The ADENOMA Study. Accuracy of Detection using Endocuff Vision™ Optimization of Mucosal Abnormalities: study protocol for randomized controlled trial

Authors

Roisin Bevan[1], Wee Sing Ngu[1], Brian P. Saunders[2], Zacharias Tsiamoulos[2], Paul Bassett[3], Zoe Hoare[4], Colin J. Rees[1]

Institutions

[1] South Tyneside NHS Foundation Trust, Harton Lane, South Shields, Tyne and Wear, UK
[2] Wolfson Unit for Endoscopy, St Mark's Hospital, Harrow, Middlesex, UK
[3] 40 Longwood Lane, Amersham, Bucks, UK
[4] North Wales Organisation for Randomised Trials in Health, Bangor University, Holyhead Road, Bangor, Gwynedd, UK

submitted 3. June 2015
accepted after revision
1. October 2015

Bibliography
DOI http://dx.doi.org/10.1055/s-0041-107900
Published online: 27.11.2015
Endoscopy International Open 2016; 04: E205–E212

E-ISSN 2196-9736

Corresponding author
Wee Sing Ngu
South Tyneside NHS Foundation Trust
Harton Lane
South Shields
NE34 0PL
UK
Fax: +44-191-2032930
wngu@nhs.net

Background: Colonoscopy is the gold standard investigation for the diagnosis of bowel pathology and colorectal cancer screening. Adenoma detection rate is a marker of high quality colonoscopy and a high adenoma detection rate is associated with a lower incidence of interval cancers. Several technological advancements have been explored to improve adenoma detection rate. A new device called Endocuff Vision™ has been shown to improve adenoma detection rate in pilot studies.

Methods/Design: This is a prospective, multicenter, randomized controlled trial comparing the adenoma detection rate in patients undergoing Endocuff Vision™-assisted colonoscopy with standard colonoscopy. All patients above 18 years of age referred for screening, surveillance, or diagnostic colonoscopy who are able to consent are invited to the study. Patients with absolute contraindications to colonoscopy, large bowel obstruction or pseudo-obstruction, colon cancer or polyposis syndromes, colonic strictures, severe diverticular segments, active colitis, anticoagulant therapy, or pregnancy are excluded. Patients are randomized according to site, age, sex, and bowel cancer screening status to receive Endocuff Vision™-assisted colonoscopy or standard colonoscopy on the day of procedure. Baseline data, colonoscopy, and polyp data including histology are collected. Nurse assessment of patient comfort and patient comfort questionnaires are completed post procedure. Patients are followed up at 21 days and complete a patient experience questionnaire. This study will take place across seven NHS Hospital Trusts: one in London and six within the Northern Region Endoscopy Group. A maximum of 10 colonoscopists per site will recruit a total of 1772 patients, with a maximum of four bowel screening colonoscopists permitted per site.

Discussion: This is the first trial to evaluate the adenoma detection rate of Endocuff Vision™ in all screening, surveillance, and diagnostic patient groups. This timely study will guide clinicians as to the role of Endocuff Vision™ in routine colonoscopy.

Study registration: ISRCTN11821044.

Introduction

Background

Colonoscopy is considered to be the optimal procedure for bowel cancer screening and diagnosis of colonic pathology. However, it remains an imperfect tool for cancer prevention. Missing lesions during colonoscopy is implicated as one of the primary reasons for interval colorectal cancers, with a clear correlation between adenoma detection rate (ADR) and interval cancers demonstrated in a few trials [1,2]. Adenoma detection is the most important contemporaneous marker of mucosal visualization and of high quality colonoscopy [3,4]. Variation in ADR exists within the UK, although there has been an improvement in the interval between two large audits of colonoscopy quality [5,6]. Reasons for non-detection of a lesion at colonoscopy include: suboptimal technique; shorter withdrawal time; inadequate bowel preparation; presence of flat, depressed or subtle lesions; and the inability to visualize the proximal side of haustral folds, flexures (blind spots), rectal valves, and ileocecal valves [7,8]. Optical imaging innovations and technological developments in the field of colonoscopy have attempted to decrease the adenoma miss rates with the introduction of high definition endoscopes, electronic chromoendoscopy (such as narrow-band imaging), wide-angle colonoscopies and retrograde viewing devices [9,10]. Lesions located on the proximal sides of colonic folds may be missed during standard conventional colonoscopy [11]. Although views may be improved with dynamic patient position changing and routine retroflexion, these maneuvers may not be effective, parti-

cularly in the narrower colonic segments, even with the use of a pediatric colonoscope or gastroscope [12,13]. Currently available transparent caps and hoods, attached at the tip of the scope, have been used to hold down folds and improve visualization in the forward view. However, they make the tip section of the scope more rigid and longer, and this may impair scope insertion in an angulated sigmoid colon [14,15].

A preliminary pilot evaluation study has demonstrated a potential benefit in terms of mucosal visualization and adenoma detection when using Endocuff Vision™ [16]. Published work on the improved ability to undertake therapy using Endocuff Vision™ has additionally demonstrated advantages gained by obtaining scope tip stability and a safer operational platform [17].

