A pilot, single-center, single-arm, feasibility study evaluating a polyp measurement device in patients undergoing screening or surveillance colonoscopy

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NYULMC Study Number:	s18-02047
NCT Number:	NCT03856255
Funding Sponsor:	NYU School of Medicine Division of Gastroenterology 240 East 38th St. 23rd Floor New York, NY 10016 212-263-3095
Study Product:	Napoleon^{TM} endoscopic polyp measurement device
Study Product Provider:	Micro-Tech Endoscopy USA

Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), 21 CFR Parts 50, 56, 312, and 812 as applicable, any other applicable US government research regulations, and institutional research policies and procedures. The International Conference on Harmonisation ("ICH") Guideline for Good Clinical Practice ("GCP") (sometimes referred to as "ICH-GCP" or "E6") will be applied only to the extent that it is compatible with FDA and DHHS regulations. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

Specific Aims

The aims of this study are:

1. To evaluate the feasibility of using a 0-20mm catheter with an attached measurement device in measuring the size of polyps detected during a screening or surveillance colonoscopy, and
2. To compare the measurements ascertained with this device with those measurements obtained through standard, device-free optical assessment.

Introduction, Background Information and Scientific Rationale

Background and Significance

Colorectal cancer is the second-leading cause of cancer death in the United States (1). Colorectal cancer screening is recommended to begin at age 50 years for most men and women at average risk for this disease (2). Colonoscopy is a gold standard method of screening for colorectal cancer, allowing for the detection and removal of colorectal polyps, some of which can progress into malignancy. The literature has shown that the removal of polyps during a colonoscopy results in decreased incidence and mortality related to colorectal cancer (3-4). Indeed, the last decade has shown a decline in colorectal cancer incidence and mortality in adults over age 50, largely due to increased colonoscopy screening (5). Currently, the risk of a patient developing colorectal cancer and thus time intervals for colonoscopy surveillance post-polypectomy is determined by the number, pathology, and size of the polyps that are observed and removed during the colonoscopy procedure. Current surveillance guidelines indicate the need for a shorter interval before the next colonoscopy for patients who have one or more polyps that are 10mm or larger (6). In addition, different polypectomy techniques are indicated for the treatment of polyps less than 20mm in size. For example, cold forceps may be appropriate for removal of 1mm to 2mm polyps, cold snare for polyps less than 10mm, and hot-snare resection for polyps 10mm to 19mm (7). Yet, while the number and pathology of polyps are easily obtained and verified, it is standard practice for the size of a polyp to be assessed through endoscopist optical visualization alone, without use of an objective device or standard by which to measure it. Often, the endoscopist will compare the size of the polyp to the size of the snare loop to estimate and document the size of the polyp(s). However, with the size of a polyp being a major indicator of malignant potential as well as an indicator of appropriate polypectomy technique and surveillance intervals, a device with which to take and document accurate and objective measurements of polyps during colonoscopy holds the potential for health benefits. In addition to having a potential clinical benefit for each patient in terms of polypectomy and surveillance intervals, as an objective indicator of polyp size, this technique also holds promise for use in future studies that evaluate polyp size as an indicator of potential malignancy (or future malignancy) and for use by national clinical guidelines committees who may utilize these objective data to update future screening and surveillance recommendations.

Measurement Device

This study incorporates the use of the Micro-Tech Endoscopic Gauge, a newly developed device (not FDA approved) for utilization during colonoscopy to allow the accurate and objective measurement of each polyp. The device is a retractable, expandable/collapsible "ruler" measuring from 0mm to 20mm, with demarcations every 5 mm, and is attached to a catheter. Like a standard colonoscopy snare, the catheter with attached measuring device is inserted through any standard colonoscope or gastroscope with an endoscope instrument channel. The endoscopist extends the catheter with measuring device through the colonoscope, places it adjacent to the polyp, views and records the measurement of the polyp beside its longest axis according to the device, and retracts the catheter with measuring device back into the colonoscope. This process is currently the same as that used with a polypectomy snare utilized during colonoscopy to estimate the size of a polyp relative to the size of the polypectomy snare. The device is single use and sterile.

Using this device, the investigators of this study will seek to prove feasibility of utilization of this device during colonoscopy screening and surveillance procedures for the purpose of accurately measuring polyps. They will observe and identify factors related to viability such as whether the device is easily inserted and retracted, whether the device is easily placed adjacent to the polyp in all anatomic areas of the colon and rectum, and the quality of visibility of the measurement device when inside the colon or rectum (and adjacent to the polyp). They will also document and compare the measurements taken with the device to those taken by the standard optical method without use of a measurement device.

