Capsule Endoscopy for HEmorrhage in the ER (CHEER)

Protocol Identifying Number: ISR-2016-10770

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Investigator Initiated Research

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STATEMENT OF COMPLIANCE

The study will be conducted in accordance with the International Conference on Helsinki guidelines for Good Clinical Practice (ICH E6), and the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46). All personnel involved in the conduct of this study have completed human subjects' protection training.

SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments provide the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator or Clinical Site Investigator:

Signed: _____ Date: _____

Name:

Title:

TABLE OF CONTENTS

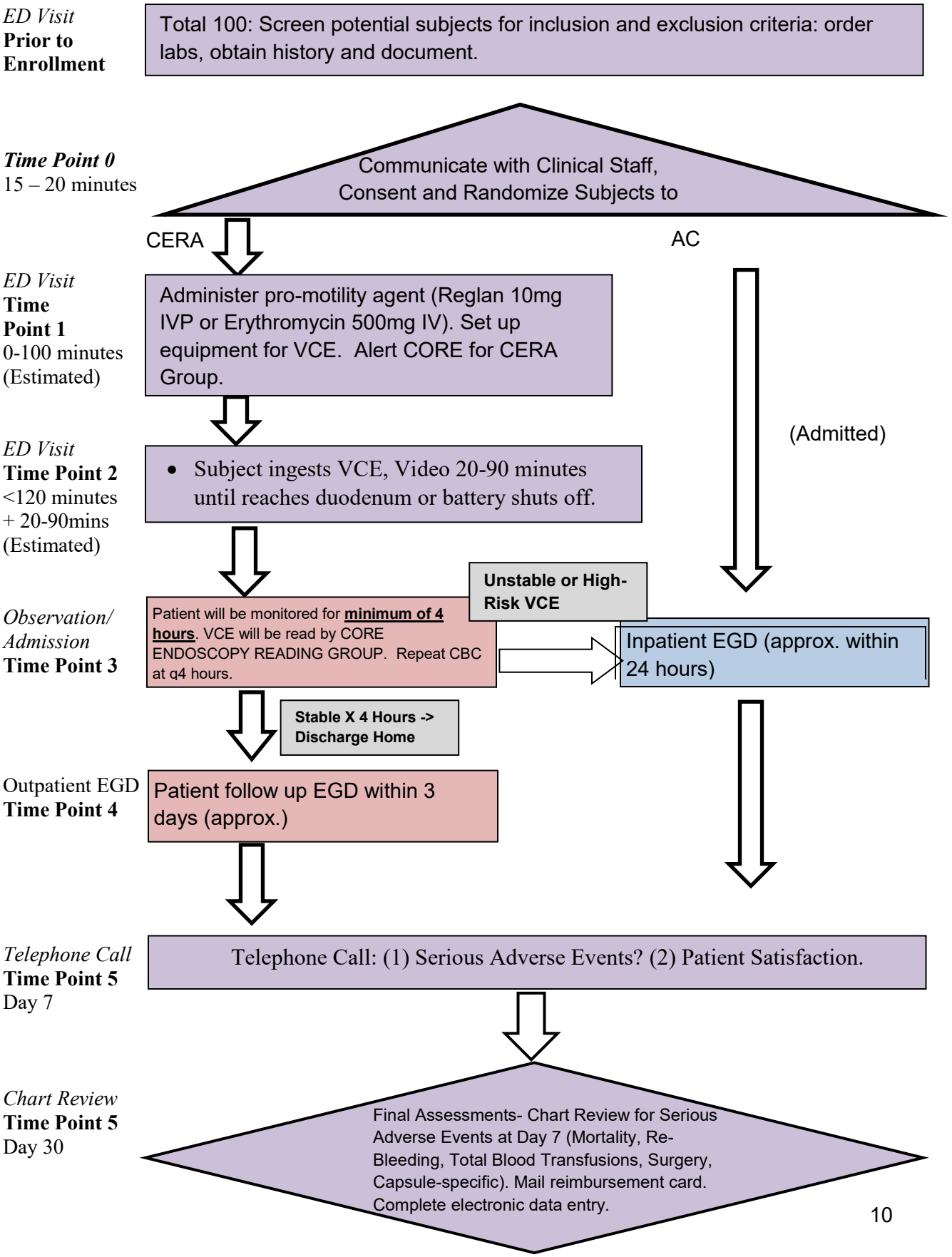
LIST OF ABBREVIATIONS

AC	Active Control
CE	Capsule Endoscopy (Risk Assessment)
CERA	Capsule Endoscopy Risk Assessment
CFR	Code of Federal Regulations
CHEER	Capsule Endoscopy for HEmorrhage in the ER
CORE	Central Reading Group for Endoscopy
ED	Emergency Department
EGD	Esophagogastroduodenoscopy
GBS	Glasgow Blatchford Score
GI	Gastrointestinal
ICH	International Conference on Harmonization
IRB	Institutional Review Board
NIH	National Institutes of Health
RC	Research Coordinator
ST	Standard (Risk Assessment)
UGIB	Upper GI Bleed
US	United States
VCE	Video Capsule Endoscopy

PROTOCOL SUMMARY

Title:	Capsule Endoscopy for HEmorrhage in the ER (CHEER)
Précis:	This is a multi-center randomized controlled trial examining the use of Video Capsule Endoscopy (VCE) to discharge low-moderate risk patients with suspected upper gastrointestinal bleeds (UGIB) from the Emergency Department (ED.) We will enroll 100 subjects at 4 sites who present with signs of hemodynamically stable UGIBs and compare VCE risk assessment to an Active Control (AC) group who receive inpatient upper endoscopy (EGD).
Objectives:	Primary: Our primary goal is to determine whether ED VCE is able to discharge low risk patients for outpatient management of upper GI bleeds. Secondary: Our secondary objective is to estimate the sensitivity and specificity of VCE compared to subsequent EGD in the detection of serious bleeding lesions in the upper gastrointestinal (GI) tract. Sample size is 100 patients, age ≥ 18 in 4 urban EDs, mixed gender, mixed race, hemodynamically stable with possible co-morbidities.
Population:	Study subjects will be enrolled from larger pool of adult ED patients presenting with acute overt UGIB defined as bloody emesis and/or coffee ground vomiting and/or melena within the previous 48 hours.
Number of Sites:	4
Study Duration:	12 months
Subject Participation Duration:	30 days
Estimated Time to Complete Enrollment:	1 year

Schematic of Study Design:



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2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 Background Information

Upper gastrointestinal (GI) hemorrhage is the primary diagnosis for 300,000 annual Emergency Department (ED) admissions in the US. The challenge for the ED is to determine whether a patient with a suspected upper GI bleed (UGIB) needs urgent intervention (i.e. hospital admission for endoscopy, surgery and/or transfusion) or can be safely discharged for outpatient management. The Glasgow-Blatchford Score (GBS) was developed to identify GI bleeds that require hospital admission and urgent intervention. The GBS has a high sensitivity but low specificity. For high risk bleeds, standard of care is hospital admission and a performance of esophagogastroduodenoscopy (upper endoscopy or EGD) within 24 hours. However, many US hospitals do not have the resources to perform EGD on all patients suspected to have UGIB within 24 hours of admission.[1] As a result, a significant proportion of patients with low-risk bleeds are admitted to the hospital for observation and may never receive EGD and many patients with high-risk lesions receive delayed care because of the inability to discriminate low risk from high risk bleeding events.

Video capsule endoscopy (VCE) was initially approved in 2001 by the Food and Drug Administration as a noninvasive diagnostic test for occult UGIB. This technology represented a significant advance in the investigation of intestinal diseases. Indications that have been validated include cryptogenic gastrointestinal bleeding, familial polyposis, and intestinal lesions in patients with Crohn's disease. Based on recent evidence, VCE represents a novel strategy to perform rapid diagnosis of suspected UGIB, portal hypertension, non-cardiac chest pain, gastroesophageal reflux disease in the emergency department (ED). There are limited numbers of EDs in the United States that have used VCE on trial- and protocol-based patient studies, but the results are encouraging.[2] Given the expanding role of advanced diagnostic and point-of-care testing in US EDs, VCE has great potential for future evaluation of ED gastrointestinal complaints.

