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Robotics in Colonoscopy

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Abstract

Colorectal cancer is the second leading cause of mortality in men and women in the United States. While there is a definite advantage regarding the use of colonoscopies in screening, there is still a lack of widespread acceptance of colonoscopy use in the general public. This is evident by the fact that up to 75% of patients diagnosed with colorectal cancer present with locally advanced disease. In order to make colonoscopy and in turn colorectal cancer screening a patient friendly and a comfortable test some changes in tool are necessary. The conventional colonoscope has not changed much since its development. There are several new advances in colorectal screening practices. One of the most promising new advances is the advent of robotic endoscopic techniques.

INTRODUCTION

Colorectal cancer is the second leading cause of mortality in men and women in the United States. Guidelines for early detection of colorectal cancer include: fecal occult blood sampling annually, flexible sigmoidoscopy every five years, or colonoscopy every ten years.[1] Colonoscopies have been one of the main stays for colorectal cancer screening. Screening colonoscopies have led to a decrease in both distal and proximal colon cancer mortality rates compared to no screening.[2] While there is a definite advantage regarding the use of colonoscopies in screening, there is still a lack of widespread acceptance of colonoscopy use in the general public. This is evident by the fact that up to 75% of patients diagnosed with colorectal cancer present with locally advanced disease.[3] It is also evident by the fact that half of all patients referred for a colonoscopy failed to complete the exam.[4] In 2012 65% of US adults were current with colorectal screening guidelines, and 27.7% of adults have never been screened.[5]

The risk factors for nonadherence to screening includes: female sex, younger age, and insurance type. Females who generally have higher use of preventative services use endoscopic screening significantly less than males, and a study done in 2004 showed that less than one fourth of women reported using endoscopic procedures for screening in the previous five years.[6] Two of the biggest barriers to receiving screening colonoscopies are fear of pain and belief that screening is not necessary if the patient is asymptomatic.[7] The

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fear of pain or complications stems from the rates of serious complications. 2.8 serious complications (perforation, hemorrhages, diverticulitis, or severe abdominal pain) occur per 1,000 patients undergoing colonoscopy.[8] Colonoscopy also has the undesired necessity of sedation, and the embarrassment that the patient experiences.[9] The discomfort experienced during colonoscopy is due to the semi-rigid tube design of conventional endoscopes. Another barrier to effective treatment is lack of completion of colonoscopy. This usually occurs due to either an angulated sigmoid colon or a redundant colon.[10]

In order to make colonoscopy and in turn colorectal cancer screening a patient friendly and a comfortable test some changes in tool are necessary. The conventional colonoscope has not changed much since its development. There are several new advances in colorectal screening practices. One of the most promising new advances is the advent of robotic endoscopic techniques.

ROBOTIC CAPSULES

One of the greatest limitations to the current endoscopic techniques available today is the lack of information that can be gathered about the small intestine. Colonoscopy only reaches the terminal ileum and esophagogastroduodenoscopy only reaches the proximal portion of the small intestine. Push enteroscopy is capable of viewing the small intestine, but has some serious complications including perforations, abdominal pain, and pancreatitis.[11,12] The wireless capsule endoscopic devices were designed to be able to capture images from the small bowel to make up for this deficit of the other devices. Capsule endoscopy has since been shown to have a higher diagnostic yield compared to push enteroscopy.[13] The first capsule to be produced for small bowel diagnostics was the MTA2. This capsule was able to have a field of view of 140 degrees, had a magnification factor of 1:8 and a resolution of 0.1 mm.[14] The pill is then carried throughout the GI tract via peristalsis. The pill captures 2 images per second and can capture about 55,000 pictures throughout the GI tract. The clinical importance of this capsule device is mainly in the diagnostic information that can be gathered in the small intestine. It has been validated as a better diagnostic tool compared to traditional techniques for occult GI bleed, Celiac disease, and Crohn’s disease.[15–17] While the capsule is good for diagnosing an occult GI bleed some studies have demonstrated that this does not affect the outcome.[18–20] The biggest complication associated with this capsule is capsule retention; this can occur more frequently in patients with Crohn’s disease due to the risk of stricture.

