Comparison of the use of Wireless Capsule Endoscopy with Magnetic Resonance Enterography in Children with Inflammatory Bowel Disease

NCT # 02182947
March 20, 2014
Revised January 31, 2017

Comparison of the use of Wireless Capsule Endoscopy with Magnetic Resonance Enterography in Children with Inflammatory Bowel Disease

Principal Investigator:
Nadia M Hijaz, MD, Assistant professor of Pediatric, Division of Gastroenterology Hepatology and Nutrition, University of Missouri Kansas City, Children Mercy Hospital Kansas City, 2401 Gillham Road, Kansas City, MO 64108 USA nmhijaz@cmh.edu

Co-Investigators:
Thomas M Attard, MD, Professor, Division of Gastroenterology Hepatology and Nutrition, University of Missouri Kansas City, Children Mercy Hospital Kansas City, 2401 Gillham Road, Kansas City, MO, 64108 USA tmattard@cmh.edu

Jennifer M Colombo, MD, Associate Professor, Division of Gastroenterology Hepatology and Nutrition, University of Missouri Kansas City, Children Mercy Hospital Kansas City, 2401 Gillham Road, Kansas City, MO, 64108, USA jmcolombo@cmh.edu

Neil J Mardis, MD, Pediatric Radiologist, Division of Radiology, University of Missouri Kansas City, Children Mercy Hospital Kansas City, 2401 Gillham Road, Kansas City, MO 64108 USA njmardis@cmh.edu

Craig A Friesen, MD, Professor, Division of Gastroenterology Hepatology and Nutrition, University of Missouri Kansas City, Children Mercy Hospital Kansas City, 2401 Gillham Road, Kansas City, MO USA 64108, USA cfriesen@cmh.edu.

Study Site(s): Children's Mercy Hospital

Protocol Version: (*2.0)* **Protocol Date:** March 20, 2014

1. STUDY OBJECTIVES/HYPOTHESIS

Primary Objective(s)

Primary aim: Compare the diagnostic yield of Magnetic Resonance Enterography (MRE) with Small-Bowel Capsule Endoscopy (SBCE) in pediatric patients with known

Inflammatory Bowel Disease (IBD) including Crohn's disease (CD) or indeterminate colitis (IC).

Secondary Objective(s)

1. To determine the detection rate of small bowel disease / complications, subjected to a strategy of Wireless Capsule Endoscopy (WCE) – small bowel screening / surveillance vs MRE in a pediatric tertiary medical institution.
2. Compare sensitivity and specificity of both MRE and WCE in identifying patients with active vs. inactive CD and IC as defined by the Pediatric Crohn's disease activity index.
3. To correlate the findings detected on WCE by Lewis score with Crohn's disease activity index.

2. BACKGROUND

Crohn's Disease CD represents a chronic idiopathic disorder primarily involving the gastrointestinal tract. Although any part of the gastrointestinal tract can be involved, the most common pattern in paediatric patients is ileocecal involvement. More proximal small intestinal involvement is more common in pediatric patients with a prevalence of up to 20%[1]. The clinical presentation and sequelae of small intestinal involvement in Crohn's Disease is varied and include nutritional sequelae resulting in growth delay and including iron deficiency anemia, stricture formation, obscure abdominal pain and eventually obstruction[1,2]. Small intestinal screening in suspected Crohn's Disease and periodic small intestinal surveillance in known cases is the current accepted standard of care [1]. There are several modalities that can be employed toward visualizing the small intestine although there is no gold standard[1]. Options include contrast studies including small bowel series and computed tomography enterography (CTE). Gadolinium enhanced MRI imaging (GAD MRI) of the abdomen and small bowel enema are technically more demanding but may be more sensitive in early disease.

