as shown on Fig. 5.1.

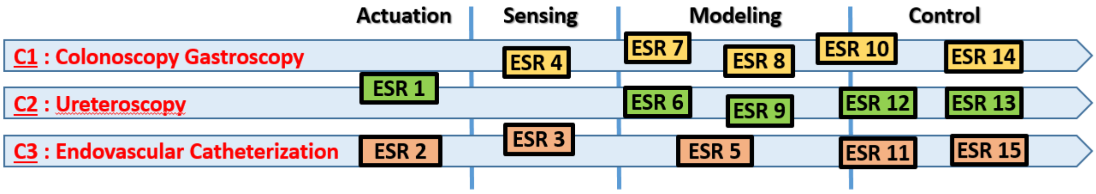
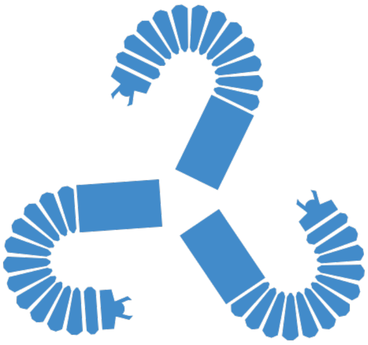


Figure 5.1: Relation between the technical challenges posed by the clinical use cases and the ESRs projects in the ATLAS

The development of new actuation technologies will benefit all clinical scenarios. Indeed, flexible, slender yet agile devices or even untetethered diagnostic tools will make possible new interventions and fine manipulations. Sensing and modeling will enable localizing the endoscope or catheter within the anatomy it is evolving into, as well as estimating its shape. Such sensing modalities will also allow identifying the nature of tissues, which in turn will allow our developed control algorithms to take more informed decisions. Such decisions may be dependent on the type of gesture being performed as well as the phase of the surgery and the tools being used. Phase and tool detection as well as episode segmentation will provide decision algorithms with curcial information with this regard.



The ATLAS project

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ATLAS-D10.1-1.0

Horizon 2020

Bibliography

[1] Rui Castro et al. "Solutions for submucosal injection: What to choose and how to do it". In: *World journal of gastroenterology* 25.7 (2019), p. 777.

[2] Hyuk Soon Choi and Hoon Jai Chun. "Accessory devices frequently used for endoscopic submucosal dissection". In: *Clinical endoscopy* 50.3 (2017), p. 224.

[3] Gary C Curhan. "Epidemiology of stone disease". In: *Urologic Clinics of North America* 34.3 (2007), pp. 287–293.

[4] Jean De La Rosette et al. "The clinical research office of the endourological society ureteroscopy global study: indications, complications, and outcomes in 11,885 patients". In: *Journal of Endourology* 28.2 (2014), pp. 131–139.

[5] Islam Y Elgendy et al. "Does the baseline coronary lesion length impact outcomes with IVUS-guided percutaneous coronary intervention?" In: *Journal of the American College of Cardiology* 68.5 (2016), pp. 569–570.

[6] J Ferlay, HR Shin, F Bray, et al. *GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10*. International Agency for Research on Cancer. 2010.

[7] P Geavlete et al. "Ureteroscopy–an essential modern approach in upper urinary tract diagnosis and treatment". In: *Journal of medicine and life* 3.2 (2010), p. 193.

[8] Guido Giusti et al. "Current standard technique for modern flexible ureteroscopy: tips and tricks". In: *European urology* 70.1 (2016), pp. 188–194.

[9] Takuji Gotoda et al. "A new endoscopic mucosal resection procedure using an insulation-tipped electrosurgical knife for rectal flat lesions: report of two cases". In: *Gastrointestinal endoscopy* 50.4 (1999), pp. 560–563.

[10] Russell I Heigh et al. "Use of Electromagnetic (EM) Colonoscope to Assess Maneuvers Associated with Cecal Intubation". In: *Gastrointestinal Endoscopy* 67.5 (2008), AB322–AB323.

