Robotically controlled magnetic capsule endoscopy: new method in the non-invasive diagnosis and screening of upper GI tract disorders

PhD Thesis

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Szeged, 2023

1. Introduction

According to current guidelines, small-bowel capsule endoscopy is the diagnostic method of first choice in patients with obscure gastrointestinal bleeding (bleeding of unclear origin), as well as known or suspected small bowel diseases. (1). Capsule endoscopes currently used in the daily routine drift passively through the gastrointestinal tract, relying on its peristaltic activity for passage. A technology allowing active locomotion of the capsule endoscope would be a significant step forward leading to improved diagnostic accuracy. Robotic control and magnetic assisted free-hand control of the magnetic capsule endoscope were compared in an ex vivo study in 2010. Robotic control was found to be successful in achieving the target in 87% of the cases while manual control was successful in 37%, a finding which confirmed the advantage of robotic control (2). Today, the best answer to these technological challenges seems to be provided by the Ankon NaviCam robotically manoeuvred magnetically controlled capsule endoscopy (MCCE) locomotion system, the prototype of which was first presented in 2012. (3, 4). In recent years, publications on magnetic assisted capsule endoscopy of the stomach have been dominated by discussions of robotically controlled systems. A review published in 2021 found robotically controlled magnetic capsule endoscopy similar to gastroscopy in terms of diagnostic accuracy, while the former had the advantage of greater safety, better tolerability, avoidance of sedation, and a lower risk for infection transmission. It is, however, unsuitable for treatment or biopsy (5). MCCE was approved by the Chinese Food and Drug Administration in 2017, and also approved in the EU and USA in 2017 and 2021 (CE and FDA) (6). In Europe, robotically controlled MCCE systems are currently available at two sites (Sheffield, UK and Székesfehérvár, Hungary), both NaviCam systems developed by Ankon Ltd.

2. Aims

2.1 EVALUATION OF THE SAFETY AND FEASIBILITY OF MAGNETICALLY CONTROLLED CAPSULE ENDOSCOPY (MCCE) IN THE EXAMINATION OF THE ENTIRE UPPER GASTROINTESTINAL TRACT INCLUDING THE OESOPHAGUS, THE STOMACH AND THE SMALL BOWEL

Objectives and aims of our present study include: establishing a preparation methodology to facilitate better mucosal visualization in the stomach and, furthermore, defining and presenting patient positions and standard examination techniques to be used in MCCE; evaluation of the possibility of transpyloric transit by magnetic control and presentation of related results; assessment of the safety and potential complications of the methodology, as well as the feasibility of the complete exploration of the stomach and the small intestine; and finally, comparing the results of standard gastroscopy and MCCE in patients population under the age of 40 and referred due to symptoms of functional dyspepsia.

2.2 EVALUATION OF THE DIAGNOSTIC YIELD AND SAFETY OF MAGNETICALLY CONTROLLED CAPSULE ENDOSCOPY (MCCE)

MCCE, capable of guiding the capsule endoscope in the stomach, may become an alternative to gold-standard gastroscopy in special patient populations, primarily in screening for upper gastrointestinal tract disorders, or may function as a non-invasive procedure prior to gastroscopy. MCCE is non-invasive, does not require sedation, and is better tolerated by patients, as shown in previous studies. In our publication, which is the first to evaluate MCCE in a European patient population, our aim is to present the results obtained in patients undergoing MCCE for gastric or small bowel indications; to discuss the diagnostic yield, efficacy and safety of MCCE; and to compare the results obtained with MCCE and conventional gastroscopy, respectively, in a selected patient population.

3. Methods

3.1 Technical Methods

The MCCE system used in our study (Ankon Technologies Co. Ltd.) includes a special static magnet with robotic and manual guidance, a movable examination table, and a computer workstation with ESNavi software controlling the magnetic system while allowing inspection of the images. The magnetic robotic C-arm generates an adjustable magnetic field outside the patient’s body with a maximum strength of 0.2 T, which allows precise controlled movements in three spatial directions. During the procedure, the physician guides the magnetic capsule by two joysticks. A gyroscope helps follow the tilt angle and viewing direction of the capsule on the control panel. The system is capable of real-time transmission of images and signals between the capsule endoscope and the control station allowing the physician or a trained health professional to carry out capsule endoscopy in the stomach. By modifying the magnetic vectors and axes using a computer-based software, these robotic systems can automatically run the mapping of the gastric mucosa, even without the direct intervention of a physician. An average of 9-10,000 still images of the oesophagus and gastric mucosa are taken during a 20-25 minute gastric MCCE scan.

