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TITLE: A comparison of early deployment of a video capsule (Endocapsule EC-10: Olympus Tokyo. Japan) in the Emergency Department versus conventional work-up of non-hematemesis gastrointestinal bleeding [NHGIB].

NCT02442830

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1) Title

A comparison of early deployment of a video capsule (Endocapsule EC-10: Olympus Tokyo. Japan) in the Emergency Department versus conventional work-up of non-hematemesis gastrointestinal bleeding [NHGIB].

2) IRB Review History*

Not applicable.

3) Objectives*

The objectives of this study are to test whether there are statistically significant differences between the conventional workup of NHGIB by endoscopy [upper, lower and other tests], compared with deployment of a video capsule VCE as the first test followed by the most appropriate endoscopic procedure based on VCE findings, if needed. We propose to examine differences in time to diagnosis, reduction in numbers of procedures, and length of stay between a conventional workup protocol and our proposed protocol of early capsule endoscopy deployment.

4) Background*

After 40 years of considering gastrointestinal bleeding as upper or lower and largely ignoring the small intestine, there is accumulating evidence that the conventional approach to the assessment of NHGIB could be improved by early deployment of a video capsule as the first diagnostic test. Currently, video capsule endoscopy is considered the gold standard as the diagnostic test for small intestinal bleeding. In a recent study at UMass of 336 patients who presented to the ED with complaints of gastrointestinal bleeding 36 patients (10.7%) were given a video capsule during their stay.¹

In patients with hematemesis, upper endoscopy remains the diagnostic and therapeutic modality of choice. However patients with melena and hematochezia may benefit from early VCE since both signs and symptoms provide poor localization as to the origin of bleeding. Data from our previous study suggests that the ingestion of a video capsule in the emergency department could quickly and non-invasively provide clinicians accurate data as to the origin of the bleeding. This information could provide a guide to further management of the patient. Video capsule endoscopy is able to visualize bleeding in the esophagus, stomach, duodenum, small intestine and right colon, thereby eliminating the guess work of deciding which endoscopic approach to use.

At UMass, we have shown that of the 36 patients who received a video capsule, 26 (72.2%) had diagnostic studies (i.e. bleeding was identified). In comparison, 152 patients required upper endoscopy (of which 52.9% were diagnostic) and 64 patients required colonoscopy (of which 47%

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were diagnostic). Of those 26 patients with diagnostic capsule studies, 13 also required upper endoscopy, 1 required a colonoscopy, and 4 required both a colonoscopy and endoscopy. It is important to recognize, however, that often capsule studies are performed AFTER upper endoscopy and colonoscopy and performed and are negative. This sequence is the conventional work up of bleeding. Despite being performed later in the hospital course of our patients, capsule studies have a high diagnostic yield. In reality VCE is used uncommonly in acute bleeding because it is rarely considered in the context of acute GI bleeding

In this study, we propose the approach of using the video capsule as the first diagnostic test PRIOR to colonoscopy and endoscopy; this may lead to a shortened time to diagnosis, a reduction in length of stay, and a reduction in numbers of procedures due to early, accurate localization of the source of bleeding. All of these components could result in better quality of care and cost containment.^{1,2} Further, it is known that 80% of patients stop bleeding spontaneously. Thus the earlier they are examined the more likely the origin of the bleeding is likely to be found

The use of capsule endoscopy has been approved by the FDA since 2001 for small intestinal bleeding obscure GI Bleeding]. It is very safe, no deaths associated with its use have been reported. More than two million capsule have been used and obstruction and perforation are extremely rare.

Interest in the broader use of VCE is accumulation. In 2004 Sachdev et al reported a pilot study on the use of early use of VCE in acute NHGIB. This showed a 50% reduction to time to diagnosis in 24 patients. More recently studies of VCE deployed in the ED, in patients with upper GI bleeding showed improved management. Our group recently demonstrated that the closer a video capsule is performed to the time of bleeding the higher the likelihood of locating the sources and the higher the therapeutic intervention rate.³ We also have demonstrated that the use of capsule endoscopy in patients with NHGIB has a higher diagnostic yield than does colonoscopy. With improved diagnostic yields, capsule endoscopy may help clinicians by providing guidance in the management of patients with NHGIB.