VCE offers potential advantages over traditional EGD including the ability to be performed 24 hours a day without sedation and interpreted at the bedside by emergency physicians. In addition, VCE is much less invasive, is painless, and enables the patient to pursue normal daily activities after the procedure. ED physicians may use the information to make real-time decisions regarding the need for hospitalization, endoscopic hemostasis, and risk stratification. Real-time imaging has been shown to be helpful in early diagnosis of bleeding lesions [1], and the videos generated can be sent to an off-site specialist for an over-read after the initial ED interpretation. This workflow is similar to that of many current ED diagnostic tests such as electrocardiograms and radiology examinations. This ability to transmit images could become especially important in rural communities or in communities that have limited access to a gastroenterologist. Incorporation of VCE into ED practice could follow a trajectory similar to that of point-of-care ultrasonography, an imaging modality in which ED physicians have become increasingly skilled and for which indications continue to expand [2].

In patients requiring VCE, most contraindications are relative and the procedure has been performed safely in a variety of clinical settings [3]. Pacemakers and other electrical medical

devices are not a contra- indication to the procedure with newer versions of the capsules. The only absolute contraindications are bowel obstruction and pregnancy [4]. There is a low risk of non-natural excretion of the capsule estimated at less than 1 in 100 [5]. In general, the procedure poses significantly less risk than traditional EGD, and multiple studies have shown that VCE is well tolerated in ED patients with suspected acute UGIB [6-8].

The American Society of Gastrointestinal Endoscopy states that credentials for VCE should be determined independently from other endoscopic procedures such as colonoscopy, sigmoidoscopy, or any other endoscopic procedure [9]. The American Society of Gastrointestinal Endoscopy emphasizes sound medical training, appropriate patient selection, correct interpretation, and continued medical management for all patients. VCE requires only image interpretation and does not require procedural skill training associated with other endoscopic procedures; therefore, ED physicians can meet these criteria with basic training.[3]

In a study of 25 subjects, VCE interpretation by emergency physicians demonstrated excellent agreement with gastroenterologists for the presence of fresh or coffee-ground blood (0.96 overall agreement; κ ¼ 0.90) [7]. In another study, 126 emergency physicians were asked to look at standardized videos from ED patients who presented with acute UGIB. Compared with expert gastroenterology-adjudicated interpretation, the sensitivity of ED physicians to detect blood was 0.94% (95% CI: 91%-96%) and specificity was 87% (95% CI: 80%-92%) [10].

Gastrointestinal hemorrhage is a common emergency condition, and the severity ranges from benign to life threatening. Risk stratification of acute UGIB is challenging in the ED because traditional diagnostic approach using the physical exam, lab testing and radiographic studies is too nonspecific to be used without adjunctive endoscopy. As a result, many patients with an ultimately benign clinical course are admitted to the hospital and incur considerable costs. Without an ED-based endoscopy, alternative means to risk stratify patients with signs of UGIB include performing nasogastric aspiration, which is uncomfortable for patients [11], using clinical decision rules, such as the Rockall Risk Score and Glasgow-Blatchford Score, or admitting all patients with suspected upper gastrointestinal bleed for endoscopy [12].

Most endoscopy capsules are manufactured for use in the small bowel, but the esophageal capsule endoscope (PillCam UGI, Medtronic) is designed to visualize the upper gastrointestinal tract. The esophageal VCE is equipped with 2 cameras at either end that take 35 pictures per second for 30 minutes. Initial studies with early-generation esophageal VCE demonstrated a sensitivity of 92% and specificity of 95% to diagnose chronic reflux esophagitis [13]. In addition, the sensitivity and the specificity were found to be 97% and 99%, respectively, for the diagnosis of Barrett esophagus and 89% and 99%, respectively, for diagnosis of esophagitis [13].

The use of esophageal VCE in the ED to directly visualize the upper gastrointestinal tract and identify presence or absence of blood is a novel approach that has been studied in 4 ED-based studies. First, Rubin et al [14] studied 24 patients who presented to the ED with signs of UGIB. In this study, patients were randomized to either receive a VCE in the ED with real-time interpretation or receive standard care. Of the 12 patients in the experimental group, 7 had

bleeding detected on VCE and all had bleeding confirmed with subsequent EGD within 6 hours of hospital admission. Of the 4 patients who had a negative result on VCE (1 could not tolerate a VCE), all 4 had subsequent negative findings on EGD. On average, patients in the experimental group had an EGD performed sooner than the control group, but there was no change in clinical outcomes.

Gralnek et al [6] studied 41 patients who presented to the ED with UGIB and each received both a nasogastric tube and VCE. All patients had an EGD performed in the hospital within 12-24 hours after presentation. Of the 41 patients, 18 had blood in the upper gastrointestinal tract detected by EGD; capsule endoscopy detected blood in 83% (15/18) of these cases compared with a nasogastric aspiration, which detected blood in 33.3% (6/18). It is important to note that in 9 of these patients, the capsule detected blood in the duodenum, when nasogastric aspiration was reported to be either clear or bilious. Lack of detection of post-pyloric bleeding is an important limitation of nasogastric aspiration. Patients preferred VCE over nasogastric aspiration.

A third study conducted in the ED on the use of VCE enrolled 25 subjects with acute upper gastrointestinal hemorrhage [7]. In this study, Meltzer et al demonstrated an 88% sensitivity (95% CI: 65%- 100%) and 64% specificity (95% CI: 35%-92%) for the detection of fresh blood compared with an EGD performed with 24 hours. Capsule endoscopy missed a bleeding lesion located in the post- pyloric region, which was not imaged because of expired battery life (30 minutes).

Most recently, the use of esophageal VCE in the ED was compared with the validated triage system, the Glasgow-Blatchford Score, to identify the number of patients who may be suitable for outpatient care [8]. Patients who presented to the ED for suspected acute UGIB were enrolled and administered esophageal VCE. For capsules that passed the pylorus and reached the duodenum, high-risk lesions were detected with a 95% sensitivity (95% CI: 72%-100%) and a 92% specificity (95% CI: 73%- 99%) compared with the Blatchford Score that demonstrated a 94% sensitivity (95% CI: 72%-100%) and a 16% specificity (95% CI: 5%-37%).

There has been one feasibility study published to test whether VCE can reduce hospital admissions in patients with suspected UGIB. In a prospective randomized controlled trial in which patients who presented with symptoms or signs suggestive of UGIB were randomized to receive either the standard treatment of hospital management versus VCE. Patients were also graded by Glasgow Blatchford score (GBS) at the ED for assessment of need of hospital admission. In this study, seventy-one patients fulfilled the recruitment criteria, with 37 subjects randomized to the VCE group and 34 subjects randomized to standard group. Seven VCE patients with active bleeding or significant endoscopic findings were admitted to the hospital compared with the standard group in which all 34 patients were admitted. There was no difference in the clinical outcome in terms of recurrent bleeding and 30-day mortality. In addition, hospital admission was also greatly reduced if VCE results were used instead of the GBS to determine whether patients were admitted or managed in the outpatient setting.[9]

In all ED studies that have been conducted for acute upper gastrointestinal hemorrhage, VCE has performed well when it travels through the pylorus. However, several high-risk lesions were missed if the VCE did not travel through the pylorus before the battery expired. The time to pass the pylorus is variable. At 60 minutes, 98% of capsules visualize the duodenum [6]; when the battery life is only approximately 20-30 minutes, approximately 50% visualize the duodenum (12/25 [7], 44/83 [8], and 7/12 [14]). In one study, the single missed active bleeding occurred in a patient who was bleeding in the post-pyloric duodenum and in whom the VCE battery expired before reaching the post-pyloric region [7]. For standard EGD, the use of pro-kinetic agents such as erythromycin or metoclopramide has improved mucosal visualization and has been increasingly used before the procedure. This strategy, combined with 60 minutes of visualization, will likely increase the accuracy of VCE as well.