Endocuff Vision™

The Endocuff™ (ARC Medical Design Ltd and Diagmed, UK) is a new device (CE marked in UK) made of a soft plastic material with a unique dynamic shape (**Fig. 1**). The core is made of polypropylene and the 'finger-like' projections are made of a thermoplastic elastomer. Endocuff™ comes in four color coded sizes (purple, blue, green and orange) to fit a range of pediatric and adult colonoscopes. The first version of Endocuff™ comprised backwards pointing (proximal and distal to the scope tip) flexible 'finger-like' projections at intervals around the device circumference with the following dimensions in different cuff sizes (length of 23.8 mm × diameters of 16.1/16.7/17.2/18.5 mm with the finger-like projections folded back and 32.6/33.1/33.6/34.8 mm with the finger-like projections opened out). The new version of Endocuff ™ (the Endocuff Vision™) that is utilized during the clinical trial, however, has only one proximal row of more rounded finger-like projections to eliminate any mucosa lacerations that were observed with the first version (**Fig. 2**). Both versions are mounted at the tip of the scope and held on by friction (pull-off force is a minimum of 10 Newton). The chief investigators have used the Endocuff Vision™ extensively, and report no occasions of cuff dislodgment. The Endocuff Vision™ aims to improve access in the large bowel by flattening colonic folds and manipulating them away from the field of forward view.

Use of the Endocuff Vision™ is contraindicated in:

I. known colonic strictures, or

II. active inflammatory disorders such as acute infective colitis, colonic Crohn's disease, ulcerative colitis, and acute diverticulitis.

Endocuff Vision™ is placed snugly around the colonoscope tip before insertion (**Fig. 3**). It does not project beyond the tip of the scope, providing an unrestricted view. It does not trap fecal residue. It helps anchor the scope tip against the bowel wall to provide a stable platform of access. The soft, elastic projections are pushed back (recoiled) towards the scope shaft during insertion but evert during withdrawal to hold colon folds away from the field of view.

Endocuff Vision™ may therefore benefit:

1. Patients: More accurate examinations with lower rates of missed polyps. This will ensure that the most accurate endoscopic surveillance program is selected.
2. NHS and other Healthcare providers: Reduced risk, with fewer polyp 'misses', and improved ADR, with a potential correlating reduction in interval cancer rates.

Hypotheses

We hypothesize that the Endocuff Vision™ will improve ADR by possibly providing better fold retraction, a wider field of view and better scope tip stabilization. We also hypothesize that Endocuff Vision™ may have a positive effect on scope insertion time, cecal or terminal ileal intubation, and patient comfort and satisfaction.

Fig. 1 Endocuff™; First version of Endocuff™ with one proximal and one distal row of finger-like projections (personal photograph taken by the authors).

Fig. 2 Endocuff Vision™; The updated version which is being used in this trial which has one proximal row of finger-like projections (personal photograph taken by the authors).

Fig. 3 Endocuff Vision™; The Endocuff Vision™ mounted at the tip of the colonoscope (personal photograph taken by the authors).

Primary objective

The primary objective is to ascertain, if there is a difference in adenoma detection rate between Endocuff Vision™-Assisted Colonoscopy (EAC) and Standard Colonoscopy (SC) patient groups.

Secondary objectives

The secondary objectives are:

1. to ascertain, if there is a difference in mean adenomas detected per procedure (MAP2) between EAC and SC;
2. to establish the rate of cuff exchange (that is, how often the cuff has to be removed);
3. to demonstrate non-inferiority of cecal intubation rates and insertion time to cecum between EAC and SC;
4. to demonstrate non-inferiority in complete withdrawal time in procedures where no polyps are detected between EAC and SC;

5. to demonstrate non-inferiority of patient satisfaction with EAC compared to SC;
6. to identify any difference in future colonoscopic workload produced by increased ADR in terms of number of potential follow-up procedures based on British Society of Gastroenterology (BSG) adenoma surveillance guidelines between the EAC and SC groups;
7. to identify the prevalence of proximal sessile serrated polyps between EAC and SC groups;
8. to ascertain the distribution of polyps in the colon in EAC and SC groups by location;
9. to compare the ADR of NHS Bowel Cancer Screening Programme (BCSP) and non-BCSP colonoscopists;
10. to compare the ADR of the first 20% of patients scoped by each colonoscopist with the last 20% of patients in each arm to identify any changes in ADR, and
11. to compare the baseline ADR of each colonoscopist before trial recruitment with their individual ADR in patients where Endocuff Vision™ was not used.

These outcomes will be analyzed on an intention-to-treat basis.

Methods

Study design

This clinical, randomized, multicenter study will be conducted in subjects referred and scheduled for screening or surveillance colonoscopy via the BCSP, diagnostic or surveillance colonoscopy through the symptomatic NHS service, and will compare EAC with SC.