Potential Risks

A colonoscopy is generally a safe procedure, but with any procedure there are risks and not all risks can be known at this time regarding the use of this device. Perforation, bleeding, or infection of the colon are rare side effects from this test. The overall length of the colonoscopy may be extended by a few minutes as the physician measures a suspected polyp or polyps.

Research Design and Methods

General Study Design

This is a single-center, single-arm, non-randomized feasibility study to evaluate the feasibility of the Micro-Tech Endoscopic Gauge, an expandable/collapsible, retractable measuring device (0-20mm), to be used to measure any polyp (up to 20mm in size) detected during a screening or surveillance colonoscopy in patients age 50 to 85 years.

Primary Endpoints

The primary endpoints for this study are

1. Ease of use in advancing the measuring device catheter through the working channel of the colonoscope (Question 2)
2. Ease of extending and retracting the measuring device from the catheter (Question 3)
3. Ease of use in placing the measuring device adjacent to the polyp in order to determine a measurement (Question iv)
4. Ease of use in taking a picture that included the measuring device and polyp in order to photo-document the measurement reading (Question v)

Secondary Endpoints

Secondary endpoints for this study include:

1. Size of polyp measured by the device versus measured by standard, device-free optical visualization (Questions ii, iii)
2. Boston Bowel Preparation Scale score (Question 4)
3. Size and anatomic location of each polyp detected (Question i)

Study Enrollment and Withdrawal

Inclusion criteria:

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Individuals age 50-85 years old, who require an outpatient screening or surveillance colonoscopy
2. Ability to give consent

Exclusion criteria:

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Pregnancy
2. Inflammatory bowel disease

Study-wide number of subjects:
The total number of patients required to complete this feasibility study will be 50. It is expected that approximately 150 participants will be enrolled in order to produce 50 evaluable participants. This is a single site study and all patients will be enrolled at NYU Langone.

Method of Subject Identification and Recruitment
Patients who meet the inclusion criteria (below) and who are or will be scheduled for a screening or surveillance colonoscopy at NYU Langone Medical Center's Ambulatory Care Center (240 East 38 Street, floor 23) will be eligible for recruitment to the study.

Potential patients that have their colonoscopy scheduled will be contacted by the study team to discuss the measuring device study. A copy of the consent form will be provided to them for review and all questions will be answered. If interested, the patient can sign the study consent the same day as the procedure when they sign procedure consent.

Study-wide recruitment:
A study investigator or appropriately designated study team member will present patients who are or will be scheduled at NYU Langone Health's Ambulatory Care Center for a screening or surveillance colonoscopy with the opportunity to participate in the study.

Study Duration:
The study will begin accrual after IRB approval of the research protocol. The investigators anticipate the study will take up to 2-3 months to complete subject accrual. The estimated time for completion of the study analysis is July 2019.

For each patient, participation will include an in-depth discussion about the study, including potential risks and benefits, with a member of the study team.

Participant Withdrawal or Termination
Participants are free to withdraw from participation in the study at any time upon request. An investigator may terminate participation in the study if:

- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
- Any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
- Polyps are not detected during the colonoscopy

Informed consent:
Informed consent will be obtained for the colonoscopy with use of the investigational measuring device. A study investigator or appropriate designee will provide, explain, answer questions about the study prior to the patient's scheduled colonoscopy date. Clinical informed consent for the colonoscopy procedure will be obtained separately at NYU Langone Health's Ambulatory Care Center.

Study Agent and/or Procedural Intervention

Study Agent

The Napoleon^{TM} endoscopic polyp measurement device is a sterile, single-use endoscopic device, intended to be used endoscopically to measure appropriately the size of polyps within the GI tract. It is sterilized by ethylene oxide to achieve the Sterility Assurance Level (SAL) of 10^{-6} and placed in a sterility maintenance package to ensure a shelf life of 2 years. The endoscopic polyp measurement device mainly includes a distal measurement tip, support arm, wire cable, outer tube and handle assembly.

Intended Use

The measurement device is intended to be used as an endoscopic reference when estimating the size of a feature under endoscopic examination.

Device Administration

The device reaches target tissue through the working channel of endoscope, slowly advance the finger rings to advance the distal tip of the measurement device. Position close to the feature to be measured and read the markings of the tip to document the size of the feature. Pull back the slider to retract the distal tip prior to removing the device from the instrument channel. Upon completion of the procedure, remove the instrument from the endoscope and discard appropriately based on institutional protocols. The endoscopists using the device are board certified gastroenterologists with extensive endoscopy training and experience. The device used for this study is extremely similar to catheter devices that are currently in use. Specific training on use of the device will be provided by the PI to each of the endoscopists.

