



# Diagnostic accuracy of computed tomography colonography for tumor depth in colorectal cancer: A systematic review and meta-analysis

Nobuaki Hoshino<sup>\*</sup>, Takashi Sakamoto, Koya Hida, Yoshiharu Sakai

Department of Surgery, Kyoto University Graduate School of Medicine, 54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto, 606-8507, Japan

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## ABSTRACT

**Background:** Accurate preoperative determination of tumor depth is a major concern in colorectal cancer. Assessment of tumor depth can influence the treatment strategy for colorectal cancer, but there is currently no universal diagnostic standard. This review sought to evaluate the diagnostic performance of computed tomography (CT) colonography for tumor infiltration depth in colorectal cancer.

**Methods:** The PubMed, Scopus, and Cochrane Central Register of Controlled Trials databases were searched to identify studies that compared the tumor depth using CT colonography with that determined using pathological assessment. Relevant data were extracted from the eligible studies by two review authors working independently. Any disagreement was resolved by discussion. The quality of the studies was assessed using the QUADAS-2 tool. The diagnostic performance of CT colonography for tumor depth in colorectal cancer was evaluated by meta-analysis using sensitivity and specificity values and diagnostic odds ratios.

**Results:** The systematic literature search identified 16 eligible studies. The pooled sensitivity and specificity values and diagnostic odds ratios were 97.8% (95% confidence interval [CI] 88.1–99.6), 76.4% (95% CI 59.9–87.5), and 142.6 (95% CI 20.0–1071.0) for T2 invasion, 97.7% (95% CI 92.1–99.3), 83.5% (95% CI 75.9–89.0), and 212.1 (95% CI 50.6–888.1) for T3 invasion, and 84.9% (95% CI 61.7–95.1), 97.5% (95% CI 93.2–99.1), and 219.5 (95% CI 37.8–1273.6) for T4 invasion, respectively.

**Conclusions:** CT colonography was found to have high diagnostic performance and was useful for determining tumor depth in colorectal cancer.

## 1. Introduction

Accurate diagnosis of tumor depth is a major concern in the treatment strategy for colorectal cancer. The standard treatment for colorectal cancer is surgical resection with lymph node dissection [1]. However, local (endoscopic or transanal) resection without lymph node dissection may be sufficient to cure early-stage disease [1–3], whereas preoperative treatment including chemotherapy and radiotherapy or extended surgery may be needed to achieve curative resection in patients with advanced disease [4]. Preoperative diagnosis of tumor depth can influence the treatment strategy for colorectal cancer, and the diagnostic performance of computed tomography (CT) in this regard has been investigated [5]. However, the diagnostic accuracy of CT may be insufficient to accurately assess tumor depth. In this review, we investigate the diagnostic performance of CT colonography in estimation of tumor depth of colorectal cancer.

## 2. Material and methods

### 2.1. Inclusion criteria

Studies that compared tumor depth obtained by CT colonography with that determined by pathologic assessment in patients with colorectal cancer were considered for inclusion in this review, regardless of the type of study. Pathological findings were set as the reference standard. Studies that reported both sensitivity and specificity were included. CT colonography was defined to be 3-dimensional in this review.

### 2.2. Literature search

A systematic literature search of the PubMed, Scopus, and Cochrane Central Register of Controlled Trials electronic databases was conducted on August 8, 2018. The search was performed with no restriction of publication date, and the search terms included “colon cancer,”

<sup>\*</sup> Corresponding author.

E-mail address: [hoshinob@kuhp.kyoto-u.ac.jp](mailto:hoshinob@kuhp.kyoto-u.ac.jp) (N. Hoshino).

“rectal cancer,” “colorectal cancer,” “CT,” “colonography,” “enema,” and related terms (Table S1).

