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# The predictive value of non-enhanced CT radiomics in differentiating early and advanced T-staging of colon cancer

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**Abstract**

This study aimed to assess the diagnostic value of non-enhanced CT radiomics in preoperatively differentiating early-stage (T1–T2) from locally advanced (T3–T4) colon cancer, addressing the limitations of conventional empirical staging. A retrospective analysis was conducted on 170 patients with surgically confirmed primary colon cancer who underwent non-enhanced CT scans within 1 week before surgery. Three-dimensional segmentation of colonic tumors was performed on the non-enhanced images, followed by automated extraction of radiomic features. Feature selection was executed using the minimum redundancy maximum relevance (mRMR) algorithm, and key features associated with cancer stage were identified using the least absolute shrinkage and selection operator logistic regression. The performance of the radiomics model was compared with conventional T-staging by radiologists. The cohort comprised 170 patients with an average age of 61.69 ± 13.22 years, 43.3% of whom were female, and 75 (44.1%) presented with early-stage disease. Eight radiomic features from non-enhanced imaging were ultimately included. The radiomics model achieved an area under the curve (AUC) of 0.85 (95% confidence interval: 0.78–0.92) in the training set and 0.84 (95% confidence interval: 0.74–0.95) in the test set, with corresponding accuracies of 0.70 and 0.78, sensitivities of 0.87 and 0.87, and specificities of 0.69 and 0.71, respectively. Additionally, in the training set, the radiomics model (AUC = 0.85) significantly outperformed empirical T-staging by radiologists (AUC = 0.71, $P < .009$). A similar trend was observed in the test set, where the radiomics model (AUC = 0.85) surpassed empirical T-staging (AUC = 0.76), although this difference was not statistically significant ($P = .27$). Non-enhanced CT radiomics demonstrated superior performance over conventional radiologists' T-staging in distinguishing early from advanced colon cancer stages.

**Abbreviations:** AUC = area under the curve, CI = confidence interval, CT = computed tomography, ICC = intraclass correlation coefficients, LASSO = least absolute shrinkage and selection operator, MRI = magnetic resonance imaging, mRMR = minimum redundancy maximum relevance, ROI = region of interest.

**Keywords:** colon cancer, non-enhanced CT, radiomics, T-staging

## 1. Introduction

Colorectal cancer stands as the 3rd most commonly diagnosed cancer and the 3rd leading cause of cancer-related deaths among both men and women. However, it ranks second in total cancer-related mortality and is the leading cause of death in men under 50 years old.[1] Approximately 60% to 70% of colorectal cancer cases are colon cancer. The early

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*The authors are responsible for all aspects of the work, ensuring that any questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved. This study was conducted following the Declaration of Helsinki (revised in 2013). The research received approval from the Ethics Committee of Zhujiang Hospital of Southern Medical University, and individual consent was waived for this retrospective analysis.*

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symptoms of colon cancer are often difficult to detect, leading to delayed diagnoses and significantly affecting patient prognosis. Early detection and precise clinical staging are crucially linked to the disease's prognosis. Therefore, detailed preoperative clinical analysis is essential for determining the best treatment approach.[2] Tumors infiltrating different layers of the intestinal wall respond differently to surgical interventions at various stages. Tumors confined to the submucosa or muscularis propria without penetration (T1–T2 stage) are typically treated with surgical resection. In contrast, for colon cancer cases extending beyond the muscularis propria (T3–T4 stage), personalized chemotherapy is recommended to lower the recurrence rate and improve survival rates. Thus, accurate preoperative T-staging is critical in deciding the appropriate treatment strategy for colonic cancer.