There is growing concern with recurrent radiation exposure particularly from routine radiologic modalities in children [3], this is especially relevant in pediatric Crohn's Disease in so far as CT entercolysis abdomen and small bowel series are often seen as complementary [3]. Although small bowel series is accepted as a routine diagnostic modality in pediatric IBD if fluoroscopy time is kept to a minimum, its limitations are well defined and are especially relevant in the early stages of IBD wherein fistulising, stricturing disease is less common. Magnetic resonance enterography (MRE) has a diagnostic effectiveness comparable to other radiological modalities for evaluation of adult patients with CD, [1,2]but without radiation exposure. However it is limited by expense, the availability of the requisite equipment and software, need for sedation in pediatric population, limited expertise in accurate interpretation especially in early lesions such as are more common in pediatric IBD, and overall insensitivity to early mucosal lesions including vascular abnormalities.

Alternative modalities for small bowel imaging are being studied and include the routine use of wireless-video capsule endoscopy (WCE) which allows visualization of the small-bowel mucosal lesions in Crohn's disease [4]. Because the risk for capsule retention in suspected or established Crohn's disease is significantly increased; in some series up to 13%; pre WCE small bowel imaging or patency capsule has become standard of care.

The main indications for WCE in Crohn's disease are to establish the diagnosis, to assess disease prognosis, disease activity, and mucosal healing post therapy, and to define the extent and severity of disease [5]. A small, prospective study of 27 patients suspected to have Crohn's disease, revealed a sensitivity of 93% and specificity of 84% for the WCE examination compared to surgical and enteroscopic tissue samples, and demonstrated a significant change in their management [6]. Another prospective randomized blinded study adults (N = 21) reported the sensitivity and specificity of CD in terminal ileum were 100% and 91% by WCE[7]. Jenson suggested WCE as first line modality for detection of small bowel CD beyond the reach of colonoscopy [7]. In adults with known CD, Karoui et al evaluated WCE in a prospective study (N = 20) comparing it to radiological techniques and concluded that WCE is more accurate in detection of small bowel lesions in CD[8].

In a small retrospective study (N=7), most older children and adolescents with unexplained growth failure and normal small bowel series were found to have Crohn's disease involving the small intestine [9]. A recent prospective study performed in 60 pediatric patients with suspected crohns showed both MRE and WCE appeared complementary methods for the detection of Crohn's disease in suspected CD patients. Both have a high degree of accuracy, sensitivity, and specificity at 98.3%, 100%, 97.6%, and 91.9%, 90.9%, 92.3%, respectively [10]. Another large prospective study in children (N=117) with established or suspected CD demonstrate a statically significant diagnostic yield of WCE in reclassifying indeterminate colitis IC into CD (60%), detection of CD lesions in known CD (41%) and establishing new diagnosis in suspected CD(50%) compared to other radiological modalities[11].

Overall tolerance and safety: WCE is safe in children approximately 9 years of age and older, endoscopic placement is feasible in individuals refusing or unable to swallow the capsule but adds to the potential morbidity and expense of the procedure. WCE has been safely performed in children as small as 11.5 kg [4]. Jensen and colleagues studied the factors associated with incomplete WCE studies and their diagnostic yield in pediatric patients. In this study, 22% of the WCE studies were incomplete, and in 12 (44%) of these were normal pre-WCE radiologic findings [4].

WCE should be used with caution and most likely contraindicated in patients with known swallowing disorders, gastrointestinal obstruction and fistulas. The risk for WCE retention (which is defined as capsule remains in digestive tract for a minimum of 2 weeks or it requires direct intervention to aid in its passage) in Crohn's disease patients is estimated to be 5%–13% [12]. Even though Crohns disease is reported to have the most

common retention rate it is reported in metanalysis that retention rate is 2.6% in all prospective and retrospective studies [13].

Atay and colleagues investigated the risk factors for capsule retention in their cohort (n = 207) of pediatric patients studied by WCE[14]. Capsule retention complicated 1.4% of studies; all in known Crohn's patients. The risk in known CD patients was therefore 5.2%, and rose to 37% if there had been a prior small bowel series showing small bowel disease, and to 43% if the patient's body mass index was less than the 5th percentile, presumably indicative of more severe, longstanding small bowel involvement [14].