### 2.3. Study selection and data collection

The titles and abstracts of articles identified by the literature search were independently screened by two of the review authors (NH, TS) to determine whether they met the inclusion criteria. After screening, the full texts of the articles were assessed before final inclusion in the review. Duplicate publications were excluded by referring to the study titles and author names. During the screening process, any disagreement between the two reviewers was resolved by discussion. All data were extracted by the same two reviewers and checked for accuracy.

### 2.4. Assessment of methodological quality

The QUADAS-2 tool was used to evaluate the quality of the included studies [6] in two categories: risk of bias and applicability concerns. The risk of bias category includes four domains: patient selection, index test, reference standard, and flow and timing. The applicability concerns category includes three domains: patient selection, index test, and reference standard. The risk of each domain was judged to be high, low, or unclear.

### 2.5. Statistical analysis

Sensitivity and specificity were calculated for each study and shown as forest plots by Review Manager (Cochrane Collaboration, London, UK) [7]. Heterogeneity is often found in meta-analyses of diagnostic accuracy [8]. Bivariate meta-analysis of sensitivity and specificity was performed using STATA 13.0 software (Stata Corporation, College Station, TX, USA) [9], and the pooled sensitivity and specificity values and diagnostic odds ratios for T2, T3, and T4 invasion were calculated because the analysis can allow for variability in the included studies. A summary point estimate with a 95% confidence region was created by Review Manager according to the Cochrane Library [8]. The diagnostic performance was judged to be high when both the sensitivity and the specificity were > 80% and the diagnostic odds ratio was > 10.

## 3. Results

### 3.1. Study selection

The literature search identified 1474 articles potentially eligible for inclusion in the meta-analysis. After exclusion of 553 duplications, the titles and abstracts of the remaining 921 studies were screened. Then, 58 full-text articles were assessed to determine whether they met our inclusion criteria. Finally, 16 studies were included in the meta-analysis (Fig. 1) [10–25].

### 3.2. Characteristics of included studies

The 16 studies included in the meta-analysis were reported from 7 countries between 2002 and 2018. All 16 studies had a cohort design; 13 were prospective and 3 were retrospective. Twelve studies involved colorectal cancer, 3 involved colon cancer, and 1 study involved rectal cancer (Table 1).

### 3.3. Methodological quality

A summary of the methodological quality of the included studies is shown in Table 2.

#### 3.3.1. Risk of bias

In total, 8 studies were judged to be at low risk of bias and 8 to be at unclear risk in the patient selection domain; 11 studies were judged to

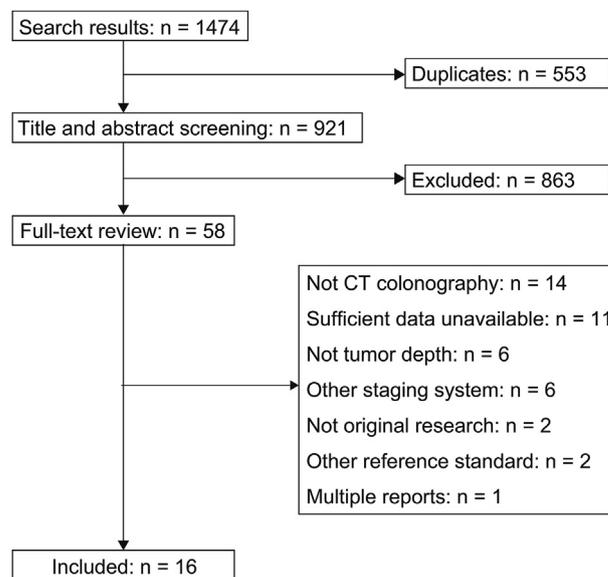


Fig. 1. Flow diagram of study selection. CT, computed tomography.

be at low risk, 3 at high risk, and 2 at unclear risk in the index test domain. All studies were judged to be at low risk in the reference standard domain. Seven studies were judged to be at low risk, 1 at high risk of bias, and 8 at unclear risk in the flow and timing domain.

#### 3.3.2. Applicability concerns

All studies were judged to be at low risk in the patient selection, index test, and reference standard domains.

