Protocol

Noncontact magnetically controlled capsule endoscopy for infection-free gastric examination during the COVID-19 pandemic: a pilot, open-label, randomized study

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CHAPTER 1: ADMINISTRATIVE INFORMATION

1.1 Title

- Noncontact magnetically controlled capsule endoscopy for infection-free gastric examination during the COVID-19 pandemic: a pilot, open-label, randomized study

1.2 Trial registration

- ClinicalTrials.gov identifier: NCT04389333

1.3 Protocol version

- Version 1.0 published on Feb 3rd, 2020.

1.4 Details of applications

- Investigation site (institution): Changhai Hospital
- Principal investigator: Zhuan Liao

CHAPTER 2: INTRODUCTION

2.1 Introduction and rationale

COVID-19, a respiratory disease that spreads via direct contact or through droplet transmission, has caused a major disruption in the healthcare system since it was first identified in 2019 [1]. Endoscopic procedures during the pandemic were divided into urgent endoscopy, semi-urgent endoscopy, and elective endoscopy, with the aim of preventing infection among healthcare professionals and providing necessary medical services [2]. For patients who required urgent gastroscopy, the face-to-face contact with endoscopists, aggressive suctioning, and coughing [3] during examination brought opportunities for transmission. Considering the reduced endoscopy volume in most endoscopy departments, diagnosis of patients who needed semi-urgent endoscopy and elective endoscopy may have been delayed [4]. Therefore, focusing on how to return to gradually return to provision of routine endoscopy services while maintaining safety for endoscopists deserves attention [5].

Capsule endoscopy provides a great view of the gastrointestinal tract through use of a miniature, pill-sized camera and it is as accurate as other gastrointestinal endoscopy modalities [6]. Its unique advantages include single use, excellent tolerance, and minimal medical staff requirement, which reduces the risk of exposure to pathogenic microorganisms and cross-infection [7] and makes it an appropriate method for examining and triaging an endoscopy department during the COVID-19 pandemic [8].

However, capsule endoscopy cannot be used to avoid face-to-face contact between endoscopists and patients who have asymptomatic COVID-19 cases [9]. Herein, we describe a novel noncontact magnetically controlled capsule endoscopy (ncMCE) system using a remote control system to separate endoscopists and patients physically, which was developed and tested in our medical center [10,11]. The objective of the present study was to evaluate the feasibility and safety of ncMCE for gastric examination.

2.2 Study design

This study was a pilot, open-label, randomized controlled trial approved by the institutional review board of Shanghai Changhai Hospital and registered at ClinicalTrials.gov (NCT 04389333). All of the diagnostic and therapeutic modalities were carried out in accordance with the approved guidelines.

2.3 Monitoring plan

During the clinical trial, the clinical trial inspector appointed by the bidding unit will conduct regular on-site inspection visits to the research hospital. The clinical trial supervisor is the main contact between the applicant and the researcher. The inspectors must follow the quality management standards and SOP of clinical trials of medical devices, visit the experimental units regularly or according to the actual situation for clinical supervision, urge the progress of clinical trials, check and confirm the correctness and completeness of the records and reports of all data and the input of case reports, and be consistent with the original data, so as to ensure that clinical trials are carried out in accordance with the clinical trial plan.

The specific contents of the inspectors include:

- Confirm that facilities remain acceptable.
- Ensure the implementation of the test plan by researchers during the experiment.
- Verify that all data records and reports are correct and complete and consistent with the original data.
- Research instruments should be supplied, stored, distributed and retrieved in accordance with relevant regulations, and to make corresponding records;
- The violation of the scheme and SAE should be faithfully recorded and remedied in time.
- Perform source data verification and review.
- Complete a written monitoring report after each visit.

An independent Data and safety monitoring committee (DSMC) appointed by the ethics committee, the Shanghai and National Medical Products Administration provided trial regular oversight.