The Patency Capsule (Agile ®) was developed, tested, and shown to greatly curtail the possibility of small bowel capsule retention and therefore obviate the need for surgery[15]. A pre-WCE, patency capsule (PC) strategy has completely removed the incidence of capsule retention[15]. The caveat to PC testing is that it also impacts the utility of WCE overall in so far as a proportion of patients cannot thus be studied (failed PC passage). The Patency capsule is identical in shape and size to the actual WCE device but in the presence of small intestinal enzymes it will dissolve starting at 30 hours post ingestion, thus slow passage or retention of PC in the small bowel signals a risk of capsule retention and are usually interpreted as a contraindication for WCE.[16]

The safety of PC was evaluated in a multicenter clinical trial (N=106) with known Crohn's disease and intestinal strictures which showed that all cases had a complete passage of WCE if patency capsule proved patency[15] . Adverse events of PC were reported in 17/106 patients such as abdominal pain was managed with conservative management. One case developed obstruction and underwent surgery which seems unrelated to the patency capsule because it was not retained at the time of surgery (1/106) [15]. Another retrospective study by Cohen showed that after successful passage of the patency capsule in 19 patients, who proceed to have WCE after one week with one patient experiencing capsule retention[17]. The results of the study led to the diagnosis of CD and the patient subsequently underwent a needed ileocecal resection [17].

RATIONALE

Most of the studies evaluating the roles of MRE and WCE conducted in pediatric patients have been retrospective with the main goal of making a diagnosis in patients with suspected IBD. The current study is the first prospective study in children with known IBD assessing the roles of MRE and WCE in identifying disease exacerbation. This study will help to identify if capsule endoscopy is superior or complementary to MRE in the evaluation of suspected disease exacerbation in IBD patients.

3. STUDY DESIGN

- Prospective single blinded comparison of a cohort of pediatric patients with indeterminate colitis (IC) or Crohn's disease (CD) who are scheduled to undergo

routine small bowel screening or surveillance using MRE. Subjects will swallow a patency capsule (PC) to study bowel patency. If MRE shows stenosis or stricture subject and caregivers will be given the opportunity to continue with the study or withdraw. Those patients, who pass an intact PC, usually within 40 hours, will ingest the wireless capsule endoscopy (WCE). The WCE will be performed within 1 week of completion of MRE. Both modalities diagnostic yields will be compared to detect Crohn's disease lesions/complications and correlate the findings with Pediatric Crohn's Disease Activity Index (CDAI).

4. TARGET STUDY POPLUATION SPECIFICS

Study participants (n=50) ages 4 – 17.99 years of age will be recruited for this study. Patients will be identified for recruitment after an initial evaluation in gastroenterology clinic at Children's Mercy (CM), if they are diagnosed with IBD and planned to have MRE as part of standard of care for clinical indication to evaluate small bowel disease.

Inclusion Criteria;

- Patients aged 4 to 17.99 years at time of investigation
- IBD/CD and IBD/IC diagnosed based on standard clinical – histologic criteria
- Patient is scheduled to have MRE as standard of care for evaluation of disease severity/ complication.
- Signed permission/assent/consent

Exclusion Criteria:

- IBD diagnosis not established
- Recent intestinal tract surgery / resection involving small bowel
- Use of NSAIDs 4 weeks prior to the Capsule endoscopy study.
- Patients are on prokinetic medication.
- Swallowing disorders, esophageal stricture or patients unable to swallow the capsule.
- Presence of gastrointestinal obstruction or ileus.
- Patient with implanted electro-medical device or pacemakers.

5. STUDY PROCEDURES

- Prior to MRE visit:
    - The provider ordering the MRE will contact a member of the study team to let them know an MRE for a patient has been scheduled.
    - Team members will have the option of calling the parent/authorized representative of the family to ask if they would like to hear about the study. If yes, the team member will explain the study and follow protocol for telephone consent or agree to meet with the family when the patient comes in for his/her MRE.

- Standard of Care MRE visit:

  - At the MRE procedure visit, if not previously consented, the subject and family will be approached by a member of the study team to explain the study and ask if they would like to participate. If a subject is unable to stay after MRE to complete patency capsule procedures, the family can choose to return in the next 1-2 days to any CMH GI location with study staff to complete the procedure.