While the early capsule types are useful to provide some information, it is still limited in its clinical practicality. The ability to start and stop the capsule depending on the location in the gastrointestinal tract is very important, and because of this there has been a shift towards creating capsules that can move actively throughout the intestinal tract. Olympus has created a capsule that is capable of moving throughout the intestinal tract via the use of magnetic actuation. This capsule has an internal permanent magnet which allows it to be steered externally via the use of a magnetic field. The magnetic field allows for manipulation of position, orientation and posture of the capsule. It can even be manipulated to rotate in a forward or reverse direction. The capsule is also charged via electromagnetic induction which negates the need for an internal battery source.[14]

Movement of the capsule can also be controlled through the use of electric stimulation. Galvanic stimulation of the gut wall has been shown to be able to propel devices through the GI tract quicker.[21] To test the possibility of using electric stimulation to propel a device, a small ovoid shaped device with electrodes mounted on the sides was designed. When in the gut two or more of the electrodes are touching the wall so that when a voltage is applied a current flows through the wall which causes the muscles to contract and push the capsule forward. The device was tested *in vivo* and *in vitro.* The in vitro study found that the best device had a taper of 40 degrees, this device was then the one used *in vivo*. The *in vivo* studies showed that the rate of progression through the small intestine was rapid compared to the time it takes for Sonde-type endoscopy. The appropriate diameter of device however is still not known for humans since these devices were tested in pigs. More studies will need to be done to determine if this type of movement would be possible in humans, and if it is possible more testing will need to be done to optimize the speed and size of the device.

Another new type of capsule style has been designed with small legs that allow for better control of movement. The legs are also theorized to allow for good control of trajectory so that sensitive areas of the intestine can be avoided, they are also expected to have lower contact point pressures, and because no insufflation is needed they are expected to reduce the pain experienced by the patient.[22] There are multiple types of this capsule currently being tested. One such capsule consists of eight legs and two microelectronic magnets and a gear system for controlling the legs, this is what allows for active locomotion throughout the gastrointestinal tract. A camera and a light source are also included in the capsule. The capsule is powered by a small cable that is connected to the capsule.[22] This capsule was tested for feasibility in three different parameters: a closed straight phantom model, a lower-GI phantom model, and *in-vivo*. The closed straight model consisted of a section of colon tissue that was fixed at both ends. This model was used to determine the optimal leg angles to allow for propulsion. The capsule was monitored from the other side using a traditional endoscope, and the capsule was timed to see how long it took to go twenty seconds in the colon. The lower-GI phantom model consists of an anatomical model of the abdomen with accessories for the various organs and attachment sites for where the intestine should be placed. The intestine is then placed so that all of the angles of the colon are similar to the angles that would be present *in-vivo*. The locomotion parameters were set using the results from the previous closed straight test. After this testing the capsule was then tested *in-vivo* in a pig. The first test could be optimized so that the capsule moved 20 cm in 4.9 minutes.[22] The second test showed that the capsule could pass through nearly all parts of the colon; however, the capsule needed some help around the hepatic and splenic flexures. The average time for the lower GI passage was about 55 minutes.[22] The *in-vivo* test demonstrated that the capsule was able to move against peristalsis without damaging the colon. Due to the increased procedural time and inability to circumvent the flexures the capsule is not yet currently ready to be utilized.

While a majority of the capsules currently available have been created specifically to help diagnose small intestine pathology, there are some emerging capsules that have been developed for esophageal or colon pathologies as well. The Pillcam colon capsule has been designed to help identify colonic pathology. The Pillcam capsule also has a lower diagnostic yield compared to traditional colonoscopy in terms of diagnosing colorectal polyps.[23] The study consisted of 328 patients who were tested both with the capsule and with the traditional colonoscopy method. The sensitivity and specificity of the capsule to detect polyps was 64% and 84% respectively.[23] This is significantly lower than the colonoscopy currently used, and suggests that the capsule should not be used to diagnose colorectal cancer or polyps. One study did demonstrate that the colon capsule could be a feasible modality in those patients who have contraindications to colonoscopy, refused colonoscopy, or have had an incomplete colonoscopy.[24] While the capsule was not as effective for diagnosing colorectal polyps, the capsule was shown to be effective in assessing the severity and extent of Ulcerative colitis when compared to traditional colonoscopy.[25] The roles of the different types of capsules have not fully been elucidated and will require more research to fully develop a feasible protocol for the use of these new devices.

