Refining CT colonography methods
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Chapter 1

Introduction and outline of the thesis

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Chapter 1

Introduction

Colorectal cancer is one of the leading causes of cancer-related mortality. It is estimated that in developed countries in 2008, 727,400 individuals were diagnosed with colorectal cancer and 320,100 died as a consequence of this disease [1]. Most colorectal cancers are thought to develop from adenomas through the so-called adenoma-carcinoma sequence [2]. Adenomas and especially advanced adenomas have a risk of developing into cancer. An advanced adenoma is defined as an adenoma ≥ 10 mm, with villous histology (≥ 25% villous) or with high-grade dysplasia. Advanced adenomas and carcinomas combined are known as advanced neoplasia. Despite improvements in treatment of colorectal cancer, mortality has not decreased to a considerable extent [2]. The most important reason is the presence of extensive disease at the time of diagnosis.

Early detection of colorectal cancer and prevention by removing the precursors of colorectal cancer (adenomatous polyps) by screening is possible and at this moment seems to be the most feasible solution to substantially reduce incidence and mortality of colorectal cancer [2]. Several screening techniques are available, including faecal occult blood test, sigmoidoscopy, double-contrast barium enema, colonoscopy and CT colonography. For the selection of the future colorectal cancer screening test all benefits and drawbacks have to be studied and weighted.

CT colonography is a structural radiologic examination to evaluate the colorectum for polyps and cancers. It has replaced double-contrast barium as preferred imaging modality for this purpose [3–5]. After an oral bowel preparation and colonic insufflation, an abdominal CT acquisition is performed in both prone and supine position. Images are reconstructed to allow for three-dimensional evaluation (i.e. virtual colonoscopy) in addition to two-dimensional evaluation (Figure 1). The accuracy for colorectal cancer detection of this technique is comparable to colonoscopy and it is also an accurate method for the detection of advanced adenomas [6–11]. It is therefore used as an alternative for colonoscopy, or when colonoscopy is incomplete. Furthermore its role as a potential screening tool is under continuous investigation [10, 12, 13]. The less invasive character of CT colonography compared with colonoscopy (e.g. no sedation, less purgative bowel preparation and only small flexible rectal catheter in the rectum for the insufflation) may have important advantages in terms of acceptance and therefore likely the adherence in screening.
Figure 1 shows correlative three-dimensional (left) and two-dimensional (right) CT colonography images. The three-dimensional (virtual colonoscopy) viewing method shown here is called the ‘unfolded cube method’. A 15 millimetre pedunculated villous adenoma is pointed out with the solid white arrows. The dashed arrow shows the content of the bowel that is tagged with iodinated contrast medium, and is therefore white on the image. Notice that there is contrast material posterior to the polyp on the two-dimensional image. On the three-dimensional image the contrast material is not seen because it has been electronically removed using ‘electronic cleansing’. The bowel pointed out with the dashed arrow is very well distended. One can imagine this causes stretching of the bowel wall and therefore colonic cramps. Finally notice that on the two-dimensional images not only the colon is seen but also other abdominal (extracolonic) structures.

Insufflation of the colon is required to visualise the complete colonic wall. Colonic insufflation can be performed manually and with room air, but automatic insufflation of carbon dioxide is the preferred method [5, 14]. Furthermore, the use of two scan positions increases the number of segments with adequate distension [15]. Unfortunately the insufflation causes painful colonic cramps and affects the acceptance of the technique [16–18]. To reduce colonic cramps a spasmolytic (hyoscine butylbromide or glucagon hydrochloride) is often given before insufflation. The spasmolytic may also improve distension and possibly reduce image artefacts. No differences have been detected in a direct comparison of distension and burden between both spasmolytics [19]. Although spasmolytics reduce the colonic spasms, the colonic cramps still cause considerable pain and burden. In some studies, the pain and burden even compare unfavourable with colonoscopy under conscious sedation [16–18, 20]. Reduction of insufflation pain may improve CT colonography acceptance. Therefore efforts should be made to further reduce the pain and burden of CT colonography insufflation.