Patients will be recruited from six participating hospital sites within the Northern Region Endoscopy Group and St Mark's Hospital, London. Recruitment will begin at South Tyneside District Hospital, North Tees Hospital, and St Mark's Hospital as part of an "internal pilot" for 1 month, to allow for testing of the protocol and data collection process. Any protocol amendments will be disseminated to all participating sites. The study data will be collected and analyzed by the principal investigators.

Planned recruitment is for 1772 patients. These patients will have been referred for a colonoscopy at one of the participating sites. All potential participants will be sent or given a patient information leaflet about the study when their colonoscopy paperwork is sent or given to them, allowing adequate time to read the information leaflet (at least 24 hours) before consenting to the study. On attending the endoscopy unit for their procedure, they will be approached by a member of the research team, and given the opportunity to discuss the study. If they are willing to proceed with the study, they will complete written consent forms, and baseline data will be collected. They will then be randomized to either EAC group or SC group using a computer generated randomization tool. The procedure will be performed, and intraprocedure data collected by a member of the research team onto a case report form. Any polyps detected and removed will be followed up, and histological diagnosis recorded post procedure by the research team (**Fig. 4**, **Fig. 5**). All colonoscopies will be calibrated and serviced according to local guidelines.

Patients will remain in the study for 21 days to allow collection of standard post-colonoscopy complication data through review of medical notes after the 21-day period has elapsed. Serious Adverse Events (SAEs) will also be recorded for all patients from the time of colonoscopy to 21 days post procedure. There will no additional follow-up visit needed as a result of this. The timing of outpatient appointments and results will not be affected by the study and will be as standard for each unit. Data will be collated and analyzed by the research team. Adverse events will be classified by the research team.

Data collected before colonoscopy:

1. patient demographics (age, gender);
2. indication for colonoscopy, and
3. past abdominal surgical history.

Data collected during the colonoscopy procedure:

1. polyps detected (total number, plus for each polyp seen: location; size; morphology; removed (Yes/No); removal method);
2. extent of examination;
3. insertion time to cecum;
4. insertion time to terminal ileum (if applicable);
5. withdrawal time;
6. position change;
7. use of bowel preparation;
8. use of carbon dioxide insufflation;
9. patient satisfaction and comfort scores, and
10. immediate complications.

Data collected post procedure:

1. polyp histology;
2. complications up to 21 days, and
3. adverse events.

Inclusion criteria

All patients who are attending for screening, surveillance or diagnostic colonoscopy will be invited to the study. Patients should be aged 18 and over and have the ability to give informed consent.

Exclusion criteria

The exclusion criteria are:

1. patients with absolute contraindications to colonoscopy;
2. patients with established or suspicion of large bowel obstruction or pseudo-obstruction;
3. patients with known colon cancer or polyposis syndromes;
4. patients with known colonic strictures;
5. patients with a known severe diverticular segment (that is likely to impede colonoscope passage);
6. patients with active colitis (ulcerative colitis, Crohn's colitis, diverticulitis, infective colitis);
7. patients lacking capacity to give informed consent;
8. patients on clopidogrel, warfarin, or other new generation anticoagulants who have not stopped this for the procedure;
9. patients who are attending for a therapeutic procedure or assessment of a known lesion, or
10. pregnancy.

Withdrawal criteria

During colonoscopy, Endocuff Vision™ will be withdrawn in situations where:

1. there is an acute angulation in a fixed sigmoid colon rendering scope insertion not feasible with the Endocuff Vision™ mounted;
2. there is a new diagnosis of polyposis syndrome;
3. there is a new diagnosis of active colitis (where the endoscopist is concerned with regard to the risk of mucosal damage);
4. there is identification of a new colonic stricture, or
5. there is a new cancer diagnosis and progression of the colonoscope with the Endocuff Vision™ attached is not possible.

