Screening for colorectal cancer, where are we now?

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Colorectal cancer (CRC) screening is being implemented around the world based on the screening recommendations issued by most professional societies. Little is known about the best screening modality. For a successful population-based programme it has to have:

(1) Patient acceptance of the screening modality in different demographic groups.
(2) Effective implementation strategies in different regions around the world.

Faecal occult blood testing, sigmoidoscopy, virtual colonoscopy and stool DNA testing are all valid screening modalities and have been proven effective in reducing CRC mortality. However, colonoscopy is currently the best screening modality for the prevention and early detection of CRC [1,2].

This review will focus on new endoscopes on the horizon.

There are several major drawbacks associated with the "gold standard" colonoscopy: low patient compliance is a major obstacle preventing a large scale implementation of this programme [3]. Patient compliance is limited because of the embarrassment [3–5], the preparation [6] and the fear of pain and discomfort that are associated with the procedure [6–9]. Concerns regarding the risk in an invasive procedure and the high costs further decrease the success of screening colonoscopy [10,11]. High polyp miss rates in some reports are another issue of concern [12,13].

These limitations highlight the need for a better colonoscopic procedure (Table 1).

Table 1
The ideal colonoscope

1. Disposable.
2. Low cost.
3. Skill-independent.
4. No sedation.
5. Self-propelling.
6. A better vision system
7. Records the procedure on a CD.
8. Therapeutic option.

Protectiscope™ (Stryker, Kalamazoo, MI, USA)

This is the first disposable device on the market that protects the scope and enhances its advancement. The Protectiscope was approved in 2004 by the US Food and Drug Administration. The disposable component is inserted through the endoscope before initiating the procedure and is discarded at the end of it, protecting the outer surface of the scope from contamination. It is a standard colonoscope with all the regular working channels. Another advantage of this scope is the ease of advancement, which is achieved by using a second air pressure system that pumps air into the space between the shaft of the scope and the protective sleeve, producing a small forward force just below the tip of the scope that makes the scope easier to push.

In a pilot study in 178 subjects, a cecal intubation rate of 90% ($n = 161$) was reported. Biopsies and polypectomies were performed without any difficulties. The procedure had to be terminated because of device malfunction in three patients, but there were no major complications. The sheath barrier proved to be effective against infection.

However, the entire project was recently put on hold, following a disappointing attempt to use the device in a community setting. The company decided to abandon the assisted colonoscopy features and is now concentrating on the disposable component (N. Arber, Tel Aviv Medical Center).

Neoguide Systems Inc (San Jose, CA, USA)

An "intelligent" colonoscope with 15 identical bendable computer-controlled segments behind a steerable and controllable tip. The segments are directed to follow the lead segment at each given depth. There

are two sensors; the tip position sensor, which continuously measures tip position, and the external position sensor, which continuously measures tip depth. Based on these measurements and by using computer algorithms the device builds a real-time, three-dimensional map of the colon. This enables control of the entire shape of the scope and not just its tip. This way, looping and stretching of the mesentery can be completely prevented, thereby reducing the time of insertion and the induced pain [14]. Biopsies and polypectomies through a standard working channel are possible. In a first clinical study the cecum was reached in 11 out of 12 cases, in five of them in less than 3 min. Despite the initial enthusiasm, research and development of this device was recently halted (N. Arber, Tel Aviv Medical Center).

The Invendoscope™ (Invendo Medical, Kissing, Germany)

This is a hand steered disposable colonoscope, which is propelled by a motorized unit. All endoscopic activities are controlled by a hand-held unit. It uses "inverted sleeve" technology. Wheels are rolled on the inner side of an inverted sleeve, so that the sleeve is rolled inside out, drawing the colonoscope deeper into the colon by 10-cm each time. Similarly, the driving wheels move backwards when the colonoscope is pulled out. Optimal and easy steering of the colonoscope is achieved by the ability to deflect the tip, in any direction, by 180º. The scope is slightly smaller and more flexible; nevertheless, it has working channels all similar to normal scopes. A prospective, single-arm, pilot study in 39 healthy unsedated volunteers was recently published [15]. The procedure was prematurely terminated in five subjects due to technical problems and they were excluded from the study. The cecum was reached in 82% of the remaining 34 cases. No complications were encountered. It should be noted that only limited time was spent on inspection of the mucosa while withdrawing the instrument [15]. It is the intention of the company to launch this device in 2009 (N. Arber, Tel Aviv Medical Center).

