



Application of dual-layer spectral detector computed tomography to evaluate the expression of Ki-67 in colorectal cancer

Yu-Li Wang^a, Han-Wen Zhang^{a,*}, Yong-Qian Mo^a, Hua Zhong^a, Wei-Ming Liu^a, Yi Lei^a, Fan Lin^{a,*}

^aDepartment of Radiology, The First Affiliated Hospital of Shenzhen University, Health Science Center, Shenzhen Second People's Hospital, Shenzhen, China

Abstract

Background: Compared with traditional computed tomography (CT), dual-layer spectral detector CT (SDCT) shows significant improvement in imaging soft tissues of the digestive tract. This work aimed to explore the application of SDCT to evaluate the expression of the molecular marker Ki-67 in colorectal cancer.

Methods: We retrospectively analyzed the imaging data of the SDCT (IQon Spectral CT; Philips Healthcare) of 45 patients with colorectal cancer in our centre. We used Spearman's test for the imaging parameters (reconstruction of 40, 70, and 100 keV virtual monoenergetic images [VMIs] and the slope of the Hounsfield unit attenuation plot [VMI Slope] based on venous phase CT images, the arterial phase iodine concentration [AP-IC] and venous phase iodine concentration [VP-IC], and the effective atomic number [Z effect]) and correlation analysis for the Ki-67 index. Multivariate logistic regression was used to eliminate confounding factors. We evaluated the expression level of Ki-67 and drew the receiver operating characteristic curve.

Results: The 40-keV VMI, VMI Slope, and AP-IC were found to better reflect the Ki-67 index in patients with colorectal cancer with statistical significance. The 40-keV VMI (r = -0.612, p < 0.001) and VMI Slope (r = -0.523, p < 0.001) were negatively correlated with the Ki-67 index, and AP-IC (r = 0.378, p = 0.010) was positively correlated with the Ki-67 index. The other indexes (p > 0.05) were not statistically significant. The SDCT parameters demonstrated good performance, with area under curves of 0.785 for 40-keV VMI and 0.752 for AP-IC. **Conclusion:** The SDCT parameters 40-keV VMI and AP-IC can be used for preliminary evaluation of the Ki-67 index in colorectal cancer.

()

Keywords: Colorectal neoplasms; Delivery of health care; Humans; Iodine; ROC curve

1. INTRODUCTION

Colorectal cancer is a common malignant tumor of the digestive tract, and it usually occurs in people 40 to 60 years of age. Tumors usually develop at the junction of the sigmoid colon and rectum. At present, studies have shown that a low-fiber diet, genetics, a faster pace of life, high fat, and other factors can influence the incidence and mortality of colorectal cancer, which has increased year over year. Usually, patients are prone to various manifestations, such as weight loss, low fever, and fatigue, due to factors such as toxin absorption, tumor ulceration, and blood loss. With

Dr. Fan Lin, Department of Radiology, The First Affiliated Hospital of Shenzhen University, Health Science Center, Shenzhen Second People's Hospital, 3002 SunGangXi Road, Shenzhen, China. E-mail address: foxetfoxet@gmail.com (F. Lin.). Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article. Journal of Chinese Medical Association, (2022) 85: 610-616.

Received October 18, 2021; accepted January 17, 2022.

doi: 10.1097/JCMA.000000000000706.

continuous progression of the disease, abdominal masses, intestinal obstruction, and other symptoms can develop, which can seriously threaten the health and quality of life of these patients.¹