2.8 Ethical issues

Before implementation of the clinical investigation, the investigator shall submit the clinical investigation plan (CIP), informed consent and other relevant documents to the medical ethics committee of the hospital where the clinical investigation will be

implemented. Only after ethical approval is obtained from the Ethics Committee, the study can get underway. Any modification to the CIP must be approved by the ethics committee before implementation. Serious adverse events (SAEs) that occur during the clinical investigation should be timely submitted to the Ethics Committee in written form.

This trial will be conducted in accordance with the protocol, Good Clinical Practice (GCP) and applicable regulatory requirements. All investigators undertaking this work have undertaken the necessary GCP training.

2.9 Benefits and risks assessment, group relatedness

In ncMCE group, patients could not only have systematic physical examination for free, but also have the possibility of FC-related symptoms improvement. The risks are that of vibration, capsule swallowing and re-interventions (surgery, endoscopy, radiology).

In placebo group, the same systematic physical examination and professional medical advice were provided throughout the study period. The risks are that of capsule swallowing and re-interventions (surgery, endoscopy, radiology).

The AEs including gastrointestinal (GI) symptoms such as abdominal pain, bloating, fever, nausea, vomiting, diarrhea; abnormal results of physical examinations and laboratory tests and capsule retention. All AEs reported spontaneously by the 107 subjects or observed by the investigator or his staff will be recorded.

Re-interventions (surgery, endoscopy, radiology) should be applied when necessary for safety consideration.

CHAPTER 3: ELIGIBILITY AND SCREENING

3.1 Study Population

This study was a pilot, open-label, randomized controlled trial approved by the institutional review board of Shanghai Changhai Hospital and registered at ClinicalTrials.gov (NCT 04389333). All of the diagnostic and therapeutic modalities were carried out in accordance with the approved guidelines.Beginning on March 26, 2020, we consecutively recruited 40 patients in Changhai Hospital using predefined inclusion criteria and exclusion criteria. After fully understanding the procedure of ncMCE and this study, patients who gave informed consent were randomly assigned into ncMCE and MCE groups (in a 1:1 ratio) by using a stratified block randomization (fixed block size four). Randomization was based on a computer-generated list of random numbers using SPSS software (version 22.0, SPSS Inc., Chicago, Illinois, United States). Only after the enrolled participants completed all baseline assessments did the endoscopist inform them about their allocation. Eligible patients were adults ($\geqslant$ 18 years of age) undergoing outpatient MCE. Patients with any of the following conditions were excluded: (1) dysphagia or symptoms of gastric outlet obstruction, suspected or known intestinal stenosis, overt gastrointestinal bleeding, fistulas and strictures; (2) history of upper gastrointestinal surgery or suspected delayed gastric emptying; (3) poor general condition, asthma or claustrophobia; (4) implanted metallic devices such as pacemakers, defibrillators, artificial heart valves or joint prostheses; (5) pregnancy or mental illness; (6) current participation in another clinical study; or (7) difficulty communicating.

3.2 Diagnostic work-up before randomization

3.2.1 Body temperature measurement and nucleic acid test

For safety reasons, we conducted nucleic acid test and body temperature test for each patient undergoing MCE before entering the examination room.

3.2.2 Informed consent

The principles of informed consent in the current edition of the Declaration of Helsinki will be implemented. Written informed consent will be obtained from patients before inclusion in the trial.

The investigator must introduce this study in detail to the patients, including content, purpose, intended efficacy, possible AEs, and countermeasures before signed the informed consent and patients will be given as much time as they need to make a decision.

The informed consent form shall be signed jointly by the investigator and the patient. It is in duplicate, and each party maintains one copy.