- Post Consent:

  - Subject will have lab draw for: Hemoglobin/Hematocrit (Hgb/Hct), erythrocyte sedimentation rate (ESR), Albumin.
    - Lab draw at time of standard of care IV placement for MRE if possible
    - If not possible to complete at MRE subject may have at the time of patency capsule or WCE visit.
    - If the subject has had these labs drawn for standard of care in the last 2 weeks, those values will be used in place of this lab draw

  - Patency capsule (performed as a part of the research study): A dissolvable capsule the same size as the PillCam SB capsule, with a radio frequency identification (RFID) tag (size 3mm x 13mm) packed in a lactose and barium powder. If the capsule is retained more than 80 hours it will dissolve into small pieces that can pass naturally through the GI tract after 2-5 days. Due to its ability to dissolve it is unlikely that if the capsule is retained that it will cause any further complications.

  - Subject will swallow the capsule. They will then follow the below schedule.

    - 0-2 hours nothing to eat or drink

    - 2-4 hours clear liquid only

    - 4+ hours may eat and drink freely

    - Miralax dose at the time the child can eat: Less than 5 years of age 2 doses (34 grams), 5-10 years of age 3 doses (51 grams), greater than 10 years of age 4 doses (68 grams).

    - *Due to the age range of subjects in the study they will likely be in school during the time they are enrolled in the study. To allow for greater flexibility for families. The patency capsule can be swallowed at home or with a parent/caregiver at school during the lunch period. The patient or caregiver must record the exact time the pill is swallowed to calculate*

time till x-ray. This will allow for the subsequent miralax dose and any necessary x-rays to take place after school hours.

- Subjects should not be around electromagnetic fields while PC procedure is performed

- Subject will receive Miralax and instructions for WCE home prep.

- Post Patency Capsule Swallow

  - A follow up phone call will take place with the subject and family the day following patency capsule ingestion. Subjects will return to CM radiology for an abdominal x-ray within 28-40 hours, as close as possible to 30 hours after swallowing the patency capsule unless they report to the study team that they visibly saw the excreted capsule. If the patency capsule has passed through the bowel then the subject will continue with WCE procedures.

  - *The study doctor or the subjects regular GI doctor or an appropriate delegate will discuss the results of MRE and patency capsule with the subject and guardian to decide if is a possible increased risk of retention and families will be able to decide if they would like to continue with study procedures. GI providers will be added to the MARS electronic IRB submission form and listed as study staff when they refer a subject so they are identified as being able to participate in these study procedures.*

- WCE Visit

  - The subject will return to the GI clinic to complete the WCE 5 days (± 2 days) from the time of patency capsule ingestion. Subject dietary restrictions the day before the wireless capsule endoscopy (WCE) visit.

    - To allow for greater flexibility for those subjects who are in school at the time of study procedures. The miralax prep may be started after school however the no solid foods after noon must still be observed.

    - Subject will fast for 8 hours overnight.

  - WCE visit (approximately 1 hour) - performed as a part of the research study.

    - The WCE used in this study is the PillCam SB video capsule (Given Imaging, Israel) that measures 11mm × 26mm and weighs less than 4 g.

    - Subjects will wear a belt sensor around their waist and a recording device attached to it for the duration of the WCE study. device

- Subject will be asked questions about any symptoms and/or new medications.
- Subject will swallow the capsule in GI procedure room.
- Subjects should not be around electromagnetic fields while WCE procedure is performed
- Subject may drink clear liquids 3 hours after ingesting the capsule
- Subject may eat solid foods 6 hours after ingesting the capsule, respectively.
- Subjects will be asked to return to the GI procedure room to return the belt sensor 8-12 hours after ingesting the WCE