Video capsule endoscopy (VCE; Given Imaging Ltd., Yoqneam, Israel)

VCE was approved for clinical use at the beginning of the century (reviewed in [16]). In 2008 it was suggested as a safe, non-invasive, non-sedation-requiring, alternative modality for CRC screening. The current colonic capsule measures 11×31 mm and has a camera on both sides of the VCE. It takes four pictures per second, has an automatic light control, and a total operating time of 10 h. The capsule is activated upon swallowing, stays on for 1–2 min, than enters a sleep mode for 2 h while passing the small intestine and upon reaching the terminal ileum. A meticulously clean colon is essential for the procedure. A novel and tidious colonic preparation regimen has been developed to ensure a clean colon, and to enchance capsule propulsion through the entire length of the colon within 10 h while the batteries are still active. Detailed information on this preparation can be found elsewhere [17,18].

In two trials [17,18], VCE and conventional colonoscopy were performed in tandem. In the Israeli study, there were three rounds of assessment and the sensitivity and the specificity of VCE steadily increased with each round (56%, 69%, 76%, and 69%, 81%, 100%, respectively) [17]. In the Belgian study, the positive predictive value (PPV) and negative predictive value (NPV) of significant polyp detection with VCE were 36% and 86%, respectively [18]. No complications were encountered in either study.

The first European multi-centre study of VCE included 320 participants from eight centres. VCE was performed first, followed by conventional colonoscopy. The capsule was expelled within 10 h in 93% of the subjects. The sensitivity and specificity were disappointingly low (64% and 84%, respectively). The PPV was 60% and the NPV was 86%.

In a recent position statement on CRC screening modalities, the American Cancer Society recommended against the use of VCE for screening and early detection of CRC, as the colon can not be well and accurately visualised [19].

The Aeroscope (GI View Ltd, Ramat Gan, Israel)

The Aeroscope is a miniaturised, disposable, ultra-flexible, self-propelling and self-navigating endoscope. It advances in the colon due to minimal air pressure which is gradually built up behind it, thus minimising the force applied to the colonic wall and the mesentery, hence decreasing discomfort, pain and the risk of perforation. The Aeroscope's visual system enables 360º viewing of the colonic mucosa. The first animal experiment was reported in 2006 [20]. Since then, more than 800 runs have been conducted in pigs (N. Arber, Tel Aviv Medical Center). Clinical feasibility of the device was successfully demonstrated in 12 healthy volunteers, with a cecal intubation

rate of 85% [21]. *In vitro* and *in vivo* studies showed detailed visual inspection, with only minute blood vessels (<1 mm) evident without the need for tip manipulation [22]. A total of 116 subjects have undergone testing with this device and no clinically significant complications have been reported to date (N. Arber, Tel Aviv Medical Center).

In a study performed at the beginning of 2008, the rate of cecal intubations was <80%. The company is currently improving the device so that it may be able to compete with conventional colonoscopy. A study completed in December 2008 showed a better rate of cecal intubation (>90%) than that achieved with conventional colonoscopy, but the time to cecal intubation was too long, averaging ~30 min (data not shown). More clinical studies in humans are planned in 2009 in Israel and Croatia, with regulatory studies scheduled in 2010.

Summary

The most important disadvantage of the currently available colonoscopes is the need for bowel preparation [23]. Preparation less virtual would be an attractive option. The cost of the new endoscopic methods for colorectal cancer screening is another issue, and needs to be reduced to less than US$200 if large-scale use is intended. Proof of concept for the new endoscopes has been achieved, although significant improvements are still required before colonoscopy can be replaced.

Conflict of interest statement

Dr. Arber is a member of the scientific advisory board of GI View Ltd, Ramat Gan, Israel.

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