Computed tomography (CT) imaging, characterized by its rapidity, precision, and the ability to offer a comprehensive evaluation of the patient's systemic status and metastatic presence, stands out as a preferable option. The Union for International Cancer Control endorses the utilization of CT imaging as an integral component of routine screening and preoperative assessment in populations at elevated risk for colorectal carcinoma.[3]

Traditional CT scans often face limitations in the information they capture, typically relying on empirical methods for analysis and diagnosis. In contrast, radiomics represents an emerging noninvasive multidisciplinary technology based on conventional imaging data.[4] It involves extracting high-throughput quantitative features, transforming medical images into high-dimensional, utilizable data, and aims to link large-scale image data mining with clinical and biological endpoints. For example, radiomic models based on CT images have been utilized to predict the histopathology (adenocarcinoma or squamous cell carcinoma)[5,6] and tumor stage[7] of lung cancer, as well as micropapillary patterns in lung adenocarcinoma.[8] In the field of colorectal cancer staging, Lu et al[9] analyzed texture features from apparent diffusion coefficient images of rectal cancer patients and found that homogeneity and energy were significantly higher in T1–T2 stages compared to T3–T4 stages. Likewise, Caruso et al[10] developed a radiomic model to identify high-risk colonic cancer (T4) in nonmetastatic patients, with the model achieving an area under the curve (AUC) of 0.75 in an external cohort study, effectively stratifying high-risk colonic cancer cases. Furthermore, Ma et al[11] used radiological features extracted from T2-weighted magnetic resonance imaging (MRI) to predict rectal cancer T-staging (T1–T2 vs T3–T4), achieving a prediction accuracy of 0.762.

Differences in T-staging between colon and rectal cancers are attributed to the absence of a serosal layer in the lower rectum, leading to variations in pathological T3–T4 staging between the 2. Consequently, imaging characteristics specific to T3–T4 stages may differ. Research focused specifically on the T1–T2 and T3–T4 staging of colon cancer remains limited.

To address this gap, we have developed a least absolute shrinkage and selection operator (LASSO) regression model utilizing CT scans from colon cancer patients. We then compared this model with radiologists' empirical staging to evaluate its effectiveness in staging, intending to provide more accurate preoperative guidance for colon cancer patients.

## 2. Method

### 2.1. Patient information

This retrospective study was approved by the ethics review committee of our hospital (Ethics Approval No. 2023-KY-226-01), and an exemption from the requirement for patient informed consent was granted. The case cohort included 171 postoperative colon cancer patients diagnosed between January 2020 and December 2022, all of whom were confirmed via pathology. The histopathological diagnosis adhered to the criteria outlined in the 8th edition of the American Joint Committee on Cancer[12] staging manual. According to this staging system, T1–T2 stages are classified as early stages, while T3–T4 stages are considered locally advanced.

Inclusion criteria for the study were: cases pathologically confirmed as colon cancer following surgery; absence of contraindications to CT scans such as iodine allergy, liver or kidney impairment, or congestive heart failure; non-enhanced CT scans; no prior radiation or chemotherapy for cancer before surgery; and patients aged 18 years or older with retrievable clinical data from the medical records system, including pathological details, gender, and age. Exclusion criteria included: cases pathologically confirmed as rectal cancer post-surgery; patients with concurrent malignant tumors; and cases with insufficient clinical data. The detailed flow chart is shown in Figure 1.

### 2.2. CT protocols

All patients underwent a comprehensive preoperative non-enhanced Multi-Slice CT examination. The imaging data were meticulously collected using the Philips Brilliance series (64, 128) and Philips Brilliance iCT (256), with standardized scanning parameters maintained at 120 kVp using automatic tube current modulation technology (DoseRight). The pitch was set at 0.925. For non-enhanced reconstruction, both slice thickness and interval were set at 5 mm (Table 1). The scan range extended from the dome of the diaphragm to the inferior margin of the pubic symphysis. During the scan, patients were positioned in a supine posture.

### 2.3. CT image analysis

The segmentation of all colon cancer cases was precisely executed by an abdominal radiologist with 8 years of experience in the field (H.B.S.). These seasoned professionals meticulously performed volumetric segmentation of the colon cancers from preoperative non-enhanced CT scans using the open-source MITK software (version 2023.04, available at https://www.mitk.org/wiki/). To ensure objectivity and fairness in the analysis, the readers were blinded to all clinical and histological data, though basic information about the tumor location was provided to facilitate accurate segmentation and qualitative evaluation. The region of interest (ROI) underwent thorough manual slice-by-slice delineation, meticulously covering the entire volume occupied by colon cancer. Surrounding mesenteric fat and healthy colonic walls were deliberately excluded during the segmentation process (see Fig. 2). Finally, a radiologist (Z.B.W.) reviewed and confirmed all ROIs to ensure the quality of tumor delineation. Meanwhile, we randomly selected 14 anonymized imaging data from 170 patients, and the radiologist (H.B.S.) re-delineated the colon cancer lesions 1 month later. This process aimed to verify the stability of the features used for subsequent modeling.