The cost of the VCE is an important factor that affects future use in the ED. The physician Medicare national average fee is $705 for the PillCam UGI and $50 for the professional fee. Although expensive, VCE may be cost-effective if it safely reduces hospital admissions or emergency EGD. For comparison, in 2011, 236,000 patients received an EGD (International Classification of Diseases, Ninth Revision code 45.13) in the hospital for an upper UGIB, the median length of stay was 4.0 days, and the median charges were $23,549.17 [12].

A decision-analytic model showed that VCE is cost effective for low- to moderate-risk patients despite increased upfront costs compared with clinical decision rules or nasogastric tubes. The use of VCE in the ED can potentially lead to more patients being safely discharged from the ED. The hospital admission is the single most expensive decision made by an emergency physician. Chandran et al [8] showed that the higher sensitivity of VCE compared with the Glasgow-Blatchford Score would have saved $1691 per VCE by increasing the number of patients who could receive an outpatient EGD.

Currently, the VCE does not replace the need for traditional EGD when hemostasis or biopsy is needed. Technological advancements may allow a VCE operator to control movement of the capsule, collect biopsy samples, and perform therapeutic functions.

2.2 Rationale

We believe there is an opportunity to improve the risk stratification of acute UGIB that presents to the Emergency Department through the use of Video Capsule Endoscopy. Our primary hypothesis is that VCE allows for safe outpatient management of ED patients with suspected upper GI hemorrhage. A multicenter randomized control trial is proposed to investigate the safety of this diagnostic modality.

2.3 Potential Risks and Benefits

2.3.1 Potential Risks

Patients for whom study enrollment may interfere with standard clinical care will not be enrolled. Alternatives to study participation are for patient to receive standard of care treatment for UGIB.

We have considered a variety of potential risks to participants including cognitive, affective, physical, legal/confidentiality and economic risks. The PillCam UGI is manufactured by Medtronic and has been FDA approved with a robust published safety profile since approval in 2004.

The physical risks associated with the PillCam are generally related to potential non-natural excretion. There is a small risk that the capsule could become stuck in the stomach or bowel. Based on published and unpublished data, the PillCam Small Bowel (SB) capsule has been reported to be retained in the GI tract for periods of at least 23 months without adverse events. The capsule has been shown to remain intact, without symptoms, for months. In fact, a large retrospective review by Chaifetz, et al. found that a retained capsule often leads to a diagnosis. Furthermore, the device is made of biocompatible materials and its internal parts are non-toxic. The incidence of capsule retention has been reported to be less than 1% but this figure may be higher in Crohn's disease or other conditions. The rate of surgical removal was noted to be 0.75% (Barkun JS, Friedman S. Am J Gastroentrol 2002; 97:A83).

Surgery may be required to remove a retained capsule. In general, if a patient does not pass the PillCam naturally through the upper GI tract due to gastroparesis, an EGD will be sufficient to retrieve the capsule. Given that most patients will receive an EGD as part of their standard work-up for the disease, this does not pose a significant increased risk. Patients who are at increased risk of capsule retention are not appropriate study subjects including people with swallowing disorders or with known or suspected gastrointestinal obstructions, strictures or fistulas.

Pregnant women will not be included.

Also, people with cardiac pacemakers or other implanted electro-medical devices will not be given the PillCam given a theoretical risk that the devices could interact.

Patients will be advised not to have an MRI for 30 days and to consult with their doctor prior to receiving an MRI in the future. For patients who are unsure whether they excreted the PillCam, *an abdominal X-Ray may be required as an outpatient to confirm passage.*

In order to maximize safety for all study subjects, only consented and enrolled subjects will be administered the PillCam under the personal supervision of the PI or under the supervision of a sub-investigator/trained research associate responsible to the PI. In addition, the PillCam will be stored in a secure, limited access area. Product accountability log must include the protocol number, investigative site name, product name, medical units (i.e., video capsules), serial number and subject ID number.

We anticipate low cognitive risk to participants. Diagnosis of source of gastrointestinal bleeding lesion is presumably one of the reasons the patient presented for emergency care. We do not anticipate an affective risk to participants. Some participants may be bothered by the knowledge that the device will pass naturally and may take several days to be excreted.

We believe the study poses a low privacy risk to subjects as all data will be encrypted and no PHI will be stored with data.

Finally, the study has a low economic risk since the device and the interpretation of the device are not being billed to the subject or his/her insurance company. *The only economic risk may result from an unanticipated complication of the device that will not be covered by Medtronic, LTD, the manufacturer of the pill camera, GWUH or MFA.*

Minor adverse events that occur will be reported directly to the principal investigator and overall study coordinator at the next business day. Minor adverse events include inability to tolerate capsule, discomfort swallowing capsule, issues regarding video capture, issues regarding video transmission, erroneous video interpretation that has no significant impact on clinical care, protocol deviations, reactions to medication (pro-motility agent), delays in endoscopy interpretation, delays in EGD and others. All minor adverse events will be shared with the entire research team at regularly scheduled monthly calls or sooner at the PI's discretion.

Any major adverse events that occur will be reported directly to the principal investigator who will be available to study subjects 24 hours a day. Severe adverse events will be reported to the entire research team, the DSMB and to IRB within 24 hours. Updates will be provided after a full investigation is completed. Since the PillCam is an FDA-approved device and not an experimental device, all SAE's will also be reported to the FDA. Potential major adverse events include missed high-risk lesions, delayed definitive care, patients who are discharged from hospital and experience a major outcome (see below), capsule retention in the small bowel, and any serious outcome that may be related to study protocol. A DSMB will be formed that includes experts in emergency medicine, gastroenterology and research methodology. DSMB will meet annually during which a report will be produced by PI and as needed for SAE's.

2.3.2 Potential Benefits

Immediate potential benefits include a focused effort by the research team to ensure that an EGD is performed within 24 hours of ED presentation for all subjects who are admitted and within 72 hours for all subjects who are discharged from the ED. In addition, some subjects may avoid hospitalization and have their symptoms managed as an outpatient. Long-term potential benefits include better management of a condition that is common and can recur.

2.3.3 Discussion

The typical primary care, urgent care or emergency care provider is unable to evaluate common and serious conditions of the gastrointestinal tract such as a bleeding peptic ulcer. As such, more than 80% of patients who present to US ED's with suspected bleeding in their upper GI tract require hospitalization, procedural sedation by an anesthesiologist, and a traditional tube-based upper endoscopy by a gastroenterologist. While this traditional process is safe and effective, it is not efficient for low-risk patients and not timely for all high-risk patients. The opportunity to bring VCE to the front-lines of US medical care will revolutionize how we manage upper GI bleeding and shed light on critical diseases that have heretofore been hidden from providers. This trial is an important step toward demonstrating that VCE is a safe and effective tool to risk-stratify upper GI bleeding and improve quality of emergency care for all patients.

3 OBJECTIVES

3.1 Study Objectives

Our primary goal is to test whether ED Video Capsule Endoscopy (VCE) is able to safely discharge low risk patients for outpatient evaluation and management. Our secondary objective is to estimate the sensitivity and specificity of VCE compared to subsequent EGD in the detection of serious bleeding lesions in the upper gastrointestinal (GI) tract.

3.2 Study Outcome Measures

3.2.1 Primary Outcome: (1) Percent Discharged Home. Assumption is that 100% of Active Control (AC) group will be admitted.
3.2.2 Secondary Outcome: Sensitivity and specificity of VCE compared to EGD. *Endpoints will be defined in the following way:*

Positive Video Capsule Endoscopy will be defined as:
1. Fresh blood or evidence of active bleeding visualized in upper GI tract.
2. Coffee ground blood visualized in upper GI tract, but no active bleeding seen.
3. A High Grade Non-Variceal Lesion (Forrest Ia, Ib, IIa or IIb).
4. Signs of Variceal Hemorrhage.
5. Signs of malignancy visualized in upper GI tract.