#### 3.4. Diagnostic performance

The sensitivity and specificity of CT colonography for T2, T3, and T4 invasion in each study is shown with the 95% confidence interval (CI) values in Fig. 2. Summary estimates obtained by the bivariate approach are shown in Fig. 3. The pooled sensitivity and specificity values and diagnostic odds ratios were 97.8% (95% CI 88.1–99.6), 76.4% (95% CI 59.9–87.5), and 142.6 (95% CI 20.0–1017.0) for T2 invasion, 97.7% (95% CI 92.1–99.3), 83.5% (95% CI 75.9–89.0), and 212.1 (95% CI 50.6–888.1) for T3 invasion, and 84.9% (95% CI 61.7–95.1), 97.5% (95% CI 93.2–99.1), and 219.5 (95% CI 37.8–1273.6) for T4 invasion, respectively.

## 4. Discussion

In this review, we investigated the diagnostic performance of CT colonography for tumor depth using sensitivity and specificity values and diagnostic odds ratios. CT colonography showed high diagnostic performance for T2, T3, and T4 invasion.

Accurate diagnosis of tumor depth helps in the selection of the optimal treatment strategy for colorectal cancer. For T1 tumors, local resection, including endoscopic and transanal resection, can be a useful therapeutic option instead of surgical resection [1–3]. Clearly, there is a considerable difference between surgical resection and local resection in terms of the invasiveness of the procedure for patients. Although there is no consensus regarding the indications for local resection because of the potential for recurrence using this strategy, some patients benefit from local resection due to it being less invasive [1–3]. In contrast, the presence of a T4 tumor can influence the indications for preoperative chemotherapy and/or radiotherapy [4,26] and a surgical approach, either open or laparoscopic, to achieve radical surgery [27].

In a meta-analysis of studies of the diagnostic performance of CT for tumor depth of colon cancer, Leufkens et al. [28] reported pooled

**Table 1**  
Characteristics of studies included in this review.

Study	Year	Design	Country	Lesions (n)	Type of cancer	Assessment approach (No. of readers for each CTC, n)	Reference standard
Chung [10]	2005	Prospective, cohort	Korea	21	Colorectal	Consensus (2)	Pathology findings
da Fonte [11]	2012	Prospective, cohort	Brazil	25	Colorectal	Consensus (2)	Pathology findings
Flor [12]	2013	Prospective, cohort	Italy	75	Colorectal	Consensus (2)	Pathology findings
Kayashima [13]	2008	Prospective, cohort	Japan	40	Colon	Consensus (2)	Pathology findings
Kim [14]	2007	Prospective, cohort	Korea	73	Colorectal	Independent (1)	Pathology findings
Laghi [15]	2002	Prospective, cohort	Italy	33	Colorectal	Consensus (2)	Pathology findings
Maras-Simunic [16]	2009	Prospective, cohort	Croatia	41	Colorectal	Consensus (2)	Pathology findings
Morimoto [17]	2018	Retrospective, cohort	Japan	155	Colon	Consensus (2)	Pathology findings
Nagata [18]	2004	Prospective, cohort	Japan	319	Colorectal	Independent (2)	Pathology findings
Narayanan [19]	2014	Prospective, cohort	India	26	Colorectal	Consensus (2)	Pathology findings
Sato [20]	2017	Retrospective, cohort	Japan	86	Colon	NR (NR)	Pathology findings
Schaeffer [21]	2014	Prospective, cohort	Germany	18	Colorectal	Consensus (2)	Pathology findings
Shida [22]	2017	Prospective, cohort	Japan	45	Rectal	Consensus (6+)	Pathology findings
Singh [23]	2015	Prospective, cohort	India	22	Colorectal	NR (NR)	Pathology findings
Stagnitti [24]	2015	Prospective, cohort	Italy	127	Colorectal	Consensus (2)	Pathology findings
Utano [25]	2008	Retrospective, cohort	Japan	246	Colorectal	Consensus (3)	Pathology findings