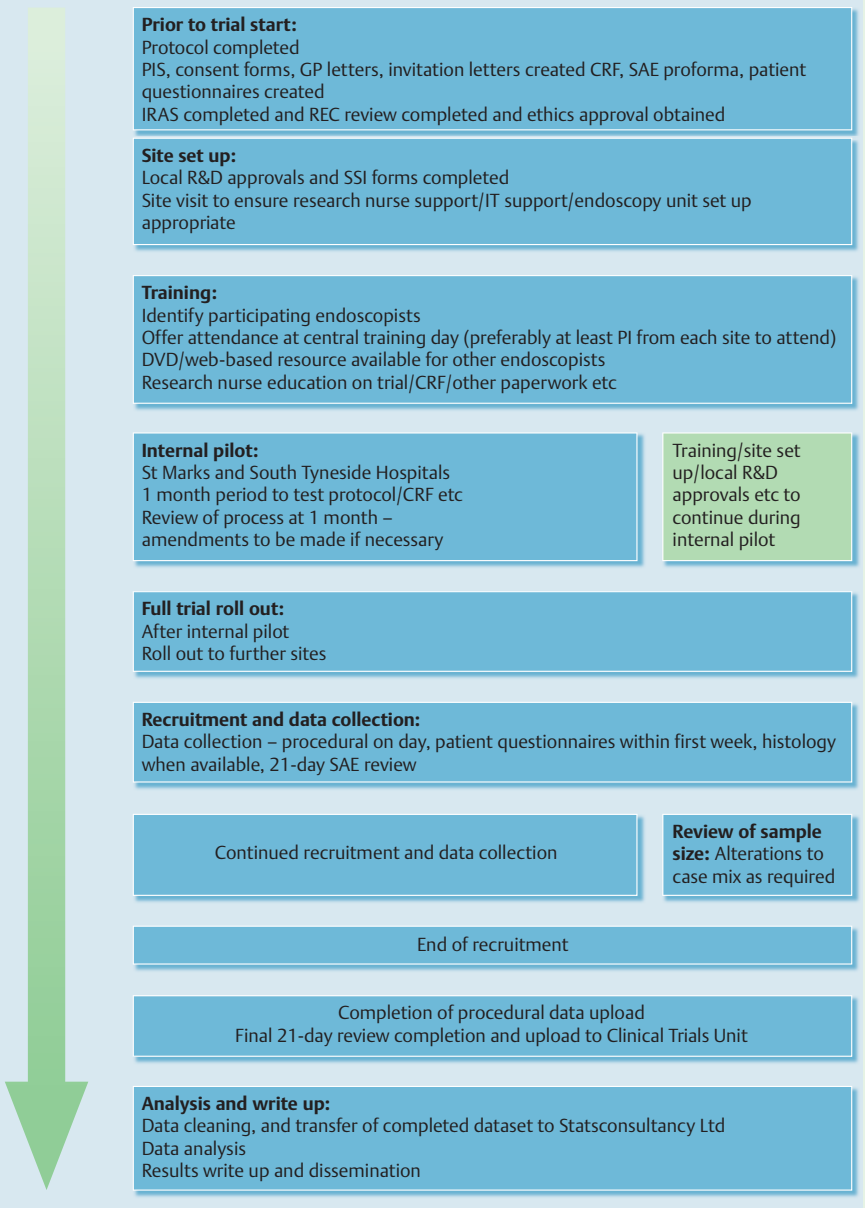

Fig. 4 Trial flow chart.

Setting/participating centers

Seven NHS hospital sites are participating and will enroll patients. Six participating sites within the Northern Region Endoscopy Group are district general hospitals. St Mark's Hospital in London is a tertiary referral center for endoscopy.

Randomization

Patients will undergo stratified randomization into EAC or SC groups based on age, gender, hospital site, and BCSP status. This is done by a computer generated system using a dynamic adaptive algorithm [18] in collaboration with North Wales Organisation for Randomised Trials in Health (NWORTH) Clinical Trials Unit.

Participating colonoscopists and training with Endocuff Vision™

Trial recruitment will involve a maximum of 10 colonoscopists at each site, and colonoscopists will be chosen to reflect the range of experience. At each site, a limited number (maximum four) of BCSP colonoscopists will be selected. All colonoscopists at participating units will undergo theoretical and practical sessions of training (using online/DVD tutorials) with Endocuff Vision™ and will have a lifetime experience of at least 20 cases with the device before study commencement. At least one endoscopist from each site will attend the training day where the study will be discussed, use of the Endocuff Vision™ demonstrated and online/DVD tutorials provided for training of other endoscopists.

Adverse events

The risks of adverse events (AEs) for EAC are believed to be equivalent to SC, including bleeding and perforation risks. There are also AEs related to sedation such as cardio-respiratory compromise that are similar in both EAC and SC procedures.

However, the study will measure AEs, which will be recorded in the patients' medical notes and on case report forms. AEs will be recorded for the 21-day period from the day of colonoscopy, or until withdrawal from study. Adverse events are defined as any new medical occurrence, or worsening of a pre-existing medical condition in a patient. There are no known complications or AEs from Endocuff Vision™. All AEs will be graded as mild, moderate,