Negative VCE:
5. Clean stomach and duodenum, no fresh blood or coffee ground.
6. Upper GI pathology non-causative/ incidental.
7. A low grade non-Variceal lesion (Forrest IIc, III).

An Inconclusive VCE:
8. Any capsule that does not pass the pylorus before battery life is expired (and does not detect lesion in stomach or esophagus).

Positive EGD
1. Fresh blood or evidence of active bleeding.
2. Coffee ground but no active bleeding seen.
3. A High Grade Non-Variceal Lesion (Forrest Ia, Ib, IIa or IIb).
4. Signs of Variceal Hemorrhage.

Negative EGD
5. Clean stomach and duodenum, no fresh blood or coffee ground.
6. Upper GI pathology non-causative/ incidental.
7. A low grade non-variceal lesion (Forrest IIc, III).

Other Outcomes:
1. Patient satisfaction with the VCE procedure. (Form Used: *CHEER #4*)

2. GI Physician Final Read and Site physician agreement of VCE results. (Form Used: *CHEER #5*)
3. Serious Adverse Events at Day 7 and Day 30 (Mortality, Re-Bleeding, Total Blood Transfusions, Surgery, Capsule-specific). (Form Used: *CHEER #7*)
4. ED Length of Stay (hours).
5. Hospital Length of Stay (days).
6. Cost-effective analysis.
    - At conclusion of study, we will construct a model using standard decision analysis software to examine the cost-effectiveness of three available strategies for a base-case patient who presents to the ED with either mild or moderate risk scenarios (by Glasgow-Blatchford Score) for requiring invasive hemostatic intervention (i.e., endoscopic, surgical, etc.) The three available diagnostic strategies are (1) direct imaging with video capsule endoscopy performed in the ED, (2) risk stratification using the Glasgow-Blatchford score, and, finally, (3) an admit-all strategy.

4 STUDY DESIGN

4.1 Study Design: Randomized Controlled Trial

4.2 Proposed Sites: GWU, Temple, Duke and other additional sites TBD.

4.3 Patient Safety: The study will be conducted in compliance with Declaration of Helsinki and ICH-GCP guidelines. Study design will be vetted by the local IRB at each participating institution prior to commencement.

4.4 Study procedure:

1. Screen potential patients with signs of upper GI bleeding (melena, h/o hematemesis or coffee-ground emesis) from general pool of ED patients. (Form used, *CHEER:1*)

2. Patients who screen as eligible will be approached about potential interest, to review of inclusion and exclusion criteria, and obtain informed consent. (*See below for full list of inclusion/ exclusion criteria.)*

3. Research Coordinator will calculate traditional risk stratification scores (Glasgow – Blatchford and Rockall).

4. All consented patients will be given a study ID and recorded in enrollment log. (Form used, *CHEER:2)*

5. Once enrolled, all subjects will be randomized to either Active Control (AC) [admission plus EGD within hospital stay] or experimental Capsule Endoscopy Risk Assessment (CERA) in ED.

6. Only patients randomized to the experimental arm will receive video capsule endoscopy in the emergency department. 20 to 60 minutes before capsule ingestion, each patient in the experimental arm receives a single dose of intravenous metoclopramide 10 mg (or erythromycin 500mg intravenously if there is a contraindication), which helps to promote gastric motility and improves visualization of the gastric mucosa at endoscopy. The Research Coordinator (RC) will prepare the patient for VCE. (*See below for description of procedure.*)

7. Within 2 hours of presenting to the ED, patient will ingest video capsule-- RC will monitor progress on real-time viewer for passage through pylorus. Upon passing the pylorus, we will record 5 more minutes of video or until battery runs out – whichever occurs first.

8. Patient data will be completed using a standardized data collection tool including the following elements: chief complaint of patient, history of present illness, past medical history, pertinent lab findings, current medications, vital signs, focused physical exam findings and all relevant treatments administered during the ED and hospital stay. (Form Used, *CHEER:3)*

9. At completion of VCE, patient satisfaction regarding VCE will be assessed in patients in the experimental group. (Form used, *CHEER: 4)*

10. For Active Control (AC) group each patient will be admitted.

    During hospital admission, EGD will be performed on all subjects and hemostasis therapy applied as necessary. The study team decided against mandating that EGD be performed within 24 hours of hospital admission. This is a pragmatic trial. The longer the duration between the inpatient EGD and the ED VCE the greater the likelihood of discrepancy in the findings that may be due to a change in the lesion as part of its natural course or due to treatments delivered. However, the primary objective of the study is not to evaluate diagnostic accuracy of the ED VCE. The study team decided it was more important to enroll subjects in a timely manner than exclude subjects because the inpatient EGD was not completed within 24 hours.

    For the experimental CERA group, subjects will be monitored for a minimum of 4 hours after ingestion. VCE will be undergo a formal review after completion of the VCE by a staff gastroenterologist with extensive experience in VCEs of the small bowel, colon, and esophagus. Both research personnel and the gastroenterologist will undergo a capsule training program organized by Medtronic and receive accreditation after the training.

11. Subjects in the experimental arm who have no sign of active bleeding, show no serious endoscopic findings on capsule, and have stable hemoglobin, blood pressure and heart rate for at least 4 hours will be discharged from the ED. Discharged CE patients will be scheduled to have an outpatient EGD within 3 days post discharge. Patients will be instructed to return to the ED sooner if signs of new bleeding develops. The Research Coordinator will facilitate setting up this appointment for the patient.

    Any subject in the experimental arm with a positive VCE or a negative VCE but has a drop in Hemoglobin ≥ 3 at 4 hours or an elevated HR or low BP will be admitted. A hemoglobin drop between 2 and 3 will NOT automatically transfer patient to active control arm. In these cases, decision to proceed will be up to discretion of treating physician. We anticipate that all admitted patients in the experimental arm will undergo EGD in the hospital (same as AC arm.)

12. Primary Outcome: (1) Percent Discharged Home. Assumption is that 100% of Active Control / standard risk assessment will be admitted.

13. Secondary Outcome: Sensitivity and specificity of VCE compared to EGD

14. Safety outcomes. Patient will be followed for clinical course and EGD results. Day 7 and Day 30, subject follow-up by telephone (if home) or in person (if still in hospital) to assess for adverse events or recurrent bleeding episode. (Form Used, *CHEER: 6*,*7)*

15. All VCE's will be re-read by offsite gastroenterologists who are blinded to the first interpretation and the patient.

5 STUDY ENROLLMENT AND WITHDRAWAL

5.1 Subject Inclusion Criteria

Individuals aged ≥ 18 years presenting to the Emergency Department with “likely upper GI bleed” (typically bloody emesis and/or coffee ground vomiting and/or melena) that has occurred within the previous 48 hours.

5.2 Subject Exclusion Criteria

1. Upper GI Bleed with hemodynamic instability (BP<90 mmHg, pulse>120 beats per minute, and Hgb < 9 g/dL)
2. High Risk Upper GI Bleed (Glasgow Blatchford Score* ≥ 6)
3. Signs, symptoms or history of liver cirrhosis or liver failure
4. Signs, symptoms or history of decompensated heart failure or congestive heart failure
5. Presumed Pregnant, trying to conceive or breastfeeding
6. Known history of gastric cancer
7. Known history of gastric or esophageal varices
8. GI surgery within the last 6 months
9. Prior enrollment in the CHEER Study
10. Prisoner or Ward of State
11. Trouble swallowing, suspected bowel obstruction or perforation, per treating clinician
12. Past UGI tract surgery (e.g., Bilroth I or II, esophagectomy, gastrectomy, bariatric procedure) that changes Gastrointestinal anatomy
13. Known history of gastroparesis, esophageal stricture or Crohn’s disease
14. Altered mental status that limits the ability to swallow a capsule
15. Expected to have Magnetic Resonance Imaging (MRI) examination within 7 days
16. Consumed medications within the past 12 hours that may coat the upper GI tract such as antacids or sucralfate or Maalox and potentially limits capsule visualization
17. Patient either refuses or is unable to get traditional EGD
18. Patient does not have reliable contact information – no phone, no permanent address
19. Patient refuses
20. Unable to provide written consent
21. Non-English speaker
22. Suspected middle or lower GI bleeding
23. Treating ED Physician is not amenable to admission or discharge based on randomization or Video Capsule Endoscopy results.