CTC, computed tomography colonography; NR, not reported.

sensitivity and specificity values of 0.77 and 0.03, respectively. In another meta-analysis, Nerad et al. [5] reported pooled sensitivity and specificity values of 0.90 and 0.69, respectively, for T3 invasion and 0.77 and 0.70 for deep T3 invasion. In both meta-analyses, the diagnostic performance of CT for tumor depth was not particularly high for colon cancer. However, the findings of Nerad et al. [5] also suggested that CT colonography potentially had high diagnostic performance. Their meta-analysis included only two studies of CT colonography, for which the pooled sensitivity and specificity values were 0.97 and 0.81, respectively. Another meta-analysis investigated the value of CT colonography as an alternative to colonoscopy for screening in view of its less invasive nature, and found that it had high sensitivity (96.1%, 95% CI 93.8–97.7) in the detection of colorectal cancer [29]. Furthermore, CT colonography can provide more information than CT with regard to the appearance of a tumor and intestinal wall deformity [30]. In the present review, we investigated the diagnostic performance of CT colonography for tumor depth in colorectal cancer by performing a meta-analysis because we think that CT colonography enables more accurate diagnosis of tumor depth in colorectal cancer. The results of this meta-analysis show the high diagnostic performance of CT colonography for tumor depth in colorectal cancer. We judged the diagnostic performance based on the sensitivity, specificity, and diagnostic odds ratio. As far as we know, there are currently no definite criteria for the classification of diagnostic performance. Thus, we set the criteria for high

diagnostic performance as described above according to the previous studies [5,28,31].

Colonoscopy is also useful in the diagnosis of tumor depth, and several types of classifications have been proposed [32,33]. The main purpose of endoscopic evaluation of tumor depth is to judge whether the tumor can be resected endoscopically and focuses on accurate detection of tumor invasion to the submucosal layer (T1 invasion). In contrast, CT colonography focuses on T2, T3, and T4 invasion and has high diagnostic performance, especially for T3 and T4 invasion. Therefore, CT colonography and colonoscopy can be considered to have different roles in assessment of tumor depth.

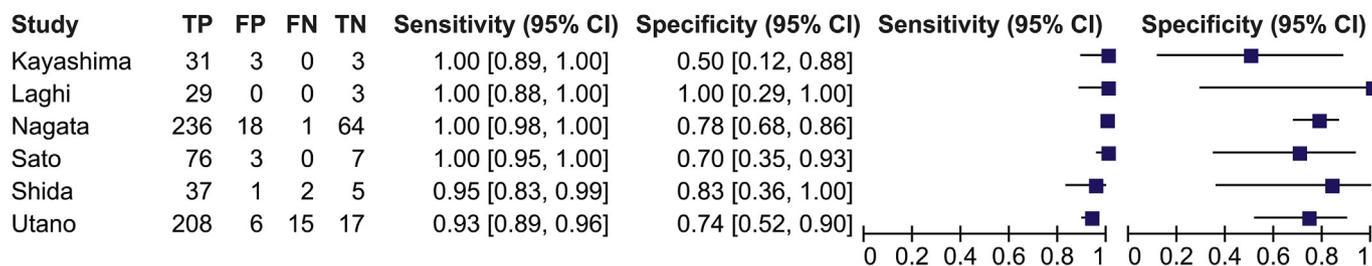
The strength of this review is that all the included studies used pathological findings as the reference standard, which ensures an accurate diagnosis. Furthermore, most of the CT colonography studies had a prospective design and had multiple CT colonography readers, which would minimize bias. However, this review also has some limitations. Heterogeneity among the included studies was inevitable because we included studies from various countries where there may be differences in CT equipment and protocols. Moreover, our meta-analysis did not differentiate between cancers of the colon and those of the rectum because most of the included studies reported the combined data of colon and rectum.