At times due to Crohn's disease a portion of the bowel can become inflamed and narrowed. These stenosed/strictured areas are not often easily identified until a patient has symptoms of bowel obstruction. It is possible that the capsule may identify these areas because it is not able to pass through the decreased space in the lumen. If the family or subject does not visually see the capsule pass within 2 weeks from the time of capsule ingestion, then an x-ray will be performed to assess if it is retained in the bowel. If the capsule is retained, the PI or Sub-I will notify the subject's primary GI physician about the finding and medical management will be attempted to reduce the subject's inflammation so that the capsule may pass through. In some cases the capsule may identify such a diseased portion of the bowel that it needs to be surgically removed. This capsule retention due to a strictured portion of the bowel will not be considered an adverse event. It will be considered an incidental finding of the subject's disease process. The subject and their 3rd party payor will be responsible for the treatment of these incidental findings.

6. DATA COLLECTION

Data Collection Procedures

- The subject's medical record will be reviewed for data collection to include but not limited to, subject demographics, medical and surgical history, imaging results initial disease presentation and patient current clinical status. Data will be collected on a separate paper data collection form.
- The capsule images will be independently interpreted by the PI initially and then confirmed by two gastroenterologists with 4 - 10 years of experience in capsule endoscopy. The results will be reported in the subject's medical record as they would be for standard of care in compliance with the CMH policy on medical record documentation of research subjects. The subjects regular GI provider will review the results of the WCE and consider the results when making decisions about the subjects treatment plan. We will be using the capsule endoscopy data collection form including the Lewis scoring system that is automatically

calculated and included in the RAPID® software. Lewis score is a WCE ranking of inflammatory activity into three levels based on erythema, stenosis, edema and erosions in small intestinal tertiles: 1) no disease or clinically insignificant disease (LS<135); 2) mild disease (135≤LS≤790); and 3) moderate or severe disease (LS>790).

- The study will be considered negative if no abnormalities were seen and as positive if clear abnormalities of the SB mucosa (i.e. ulcerations, erosions, polyps, vascular lesions, and bleeding lesions) were observed. White lesions within a crater with surrounding erythema were considered ulcers, whereas small superficial white lesions, even with surrounding erythema, were considered erosions. If no abnormalities or non-specific findings (such as erythematous spots or mucosal breaks) were seen the examination was considered non-specific or normal.

- The examiners of WCE and MRE will be blinded to each other's findings but will be aware of the patient's history and laboratory data.

- To reduce variation in MRE readings, one radiologist will retrospectively review the MRE for all subjects to provide a consistent assessment of the extent of the subjects' disease.

Records to be kept

Information will be collected on a paper data collection sheet and entered in an electronic database. Additionally if a research team member chooses they may complete the data collection form electronically by typing results into the electronic word document version of the data collection sheet and saving it to the internal CMH server. Data collection forms will be identified only by assigned subject study ID, date of service and will be retained indefinitely. The electronic database will only retain assigned subject study ID numbers and will be retained indefinitely. An electronic master subject list will include subject name, MRN, dates of service and study assigned ID number. The electronic master subject list will be retained indefinitely. A pre-recruitment log with patient name, MRN and date of MRE will be used to track and keep record of those subjects approached for study participation. The pre-recruitment log will be destroyed at the time enrollment is completed. The WCE procedure uses a software installed on the hard drive of the password protected CMH GI procedure room computer. The images from the study and subject name, MRN, and date of birth will be retained indefinitely on the hard drive. The information entered into the medical record will be retained indefinitely.

Secure Storage of Data

Paper/physical Documents: These documents will be stored in a file cabinet in the locked research room in the GI clinic:

- Signed Permission/Assent/Consent
- Paper Data Collection Forms

Electronic Documents: These documents will be kept on the secure internal CMH server, in a restricted access folder:

- Data Collection form
- Master Participant List
- Pre-recruitment Log
- Data Collection Database

7. STUDY DURATION/STUDY TIMELINE

Stage 1: recruitment and study procedures, fall 2013-Fall 2014
Stage 2: data analysis, fall 2014- winter 2014
Stage 3: publication, 2015