Device Calibration

Acquisition

Describe how study agent will be acquired and shipped to investigator by Micro-Tech.

Method of Assignment/Randomization

This is a single arm study and all patients will be utilizing the same measuring device.

Appearance, Packaging, and Labeling

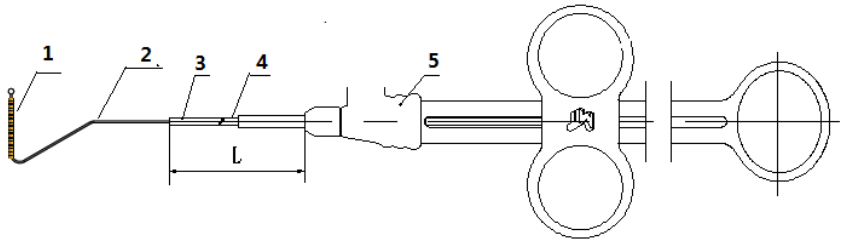
Include description that device will be labeled in accordance with 21 CFR 812.5.

Product Storage

The measurement device will be stored separately from commercial catheter devices in a cool, dry, clean, well-ventilated, and non-corrosive gas environment. The contents are sterile and the packaging will be inspected for signs of any damage prior to use. The product has a shelf life of 2 years and the expiration date will be verified. If the packaging or device shows any sign of damage, it will be discarded.

Include description that investigational product will be stored separately from commercial product. Provide information regarding how device will be evaluated prior to procedure (e.g. disposing of device if packaging seal broken.)

Device Specifications



1. Distal Measurement Tip 2. Support Arm 3. Wire Cable 4. Outer Tube 5.Handle Assembly

Fig. l Schematic diagram of Endoscopic Polyp Measurement Device

The device has a diameter of 2.3mm, a working length of 230cm, and the length of the distal measuring tip is 15mm±2mm.

Procedures for Training Investigators

Include description that PI will train (and possibly supervise) staff administering device. Mention that training will be documented.

Study Intervention

On the day of the procedure, the study investigator or study team member will obtain/confirm informed consent for the study and assess/reassess study eligibility. Women of Child Bearing Potential (WOCBP) are administered a pregnancy test as part of standard procedure prior to the colonoscopy and the study coordinator or investigator will confirm a negative result prior to enrolling the patient. A study investigator will perform the colonoscopy with use of the investigational measurement device. If and when a polyp is found, the investigator will note the type of polyp, location of polyp, and estimated size via standard optical visualization methods. The investigator will then apply the investigational measuring device and record the size according to the device, and take a photo using the colonoscope. Photos taken will not be stored with any identifiers. A study team member will record these findings for each polyp during the procedure as outlined in the Measuring Device Procedure Questionnaire. The questionnaire will be finished once the physician has completed the procedure.

After completion of the colonoscopy, patients will be assessed for adverse reactions and complications according to standard protocol in the endoscopy unit. This includes an immediate assessment after the procedure and again approximately 24 hours after the procedure during a routine post-procedure follow-up phone call.

Any data generated from this study will not be used to guide patient care without confirmation using other standard clinical practices

Study Schedule

Screening

- Obtain informed consent of potential participant verified on written informed consent
- Review medical history to determine eligibility based on inclusion/exclusion criteria
- Confirm negative pregnancy test for WOCBP

Intervention

- Verify inclusion/exclusion criteria
- Colonoscopy and measurement of polyps, if detected
- Collection of data via Measuring Device Procedure Questionnaire

24 Hour Follow-Up Call (+/- 12 hrs)

- Adverse events experienced after procedure

Study Exit

After completing the 24 follow-up call, subjects will be exited from the study.

Data Storage

Study participant data, which is for purposes of statistical analysis and scientific reporting, will be maintained in a study specific NYU REDCap. This will not include the participant's identifying information. Individual participants and their research data will be identified by a unique study identification number (001, 002, etc).

Statistical Method

This study will include patients from approximately 10 physicians, with each physician enrolling a similar number of patients to maintain consistency. Each physician will be completing the Measuring Device Questionnaire (Appendix 1). The scores from the physicians will be averaged to produce an independent variable for comparison.