### 2.4. Feature extraction

A total of 100 quantitative imaging features were extracted from these CT images using PyRadiomics (version 3.0, Python 3.10, accessible at https://pyradiomics.readthedocs.io/en/latest/). These extracted features were categorized into 3 groups: 1st-order statistics, which include 18 descriptors quantifying the voxel intensity distribution within the CT images using basic statistical metrics; shape-based features, encompassing 14 3-dimensional characteristics that describe the shape and size attributes of the segmented region; and Texture features, quantifying the heterogeneity changes within the ROI through the computation of the gray level co-occurrence matrix (22 features), gray level run length matrix (16 features), gray level size

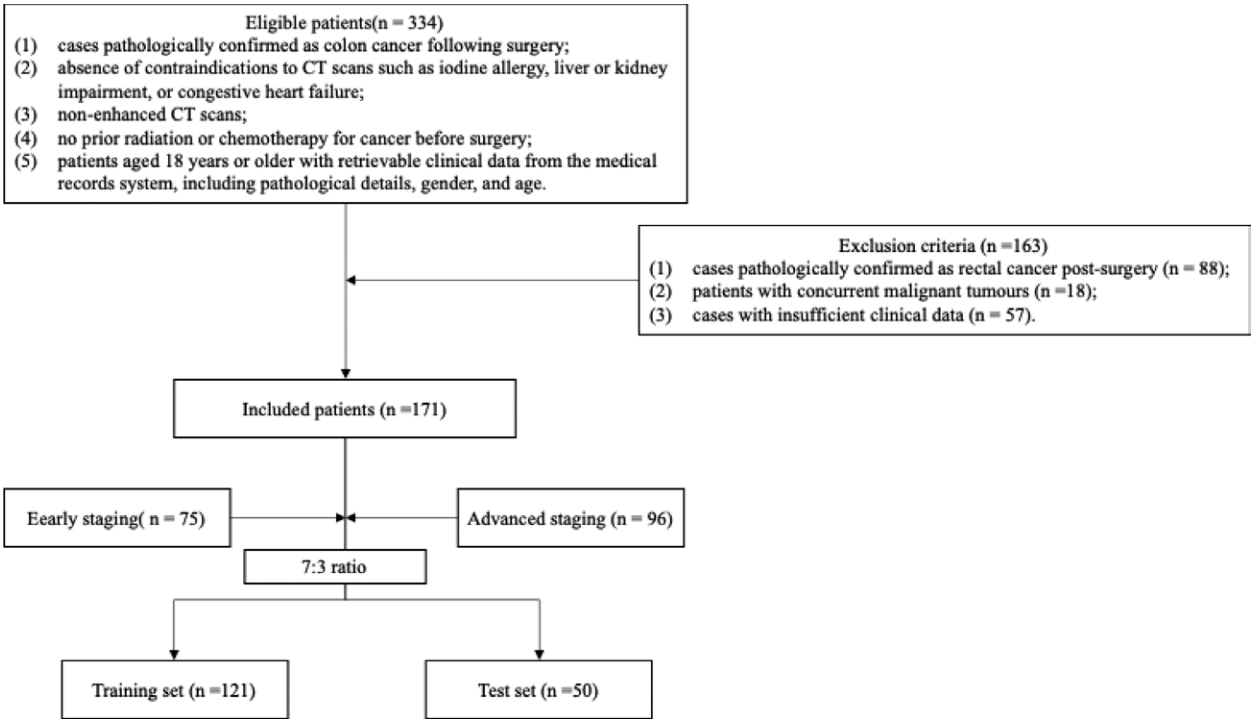


**Figure 1.** The flowchart of the study population.

**Table 1**

**CT imaging protocol for patients.**

| CT information | Parameters | |
|---|---|---|
| CT system | Philips Brilliance 64/128, Philips Brilliance iCT | |
| CT scans | Tube voltage | 120 kVp |
| | Tube current | Automatic tube current modulation technology (DoseRight) |
| | Scan pitch | 0.925 |
| CT imaging | No-enhanced CT | No contrast |
| Image reconstruction | Image matrix | 512*512 |
| | Reconstruction thickness | 1 mm or 5 mm |

