Conventional CT for the Prediction of an Involved Circumferential Resection Margin in Primary Rectal Cancer

Steven V.R.C. Wolberink\textsuperscript{a,g} Regina G.H. Beets-Tan\textsuperscript{b} Danielle F.M. de Haas-Kock\textsuperscript{c}  
Mark M. Span\textsuperscript{e}  Eric J. van de Jagt\textsuperscript{d} Cornelis J.H. van de Velde\textsuperscript{f} Theo Wiggers\textsuperscript{a,g}

\textsuperscript{a}Department of Surgery, University Medical Center Groningen, Groningen; \textsuperscript{b}Department of Radiology, University Hospital Maastricht; \textsuperscript{c}Department of Radiation Oncology (MAASTRO), Research Institute GROW, University Hospital Maastricht, Maastricht; \textsuperscript{d}Department of Radiology, University Medical Center Groningen; \textsuperscript{e}Office for Medical Technology Assessment, Groningen, and \textsuperscript{f}Department of Surgery, Leiden University Medical Center, Leiden; \textsuperscript{g}Department of Radiology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

**Conclusion:** Conventional CT scan lacks sensitivity for a clinical use in the preoperative assessment of an involved CRM in primary rectal cancer. Modern multislice spiral CT will probably resolve some of the problems of conventional CT; however, further research is needed to establish its role.

**Key Words**  
Rectum, computed tomography \cdot Neoplasms \cdot Rectal cancer surgery \cdot Circumferential resection margin

**Abstract**

**Purpose:** To determine the accuracy of conventional computed tomography (CT) scan in the preoperative prediction of an involved circumferential resection margin (CRM) in primary rectal cancer.  

**Methods:** 125 patients with biopsy-proven adenocarcinoma of the rectum underwent CT of the abdomen before undergoing total mesorectal excision. Scans were scored by three observers, differing in experience. The main outcome was yes/no involvement of the CRM. Histology was taken as reference standard.

**Results:** For the most experienced observer, observer A, sensitivity was 46.7% and specificity 92.6%. For observer B, sensitivity was 46.7% and specificity 89.5%. For the least experienced observer C, sensitivity was 43.3% and specificity 92.6%. Inter-observer variability was good between observers A and B ($\kappa$ 0.648), B and C ($\kappa$ 0.648), and intermediate between A and C ($\kappa$ 0.542). Discrepancies occurred in a total of 34 patients; 25 had a CT scan of low technical quality, 10 an anteriorly located distal tumor.

**Introduction**

Successful treatment of primary rectal cancer means achieving a free circumferential resection margin (CRM). Total mesorectal excision (TME) is now the standard treatment, allowing recurrence rates below 10% [1–5]. In addition to TME, neoadjuvant treatment decreases the local recurrence rate even more to rates as low as 6% [6–15]. To assign the optimal neoadjuvant treatment strategy however, patients with rectal cancer high at risk of local recurrence need to be identified. The CRM is known to be one of the main risk factors in rectal cancer surgery [16]. A reliable prediction of the CRM by preoperative imaging is therefore important.
Recent publications have shown that MRI using phased-array coils can predict the CRM preoperatively with high accuracy [17–19].

Despite the widespread use of computed tomography (CT) in tumor staging, so far its role in the preoperative assessment of the CRM in rectal cancer staging has not been determined. In contrast to MRI, CT is more available, less expensive and less time-consuming. Furthermore, if CT would work for CRM assessment in rectal cancer patients, it would become a potential one-stop shop whole-body staging tool allowing accurate local and distant staging in one single examination.

The aim of this study is to investigate the accuracy of conventional CT for the prediction of an involved CRM in patients with primary rectal cancer.

Materials and Methods

The study was approved by the institutional review board.

Study Population

The study was performed on a retrospective basis. A cohort of patients was drawn from an existing database from the Dutch TME trial [9]. All 600 patients registered to have had a preoperative CT scan were included. All patients had a biopsy-proven, primary adenocarcinoma of the rectum, deemed primarily resectable on the basis of clinical evaluation, endoscopy and/or imaging. All patients underwent a conventional CT scan of the abdomen/pelvis before undergoing either surgery or radiotherapy. All patients underwent TME surgery performed by expert surgeons or surgeons trained by these experts to perform TME surgery. Pathologists were trained to dissect the resection specimen according to the protocol of Quirke et al. [20] and histopathology was taken as the reference standard against which the CT findings were compared. Overall accuracy, sensitivity and specificity of the prediction of involvement of the mesorectal fascia. The direction of the tumor penetration through the rectal wall was recorded as it is this direction which determines the shortest distance from the tumor to the mesorectal fascia (the CRM). In addition, the distance to the anale verge of the tumor and sites of extramesorectal growth were registered. For the prediction of the involvement, the direction of an involved fascia and the infiltration of mesorectal fat, the following confidence levels were scored:

- 0 = definitely not
- 1 = probably not
- 2 = possibly so
- 3 = probably so
- 4 = definitely so

Analysis and Statistics

The distance from the tumor to the mesorectal fascia on pathology was taken as the reference standard against which the CT findings were compared. Overall accuracy, sensitivity and specificity of the prediction of involvement of the CRM were calculated using cross-tabulation statistics. Receiver operating characteristic (ROC) analysis for the prediction of an involved mesorectal fascia were performed on the data generated by the confidence level scoring of the three observers. For each observer the accuracy of the CT for the prediction of an involved CRM was measured by calculating the area under the curve (AUC). Differences in accuracy between the observers were evaluated by a pairwise comparison of their respective areas under the ROC curve. The inter-observer agreement was measured using the linear weighted κ statistic by pairwise comparison of the accuracy of the three observers for the prediction of an involved CRM. Statistical analysis was performed using the software package SPSS® for Windows Version 11.0 (SPSS, Chicago, Ill., USA).