Addendum to Protocol Statistical Method: Due to the Covid-19 breakout, we have to close our study early. We have 3 physicians who treated 5 patients each; 1 physician who treated 4 patients; 1 physician who treated 3 patients and 1 physician who treated 1 patient. For each of these 6 physicians, we obtain the average score of the patients he had treated. We then obtain the weighted mean of these average scores for the 6 physicians using the number of patients treated by each of the physicians as the weight. By the above sample size we can provide a two-sided 95% confidence interval with a distance from the mean (of the 6 physicians) to the limits equal to the 1.96*square root of $(0.043*\sigma^2+0.147*\rho*\sigma^2)$, where σ^2 is the true variance of patient's assessment score and ρ is the correlation of the patients' assessment

scores for the same physician. For example, if σ^2 is 10 and ρ is 0.5, then we will get a 95% confidence interval with width 4.2.

Sample Size Considerations

Approximately 30% of patients undergoing a colonoscopy at age 50 have polyps (8). For the purposes of accruing data on patients with polyps at the time of colonoscopy, we intend to enroll approximately 150 patients with the anticipation that 30% will have polyps to be removed. By using 10 physicians, for each of the primary endpoints individually, we can produce a two-sided 95% confidence interval with a distance from the mean to the limits that is equal to 0.715 standard deviation. Each physician will accrue 50 patients equally assigned to the 10 physicians (5 patients/physician). The average scores of the 5 patients accrued will be used for the estimate of each physician.

Safety

Safety Monitoring

Dr. Brian Bosworth will serve as the independent physician responsible for systematic oversight of the study and review of accumulated data and safety information to ensure proper conduct of protocol, compliance, data accuracy and integrity, and subject safety. Dr. Bosworth serves as the chief of medicine at NYU Langone's Tisch Hospital, is a board-certified Gastroenterologist, and is a member of the educational committee of the American Society for Gastrointestinal Endoscopy. Dr. Bosworth will monitor any adverse events related to study procedures, and provide findings to the PI, who will ensure accurate and timely reporting of important events to the IRB, as required. All subjects' medical records will be reviewed to assess for any possible adverse events that occurred between point of enrollment (introduction of the study device into the colonoscope) and study exit (completion of 24 Hour Follow-Up Call.) Safety data related to incidents of perforation, bleeding, or infection of the colon will be evaluated after every 5 subjects. Due to the short timeline of the study, the PI will submit progress/data safety monitoring reports to the IRB at the conclusion of the study or at the time of the continuing review, if reached.

Definition of Adverse Events

An adverse event is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study.

Assessment of Adverse Events

All adverse events will have their relationship to the study device assessed:

- **Related** – there is a reasonable possibility that the study device caused the adverse event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study agent and the adverse event.
- **Not Related** – there is not a reasonable possibility that the administration of the study agent caused the event, or an alternate etiology has been established.

Additionally, the following guidelines will be used to describe severity:

- **Mild** – events require minimal or no treatment and do not interfere with the participant's daily activities
- **Moderate** – events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – events interrupt a participant's usual daily activities and may require systemic drug therapy or other treatment. Severe events are usually life-threatening or incapacitating.

Adverse Event Reporting

The Principal Investigator shall be responsible for reporting adverse events to the NYULMC IRB according to their policies and procedures.

Study Halting Rules

Individual subjects will be removed from active study if any of the stopping conditions below are met at any time:

- Withdrawal of consent
- PI or any regulatory authority believe that withdrawal is necessary for the subject's health, well-being, or best interests

Stopping conditions for the study as a whole:

- Principal investigator or independent physician decide collectively that investigations should be terminated
- One severe adverse event is determined to be related to the study device
- Institutional Review Board terminates the study
- Target enrollment has been achieved

The Principal Investigator will inform the NYULMC IRB and implement appropriate protocol modifications to ensure human subjects safety.

Study Finances

Funding Status

There is no funding being provided for this study. There are no additional costs to the patient for participating in this study. There is no cost to the medical institution related to this study or the addition of the measuring device to the colonoscopy procedure. The measuring device is provided at no cost by Micro-Tech Endoscopy USA.

Human Subjects Research Protection from Risk

Risk to Subjects

A screening or surveillance colonoscopy is associated with the risk of rare complications, such as perforation, bleeding, and infection. The investigational measuring device is similar to the standard devices, such as a polypectomy snare, that are already being used in standard practice during the procedure. No additional risks are expected with the addition of the measuring device to the colonoscopy procedure.

Adequacy of Protection Against Risks

As per standard practice, patients will be informed of the potential risks of a colonoscopy as part of the informed consent process. Patients will be informed that there are no anticipated additional risks from the use of the investigational device, but that not all risks may be known. All efforts will be made to ensure patient confidentiality and assurance of HIPAA compliance. Subjects' data will be de-identified, using a protocol-specific unique code that will be used for all further data management. A list matching the patient medical record number to the protocol specific unique code will be kept in a locked cabinet under the control of investigators. There will be no data entry or interpretation outside of NYU. The names of the patients will not be released to any outside organizations or to persons not involved with the investigation. They will not be revealed in written reports or publications detailing the research findings.