ROBOTICALLY CONTROLLED ADVANCED COLONOSCOPIES

The current colonoscopy technique can be used for small resections and diagnostic imaging, however if a larger resection was needed, traditional endoscopic methods are not feasible. This has led to the push for more advanced endoscopes that can perform these tasks. The advanced endsocopes have been designed to have more dexterity than the current endoscopes available now. While these instruments allow for more dexterity, they are much harder to control, requiring multiple physicians to be involved in the procedure. These endoscopic devices are also not controlled intuitively and have multiple degrees of freedom which make control harder.[26] The Anubis endoscope system is one of these advanced endoscopes, and it has three degrees of freedom, insertion, rotation, and bending. The instrument is designed to be controlled manually by using a control handle that can move forwards and backwards and it can be rotated to maneuver the instrument. There is also a lever that allows for control of bending. A robotically controlled device was set-up to make the control of the instrument easier to manage. This device was designed to reduce the hysteresis on the system. Hysteresis is the dependence of a system on both its current environment and past environment. Essentially, the more hysteresis that the endoscope has, the harder it is to control. The robotic controls were then tested versus the manual control of these devices by using a tapping experiment in which the operator would locate and tap on a fixed target.[26] The robotic method consists of the endoscopic device being controlled by an Omega 6 haptic device. Insertion is controlled by moving the pen forwards and backwards and the orientation of the pen controls the rotation and bending of the instrument. The two control methods were shown to have significantly different task completion times. The robotic control using the haptic device had a quicker completion time and it was more intuitively designed for control.[26] Another study was done which compared the traditional control methods versus the use of haptics steering, and the use of the haptics steering interface but without actually using haptics. This second comparison was done to see if the steering interface alone accounted for the quicker completion time. The results of the study showed that experts were actually faster at the conventional method of steering.[27] This was attributed to the fact that the experts had spent much more time working with the conventional method and not much time with the newer method. The advanced endoscopes which were originally very complex to control and thus impractical are now easier to control through the use of robotics, and this can lead to more widespread use of these endoscopes that are capable of performing more complex tasks than the current endoscopes available.

Robotic control has also been tested on magnetic steering of endoscopic capsules. As described earlier, magnetic fields can be used to manipulate the movement of ingested capsules. This magnetic field can be either controlled manually or with robotic assistance. The two modalities were tested both *ex vivo* and *in vivo.* For the *ex vivo* testing a segment of colon was used, and the capsule was maneuvered through the colon, visualizing and contacting targets on the colon wall. Completion time and number of targets reached was recorded, the robotically assisted control reached more targets while the manual control was quicker. In the *in vivo* study the robotically assisted control had higher precision and reliability.[28]

Inchworm Robotic Endoscopes

Several generations of inchworm robotics have been created by Dario et al.[29,30] These robots are pneumatically controlled and the robot drags a cable that is connected to an external unit through the colon. The external unit provides the pneumatic actuation signals to the robot and the endscopist can see how the robot is functioning through this external unit.[31] The robots are made up of two different actuators, a clamper and an extensor. The clamper binds to the colon while the extensor uses positive displacement to push the robot along the colon. Through the use of these two devices the robot is able to inch along the colon. Experiments have demonstrated that these robot types are able to advance through the descending colon without the complication of looping that is seen using traditional endoscopes. Looping is caused by the formation of a semicircle in the traditional scope. Once this circle is formed, when you advance the scope any further it just makes the loop larger without actually advancing the tip of the scope. This causes discomfort to the patient and it impedes further progress of the scope. Looping is responsible for about 90% of the discomfort experienced during these procedures, so reducing looping can seriously improve the patient perceived outcome of the procedure.[32] While these robots have shown some progress, there are still several limitations. First, these robots are unable to make it to the cecum because of their size. The air pipe and cable are too large for the device to make it all the way to the cecum. Secondly, they are fairly hard to navigate which is a factor that will need to be overcome before these devices will be able to replace the traditional endoscope.

Similar to the clamping and extending model of Dario's robotic endoscopes is the prototype proposed by Lin et al.[33] This device has locomotion that is based on anchoring and extending itself through the intestine. The prototype was tested in *in vitro* experiments where its locomotion efficiency was around 50% in the pig's small bowel. The study demonstrated the feasibility of this device although the diameter of the small bowel does make it less effective, and the device would need to be made smaller in order to increase the mobility of the device.

Another type of earthworm robotic endoscope was designed to move through the intestinal tract in a slightly different manner. This specific prototype was 7 mm in diameter and 64 mm in length.[34] This robot is small enough to easily pass through all of the portions of the gastrointestinal tract. The robot is composed of multiple segments that can move forward one segment at a time, similar to an earthworm's motility. This robot was able to move steadily through different mediums, but it still needs to be tested *in vitro* before its efficacy can be assessed.