A variety of factors, genes, and cytokines are well known to be involved in the occurrence and development of colorectal cancer. The detection of cancer-related proteins helps to detect cancer early and prevent its development. Ki-67 is a protein in the nucleus and is closely related to cell proliferation (the degree of cell division).² Studies have shown that Ki-67 is a late-stage immune marker for cell entry into cell proliferation, and it is closely related to tumor differentiation and metastasis and is widely used as a marker for clinical cell proliferation. Ki-67 is expressed at low levels in normal tissues and at high levels in tumor cells. In patients with colorectal cancer, Ki-67 can promote tumor cell proliferation and may have a synergistic effect in promoting tumor angiogenesis and tumor cell hyperproliferation. These factors interact with each other through tumor angiogenesis and promote the development of colorectal cancer.³ Ki-67 is also a key indicator for colorectal cancer preoperative chemoradiotherapy (CRT),⁴ as it can be used to determine the degree of efficacy of CRT in patients.⁵ CRT can reduce the size and stage of the tumor, making the tumor easier to be removed by surgery. Current study has shown that the expression of Ki-67 can reflect the effect of this treatment. At the same time, it is also closely related to patient prognosis and tumor cell metastasis. In the study by Hotta et al, compared to the nuclear-tomass ratio or vascular permeability changes, Ki-67 and lymph

www.ejcma.org

()

^{*}Address correspondence. Dr. Han-Wen Zhang, Department of Radiology, The First Affiliated Hospital of Shenzhen University, Health Science Center, Shenzhen Second People's Hospital, 3002 SunGangXi Road, Shenzhen, China. E-mail address: zhwstarcraft@outlook.com (H.-W. Zhang.).

Copyright © 2022, the Chinese Medical Association. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/ by-nc-nd/4.0/)

Original Article. (2022) 85:5

nodes determined the recurrence-free survival rate and overall survival rate of patients.⁶

The formulation of an individualized treatment plan for patients with colorectal cancer relies on the evaluation of the malignant degree of the tumor in preoperative imaging. Due to the poor resolution of traditional computed tomography (CT) soft tissues, it is sometimes difficult to evaluate the depth of invasion, lymph node staging, and postoperative evaluation.⁷ In clinical practice, magnetic resonance imaging (MRI) is usually used for more in-depth research.8 For colorectal cancer patients, imaging omics research is mostly based on MRI.9 Among the studies using Ki-67, a number of MRI studies have shown that using the apparent diffusion coefficient value of diffusionweighted imaging (DWI) or the D value of intravoxel incoherent motion using its derivative technology have good judgment value for the performance of Ki-67.¹⁰⁻¹² However, regardless of whether DWI or its derivative technology is used, because the scanning time is very long, patients need to have a good respiratory status and some patients with more serious conditions cannot tolerate this examination well.

However, the appearance of dual-layer spectral detector CT (SDCT) has greatly improved the imaging of soft tissues. CT energy imaging can provide multiparametric information that conventional CT imaging cannot without increasing the radiation dose.¹³ It also has advantages in improving the sensitivity and qualitative accuracy of lesion detection, allowing for determinations of material composition and reducing metal artifacts.14 In addition to the anatomical information that can be obtained by conventional CT, it can yield a variety of energy spectrum images and allows for quantitative analysis methods to be performed through postprocessing, such as virtual plain scan, virtual monoenergetic image (VMI), iodine concentration (IC), effective atomic number (Z effect), and other functions. This provides more valuable information for the diagnosis of tumors and disease.¹⁵ At present, it is widely applied to the central nervous system, as well as the cardiovascular system and urinary tract.^{16,17} At present, SDCT is relatively rarely applied to patients with colorectal cancer, and there have been no reports on the Ki-67 index in colorectal cancer. At present, there is only one report on the Ki-67 index in patients with rectal cancer using dual-energy CT (DECT), which was conducted by Fan et al.¹⁸

By evaluating the Ki-67 tumor proliferation index before surgery, the treatment team can better predict patient prognosis and formulate the surgical procedure and treatment plans. The purpose of this study was to perform a correlation analysis with the various parameters of SDCT and the pathological index of colorectal cancer (Ki-67) and to explore the application of SDCT in this disease.