[11] Valentin Ignatov et al. "Endoscopic submucosal dissection for early colon cancer". In: *Colorectal Cancer: From Pathogenesis to Treatment* (2016), p. 165.

[12] D Brooke Johnson and Margaret S Pearle. "Complications of ureteroscopy." In: *The Urologic clinics of North America* 31.1 (2004), pp. 157–171.

[13] Yoon Suk Jung and Dong Il Park. "Submucosal injection solutions for endoscopic mucosal resection and endoscopic submucosal dissection of gastrointestinal neoplasms". In: *Gastrointestinal Intervention* 2.2 (2013), pp. 73–77.

[14] Gurjaipal Kang. "Endovascular approach to iliac artery stenosis and restenosis". In: *Indian Heart Journal* 67.6 (2015), pp. 514–517. ISSN: 00194832. DOI: `10.1016/j.ihj.2015.09.034`.

[15] Nikolaos Konstantinidis et al. "New Advances in Chronic Total Occlusions". In: *Interventional Cardiology Review* 9.3 (2014), p. 208.

[16] Takashi Kubo et al. "Superficial calcium fracture after PCI as assessed by OCT". In: *JACC: Cardiovascular Imaging* 8.10 (2015), pp. 1228–1229.

[17] S. H. Lee et al. "Colonoscopy procedural skills and training for new beginners". In: *World J. Gastroenterol.* 20.45 (Dec. 2014), pp. 16984–16995.

[18] Pietro Mascagni et al. "Democratizing Endoscopic Submucosal Dissection: Single-Operator Fully Robotic Colorectal Endoscopic Submucosal Dissection in a Pig Model". In: *Gastroenterology* 156.6 (2019), pp. 1569–1571.

[19] Nicole L Miller and James E Lingeman. "Management of kidney stones". In: *Bmj* 334.7591 (2007), pp. 468–472.

[20] Yoshihiro Morino et al. "Predicting Successful Guidewire Crossing Through Chronic Total Occlusion of Native Coronary Lesions Within 30 Minutes". In: *JACC: Cardiovascular Interventions* 4.2 (2011), pp. 213–221. DOI: `10.1016/j.jcin.2010.09.024`.

[21] Craig R Narins. "Access strategies for peripheral arterial intervention." In: *Cardiology journal* 16.1 (2009), pp. 88–97. ISSN: 1897-5593.

[22] RC Newton et al. “Probe tip contact force and bowel distension affect crypt morphology during confocal endomicroscopy”. In: *Gut* 60.Suppl 1 (2011), A12–A13.

[23] Eugenia Nikolsky and Roxana Mehran. “Understanding the consequences of contrast-induced nephropathy”. In: *Reviews in cardiovascular medicine* 4.S5 (2019), pp. 10–18.

[24] L. Norgren et al. “Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II)”. In: *J. Vasc. Surg.* 45 Suppl S (Jan. 2007), pp. 5–67.

[25] Hiroyuki Odagiri and Hideo Yasunaga. “Complications following endoscopic submucosal dissection for gastric, esophageal, and colorectal cancer: a review of studies based on nationwide large-scale databases”. In: *Annals of translational medicine* 5.8 (2017).

[26] H Ono et al. “Endoscopic mucosal resection for treatment of early gastric cancer”. In: *Gut* 48.2 (2001), pp. 225–229.

[27] Tsuneo Oyama et al. “Endoscopic submucosal dissection of early esophageal cancer”. In: *Clinical Gastroenterology and Hepatology* 3.7 (2005), S67–S70.

[28] Jun Chul Park et al. “Predictive factors for local recurrence after endoscopic resection for early gastric cancer: long-term clinical outcome in a single-center experience”. In: *Surgical endoscopy* 24.11 (2010), pp. 2842–2849.