    * As a modification, the GBS Score modified from the traditional GBS score to reduce the Hemoglobin cut-off for 6 points from 10g/dL to 9 g/dL (see Appendix B, CHEER 4; patient screening)

5.3 Strategies for Recruitment and Retention

Patients will be screened and recruited through the Emergency Department. Research assistants will be monitoring chief complaints and then reviewing the patient record, interview with provider and patients for inclusion and exclusion criteria.

5.4 Subject Withdrawal

5.4.1 Reasons for Withdrawal

A subject can withdraw at any time and for any reason. Subject should provide written notice to PI as to withdrawal intent. The PI can withdraw a patient from the study for noncompliance issues or serious medical conflicts.

5.4.2 Handling of Subject Withdrawals

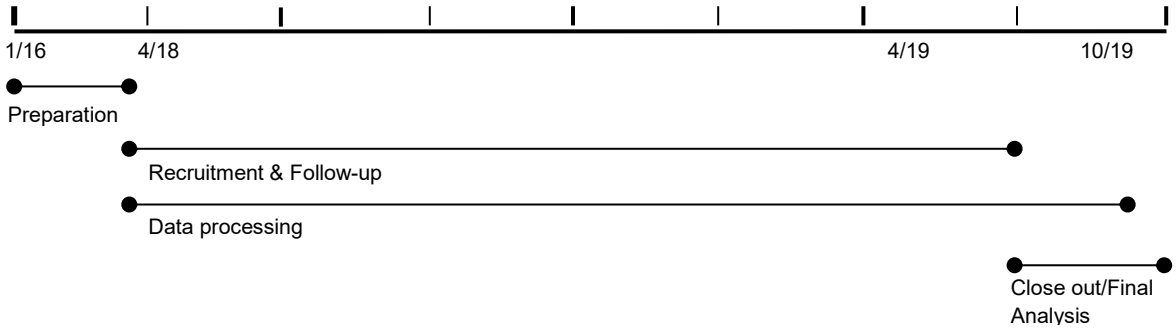
If subject withdraws from the study, no further contact will be attempted or made by study staff. If patient is withdrawn from study by PI for non-compliance or health related concerns, study staff will notify subject via phone call and/or IRB approved letter if direct contact cannot be made.

5.5 Premature Termination or Suspension of Study

Notification of all study subjects. No further data collection.

6 STUDY TIMETABLE

6.1 Timeline



December 2016 through April 2018 will be used for preparing and finalizing protocol, source documents and preparing submission for the IRB.

During this time, we will also:

- create the real time read group
- create training plan
- finalize DSMB members

6.2 Data Collection Period

April 2018- April 2019 will begin screening and recruitment. PI will travel to sites to ensure consistency with using source documents, data base entry and reading results from PillCam

6.3 Final Analysis

April 2019-November 2019 will be for data cleaning, data analysis and manuscript preparation and submittal.

7 STUDY PROCEDURES

7.1 Screening and Randomization

Potential study subjects will be identified while present in the Emergency Department. While the patient is in the ED, a member of the research team will be notified. This researcher will determine if the patient meets the inclusion and exclusion criteria. If the patient meets enrollment criteria, the study protocol will be explained to the patient. If they express interest in participation, informed consent will be obtained, randomization will take place, study procedures followed, and follow-up with GI for EGD will be arranged before the patient is discharged from the ED.

7.2 Procedural Treatment Protocol

7.3 Study Outcomes

7.3.1 Primary Outcomes

Our primary goal is to test whether ED Video Capsule Endoscopy (VCE) is able to safely discharge low risk patients for outpatient evaluation and management.

7.3.2 Secondary Outcomes

Our secondary objective is to estimate the sensitivity and specificity of VCE compared to subsequent EGD in the detection of serious bleeding lesions in the upper gastrointestinal (GI) tract.

7.4 Baseline Procedures

In this randomized clinical trial, the following data and procedures will be performed at screening:

- Informed consent
- Eligibility
- Medical history
- Physical exam
- Medications
- Labs

7.5 Patient Management and Follow-up

After randomization, patients are contacted on days 7 and 30. All the interventions and clinical follow-up in this study are those normally performed in the treatment of patients diagnosed with Upper GI Bleed. The only treatments that are not routine are the VCE PillCam event, read and subsequent discharge to home. Follow–up data will be collected in one of three ways: telephone follow-up is the most preferred method, but email communication or texting to the patient's cell-phone can also be used, in the case that a telephone call is not feasible.

7.6 Adverse Event Reporting

Detailed information concerning adverse events will be collected and evaluated throughout the conduct of the protocol. Results of clinical observations, laboratory tests, and reported events form the basis for evaluating the safety profile of this therapy. At all contacts, patients will be questioned regarding side effects or symptoms associated with the study medication which are as follows:

- Difficulty swallowing the PillCam UGI
- Capsule stuck in the stomach or bowel
- Inability to pass PillCam naturally through a bowel movement
- Surgical intervention
- Aspiration
- Possible skin irritation from the sensors

The clinical center will report adverse events to the coordinating center in a timely fashion. The coordinating center will summarize and report adverse events to the DSMB.

Additional procedures are warranted for cases of serious adverse events which is defined by the FDA as a patient outcome that is: (1) death; (2) life-threatening, i.e., the patient was at substantial risk of dying at the time of the adverse event or it is suspected that the use or continued use of the product would result in the patient's death; (3) hospitalization (initial or prolonged); (4) disability, i.e., resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life; (5) congenital anomaly, i.e., there are suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child; (6) requires intervention to prevent permanent impairment or damage. Serious adverse events will be reported immediately to the Study PI, site PI and the local IRB. The PI will notify the DSMB.

The only indication for breaking the randomization code is when it is medically necessary to unmask the study drug assignment to be able to treat the patient, such as an allergic reaction or severe side effect that appears to be related to the medication.

8 QUESTIONNAIRE ADMINISTRATION

Data will be collected on standardized forms on which nearly all responses have been pre-coded. Each form is briefly described below:

8.1 Cheer 1: Screening Log

Screening Log lists all patients screened for the study and some demographic data.

8.2 Cheer 2: Eligibility and Randomization Form

Eligibility and randomization form will collect the specific inclusion and exclusion criteria for study consent and participation.

Affix randomization label on this form.

8.3 Cheer 3: Patient Data Collection Form

Patient data collection form is completed for all randomized patients. This form includes detailed medical data obtained during screening for the study.

8.4 Cheer 4: Video Capsule Endoscopy Data Collection sheet

This form is completed by the Gastroenterologist completed the VCE read.

8.5 Cheer 5: EGD Data Collection Sheet

This form is completed by the Gastroenterologist completing the EGD read Interpretation Form.

8.6 Cheer 6: Patient Satisfaction

This form is completed during the day 7 and day 30 follow up contact.

8.7 Cheer 7: Patient Follow up

This form is completed during the day 7 and day 30 follow up contact, please verify information via EHR if necessary.

8.8 Cheer 8: Hospitalization Course/ Chart Review

This form collects information on the hospitalization and procedures during the patient's hospital stay.

8.9 Cheer 9: Adverse Event Form/ Serious Event From

This form is completed if patient reports any AE or SAE's. Report to PI within 24 hours, SAE's are reported immediately.

8.10: Cheer 10: Protocol Deviation

This form is completed if there is a deviation from the protocol at any time during the patient's course of participating in the study.

9 WEB DATA ENTRY SYSTEM

For this protocol, web data entry screens corresponding to the study forms listed above will be developed and maintained by GWU. Clinical center staff will enter data into the RedCap database for de-identified data. GWU is no longer able to maintain identifying information in RedCap.