This protocol is be the first attempt to prospectively examine this concept in a large randomized prospective trial. The questions are, can early capsule intervention decrease time to diagnosis, numbers of procedures and hospital length of stay in patients with non-hematemesis gastrointestinal bleeding.

References:

1. Jawaid S GB, Singh, A, Marshall C, and Cave D. . The epidemiology of gastrointestinal bleeding in an academic emergency department as a basis for

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reconfiguring the conventional approach to its diagnosis and management. .
Gastrointestinal Endoscopy 2013;77:Supplement, Page AB483.

2. Jawaid S MN, Gondal B, Maranda L, Marshall C, Charpentier J, Singh A, Foley A, and Cave D. . A reconsideration of the diagnosis and management of gastrointestinal bleeding based on its epidemiology and outcomes analysis. Gastrointestinal Endoscopy 2014;79:Supplement, Page AB231.
3. Singh A, Marshall C, Chaudhuri B, et al. Timing of video capsule endoscopy relative to overt obscure GI bleeding: implications from a retrospective study. Gastrointest Endosc 2013;77:761-6.

5) Inclusion and Exclusion Criteria*

Inclusion Criteria:

- Age greater than 18 years old
- New onset of melena or hematochezia
- Able to sign consent
- Hemodynamically stable (i.e. blood pressure >100/60 or pulse <110 at the time of consent)
- ED must plan to admit patient to the hospital or Clinical Decision Unit.

Exclusion criteria:

- Adults unable to consent
- Individuals who are not yet adults (infants, children, teenagers)
- Pregnant women
- Prisoners
- Prior history of gastroparesis
- Prior history of gastric, or small bowel surgery
- Prior history of inflammatory bowel disease
- Concern for infectious colitis
- Non-English speaking
- Evidence of dysphagia at the time of presentation
- Presence of bright red blood per rectum
- Allergy to metoclopramide or erythromycin
- Code status of DNR/DNI or CMO
- Prior history of abdominal radiation
- Presence of ICD or pacemaker or other implanted electronic devices
- Abdominal pain suggesting an acute abdomen or obstruction. In clinical practice, only patients with crampy abdominal pain due to

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Crohn's disease, previous intestinal surgery and a previous history of radiation therapy require a patency capsule or CT enterography before capsule endoscopy.

- Patients who cannot undergo surgery

6) Study-Wide Number of Subjects*

Not applicable – not a multi-site study

7) Study-Wide Recruitment Methods*

Not applicable – not a multi-site study

8) Study Timelines*

1. The participation of individual subjects in this study will be approximately 31-40 days (the length of their hospitalization plus an additional thirty days for follow up).
2. The duration anticipated to enroll all study subjects is about 24 months.
3. The estimated date for the investigators to complete this study and data analysis is two years.

9) Study Endpoints*

The primary endpoint will be time to diagnosis. Secondary endpoints will include hospital length of stay, number of invasive procedures, blood product transfusions.

10) Procedures Involved*

Screening

Patients presenting to the Emergency Room with NHGIB (defined as melena or hematochezia) will be identified by a member of the ED staff.

Once a subject is identified a page will be sent to a member of the research team (i.e. ED screener, research staff member, GI fellow on call, or GI attending on call) from the ED. In addition to this, the clinical research coordinator and or GI fellow will screen the Emergency Department triage software for patients who are listed as having NHGIB. Based on prior experience Ref Sachdev we expect for every 3 patients asked to participate in the study, there will be 1 patient who agrees to participate. In the emergency department study already cited, the Emergency Department at UMass sees about 350 patients annually for GI bleeding. Of these patients, approximately 230 patients have NHGIB. Given the 3:1 screening ratio, we would expect approximately 75 NHGIB patients every year to agree to participate in the study. In 24 months, we would expect to recruit up to 160 patients to our study.

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Once a subject is identified the subject will then be seen and examined by the GI fellow and attending as per standard of care and asked to participate in the study

Randomization

If inclusion/exclusion criteria are met, the consent discussion takes place and only if the subject agrees and consent is obtained, then the subject is randomized to the “Early Capsule Group” or “Conventional workup Group.” All patients in the “Early Capsule group” will receive the video capsule. Only some of the patients in the “Conventional Workup Group” will receive the capsule as indicated by what is considered the standard workup.