CHAPTER 4: INTERVENTIONS AND OUTCOMES

4.1 MCE system and ncMCE system

The MCE system (Ankon Technologies Co., Ltd. Shanghai, China) consists of a guidance C-arm magnet robot, a computer workstation with ESNavi software, endoscopic capsule, capsule locator, and a vest-like data recorder that can receive capsule signal from both sides [12]. The ncMCE system adds a remote control workstation and an audio-visual exchange system to the original well-established MCE system, which was developed and tested at our medical center [10]. To simplify the preparation process, we embedded the data recorder in the examination bed. The ncMCE system separates endoscopist and patients in two rooms (control room for endoscopist and examination room for patients), offering physical isolation for noninvasive gastric examination during the pandemic [11].

4.2 Study intervention

- Patients were required to report personal history and have chest computed tomography or nucleic acid testing to exclude COVID-19 infection within 3 days before their examination. Patients who are confirmed to have a COVID-19 infection and symptoms of pneumonia should be treated at special medical institutions first. Only when this population needs immediate endoscopy should those procedures be done in specific wards that have COVID-19 infection prevention protocols in place [13]. On arrival at the hospital in the morning after an overnight fast (> 8 hours), each patient took a 400-mg simethicone suspension dissolved in 100 mL water 40 minutes before they ingested the capsule ingestion according to standardized gastric preparation [14]. Another 800 to 1000 mL of water could be taken 10 minutes before capsule ingestion to distend the stomach [12]. Then, a patient’ s hands were disinfected and they were given the data recorder after entering the examination room. Next, a patient laid down on the examination bed next to the computer workstation, assumed the supine or left-lateral decubitus position, and swallowed the capsule, which had already been activated. An endoscopist controlled capsule movement with the help of a magnet robot using two joysticks in front of the workstation or automatically using a default mode. To ensure that the gastric mucosa was completely visualized, the endoscopist directed a patient to change position to supine and right-lateral decubitus. In the ncMCE group, a patient and the endoscopist entered two rooms through different routes and gastric preparation was under the remote guidance [15]. The audio-visual exchange system provided a platform for the endoscopist to see and communicate with a patient during examination. The data recorder was embedded in the examination bed to avoid cross-infection of COVID-19 among patients and simplify the disinfection process.Enhanced personal protective equipment (PPE) including an N95 mask, isolation gown with water resistance, head cover, eye protection, and face shield [11] should be worn by medical staff in the capsule endoscopy examination room when performing MCE. The steps for donning and doffing PPE were strictly followed, according to the standard process [16]. Medical masks were used as basic PPE for endoscopists in the ncMCE group (Supplementary material, Table 1) [17]. After each examination, the returned data recorder was disinfected using ultraviolet light, 75% alcohol, or ethylene oxide and the sheets on the bed were replaced.

4.3 Study outcomes

4.3.1 Primary efficacy outcome

The primary endpoints were feasibility assessed by completion rate (CR) and safety evaluated by the occurrence of AE. CR was defined as complete observation of the cardia, fundus, body, angulus, antrum, and pylorus of the stomach with no technical failure. Technical failure included incomplete observation, direct contact in the ncMCE group, and examination discontinuation. The safety of ncMCE was evaluated 2 weeks after the procedure for any AEs, such as infection with SARS-CoV-2 and capsule-related AEs including abdominal pain, nausea, vomiting, and capsule impaction or retention. In the current study, the endoscopist was continuously monitored for infection until 2 weeks after the last examination.

4.3.2 Secondary efficacy outcomes

Secondary endpoints included maneuverability score, pre-procedure perception and post-procedure satisfaction of patients, gastric examination time (GET), and diagnostic yield (DY). The maneuverability of the ncMCE system was evaluated with a questionnaire that consisted of signal transmission quality (stability and fluency), endoscopist comfort (strength needed to control joysticks and degree of fatigue), visualization of gastric mucosa (whether the mucus, foam in the stomach, and gastric fullness affected observation of gastric mucosa) and compliance of patients (patient ability to readily and correctly follow verbal instructions to change positions to assist in optimizing gastric views). The score for each index was 1 to 5, with 1 as the worst and 5 as the best, respectively, and a total ranging from 4 to 20. All patients were asked about the comfort and acceptability of the procedure using an improved pre-procedure perception and post-procedure satisfaction questionnaire, which was reviewed ease of swallowing, pain or discomfort experienced during and after the procedure, overall tolerability and convenience of the procedure, and knowledge, necessity for, and acceptability of ncMCE (Questionnaire 1) [18]. GET was defined as the time taken for gastric examination and determined using a digital stopwatch in the ESNavi software. DY or detection rate was calculated using the following formula: number of patients with positive findings divided by the total number of patients that underwent examination.