2. METHODS

2.1. Patients

From March 2020 to August 2021, 90 patients with colorectal space occupied by SDCT scans (IQon Spectral CT; Philips Healthcare, the Netherlands) were enrolled in our centre. The inclusion criteria were as follows: (1) enhanced SDCT scan of the abdomen and pelvis before operation and surgical treatment within 1 week after examination; (2) diagnosed with colorectal cancer after surgery and obtained complete Ki-67 pathological results. The exclusion criteria were as follows: (1) CT image quality that did not meet the evaluation requirements (such as titanium clip artifacts etc); (2) lesions that were too small affected the selection of the region of interest (ROI; such as carcinoma in situ); and (3) rectal cancer recurrence or neoadjuvant therapy before surgery. Finally, a total of 45 patients were enrolled, including 18 males and 27 females, aged 32 to 84 (mean \pm SD, 62 \pm 14) years. This study was approved by the local ethics committee.

2.2. Dual-layer spectral detector computed tomography scanning solution

An SDCT (IQon Spectral CT) was used for scanning. Before the CT examination, the patient fasted for 4 to 6 hours without intramuscular injection of antispasmodic drugs or oral contrast agents. The scan range was from the top of the diaphragm to the level of the lower edge of the bilateral symphysis pubis. The scanning parameters used are as follows: the width of the collimator was 64×0.625 mm, the tube voltage was 120 kVp, automatic tube current control technology (78-145 mA) was adopted, the radiograph tube rotation speed was 0.5 s/cycle, and the pitch was 0.969. The reconstruction layer thickness was 1.0 mm, and the layer spacing was 0.5 mm. The enhanced scan used contrast agent intelligent tracking threshold trigger technology. The trigger point was set in the abdominal aortic lumen at the celiac trunk. The trigger threshold was 120 Hounsfield units (HUs). The venous phase started to be collected 30 seconds after the end of the arterial phase scan. Iopramide (350 mg/mL iodine concentration) was used as the contrast agent at a dose of 1.2 mL/kg, and the injection rate was 3.0 mL/s.

2.3. Imaging and pathological specimen analyses

A Philips SpDS image workstation (Spectral Diagnostic Suite 6.5) was used to reconstruct VMIs based on CT venous phase images (the best period of clinical observation: because colorectal cancer lesions are clearly displayed in the venous phase and it is easy to observe the edge of the lesion, thus, the venous phase image is usually selected as the labeling object). The VMI was reconstructed every 30 keV in the range of 40 to 100 keV to obtain 40-, 70-, and 100-keV VMIs, and the slope of the HU attenuation plot (VMI Slope: slope, 40/100 keV value) was calculated. At the same time, the arterial phase IC (AP-IC) and venous phase IC (VP-IC) images and Z effect were obtained through the postprocessing workstation to obtain 7 sets of images. Two radiologists with extensive experience used a blinded method to jointly evaluate the tumor area and divide it as follows: select the largest tumor level and place the circular ROIs in the most obvious area of tumor enhancement, avoiding the tumor edge, intestinal wall blood vessels, and tumor necrosis area and surrounding inflammatory reaction area. The ROI is set to 25 to 200 mm² in size. Without changing the size and position of the ROI, by adjusting different keV values, measure the average HU of the corresponding parts in the three groups of VMI. At the same time, measure the IC value and Z effect.

Using the immunohistochemical streptavidin-peroxidase method, specimens were collected, fixed, dehydrated, embedded, sectioned, and deparaffinized. Mouse anti-human Ki-67 monoclonal antibody was added, and the sections were stained with hematoxylin and eosin, mounted on slides, and viewed under a microscope. The nuclei of positive cells were stained brown. A total of 1000 cells were randomly selected, and the positivity rate was calculated.

2.4. Statistical analysis

We used the Statistical Package for the Social Sciences (SPSS v. 19; Chicago, IL) for statistical analysis. The intra/interclass correlation coefficients (ICCs) were used to calculate consistency between reviewers. A two-sided p value <0.05 was considered statistically significant. Because the imaging data did not conform to a normal distribution, we used the Spearman's test combined with the Ki-67 index for the correlation analysis to compare and evaluate various imaging measurement parameters. p < 0.05 was considered to indicate statistical significance.