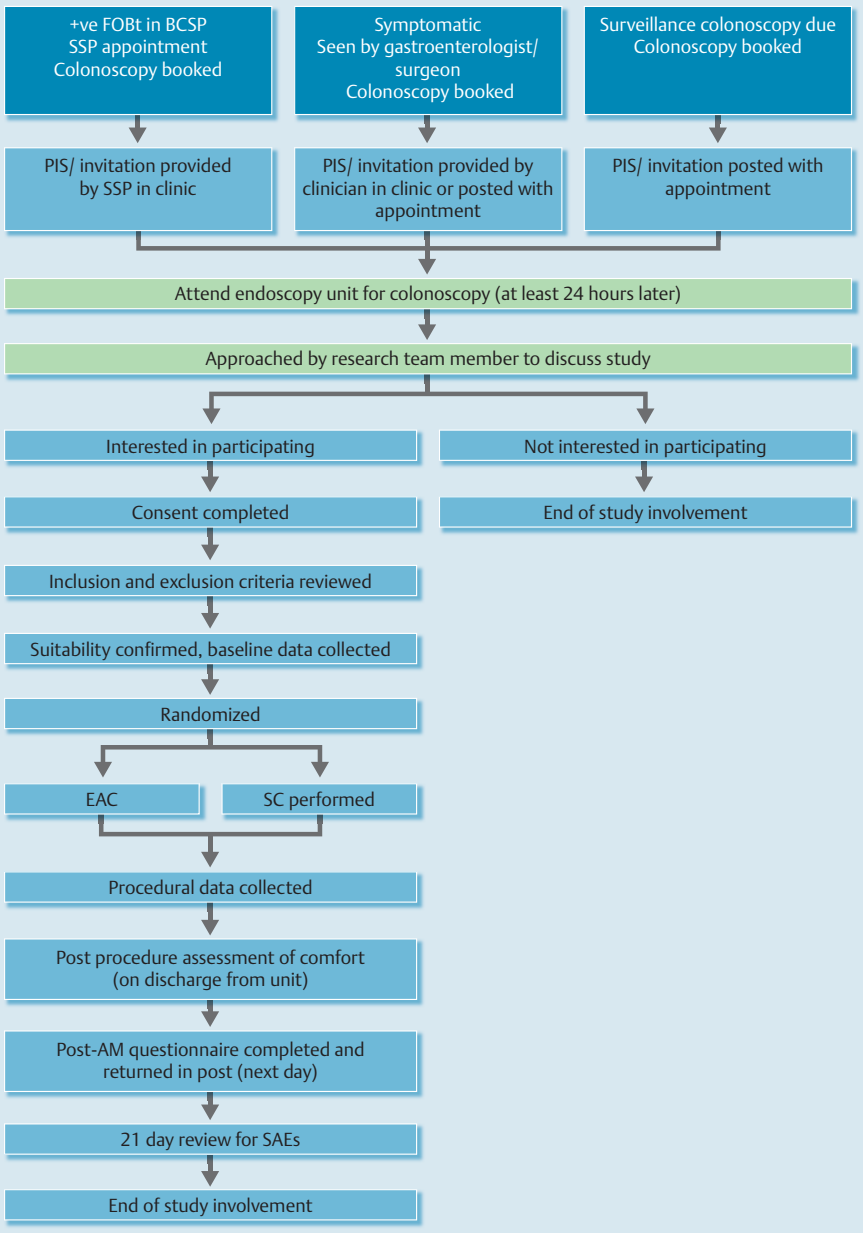

Fig. 5 Patient flow chart.

or severe, and will be assessed by an Investigator to define the relationship to the Endocuff Vision™.

All Serious Adverse Events (SAEs) will be treated clinically as appropriate and reported to the trial team within 24 hours of the research team becoming aware of the event, using the study-specific SAE Form. Any related and unexpected SAEs will be notified to the main NHS research ethics committee within 15 days of the trial team becoming aware of the event, using the National Research Ethics Service SAE form.

An event will be considered to be serious if it:

1. results in death;
2. is life threatening;
3. results in hospitalization or prolongation of existing hospitalization (exceptions to this are routine planned admissions, including admission for colonoscopy procedures as part of this study);
4. leads to persistent significant disability or incapacity, or
5. is otherwise considered to be medically significant by the Investigator.

SAEs will be recorded and reported from the time of colonoscopy until 21 days following the colonoscopy or until the time of withdrawal. SAEs will be assessed for expectedness, severity, and relatedness to the Endocuff Vision™ device. SAEs will be followed until resolution, death, or until resolution with sequelae. In addition, SAEs must be recorded in the Case Report Form on the Adverse Events section. SAEs will be reported even if they are considered to be expected events or unrelated events by the Investigator.

All AEs and SAEs will be reported and discussed with the Data Monitoring Committee. The Chair of the Data Monitoring Committee will, as appropriate, discuss AEs with two independent clinicians to assess the relationship of these AEs to the Endocuff Vision™ device. The results of this will also be presented to the Trial Steering Committee.

Assessment and follow-up

Clinical follow-up will be as per routine clinical practice for the respective unit. Colonoscopy related complications are routinely recorded up to 21 days post-procedure. All patients will have their post colonoscopy surveillance interval (according to BSG [19] or BCSP [20] guidelines) recorded in the Case Report Form, where appropriate. In the case of incomplete colonoscopy, the reason for this will be recorded. Eligible, consented patients will remain in the study for 21 days following colonoscopy. SAEs will also be reported for the 21-day period post colonoscopy for all patients in the study. We will review complication data and adverse events at 21 days by the most appropriate method for the population at each local site. This will consist of either a phone call to the patient or review of medical notes and hospital databases. If a patient presents to a different hospital post procedure to the hospital where the colonoscopy was performed, we will contact their General Practitioner to obtain information with regard to the event. This collection of data can occur up to 14 days after the end of the 21-day follow-up period, but will only include data within the 21-day window. No additional visits are required for patients who enter the study. Any follow-up appointments post-colonoscopy will be as per routine care for the respective unit. The timescale for the outpatient appointment and subsequent care will be unaltered by participation in the study.