3.2 Validation of the method

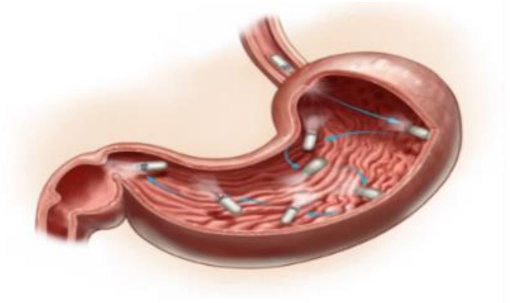
In the learning phase of the application, an in vitro study was designed to compare manual and automated manoeuvring. In the test, 12 different coloured disks numbered by quadrants were attached to the outside of a transparent plastic stomach model of authentic anatomical size fully filled with water. The percentage ratio of disks in the visual field was used to compare mucosal visualisation. The automated modalities were able to visualise 97.5% and 100% of the disks in all four quadrants with the small to medium-sized and the medium to large stomach protocols, respectively. Trainee operators could visualise 76% of the disks for the first time and 85.4% for the second during a period of time identical with that of the automated algorithm. The average time needed to explore the entire stomach was 749 s in manual mode and 390 s with the longer automated protocol (7).

3.3 Examination procedure

Contraindications for MCCE are the same as those for conventional capsule endoscopy and magnetic resonance imaging (MRI). On the day of the examination, first a Helicobacter pylori urea breath test (UBT) was performed. Unlike conventional small bowel capsule endoscopy, capsule exploration of the stomach requires appropriate cleanliness and distension of the stomach for optimal mucosal visibility. We performed a prospective study involving 60 patients and two different cleaning protocols were compared. The combined preparation method significantly reduced the average percentage of covered areas by mucus (8). After complete mapping of the gastric mucosal surface, active transpyloric propulsion of the capsule was attempted in all patients with the help of the external magnetic field. If neither active, nor passive transpyloric passage was successful within 60 min, 10 mg intravenous metoclopramide was administered.

3.4. Examination of the oesophagus, stomach and duodenum

To achieve optimal gastric mucosal visualisation and standardisation of the MCCE protocol in the stomach, we defined nine different stations with three different patient positions. Changing the patient position from the left lateral decubitus to the supine and right lateral position is necessary to combine gravity and magnetic force, which improves capsule maneuvering. The image below summarises capsule stations and camera orientations in a schematic figure. (by Zoltán Tóbiás M.D.)



4. Patients

The first study included 284 patients, 149 of them male (52.5%) and 135 female (47.5%), with a mean age of 44 years. The indications for MCCE were the same as those for conventional small bowel endoscopy (9). For the second study, patients with complaints suggesting functional unexplored dyspepsia without alarm symptoms were selected. 270 patients were entered in this study. A real-time AI-based focal lesion detecting software was also applied during the examinations. In 31 cases MCCE detected severe, potentially erosive gastritis or focal lesions in the area of the cardia, stomach or duodenum associated with Helicobacter positivity (with the exception of foveolar hyperplastic polyps smaller than 5 mm associated with PPI medication), standard gastroscopy and biopsy were also performed on the same day.