()

Wang et al.

All statistical graphs were made using GraphPad Prism 7 (Prism 7; La Jolla, CA).

We divided patients into a high-expression group (>50%, n = 28) and low-expression group (\leq 50%, n = 17) based on Ki-67 expression. According to the expression level of Ki-67, the continuous and classification variables of all patients are represented as the mean ± SD and n (%), respectively. The Mann-Whitney *U* test was used to compare continuous variables between low and high Ki-67 expression. A *p* value <0.05 was considered to be statistically significant. A univariate logistic regression analysis was performed to select parameters with predictive significance for Ki-67 expression. The parameters of *p* < 0.05 were selected to construct multivariate logistic regression to eliminate confounding factors. Receiver operating characteristic curve (ROC) analysis was used to evaluate the diagnostic capabilities of the SDCT parameters, including calculation of the area under curve (AUC) value and 95% CI.

3. RESULTS

The age and sex of the patients and the Ki-67 index of colorectal cancer were not statistically significant. The interobserver agreement of all measurements between the two reviewers was excellent, with ICC values greater than 0.80. Basic patient information, imaging information (average of the ROI values taken by two radiologists), and pathological information are shown in Supplementary Table 1, http://links.lww.com/JCMA/A134.

3.1. Associations between SDCT continuous variables and Ki-67 expression

The results of the Spearman-related tests are shown in Table 1. The results indicate that 40-keV VMI, VMI Slope, and AP-IC are statistically significant. Among them, the results for 40-keV VMI (r = -0.612, p < 0.001), VMI Slope (r = -0.523, p < 0.001), and AP-IC (r = 0.378, p = 0.010) indicated that the HU value of 40 keV was negatively correlated with the Ki-67 index, VMI Slope, and AP-IC and that the Ki-67 index was positive (Fig. 1). However, there was no significant correlation between the VP-IC, Z effect, 70-keV VMI, and 100-keV VMI.

We performed a Mann-Whitney *U* test on the basic information of patients and SDCT parameters (Table 2), and the results of the univariate logistic regression showed that VMI Slope (p = 0.04), 40 keV (p < 0.001), and AP-IC (p = 0.08) were good predictors of Ki-67 expression. The results of the multivariate logistic regression showed that VMI Slope (p = 0.478) was not a good predictor of Ki-67 expression, whereas 40 keV (p = 0.048) and AP-IC (p = 0.050) were; therefore, VMI Slope was eliminated as a confounding factor. The ROC showed good performance, with AUCs of 0.785 for 40 keV VMI and 0.752 for AP-IC (Fig. 2).

Table 1

Spearman correlation analysis of Ki-67 index and spectral detector computed tomography parameters in patients with colorectal cancer

	40-keV	70-keV	100-keV				Ζ
	VMI	VMI	VMI	VMI Slope	AP-IC	VP-IC	effect
Correlation coefficient	-0.612	-0.290	-0.201	-0.523	0.378	0.050	0.035
p	< 0.001	0.053	0.185	< 0.001	0.010	0.742	0.819

p < 0.05 indicates statistical significance. A correlation coefficient closer to 1 indicates that the correlation of the parameter is stronger. Negative values represent a negative correlation. AP-IC = arterial phase iodine concentration; VMI = virtual monoenergetic image; VP-IC = venous phase iodine concentration.