Aer-O-Scope

The aer-o-scope is another type of pneumatically controlled self-propelling endoscope, similar to the inchworm robotics developed by Dario. The scope is composed of two separate units, a disposable unit and a work station. The disposable unit consists of a rectal introducer, a supply cable, and a scope with a scanning balloon.[35] The balloon on the introducer seals the anus and then the colon is insufflated. The gas pressure is what propels the scanning balloon. There are multiple sensors that are used to regulate the pressure in the colon to insure that the pressure does not exceed a predetermined setting. Once the balloon makes it to the cecum the pressures are reversed and this pushes the balloon back towards the rectum. To test the feasibility of this device a study was done in 20 pigs. The study showed that the device could reach maximum insertion in 80–90% of the procedures performed.[36] This device was then tested *in vivo* in twelve human subjects and the device was able to reach the cecum in ten of the subjects. In the two subjects that the cecum could not be reached, a traditional colonoscopy also could not reach it. In one of the cases the patient had a redundant colon and in the other case the pain was too great to proceed all the way to the cecum. Only two of the subjects requested analgesics during the procedure.[35] The viewing capability of this device was then tested *ex vivo*. In the *ex vivo* study small beads were sewn into porcine colon. The sensitivity of the aer-o-scope was 97.4%.[37] A main benefit of this device is that it decreases the looping seen in standard endoscopies because rather than being pushed, it follows a pressure gradient. The major problem with this device is that it can only be used for screening and not therapy. It does not have any accessories available to remove polyps so it will not be able to replace the standard colonoscopy that is done therapeutically.

Autonomous Colonic Endoscope

The idea of autonomous endoscopes has led to the development of a new type of endoscope that does not have any attached cables and can be controlled through reinforcement learning. The locomotive principle consists of a front body with a helical fin and a rear body that has a helical fin that rotates in the opposite direction. When moving forward the front body rotates clockwise and the rear body rotates counter-clockwise, in this manner the robotic endoscope moves in a forward manner through the colon.[38] The fins are composed of a thermoplastic elastomer which is advantageous for three main reasons: ease of deformability, ductility, and workability. The ease of deformability means that it has a low degree of stiffness and is thus more compliable to the colon and less likely to damage the colonic walls. The ductility means that it can undergo deformation without breaking, and the workability means that the material is easy to mold into the fin structures. The robotic endoscope also has three universal joints that allows for it to passively bend in the colon. The software in the robotic endoscope relies on two different learning algorithms, Q-learning, and SARSA (State-Action-Reward-State-Action). These learning algorithms allow the robot to learn how to move throughout the colon. The robotic endoscope was then tested in living swine colon. The endoscope was able to move at a speed of 11 mm per minute and there was no structural damage to the colon in this set up.[38] One of the limitations to this design is that it is possible for the endoscope to become stuck in the colon if the colon is either too narrow or too wide. If it is to wide there will not be an appropriate amount of thrust force that can be generated and so the fins will not end up propelling the robot. After further testing the robot was able to achieve a top speed of 134 mm/minute which would equate to performing a colonoscopy in about eleven minutes. Another main drawback of this type of robotic endoscope is that at its current state it cannot traverse bent areas. This means that it would not be able to fully navigate to the cecum, however there is a newer device being built that will be able to do this. It will have two motors and an active bending system that will allow it to drive the flexures and tighter areas more effectively.

Claytronics in Endoscopy

One of the major limitations to many of the common robotic endoscopes is that they are of a fixed size and shape. This means that they cannot always traverse the tighter areas of the gastrointestinal tract efficiently. This has led to the push for using programmable matter in colonoscopy. Programmable matter is a category of materials that can change its physical parameters based on user input. This allows the material to change shape, size, texture and color. Claytronics is one type of programmable matter that is currently being tested and is thought to be advantageous in colonoscopies. The claytronics consists of millions of cooperating individual particles that can sense the environment and can sense the other particles, and perform computation to move about the other particles to make new shapes.[39] Claytronics in endoscopy could increase the mobility, control, and imaging techniques of the current colonoscopy. The ability of the material to be able to change shape and size will be helpful in navigating through the colon, and will also allow for the material to bypass any waste that is present from inadequate preparation. The material will also make perforations less likely to occur because the material is more flexible than the traditional endoscopes. The programmable material could also increase the imaging modality. This would occur because these particles could compile all of their images to form a highly resolved image that is 360 degrees. The traditional endoscopes only have a view of around 140 degrees so this would greatly enhance the imaging.[39] While the idea of using programmable material in colonoscopy is promising, there is still much work to be done before the device would be ready in humans.

Colonosight

The colonosight system is a self-advancing single use endoscope currently approved by the FDA.[40] The colonosight system consists of a reusable endoscope with LED’s and a camera at the tip, a disposable sleeve, a system control unit, a thermal pinch cutter, a video monitor, and a therapeutic device cover. The advantages of this device include protection of the endoscope due to the disposable sleeve, easier scope advancement due to the pulling mechanism, and the LED light source at the tip of the probe.[41] The machine works by means of an outer sheath that can be insufflated to pull the endoscope through the colon. This pull eliminates some of the need to generate a pushing force on the colon and can be helpful in reducing the occurrence of looping. In a study performed to test the colonosight system in 178 human patients, the cecum was reached 90% of the time with a mean time of 11.2 minutes.[42] There were also no complications noted in the study. The general impression of the physicians who used these devices was that the pulling capability of the endoscope helped them perform the procedure easier than the standard colonoscopy.

