Ontario Health Technology Assessment Series 2009; Vol. 9, No. 8

Magnetic Resonance (MR) Colonography for Colorectal Cancer Screening

An Evidence-Based Analysis

Presented to the Ontario Health Technology Advisory Committee in June, 2008

September 2009

Ontario

Medical Advisory Secretariat
Ministry of Health and Long-Term Care

Suggested Citation

This report should be cited as follows:

Medical Advisory Secretariat. Magnetic resonance (MR) colonography for colorectal cancer screening: an evidence-based analysis. *Ontario Health Technology Assessment Series* 2009;9(8).

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ISSN 1915-7398 (Online)
ISBN 978-1-4249-9609-4 (PDF)

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List of Abbreviations

AUC	Area under the curve
CI	Confidence interval(s)
CRC	Colorectal cancer
CT	Computed tomographic
CTC	Computed tomographic colonography
FPR	False positive rate
GP	General practitioner
MAS	Medical Advisory Secretariat
MR	Magnetic resonance
OR	Odds ratio
OHTAC	Ontario Health Technology Advisory Committee
RCT	Randomized controlled trial
RR	Relative risk
SD	Standard deviation
SROC	Summary receiver operating characteristic
TPR	True positive rate

Glossary

Average risk for colorectal cancer	The risk of developing colon cancer among people 5o years of age and older who do not have any other risk factor for colorectal cancer
Cecum	The proximal section of the colon
Neoplasia	Abnormal growth of cells that may be benign or malignant
Segmental unblinding	A technique used in virtual colonoscopy studies for cases of discrepancy between the results of CT colonography and colonoscopy. In the technique, findings of CT colonography are revealed to the endoscopist after initial examination of each colonic segment. If a lesion was found at CT colonography but not at the initial colonoscopy, the endoscopist re-examines that segment to see whether the finding in CT colonography is a true positive or a false positive.
Sigmoid colon	The distal section of the colon
Virtual colonoscopy	A method used to detect colorectal cancers and polyps using CT or MR colonography

Background

The colorectal cancer (CRC) screening project was undertaken by the Medical Advisory Secretariat (MAS) in collaboration with the Cancer Care Ontario (CCO).

In November 2007, the Ontario Health Technology Advisory Committee (OHTAC) MAS to conduct an evidence-based analysis of the available data with respect to colorectal cancer diagnosis and prevention. The general purpose of the project was to investigate the effectiveness, cost effectiveness, and safety of the various methods and techniques used for colorectal cancer screening in average risk people, 50 years of age and older.

The options currently offered for colorectal cancer screening were reviewed and five technologies were selected for review:

- Computed tomographic (CT) colonography
- Magnetic resonance (MR) colonography
- Wireless capsule endoscopy (PillCam Colon)
- Fecal occult blood test (FOBT)
- Flexible sigmoidoscopy

In this review, colonoscopy was considered as the "gold standard" technique by which the effectiveness of all other modalities could be evaluated. An economic analysis was also conducted to determine cost-effectiveness of different screening modalities.

Evidence-based analyses have been prepared for each of these technologies, as well as summary document that includes an economic analysis, all of which are presented at the MAS Web site: http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html

Objective

The objective of this review was to evaluate the diagnostic accuracy of magnetic resonance (MR) colonography for identification of cancers and adenomatous polyps in the colon and rectum in average risk people, 50 years of age and older, in the context of colorectal cancer (CRC) screening.

Colorectal Cancer Screening

The objective of CRC screening is to reduce the burden of CRC and thereby the morbidity and mortality rate of the disease. It is believed that this goal can be achieved by regularly screening the average-risk population, enabling the detection of cancer at early, curable stages, and polyps before they become cancerous. Several methods of screening for CRC screening have been proposed by various organizations, each with their own advantages and disadvantages. There is no single infallible technique for detection and thus there is an ongoing need for improvement of screening methods. However, as with other screening tests, an effective screening technique for CRC should, at a minimum, be feasible, accurate, safe, acceptable, and cost-effective.

Optical Colonoscopy

Colonoscopy is currently considered the gold standard for detection of colorectal neoplasia, yet its true sensitivity is difficult to determine. The success of the technique in identification of colorectal lesions is highly dependent on the skills of the endoscopist. The initial measures of sensitivity of colonoscopy for adenomas were made by tandem colonoscopy studies. (1;2) Rex et al. (1) determined miss rate of colonoscopy by same day back-to-back colonoscopy, which was shown to be 13% for adenomas 6-9 mm, and 6% for adenomas ≥ 10 mm. Right colon adenomas were missed more often (27%) than left colon adenomas (21%), but the difference was not statistically significant. Hixson et al. (2) studied the colonoscopic miss rate in a blinded trial. In the study, colonoscopy identified all of the 63 lesions that were ≥10 mm, while 12% of the 6-9 mm lesions were missed.

More recently, the technique of segmental unblinding in CT colonography studies has been used to demonstrate the true sensitivity of colonoscopy for detection of adenomas. This technique is, however, an unreliable method for determination of sensitivity of colonoscopy for polyps <10 mm in size. Pickhardt et al. (3) used the technique of segmental unblinding and reported that colonoscopy had a higher sensitivity for detection of patients with adenomas ≥6 mm (90%) than that for detection of patients with adenomas ≥10 mm (88%).

The interior lining of the colon from anus to cecum can be visualized through colonoscopy, allowing for a high rate of detection for potentially curable CRCs and precancerous adenomatous polyps. The advantage of colonoscopy is that it allows detection, biopsy, and removal of the lesions identified. A single session detection and treatment would thus be more convenient for patients. In addition, the longer interval between repeat screens has the potential to minimize the costs associated with two-stage screening with other tests. The drawback of the technique is that it is invasive and is associated with clinically important complications such as bleeding and/or perforation, but the likelihood of these risks are small and they are more commonly associated with polypectomy and/or biopsy. (4) The risk of perforation is higher in the presence of conditions such as active colitis, inflammation, diverticular or ischemic disease, and prior irradiation. Although colonoscopy is not routinely indicated for patients with inflammatory bowel disease, it may be indicated for patients with ulcerative colitis of more than 10 years' duration because of an increased risk of carcinoma. I

A study conducted among the United States Medicare population examined the risk of colonic perforation following colonoscopy and sigmoidoscopy. (5) Overall, 77 perforations occurred following 39,286 colonoscopies (incidence = 1.96/1,000 procedure). The risk of perforation for those who underwent screening colonoscopy (n = 20,163) was thus 1.3/1,000. In a separate Swedish study (6) involving 6,066 diagnostic and therapeutic colonoscopies, bleeding and perforation occurred in 0.2% and 0.1% respectively, with no colonoscopy related mortality. Bleeding was confined to therapeutic colonoscopy and occurred immediately (mainly after removal of large polyps with thick stalks). Perforation at diagnostic colonoscopy occurred in the left colon and was diagnosed sooner than perforations due to therapeutic colonoscopy where the cecum was the most frequent site. Again, bleeding was correlated to the experience of endoscopist.

It should also be noted that colonoscopy does fail to reach the cecum in 5% to 10% of average-risk people due a variety of reasons such as tortuousity or malrotation of the loops, bowel spasm, diverticulitis or diverticulosis, ischemic colitis, colonic configuration from previous surgery, obstructive tumors, external compression from masses or hernia. (7)

Though there are no published randomized trials, there is indirect evidence that the technique can reduce the overall incidence and mortality of CRC. Colonoscopy was an integral part of the FOBT clinical trials that demonstrated reduction in mortality through CRC screening.

Existing techniques for CRC screening generally fall into the following three categories:

Endoscopic techniques:

- Optical colonoscopy
- Flexible sigmoidoscopy (FS)

Stool-based techniques:

- Fecal occult blood test (FOBT)
- Fecal Immunochemical Test (FIT)
- Fecal DNA testing

Imaging techniques:

- Virtual colonoscopy techniques using:
  a) Computed tomographic colonography (CT colonography)
  b) Magnetic resonance colonography (MR colonography)
- Wireless capsule endoscopy (PillCam Colon)
- Double-contrast barium enema (DCBE)

MR Colonography

MR colonography is a noninvasive method for evaluating the entire colon. Potential uses include staging of colorectal pathology and detection of cancer and precancerous lesions. It also allows for the evaluation of extracolonic pathologies including cancer metastases. In the context of CRC screening, the absence of ionizing radiation in MR colonography provides an advantage over computed tomographic (CT) colonography, in which repeat examinations every 5 years expose patients to potentially significant amounts of ionizing radiation.

Bowel preparation is performed in a way similar to that required for CT colonography or optical colonoscopy and different substances for bowel preparation are commercially available. Patients must be screened for general contraindications to magnetic resonance imaging (MRI) including the presence of metallic implants or severe claustrophobia. As with CT colonography, distension of the colon is a prerequisite for procedure and can be achieved using water, air, or carbon dioxide. Also similar to the procedure in CT colonography, patients can be imaged in the prone and supine positions.

Dark Lumen and Bright Lumen Techniques of MR Colonography

Methods of MR colonography are classified into bright lumen and dark lumen. In the bright lumen technique, colorectal lesions are shown as dark filling defects of low signal on a bright background of distended colon, while with the dark lumen technique, colorectal lesions are shown as white on a dark background of distended colon. In the dark lumen technique, the intravenous application of paramagnetic contrast agents allows visualization of the colorectal wall, discriminating it from the dark colonic lumen. This reduces the incidence of false positive findings. Residual stools or air bubbles that might mimic polyps in the bright lumen technique, remain dark. (8) The bright lumen technique is, however, less affected by movement of the patient and may be preferable in patients unable to hold their breath. (9)

Literature Review of Effectiveness

Research Questions

1. What is the accuracy of MR colonography in detection of CRCs and polyps in individuals 50 years of age and older compared with the gold standard optical colonoscopy?
2. How safe is the MR colonography procedure in the context of CRC screening?