8. STATISTICAL CONSIDERATIONS

Measures

1. Detection rate of upper intestinal lesions in known IBD – CD undergoing WCE vs radiologic modality.
2. Definitive diagnosis of SB involvement of patients undergoing WCE vs radiologic modality in indeterminate IBD.
3. Complication rate for WCE vs 1st radiologic testing
4. Retention rate of WCE
5. The Crohn's disease activity index and it is relation with the findings on both modalities
6. Lewis score on WCE

Sample size determination

With a sample size of 34 participants we will have 80% power probability to detect the 23 % difference in IBD small intestinal MRE findings and WCE detection rate similar to previously reported pediatric studies [11]. This determination uses a Chi-Square test and a two-sided significance level of 0.05. Subjects whose MRE results show findings that are contraindicated with WCE will be considered screen failures. We anticipate around 20% screen failure rate and intend to recruit 40 subjects to obtain a sample size of 34 evaluable subjects.

Data Analyses

The disease activity detection rate of MRE and WCE will be compared using McNemar's test and Chi square test. The sensitivity and specificity of both tests will be calculated based on a gold standard of classifying disease activity using Crohn's disease activity index (CDAI). The person correlation coefficient or spearman rank correlation coefficient

will be utilized to assess agreement between lewis capsule endoscopy score and CDAI. All p values will be 2 sided with statistical significance evaluated at 0.5 alpha level.

HUMAN SUBJECTS

Institutional Review Board (IRB) Review and Informed Consent

This protocol, and any subsequent modifications, will be reviewed and approved by the Pediatric IRB at The Children's Mercy Hospital & Clinics.

We request a partial Waiver of HIPAA Authorization for pre-recruitment activities.

Potential participants will be identified at the time of a clinic appointment or prior to their scheduled MRE appointment in radiology. IBD program coordinators or GI providers will notify a research staff member of a potential participant's eligibility. The family will be approached at a clinic visit about participation. If the research staff is notified at a time that the family is not in the clinic a member of the study team will call the family to introduce the study to them briefly and ask if they can talk with them about the study prior to their MRE. A recruitment flyer and permission assent form can be sent to the family prior to the appointment via e-mail, fax or postal mail should they request it. The recruitment flyer will also be made available in the GI Clinic.

Prior to drawing any blood or performing any other procedures related to this study, the permission/assent form or consent form will be reviewed carefully with the participant (and parent) in person or by telephone in extenuating circumstances (i.e. out-of-state non-custodial parent, divorce, or separation).

Telephone consenting may be necessary for this study due to fasting procedures required prior to the subjects standard of care visit so the subject may continue at the same visit with research procedures. All questions will be answered and signatures will be obtained by study staff form the parent before procedures begin on the child. The PI will ensure the procedures for securing telephone consent are followed.

Subject Confidentiality

Paper/physical Documents: These documents will be stored in a file cabinet in the locked research room in the GI clinic:

- Signed Permission/Assent/Consent – will contain subject and caregiver name and subject MRN, date of consent, retained indefinitely.

- Paper Data Collection Forms – subject study ID, date of service, retained indefinitely

Electronic Documents: These documents will be kept on the secure internal CMH server, in a restricted access folder):

- Data Collection Forms – subject study ID, date of service, retained indefinitely

- Master Participant List - subject name, MRN, date of service, assigned study ID number, retained indefinitely.
- Pre-recruitment Log – subject name, MRN, date of MRE, deleted upon completion of enrollment.
- Data Collection Database - de-identified, retained indefinitely

WCE software - The images from the study and subject name, MRN, date of service, capsule ID number and date of birth will be retained indefinitely on the hard drive. The information entered into the medical record will be retained indefinitely.

Study Modification/Discontinuation

The study may be modified or discontinued at any time by the IRB, the OHRP, the FDA or other Government agencies as part of their duties to ensure that research subjects are protected.

9. PUBLICATION OF RESEARCH FINDINGS

Results are intended to be presented at the national Gastroenterology and Inflammatory Bowel Disease conferences.
Results are intended to be published in the Gastroenterology journals.