Each site will maintain their own record keeping for maintaining their source documentation for patient information pertaining to follow up contact and file collection of physical source documentation. Please follow your institutional IRB for record maintenance.

10 ASSESSMENT OF SAFETY

10.1 Unanticipated Problems

10.1.1 Capsule Retention, Capsule Retention, Group Crossover

10.2 Serious Adverse Events

Serious adverse events will be reported immediately to the Study PI and the local IRB. Additional procedures are warranted for cases of serious adverse events which is defined by the FDA as a patient outcome that is:

(1) Death;
(2) Life-threatening, i.e., the patient was at substantial risk of dying at the time of the adverse event or it is suspected that the use or continued use of the product would result in the patient's death;
(3) Hospitalization (initial or prolonged);
(4) Disability, i.e., resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life;
(5) Congenital anomaly, i.e., there are suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child;
(6) Requires intervention to prevent permanent impairment or damage.

If a patient in either group experiences any of the aforementioned six outcomes that may be possibly related to the research protocol, including but not limited to the following categories of risk:

(1) Missed gastrointestinal lesion;
(2) Capsule ingestion;
(3) Capsule retention;
(4) Delayed definitive care;

10.3 Reporting Procedures

All adverse events get reported to site IRB, to study PI and DSMB.

11 HYPOTHESIS AND ANALYSIS

11.1 Study Hypotheses

We hypothesize that there will be no significant difference in the hospital admission rate among subjects diagnosed with a high-risk lesion between the two study groups whereas there will be a significant difference in the hospital admission rate among subjects with a low risk lesion.

11.2 Sample Size Considerations

With 100 patients, we will have adequate power (i.e. ≥ 80%) to detect a 25% difference or greater in admission rates for subjects with low risk lesions with p- value less than 0.05. We assume that the controls will a 100% admission rate. We anticipate 20% or less of all subjects to be diagnosed with a high-risk lesion, we are unlikely to have adequate power to detect a significant difference in the hospital admission rate between the two study groups.

11.3 Final Analysis Plan

The analysis will be conducted in several stages. First, we will compare the baseline characteristics of the two study groups to determine if randomization was successful. We will also compare the baseline characteristics of the study samples by enrollment site. Second, we will compare the VCE and EGD results and classify all study subjects according to whether there is a high versus low risk lesion present. The VCE and EGD results may differ because they are not being performed at the same time and GI bleeds can resolve or change so it is unlikely that there will be perfect agreement between the two modalities. In cases where one modality identifies a low risk lesion and the other one a high-risk lesion, we will classify the lesion as high risk. If the VCE could not adequately visualize the tract, we will classify the results according to the EGD. We will compare the sensitivity and specificity of VCE and EGD for identifying high risk lesions. Finally, we will separately compare the admission rates of high-risk lesions and low risk lesions between the two study groups. We will compare admission rates aggregated across the four study centers as well as within each study center.

For tertiary outcomes, we will compare the outcomes by study group using a chi-square test statistic if the outcome is categorical such as the presence of an adverse event and a t test (normally distributed) or median test (non-normally distributed) if the outcome is continuous such as hospital or ED length of stay.

11.4 Cost-Effective Analysis

A cost-effective model will be constructed to determine if the increased upfront cost of VCE is offset by the decreased cost due to fewer admissions.

12 STUDY OVERSIGHT

A Data Safety Monitoring Board (DSMB) consisting of appropriately qualified independent experts has been appointed by the PI to provide review of data on patient safety and study progress. The membership roster is maintained by Site PI and study coordinator and is available from them as needed. PI will provide reports including adverse events. A summary of DSMB deliberations will be prepared distributed to the subsites to submit to their IRB.

The Data and Safety Monitoring Board provides ongoing evaluation of the study progress including patient accrual and retention, monitoring of adverse events, and the adequacy and efficiency of the analysis plan to discern outcomes that might require study modifications, or result in early cessation of the study due to its benefits or harms. The DSMB does not evaluate the scientific merit or methodology of the study, nor does it directly participate in the execution of a study's protocol, monitor the budget, or approve sub-protocols or other modifications to the study.

The major responsibilities of the Board are:

- To review the data analysis plan and make recommendations for additions or changes to the plan.
- To assess the performance of each participating center and make appropriate recommendations regarding continuation, probationary status, or termination.
- To consider patient accrual, overall study progress (timeline and follow-up participation), adverse effects and patient safety, treatment effectiveness/futility, and proper monitoring and reporting by the study team as these affect the ethical treatment of participants or the ethical conduct of research.
- Report to the PI on any perceived problems with study conduct, enrollment, sample size, and data collection.

12.1 Site Visits

PI and study coordinator will visit all sites a minimum of once annually and each site will engage in monthly calls.

12.2 Monthly Reports

Monthly Recruitment Reports - reports of the number of people screened and enrolled by month. Reports detailing recruitment, baseline patient characteristics, data quality, incidence of missing data and adherence to study protocol.

12.3 Annual Reports

Data and Safety Monitoring Board (DSMB) Reports - The DSMB will prepare a written report which includes patient recruitment, baseline patient characteristics, center performance information with respect to data quality, timeliness of data submission and protocol adherence (in addition to safety and efficacy data). The reports also include adverse events, loss to follow-up and all outcome variables as described previously in this protocol.

13 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Study staff will maintain appropriate medical and research records for this study, in compliance with ICH E6, Section 4.9 and regulatory and institutional requirements for the protection of confidentiality of subjects.

14 QUALITY CONTROL AND QUALITY ASSURANCE

QC procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written SOPs, the monitors will verify that the clinical trial is conducted, and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

15 ETHICS/PROTECTION OF HUMAN SUBJECTS

15.1 Good Clinical Practices

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46 and/or the ICH E6.

15.2 Institutional Review Board

The protocol, informed consent form(s), recruitment materials and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented in the study.

15.3 Informed Consent Process

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Extensive discussion of risks and possible benefits of study participation will be provided to participants and their families, if applicable. A consent form describing in detail the study procedures and risks will be given to the participant. Consent forms will be IRB-approved, and the participant is required to read and review the document or have the document read to him or her. The investigator or designee will explain the research study to the participant and answer any questions that may arise. The participant will sign the informed consent document prior to any study-related assessments or procedures. Participants will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. They may withdraw consent at any time throughout the course of the study. A copy of the signed informed consent document will be given to participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study. The consent process will be documented in the clinical or research record.

15.4 Exclusion of Women, Minorities, and Children (Special Populations)

All adults will be included. Children will be excluded because upper GI bleed is typically a disease of adults.

15.5 Participant Confidentiality

All records will be confidential. Subjects will not be identified in any reports or publications of this study. It is possible that representatives of regulatory agencies and from the study's sponsor may come to (the university/hospital) to review study information. In that situation, copies of the relevant parts of the study records will be released with all identifying information removed. Access to study records will be limited to those who need the information for purposes of this study, as well as your health care providers should they need access to the information. All records are kept in a secure location and access is limited to research study personnel.

16 DATA HANDLING AND RECORD KEEPING

16.1 Data Management Responsibilities

Each participating site will maintain appropriate medical and research records for this trial, in compliance with ICH E6 and regulatory and institutional requirements for the protection of confidentiality of participants. As part of participating in this study, each site will permit authorized representatives of the PI to examine (and when permitted by applicable law, to copy) clinical records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress, and data validity.

Source data are all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Examples include, but are not limited to, hospital records, clinical and office charts, laboratory notes, memoranda, recorded videos of upper Gi tract, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, and participant files and records kept at the pharmacy, at the laboratories, and medico-technical departments involved in the clinical trial. It is acceptable to use CRFs as source documents. Except for videos, all data will be collected on CRFs.

Study participation will also be recorded in the medical record to ensure that anyone who would access the patient medical record has adequate knowledge that the patient is participating in a clinical trial.

16.2 Data Capture Methods

Data will be captured both via hand written source documents and a centralized web-based data entry system. The centralized web system will be Redcap and will be administered by GWUH.