CHAPTER 5: DATA MANAGEMENT

5.1 Case report forms

The case report form is filled out by the researcher, and each enrolled case has one. After the completed case report form is checked by the clinical inspector, the first link is handed over to the data manager for data entry and management. CRF should include the patient's name, gender, age, identification (ID) number, phone number, address, diagnosis, clinical evaluation index, etc. During the study, the data of GET, maneuverability questionnaire, pre-procedure perception and post-procedure satisfaction questionaire, diagnostic results, combined medication and AEs were recorded in the CRF.

CRFs will be treated as confidential documents and held securely in accordance with regulations. CRFs shall be restricted to the personnel approved by the Chief Investigator and recorded on the ‘Study Delegation Log.’ The investigator shall sign the CRF to confirm the accuracy of the data recorded.

5.2 Data collection

Information on the basic characteristics of the enrolled patients was collected prospectively. Each patient was followed up for 2 weeks by telephone and hospital information system to confirm capsule excretion and any adverse events (AEs), including COVID-19 infection. The maneuverability questionnaire for the endoscopist and improved questionnaire on pre-procedure perception and post-procedure satisfaction for patients were completed after the examination. To avoid systematic bias, a single endoscopist (W.Z.) performed each examination and made the diagnoses for all enrolled patients immediately. The evaluation of completion was made by another blinded researcher (J.H.Z.).

5.3 Data entry and modification

Data entry and modification: The data of CRF were input by the independent double-entry method. Data managers check the data in the case report form and find out that questions are asked by clinical inspector. Data managers modify and confirm the data according to the researchers' answers, and if necessary, a clinical inspector can issue the questionnaires again.

After data entry and inspection, data managers, main researchers, bidders and statistic analysts jointly audit the data, and complete the final definition and judgment of the analysis population.

5.4 Data summary and report

The principal investigator writes a clinical investigation summary report in accordance to CONSORT guidelines and archives the data. Any changes to the original statistical plan should be stated and justified in the CIP and/or in the final report.

CHAPTER 6: SAFETY REPORTING AND MEDICAL MANAGEMENT

6.1 Adverse events

6.1.1 Definition

6.1.1.1 Adverse event (AE)

An AE is any adverse medical event, unintended disease or injury, or any unfavorable clinical sign (including an abnormal laboratory finding) that occurs to the subject, user, or another person, whether or not related to the investigational device. This includes events related to:
All events related to the investigation or control device.
All events related to the investigation process (all processes in the CIP).
Note: For users or others, the AEs here are limited to all of those related to the investigational device.

6.1.1.2 Adverse device effect (ADE)

Adverse events related to use of investigational medical device:
Include AEs caused by inadequate or inappropriate descriptions of usage, deployment, implantation, installation, operation, or any fault of the investigational medical device.
Include AEs caused by use error or deliberate misuse of the investigational medical device.

6.1.1.3 Adverse event severity determination

Observe the procedure, severity, actions taken and outcome of AEs and fill them in the adverse event report form. According to the following criteria, the severity of AEs can be classified into mild, moderate, and severe.
Mild: Transient or mild discomfort that does not affect daily life and action; no special measures or medical intervention/therapy required.
Moderate: Mild effect on daily life and activity; take measures or medical intervention/therapy if necessary.
Severe: Serious effect on daily life and activity; special measures or medical intervention/therapy required; hospitalization if necessary.