**Table 2**  
Summary of assessment of methodologic quality of included studies.

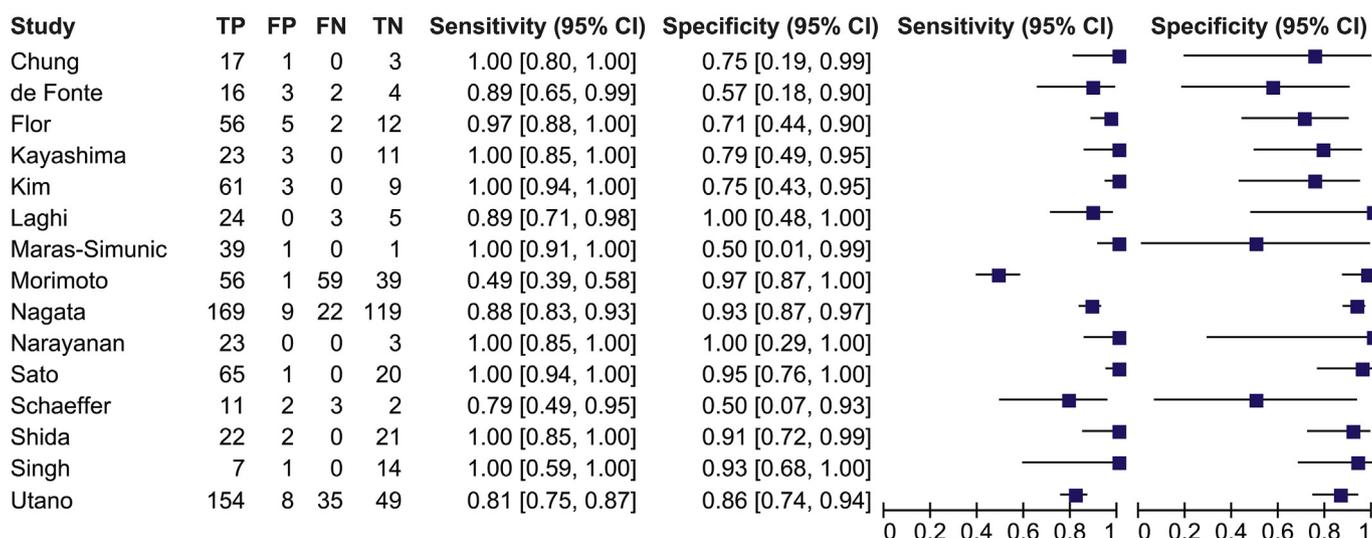
Study	Risk of bias			Concerns about applicability			
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Chung	+	+	+	+	+	+	+
da Fonte	+	+	+	+	+	+	+
Flor	+	+	+	+	+	+	+
Kayashima	+	+	+	+	+	+	+
Kim	?	-	+	?	+	+	+
Laghi	?	+	+	?	+	+	+
Maras-Simunic	?	+	+	+	+	+	+
Morimoto	?	-	+	?	+	+	+
Nagata	?	+	+	?	+	+	+
Narayanan	+	+	+	+	+	+	+
Sato	?	?	+	?	+	+	+
Schaeffer	+	?	+	?	+	+	+
Shida	+	+	+	+	+	+	+
Singh	?	+	+	-	+	+	+
Stagnitti	?	+	+	?	+	+	+
Utano	+	-	+	?	+	+	+

+, low risk; -, high risk; ? unclear risk.