5. Results

UBT tests performed prior to MCCE revealed Helicobacter pylori (HP) positivity in 32.7% of the cases. No significant association between the HP status and the type (proximal or distal), distribution (diffuse or focal) or severity (minimal or active erosive) of the gastritis visualised on MCCE was found. The mean gastric, small bowel and colon transit times with MCCE were: 47 min 40 sec (M/F: 44 min 15 sec/51 min 14 sec), 3 h 46 min 22 s (M/F: 3 h 52 min 44 s/3 h 38 min 21 s) and 1 h 4 min 34 s (M/F: 1 h 1 min 16 s/1 h 8 min 53 s), respectively. Average total time of MCCE procedure: 5 h 48 min 35 s (M/F: 5 h 46 min 37 s/5 h 50 min 18 s). The diagnostic yield for detecting any abnormalities in the stomach and the small bowel with MCCE was 81.9%: 68.6% for minor pathologies and 13.3% for major pathologies. In the stomach, tumours, ulcers and polyps were considered major, while signs of gastritis, erosions and small fundic gland hyperplastic polyps were minor pathologies. In the small bowel, signs of Crohn's inflammation with ulcerative lesions, polyps, cancers, SETs and celiac disease were the major, and non-specific inflammations, erosions, diverticula's, polypoid lymphoid hyperplasia and angiodysplasias the minor pathologies. 25.8% of the abnormalities were found in the small bowel, and 74.2% were in the stomach. The diagnostic yield for the stomach/small bowel was 4.9%/8.4% for major pathologies and 55.9%/12.7% for minor pathologies. The distribution of pathologies detected by MCCE is shown in Table.

	Gastric polyp	**Gastric ulcer**	**Coeliac disease**	**Crohn's disease**	**Gastritis**	**Small intestinal diverticula**	**AVM**	**Aspecific small intestinal inflammation**
Pathologies	5	9	1	21	159	1	26	9

Patients who tested positive in UBT with associated gastric complaints or were found to have gastric pathologies in MCCE were prescribed a HP eradication course in accordance with the guidelines, and the outcome was followed up.

Our team developed a modified oesophageal protocol for MCCE, which significantly improved visualisation of the oesophageal body and distal oesophageal mucosa compared to earlier conventional capsule ingestion techniques (10). The modified protocol allowed a significant increase both in average transit time in the oesophagus and in the number of images taken by the capsule camera: 82 sec vs 24 sec, and 423 vs 120 still images. Furthermore, visibility of the partial and full circumference of the Z-line increased to 90% vs 36% and 76% vs 23%, respectively, compared to the conventional protocol. This means that endoscopic signs of erosive reflux disease and Barrett's oesophagus could be detected in more than two-third of the patients using the modified procedure.

The capsule's active magnetic movement through the pylorus was successful in 41.9% of all patients (automated protocol in 56 patients and manual control in 63 patients). In 18 (M/F: 6/12) patients (6.3%), small bowel visualisation with MCCE was incomplete. According to ESGE guidelines, the procedure and the technology are considered acceptable if at least 80% of small bowel examinations are successfully completed. The optimal target value is 95%, very close to the 93.7% rate we achieved with combined gastric and small bowel MCCE. There were 13 occurrences of incomplete examinations because of capsule battery exhaustion. In 3 of these 13 cases, the capsule was shut down within 5 h of operation, suggesting manufacturing flaw. In the remaining 10 patients, incompletion of the study was due to delayed small intestinal transit; in these cases the average total examination time was 9 h 12 min 9 s, and from the pylorus to the last image, the average transit time was 8 h 26 min 4 s. The examination was discontinued sooner than planned in 3 cases on the patient's request. If these 3 cases are not considered in the statistics, 96% of the capsule endoscopies performed for small bowel indications in our MCCE study were completed in the stomach as well as the small intestine, which proves that the technology is suitable for exploration of the entire upper gastrointestinal tract.