CT colonography is performed after an oral bowel preparation as otherwise colorectal cancer and polyps will be obscured by stool. Although the CT colonography preparations are generally less purgative than in colonoscopy, some
purgation is desired to create mixing of bowel content and tagging agent (iodine and/or barium) [5]. Tagging causes a large contrast between bowel content and colonic lesions because it increases the CT value of the fluid or stool as compared to the bowel wall and lesions. Well-tagged fluid levels make optimal CT colonography reading possible. Another advantage of tagging is that it allows less purgative bowel preparations and the use of electronic stool removal (electronic cleaning). Less purgative bowel preparations do however make a full colon three-dimensional evaluation impossible as either the contrast material obscures the colonic wall or - in case of electronic cleansing - substantial artefacts (‘floating debris’) interfere with reading the examination [21]. This is a limitation as a combination of two-dimensional and three-dimensional read is considered state of the art [14, 22]. The lack of a three-dimensional read is detrimental to all but especially to inexperienced readers. In these individuals a primary three-dimensional read (initial three-dimensional read with two-dimensional problem solving) has been shown to lead to improved polyp sensitivity and is therefore mandatory for these readers [23]. An improved electronic cleansing algorithm may allow for the combination of a reduced preparation and three-dimensional reading. Further reduction of burden of the oral bowel preparation would be beneficial for CT colonography acceptance, especially when omitting the oral bowel preparation would be possible.

**Dual-energy** CT is not a new technique, but since a few years simultaneous acquisition of low- and high voltage scans (e.g. 80 or 100 and 140 kV) is possible [24]. The information that is thus obtained enables more accurate differentiation between tissue types with different effective atomic numbers [25]. Dual-energy CT has the ability to differentiate iodine or barium very well from other tissues or materials with lower atomic numbers. Additionally iodine-only images can be created with post-processing. One dual-energy CT colonography study has evaluated the feasibility of characterising lesions by their uptake of intravenous iodine contrast medium only [26]. This may obviate the need for an oral bowel preparation. These authors were able to differentiate colorectal cancer from non-enhancing (non-tagged) stool using intravenous contrast medium uptake. This study however concerned only one colorectal cancer. Whether all colorectal cancers are visible on dual-energy CT and whether iodine-only images may improve the detection is unknown.

CT systems use ionising radiation dose which may cause damage to DNA and therefore result in cancer later in life [27]. Therefore one has to use the lowest
radiation dose possible. CT colonography scan parameters were initially based on clinical abdominal CT protocols, and later on were adjusted to lower dose settings. Dose reduction is possible because essential differences exist between the two examinations with regard to the kind of details that have to be visualised. In clinical intravenous contrast medium enhanced abdominal CT subtle contrasts between the different soft tissues are important and may be obscured when the images are too noisy. Therefore, a relatively high dose is required in order to reduce the noise. In CT colonography examinations, on the other hand, target lesions (colorectal cancer and adenomatous polyps) remain visible in much noisier images [28]. This is due to the large contrast between the bowel wall and intraluminal gas. The use of newer CT equipment with more efficient use of radiation dose or new reconstruction techniques (e.g. iterative reconstruction algorithms) as well as stricter guidelines may contribute to a reduction in radiation dose [14, 29–32]. Therefore the benefit-risk ratio may change over time and the radiation risk has to be weighed against the potential benefits of screening with CT colonography.