a



b



c

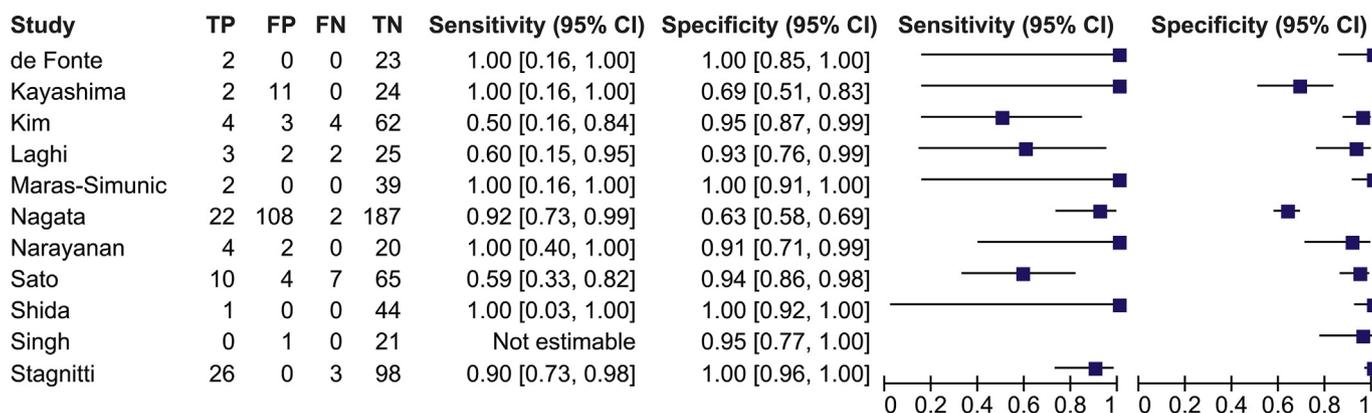


Fig. 2. Sensitivity and specificity values with 95% confidence intervals for each included study. CI, confidence interval; FN, false negative; FP, false positive; TN, true negative; TP, true positive. a: T2 invasion, b: T3 invasion, c: T4 invasion.

5. Conclusions

CT colonography showed high diagnostic performance and was useful for diagnosing tumor depth in colorectal cancer.

Declarations of interest

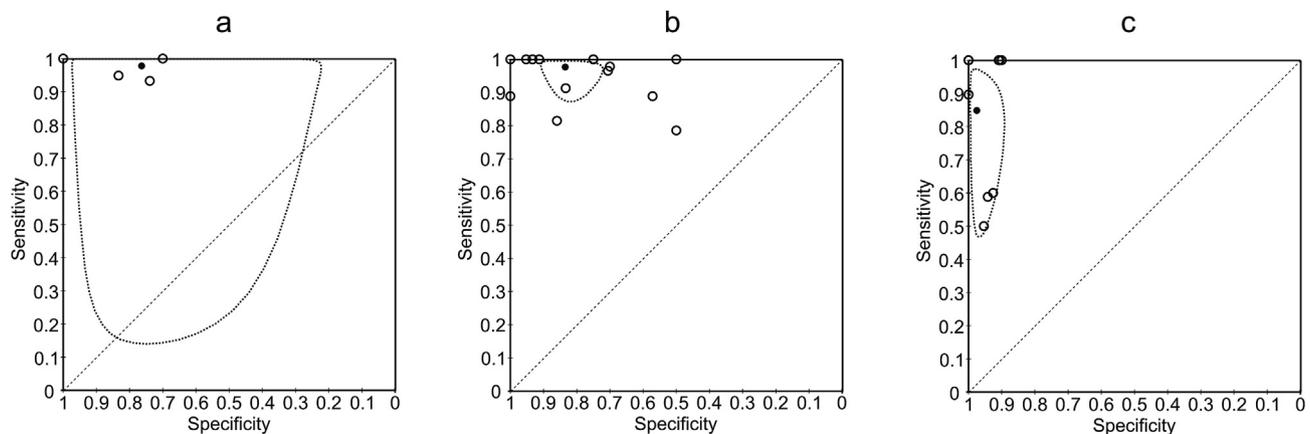
None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://>



**Fig. 3.** Summary point estimates for sensitivity and specificity of computed tomography colonography in the assessment of tumor depth in colorectal cancer. White spots indicate the points for each study, the black dot indicates the summary point estimate, and the dotted line outlines the 95% confidence region. a: T2 invasion, b: T3 invasion, c: T4 invasion.

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