In the second study, 28.6% of the patients with complaints suggesting unexplored functional dyspepsia were HP positive; these patients were prescribed an eradication course following the MCCE examination. MCCE findings were negative in 40 patients (14.8%), i.e. no diffuse or focal abnormalities were detected either in the distal oesophagus or the stomach. Mild gastritis was found in 102 patients (37.8%). MCCE detected the following pathologies in the oesophagus or the stomach: erosive reflux 73 (27%), suspected short Barrett's metaplasia 6 (2.2%), erosive or active gastric outlet inflammation 76 (28.1%), duodeno-gastric biliary reflux 45 (16.7%), foveolar hyperplasia 25 (9.2%), solitary gastric polypoid lesion 9 (3.3%), pangastritis 6 (2.2%), gastric ulcer 5 (1.9%), suspected intestinal metaplasia 4 (1.5%), signs of increased portal pressure and AVM 3 (1.1%), and gastric lesion characteristic of early focal malignancy 1 (0.3%), which was later diagnosed as B-cell lymphoma based on the biopsy taken during gastroscopy. In cases requiring biopsy, gastroscopy was also performed on the day of the examination if agreed by the patient. The results of the 31 patients (11.5%) undergoing gastroscopy are summarised in Table. The results obtained by gastroscopy correlated well with those of MCCE, both for focal and diffuse lesions. Lesions that appeared to be ulcers on enlarged capsule images were found to correspond to erosions in gastroscopy, and MCCE more often suggested gastritis, which was then unconfirmed macroscopically by conventional upper pan endoscopy.

	Gastritis	Polyp	Erosion	Gastric ulcer	Foveolar hyperplasia	Early gastric neoplasia
Visible with both methods	22	3	15	3	3	1
Only visible on MCCE	9	0	3	2	0	0
Only visible on gastroscopy	0	0	2	0	0	0

Complications: In 2 patients, oesophageal spasm in the corpus caused the capsule to get stuck; the capsule was successfully moved to the stomach with endoscope in both patients, later eosinophil oesophagitis was confirmed by biopsy with conventional endoscope in both patients. In 2 cases there was capsule retention due to narrowed bowel lumen caused by Chron's-like ulceration; both cases were resolved with anti-inflammatory medication and did not require surgery or endoscopic intervention. In 5 patients the capsule failed to empty from the stomach for as long as 5 hours; in these cases, the capsule was captured in a loop by endoscopy and passed to the descending duodenum through the pylorus. There were no severe adverse events or complications requiring hospitalisation, or definitive capsule retention, either during the study period or in the total of 1,400 MCCEs performed since then. (11).

6. Discussion

Data in the literature show that the distal section of the oesophagus, Z-line, cardia, fundus, corpus, angulus, antrum and pylorus can be visualised well and completely using the NaviCam capsule in more than 95% of patients (7). In an average case, exploration of the entire gastric lining takes 20 to 30 minutes. In 40 to 59% of the cases, the capsule can successfully be guided by magnetic control through the pylorus, which significantly reduces gastric transit time compared to conventional capsule endoscopy. As the total operation time of a NaviCam magnetic capsule endoscope is 10 to 12 hours depending on image recording speed, having surveyed the stomach one capsule is able to explore the entire small intestinal mucosa as well. In addition, if the capsule camera in the bulbus is turned toward the pylorus capturing the descending duodenum, the Vater papilla can also be visualised, which is feasible in 30% of all magnetic assisted capsule endoscopy procedures (12).

No studies similar to the one we conducted where the entire upper gastrointestinal tract, including the stomach and the small bowel, was explored with the same capsule endoscope during MCCE have been carried out in Europe and published in the literature. Denzer et al. published a blinded, prospective trial with the Intromedic manually controlled MCCE. The capsule accuracy was 90.5%, compared to gold-standard gastroscopy under sedation with propofol. (13).

An inherent limitation of our study was that gastroscopy was performed only in a limited number of patients. However, several previous studies demonstrated excellent diagnostic value and high accuracy compared to gastroscopy. (14 A meta-analysis in 2021 reviewed 7 studies involving a total of 916 patients and 745 gastric lesions. Mean examination time was 21.92±8.87 min and overall sensitivity was 87% [95% (CI), 84%-89%]. (15).

Due to the huge number of negative images, evaluation of capsule endoscopy is particularly time-consuming, therefore, while capsule endoscopy is a patient-friendly, non-invasive procedure, with the evaluation techniques currently used it can hardly be called doctor-friendly, which is clearly a major obstacle to its wide-spread use. Application of AI can reduce the time required for the procedure and consequently its cost, and can also improve accessibility. The Ankon MCCE system is the first in the world to use a CE- licensed computer algorithm (ProScan) developed on an AI deep-learning network, which can separate images containing abnormalities from negative ones and select the former in small bowel capsule examinations, thus making evaluation easier. (16)

In summary, review of the international literature, as well as our own results and experience with the new MCCE technique suggest that capsule endoscopy, already a gold standard in small bowel investigations, in the future may offer a non-invasive alternative in the diagnosis of upper gastrointestinal tract disorders, due to magnetic navigation, robotics, automated control, and fast evaluation made possible by the use of artificial intelligence.