10. REFERENCES

1. Cuffari C, Dubinsky M, Darbari A, Sena L, and Baldassano R. Crohn's Jejunoileitis: The Pediatrician's Perspective on Diagnosis and Management. *Inflamm Bowel Dis* 2005;11(7):696-704.

2. Differentiating Ulcerative Colitis from Crohn Disease in Children and Young Adults: Report of a Working Group of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the Crohn's and Colitis Foundation of America Journal of Pediatric Gastroenterology and Nutrition 2007; 44: 653-674

3. Levi Z, Fraser E, Krongrad R, et al. Factors associated with radiation exposure in patients with inflammatory bowel disease. *G Aliment Pharmacol Ther*. 2009; 30:1128-1136.

4. Jensen MK, Tipnis N, Bajorunaite R, Sheth M, Sato T, Noel R. Capsule endoscopy performed across the pediatric age range: indications, incomplete studies, and utility in management of inflammatory bowel disease. *Gastrointest Endosc.* 2010 ;72:95-102.

5. Ladas SD, Triantafyllou K, Spada C, et al . European Society of Gastrointestinal Endoscopy (ESGE): recommendations (2009) on clinical use of video capsule endoscopy to investigate small-bowel, esophageal and colonic diseases; ESGE Clinical Guidelines Committee. *Endoscopy.* 2010 ;42:220-227.

6. Girelli C, Porta P, Malacrida V, Barzaghi F, Rocca F. Clinical outcome of patients examined by capsule endoscopy for suspected small bowel Crohn's disease. *Dig Liver Dis*. 2007;39:148–154.

7. Jensen MD , Nathan T, Rafaelsen SR, Kjeldsen J. Diagnostic acuuracy of capsule endoscopy for small bowel Crohns disease is superior to that of MR enterography or CT enterography. *Clin Gastroenterol Hepatol.* 2011;9:124-129.

8. Karoui S, Ouerdiane S, Nouira K, et al. Evaluation of small bowel involvement in crohns disease by small bowel. Bowel videocapsule a prospective comparative study with Computed Tomography enteroclysis and small bowel radiography. *Tunis Med.* 2011;89 :445-451.

9. Moy L, Levine J. Capsule endoscopy in the evaluation of patients with unexplained growth failure. *J Pediatr Gastroenterol Nutr.* 2009 ; 48(5):647-650.

10. Casciani E, Masselli G, Di Nardo G,et al. MR enterography versus capsule endoscopy in paediatric patients with suspected Crohn's disease. *Eur Radiol.* 2011; 21:823–831.

11. Di Nardo G, Oliva S, Ferrari F, et al. Usefulness of wireless capsule endoscopy in pediatric inflammatory bowel disease. *Dig and Liver Dis.* 2011;43: 220-224.

12. Cheifetz A, Korenbluth A, Legnani P, et al. The risk of retention of the capsule endoscope in patients with known or suspected Crohn's disease. *Am J Gastroenterol.* 2006; 101: 2218–2222.

13. Zhuan L, Rui G, Can X, Zhao-Shen L. Indication and detection, complesion and retention rates of small bowel capsule endoscopy: a systematic review. *Gastrointestinal Endoscopy.* 2010; 71 : 280–286.

14. Atay O, Mahajan L, Kay M, Mohr F, Kaplan B, Wyllie R. Risk of capsule endoscope retention in pediatric patients: a large single-center experience and review of the literature.*J Pediatr Gastroenterol Nutr*. 2009;49(2):196-201.

15**.** Herrerias JM, Leighton JA, Costamagna G, et al. Agile patency system eliminates risk of capsule retention in patients with known intestinal strictures who undergo capsule endoscopy. *Gastrointest Endosc.* 2008; 67: 902-909.

16. Caunedo-Alvarez A, Romero-Vazquez J, Herrerias-Gutierrez JM**.** Patency and agile© capsules*. World J Gastroenterol*. 2008;14(34):5269-5273.

17. Cohen S, Ephrath H, Lewis J, et al. Pediatric Capsule Endoscopy: Review of the Small Bowel and Patency Capsules. *J Pediatr Gastroenterol Nutr.* 2012; 54: 409-413.