Sample size

The study is powered to detect a difference in the ADR between two groups. There will be two subgroups of participants – those undergoing colonoscopy via the BCSP, and those with symptoms or being followed up in the general, non-screening, NHS service. ADR varies between these two groups; in the BCSP screening population, ADR is approximately 45 %, and in the non-screening population, 16 %. A difference in ADR of 5 – 10 % would be of clinical importance (5 % in the non-screening cohort, and 10 % in the screening cohort).

Preliminary work on BCSP participants at one of the Chief Investigators' sites suggests that such a rise in ADR for EAC procedures is possible. The proportion of screening to non-screening participants is anticipated to be approximately 20:80. Mean ADR for the whole group is therefore 21.8 %, and a 6 % increase in ADR to 27.8 % is deemed to be clinically significant. Therefore, to demonstrate a 6 % increase in ADR with a 5 % significance level and 90 % power using a one-sided test, it is calculated that 886 patients per group are required for the study, 1772 patients in total (**Fig. 6**).

Data analysis

The primary outcome is adenoma detection rate. A chi-squared test will be used to compare this outcome between groups. A secondary outcome is the number of adenomas detected per procedure. This is likely to have a positively skewed distribution, and so the Mann-Whitney test will be used to compare between groups. An additional secondary outcome is the proportion of patients who require a follow-up procedure (based on BSG adenoma surveillance guidelines), which will be compared between groups using the chi-squared test.

Other secondary outcomes will be examined on a non-inferiority basis, namely cecal intubation rate, insertion time to cecum, withdrawal time in procedures where there are no polyps, and patient satisfaction. The margin of non-inferiority will be set for all outcomes. For the continuous outcomes, one-sided 97.5 % confidence interval for the mean difference between groups will be calculated. For the binary outcomes, a one-sided 97.5 % confidence interval for the difference in proportions will be calculated. Non-inferiority will be assumed if the bound of the confidence interval does not cross the point of non-inferiority. The rate of cuff exchange will be calculated in the EAC group, along with a corresponding confidence interval. The analyses will be performed on an intention-to-treat basis. Data and all appropriate documentation will be stored for a minimum of 15 years after completion of the study, including the follow-up period.

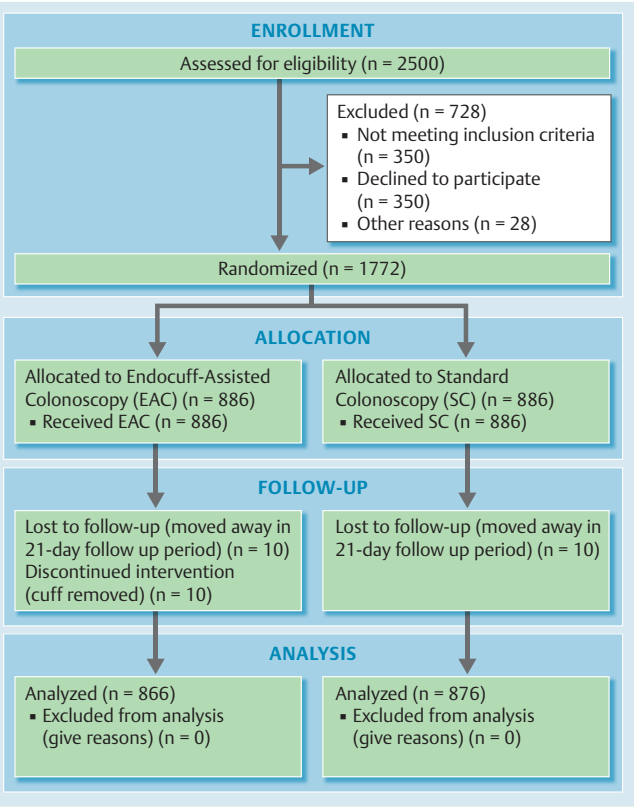

Fig. 6 CONSORT 2010 Flow Diagram for reporting of trials.

Data monitoring

The trial is supervised by the Data Monitoring Committee which consists of an independent chair, with two independent clinicians and an independent statistician. The aim of the Data Monitoring Committee is to safeguard the interests of trial participants, assess the safety and viability of the intervention during the trial, and monitor the overall conduct of the clinical trial. The Data Monitoring Committee will meet every 4 months.

Trial Management Group

The Chief Investigator has overall responsibility for the study and will oversee all study management. The Trial Management Group will be responsible for the day-to-day running of the trial. The Trial Management Group will be supported by and report to an independent Trial Steering Committee. The Trial Management Group will meet every 2 months.