6.1.2 Recording

All AEs reported by the patients or discovered from Electronic Medical Record were assessed for severity and relationship with study treatment by the investigators, with appropriate measures taken in time and detailedly documented.

6.2 Serious adverse events

6.2.1 Definition

SAEs can be defined as any events leading to death or serious deterioration of health during clinical trials, including:
Fatal disease or injury;
Leading to permanent defect of body structure or function;
Requires hospitalization;
Medical or surgical intervention is needed to avoid permanent defects in body structure or function.

6.2.2 Measurements and reporting

Table List of contact information for SAE reporting

Contacts	phone or fax
Changhai Hospital	Tel.: +86-021-31162338
Shanghai Municipal Food and Drug Administration	Tel.: +86-021-23111111
State Food and Drug Administration	Tel.: +86-010-88331776

When SAE occur in our clinical trials, the researchers should immediately take appropriate treatment measures for the subjects, and report in writing to the management department of clinical trials of medical devices in the clinical trial institutions under their jurisdiction and notify the applicants.

SAEs had to be reported the principal investigator and to DSMC, ethics committee and the local provincial food and drug administration within 24 hours. For death events, the investigation sites and investigator should provide the ethics committee and sponsor with all information they need.

6.3 Unexpected adverse device events (UDAE)

Unexpected adverse device events refer to serious adverse health or safety effects, life-threatening problems or deaths caused by or associated with devices that are unaware of their nature, severity or frequency in research programs, instructions for use and instructions for clinical trials, or any other serious unexpected problems related to ncMCE.

6.4 Relationship determination

The reporting investigator will complete the SAE report in the CRFs, including date of event, admissions, diagnosis details, date of discharge， whether result in the experiment and its sequela. Researchers should give targeted treatment and follow-up to AEs until symptoms disappear or remain stable.

Any adverse event should be judged on the basis according to the following criteria:

Irrelevant: There was no correlation between AE and the use of ncMCE .

possibly irrelevant: The occurrence of AE is more likely to be related to other factors, such as combination of drugs or accompanying diseases, or the occurrence time of AE indicates that it is unlikely to have a causal relationship with ncMCE .

Possibly relevant: AE may be caused by the use of ncMCE . There is a reasonable time sequence for the occurrence of incidents and the use of research-related devices and can exclude the effect of concomitant treatment and combined medication.

Affirmative relevant: The type of adverse event has been identified as a side effect of ncMCE and cannot be explained by other reasons. The occurrence order of the event strongly suggests causality.

6.5 Device deficiency

Device deficiency refers to deficiency of a medical device in identification, quality, durability, reliability, safety or performance. Medical device deficiencies include malfunction, misuse or use error and inadequate labeling.

The investigator shall record the discovered device deficiencies during the clinical investigation and analyze the cause of the event together with the sponsor, form a written analysis report, and propose a suggestion on continuation, suspension or termination of the investigation, which will be reported by the medical device clinical investigation management department to the Ethics Committee for review.

Both investigators and subjects can make a complaint against the treatment product and control product at any phase of the clinical study.

CHAPTER 7: MISCELLANEOUS CONSIDERATIONS

7.1 Trace to the source

Source data refers to original record of clinical findings, observations, and other activities in the clinical investigation, as well as all information in its approved copy, which can be used for clinical investigation reconstruction and evaluation. This clinical investigation includes: name, date of birth and gender of subjects; investigation identification code, CIP number, name of the investigational device; start date of subjects screening or enrolling; investigational device use date and quantity; signature of investigators; serious adverse events and handling information; date of collection, outcomes and date of report of laboratory specimens, signature of inspector; signature of CRA.

A source file is a printed file, a video file, or an electronic file containing source data. Informed consent form, subjects screening form and enrollment log, subject identification code list, medical documents of subjects (such as medical records or investigation medical records, including physical and chemical examination reports), investigational device use records, lab records, serious adverse event report and memo. The source file is the first-hand source of clinical investigation data records. Any observations and examination results in the clinical investigation shall be recorded the source file in a timely, accurate, complete, standardized and authentic manner.

