CT colonography for screening of patients at increased risk for colorectal cancer: accuracy, patient acceptance and radiation issues
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Summary and Conclusions
Summary

The studies in this thesis on CT colonography addressed several criterions that determine to a large extent the efficacy of this examination in colorectal cancer screening and surveillance: accuracy and patient acceptance. Also, the possibilities to estimate the potential risks related to screening with CT colonography, imposed by the use of ionizing radiation, were investigated and efforts were made to assess the feasibility to substantially reduce this risk.

In chapter 2, we aimed to investigate the accuracy of CT colonography in patients at increased risk for colorectal cancer, with colonoscopy as the reference standard. To compensate for the miss rate of the reference standard, we performed a second look colonoscopy to verify the nature of large false positive findings of CT colonography that could not be explained based on review of the colonoscopy video. These results were subsequently incorporated in the analysis. In this way we found that CT colonography had a similar ability to identify patients with large colorectal polyps as colonoscopy, which is the recognized gold standard for the detection of polyps. Almost all sessile and pedunculated polyps ≥6 mm were detected with CT colonography. Most flat lesions, which are known to have a high malignant potential, however, were overlooked with CT colonography. In retrospect, 5 out of 10 missed flat lesions could be identified in the CT colonography images, among which an adenomatous polyp and a cancer. Early signs indicate that scanning with thinner collimation, addition of a primary 2D review, and additional training might help to improve the detection of such lesions. Another limitation that came into view was the high number of false positive findings, especially in the medium and small size category. Although, it is very likely that a certain proportion of these findings are based on true polyps that were missed by the reference standard, another part will constitute residual fecal material. Tagging of stool with contrast agents and scanning with thinner slices can be expected to improve the discrimination of fecal material from polyps, without reducing the sensitivity.

Patients with a personal or family history of colorectal adenomas or cancer are well known to be at increased risk for colorectal cancer and many organizations recommend colonoscopic screening of these patients, but even in these groups utilization of colorectal screening varies widely. Disadvantages of colonoscopy are the attendant discomfort, a reason that is frequently mentioned to decline screening, and the small but definite risk for complications. In chapter 3 we compared patient preferences
between CT colonography and colonoscopy in a five-week follow-up study and found that increased-risk patients significantly preferred CT colonography over colonoscopy, both directly after both examinations and five-weeks later. The preference for CT colonography had decreased significantly, however, over the follow-up period. Initially, experience parameters such as pain and embarrassment were strongly associated with preference, but at the second preference measurement five weeks later, the influence of experience parameters decreased. Instead the influence of outcome parameters, such as the presence of polyps, emerged.

Due to its acceptable accuracy and its patient friendly character, CT colonography can be considered as an attractive alternative to conventional colorectal screening methods. An important drawback remains the fact that individuals that undergo this examination are exposed to ionizing radiation. Because no recent data exist on the effective doses that are used to perform CT colonography, no estimates as to the risk resulting from this examination can be made. In chapter 4 the results of an inventory among institutions that perform research on CT colonography are reported. It appears that the present (2004) median effective dose for CT colonography in prone and supine position results in an effective dose of 10.0 mSv. When analyzed in time, it appeared that although radiologists increasingly used multislice scanners and scan with increasingly thin sections, the effective doses remained approximately constant. This is caused by a trend to use lower tube charge (mAs). When the median effective dose is translated into a risk for individuals aged 50, this dose may induce one fatal cancer in 4000 persons, which may become manifest after a latent period of up to a few decades.

In chapter 5 we report a study on the use of low dose scan protocols for CT colonography. In this study we compared three dose levels, 12, 6 and 3.6 mSv (corresponding with 100, 50 and 30 mAs) in three identical patient groups. It is our opinion that such a set-up is preferable to a comparison of different dose levels in different patient groups, as the differences in polyp detectability between two mAs levels can be attributed to the dose levels. We achieved this by simulating lower dose CT scans based on the raw transmission measurements of CT colonography examinations of 50 patients. In this study it appeared that although image quality decreased significantly in the simulated 30 mAs scans, the sensitivity and specificity remained unimpaired. As expected, the patient circumference as measured midway between the lowest rib and the iliac crest appeared to be a determinant of image quality.
Driven by the results of chapter 5, we were interested to find the lowest magnitude of dose that is compatible with polyp detection. In chapter 6 we report an experimental study performed in 15 patients with polyps ≥5 mm in which we compared the numbers of true and false positive findings at five mAs levels, ranging from medium to very low (12, 3, 0.8, 0.2 and 0.05 mSv, corresponding with 100, 25, 6.3, 1.6 and 0.4 mAs). The two lowest dose levels cannot be attained with presently available CT scanners. In this study we applied the same simulation method as in chapter 5. It appeared that in the simulated scans at mAs levels as low as 1.6, detection of polyps ≥5 mm decreased only slightly, but not significantly. Detection of polyps ≥10 mm, although only few in number in this study (n=5), was constant down to a mAs level of 0.4, the lowest level tested. It appeared that location of the polyp -in the pelvic or the abdominal colon segments- influenced the detection rates at very low dose level; detection of polyps in the pelvic colon segments decreased significantly when the 100 mAs data were compared with the simulated 0.4 mAs data, whereas detection of polyps in the abdominal segments did not. This study indicates that dose levels that are used to date could theoretically be reduced as much as 20 to 60 times, resulting in an identical reduction in the risk to induce cancer. Use of such low doses in colorectal cancer prevention would virtually eliminate the drawback of exposure to ionizing radiation. Before implementation of very low dose scan protocols in practice can be recommended, studies on the accuracy of real low dose CT colonography in consecutive patients are needed to confirm our findings that are obtained in an experimental setting.