CT = computed tomography.

zone matrix (16 features), and gray level dependence matrix (14 features), totaling 68 features.

### 2.5. Feature selection and model building

Prior to feature selection, *Z*-score normalization (Eq. [1]) was utilized to standardize radiomic features, ensuring their range was confined between 0 and 1.

This step aimed to reduce the computational load associated with high-dimensional features and mitigate the potential impact of redundant features on classification accuracy. After normalization, an intraclass correlation coefficients (ICC) analysis was performed on the radiomic features of the imaging data from the 14 randomly selected patients who underwent 2 rounds of lesion delineation. Consistency features were then derived, and the minimum redundancy maximum relevance (mRMR) method was applied to select features. This method identified the top 15 features with the highest mRMR scores as the key contributors.

Before model construction, all data were divided into training and testing sets in a 7:3 ratio. Consequently, a LASSO logistic regression model was developed using 10-fold cross-validation on the training dataset. This process identified the tuning parameter λ,[13] determining the optimal number of features that significantly impact T-staging. Finally, a radiomic score (rad_score) was calculated for each patient based on their respective LASSO coefficients, representing the importance of each feature:

$$z = (x - \mu)/\sigma_{(1)}$$

$x$ is an observed value, $\mu$ is the mean, and $\sigma$ is the standard deviation.

### 2.6. Radiologist's empirical staging

The empirical T-staging (T1, T2, T3, T4) was provided by a radiologist (with 8 years of abdominal diagnostic experience, H.B.S.) based on non-enhanced images. Early-stage colon cancer was classified as T1 and T2, while advanced stage was classified as T3 and T4. Using the same training and testing sets as the radiomics analysis, a logistic regression model was then constructed to determine the performance of the empirical staging.

### 2.7. Model evaluation

The performance of both the radiomics model and the empirical staging model was evaluated using metrics such as the receiver operating characteristic curve, AUC, accuracy, sensitivity, and specificity.

## 3. Results

### 3.1. Study population

The study enrolled a total of 170 patients, with an average age of 61.69 ± 13.22 years. Females constituted 43.3% of the total participants. According to the T-staging system, 75 patients were categorized into the T1–T2 stage, including 46 males and 29 females, with an average age of 61.27 ± 11.02 years. Additionally, 95 cases were classified under the T3–T4 stage

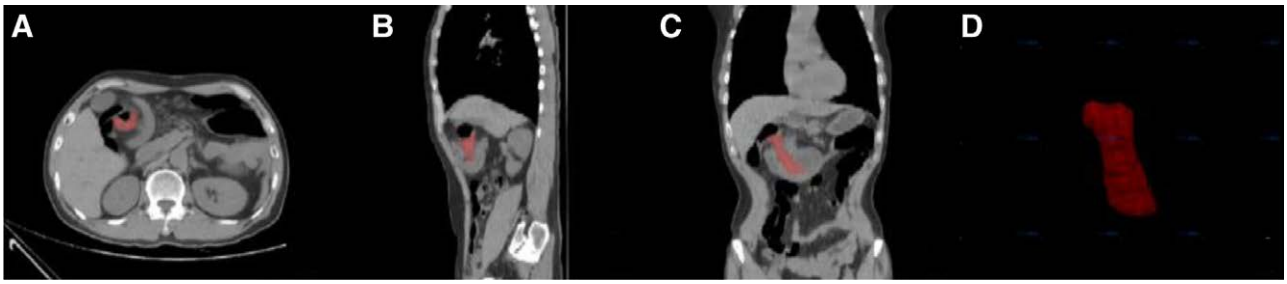


**Figure 2.** A 55-year-old male patient with a tumor located in the transverse colon. It illustrated the patient's 3-dimensional colon cancer tumor segmentation. Figure A, B, and C respectively represented the axial, sagittal, and coronal tumor segmentation images, while Figure D showed the 3-dimensional rendered volume image.