16.3 Schedule and Content of Reports

The recruitment and follow-up periods begin in April 2017 and continue through April 2018. Data queries are generated and resolved during this time period through June 2018. Data close-out will be performed immediately following end of recruitment period.

16.4 Study Records Retention

Study records will be maintained for at 3 years post study closure and per IRB specifications.

16.5 Protocol Deviations

Protocol deviations will be maintained through protocol deviations source documentation that is entered into the centralized databased. Protocol deviations will also be reported directly to study PI within 24 hours.

17 PUBLICATION/DATA SHARING POLICY

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

18 LITERATURE REFERENCES

White CM, Kilgore ML. PillCam ESO Versus Esophagogastroduodenoscopy (EGD) in Esophageal Variceal Screening: A Decision Analysis. J Clin Gastroenterol. 2009 Aug 5. [Epub ahead of print] PubMed PMID: 19661814.

Moglia A, Menciassi A, Dario P, Cuschieri A. Capsule endoscopy: progress update and challenges ahead. Nat Rev Gastroenterol Hepatol. 2009 Jun;6(6):353-62. Review. PubMed PMID: 19434097.

Lapalus MG. Esophageal capsule endoscopy vs. EGD for the evaluation of portal hypertension: a French prospective multicenter comparative study. Am J Gastroenterol. 2009 May;104(5):1112-8. Epub 2009 Mar 31.

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Westerhof J, Koornstra JJ, Weersma RK. Capsule endoscopy: a review from the clinician's perspectives. Minerva Gastroenterol Dietol. 2008 Jun;54(2):189-207. Review. PubMed PMID: 18319691.

Gralnek IM, Adler SN, Yassin K, Koslowsky B, Metzger Y, Eliakim R. Detecting esophageal disease with second-generation capsule endoscopy: initial evaluation of the PillCam ESO 2. Endoscopy. 2008 Apr; 40(4):275-9. PubMed PMID: 18389444.

[9] Sung J.J.Y., Tang R.S.Y., Ching J.Y.L., Rainer T.H., Lau J.Y.W. Use of capsule endoscopy in the emergency department as a triage of patients with GI bleeding. (2016) Gastrointestinal Endoscopy, 84 (6), pp. 907-913.

APPENDICES

18.1 APPENDIX A: Schedule of Events

2017

December - February Consensus building. Protocol Development

2017

January-December	IRB submission at all sites
January-December	Contract between primary site GW and all enrolling sites
January- December	DSMB formation, steering committee convene, central CE reading team call schedule established for March 2017 to March 2018

2018

March	CE training and Site Visit by PI and team
April	Enrollment kick off
April-April	Monthly Calls for entire team. Status reports.

2019

April	Target Enrollment Reached, End recruitment
April	DSMB report prepared
June	Data Cleaning
August	First manuscript Draft Prepared
September	Manuscript Submitted (To be discussed: Dissemination plan.)

18.2 APPENDIX B – Document List

Cheer 1: Screening Log

Cheer 2: Eligibility

Cheer 3: Patient Data Collection Form

Cheer 4: Patient Screening; GBS Score

Cheer 5: Patient Lab Values Pre- PillCam

Cheer 6: Patient Lab Values Post-PillCam

Cheer 7: Video Capsule Endoscopy Data Collection sheet

Cheer 8: EGD Data Collection Sheet

Cheer 9: Patient Satisfaction Day 7 and Day 30

Cheer 10: Patient Follow up Day 7 and Day 30

Cheer 11: Patient Chart Review

Cheer 12: Adverse Event Form/ Serious Event From

Cheer 13: Protocol Deviation

18.3 Screening Log

CHEER 1 SCREENING LOG

	Project Name:	CHEER			Site# + PI Name	GW + Meltzer
Screen #	Screening Type	Patient Initials	Pre-Screen Date	Pass/Fail	Screen Failure Reason	Notes
1	Pre-Screen	AB	4/1/2017	Fail	Exclusion #1- Hemodynamic Instability	
2						
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18.4 Patient Screening

Patient Screening

Record ID _____ Date of Screening _____Initials of Person Completing Form_____

1.Age of 18 or older

Yes No (Must be YES to be eligible for study)

2.Evidence of likely acute upper GI bleed (melena, hematemesis (bright red or coffee-ground) in the last 48 hours?

Yes No (Must be YES to be eligible for study)

3. Treating ED Physician is amenable to admission or discharge based on randomization and/or results of video capsule endoscopy.

Yes No (Must be YES to be eligible)

4.Upper GI Bleed with hemodynamic instability (BP<90 mmHg, pulse>120 beats per minute, and Hgb<9 g/dL)

Yes No (Must be NO to be eligible for study)5. High Risk Upper GI Bleed (Glasgow Blatchford Score ≥ 6)

Yes No (Must be NO to be eligible for study)**5. Presumed pregnant, trying to conceive or breastfeeding**

Yes No (Must be NO to be eligible for study)

6. Signs, symptoms, or history of liver cirrhosis or liver failure

Yes No (Must be NO to be eligible for study)

7. Signs, symptoms, or history of decompensated heart failure or congestive heart failure

Yes No (Must be NO to be eligible for study)

8. Known history of gastric cancer

Yes No (Must be NO to be eligible)

9Known history of gastric of esophageal varices

Yes No (Must be NO to be eligible for study)

10. GI surgery within the last 6 months

Yes No (Must be NO to be eligible for study)

11. Prior enrollment in the CHEER Study

Yes No (Must be NO to be eligible for study)

12. Prisoner or Ward of State

Yes No (Must be NO to be eligible for study)

13. Trouble swallowing, suspected bowel obstruction or perforation, per treating clinician

Yes No (Must be NO to be eligible for study)

14. Past UGI tract surgery (e.g., Bilroth I or II, esophagectomy, gastrectomy, bariatric procedure) that changes Gastrointestinal anatomy

Yes No (Must be NO to be eligible for study)

15. Known history of gastroparesis, esophageal stricture or Crohn's disease

Yes No (Must be NO to be eligible for study)

16. Altered mental status that limits the ability to swallow a capsule

Yes No (Must be NO to be eligible for study)

17. Expected to have Magnetic Resonance Imaging (MRI) examination within 7 days

Yes No (Must be NO to be eligible for study)

18. Consumed medications within the past 12 hours that may coat the upper GI tract such as antacids or sucralfate or Maalox and potentially limits capsule visualization

Yes No (Must be NO to be eligible for study)

19. Patient either refuses or is unable to get traditional EGD

Yes No (Must be NO to be eligible for study)

20. Patient does not have reliable contact information – no phone, no permanent address

Yes No (Must be NO to be eligible for study)

21. Patient refuses

Yes No (Must be NO to be eligible for study)

22. Unable to provide written consent

Yes No (Must be NO to be eligible for study)

23. Non-English speaker

Yes No (Must be NO to be eligible for study)

24. Suspected milddle or lower GI bleeding

Yes No (Must be NO to be eligible for study)

If eligible and consented, affix VCE label here.

18.5 Patient Data Collection

Patient Data Collection

Initials of Person Completing Form _____Time _____

Gender Male Female

Race White Black Asian Native American Other If other, please indicate

Ethnicity (self-report) Hispanic Not Hispanic

Date and time patient last ate _____

Have you had any bloody or black "tar" stools in the past 24 hours? Yes No

Have you had bloody or coffee ground vomit in past 24 hours? Yes No

Have you felt weak or light headed in past 24 hours? Yes No

Have you passed out or lost consciousness in the past 24 hours? Yes No

How long ago did this episode of bleeding first start?

Less than 4 hours

Between 4 and 12 hours

Between 12 and 24 hours

Between 1-2 Days

More than 2 Days

Unsure

Any allergies? Yes No

Please list allergies _____

Is patient on any current medications? Yes No

Please list medications _____

Currently taking Proton pump inhibitor (PPI) Antacids?