Primary Outcomes

- Detection of CRCs in patients 50 years of age and older
- Detection of colorectal polyps in patients 50 years of age and older

Methods

Outcome Measures

- Sensitivity for cancer detection
- Per-patient sensitivity and specificity for large, medium-sized, and small polyps
- Per-polyp sensitivity for large, medium-sized, and small polyps

Inclusion Criteria

- Prospective studies comparing accuracy of MR colonography with optical colonoscopy (OC) for detection of CRCs and polyps
- Studies using MR colonography before colonoscopy
- Studies reporting either per-patient or per-polyp sensitivities/specificities
- Studies reporting results in absolute numbers
- Studies including 20 or more patients

Exclusion Criteria

- Retrospective studies
- Studies of areas other than the colon
- Studies addressing other diseases of the colon
- Studies addressing technical, educational, or other aspects of MR colonography
- Studies that did not report accuracy data

Data Extraction

The following data were extracted for analysis:

- Study characteristics
- Number of procedures completed
- Number of identified cancers
- Number of patients diagnosed with polyp (separately for categories of polyp size)
- Number of individual polyps identified by MR colonography (separately for categories of polyp size)
- Experience of radiologists

Data Analysis

Summary Receiver Operating Characteristic (SROC) methodology was used as a summary measure of the accuracy of MR colonography for identifying patients with different sizes of polyp. SROC curves and forest plots of sensitivities and specificities were produced using MetaDisc software. (10) Area under curve (AUC) and Index Q (a point on the curve where sensitivity equals specificity) were used as summary measures of the accuracy of MR colonography for the identification of patients with polyps of different size.

Pooled sensitivity and specificity and 95% CI, along with related forest plots, were constructed for per-polyp sensitivity for different size polyps. Pooled sensitivities were also used to demonstrate the accuracy of MR colonography for the identification of individual polyps of different size.

The cancer detection rate of MR colonography was calculated by dividing the total number of patients with CRC identified by MR colonography by the total number of patients with CRC identified by colonoscopy

Literature Search

A search of electronic databases [OVID MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, The Cochrane Library, and the International Agency for Health Technology Assessment (INAHTA/CRD) database] was undertaken to identify evidence published from January 1, 2003 to January 30, 2008. The search was limited to English-language articles and human studies. The search strategy is detailed in Appendix 1. The literature search identified 620 citations for virtual colonoscopy, of which 14 met inclusion criteria (see Table 1).

Table 1: Evidence Levels of Included Studies

Study Design	Evidence Level	Number of Eligible Studies
Large RCT, systematic review of RCTs*	1	0
Large RCT unpublished but reported to an international scientific meeting	1(g)	0
Small RCT	2	0
Small RCT unpublished but reported to an international scientific meeting	2(g)	0
Non-RCT with contemporaneous controls	3a	14
Non-RCT with historical controls	3b	0
Non-RCT presented at international conference	3(g)	0
Surveillance (database or register)	4a	0
Case series (multisite)	4b	0
Case series (single site)	4c	0
Retrospective review, modeling	4d	0
Case series presented at international conference	4(g)	0

*RCT refers to randomized controlled trial; g, grey literature.

Results of Literature Review

Fourteen trials representing a total of 1,305 patients met the inclusion criteria. The studies originated from five countries and the mean age of the patients ranged from 49.6 to 69 years. All of the studies used MR colonography with MRI equipment with a gradient strength of 1.5 T and one study also examined some patients (16%) using a field strength of 3 T. Most of the studies applied standard bowel preparation, while no bowel cleansing or limited bowel preparation was applied in 3 studies. (11-13). The design characteristics of the reviewed studies are summarized in Table 2, while the inclusion and exclusion criteria of each are detailed Appendix 2.

Table 2: Characteristics of the Studies on MR Colonography

Study	Country	Patients	Gender M/F	Age, years, Mean ± SD (Range)	MR System	Colonography Technique
Kuehle et al., 2007 (11)	Germany	315	NR	(50–81)	1.5 T	Dark lumen
Florie et al., 2007 (12)	The Netherlands	200	128/72	58 ± 12 (23–84)	1.5 T (n=168) 3 T (n=32)	Bright lumen
Saar et al., 2007 (14)	Switzerland	120	56/64	69 (22–87)Ŧ	1.5 T	Bright lumen
Zhang et al., 2007 (15)	China	22	9/13	58.6 (46–86)	1.5 T	Dark lumen
Hartmann et al., 2006 (16)	Germany	92	52/40	61.5 ± 14.5 (25–82)	1.5 T	Dark lumen
Ajaj et al., 2006 (17)	Germany	72	37/35	56.4 (39–71)	1.5 T	Dark lumen
Goehde et al., 2005 (13)	Germany	42	18/24	NR (23–75)	1.5 T	Dark lumen
Lauenstein et al., 2005 (18)	Germany	37	14/24	49.6 (18–89)	1.5 T	Dark lumen & bright lumen
Bielen et al., 2005 (19)	Belgium	23	16/7	60 (43–73)	1.5 T	Dark lumen
Leung et al., 2004 (20)	China	156	74/82	55.2 ± 9.1	1.5 T	Dark lumen
Lam et al., 2004 (21)	China	34	17/17	54.9 (38–70)	1.5 T	Dark lumen
Ajaj et al., 2004 (22)	Germany	50	28/22	NR (44–77)	1.5 T	Dark lumen
Ajaj et al., 2003 (23)	Germany	122	56/66	60.2 (17–90)	1.5 T	Dark lumen
So et al., 2003 (24)	China	22 (20)†	8/14	55.5	1.5 T	Dark lumen

*F indicates female; M, male; NR, not reported; SD, standard deviation; T, Tesla.

†Number analyzed.

Ŧ=Median age reported;

In terms of technique, MR colonography was performed in the prone positioning in six studies, in the supine positioning in one study, and in both positions in seven studies (see Table 3). One of these studies (18) performed MR colonography in the supine and prone positions for bright lumen images and using supine positioning only for dark lumen images. Most of the studies applied a dark lumen technique (n=11) via rectal administration of either warm tap water (n=5), air (n=4), warm tap water in one group and air in another group (n=1), or using fat enema (n=1) as a contrast agent. (15) In those studies that applied a bright lumen technique (as well as those that used a dark lumen technique with air as a contrast agent), patients were generally imaged in both the supine and prone positions. In the one study in which fat was used as a contrast medium, the medium was composed primarily of salad oil, acacia, menthol, and distilled water. The authors considered this mixture to be safe and more cost-effective than paramagnetic contrast mediums such as gadolinium, while being less sensitive to susceptibility artifacts than air.

In most studies, optical colonoscopy was performed on the same day as MR colonography. Three studies that applied limited or no bowel preparation (11-13) performed optical colonoscopy 1 to 4 weeks after MR colonography. In two studies (11;12) repeated colonoscopy was considered for lesions seen only in MR colonography, while in a third study (12) it was deemed unnecessary for all cases. In one study (11), MR colonography found lesions in 22 patients but only three were confirmed by repeat colonoscopy. Thus, false positive findings were recorded for 19 patients. Segmental unblinding was performed in only one study, (20) in which MR colonography yielded three false positive findings.

Most of the studies reported the number of incomplete colonoscopy and MR colonography examinations, but in most trials, patients with incomplete procedures were excluded. Two studies reported incomplete MR colonography, which were mainly due to water leakage, pain, failure to hold breath, and/or air in the colon. The lowest rate of complete colonoscopy was observed in the study by Zhang et al. (15) This study had the highest prevalence of cancer (72.7%), and incomplete colonoscopies were all due to stenosis of the colon.

Reported incomplete colonoscopy across the studies was mainly due to:

- tumor obstruction
- stenosis/stricture due to conditions such as ulcerative colitis
- poor bowel preparation
- elongated bowel segments
- tortuosity of the colon
- redundant sigmoid colon
- abdominal pain

Table 4 shows the rate for completed colonoscopy and MR colonography.

Table 3: Technical Characteristics of MR Colonography Studies

Study	Bowel Cleansing	Patient Positioning	Bowel Distension	Oral Tagging Agent	IV Contrast Agent	Time for Colonoscopy
Kuehle et al., 2007 (11)	No prep, no dietary restriction	Prone	Warm tap water	Gastrographin Barium Locust bean gum	Gadolinium compound	Within 4 weeks
Florie et al., 2007 (12)	Limited	Supine & prone	Water mixed with gadolinium-based contrast agent	Gadolinium	None	Within 2 weeks
Saar et al., 2007 (14)	Standard	Supine & prone	Water mixed with gadolinium-based contrast agent	None	None	Same day
Zhang et al., 2007 (15)	Standard	Supine	Fat contrast medium	None	Gadopentetate dimelumine	NR
Hartmann et al., 2006 (16)	Standard	Prone	Warm tap water	None	Gadobenate dimeglumine;	Same day
Ajaj et al., 2006 (17)	Standard	Prone	Warm tap water	None	Gd BOPTA, MultiHance	Within 36 hours
Goehde et al., 2005 (13)	No prep	Prone	Warm tap water	Highly concentrated barium sulphate	Gd BOPTA, MultiHance	7–21 days after MRC
Lauenstein et al., 2005 (18)	Standard	BL*: Supine & prone DL: Supine	Warm tap water	None	BL: None DL: Gd BOPTA, MultiHance	Same day
Bielen et al., 2005 (19)	Standard	Supine & prone (n=20) Supine (n=3)	Air	None	None	Same day
Leung et al., 2004 (20)	Standard	Supine & prone	Room air	None	None	Same day
Lam et al., 2004 (21)	Standard	Supine & prone	Room air	None	None	Same day
Ajaj et al., 2004 (22)	Standard	Prone	Warm tap water (n=25) Room air (n=25)	None	Gd BOPTA, MultiHance	Same day
Ajaj et al., 2003 (23)	Standard	Prone	Warm tap water	None	Gd BOPTA, MultiHance	Same day
So et al., 2003 (24)	Standard	Supine & prone	Room air	None	None	NR

*BL indicates bright lumen; DL, dark lumen; MRC, Magnetic resonance colonography, NR, not reported.