category, comprising 50 males and 46 females, with an average age of 62.02 ± 14.78 years. Furthermore, based on the radiologist's empirical staging, there were 3 cases in T1, 69 in T2, 66 in T3, and 32 in T4. Table 2 outlined the baseline clinical data and patient demographics.

### 3.2. Feature extraction and model evaluation

After performing ICC analysis to assess feature consistency, features with an ICC 10.8 were selected, resulting in 57 retained features. Following the application of the mRMR feature selection method, the top 15 features with the highest mRMR scores were identified.

This was followed by a 10-fold cross-validation using LASSO logistic regression. Figure 3A illustrates the binomial deviances and coefficients obtained after adjusting with different lambda (λ) values. Ultimately, a set of 8 features with nonzero coefficients was chosen, as shown in Figure 3B (refer to Table 3). These features are associated with the optimal λ value of 0.0094, as displayed in Figure 3A. The selected features included 4 texture features, 3 shape features, and 1 first-order feature. Among these, the top 3 features with the highest coefficients were: original_glszm_ZonePercentage, original_shape_Sphericity, and original_shape_LeastAxisLength, with coefficients of –0.964, –0.884, and 0.879, respectively (Table 3, Fig. 3C).

In both the training and testing datasets, the radiomic features (rad_score) of patients in stages T3–T4 were consistently higher than those in stages T1–T2 (all $P < .001$, as shown in Fig. 3D). These features are derived from the selected features and their respective coefficients. The calculation formula is as follows: rad_score = 0.879*original_shape_LeastAxisLength – 0.276*original_firstorder_90Percentile + 0.29*original_glrlm_RunVariance –0.964*original_glszm_ZonePercentage-0.884*original_shape_Sphericity – 0.445*original_shape_Maximum2DDiameterColumn-0.099*original_glcm_ClusterShade + 0.044*original_gldm_DependenceVariance + 0.361

In the training set, the radiomics model achieved an AUC value of 0.85 (95% CI: 0.78–0.92) as depicted in Figure 4A. The corresponding accuracy was 0.77, sensitivity was 0.87, and specificity was 0.69. In the testing set, the radiomics AUC value was 0.85 (95% CI: 0.74–0.95) as shown in Figure 4B. The accuracy was 0.78, sensitivity was 0.87, and specificity was 0.71 (Table 4). After performing the DeLong test, no statistically significant difference was found between the AUCs of the training set and the test set ($P = .9375$).

### 3.3. Empirical staging model

The performance of the empirical staging model in the training set achieved an AUC value of 0.71 (95% CI: 0.63–0.79), as shown in Figure 4C. The corresponding accuracy was 0.72, sensitivity was 0.73, and specificity was 0.69. In the testing set, the AUC value was 0.76 (95% CI: 0.63–0.88) as shown in Figure 4D, with an accuracy of 0.76, sensitivity of 0.79, and specificity of 0.73 (refer to Table 4).

**Table 2**

**Patient demographics and primary colon cancer characteristics.**

| Characteristic | Total cases | Early staging | Advanced staging |
|---|---|---|---|
| All the dataset number of samples | 170 | 75 | 95 |
| Age (average ± SD) | 61.69 ± 13.22 | 61.27 ± 11.02 | 62.02 ± 14.78 |
| Sex | | | |
| Female | 73 (42.9%) | 29 (37.4%) | 46 (47.4%) |
| Male | 97 (57.1%) | 46 (62.6%) | 50 (52.6%) |
| T-staging | | | |
| T1 | 26 | 26 | – |
| T2 | 49 | 49 | – |
| T3 | 61 | – | 61 |
| T4 | 34 | – | 34 |
| Empirical T-staging | | | – |
| T1 | 3 | 3 | – |
| T2 | 69 | 69 | – |
| T3 | 66 | – | 66 |
| T4 | 32 | – | 32 |

SD = standard deviation.