We will assign patients to study ID numbers consecutively by the order of which they are enrolled in our study. For the Randomization Process we will be utilizing a random sorting generator to assign integers in a random order, corresponding to study IDs which allows researchers to randomly assign study participants into specific study groups. Assignments are put into a mail merge, locked with a password, and printed, then put into a sealed, security envelope, which is sealed with a Study ID sticker. The Randomization Scheme will allow us to attach particular Study ID numbers randomly to particular groups based on our criteria to have 80 subjects in the early capsule group and a comparable number in the conventional workup group. The envelope is only opened once all entry criteria have been met and the subject will be assigned a group. Subjects with a Study ID ending in 1-100 will be enrolled at University Campus. Subjects with a Study ID ending in 101-120 will be enrolled at Memorial Campus. Subjects with a Study ID ending in 121-160 will be enrolled at either campus, depending on enrollment. Enrollment will be competitive at the two locations and there is no specific quota to be reached at either location.

We plan to enroll up to 160 subjects in our study. 80 subjects will be randomized to the “early capsule” deployment group. This means that this group of subjects will have a VCE deployed as soon as possible after presentation to the ED, once the consent process has taken place, eligibility has been confirmed, and the subject has met the standard of care guidelines for preparation before capsule ingestion. Standard preparation for capsule ingestion means that a patient cannot eat for 10 hours prior to deployment of the capsule. Therefore, patients in our study will be asked when they had last eaten. If patients report that they have not eaten anything over the past 10 hours we will deploy the capsule immediately. If, however, patients say that they have eaten something over the past 10 hours we will take note of when they believe they last ate and will deploy the capsule 10 hours after the time that they last ate. In the pilot [Sachdev] study all patients in the early capsule arm received the capsule within a mean of 4 hours of admission to the ED, and none had food in the stomach on capsule examination.

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Procedure

Capsules are swallowed with a small [4-12 oz.] amount of water. As noted above, patients will not have the capsule deployed until it has been confirmed that 10 hours have passed since the patient had last eaten.

Patients are allowed to take medications up to two hours prior to ingesting the capsule (which is standard of care).

Immediately following ingestion of the VCE a research staff member will use the capsule's Real-Time Viewer (RTV) to inspect for blood in the stomach. At 40-60 minutes following VCE ingestion, a staff member will again use the RTV to confirm that the capsule has entered the small bowel. If the capsule at that time is still in the stomach a prokinetic agent (either metoclopramide or erythromycin, [these agents are commonly used in patients with upper GI bleeding to help get blood clot out of the stomach prior to upper endoscopy to help clear the stomach to improve the chance of finding the source of bleeding]). Based on experience the need for either prokinetic agent is in approximately 1 out of 8 patients. If a prokinetic agent is required a staff member will check within another 40-60 minutes to again verify that the capsule has moved to the small intestine. No further prokinetic will be given. Four hours after ingestion, a staff member will used the RTV to again check for blood. This the mean small intestinal transit time of the small intestine. If the VCE is in the cecum, the study will be stopped and data will be downloaded to the workstation and processed into a video. If the VCE has not reached the cecum, at four and eight hours after ingestion, a staff member will again check the RTV to see if blood is present and/or the ileocecal valve has been passed. Data from the capsule recorder will be downloaded to a workstation as soon as possible.

The PI or sub-investigator will then view the video of the capsule recording [it takes about 5 minutes to establish if there is bleeding and where it is coming from. More detailed analysis will take about 15 minutes]. As soon as the capsule recording has been reviewed the PI or sub-investigator will inform the patient's attending gastroenterologist as to where the bleeding is coming from or that bleeding is not seen ideally within 1-4 hours from the time of stopping the capsule recording.

Depending on the findings a recommendation will be made as to the next most appropriate test. See attached Figure 1. If blood is found in the esophagus, stomach or duodenum an upper endoscopy is recommended. If blood is seen in the small intestine, it will be recommended that the subject next have a push enteroscopy, deep enteroscopy, or angiography. If blood in right colon, colonoscopy may be performed or deferred to colonoscopy as an outpatient, if active bleeding has ceased. If the capsule study is not diagnostic and no blood is seen in the GI tract and there is no ongoing hematochezia, the subject will be placed in ED observation for up to 23 hours and evaluated for potential discharge and follow-up by gastroenterology as an outpatient.

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If no bleeding/ blood or a likely source is found. These individuals will be considered for observation, early discharge and follow up in the GI outpatient setting.