Table 4: Percentages of Optical Colonoscopy and CT Colonography Completed

Study	Completed Colonoscopy, %	Completed MRC, %	Reported Adverse Events
Kuehle et al., 2007 (11)	94.4	98.4	1 perforation after OC due to chronic diverticulitis
Florie et al., 2007 (12)	100	100	NR
Saar et al., 2007 (14)	95	100	2 perforations after OC (1 due to infiltrating ovarian cancer, 1 due to removal of a 30 mm sessile adenoma)
Zhang et al., 2007 (15)	81.8	100	NR
Hartmann et al., 2006 (16)	94	100	NR
Ajaj et al., 2006 (17)	100	100	None
Goehde et al., 2005 (13)	100	100	Unpleasant feeling of fullness and painful constipation in many patients who consumed highly concentrated barium sulphate. Inspection of MR site toilet showed cement-like consistency of the stool after MRC in many patients. No complication due to sedation or therapeutic intervention for OC was noted.
Lauenstein et al., 2005 (18)	100	100	NR
Bielen et al., 2005 (19)	NR	NR	NR
Leung et al., 2004 (20)	99.4	95.2	13 transient episodes of hypoxia and 10 transient episodes of hypotension, 2 episodes of hemorrhage (after polypectomy or due to tumour) in patients undergoing OC
Lam et al., 2004 (21)	100	100	NR
Ajaj et al., 2004 (22)	NR	NR	Spillage of water on the scanner in the case of 2 patients who underwent water-distended MRC*
Ajaj et al., 2003 (23)	92.6	NR	NR
So et al., 2003 (24)	90.1	100	NR

*MRC indicates magnetic resonance colonography; NR, not reported; OC, optical colonoscopy.

Sensitivity of MR Colonography for Cancer Detection

A total of 58 cancers were found in 1,305 patients. The prevalence of cancer in these studies ranged from 0% to 72.7%. Ajaj et al. (17) did not report whether the cancers were detected by MR colonography; however, from 54 remaining cancers, 53 were detected by MR colonography. Overall, the MR colonography detection rate for cancer was 98.2% (Table 5).

Studies reported lesions using the size categories of larger than 10 mm in diameter, 5 to 10 mm, and less than 5 mm, as well as using a combination of these categories. The cut-off threshold did vary slightly between studies, thus we considered three size categories, large, medium, and small for identified polyps. Where sufficient data was available, additional size categories were calculated (e.g., for medium to large or all size polyps) by grouping other size categories if such was not reported.

It is generally agreed that polyps less than or equal to 5 mm in diameter have a very low likelihood of becoming malignant and leading some investigators to ignore documenting polyps this small. The significance of medium-sized polyps has ignited debate, not only because sensitivity and specificity are affected, but because the interval at which the examination should be repeated will change. We included all types of polyps. Thirteen studies reported polyps regardless of their pathology while one (20) reported adenomatous polyps only.

Sensitivity and Specificity of MR Colonography for Detection of Patients With Polyps

Accuracy of MR colonography was analyzed in two different ways: identification of patient with polyps and the identification of individual polyps themselves. From a screening perspective, focusing analysis on per-patient data is more important than per-polyp data as it emphasizes the utility of the MR colonography as a screening tool. Table 6 summarizes number of true and false positives and true and false negatives for MR colonography for detection of patients with colorectal polyps of different sizes.

Summary Receiver Operating Characteristic Curves

A meta-analysis using SROC methodology was conducted to summarize the results of the studies on MR colonography performance. The SROC method was developed by Moses et al. (25) through a logistic transformation and linear regression of diagnostic accuracy data. In diagnostic technology, the threshold for a positive test varies across different studies and a tradeoff between sensitivity and specificity is not well defined. Therefore, the full picture of the test accuracy cannot be obtained, resulting in uncertainty regarding the value of the diagnostic test – a problem that can be resolved through a logistic regression.

First the true positive rate (TPR) and false positive rate (FPR) are transformed into their corresponding logits. The logit of the true positive rate is a natural log of [TPR/(1 − TPR)], and the logit of the false positive rate is the natural log of [FPR/(1 − FPR)]. The parameters of D and S (the difference and sum of the logits, respectively) are then calculated. By converting the TPR and FPR from each study to their logistic transform and plotting the sum and differences of the logistic transforms, a curve is generated and a linear model is fitted. The ideal position of a SROC curve on a SROC space is near the upper left corner, which indicates a perfect test or a perfect technique in differentiating diseased and non-diseased individuals. In a SROC curve, studies appear in the SROC space as a set of points and the curve is fitted through them. (26)

The area under curve (AUC) has been proposed as a summary measure of the overall performance of the test. A perfect test would have an AUC = 1, whereas a completely random test would have an AUC of 0.5. Index Q is another method to summarize the accuracy data. The index Q corresponds to the point on the curve in which sensitivity equals specificity. The SE (AUC) is the standard error of the AUC and SE (Q) is the standard error of the index (Q).

Table 5: Number of Cancers Detected by MR Colonography

Study	Patients	Patients With Cancer	Prevalence of Cancer, %	Cancers Detected by MR Colonography	Percentage of Cancers Detected by MR Colonography
Kuehle et al., 2007 (11)	315	1	0.3	1	100
Florie et al., 2007 (12)	200	0	0.0	0	N/A*
Saar et al., 2007 (14)	120	7	5.8	7	100
Zhang et al., 2007 (15)	22	16	72.7	16	100
Hartmann et al., 2006 (16)	92	7	7.6	7	100
Ajaj et al., 2006 (17)	72	4	5.6	NR	N/A
Goehde et al., 2005 (13)	42	0	0.0	0	N/A
Lauenstein et al., 2005 (18)	37	4	10.8	4	100
Bielen et al., 2005 (19)	23	1	4.3	1	100
Leung et al., 2004 (20)	156	4	1.9	3	75
Lam et al., 2004 (21)	34	2	5.9	2	100
Ajaj et al., 2004 (22)	50	1	2.0	1	100
Ajaj et al., 2003 (23)	122	9	7.4	9	100
So et al., 2003 (24)	20	2	10.0	2	100
Total	**1,305**	**58**	**N/A**	**53**	**98.2**

*N/A indicates not applicable; NR, not reported.

Table 6: Sensitivity and Specificity of MR Colonography for Detection of Patients According to Polyp Size

Study*	>10 mm		5–10 mm		<5 mm		≥5 mm		All sizes	
	True Positive	True Negative	True Positive	True Negative	True Positive	True Negative	True Positive	True Negative	True Positive	True Negative
Kuehle et al., 2007 (11)	14/20†	295/295	27/45	264/270	3/56	246/259	33/52	257/263	44/121	175/194
Florie et al., 2007 (12)	≥10 mm 9/12	≥10 mm 175/188	NR	NR	NR	NR	≥6 mm 17/26	≥6 mm 116/174	NR	NR
Saar et al., 2007 (14)	NR	NR	NR	NR	NR	NR	NR	NR	47/56	62/64
Zhang et al., 2007 (15)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hartmann et al., 2006 (16)	≥10 mm 17/17	≥10 mm 75/75	6–9 mm 21/25	6–9 mm 66/67	≤5 mm 4/17	≤5 mm 43/45	≥6 mm 38/42	≥6 mm 49/50	41/46	44/46
Ajaj et al., 2006 (17)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Goehde et al., 2005 (13)	NR	NR	NR	NR	NR	NR	NR	NR	5/17	23/25
Lauenstein et al., 2005 (18)	NR	NR	NR	NR	NR	NR	NR	NR	BL: 10/12 DL: 11/12	BL: 20/25 DL: 25/25
Bielen et al., 2005 (19)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Leung et al., 2004 (20)‡	2/5	150/151	2/26	128/130	NR	NR	4/31	122/125	NR	NR
Lam et al., 2004 (21)	NR	NR	NR	NR	NR	NR	3/4	28/30	NR	NR
Ajaj et al., 2004 (22)	≥10 mm WD: 1/1 AD: 0/0	NR	6–9 mm WD: 1/1 AD: 3/3	NR	≤5 mm WD: 0/1 AD: 0/0	NR	≥6 mm WD: 2/2 AD: 3/3	NR	WD: 2/3 AD: 3/3	NR
Ajaj et al., 2003 (23)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
So et al., 2003 (24)	≥10 mm 1/1	19/19	NR	NR	NR	NR	NR	NR	NR	NR

*Some size categories were manually calculated;; WD, water-distended group; AD, air-distended group; BL, bright lumen; DL, dark lumen, NR, not reported.
†Included cancer. ‡Adenomatous polyps only were reported.

The resulting SROC curve for categories of polyp size along with its 95% confidence intervals, and related data points are shown in Figure 1. Figures 2 and 3 show the sensitivity and specificity of MR colonography for the detection of patients with large polyps. The resulting SROC curve for medium to large polyps, along with its 95% CI and related data points is shown in Figure 4. Figures 5 and 6 show the sensitivity and specificity of MR colonography for the detection of patients with medium to large polyps.