For the selection of a screening tool, costs are important. Studies indicate that CT colonography may be less cost-effective as compared to other screening options [33, 34]. However, these studies were based on assumed unit costs for CT colonography while a recent evaluation of actual costs showed substantial lower costs than assumed [35]. Nevertheless, costs reduction is important for cost effectiveness of any test and to reduce CT colonography costs, alternative reading strategies with radiographers have been studied [36, 37]. For assessment of lesions inside the colon (intracolonic findings) radiographers can be equally accurate to a radiologist [36–38]. Apart from intracolonic findings, lesions outside the colon (extracolonic findings) may be visible on the CT colonography. In symptomatic patients the assessment of extracolonic lesions is important and part of staging, such as colorectal liver metastases or lymphadenopathy in a contrast-enhanced CT colonography. Important extracolonic findings are relatively frequent in these patients [39]. In a screening population the target lesions are located in the colon and it is unclear whether the extracolonic findings on a low-dose, non-enhanced CT colonography are boon or bust. As compared to the symptomatic population, important extracolonic findings are much less common [9]. Some findings however, require further work-up or treatment. In a screening setting cost-saving strategies can be considered, such as the use of radiographers.
Outline of the thesis

This thesis is focused on refining CT colonography methods. Although CT colonography has some important advantages compared with other diagnostic and screening tests, it necessary to work on its imperfections and thereby refine the technique. In this thesis we investigate several options to improve CT colonography aspects or the knowledge about these aspects. Reading strategies, cost-effectiveness, knowledge on radiation exposure, colonic insufflation, choice of spasmolytic, bowel preparation and image processing are aspects addressed in this thesis.

In order to be competitive with other screening options, the cost-effectiveness of CT colonography has to be improved. Radiographers can read CT colonography for intracolonic findings and this may be a cost-reducing strategy [35, 38]. However a radiologist has to read all scans for extracolonic findings. In chapter 2 we therefore assess the feasibility of training radiographers to triage CT colonography for extracolonic findings. If radiographers can perform an effective triage, the radiologist has to read only a small proportion of all screening CT colonographies.

Knowledge about the benefit-risk ratio of a test is important. The benefit of CT colonography in terms of yield is well known, but the radiation risk may change over time due to new guidelines and more radiation efficient CT equipment. We therefore performed an inventory among international researchers on CT colonography to determine the currently used effective radiation dose for different CT colonography indications, which we describe in chapter 3.

Chapter 4 is a narrative review in which we summarise the literature on two important CT colonography aspects: radiation dose and colonic insufflation. Colonic insufflation is required for CT colonography because accurate polyp detection is only possible in adequately distended segments. Unfortunately insufflation causes painful cramps that limit the acceptance of this technique. Apart from the use of spasmolytics, no efforts have been made to reduce CT colonography insufflation pain. In chapter 5 and 6 we described the protocol and results of our randomised, double-blind, placebo-controlled trial to evaluate the value (especially the analgesic effect) of alfentanil in CT colonography. We hypothesised that alfentanil would provide a maximum insufflation pain reduction of 1.3 points on an 11-point numeric rating scale.

Until now no differences in burden and distension have been objectified between the two commonly used spasmolytics for CT colonography. In chapter 7 we
compared the distension and burden between these two spasmolytics within a large population screening trial.

The bowel preparation is considered a burdensome aspect of CT colonography and therefore omitting the bowel preparation would be advantageous, especially for frail and elderly patients. In these patients the primary goal of the examination is the detection of colorectal cancer while the detection of polyps is less important. A technique with intravenous contrast medium and dual-energy CT may allow cancer detection. In **chapter 8** we describe a feasibility study in which we study the visibility of colorectal cancers using intravenous contrast medium (no oral bowel preparation) and dual-energy CT and the additional value of iodine-only images.

When using a bowel preparation the preparation should be as minimal as possible. Although two-dimensional evaluation is possible with a minimal preparation, three-dimensional evaluation is currently not possible because of cleansing artefacts. However, the combination of both two-dimensional and three-dimensional images is deemed necessary for an optimal evaluation. Therefore we developed and tested a new cleansing algorithm aimed to allow three-dimensional evaluation in minimally prepared CT colonography, which we describe in **chapter 9**.

In **chapter 10 and 11** we provide a summary of this thesis with our conclusions and implications.
Chapter 1

References