For most subjects, the capsule will pass in a bowel movement within 24 - 72 hours of ingestion.

An equal number subjects [up to 80] will be randomized to the “conventional workup group”. “Conventional Workup” for NHGIB could include upper endoscopy, colonoscopy, and additional capsule or small bowel enteroscopy depending on the subject’s presentation and the results of the workup performed by the gastroenterology team. For some subjects, the VCE would be done as part of standard of care estimated that 5-15% of patients will have small intestinal bleeding. For patients requiring a video capsule endoscopy as part of “conventional workup” the patients will be given the same Olympus video capsule that is used in the “Early Capsule” group. Further management would be as standard of care. These subjects will be discharged on the recommendation of the attending hospitalist after completion of treatment.

Review and Follow-Up

During hospitalization, data will be recorded from ED pulse check, Meditech, Soarian, and Allscripts regarding fluid administration, transfusion of pRBC, initial hematocrit, times and types of procedures (e.g. upper endoscopy, enteroscopy, colonoscopy), time from entry to ED to time to diagnosis (i.e. localization of source of bleeding), admission disposition (i.e. clinical decision unit, regular floor, ICU), time of discharge. The procedures involved in the hospitalization (i.e. upper endoscopy, enteroscopy, and colonoscopy) will be done as part of standard of care. All of this information will be linked to the subject’s study ID number as described above. This data collection is for research purposes only.

In addition, the costs of the procedures will be collected through financial services. The costs that will be collected are both the fixed and variable costs associated with each patient in the study. We will also collect the direct and indirect costs allocated to each patient. All charges associated with the admission for each patient in the study will have costs allocated. This will be evaluated as an additional data point to compare the two arms of the study. No additional PHI will be collected.

Telephone Follow-Up

Subjects will also be contacted by phone by a research staff member at two different time points following their discharge from the hospital. These time points will be at 3 days (+2 days) and 30 days (+/- 3 days) following their discharge. At these time points a staff member will call a subject to obtain information about whether or not a patient has had recurrent bleeding and whether or not the patient had to be readmitted to a hospital or emergency room for

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recurrent bleeding. Please see attached form for telephone script that staff member will read along with particular questions that will be asked.

No more than three attempts will be made at each time point to reach the subject. If a message is left, it will be "Hello, this is [name] calling from UMass looking to speak with [subject]. Please call back at [number] at your earliest convenience. Thank you."

11) Data and Specimen Banking*

N/A – no data banking.

12) Data Management*

- Data analysis plan: As discussed above, data will be obtained through review of medical records. Specifically we will be looking at time to diagnosis of bleeding source, laboratory values, number of blood products transfused procedures performed, along with additional measures as described above. Once we have separated our two cohorts we will perform chi-square and standard t-tests to compare the different dependent variables in the two cohorts. We will also perform Kaplan-Meier curve analyses to compare length of stays and time to diagnosis which is the primary metric of this study.
- Steps that will be taken to secure data: All clinical data from individual subjects will be de-identified and given a study number. The study number will serve as a link between the data and the subject's identifiable information. RedCAP online encrypted database will be used to store the dataset. The database will only be accessed by the primary investigator and research assistants.
- Data will be exported for analysis as a de-identified data set. The de-identified dataset (which would be absent of any PHI) would be transferred in a password-encrypted email to the external sponsor.
- The external sponsor – Olympus Medical Systems – will have access only to the de-identified data set and will not have access to the study key with identifying health information.
- Identifier keys will be destroyed once primary data analysis is complete.
- No identifying information will be used in any report or publication generated from this study.
- Power analysis: Based on a previous retrospective epidemiology study, the average time to diagnosis for subjects presenting with non-hematemesis GI bleeding (NHGIB) who underwent a conventional workup was 30 hours (standard deviation of 6.1). Subjects with NHGIB who had an early capsule as the first diagnostic test had an average time to diagnosis of 15.9 hours (standard deviation of 12.2). This calculates an effect size of 1.49301. This is

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an effect we are looking to replicate prospectively in this study. Using this data with an assumed α of 0.05 and using a sample size of 80 subjects in the early capsule deployment group and 80 subjects in the Conventional Workup group the calculated power is 99%.

13) Provisions to Monitor the Data to Ensure the Safety of Subjects*

Throughout course of a study subject's participation in the study they will be followed for signs of adverse events to medication administration or for complications of capsule endoscopy. Adverse events will be documented as part of initial data analysis. This data analysis will be performed by the residents and fellows who are part of the study staff for this project.