The overall performance of MR colonography for identification of patients with large polyps was excellent. The SROC curve was located close to the top left corner and AUC was 0.97. Sensitivity decreased with decreasing polyp size. The AUC for medium-sized to large polyps was 0.91%.

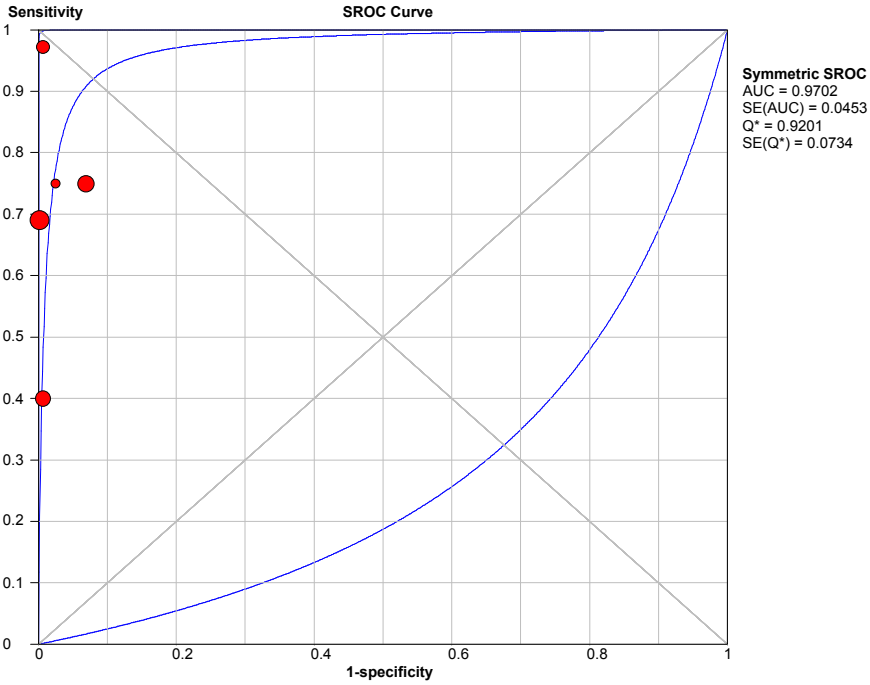


Figure 1: SROC Curve for the Detection of Patients with Large Polyps

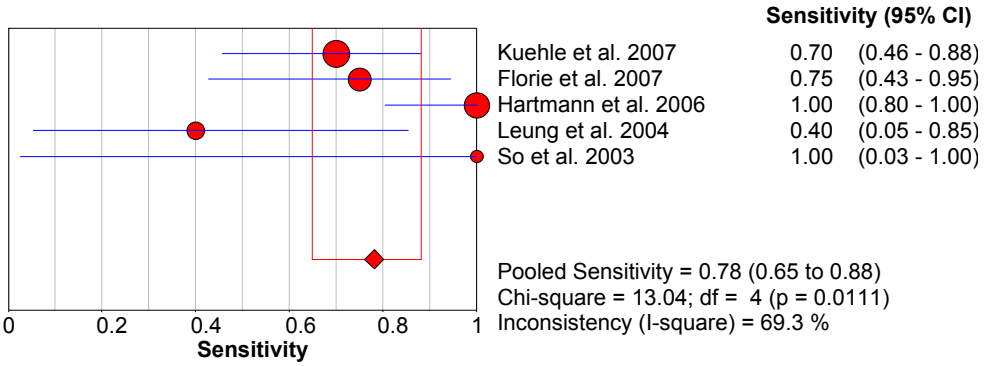


Figure 2: Per-Patient Sensitivity of MR Colonography for the Detection of Large Polyps

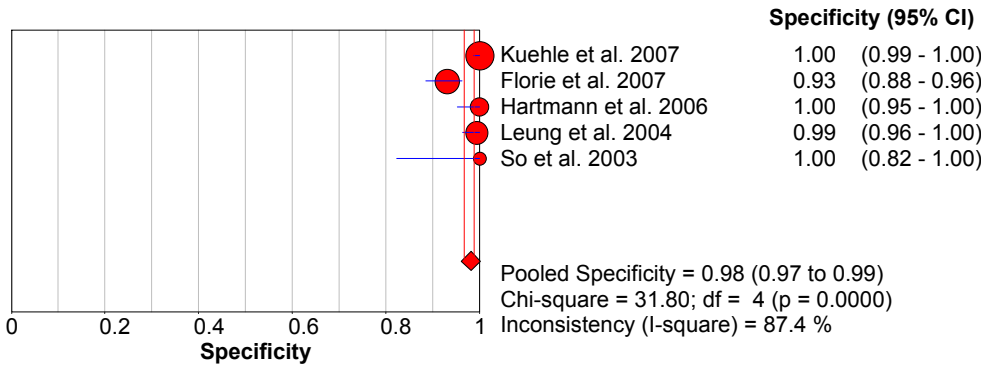


Figure 3: Per- Patient Specificity of MR Colonography for the Detection of Large Polyps

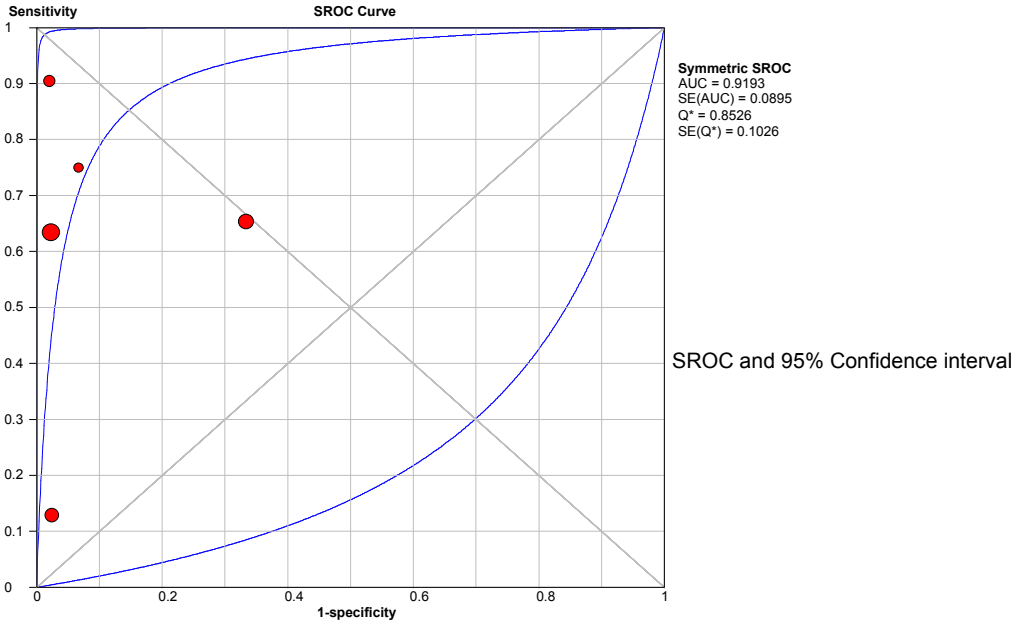


Figure 4: SROC Curve for the Detection of Patients with Medium to Large Polyps

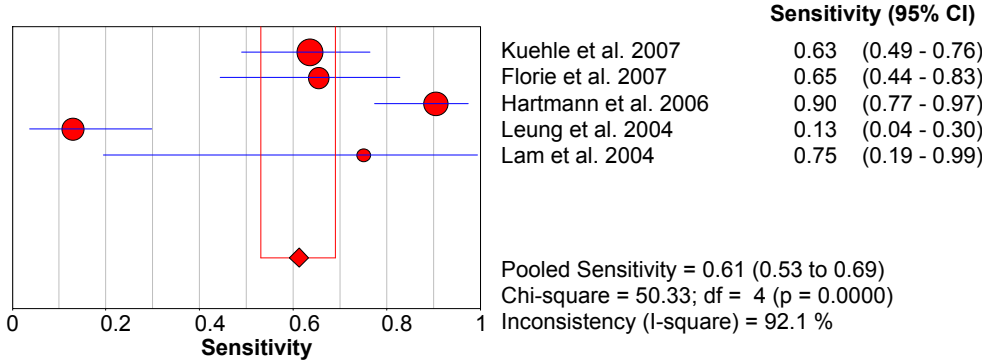


Figure 5: Per-Patient Sensitivity of MR Colonography for the Detection of Medium to Large Polyps

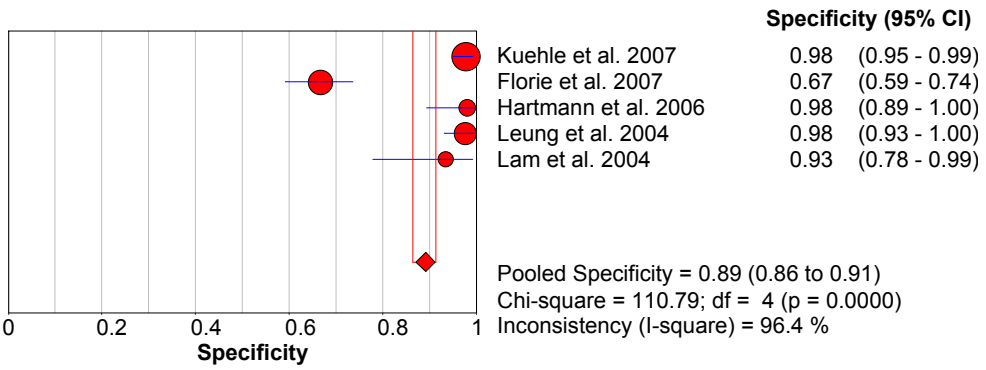


Figure 6: Per-Patient Specificity of MR Colonography for the Detection of Medium to Large Polyps

Studies were heterogeneous in per-patient sensitivity. Contrary to the sensitivity, per-patient specificity was more homogenous among the studies. It appeared that higher and homogenous specificity contributed greatly to a higher value for AUC on the SROC curve. Table 7 summarizes the resulting AUC and Q values along with their standard errors (SE).