THE ENDOTICS SYSTEM

The endotics system is composed of sterile disposable probe and a workstation. The probe has a steerable tip, a flexible body, and a tank with an electro-pneumatic connector.[43] The head contains LED lights, a camera with a 110 degree viewing angle, a water jet and an air jet that allows for rinsing and insufflation. The device is controlled by the workstation which can control the head of the endoscope in 180 degrees in every direction. The workstation also controls the rinsing insufflation, and vacuum features. The endoscope moves forward by the use of a semi-autonomous action which moves the robot in an inchworm-like fashion. The probe contains two clamps which allow for the locomotion to occur. These clamps are located at the proximal and distal ends of the probe. The locomotion occurs by a series of steps. First the proximal clamp attaches to the mucosa, next the body of the probe elongates, then the distal clamp attaches to the mucosa and the proximal clamp unattaches, the body contracts and the process begins again. A study of the forces applied by the endotics system compared to the traditional colonoscope showed that the endotics system produced forces that were 90% lower.[43] To assess the efficacy of visualization of polyps a study was performed comparing the endotics system to the traditional colonoscopy. In this study 71 patients were enrolled who had a clinical or familial risk of having polyps. These patients then underwent evaluation by both a traditional colonoscopy and the endotics system on the same day. The endotics system was shown to have a sensitivity of 93.3% and a specificity of 100% compared to the gold standard.[44]

NEOGUIDE SYSTEM

The Neoguide system was developed to help overcome the problems associated with looping in the colon. The neoguide system consists of a 16 segment insertion tube that controls the endoscope. The first segment is the leader segment and this has a position sensor. This sensor measures the tip steering while another sensor measures the insertion depth. This allows for a snaking pattern of the endoscope. Using these two sensors the computer can guide the rest of the segments to follow a similar pattern that the first segment used. The computer system can also create a real-time three-dimensional map of the tip position and insertion tube. The PACE study was designed to test the efficacy of this system in human models. In this small human study the cecum was reached 100% of the time, and it was determined to be a feasible device for performing colonoscopies.[45] To test if this new system decreases the looping formation a model was designed to simulate a colon with the four main flexures. At the flexures there were four force transducers to measure the forces applied by this new endoscope. The study also incorporated a measure of colonic displacement observed by the Neoguide system and the traditional endoscope. The Neoguide system significantly lowered the forces applied to the flexures and the colonic displacement compared to the traditional endoscope.[46] Another benefit of the Neoguide system is that the sensors allow for three-dimensional mapping of the endoscope tip. This mapping allows endoscopists to identify the location of the tip in 99% of the cases.[47] The benefits of being able to identify the shape of the scope and tip position are increased completion rates, and shorter duration of exams.[32,48–50]

INVENDOSCOPE

The invendoscope is a single-use hand-held controlled endoscope. It has an inner sheath that has a sleeve pulled over it which is attached to a propulsion connector. The connector is hooked onto an endoscopic driving unit. When the forward or backwards buttons are pressed eight drive wheels move in the driving unit, these wheels are connected to the sleeve in such a manner that the inner sheath begins to move forwards. The tip of the endoscope can be deflected electrohydraulically 180 degrees in any direction by moving a joy-stick on the hand-held controls.[51] The design of the invendoscope allows for a decreased force exerted on the colon, and therefore the discomfort experienced by the patient during the procedure. In a human study the invendoscope was able to reach the cecum in 80–90% of the patients without sedation.[51]

CONCLUSIONS

The recent advancements in robotic colonoscopy have many benefits over traditional endoscopes. These devices can give a more in depth view of the gastrointestinal tract, they decrease the pain associated with endoscopy, and they can perform more difficult procedures than the current endoscopes. While all of these newer devices have certain advantages over the traditional scopes, currently, none of these is a perfect replacement. The capsules can only be used for screening purposes and the inchworm robotics are still too large to fully navigate the colon. The most promising new development is the robotically controlled advanced endoscopes. These are proving to be beneficial for the more intricate procedures, like bowel resections; and with the haptic control devices they are easier to navigate than when they first were developed. The traditional endoscopes have greatly changed the outcome of colorectal cancer and these newer devices while showing a lot of promise still need to be improved upon before they can surpass the traditional endoscopes in screening and prevention of colorectal cancer.

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