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Assessing accuracy of PillCam Colon 2 in a screening setting: a prospective study in Italy

Submission date
17/04/2014

Recruitment status
No longer recruiting

Registration date
08/05/2014

Overall study status
Completed

Last Edited
01/09/2020

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Colon capsule endoscopy is a new technique to look at the colon. The patient swallows a capsule that is slightly bigger than an antibiotic pill. The capsule has two small cameras that can send images of the colon to an external data-recorder where the video of the examination can be stored and examined after capsule excretion. The aim of this study is to find out how accurate a new capsule is at detecting colorectal cancer and advanced adenomas.

Who can participate?
People aged 55 to 69 attending an organized population screening program, who had a positive test result at the screening test (fecal occult blood test).

What does the study involve?
Subjects who consent to be enrolled are required to follow a specific oral bowel preparation starting 2 days before the planned appointment. In the morning of the exam day, after completing the last part of the preparation, the patients will swallow the capsule. A colonoscopy will be performed following the usual procedure after the excretion of the capsule.

What are the possible benefits and risks of participating?
A trained endoscopist will review the video recorded through the capsule cameras and he will call back the patient if a lesion 10 mm or larger is found using the video from the capsule. This double check may represent an advantage for the participants. The disadvantage of participating is that participants will have to undergo a longer and potentially less acceptable bowel preparation.

Where is the study run from?
The study is run within six screening programs in four regions in Italy, coordinated by the Piedmont Regional Centre for Oncology and Prevention, in Turin, and by the Gastroenterology Unit of the Gemelli Hospital in Rome.

When is the study starting and how long is it expected to run for?
Recruitment was started in February 2014 and we expect to compete the planned recruitment within 18 months.

Who is funding the study?
The study is conducted within the regional screening programs funded by the Regional Health Authorities. Given Imaging Ltd, who developed the capsule, will supply the capsules.

Who is the main contact?
Dr Carlo Senore (Turin)
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CEI 701

Study information

Scientific Title
Assessing accuracy of PillCam Colon 2 in a screening setting: a prospective study in Italy

Acronym
CCANDY (Colon Capsule Advanced Neoplasia Detection Yield)

Study objectives
Colon capsule endoscopy (CCE) is a new technique to visualize the colon. One multicenter study evaluating CCE effectiveness in a prospective setting, in high-risk patients, showed 64% sensitivity and 84% specificity for detecting polyps ≥6 mm. The corresponding figures for advanced adenoma detection was 73% and 79%, respectively. A new PillCam Colon device has been subsequently developed to overcome some technical features which could limit its accuracy. The accuracy of the second-generation colon capsule for adenoma detection seems promising, with two studies conducted, one in Israel and the other in eight sites in Europe, showing a sensitivity of 88% and a specificity of 89% and 95% for advanced neoplasms. Available evidence concerning the diagnostic performance of this new technology is however limited both in terms of number of studies and of study size. The precision of the estimates of sensitivity and specificity are therefore not satisfactory. Also the study population was not selected according

to homogeneous criteria and in particular this device has not yet been evaluated in an average risk screening population. We plan to study the diagnostic accuracy of the new PillCam Colon device in a homogeneous study population at increased risk of harboring advanced neoplasms, based on the result of FIT screening.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Hospital Ethics Committee University Hospital S Giovanni Battista, AO CTO/Maria Adelaide (Comitato Etico Interaziendale AOU S Giovanni Battista, AO CTO/Maria Adelaide), 02/08/2013, Prot. N. 0085890; CEI 701

Primary study design
Interventional

Study design
Paired design

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Colorectal cancer

Interventions
The subjects will be required to undergo the CCE examination in the hospital endoscopy unit, where they will be monitored following the swallowing of the capsule. Participating subjects may have the option to go back home for some hours or to leave the clinic for a walk after the ingestion of the second boost, based on the local organisation and transfer times.

Bowel preparation regimen
The accuracy of colon capsule is highly dependent on the quality of bowel cleansing. For this purpose a more extensive and potentially cumbersome bowel preparation is needed than with colonoscopy. In order to reduce the patient's discomfort while ensuring the necessary quality of the bowel preparation, the following regimen will be adopted.

Day -2 All day At least 10 glasses of water
Bedtime 4 Senna tablets (12 mg each)

Day -1 All day Clear liquid diet
Evening 2 L PEG

Exam Day

Morning: 2 L PEG (45-60 minutes before capsule ingestion)
~ 8-9 am capsule ingestion
1st boost: upon small bowel detection 40 ml NaP* & 1 L water and 50 ml of Gastrografin
2nd boost: 3 hrs after 1st boost 20 ml NaP* & 0.5 L water and 30 ml of Gastrografin
Suppository: 2 hrs after 2nd boost 10 mg Bisacodyl
* PhosphoLax

No other dietary restrictions in the days preceding the exam are recommended.