Table 7: Area Under the Curve (AUC) and Index Q for MR Colonography for Detecting Patients With Different Polyp Sizes

Polyp size	AUC	SE (AUC)	Q	SE* (Q)
Large	0.9702	0.0453	0.9201	0.0734
Large & medium-sized	0.9193	0.0895	0.8526	0.1028

*SE indicates standard error.

Sensitivity of MR Colonography for Detection of Polyps According to Size

The sensitivity of MR colonography for detection of individual polyps of different size is summarized in Table 8. The sensitivity of MR colonography for detection of patients with different size polyps is displayed in Figures 7 to 14. Since sensitivity appeared to be lower in studies that applied no bowel preparation, results are shown separately for all studies (standard or no bowel preparation) and studies that used standard bowel preparation only.

A summary of the sensitivity of MR colonography for detection of polyps of different sizes is displayed is presented in Table 9. Because it appeared that more recent studies have reported higher sensitivity (probably through advancement in the technique and learning curve), their results are distinguished from earlier studies.

Table 8: Sensitivity of MR Colonography for Detection of Polyps According to Size

Study*	>10 mm	5–10	<5 mm	≥5 mm	All sizes
Kuehle et al., 2007 (11)	17/23†	34/59	16/153	51/82	67/235
Florie et al., 2007 (12)	≥10 mm 17/22	NR	NR	≥6 mm 32/44	NR
Saar et al., 2007 (14)	29/31	44/51	10/16	72/82	83/103
Zhang et al., 2007 (15)	4/5‡	5/9	0/4	9/14‡	26/35‡
Hartmann et al., 2006 (16)	≥10 mm 22/22	6–9 mm 32/41	≤5 mm 4/44	≥6 mm 54/63	58/107
Ajaj et al., 2006 (17)	NR	NR	0/65	22/25†	22/90†
Goehde et al., 2005 (13)	≥10 mm 3/6	6–9 mm 2/12	<6 mm 1/11	>6 mm 5/18	6/29
Lauenstein et al., 2005 (18) Bright lumen Dark lumen	NR	NR	≤5 mm 0/4 0/4	>5 mm 9/11 11/11	9/15 11/15
Bielen et al., 2005 (19)	≥10 mm 1/1	5–9 mm 1/1	0/4	2/3	2/7
Leung et al., 2004 (20) (Ad)	2/7	3/60	NR	5/67	NR
Lam et al., 2004 (21)	1/1	1/2	2/11	2/3	4/14
Ajaj et al., 2004 (22) Water distension Air distension	≥10 mm 1/1 0/0	6–9 mm 1/1 3/3	≤5 mm 0/1 0/0	≥6 mm 2/2 3/3	2/3 3/3
Ajaj et al., 2003 (23)	2/2	16/18	0/30	18/20	18/50
So et al., 2003 (24)	≥10 mm 1/1	5–9 mm 0/1	0/12	1/2	1/14

*Some size categories were manually calculated; Ad=Reported only adenomatous polyps;
†Included cancer.
‡Cancers were manually excluded; NR, not reported.

Table 9: Pooled Per-Polyp Sensitivity of MR Colonography for Colorectal Polyp Detection by Size

	Sensitivity of Polyp Detection, %		
Polyp Size	Standard/No/Limited BP*	Standard BP	Standard BP & Published 2005–2008
Large	82 (74–88)	89 (79–95)	95 (86–99)
Medium-sized	70 (63–76)	81 (73–87)	80 (71–88)
Large & medium-sized	75 (70–79)	85 (79–89)	86 (80–90)
Small	9 (6–13)	8 (5–13)	10 (6–17)

*BP indicates bowel preparation.

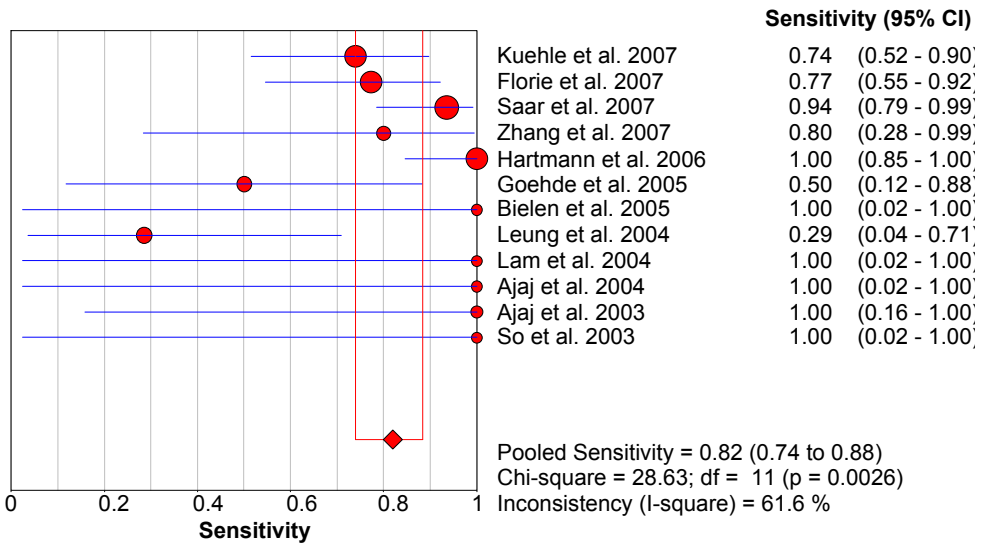


Figure 7: Sensitivity of MR Colonography for the Detection of Large Polyps (All Studies)

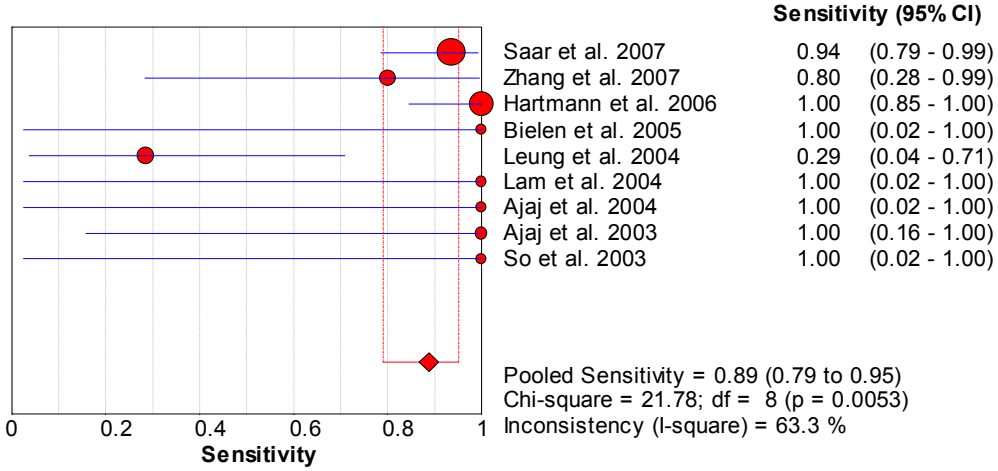


Figure 8: Sensitivity of MR Colonography for the Detection of Large Polyps (Standard Bowel Preparation)

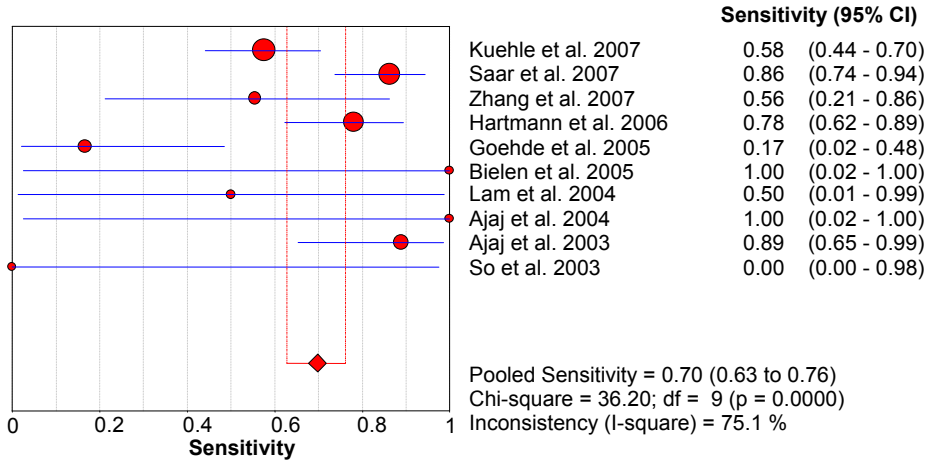


Figure 9: Sensitivity of MR Colonography for the Detection of Medium Polyps

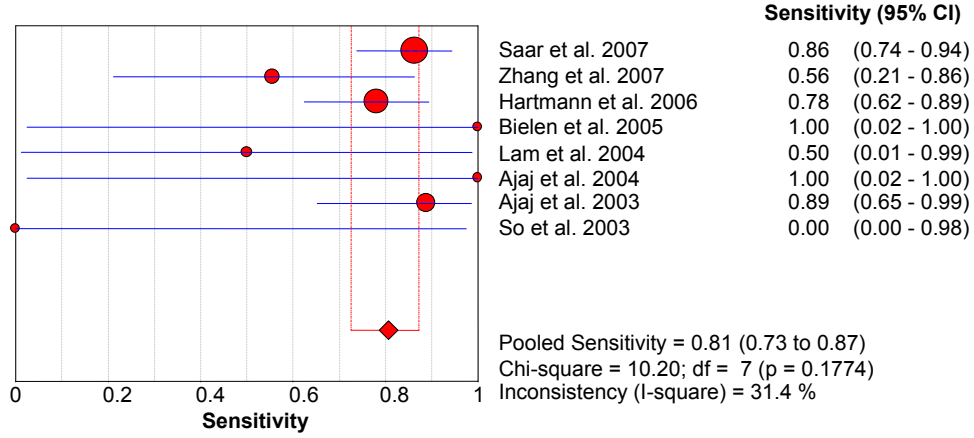


Figure 10: Sensitivity of MR Colonography for the Detection of Medium Polyps With Standard Bowel Preparation