7. Conclusions and new results

New results:

1. MCCE has been shown to be a feasible and effective method for exploration of the gastric and entire small bowel mucosa in 93.7% of tested patients. The average total procedure time was 5 h 48 min 35 s (5 h 46 min 37 s / 5 h 50 min 18 s).

2. Our team was the first to confirm that MCCE can visualize the complete upper gastrointestinal tract in one setting. Furthermore, we described in detail the methodology and published the steps and precise technique of the MCCE procedure.

3. Helicobacter pylori positivity was confirmed by urea breath tests in 32.7% of patients tested for small bowel CE indication. No significant correlation was found between the Helicobacter status and the type (proximal or antral), distribution (diffuse or focal), or severity (minimal or active erosive) of gastritis.

4. MCCE is a safe and non-invasive procedure. Mild complications occurred in 4 patients (oesophageal and small bowel CE retention in two patients each); each case could be resolved endoscopically or by conservative medication. Severe complications requiring surgery or hospitalization did not occur.

5. In vitro experiments with MCCE on plastic stomach model we revealed a 97% to 100% inner surface visibility in 20 to 30 min using automated and manually guided protocols, which confirms that the MCCE technology is suitable for complete mapping of the gastric inner surface and mucosa, if provided appropriate cleanliness and distension of the stomach with water is achieved.

6. In in vivo studies, we proved an excellent average visibility of the gastric mucosa, in patients with optimal gastric cleansing, was 100%, 100% and 97% in the antrum, corpus and fornix, respectively. Average visibility in the fundus, corpus and antrum ranged between 92.4-87.68%, 96.64-90.78% and 99.69-93.86%, respectively, due to the fact, that in some cases mucus and foam remaining in the gastric lake of the stomach.

7. Cleanliness and visibility of the gastric mucosa can be improved significantly by adding Pronase B and sodium bicarbonate to standard simethicone and 8-10 dl of clear water 30 minutes before the MCCE procedure.

8. If MCCEs conducted according to the modified oesophageal protocol first published by our team, the cardiac region and the Z-line could be partially and fully visualized in 90% and 73% of the patients, respectively, confirming feasibility of capsule endoscopic exploration of the distal oesophagus and the cardia.

9. With an active magnetic guidance of the capsule a transpyloric transit can be achieved within 30 min in 41.9% of the cases, and afterwards the Vater papilla can be fully visualized in 30% of patients.

10. The diagnostic yield for detecting any abnormalities in the stomach and the small bowel with MCCE for small intestinal indication was 81.8%, 68.6% for minor and 13.3% for major pathologies. 25.8% of the abnormalities were found in the small bowel and 74.2% in the stomach. The diagnostic yield for stomach and small bowel pathologies was 4.9% and 8.4%, for major and 55.9% and 12.7%, respectively, for minor pathologies.

11. MCCE and gastroscopy findings were compared in 31 patients who underwent both procedures on the same day. The results demonstrated high concordance and similar diagnostic effectiveness in the detection of focal and diffuse lesions.

In conclusion, combined gastric and small bowel MCCE is recommended in patients referred for small bowel capsule endoscopy (IBD, OGIB and iron deficiency anaemia), as it significantly increases the diagnostic yield of the capsule procedure. Furthermore, in view of high MCCE accuracy compared to gastroscopy, particularly in focal lesions, gastric MCCE may be considered in patients under the age of 40 with complaints suggesting functional dyspepsia without alarm symptoms in whom gastroscopy is not justified, thus reducing the number of unnecessary and invasive gastroscopic examinations, and shortening the waiting list, without risking to miss any significant gastric lesions or pathologies.

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