

# Chinese guideline for the application of rectal cancer staging recognition systems based on artificial intelligence platforms (2021 edition)

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## Development and Application of Artificial Intelligence Recognition Systems in Rectal Cancer Staging

Whether for surgical treatment or for neoadjuvant chemotherapy, imaging evaluation has become an important basis to perform the treatment plans.<sup>[1]</sup> The reading of imaging results requires a large number of experienced

radiologists to complete, but shortages and uneven distributions of personnel cause delays and biases in imaging results. Therefore, independent research and

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development of automatic recognition systems of rectal cancer staging based on artificial intelligence (AI) platforms aim to partially replace practitioners' work and achieve rapid and accurate identification of rectal cancer staging.

Faster region-based convolutional neural networks (FR-CNNs) were utilized to learn and train from a large number of images and build a network for the identification and labeling of lesions, the automatic delineation of target areas, and three-dimensional reconstruction. According to the requirements of the National Comprehensive Cancer Network guidelines, pre-operative evaluation is mainly based on the tumor-node-metastasis (TNM) staging system and the circumferential resection margin (CRM).<sup>[2]</sup> The guideline decided to take "T, N, CRM, and extramural vascular invasion (EMVI)" as the pre-operative evaluation factors of rectal cancer staging, and the AI recognition system was used to complete the evaluation of tumor staging.

### Parameters and Process of Research and Development for AI Recognition System

#### Establishment of the image database

Magnetic resonance imaging (MRI) images were acquired using GE, Siemens, Philips, and other 3.0T MRI scanners configured in most hospitals. The main scanning sequence and parameters are listed for reference in Supplementary Table 1, <http://links.lww.com/CM9/A535>. After image collection was completed, the corresponding sequence images with diagnostic value for an input in the deep neural network (DNN) were selected to establish the database.

#### Identification of parameters in the training set of the AI recognition system

Based on the decision of the expert committee, provisions were made for the identification of four parameters in the training set.<sup>[3,4]</sup> T staging was defined in MRI based on the TNM staging system of the American Joint Committee on Cancer<sup>[5]</sup> and Horvat *et al's* study<sup>[6]</sup>: (a) T1 tumors infiltrate the submucosa; (b) T2 tumors extend into the muscularis propria; (c) T3 tumors are characterized by a discontinuity of the muscularis propria, with the extension of the tumor into the mesorectum; and (d) T4 tumors are those that infiltrate the peritoneal reflection or other pelvic organs and structures. According to international consensus, the size, shape, and signal of lymph nodes (LNs) are used as the diagnostic basis for metastasis<sup>[6-8]</sup>: (a) The smallest diameter on T2 weighted image (T2WI) of MRI was  $\geq 5$  mm; (b) Irregular in shape and indistinct in edge; (c) Dispersion enhanced imaging shows high signal; and (d) Upper and lower discontinuities between the image layers were considered LN positive. For positive judgments of CRM on MRI, we adopted the criteria of the MERCURY Research Group<sup>[9]</sup>: Positive CRM was considered when the distance between the outer edge of the tumor and the mesenteric fascia was  $\leq 1$  mm. For positive judgments of EMVI on MRI, we used the scoring system from the study of Smith *et al*<sup>[10]</sup>: On MRI T2WI, (a) The moderate signal intensity was evident in the blood vessels, but the contour and caliber of these vessels were only slightly enlarged and (b) The tumor signal is clear, the vascular shape is

obviously irregular or nodular dilatation [Supplementary Figure 1A, <http://links.lww.com/CM9/A531>].

#### Identification process

Two senior imaging experts and one colorectal surgery expert were selected to jointly evaluate and mark the correlation factors of rectal cancer staging on the images at the corresponding level of the MRI sequence. In case of any inconsistency between the diagnostic results of the three experts, a fourth imaging expert was consulted, and a final conclusion was reached. For each patient, approximately three marked images with diagnostic value were selected for input into the DNN to study the DNN platform and establish the corresponding MRI image database.<sup>[11-13]</sup>

#### FR-CNN training framework

We used FR-CNN to realize the automatic detection of rectal cancer staging parameters. The system was composed of two modules: a region proposal network and a module based on the candidate areas of the FR-CNN target detector [Supplementary Figure 2, <http://links.lww.com/CM9/A532>]. Two common parts were combined into a whole and unified target detection network, and by sharing the same convolution layer, the bounding box of the suspected lesions served as the image output with the parameters of the output probability scores [Supplementary Figure 1B, <http://links.lww.com/CM9/A531>].<sup>[14,15]</sup>

#### Selection of clinical validation evaluation tools

We use receiver operating characteristic (ROC) and precision-recall (PR) curves as evaluation tools for clinical verification of the AI automatic recognition system for MRI image-assisted diagnosis. Both ROC and PR are excellent evaluation tools in the field of detection and classification involving DNNs. However, most of the area under the curve (AUC) indicators in the current studies were obtained based on ROC curves, so the AUC value of the final evaluation indicator in this study was also calculated based on the ROC curve<sup>[16]</sup> [Supplementary Figure 3, <http://links.lww.com/CM9/A533>].

### Clinical Application of the AI Recognition System

#### Result interpretation of AI recognition system

AI recognition system through deep learning and verification needs to achieve higher accuracy evaluation indexes, and ROC curve evaluation is recommended. When AUC  $\geq 90\%$  is obtained, the AI recognition system will enter the clinical application. The AI recognition system will locate and calculate probabilities for the four indicators of T staging, N staging, CRM, and EMVI of rectal cancer to provide a reference for clinicians in the judgment of pre-operative staging of rectal cancer and the formulation of diagnosis and treatment plan. When using the AI recognition system, clinicians will make accurate judgments based on the probability of each indicator. Therefore, this guideline divides the probability into three levels based on previous studies and clinical applications: Highly reliable, possible compliance, and poor compliance. The probability

of high reliability includes: T staging  $\geq 90\%$ , N staging, CRM, or EMVI  $\geq 80\%$ ; the possibility of possible compliance includes:  $90\% > T \text{ staging} \geq 70\%$ ,  $80\% > N \text{ staging}$ , CRM or EMVI  $\geq 60\%$ ; the probability of poor compliance includes: T staging  $< 70\%$ , N staging, CRM or EMVI  $< 60\%$ .

### Clinical application scenario of AI recognition system

This guideline is recommended for high-resolution MRI images of patients with rectal cancer, and the results are input into the AI recognition system to obtain the identification results of T staging, N staging, CRM, and EMVI as four parameters. For T1N0, early colorectal cancer patients, transanal local resection, transanal endoscopic microsurgery, or transanal minimally invasive surgery can be chosen. For pre-operative evaluation results that do not meet the above conditions, including the possibility of lateral LN metastasis, pre-operative neo-adjuvant chemoradiation is recommended, then secondary identification is performed using the AI recognition system. To achieve the clinical complete response (cCR), transanal local resection or watch and wait strategy is then recommended. For patients who have not reached the cCR, radical TME surgery is recommended. In addition, if the secondary identification still identifies lateral LNs metastasis in patients, selective lateral LNs dissection is recommended and performed<sup>[17]</sup> [Supplementary Figure 4, <http://links.lww.com/CM9/A534>].

### Registration

International Practice Guideline Registry (No. IPGRP-2020CN175).

### Conflicts of interest

None.

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