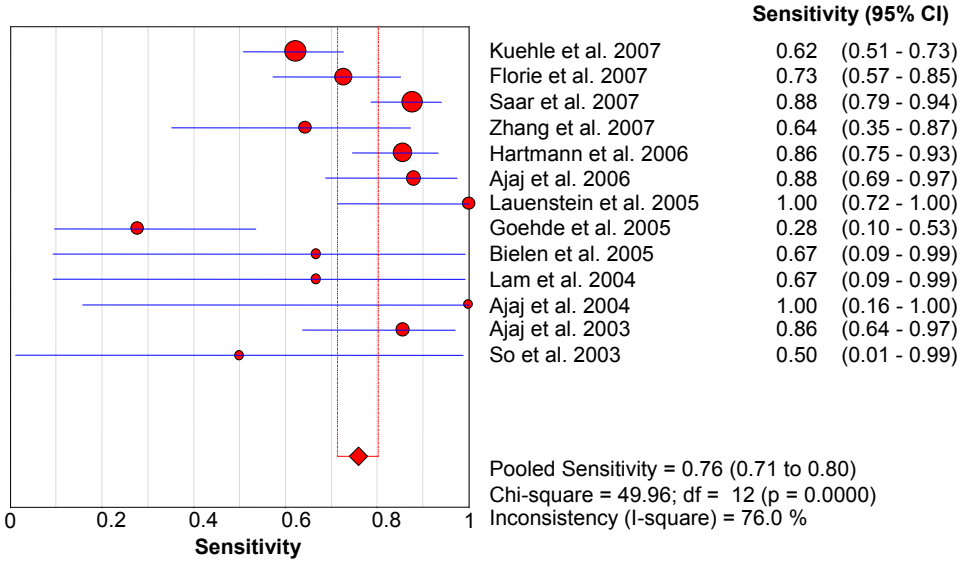


Figure 11: Sensitivity of MR Colonography for the Detection of Medium and Large Polyps

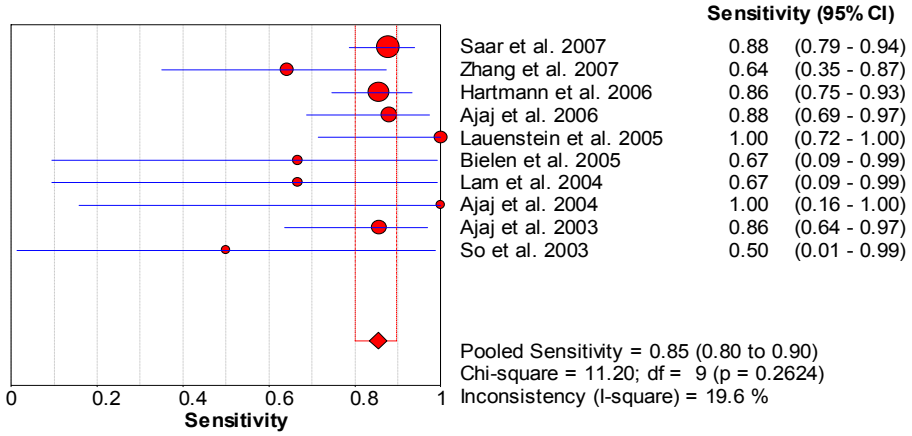


Figure 12: Sensitivity of MR Colonography for the Detection of Medium to Large Polyps With Standard Bowel Preparation

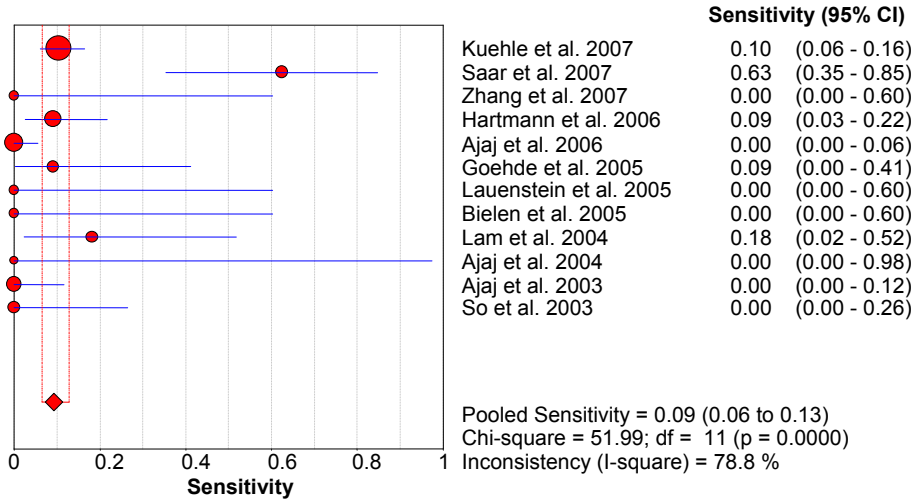


Figure 13: Sensitivity of MR Colonography for the Detection of Small Polyps

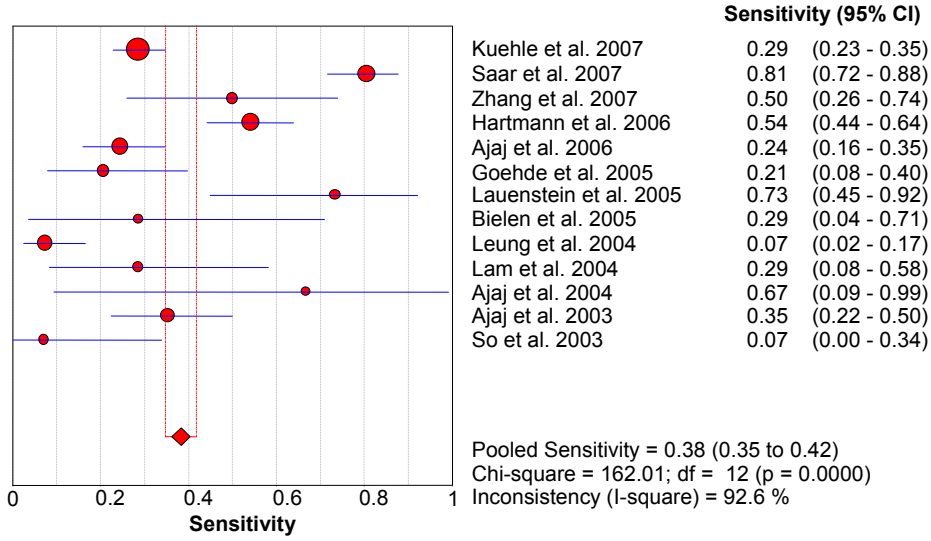


Figure 14: Sensitivity of MR Colonography for the Detection of All Size Polyps

Earlier Versus Recent Studies

Recently published studies are more likely to reflect a greater level of experience and familiarity with MR colonography on the part of participating radiologists compared with earlier studies. The range of reported sensitivities differs between those studies published since 2006 and those published between 2003 and 2005 (see Figure 15).

Regardless of the publishing year, most of the studies included in this report involved two radiologists who reviewed images independently and provided a consensus. A summary of the experience of the participating radiologists and endoscopists in the included studies is provided in Table 10.

Dark Lumen Versus Bright Lumen

The introduction of the dark lumen technique provided a further improvement in the diagnostic accuracy of MR colonography as demonstrated by Lauenstein et al. (18) This study found both the sensitivity and specificity of dark lumen to be higher than bright lumen, with the former identifying all 11 polyps larger than 5 mm in diameter (sensitivity 100%), while the bright lumen technique missed two polyps measuring 7 and 8 mm in diameter (sensitivity 81.8%). The dark lumen technique gave no false positive results as residual stool could be differentiated from colorectal lesions (specificity 100%), while the bright lumen technique yielded five false positive results because of an inability to make this distinction.

MRI Gradient Strength

Most clinical studies evaluating the performance characteristics of MR colonography have been conducted at 1.5 T. Although experience with MR colonography at 3 T is limited, the first clinical results are promising.