Given that we anticipate minimal adverse events, any adverse events that occur will be reviewed by the study staff and the Primary Investigator within one week. This would include a complete analysis of the how the adverse event occurred in order to help prevent further events going forward. At that time the Primary Investigator will also assess cumulative reports.

14) Withdrawal of Subjects*

If the patient is unable to swallow the capsule we would remove them from the study.

Patients will be withdraw from study if the bleeding source is found to be outside of the stomach or intestines.

A subject can withdraw from the study at any time per their request.

15) Risks to Subjects*

This study is investigating the benefits of re-ordering the process of the current care algorithm for NHGIB. Video capsule endoscopy is already part of standard of care for many GI bleeding workups. This is not a new diagnostic modality and no new risk is being introduced from this technology itself. There are no anticipated risks to subjects who are randomized to the early deployment of the capsule and the diagnostic yield is expected to be at least comparable to the standard deployment.

One anticipated risk is a breach of confidentiality and to minimize this risk all identifiers will be destroyed. In order to minimize this risk, as described in question 12, identifiers will be destroyed. Data collected will be analyzed using study ID numbers only.

The most significant risk of VCE is capsule retention. This risk is the same for both groups and there is no anticipated unforeseen risk with early deployment. The risks do not change based on timing. Capsule retention is when the video capsule does not complete its transit throughout the GI tract. Studies have varied in their reports of the frequency of capsule retention with rates of about 1%, ranging from 1-13% of total cases. The

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latter figure is for a study on Crohn's disease patients. If capsule retention occurs subjects may require radiologic imaging. This usually consists of a plain film of the abdomen taken 2 weeks after the capsule was swallowed to localize the capsule. They will not be kept in hospital for this. If the patient sees the capsule in their feces, this test is not needed.

Importantly, even if the capsule is retained subsequent clinical decompensation requiring endoscopic or surgical intervention is extremely rare. In most cases of capsule retention, clinical decompensation does not occur and no further therapeutic options need to be pursued. In fact, if a capsule is retained it can often be useful in defining the site of luminal abnormality that can be targeted by a clinician. Nonetheless, to minimize the risk of capsule retention in our subjects we will be screening all potential subjects for associated conditions that are commonly associated with this complication. These conditions are listed as part of our exclusion criteria for this study. Removal of a capsule may be achieved by deep enteroscopy or at the time of surgery which is usually performed to remove the cause of the retention e.g. a tumor or stricture. The capsules may be left in place, Patients have been known to safely retain the capsule for years without ill effects.

It is not expected that there is any risk that the subjects assigned to the early capsule group will require more diagnostic procedures than the conventional work-up group. The hypothesis of this study is that the early deployment group may, in fact, undergo fewer procedures and have a shorter hospitalization compared to those having a conventional work-up.

Another potential risk to the subjects in the study relates to the prokinetic medications (metoclopramide and erythromycin) which would be given if the capsule is slow to leave the stomach. Risks associated with the use of metoclopramide include allergic reactions (e.g., skin rash or difficulty breathing), extrapyramidal reactions, central nervous system effects (e.g. insomnia, headache, confusion), neuroleptic malignant syndrome, endocrine disturbances (e.g. galactorrhea, amenorrhea, gynecomastia), and cardiovascular effects (e.g. hypotension, tachycardia, bradycardia, heart failure, and AV block). The adverse effects of metoclopramide are directly correlated to the duration and dose of the drug given, so we expect the incidence of adverse effects to be minimal given that we are giving one dose only for the purpose of this study. For erythromycin, adverse effects include allergic reactions (e.g., skin rash or difficulty breathing), gastrointestinal effects (including nausea, vomiting, abdominal pain, diarrhea, and anorexia), hepatic dysfunction, pseudomembranous colitis, QT prolongation, and ventricular tachycardia.

These drugs are frequently used in patients with upper GI bleeding to help empty the stomach of clot prior to endoscopy to enhance visualization of the bleeding site(s). Single doses of these drugs have very low risk

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16) Potential Benefits to Subjects*

Subjects who receive the early capsule deployment may have a quicker diagnosis of the source of GI bleeding and may be able to receive a more definitive treatment of their bleeding source which could lead to a decreased length of hospital stay as well as fewer procedures.