7.2 Confidentiality

This agreement and the contents of this clinical trial and all ancillary information are confidential. Researcher shall bear the responsibility of confidentiality; including patent, manufacturing process and data provided by the applicant to the researcher that has not yet been published, and shall not be disclosed to any third party unless the consent of the applicant is obtained, and the confidentiality obligation still works at the end of this trial.

7.3 Discontinuation of the study

A study participant may be discontinued from the study if the investigator believes that it is not safe for the participant to continue. And subjects can withdraw from the study at any time

The sponsor should ensure that all investigators in the clinical investigation strictly follow the CIP and promptly point out when the investigation sites and investigators do not observe relevant laws, the GCP and this CIP and give a timely correction; if the situation gets worse or the inobservance remains uncorrected, the sponsor should terminate the clinical investigation, and report to the local provincial food and drug administration, and China Food and Drug Administration (CFDA).

7.4 Protocol deviation and violation

Deviations from the CIP are mainly manifested as the following:

- Loss to follow up;
- Subjects do not meet the inclusion/exclusion criteria;
- Investigators or subjects are not in strict compliance with the CIP or subject compliance is poor;
- Investigation is terminated due to adverse events.

If there is a deviation from the CIP during investigation, the investigator shall promptly notify the sponsor, the investigation sites and ethics committee.

7.5 Protocol amendments

Before clinical investigation, the CIP will be discussed and revised jointly by investigators and implementers who will sign the final copy and submit it to the ethics committee for approval before implementation.

If there is a problem with the CIP during practical implementation of the clinical investigation, a revision is necessary. The plan of revision shall be proposed to the implementer for a multi-center discussion. After then, the responsible unit will carry out revision and submit the revised CIP in a written form to the implementer and investigation units for signing. Finally, send it to the ethics committee again for approval before implementation.

If new data important related to the product for verification is found, the informed consent form must be modified and sent to the ethics committee for approval.

CHAPTER 8: STATISTICAL CONSIDERATIONS

As a pilot study to evaluate the feasibility and safety of ncMCE, the sample size was not calculated [19]. Considering the capsule endoscopy volume of Changhai Hospital during the pandemic, we planned to recruit 40 patients into two groups. Basic characteristics were presented as means with standard deviations for continuous variables such as age, body mass index (BMI), and percentages for binary variables including sex, medical history, and symptoms. Quantitative data were summarized with parametric statistics, mean and standard deviation, or nonparametric statistics, median, and interquartile range (IQR), whereas categorical data were presented as Under the condition of normal distribution and homogeneity of variance, variance analysis was used to compare the difference in mean between groups, while a K-W test was used to compare the difference in distribution between groups and Fisher’ s test was used to compare the two and disordered multi-classification data of subjects under the condition that homogeneity of variance was not satisfied. All reported Pvalues are two-sided and differences that reached $P < 0.05$ were considered statistically significant. Statistical analyses were performed with SPSS (version 22.0, SPSS Inc., Chicago, Illinois, United States).

Appendix 1.Comparison between ncMCE and MCE.

The capsule is 26.7 mm in length, 11.8 mm in diameter, and 4.5±0.5 g in weight, with a guidance magnet robot to control. The field of view is 140 degrees and the depth of view is 0 to 30 mm. After examination with an adaptive frame rate of 8 frames per second (fps), we got the image with 480×480 resolution.

	ncMCE	MCE
Data recorder	Sheet type	Vest type
Examination area	Two rooms	One room
System fixture	Guidance magnet robot Computer workstation with ESNavi software Endoscopic capsule; capsule locator Data recorder Remote control workstation Audiovisual exchange system	Guidance magnet robot Computer workstation with ESNavi software Endoscopic capsule; capsule locator Data recorder
PPE of endoscopist	Medical mask	N95 mask Isolation gown with water resistance Head cover Eye protection and face shield
Physical isolation	Yes	No

Appendix 2.Questionnaire 1 Improved questionnaire for pre-procedure perception and post-procedure satisfaction.