[29] Mathieu Pioche, Gaspard Bertrand, and Jérôme Rivory. “Endoscopic perforation during EMR or ESD: who should take care of the patient?” In: *Endoscopy international open* 6.03 (2018), E313–E314.

[30] Enrique Quintero et al. “Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening”. In: *New England Journal of Medicine* 366.8 (2012), pp. 697–706.

[31] B. Rosa, P. Mozer, and J. Szewczyk. “Robotization of a ureteroscope for automatic lithiasis vaporization”. In: *Journal of Endourology* 24.12 (2010), pp. 2112–2113.

[32] Jean JMCH de la Rosette, Thomas Skrekas, and Joseph W Segura. “Handling and prevention of complications in stone basketing”. In: *European urology* 50.5 (2006), pp. 991–999.

[33] Remzi Saglam et al. “A new robot for flexible ureteroscopy: development and early clinical results (IDEAL stage 1–2b)”. In: *European urology* 66.6 (2014), pp. 1092–1100.

[34] Yutaka Saito et al. “Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection”. In: *Surgical endoscopy* 24.2 (2010), pp. 343–352.

[35] Eline H Schreuders et al. “Colorectal cancer screening: a global overview of existing programmes”. In: *Gut* 64.10 (2015), pp. 1637–1649.

[36] Timothy G Schuster et al. “Complications of ureteroscopy: analysis of predictive factors”. In: *The Journal of urology* 166.2 (2001), pp. 538–540.

[37] George Sgourakis, Ines Gockel, and Hauke Lang. “Endoscopic and surgical resection of T1a/T1b esophageal neoplasms: a systematic review”. In: *World Journal of Gastroenterology: WJG* 19.9 (2013), p. 1424.

[38] Pari M Shah and Hans Gerdes. “Endoscopic options for early stage esophageal cancer”. In: *Journal of gastrointestinal oncology* 6.1 (2015), p. 20.

[39] Jun Shu and Gaetano Santulli. “Update on peripheral artery disease: Epidemiology and evidence-based facts”. In: *Atherosclerosis* 275 (2018), pp. 379–381. ISSN: 18791484. DOI: `10.1016/j.atherosclerosis.2018.05.033`.

[40] Kim G Smolderen et al. “Long-term prognostic risk in lower extremity peripheral arterial disease as a function of the number of peripheral arterial lesions”. In: *Journal of the American Heart Association* 4.10 (Oct. 2015), e001823. ISSN: 20479980. DOI: `10.1161/JAHA.115.001823`.

[41] Leslie H Sobin and Irvin D Fleming. “TNM classification of malignant tumors, (1997)”. In: *Cancer: Interdisciplinary International Journal of the American Cancer Society* 80.9 (1997), pp. 1803–1804.

[42] Anant Suraj Vemuri et al. “Interoperative biopsy site relocalization in endoluminal surgery”. In: *IEEE Transactions on Biomedical Engineering* 63.9 (2015), pp. 1862–1873.

[43] Tom Vercauteren et al. “Robust mosaicing with correction of motion distortions and tissue deformations for in vivo fibered microscopy”. In: *Medical image analysis* 10.5 (2006), pp. 673–692.

[44] Jing Wang et al. “Endoscopic submucosal dissection vs endoscopic mucosal resection for colorectal tumors: a meta-analysis”. In: *World journal of gastroenterology: WJG* 20.25 (2014), p. 8282.

[45] B. P. Yan et al. “Current endovascular therapy for lower extremity peripheral arterial disease: indications, outcomes and modalities”. In: *Heart Asia* 1.1 (2009), pp. 51–57.

[46] Menglong Ye et al. “Online tracking and retargeting with applications to optical biopsy in gastrointestinal endoscopic examinations”. In: *Medical image analysis* 30 (2016), pp. 144–157.

[47] Dorit E Zilberman et al. “The digital flexible ureteroscope: in vitro assessment of optical characteristics”. In: *Journal of endourology* 25.3 (2011), pp. 519–522.