17) Vulnerable Populations*

No vulnerable populations are expected to be enrolled.

18) Multi-Site Research*

Not applicable – single site research.

19) Community-Based Participatory Research*

Not applicable – not community-based participatory research.

20) Sharing of Results with Subjects*

Study results are not expected to be shared with individual subjects and subjects will not be identified in any publications; however, de-identified results may be published in publicly-available journals.

21) Setting

Initial screening of subjects will be performed in the Emergency Room at the UMass Memorial Medical Center – University Campus-University Campus and UMass Memorial Medical Center – Memorial Campus as discussed in Section 10. Review of video capsule recordings will occur at the GI endoscopy clinic at the same campus.

22) Resources Available

The Principal Investigator is a board certified gastroenterologist with extensive experience at reading video capsules. He will oversee all aspects of the research to ensure it is conducted correctly and that all staff are properly trained on their roles and responsibilities. He will be assisted by sub-investigators who are physicians (attendings, fellows, and/or residents) in the Department of Medicine and Emergency Medicine.

Gastroenterology fellows and Medicine residents will all be used to screen potential candidates for this study once they are notified by the paging process described previously. All fellows and residents will have the appropriate CITI training and will be added to the list of project personnel prior to interacting with or obtaining consent from subjects. They will be responsible for reviewing the inclusion and exclusion criteria with the subject and with obtaining consent for the capsule endoscopy if the subjects agree to take part in the study.

For subjects who agree to take part in the study, Gastroenterology fellows and Medicine residents will also be tasked with administering the capsule

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and with following the results on the RTV as described previously. Fellows and residents performing this task will have the appropriate training and experience in administering the capsule. The Principal Investigator will personally oversee the training of the fellows and residents and personally demonstrate to them how to administer the capsule. The Principal Investigator will be available for any questions that may come up if a fellow or resident has difficulty initiating the capsule. Fellows and residents may also order prokinetic agents such as metoclopramide and erythromycin as described above. The decision to order prokinetics comes after the fellows and residents have discussed using those agents with the Principal Investigator who is a world-renowned authority on capsule endoscopy and the use of prokinetic agents for the purpose of their use.

Fellows and residents also will have the responsibility to upload videos to the ShareFile environment using the capsule workstation as described. They will also communicate capsule findings from the Primary Investigator and Sub-investigator to the primary team members regarding recommendations of further workup and procedures based on the recordings. Other responsibilities will include data collection, and data analysis.

A study coordinator in this study will have a primary role of maintaining IRB communications. All individuals will be added to the Project Personnel tab prior to participation in research activities.

The time that our group will devote to this study will be approximately 2 years.

All members of the research staff will be available to the subjects for any consequences that may occur secondary to this research.

All persons who are part of this study and listed as study personnel will meet multiple times prior to initiation of the research to discuss the study protocol, procedures, and the individual duties and functions. Throughout the research project we will have frequent meetings to discuss updates on the research.

23) Prior Approvals

The Department Chair of Emergency Medicine [REDACTED] has been involved with this study since its early stages of development and is actively involved with its implementation. We have email confirmation that he has approved this research study to be performed in his department.

The 'Questions for PI Checklist' from the Subcommittee on Human Uses [SHU] of the Radiation Safety Committee [RSC] has been reviewed and

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there is no requirement for pre-approval by the subcommittee. A KUB is only performed on those patients whose capsule does not reach the cecum before the battery runs out and who do not see the capsule excreted in their feces in the 2 weeks following the procedure. This is standard of care.

The UMMS Conflicts of Interest committee is currently in the process of review this study and the PI's potential conflict of interest. Language has been added to the consent form to indicate that there is a consultant relationship. When available, the COI committee's determination letter and mitigation plan (if applicable) will be submitted in a further modification.

24) Recruitment Methods

As mentioned in Section 10, subjects with NHGIB will be identified by a member of the Emergency Department staff or one of the study staff members. Subjects will be notified of the risks and benefits of participating in this study. They will not be offered financial compensation for their participation. They will be offered an opportunity to ask any questions they have regarding this study.

25) Local Number of Subjects

The study will aim to include up to 160 subjects for this study. Up to 80 subjects will be randomized into the “Early Capsule Group” and 80 subjects will be randomized into the Conventional Workup Group.