Trial Steering Committee

The trial is supervised by the Trial Steering Committee which consists of an independent chair, independent clinician, patient and public involvement representative, and also an independent statistician. The role of the Trial Steering Committee is to supervise the trial to ensure that it is conducted to the rigorous stand-

ards set out in the Department of Health's Research Governance Framework for Health and Social Care and the principles of Good Clinical Practice. The Trial Steering Committee will meet every 6 months.

Publication policy

The Chief Investigators will take responsibility to present and publish the outcomes of the study. Study results will be disseminated through national and international symposia and local networks. The results will also be submitted for publication in international peer reviewed journals and presented to the British Society of Gastroenterology Endoscopy Research Committee, BSG guideline groups and the Bowel Cancer Screening Programme. Feedback will be given to regional and national Endoscopy leads, maximizing the exposure of findings to colonoscopists.

Study period

The study period of this trial is November 2014 to July 2016, with the participant entry period from November 2014 to June 2016.

Protocol version

The trial is on protocol version 14.0 dated 11 November 2015.

Ethical considerations

Ethics approval has been awarded via the NHS Research Ethics Committee before the study starting. There are no known additional risks to patients associated with the use of the Endocuff Vision™ device. The addition of Endocuff Vision™ will not add significantly to the duration of the procedure, although if adenoma detection rate increases significantly, the procedure may take longer due to increased polypectomy numbers. Patients will be informed of the risks associated with standard colonoscopy and consented for the procedures as per standard clinical practice in each center, in addition to a study-specific consent form which will have been discussed with the patient by the research team. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions. The ADENOMA Study is supported by the British Society of Gastroenterology Endoscopy Research Committee and has been identified as a research priority. The protocol for ADENOMA study has been reviewed and endorsed by the Bowel Cancer Screening Research Committee.

Sponsor

The trial is sponsored by South Tyneside NHS Foundation Trust District Hospital.

Discussion

Adenomatous polyps can turn into colorectal cancer through the adenoma-carcinoma sequence [21, 22]. Thus, an increase in adenoma detection and subsequent removal may reduce colorectal cancer risk. Methods to improve ADR are widely contested and have been studied via various modalities of technology. This is the first randomized controlled trial looking at the use of Endocuff Vision™ in screening, surveillance, and diagnosis of patients. Studies have shown that there is a wide ADR variation in non-screening colonoscopists with BCSP colonoscopists having a 30% higher ADR comparatively [3,23]. Although this may in part be due to the increased risk of adenomas in BCSP patients who attend because of a positive fecal occult blood test, this may also reflect higher quality colonoscopy. The Endocuff Vision™ may be of benefit in non-screening colonoscopists to increase ADR.

The NHS Bowel Cancer Screening Programme started in July 2006 with all screening endoscopists having to undergo strict accreditation criteria via the Screening Assessor Accreditation System which is a web-based application process maintained by the Joint Advisory Group in Gastrointestinal Endoscopy. All screening colonoscopists must submit audit data demonstrating a high level of performance before accreditation. Completion of an accreditation examination at an independent unit is then undertaken which consists of a multiple choice question examination and performance of two colonoscopies observed by two independent and trained examiners using objective directly observed colonoscopic procedural skills assessment criteria. Accredited colonoscopists are subjected to a rigorous ongoing audit of colonoscopic performance which includes maintaining a minimum of 150 screening colonoscopies annually and having a complication rate below the national average as outlined by the latest national or BSCP data [24]. The quality of BCSP colonoscopy has been reported widely [3].

This study's strengths are that it is conducted at multiple sites to reflect tertiary and secondary centers. Although a large scale trial, it has a simple patient recruitment process. In addition, use of the Endocuff Vision™ will not unnecessarily lengthen colonoscopy time and no additional NHS resources are required. The minimum of 20 training cases required for completion by each trial colonoscopists ensures that all colonoscopists have a minimum standard from which to progress from.

One limitation of this study is that colonoscopists are not blinded to EAC or SC groups. Alternatives that were discussed included having a different colonoscopist perform initial anal intubation or to video record each colonoscopy to be double read by a different colonoscopist after the procedure. However, this was felt to be impractical as the 'finger-like' projections of the Endocuff Vision™ occasionally come into luminal view during colonoscopy. The results of this trial will be valuable in determining the role of Endocuff Vision™ in routine colonoscopy.

Trial status

The trial is currently active.

Competing interests: None

Acknowledgments

This study is conducted on existing NHS and BCSP lists, at no extra cost to the NHS. Funding is provided by ARC Medical Design Ltd to cover the Endocuff Vision™ devices, clinical trial unit costs, and results analysis. The two chief investigators are currently full-time dedicated clinical researchers. Principal investigators will be supported by a research team (of research fellows and/or research nurses) and they will invite, assess, and consent participants, and collect data. No additional NHS resources will be required to conduct this study. Any unforeseen costs related to the study will be met by ARC Medical Design Ltd.