Materials and Methods

The study was performed on a retrospective basis. A cohort of patients was drawn from an existing database from the Dutch TME trial [9]. All 600 patients registered to have had a preoperative CT scan were included. All patients had a biopsy-proven, primary adenocarcinoma of the rectum, deemed primarily resectable on the basis of clinical evaluation, endoscopy and/or imaging. All patients underwent a conventional CT scan of the abdomen/pelvis before undergoing either surgery or radiotherapy. All patients underwent TME surgery performed by expert surgeons or surgeons trained by these experts to perform TME surgery. Pathologists were trained to dissect the resection specimen according to the protocol of Quirke et al. [20] and histopathology was taken as the reference standard against which the CT findings were compared. Overall accuracy, sensitivity and specificity of the prediction of involvement of the mesorectal fascia. The direction of the tumor penetration through the rectal wall was recorded as it is this direction which determines the shortest distance from the tumor to the mesorectal fascia (the CRM). In addition, the distance to the anal verge of the tumor and sites of extramesorectal growth were registered. For the prediction of the involvement, the direction of an involved fascia and the infiltration of mesorectal fat, the following confidence levels were scored:

- 0 = definitely not
- 1 = probably not
- 2 = possibly so
- 3 = probably so
- 4 = definitely so

Analysis and Statistics

The distance from the tumor to the mesorectal fascia on pathology was taken as the reference standard against which the CT findings were compared. Overall accuracy, sensitivity and specificity of the prediction of involvement of the CRM were calculated using cross-tabulation statistics. Receiver operating characteristic (ROC) analysis for the prediction of an involved mesorectal fascia were performed on the data generated by the confidence level scoring of the three observers. For each observer the accuracy of the CT for the prediction of an involved CRM was measured by calculating the area under the curve (AUC). Differences in accuracy between the observers were evaluated by a pairwise comparison of their respective areas under the ROC curve. The inter-observer agreement was measured using the linear weighted κ statistic by pairwise comparison of the accuracy of the three observers for the prediction of an involved CRM. Statistical analysis was performed using the software package SPSS® for Windows Version 11.0 (SPSS, Chicago, Ill., USA).
Results

Patients
The study population consisted of 125 patients: 90 male (72%) and 35 female (28%). The age of the patients ranged between 32 and 87 with a median age of 64. The study population was a good representation of the population of the TME trial [9], in age and sex as well as in distribution of T stage.

TNM Stage
There were 2 T0 tumors, 3 T1 tumors, 34 T2 tumors, 76 T3 tumors and 10 T4 tumors. Table 2 shows the histological TNM classification of the tumors and the histological CRM assessment: free (e.g. CRM neg) or involved (CRM pos).

Prediction of Involved CRM per Observer
All three observers made 125 predictions. Thus, a total of 375 predictions were made, of which 73 were incorrect (19.5%) and 302 correct (80.5%).

Observer A was correct in 14/30 patients with positive margins and in 88/95 patients with negative margins. Observer B was correct in 14/30 patients with a positive margin and 85/95 patients with a negative margin. Observer C was correct in 13/30 patients with a positive margin and 88/95 patients with a negative margin. The sensitivity and specificity for the prediction of an involved CRM per observer are given in table 3.

Inter-Observable Agreement
Inter-observer agreement for prediction of an involved CRM was high between observer A and observer B (κ 0.648), intermediate between observer A and observer C (κ 0.542), and high between observer B and observer C (κ 0.648).

Analysis of Predicted Involvement of CRM
If the confidence level of the prediction of each individual observer is taken into account, there is a rise in the specificity as confidence of the predictions increases for all three observers, as illustrated by the receiver operating curves in figures 1–3. This ROC analysis also shows that the AUC, and thus the overall accuracy is greatest for observer A (the most experienced reader) at 0.813 and the least for observer C (the least experienced reader) at 0.697.

Discussion
Conventional CT scan shows a low sensitivity but high specificity in the preoperative prediction of an involved CRM. An experienced reader performs better than a less experienced reader.

Based on the National Guidelines the main choice before the surgical treatment of rectal cancer is between short-course and long-course radiotherapy. The last one aiming on downsizing and downstaging. Preoperative assessment of the involved circumferential margin should primarily focus on a high sensitivity. A relatively low specificity results in some overtreatment with long-course radiotherapy and is less worse than under treatment in case of an involved margin.