Based on a previous retrospective epidemiology study, the average time to diagnosis for subjects presenting with non-hematemesis GI bleeding (NHGIB) who underwent a conventional workup was 30 hours (standard deviation of 6.1).

Subjects with NHGIB who had an early capsule as the first diagnostic test had an average time to diagnosis of 15.9 hours (standard deviation of 12.2). This calculates an effect size of 1.49301. This is an effect we are looking to replicate prospectively in this study.

Using this data with an assumed α of 0.05 and using a sample size of 80 subjects in the early capsule deployment group and 80 subjects in the conventional workup group the calculated power is 99%.

26) Confidentiality

Study data and information will be stored securely at the study center. All data and information will be considered confidential. No identifying information will be used in any report or publication generated from this study. All information gathered will be placed directly into an online encrypted database (i.e. RedCAP). This will include identifier information (i.e. medical record numbers) as well as study data. The data from this database will then be exported from RedCAP and will be de-identified.

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Data analysis on the exported data set will then be performed. See section #12 for additional information.

27) Provisions to Protect the Privacy Interests of Subjects (HIPAA)

A HIPAA Waiver will be submitted to use to identify potential subjects. Only those subjects who meet initial entry criteria will be approached to consider participating in the study.

Subjects will be only providing health information to the investigators in this study. They will be offered an opportunity to ask any questions they have regarding this study. All information that will be used for analysis in this study that utilizes patient health information will be password-encrypted and de-identified. HIPAA Authorization to Disclose will be obtained from subjects prior to enrollment in the study.

28) Compensation for Research-Related Injury

In the unlikely event of a research-related injury, subjects or their insurance will be responsible for coverage.

The only complication of capsule endoscopy, apart from inability of the patient to swallow the device, is true capsule retention [>> 2 weeks of retention] with or without obstruction. In this case it is the underlying disease causing the problem and the management would be covered by the patient's insurance.

29) Economic Burden to Subjects

None is anticipated from participating in the study. All costs associated with the emergency department stay, hospital admission and associated testing (including but not limited to endoscopy procedures) will be paid by the subject or insurance and the subject will be responsible for all co-pays, deductibles, etc. These are all standard of care procedures.

The patients recruited to be subjects in this study would most likely require admission to the hospital or the clinical decision unit until a thorough evaluation is completed to determine the source of bleeding. This is a clinical decision that will be made regardless of participation in this study, based on the clinical judgment of the attending physician in the emergency department.

For those in the early capsule group, the cost of using the prokinetic medications (if necessary) will also be paid by the subject or insurance as this is part of the standard of care procedures for their emergency department admission and assessment. Any subsequent intervention will be billed to the subject or insurance.

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The cost of the video capsule and its reading, both for the early capsule group and any subject in the standard of care group who receives a video capsule, will be paid for by the study and not billed to the subject or insurance.

30) Consent Process

Consent will take place in the Emergency Department. Subjects will be given as much time as they require before making a decision to provide consent. The time provided for discussing the consent process with subject will be 15 minutes or greater as the subject requires. Only the listed study staff members will be involved in the consent process. In order to minimize the possibility of coercion during the consent process, potential subjects will be notified that their care will not be altered in any way if they choose to provide or not provide consent. Also, to ensure subjects' understanding we will only recruit English-speaking subjects for this study.

31) Process to Document Consent in Writing

We will be following "SOP: Written Documentation of Consent."

32) Drugs or Devices

The video capsule that will be used in this study is the Olympus small intestinal capsule endoscopy system (EC-10 System). This system has been cleared by the FDA under 510(k) approval number K123421. This is a capsule imaging system intended for visualization of the small intestine mucosa. This is the FDA cleared labeling. There is no requirement for timing in the FDA labeling. The video capsules will be locked in our study coordinator's office. Handling and administration of the capsules will be performed by study staff members who have been trained and have experience in the tasks related to the video capsules.

A copy of the clearance document and a product manual have been added to the attachments for this study.

The two prokinetic agents that will be used as part of this study if capsule retention occurs are metoclopramide and erythromycin. Package inserts for both medications are included as attachments to this study. Metoclopramide is labeled for use in gastroparesis and not gastrointestinal bleeding. Erythromycin is not approved as a prokinetic agent; however, both drugs are often used in the hospital setting for the purposes of emptying the stomach of blood in patients with gastrointestinal bleeding.