We would like to acknowledge members of the Data Monitoring Committee – Professor Mike Bramble, Professor John McLaughlin, Dr Anjan Dhar, and Dr Ben Carter for their participation and

advice. We would also like to acknowledge members of the Trial Steering Committee – Professor Mark Hull, Dr James East, Mr Colin Everett, and Mrs Carol West for their participation and advice.

References

1 *Kaminski MF*, *Regula J*, *Kraszewska E* et al. Quality indicators for colonoscopy and the risk of interval cancer. NEJM 2010; 362: 1795 – 1803
2 *Corley DA*, *Jensen CD*, *Marks AR* et al. Adenoma detection rate and risk of colorectal cancer and death. NEJM 2014; 370: 1298 – 1306
3 *Lee TJ*, *Rutter MD*, *Blanks RG* et al. Colonoscopy quality measures: experience from the NHS Bowel Cancer Screening Programme. Gut 2012; 61: 1050 – 1057
4 *Rajasekhar PT*, *Lee TJ*, *Rutter MD* et al. Using a 'conversion factor' to estimate adenoma detection rate. Endoscopy 2012; 61: A371
5 *Bowles CJ*, *Leicester R*, *Romaya C* et al. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? Gut 2004; 53: 277 – 283
6 *Gavin DR*, *Valori RM*, *Anderson JT* et al. The national colonoscopy audit: a nationwide assessment of the quality and safety of colonoscopy in the UK. Gut 2013; 62: 242 – 249
7 *Faiss S*. The missed colorectal cancer problem. Dig Dis 2011; 29: 60 – 63
8 *Rees CJ*, *Rajasekhar PT*, *Rutter MD* et al. Quality in colonoscopy: European perspectives and practice. Expert Rev Gastroenterol Hepatol 2014; 8: 29 – 47
9 *Siersema PD*, *Rastogi A*, *Leufkens AM* et al. Retrograde-viewing device improves adenoma detection rate in colonoscopies for surveillance and diagnostic workup. World J Gastroenterol 2012; 18: 3400 – 3408
10 *Kaltenbach T*, *Friedland S*, *Soetikno R*. A randomised tandem colonoscopy trial of narrow band imaging versus white light examination to compare neoplasia miss rates. Gut 2008; 57: 1406 – 1412
11 *Fenlon HM*, *Nunes DP*, *Clarke PD* et al. Colorectal neoplasm detection using virtual colonoscopy: a feasibility study. Gut 1998; 43: 806 – 811
12 *East JE*, *Bassett P*, *Arebi N* et al. Dynamic patient position changes during colonoscope withdrawal increase adenoma detection: a randomized, crossover trial. Gastrointest Endosc 2011; 73: 456 – 463
13 *Saifuddin T*, *Trivedi M*, *King PD* et al. Usefulness of a pediatric colonoscope for colonoscopy in adults. Gastrointest Endosc 2000; 51: 314 – 317
14 *Harada Y*, *Hirasawa D*, *Fujita N* et al. Impact of a transparent hood on the performance of total colonoscopy: a randomized controlled trial. Gastrointest Endosc 2009; 69: 637 – 644
15 *Rastogi A*, *Bansal A*, *Rao DS* et al. Higher adenoma detection rates with cap-assisted colonoscopy: a randomised controlled trial. Gut 2012; 61: 402 – 408
16 *Tsiamoulos ZP*, *Kinesh PP*, *Elliott TR* et al. Does Endocuff-Vision improve adenoma detection rate at screening colonoscopy? Gastrointest Endosc 2014; 79: AB233 – AB234
17 *Tsiamoulos ZP*, *Saunders BP*. A new accessory, endoscopic cuff, improves colonoscopic access for complex polyp resection and scar assessment in the sigmoid colon (with video). Gastrointest Endosc 2012; 76: 1242 – 1245
18 *Russell D*, *Hoare ZS*, *Whitaker R* et al. Generalized method for adaptive randomization in clinical trials. Stat Med 2011; 30: 922 – 934
19 *Atkin WS*, *Saunders BP*. Surveillance guidelines after removal of colorectal adenomatous polyps. Gut 2002; 51: 056 – 9
20 NHS Cancer Screening Programmes. Adenoma Surveillance: BSCP Guidance. 2009: http://www.cancerscreening.nhs.uk/bowel/publications/nhsbcsp-guidance-note-1.pdf Accessed 25 February 2014
21 *Leslie A*, *Carey FA*, *Pratt NR* et al. The colorectal adenoma-carcinoma sequence. Br J Surg 2002; 89: 845 – 860
22 *Muto T*, *Bussey HJ*, *Morson BC*. The evolution of cancer of the colon and rectum. Cancer 1975; 36: 2251 – 2270
23 *Rajasekhar PT*, *Rutter MD*, *Bramble MG* et al. Achieving high quality colonoscopy: using graphical representation to measure performance and reset standards. Colorectal Dis 2012; 14: 1538 – 1545
24 NHS Bowel Cancer Screening Programme. Accreditation of screening colonoscopists. 2006: 1 – 43 Available from: http://www.saas.nhs.uk/Downloads.aspx