Potential Benefits to Study Subjects and Others

A potential benefit to the study subjects is the objective measurement of any polyps detected during their colonoscopy, with the documented size potentially affecting the future polypectomy technique used and surveillance intervals recommended for future procedures.

Importance of the Knowledge To Be Gained

This study will allow us to determine whether the use of the investigational measuring device is feasible during a standard colonoscopy and how the device measurements compare with those of optical visualization measurements. In addition, if the use of this device is found to be feasible, it has potential implications to change the standard of practice. The use of this device may allow for future studies, in which polyps are accurately and objectively measured. This in turn may have implications for future guidelines for polypectomy technique, surveillance intervals, and other clinical recommendations found to be related to size of the polyp.

References

1. Siegel et al. Cancer statistics, 2018. *CA Cancer J Clin*. 2018;68:7-30.

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7. Rex and Dekker. How we resect colorectal polyps < 20 mm in size. *Gastrointest Endosc*. 2018 June 14.

8. Heitman SJ et al. Prevalence of adenomas and colorectal cancer in average risk individuals: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2009 Dec;7(12):1272-8.

Appendix 1

Measuring Device Procedure Questionnaire

Physician preforming colonoscopy: _____

Study member recording questionnaire: _____

Start Time: _____

End Time: _____

For ease of use questions, answer on a scale of 1-10, with 1 being the easiest and 10 being the hardest

1. Were polyps identified? Yes / No
    a. If yes, how many? _____
    b. For each polyp, complete the following questions (reference polyp ID in procedure note):
    c. Polyp #: _____
        i. Location of measured polyp (Circle one): Cecum, Ascending colon, Hepatic flexure, Transverse colon, Splenic flexure, Descending colon, Sigmoid colon, Rectum, unidentified
        ii. Estimated size of polyp: _____
        iii. Size of polyp utilizing measuring device: _____
        iv. Ease of use in placing the measuring device adjacent to the polyp in order to determine a measurement: _____
        v. Ease of use in taking a picture that included the measuring device and polyp in order to photo-document the measurement reading: _____
    d. Polyp #: _____
        i. Location of measured polyp (Circle one): Cecum, Ascending colon, Hepatic flexure, Transverse colon, Splenic flexure, Descending colon, Sigmoid colon, Rectum, unidentified
        ii. Estimated size of polyp: _____
        iii. Size of polyp utilizing measuring device: _____
        iv. Ease of use in placing the measuring device adjacent to the polyp in order to determine a measurement: _____
        v. Ease of use in taking a picture that included the measuring device and polyp in order to photo-document the measurement reading: _____
    e. Polyp #: _____
        i. Location of measured polyp (Circle one): Cecum, Ascending colon, Hepatic flexure, Transverse colon, Splenic flexure, Descending colon, Sigmoid colon, Rectum, unidentified

ii. Estimated size of polyp: _____
iii. Size of polyp utilizing measuring device: _____
iv. Ease of use in placing the measuring device adjacent to the polyp in order to determine a measurement: _____
v. Ease of use in taking a picture that included the measuring device and polyp in order to photo-document the measurement reading: _____

f. Polyp #: _____
i. Location of measured polyp (Circle one): Cecum, Ascending colon, Hepatic flexure, Transverse colon, Splenic flexure, Descending colon, Sigmoid colon, Rectum, unidentified
ii. Estimated size of polyp: _____
iii. Size of polyp utilizing measuring device: _____
iv. Ease of use in placing the measuring device adjacent to the polyp in order to determine a measurement: _____
v. Ease of use in taking a picture that included the measuring device and polyp in order to photo-document the measurement reading: _____

g. Polyp #: _____
i. Location of measured polyp (Circle one): Cecum, Ascending colon, Hepatic flexure, Transverse colon, Splenic flexure, Descending colon, Sigmoid colon, Rectum, unidentified
ii. Estimated size of polyp: _____
iii. Size of polyp utilizing measuring device: _____
iv. Ease of use in placing the measuring device adjacent to the polyp in order to determine a measurement: _____
v. Ease of use in taking a picture that included the measuring device and polyp in order to photo-document the measurement reading: _____

2. Ease of use in advancing the measuring device catheter through the working channel of the colonoscope: _____
3. Ease of extending and retracting the measuring device from the catheter: _____
4. Boston Bowel Prep Score: _____
5. Any Adverse Events?
    a. If yes, detail below

_____

_____

PI Signature: _____

Date: _____