Pre-procedure Patient Perception

1. How anxious are you about the MCE/Nc-MCE?
   4 = not at all; 3 = slightly; 2 = moderately; 1 = excessively

2. Do you expect any pain during the MCE/ ncMCE?
   4 = not at all; 3 = slightly; 2 = moderately; 1 = excessively

3. How well do you know about Nc-MCE/the concept of Non-contact
   4 = very well; 3 = well; 2 =ever heard but not know well; 1 = never even heard

Post-procedure Patient Satisfaction

4. How would you rate the swallowing/insertion of the instrument?
   4 = very easy; 3 = easy; 2 = tolerable; 1 = difficult; 0 = very difficult

5. Did you experience pain during the procedure?
   4 = none; 3 = minor; 2 = mild; 1 = severe; 0 = intolerable

6. Did you experience discomfort during the procedure?
   4 = none; 3 = minor; 2 = mild; 1 = severe; 0 = intolerable

7. Did you experience pain after the procedure?
   4 = none; 3 = minor; 2 = mild; 1 = severe; 0 = intolerable

8. Did you experience discomfort after the procedure?
   4 = none; 3 = minor; 2 = mild; 1 = severe; 0 = intolerable

9. How would you rate the examination procedure?
   4 = very comfortable; 3 = comfortable; 2 = tolerable; 1 = uncomfortable; 0 = very uncomfortable

10. If you would be given the possibility to select an examination for diagnosing your problem, would you choose this particular procedure?
    4 = definitely yes; 3 = probably yes; 2 = maybe; 1 = probably not; 0 definitely not

11. Rate the overall convenience of the test.
    4 = very convenient; 3 = convenient; 2 = not sure; 1=inconvenient; 0 = very inconvenient

12. How much time did you miss from work or regular activities due to the test?
    4 = 0-2 hours; 3 = 3-4 hours; 2 = 5-6 hours; 1 = 7-8 hours; 0 = ＞8 hours

13. Do you think it is necessary to perform nc-MCE during the outbreak?
    4 = very necessary; 3 = necessary; 2 = not sure; 1 = unnecessary; 0 = very unnecessary

14. Do you think the Nc-MCE put you to any inconvenience?
    4 = definitely not; 3 = not; 2 = not sure; 1 = yes; 0 = definitely yes

15. Rate the overall acceptance of the test.
4 = very acceptable; 3 = acceptable; 2 = moderate; 1 = acceptable only in special situations; 0 = unacceptable

Appendix 3. Questionnaire 2 Maneuverability questionnaire

1. Rate the fluency of signal transmission.
   5 = very fluent; 4 = fluent; 3 = moderate; 2 = delayed; 1 = seriously delayed;

2. Rate the stability of signal transmission while CE is moving.
   5 = very stable; 4 = stable; 3 = moderate; 2 = instable; 1 = serious instable;

3. Rate the level of strength to control joysticks. (define MCE as 5)
   5 = very light; 4 = light; 3 = moderate; 2 = heavy; 1 = very heavy;

4. Rate the fatigue degree while controlling joysticks
   5 = very easy; 4 = easy; 3 = moderate; 2 = fatigued; 1 = very fatigued;

5. Rate the compliance of patients while performing the MCE or ncMCE.
   5 = very compliant; 4 = compliant; 3 = moderate; 2 = noncompliant; 1 = very noncompliant;

6. Rate the visualization of gastric mucosa
   5 = very clear; 4 =clear; 3 = moderate; 2 = unclear 1 = very unclear.

The signal transmission was evaluated by the quality stability and fluency and the score of it was evaluated by the average score of questions 1 and 2.
The comfort of the endoscopist was evaluated based on the strength needed to control the joysticks and degree of fatigue and the score was evaluated by averaging the scores for questions 3 and 4.