Examples include Prilosec (omeprazole), protonix (pantoprazole), prevacid (lansoprazole), aciphex (raeprazole), nexium (esomeprazole)? Yes No

Do you take any NSAIDS? Examples include aspirin, ibuprofen, Aleve, Advil, Motrin? Yes No

Do you have any of the following medical problems?

Heart attack OR Heart disease

Diabetes Mellitus

Cancer that spread

Kidney Failure OR on dialysis

Previous Smoker OR Active Smoker

Liver Disease OR Liver Cirrhosis

Ulcer or Gastritis or Acid Reflux

Hemorrhoids

Prior abdominal surgery OR pelvic surgery

inflammatory bowel disease (Crohn's OR Ulcerative Colitis)

Bowel Obstruction

Other: _____

18.6 Patient Screening: GBS Score

Patient Screening: GBS Score

Gender Male Female

Blood Urea (mg/dL)

<18.2 (0 points)

18.2-22.3 (2 points)

22.4-28 (3 points)

28-70 (4 points)

>70 (6 points)

Hemoglobin (g/dl)

>13.0 (0 points for either gender)

12.0-13.0 (1 point male 0 point female)

9.0-12.0 (3 points male 1 point female)

< 9.0(6 points for either gender)

Systolic blood pressure (mmHg)

>110 (0 points)

100-109 (1 point)

90-99 (2 points)

< 90 (3 points)

Heart rate higher than 100 bpm Yes (1 point) No (0 points)

Presentation with syncope Yes (2 points) No (0 points)

Cardiac Disease (echocardiography evidence) Yes (2 points) No (0 points)

Hepatic disease (chronic, acute liver disease) Yes (2 points) No (0 points)

Presentation with melena Yes (1 point) No (0 points)

GBS Score _____

(NOTE: GBS <6 to be eligible for the study)

18.7 Patient Lab Values Pre PillCam

Record ID _____

Date/Time Collected _____

Hemoglobin _____g/dL

18.8 Patient Lab Values Post PillCam

Record ID _____

Date/Time Collected _____

Hemoglobin _____g/dL

18.9 PillCam Data Collection

Video capsule endoscopy (PillCam) data collection

Date/Time PillCam given _____Initials person filling out form_____

Provider reading PillCam _____

Real Time or Retrospective Read_____

ON THE ACCOMPANYING VIDEO CAPSULE ENDOSCOPY IS THERE EVIDENCE OF THE FOLLOWING? (Circle all that apply)

a. Clean stomach and duodenum, i.e., no fresh blood or coffee ground

b. Upper GI pathology non-causative/ incidental.

c. A LOW grade non-Variceal lesion (Forrest IIc, III)

d. A HIGH Grade Non-Variceal Lesion (Forrest Ia, Ib, IIa or IIb)

e. Coffee ground blood

f. Fresh blood or evidence of active bleeding

g. Varices (either gastric or esophageal) or Variceal Hemorrhage

h. Other sources of bleeding

-Mallory-Weiss

-Angiodysplasia

-Gastritis

-Esophagitis

-Tumor

i. If there is a bleeding source, where is it?

-Esophagus

-Stomach

-Duodenum

-None detected

j. Did the capsule pass the pylorus before battery life expired (and does not detect lesion in stomach or esophagus.) Yes No

k. Based on your findings, would you recommend endoscopic hemostasis?

Yes

No

18.10 EGD Data Collection

Esophagogastroduodenoscopy (EGD) data collection

Date and Time EGD performed _____ Initials person filling out form_____

Where was EGD performed? Inpatient outpatient

Provider reading EGD _____

Rank of person performing EGD

Attending GI

Attending General Surgery

GI Fellow 1st Year

GI Fellow 2nd Year

GI Fellow 3rd Year +

IN THE ACCOMPANYING EGD (ENDOSCOPY), IS THERE EVIDENCE OF THE FOLLOWING? (Circle all that apply)

a. Clean stomach and duodenum, i.e., no fresh blood or coffee ground

b. Upper GI pathology non-causative/ incidental.

c. A LOW grade non-Variceal lesion (Forrest IIc, III)

d. A HIGH Grade Non-Variceal Lesion (Forrest Ia, Ib, IIa or IIb)

e. Coffee ground blood

f. Fresh blood or evidence of active bleeding.

g. Varices (either gastric or esophageal) or Variceal Hemorrhage

h. Other sources of bleeding

Other sources of bleeding

-Mallory-Weiss

-Angiodysplasia

-Gastritis

-Esophagitis

-Tumor

i. If there is a bleeding source detected, where is it?

Esophagus

Stomach

Duodenum

None detected

j. Did you perform endoscopic hemostasis?

Yes

No

If yes, what intervention? _____

18.11 Patient Satisfaction Day 7 and Day 30

Patient Satisfaction Day 7 and Day 30

I understood the reason for the pill camera

Strongly Agree

Agree

Neutral

Disagree

Strongly Disagree

I understood the procedure for the pill camera.

Strongly Agree

Agree

Neutral

Disagree

Strongly Disagree

I felt the research team answered all my questions Yes No

The pill camera was easy to swallow Yes No

I would use the pill camera again Yes No

Did you have any issues Yes No

if Yes, what are they? _____

18.12 Patient Follow-up Telephone Call Day 7 and Day 30

Patient Follow up Telephone Call Day 7 and Day 30

Initials of person completing form _____

You came to the ER on {date of visit} for possible bleeding.

Are you experienced the same or similar symptoms? Yes No

Please tell me what they are _____

(If patient is continuing to have symptoms please list)

Have you recently noticed blood in the stood? Yes No

Have you vomited any BRIGHT RED or COFFEE GROUND blood recently? Yes No

How long how has this episode of BLEEDING lasted?

Between 1-2 days

Between 3-4 days

Between 5-7 days

Never went away

Unsure

Have you noticed any bloody or black tar stools in the past 24 hours? Yes No

Have you passed out or lost consciousness in the past 24 hours? Yes No

Have you seen a gastroenterologist since you were discharged? Yes No

Did you have an upper endoscopy while you were in the hospital? Yes No

Did you have an upper endoscopy after being discharged from the hospital? Yes No

What were the results of the endoscopy?

Bleeding resolved

Bleeding persisted

New problem

Unsure

If patient has a new problem, please describe. _____

Did you have a return visit to the hospital? Yes No

Return date to the hospital? _____

Which Hospital? _____

Where you hospitalized for recurrent bleeding? _____

Did you have a second endoscopy? Yes No

What were the results? _____

When were you discharged? _____

18.13 Patient Chart Review

Patient Chart Review

Initials of person abstracting information from chart _____

Hospital discharge date _____

Blood transfusion? Yes No

Date of transfusion _____

Number of PRBC? _____

Additional endoscopy Yes No

How many? _____

Hemostatic therapy? Yes No

Surgery? Yes No

Date of surgery _____

Please describe surgery. _____

Disposition?

Home

Rehabilitation

Nursing home

Deceased

18.14 Adverse Event Form

Adverse Event Form

Initials of person completing form _____

Start Date/Time _____

Stop Date/Time _____

During PillCam Administration Yes No

Post PillCam Administration Yes No

Please describe the AE _____

Relationship to the Study Protocol/Procedures (Per Site PI)

Unrelated

Unlikely

Possibly

Probably

Definite

_____

Relationship to the PillCam (Per Site PI)

Unrelated

Unlikely

Possibly

Probably

Definite

_____

Primary Outcome

Recovered/Resolved

Under Treatment

Change in AE/SAE Characteristic

Sequelae

Fatal

Unknown

_____

Serious Event? Yes No

Life Threatening? Yes No

Required or prolonged hospitalization? Yes No

Disability? Yes No

Congenital Anomaly? Yes No

Required intervention? Yes No

Death? Yes No

Was Site PI notified? Yes No

Was the IRB notified? Yes No: If No, Why Not? _____

18.15 Protocol Deviation

Protocol Deviation

Date of Event _____

Description of the Deviation _____

Reason for the deviation _____

Corrective measures _____

Was site PI notified? Yes No

Was IRB notified? Yes No

Why Not? _____