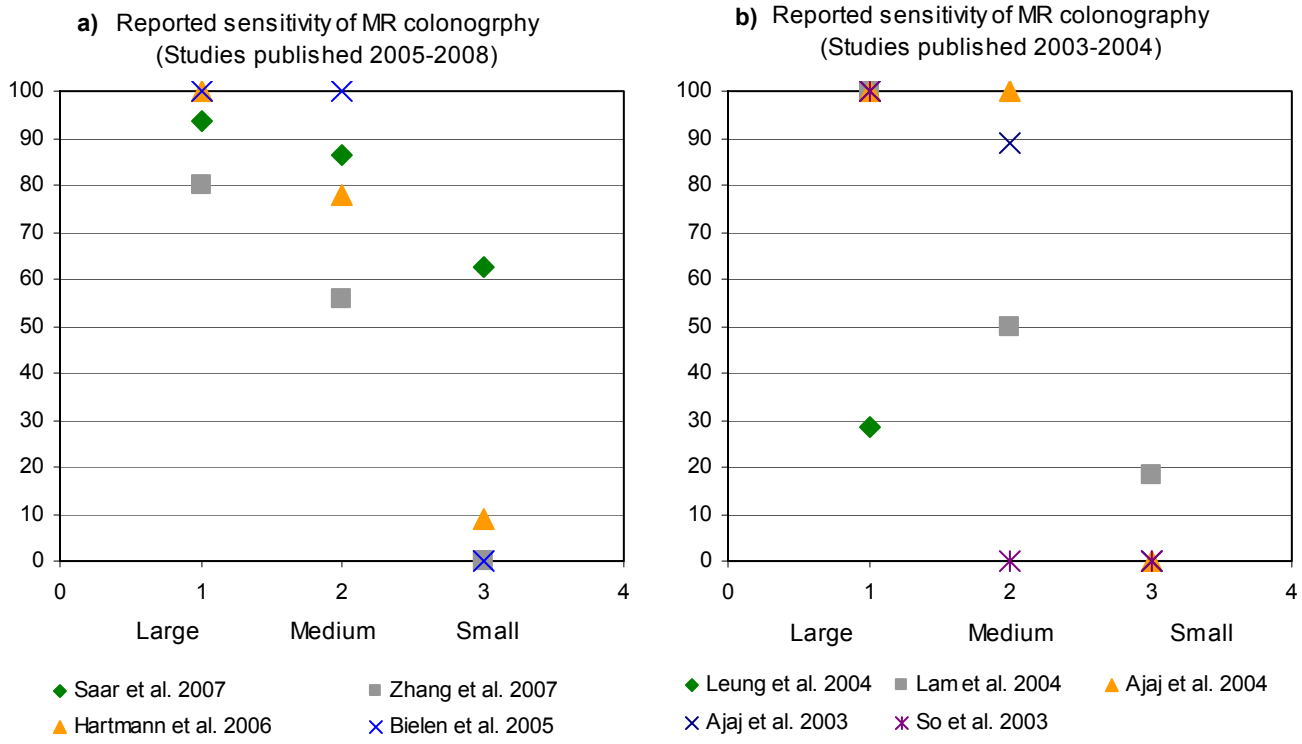


Figure 15: Sensitivity Range for Polyps of Different Sizes: (a) Earlier Studies (b) Recent Studies

Table 10: Experience of Radiologists and Practitioners

Study	Radiologist	Gastroenterologist
Kuehle et al., 2007 (11)	2 experienced radiologists	Gastroenterologist with 3 years experience in colonoscopy and >200 colonoscopies during previous 12 months (blinded)
Florie et al., 2007 (12)	1 abdominal radiologist with 11 years of clinical experience with MR imaging, 20 CTC*, and 40 MRC and 1 second year resident in radiology with 160 CTC and 40 MRC experience	Gastroenterologist or GI surgeon with 15 (3–25) years of experience and 1 GI fellow with direct supervision (blinded)
Saar et al., 2007 (14)	2 experienced radiologist with >50 MRCs. Blinded to the patient's history, clinical data, and symptoms	Experience colonoscopist with > 1,000 colonoscopies
Zhang et al., 2007 (15)	2 radiologists blinded to the colonoscopic data	NR
Hartmann et al., 2006 (16)	2 radiologist with more than 5–15 years experience and 3 gastroenterologist with more than 5 years experience in performing colonoscopy (all blinded to the results of OC)	1 gastroenterologist with at least 5 years experience in performing endoscopy (blinded)
Ajaj et al., 2006 (17)	2 radiologists with >4 years in abdominal MR imaging (blinded to the results of colonoscopy)	1 gastroenterologist (blinded)
Goehde et al., 2005 (13)	2 radiologists with >4 years in abdominal MR imaging (blinded to the results of OC)	1 gastroenterologist (blinded)
Lauenstein et al., 2005 (18)	2 experienced MR radiologists unaware of patient's history or the reason for patient's referral	1 gastroenterologist (blinded)
Bielen et al., 2005 (19)	1 radiologist familiar with abdominal imaging and virtual colonoscopy and 1 resident with limited experience in reading virtual colonoscopy	Experienced endoscopist
Leung et al., 2004 (20)	2 MR radiologists blinded to the endoscopy results	Experienced endoscopist unaware of the MRC findings on intubation of endoscopy
Lam et al., 2004 (21)	2 radiologists blinded to the endoscopy results	Experienced colonoscopist
Ajaj et al., 2004 (22)	2 experienced radiologists blinded to the colonoscopic data	NR
Ajaj et al., 2003 (23)	2 experienced radiologists	NR
So et al., 2003 (24)	2 radiologists blinded to the colonoscopic findings	NR

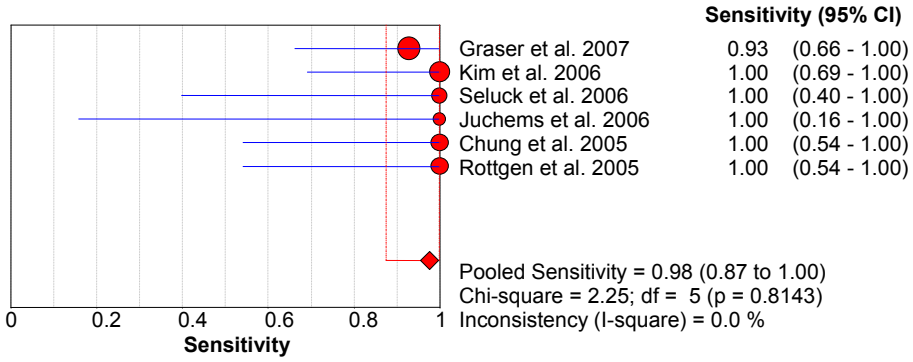
*CTC refers to CT colonography; MRC, MR colonography; NR, not reported; OC, optical colonoscopy; GI, gastrointestinal; RC, repeat colonoscopy; SU, segmental unblinding; Blinded, blinded to the results of the other test.

Adverse Events

Among 1,305 patients undergoing colonoscopy, perforation occurred in three cases. The reasons were chronic diverticulitis, infiltrating ovarian cancer, and removal of a 30 mm sessile polyp. Hemorrhage occurred in two patients following polyp removal. Water spillage was the only adverse effect reported during MR colonography. In the study by Goehde et al. (13), however, the use of highly concentrated barium sulphate for MR colonography resulted in a painful constipation and the formation of cement-like stool.

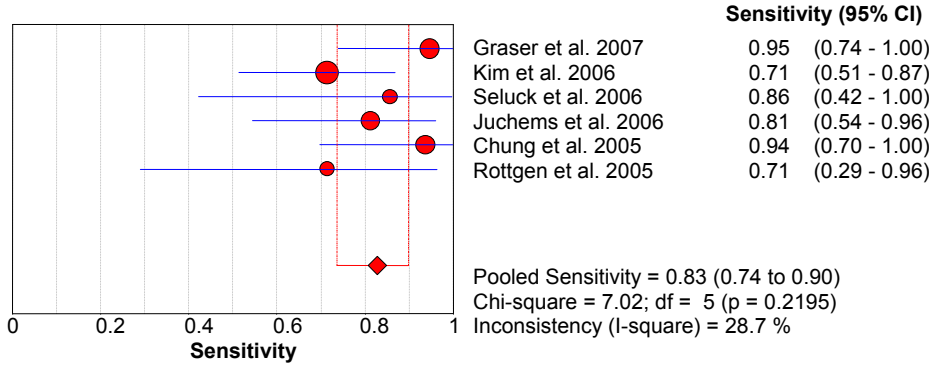
Sensitivity of MR Colonography Compared With CT Colonography

Studies on CT colonography with 16-slice or 64-slice CT equipment have reported higher sensitivity for detection of large and medium polyps than those using 1-, 4-, or 8-slice equipment (Figures 16 and 17). Figure 18 shows pooled sensitivity of both MR colonography and CT colonography for detection of cancer and different sized polyps.



Studies used 16-slice or 64-slice scanners.