Accuracy of the Prediction of an Involved CRM
Discrepancies between predicted CRM and histology occurred in 34 patients. In 25 of these 34 patients, all

Table 2. Distribution of positive and negative CRM

<table>
<thead>
<tr>
<th></th>
<th>CRM neg</th>
<th>CRM pos</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT0 N0 M0</td>
<td>2</td>
<td>–</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>pT1 N0 M0</td>
<td>3</td>
<td>–</td>
<td>3 (2.4)</td>
</tr>
<tr>
<td>pT2 N0 M0</td>
<td>28</td>
<td>–</td>
<td>28 (22.4)</td>
</tr>
<tr>
<td>pT2 N1 M0</td>
<td>5</td>
<td>–</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td>pT2 N1 M1</td>
<td>1</td>
<td>–</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>pT3 N0 M0</td>
<td>31</td>
<td>8</td>
<td>39 (31.2)</td>
</tr>
<tr>
<td>pT3 N1 M0</td>
<td>20</td>
<td>9</td>
<td>29 (23.2)</td>
</tr>
<tr>
<td>pT3 N1 M1</td>
<td>3</td>
<td>5</td>
<td>8 (6.4)</td>
</tr>
<tr>
<td>pT4 N0 M0</td>
<td>1</td>
<td>–</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>pT4 N0 M1</td>
<td>–</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>pT4 N1 M0</td>
<td>1</td>
<td>5</td>
<td>6 (4.8)</td>
</tr>
<tr>
<td>pT4 N1 M1</td>
<td>–</td>
<td>2</td>
<td>2 (1.6)</td>
</tr>
</tbody>
</table>

95 (76%) 30 (24%)

1 Two of these 9 patients had a positive CRM due to a positive lymph node.
2 One of these 5 patients had a positive CRM due to a positive lymph node.
3 One of these 2 patients had a positive CRM due to a positive lymph node.

Table 3. Sensitivity and specificity per observer for prediction of involved CRM

<table>
<thead>
<tr>
<th></th>
<th>Observer A</th>
<th>Observer B</th>
<th>Observer C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>46.7</td>
<td>46.7</td>
<td>43.3</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>92.6</td>
<td>89.5</td>
<td>92.6</td>
</tr>
</tbody>
</table>
Fig. 1. Receiver operating curve, cut-off points are for a positive prediction by observer A at confidence level definitely not, probably not, possibly so, probably so, and definitely so, respectively.

Fig. 2. Receiver operating curve, cut-off points are for a positive prediction by observer B at confidence level definitely not, probably not, possibly so, probably so, and definitely so, respectively.

Fig. 3. Receiver operating curve, cut-off points are for a positive prediction by observer C at confidence level definitely not, probably not, possibly so, probably so, and definitely so, respectively.
three observers judged the CT scan difficult to interpret due to limited spatial resolution. The main reason for the lack of sensitivity therefore seems to be of a technical nature. Most CT protocols in this study made use of thick slices (>8 mm). Therefore, the spatial resolution of the scans were too low to make any reliable predictions on margin involvement.

Most false-negatives also occurred in patients who had a distal tumor located on the anterior side of the mesorectum with a threatened margin anteriorly. In these false-negative cases the margins were often involved only by subtle tumor stranding. Because of the inherent lack of contrast resolution of CT and the insufficient spatial resolution of conventional CT techniques in this study, these tumor strands were not visualized on the CT and therefore missed by all observers (fig. 4).

Second, many disagreements between CT and histology occurred on where the tumor exactly penetrates the bowel wall. The exact location of the site of tumor penetration is essential when the site of the closest CRM has to be anticipated, because it is at this site where the mesorectal fascia should be scrutinized for any possible invasion by tumor stranding. Again, the very low contrast resolution of conventional CT prevents clear distinction between the bowel wall and tumor tissue, making it very difficult to predict the site of bowel wall penetration, resulting in misinterpretations of the site of margin involvement.

MRI being superior to CT in contrast resolution and offering simultaneous imaging in different planes can better distinguish between tumor tissue and rectal wall and is expected to perform better than CT for predicting involvement of the CRM in this specific group of distal rectal cancer. Modern state-of-the-art multislice spiral CT (MSCT) however might probably do better than conventional CT, given the ability to reconstruct thinner sections and to optimally time the bolus contrast, leading not only to an improved spatial but also to an improved contrast resolution. In addition, MSCT offers reconstructions in multiple planes (multiplanar reconstruction) thus allowing an assessment of the rectal tumor in any given plane, analog to MRI. Therefore it seems justified to investigate the role of MSCT in rectal cancer staging, because if MSCT would work, it would become a potential one-stop shop whole-body staging tool allowing accurate local and distant staging in one single examination.

**Conclusion**

Conventional CT scan lacks sensitivity for a clinical use in the preoperative assessment of an involved CRM in primary rectal cancer. Modern MSCT will probably resolve some of the problems of conventional CT; however, further research is needed to establish its role.

![Fig. 4. Example of a CT scan in which all three observers predicted a non-involve CRM. Histology however showed an involved CRM.](image)
References