After performing the DeLong test, no statistically significant difference was found between the AUCs of the training set and the test set ($P = .529$). The formula for the logistic regression model is: Logistic Model = 1.825 × Empirical Staging – 0.818.

Additionally, in the training set, the AUC of radiomic features (0.85) was greater than that of empirical staging (0.71), and a statistically significant difference was observed ($P < .009$). In the test set, the AUC of radiomic features (0.85) was greater than that of empirical staging (0.76), but no statistically significant difference was found ($P = .27$).

## 4. Discussion

The early and accurate diagnosis of colon cancer, along with precise clinical staging, significantly impacts the prognosis and treatment strategies for the disease.[2] This study demonstrated that CT radiomic features can enhance radiologists' ability to stage colon cancer on CT scans, specifically for the empirical T1–T2 and T3–T4 stages. The diagnostic performance of the radiomics model was significantly superior to the CT empirical staging model. The radiomic model achieved an AUC of 0.85 in the training cohort and 0.85 in the testing set, compared to the CT empirical staging model, which had an AUC of 0.71 in the training cohort ($P < .009$) and a testing AUC of 0.76 ($P = .27$). The results indicated that radiomics demonstrated outstanding predictive performance in both the training and testing datasets.

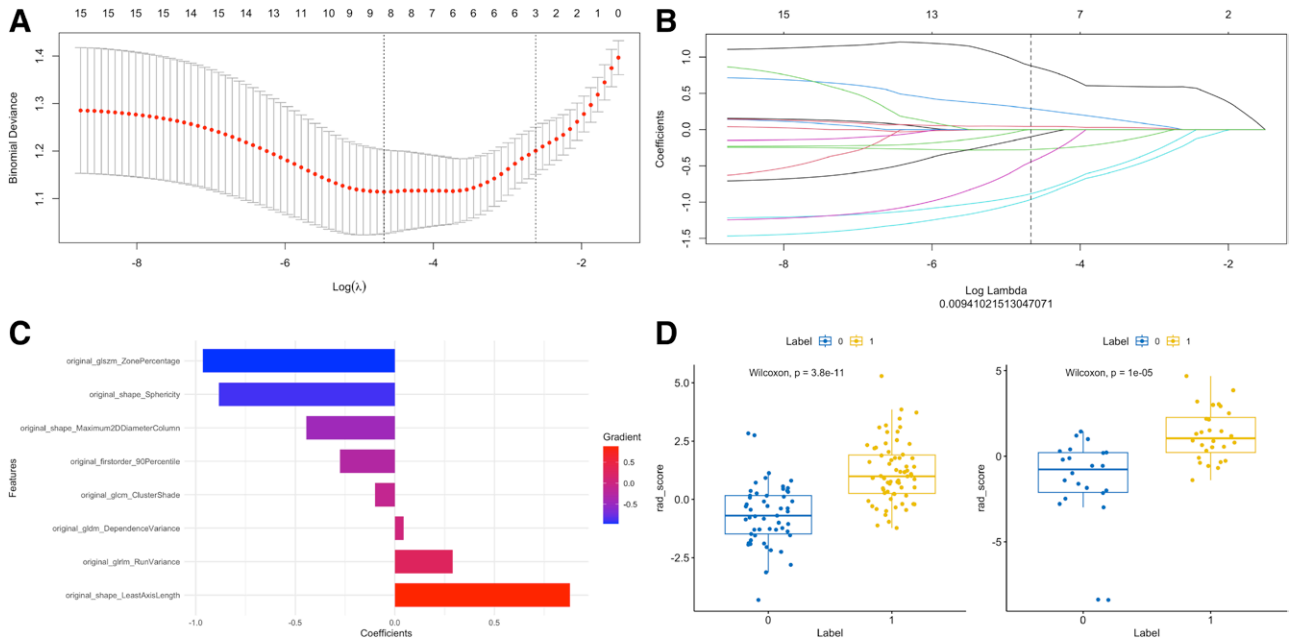


**Figure 3.** These figures illustrated the key steps in the model selection process, using 10-fold cross-validation to identify the optimal parameter (λ). This parameter was denoted by the minimum criterion, with the 1-standard error (SE) of the minimum criterion marked by vertical lines in Figure A. Figure B depicted the LASSO coefficient profiles, highlighting features with nonzero coefficients. The coefficients corresponding to the selected features are presented in Figure C. Finally, Figure D demonstrated the radiomics signature (rad_score). LASSO = least absolute shrinkage and selection operator, SE = standard error.