Although volumetric spiral CT colonography data can be reviewed three-dimensionally, most radiologists rely on two dimensional methods to review this examination. The main reason for this is that the existing 3D review methods, which resemble conventional colonoscopy, are highly interactive and result in long interpretation times. New time-efficient comprehensive 3D display modes may benefit the performance of CT colonography. In chapter 7 we report a study that validates an innovative 3D review method in 30 patients. This new review method, the unfolded cubic projection, is developed to provide a comprehensive view of the colon surface. When compared to the existing 3D review methods, the new unfolded cubic projection resulted in significantly shorter interpretation times and displayed a significantly higher proportion of colon surface. No significant differences in the detection of polyps ≥5 mm were found.
In chapter 8 we compared the unfolded cubic projection with the commonly used primary 2D review method. In a study performed in 77 patients, three reviewers reviewed all data first with a primary 3D review method and after a median interval of 8.5 months with a primary 2D review method. Sensitivity, specificity, and perceptive and interpretive errors were measured. A perceptive error was defined as a polyp or a patient with a polyp that is detected by at least one reviewer, but not all reviewers, with either the primary 2D or 3D method. An interpretive error was defined as a patient without a polyp that is correctly interpreted as such by at least one reviewer, but not by all reviewers, with either the primary 2D or 3D review method. It appeared that with the primary 3D review a higher sensitivity for the detection of large polyps was achieved than with the primary 2D review method, corresponding with less perceptive errors in the detection of polyps ≥10 mm (p = 0.06). For medium-sized polyps no significant differences were observed, but when small polyps were concerned, significantly less perceptive errors were made with the primary 3D review method. The correct identification of patients without large polyps was similar for both methods, corresponding with a similar number of interpretive errors. When patients without polyps ≥6 mm and patients without any polyp -regardless of size- were considered, significantly more interpretative errors were made with the primary 3D review method were made. We conclude that use of a comprehensive primary 3D review method improves detection rates, at the expense of a significant increase of interpretive errors. This drawback may be reduced by addition of stool tagging agents or scanning with thinner slices.
Conclusions

1. CT colonography and colonoscopy have a similar ability to identify patients with large polyps in a population at increased risk for colorectal cancer. The majority of flat lesions, however, is overlooked with CT colonography, a drawback that requires improvement.

2. Patients at increased risk for colorectal cancer prefer CT colonography to colonoscopy for surveillance, despite a 20% chance that they subsequently have to undergo colonoscopy to remove polyps.

3. At present the median effective dose that is used to perform a complete CT colonography (in supine and prone position) at institutions involved in CT colonography research is approximately 10.0 mSv. Such a dose may induce 1 cancer in 4000 individuals aged 50, which may become manifest after a latent period of up to a few decades.

4. With scanners that are widely used at present, the radiation that is used to perform CT colonography can be reduced down to 3.6 mSv, resulting in a proportionally reduction in risk. Although image quality deteriorated significantly at this level, the detection of polyps remained unimpaired.

5. Theoretically the effective dose used for CT colonography can be reduced down to levels as low as 0.2 mSv, with only a slight but not significant impairment of the detection of polyps ≥5 mm. At this dose level, which cannot be attained with currently available CT scanners, the potential risk to induce cancer with CT colonography is reduced to the bare minimum.

6. Use of the 3D unfolded cubic projection to review CT colonography significantly improves time-efficiency and colon surface visibility, when compared to ‘conventional’ 3D review.

7. Primary 3D evaluation of CT colonography results in higher polyp detection rates than with primary 2D review as with the former less perceptive errors are made.