Reading of the recorded capsule examination will be performed in each centre by experienced gastroenterologists (endoscopists) who will attend a specific training programme (see below). We plan to have two independent readings of all CCE examinations, using both the QUICK view (shrinking at 20%) programme available with the new Rapid software and the standard complete video reading.
We plan to perform whenever feasible (i.e., when the capsule will be excreted before 4.00 pm) the QUICK view reading before starting the OC, even if the results will not be available for the endoscopist performing the OC. The actual proportion of QUICK view readings performed among subjects excreting the capsule before 4.00 pm will be monitored.
A complete reading of the recorded examination will always be performed by a trained endoscopist in dedicated sessions planned within 1 week from the CCE and Optical Colonoscopy (OC) exams. This reader will be blinded to the OC results, but not necessarily to the QUICK view findings (i.e., the same reader can read the QUICK view and the complete video). Considering the relative distribution of colonic neoplasms, which are more frequent in the distal colon, the reading of the capsule examination will be started from the ano-rectal segments. Such approach would allow to assess the possible role of CCE as triage or primary screening test to select subjects who need colonoscopic assessment; we will record the time to the detection of the first lesion meeting one of the eligibility criteria for OC referral assessed in the analysis, i.e. a polyp ≥ 6 mm.
For the purposes of a full assessment of QUICK view accuracy, CCE films from all centres will be collected in a central database, they will be made anonymous and then they will be randomly assigned to readers from the different centres (each centre being eligible for reading all films of patients recruited in other centres, but not those from its patients), who will read the assigned films using the QUICK view mode. This approach will allow to have an independent assessment of all QUICK view by endoscopists who will be blinded to the complete video and to the OC results. .
All patients with lesions ≥ 10 mm visualized at the capsule examination (either at QUICK view or standard reading), but not detected at the time of OC will be invited for a second colonoscopy aimed at detecting and eventually excising the lesion identified by the capsule. This strategy allows for offering patients a more accurate examination and it allows at the same time to assess CCE performance, taking into account the fact that even the gold-standard OC can miss lesions. The accuracy of CCE for lesions ≥ 10 mm will be assessed, taking into account all such lesions detected either at the initial OC or confirmed at the second colonoscopic examination following the identification through CCE reading.
The rationale for avoiding the disclosure of the QUICK view reading results, when available before starting the OC, is related to the need to avoid systematic differences in the assessment of potentially false-positive CCE findings. Repeating the OC in some cases immediately after CCE and in other cases after some days, with a new preparation, might result in systematic differences in the quality of the bowel preparation, which affects the accuracy of the colonoscopic examination. Also, the disclosure of lesions potentially missed by OC at the time of the exam would imply an increased risk for the patient as the colon examination would have to be repeated (i.e., the endoscopist would have to insert again the scope to check for the lesion), involving eventually the excision of a large lesion. This procedure was deemed risky and cumbersome, when taking into account that in several cases it would be performed in late afternoon.
The burden for the patients should be minimal, as the expected colonoscopy miss rate of large (≥ 10 mm) lesions is expected to be low (about 1-2 patients in each center).

The colonoscopy (OC) will be performed on the same day, unless the patient requires to postpone the OC examination on the following day (we estimate that this will happen in a very small proportion of cases, i.e. <5%). Due to organizational and patient-related constraints, the exam will be started no later than 9 hours after capsule ingestion. Based on available data (Spada et al., 2012) about 85% of the capsules can be expected to be excreted at 8 hours after ingestion, this proportion rising to 88% after 10 hours. When the OC is started before capsule excretion, the endoscopist will record the site reached by the capsule and the capsule performance (specificity and sensitivity) will be assessed only over the segments which were actually examined.
All participating centers will ensure the availability of afternoon endoscopy sessions to perform the necessary exams. In all centers two endoscopists will be selected to collaborate in the study performing all the OCs. In order to ensure standardization and high quality of the examination procedure, the following recommendations have been defined:

1. Polyps up to 20 mm (based on endoscopist evaluation) should be removed in one piece (if not histology may not give details on the sizing)
2. Withdrawal time: 10 min
3. Report all polyps, as usually during screening procedures
4. Record a picture of each polyp with the open biopsy forceps aside, in order to make possible a subsequent re-evaluation of the estimated measure

All OC examinations (both the insertion and the withdrawal phase) will be recorded (HD compressed videos) and the videos will be stored to be available for review sessions. OC will be repeated by the same endoscopist who performed the first exam whenever a lesion ≥ 10 mm, missed by the initial OC, will be visualized, either at the QUICK view or at the standard reading of the capsule video. If colonoscopy is incomplete the patient will be excluded from the analysis. Excised polyps will be classified according to the WHO criteria (Jass). All the histology samples will be reviewed by a panel of expert reference pathologists.