**Table 3**

**The nonzero coefficient features was chosen in non-enhanced phase.**

| Feature | Coefficients |
|---|---|
| original_shape_LeastAxisLength | 0.879 |
| original_glrlm_RunVariance | 0.290 |
| original_gldm_DependenceVariance | 0.044 |
| original_glcm_ClusterShade | −0.099 |
| original_firstorder_90Percentile | −0.276 |
| original_shape_Maximum2DDiameterColumn | −0.446 |
| original_shape_Sphericity | −0.884 |
| original_glszm_ZonePercentage | −0.964 |

We observed that in the empirical T-staging, the model performed better in the testing set than in the training cohort. The DeLong test further indicated no statistically significant difference between the radiomic model and the empirical staging in the testing set, which may be attributed to an insufficient sample size.

Accurate identification of high-risk colon cancer is crucial to avoid overtreatment and unnecessarily exposing low-risk patients to the high morbidity associated with preoperative treatment and subsequent surgical resection. CT scans can accurately provide tumor size and the extent of invasion into surrounding organs and structures. However, when it comes to the precise differentiation of individual T stages (T1, T2, T3, T4), CT lacks accuracy due to insufficient soft tissue contrast resolution. Indeed, a previous study has shown that there is a learning curve for radiologists to adequately identify high-risk colon cancers.[14] This finding was corroborated by the results of a meta-analysis,[15] which indicated that the accuracy of CT staging for colon cancer is not yet optimal. There is a need to adopt an alternative approach to risk stratification in CT. Accurately identifying different risk groups of colon cancer will guide treatment decisions and personalized care for patients with this disease.

In recent years, radiomics has emerged as a significant field in radiology, with applications ranging from predicting muscle invasion in bladder cancer[16] to forecasting the expansion of intracranial hemorrhages[17] and preoperative classification of ovarian cysts.[18] The findings of this study demonstrated that radiomics can more accurately detect high-risk T3–T4 tumors.

In this study, we developed and tested a CT radiomics model for differentiating between T1–T2 and T3–T4 staging in colon cancer patients, and compared it with empirical T-staging provided by experienced radiologists based on non-enhanced images. In the radiomics model, we delineated the entire tumor to extract shape, 1st-order, and texture features, used mRMR for feature selection, and finally identified independent predictors for distinguishing between T1–T2 and T3–T4 stages using LASSO logistic regression.

In the training and testing sets, the radiomics AUC values were 0.85 and 0.85, respectively, surpassing the AUC values derived from radiologists' empirical T-staging (0.71 and 0.76). This demonstrated a higher discriminative performance compared to Hong et al,[19] who used radiomics to differentiate between low-risk (T1–T2) and high-risk (T3–T4) stages of colon tumors, with AUCs of 0.799 and 0.727 in the training and testing sets, respectively. Given the limited use of CT radiomics for distinguishing between T1–T2 and T3–T4 stages of colon cancer, our study also compared to some MRI radiomics studies that analyzed rectal cancer patients, such as Liu et al[20] who performed texture feature analysis on MRI images (apparent diffusion coefficient maps) to identify locally advanced rectal cancer, achieving an AUC of 0.743. Ma et al[11] also used the LASSO method to predict rectal cancer T-staging (T1–T2 and T3–T4) related features extracted from T2-weighted MRI radiomics, achieving a prediction accuracy of 0.762. Our study results exceeded those of both studies. Additionally, Dou et al[21] used LASSO regression to predict high-risk rectal staging (T3–T4 staging) in rectal cancer patients, with an AUC of 0.85, comparable to our study results.