Figure 16: Sensitivity of CT Colonography for the Detection of Large Polyps



Studies used 16-slice or 64-slice Scanners

Figure 17: Sensitivity of CT Colonography for the Detection of Medium Polyps

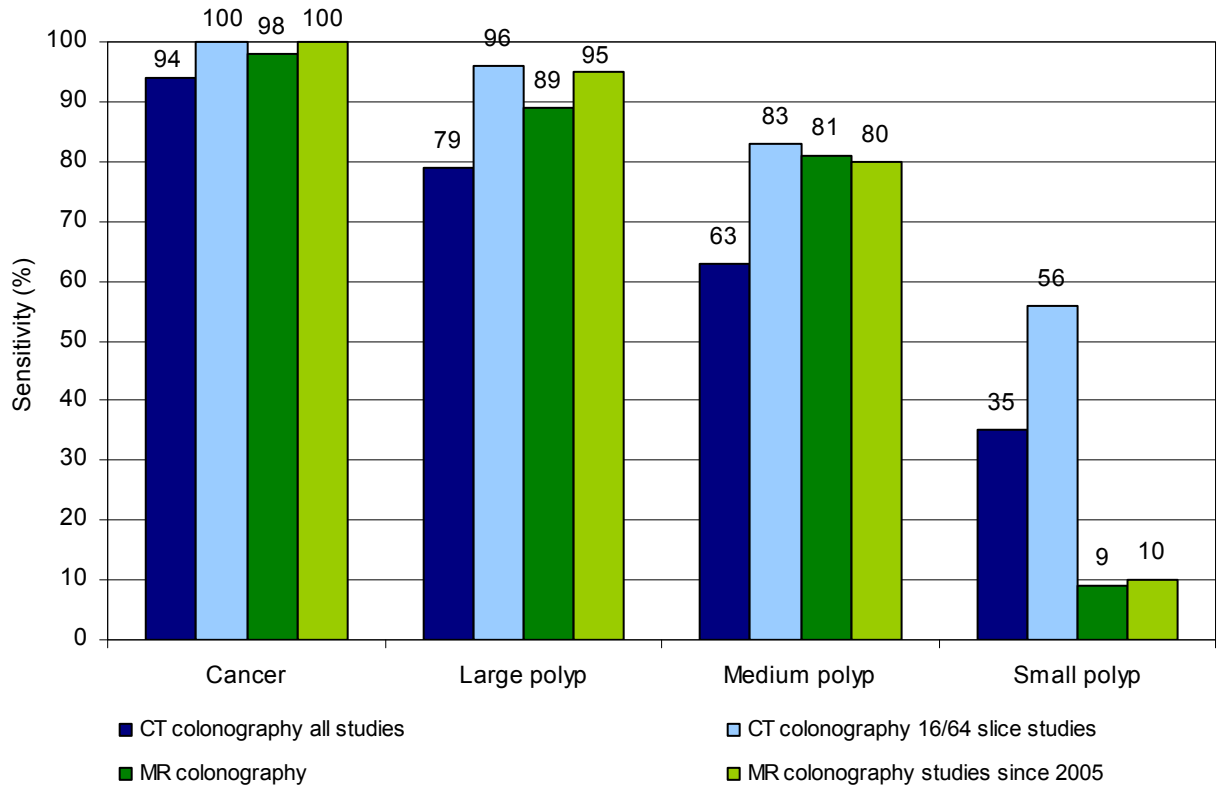


Figure 18: Pooled Sensitivity of MR Colonography Compared With CT Colonography

Conclusions

- MR colonography and CT colonography with 16-slice or 64-slice scanners have equal sensitivity for the detection of CRC, as well as for the detection of large and medium sized polyps; however, MR colonography does not carry the associated risks of ionizing radiation.
- MR colonography and CT colonography with 16-slice or 64-slice scanners can reliably detect most CRCs and large colorectal polyps; however, about 20% of medium-sized colorectal polyps will be missed by both techniques.
- None of the techniques can reliably detect small polyps and MR colonography has a much lower sensitivity for the detection of small polyps compared with CT colonography.

Appendices

Appendix 1: Literature Search Strategy

Search date: January 30, 2008
Databases Searched: MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to January Week 3 2008>
Search Strategy:

- exp Colonography, Computed Tomographic/ (727)
- (virtual colonoscopy or virtual colonography).mp. (364)
- ((ct or computed tomographic or mr or mri or magnetic resonance) adj2 (colonography or colonoscopy)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (956)
- or/1-3 (1076)
- exp Colorectal Neoplasms/ (51853)
- exp Colonic Polyps/ (2221)
- ((colon$ or colorectal or rectal or rectum) adj5 (precancer$ or pre-cancer$ or polyp$ or neoplasm$ or adenoma$ or cancer$ or dysplasia$ or neoplasia$ or tumo?r$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (62656)
- exp Precancerous Conditions/ (10419)
- or/5-8 (74178)
- 4 and 9 (845)
- limit 10 to (humans and english language and yr="2002 - 2008") (596)
- (meta analy$ or metaanaly$ or pooled analysis or random$ or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (376626)
- exp Technology Assessment, Biomedical/ or exp Evidence-Based Medicine/ (30570)
- 11 and (12 or 13) (68)
- 11 (596)
- limit 15 to (case reports or comment or editorial or letter or "review") (236)
- 15 not 16 (360)
- 14 or 17 (390)

Database: EMBASE <1980 to 2008 Week 04>
Search Strategy:

- exp Computed Tomographic Colonography/ (1026)
- (virtual colonoscopy or virtual colonography).mp. (348)
- ((ct or computed tomographic or mr or mri or magnetic resonance) adj2 (colonography or colonoscopy)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1275)
- or/1-3 (1386)
- exp Colorectal Cancer/ (31930)
- exp Colorectal Tumor/ (1892)
- exp Colon Polyp/ (6733)

- exp Colon Adenoma/ (2353)
- ((colon$ or colorectal or rectal or rectum) adj5 (precancer$ or pre-cancer$ or polyp$ or neoplasm$ or adenoma$ or cancer$ or dysplasia$ or neoplasia$ or tumo?r$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (103335)
- exp "Precancer and Cancer-In-Situ"/ (21099)
- or/5-10 (123356)
- 4 and 11 (982)
- limit 12 to (human and english language and yr="2002 - 2008") (688)
- (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or random$ or data extraction or cochrane).ti,ab. (401281)
- exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (277742)
- 13 and (14 or 15) (95)
- 13 (688)
- limit 17 to (editorial or letter or note or "review") (280)
- Case Report/ (975460)
- 17 not (18 or 19) (381)
- 16 or 20 (423)

Appendix 2: Inclusion and Exclusion Criteria of Included Studies

Study	Inclusion Criteria	Exclusion Criteria†
Kuehle et al., 2007 (11)	Screening population (Randomly selected subjects over 50 years)	Prior history of CRC or polyps, rectal bleeding, positive FOBT, altered bowel habits within the previous 12 months, colonoscopy within the previous 5 years
Florie et al., 2007 (12)	Consecutive patients with a personal of family history of colorectal polyp or cancer, scheduled for OC	Age younger than 18 years, presence of colostomy after colorectal surgery, oral or intravenous administration of another contrast medium within 48 hours prior to MR colonography, inability to hold breath for 25 seconds
Saar et al., 2007 (14)	Consecutive patients scheduled for OC including non-specific abdominal complaints, positive FOBT, follow-up after polypectomy, age over 18 years	Pregnancy
Zhang et al., 2007 (15)	Consecutive patients referred for OC (Reasons for OC: rectal bleeding, positive FOBT, altered bowel habits	General contraindications for MRI
Hartmann et al., 2006 (16)	Consecutive patients referred for OC (Reasons for OC: GI bleeding, screen for CRC, follow-up of an abnormal FOBT, iron deficiency anemia, GI symptoms such as abdominal pain, diarrhea,	Age younger than 18 years, personal or family history of genetic poly syndrome, known intolerance to MR contrast agent
Ajaj et al., 2006 (17)	Patients referred for OC for various indications including first CRC screening over 50 years of age, abdominal pain, suspected Crohn's disease or ulcerative colitis, chronic diarrhea, positive family history of CRC, positive FOBT, suspected diverticulitis	General contraindications for MRI
Goehde et al., 2005 (13)	Patients scheduled for OC in a private gastroenterologic practice	NR
Lauenstein et al., 2005 (18)	Patients referred for OC because of symptoms including rectal bleeding, positive FOBT, chronic diarrhea, positive family history of CRC	General contraindications for MRI
Bielen et al., 2005 (19)	Follow-up after resection of colorectal tumour or polyps, familial high risk for CRC, anal bleeding, suspicion of colon tumour or other pathologic conditions necessitating colonoscopy	IBD, pregnancy
Leung et al., 2004 (20)	High risk (n=86) and average risk individuals (n=79) High risk: Patients who were referred for OC because of symptoms suggestive of colorectal neoplasm, positive FOBT, family history of CRC in one or more first-degree relatives	Patients who had barium enema or colonoscopy within last 5 years, known history of IBD or diverticular disease, severe comorbid illnesses that might increase the risk of colonoscopy, current use of anticoagulants
Lam et al., 2004 (21)	Patients recruited from a health exhibition on CRC screening. Patients were stratified into high risk (n=13) and average risk groups (i.e. no symptoms suggestive of colorectal disease (n=21)	Long term use of anticoagulants, history of complicated diverticular disease or ischemic bowel, severe comorbidities such as cirrhosis or bleeding tendency
Ajaj et al., 2004 (22)	Patients referred for OC for a variety of indications, including positive family history of CRC, positive FOBT, chronic diarrhea,	NR
Ajaj et al., 2003 (23)	Patients referred for OC for various indications including abdominal pain, suspected Crohn's disease or ulcerative colitis, positive FOBT. Family history of CRC, elevated hepatic enzymes, immunosupression, chronic diarrhea, previous history of CRC, and other	NR
So et al., 2003 (24)	Patients referred for OC due to change in bowel habit and positive FOBT	NR

*FOBT indicates fecal occult blood test; GI, gastrointestinal; IBD, inflammatory bowel disease; MR, magnetic resonance; MRI, magnetic resonance imaging; NR, not reported; OC, optical colonoscopy. †Includes contraindication for MRI scanning.

References

(1) Rex DK, Cutler CS, Lemmel GT, Rahmani EY, Clark DW, Helper DJ et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. Gastroenterology 1997; 112(1):24-28.

(2) Hixson LJ, Fennerty MB, Sampliner RE, Garewal HS. Prospective blinded trial of the colonoscopic miss-rate of large colorectal polyps. Gastrointest Endosc 1991; 37(2):125-127.

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