Training
The reading of the capsule video will be performed by endoscopists having previous experience with this device, or at least with small bowel capsule examination. In addition, all readers will attend a specific training course with final evaluation of the performance level, designed for this study. The training will be designed and planned by the steering committee together with GIVEN and it will be organized by GIVEN. Two endoscopists and a nurse from each participating center will attend the training course. The two trained endoscopists will perform the readings used for the evaluation of the main outcomes of the study.
A specific training will be offered as well to nurses and health professionals who will be in charge in each center of managing subjects enrolled in the study: i.e. contacting people for enrolment, giving instructions for bowel preparation and for the management of the recorder, following subjects during the capsule examination procedure at the endoscopy unit, at the time of the exam.

Intervention Type
Device

Primary outcome(s)
The main aim of the study is to assess the accuracy (sensitivity and specificity) and the positive and negative predictive value (PPV and NPV) of PillCam Colon 2, compared to conventional colonoscopy, in detecting CRC and advanced adenomas, among subjects with a positive FIT, attending in an organised population screening programme. The primary goal will be to assess,

on a per-patient basis, the accuracy and predictive values of two different positivity thresholds for OC referral (i.e., criteria for defining a positive CCE exam): identification of least one lesion ≥ 6 mm , or of at least one lesion ≥ 10 mm. We will also assess these same parameters when using intermediate thresholds for CCE-detected lesions (i.e., lesions ≥ 7 , 8, 9 mm) in order to get information to estimate the optimal positivity cut-off.

Key secondary outcome(s)
1. To assess the potential role of CCE as a primary screening test or as a triage test to select subjects who need to be referred for colonoscopy assessment and eventually polypectomy
2. To assess CCE sensitivity and specificity by location (distal versus proximal colon) of advanced adenomas and CRC
3. Per-polyp analysis
4. The feasibility and organizational impact of the QUICK view reading in the interval between capsule egestion and the start of the OC examination, when using capsule as a triage test for colonoscopy referral

Based on the exams database, issues related to reading reliability and quality can be assessed as well:
1. The accuracy of a reading strategy which would involve stopping the CCE film review as soon as the positivity criterion has been met (i.e., a polyp of the pre-specified size has been visualised), to simulate a possible feasible and efficient approach in a screening context
2. The accuracy and reproducibility of the reading when performed by gastroenterologists, other physicians (non-gastroenterologists) and nurses
3. The validation of the QUICK view reading modality as compared to the standard complete film reading; 20% QV will be used to learn about future opportunities of QUICK view

Completion date
30/06/2015

Eligibility

Key inclusion criteria
Subjects aged 55 to 69, undergoing FIT for the first time in the context of the local population-based colorectal cancer (CRC) screening program, or those aged 60 to 69, having performed a previous test in the program, referred for OC following a positive test result, who will give their consent to be enrolled in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Other

Sex
All

Total final enrolment

Key exclusion criteria
In addition to the exclusion criteria already adopted by the population screening progammes (i. e., personal history of CRC or adenomas, or inflammatory bowel disease, hereditary syndromes [familial adenomatous polyposis (FAP), hereditary nonpolyposis colorectal cancer (HNPCC)], inability to provide informed consent, severe life-threatening disease), the presence of any of the following will exclude a subject from study enrollment:
1. Dysphagia or any swallowing disorder
2. Congestive heart failure
3. High degree of renal failure
4. Prior abdominal surgery of the gastrointestinal tract, other than uncomplicated procedures that would be unlikely to lead to bowel obstruction based on the clinical judgment of the investigator
5. Symptoms suggestive for sub-occlusion
6. History of negative large bowel endoscopy within the previous 5 years
7. Cardiac pacemaker or other implanted electro-medical device
8. Any allergy or other known contraindication to the medications used in the study. In particular history of allergic reactions after administration of iodine contrast media and history of thyroid disorders will represent a criterion for exclusion
9. Subject is expected to undergo MRI examination within 7 days after ingestion of the capsule
10. Subject with any condition believed to have an increased risk for capsule retention such as intestinal tumours, previous history of abdominal or pelvic radiotherapy, or NSAID enteropathy
11. Any condition which precludes compliance with study and/or device instructions
12. Subject currently participating in another clinical study

Date of first enrolment
01/02/2014

Date of final enrolment
30/06/2015

Locations

Countries of recruitment
Italy

Study participating centre
Via S Francesco da Paola 31
Torino
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Sponsor information

Organisation

AOU Città della Salute e della Scienza (Italy)

ROR
https://ror.org/001f7a930

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
MHS screening activity. Each centre is part of the local regional screening program, funded by the Regional Health Authority (Regione Piemonte for Turin; Regione Lombardia for Como and Milan; Regione Lazio for Rome; Regione Emilia-Romagna for Reggio Emilia)

Funder Name
Given Imaging Ltd (Israel) (supplied the capsules)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2020	01/09/2020	Yes	No