In our study, shape and texture features emerged as the most relevant radiomic characteristics for differentiating between the T1–T2 and T3–T4 stages of colon tumors.

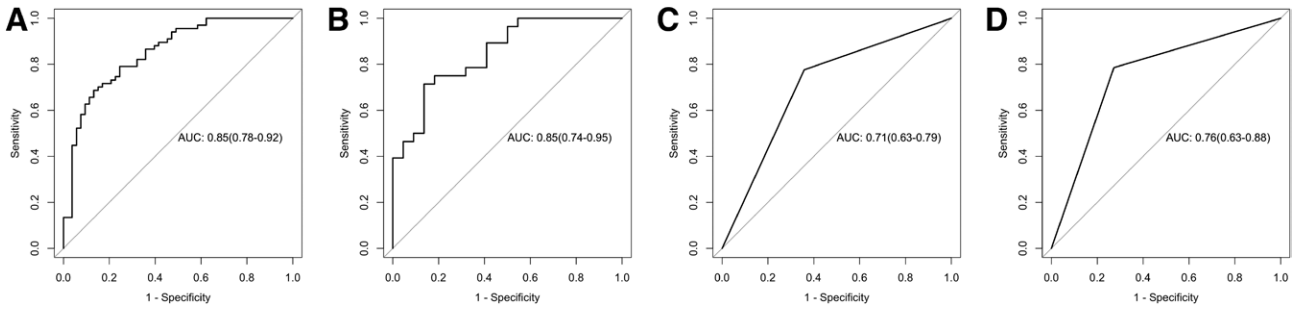


**Figure 4.** The ROC curves in both the training and testing sets. Figure A and B represented ROC curves of radiomics model in training and testing sets, respectively. Figure C and D represented ROC curves of the empirical model in training and testing sets, respectively. ROC = receiver operating characteristic.

**Table 4**

**The performance of both radiomics and empirical staging model.**

| Model | Dataset | AUC | Accuracy | Sensitivity | Specificity |
|---|---|---|---|---|---|
| LASSO | Train | 0.85 (95% CI: 0.78–0.92) | 0.77 | 0.87 | 0.69 |
| | test | 0.85 (95% CI: 0.74–0.95) | 0.78 | 0.87 | 0.71 |
| Empirical T | Train | 0.71 (95% CI: 0.63–0.79) | 0.72 | 0.73 | 0.69 |
| | Test | 0.76 (95% CI: 0.63–0.88) | 0.76 | 0.79 | 0.73 |

AUC = area under the curve, LASSO = least absolute shrinkage and selection operator.

The top 3 features with the highest coefficients were original_glszm_ZonePercentage, original_shape_Sphericity, and original_shape_LeastAxisLength, with coefficients of –0.964, –0.884, and 0.879, respectively (Table 3, Fig. 3C). This emphasized the critical role of shape features in the staging of colon cancer. These findings aligned with other studies,[22,23] which have shown the discriminative capability of tumor shape in staging.

Despite these significant findings, our study faced certain limitations. Firstly, our sample size was relatively small, and the lack of validation with data from external hospitals affected the confirmation of our model's performance. Secondly, our study did not incorporate clinical laboratory markers, nor did it explore whether laboratory markers could enhance the radiomics model. Future research should focus on multicenter, large-scale studies involving multiple manufacturers to reduce these limitations and integrate laboratory markers to enhance the predictive capability of the model.

## 5. Conclusion

Our study established CT radiomics as a superior quantitative tool for differentiating locally advanced (T3–T4) from early-stage (T1–T2) colon cancer, with AUCs of 0.85 in both the training and test sets – outperforming radiologists' empirical staging (AUC: 0.71 and 0.76, respectively), though the test set difference was not statistically significant. By capturing subvisual tumor heterogeneity, radiomics enhances preoperative risk stratification, optimizing patient selection for neoadjuvant therapy and personalized surgery. Integrating radiomics into clinical workflows may reduce staging subjectivity and improve treatment decisions in colon cancer management.

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