4. DISCUSSION

In this study, various SDCT parameters were used to evaluate the Ki-67 index in patients with colorectal cancer preoperatively, and the results showed that 40-keV VMI and AP-IC were correlated with Ki-67 expression. In SDCT, the original data space has been suppressed by anticorrelation noise, which can basically achieve a constant all-energy spectrum and low noise. A study in 2019 showed that the 72-keV VMI imaging level is basically the same as the traditional CT imaging level.¹⁹ The single energy levels of 40 keV and 50 keV can ensure a low level of noise, which is infinitely close to the 33-keV level of the iodine k edge, thereby improving the detection of lesions.²⁰ At the same time, relative to the high energy level, the soft tissue contrast is increased under the condition of 40 keV. The results of this study revealed that compared with 70 keV and 100 keV, 40 keV is correlated with Ki-67 expression in colorectal cancer; that is, as the Ki-67 index increases, the 40-keV HU level gradually decreases. At the same time, VMI Slope was also confirmed to be negatively correlated with Ki-67 expression in this study. The iodine density map can be used to make a preliminary assessment of the blood supply status and corresponding hemodynamics in tumor cells based on the iodine concentration value and increase the detection rate of lesions.²¹ In our study, there was also a significant correlation between the arterial iodine concentration and Ki-67, which is an indicator of tumor proliferation. With increasing Ki-67 expression, the AP-IC value also increased, but the VP-IC value did not show a similar performance. Z effect uses the attenuation effect of radiograph attenuation on a substance to be equivalent to a certain element, which becomes the effective atomic number diagram of the substance. A correlation between the Z effect and Ki-67 index was not found in this study (Fig. 3).

VMI is calculated from high- and low-energy data sets, which is equivalent to a CT image under a single energy ray. As the energy level decreases, the attenuation of iodine gradually increases. Low-level VMI can increase the CT value and tissue contrast of blood vessels and abnormally enhanced lesions, which is helpful for the detection of abnormally enhanced lesions. Previous reports have shown that SDCT 40-keV VMIs can increase the detection rate of gastrointestinal lesions.²² In contrast to Fan et al's research conclusion on Ki-67 using DECT, we found that the HU value at 40 keV is correlated with the Ki-67 index,18 but they did not find this correlation in their research. This phenomenon may be related to DECT and SDCT imaging technology. SDCT has a relatively unique stereo double-sided detector technology; the upper and lower spectral detectors can receive high- and low-energy-level radiograph attenuation information at the same time, which is beneficial to reduce the scanning time and maintain the integrity of the data to achieve reconstruction in the projection space, thereby improving the accuracy of energy analysis.²³ Due to individual differences, especially in elderly patients, circulatory disturbances and other reasons lead to poor vascular and tissue enhancement. Spectral CT can retrospectively use low-energy VMI images to increase the CT value of vascular enhancement and improve image quality. At the same time, we found that Ki-67 has a significant negative correlation with 40 keV. In terms of conventional understanding, the tumor malignancy increases with the increase in Ki-67 expression levels, and the imaging usually shows an increase in the degree of enhancement. The HU value of low-energy VMI images decreases as the malignancy of colorectal cancer increases. On the one hand, it shows that SDCT improves the image quality, and at the same time, it magnifies the subtle difference in the density reduction caused by the invasion of the tissue cells by the tumor. On the other hand, the VMI of SDCT distinguishes the increase in iodine density caused by highly malignant colorectal tumors with an

www.ejcma.org

()

Original Article. (2022) 85:5

J Chin Med Assoc



Fig. 1 Spearman correlation analysis scatter plot (blue line: fitted line; red dot: scatter plot; yellow area: Cl). A, Correlation analysis between Ki-67 and 40keV virtual monoenergetic image (VMI). B, Correlation analysis between Ki-67 and VMI Slope. C, Correlation analysis between Ki-67 and arterial phase iodine concentration (AP-IC).

Table 2

Clinical characteristics, imaging characteristics, and SDCT parameters based on differences in Ki-67 expression

	Ki-67 expression level			
 Variable	Low (n = 17)	High (n = 28)	p	
Clinical characteristics				
Age, y	63.00 ± 13.17	61.69 ± 28	0.981	
Sex			0.456	
Male	7 (41.2%)	10 (35.7%)		
Female	10 (58.8%)	18 (64.3%)		
Location				
Colon	12 (70.6%)	13 (46.4%)		
Rectum	5 (29.4%)	15 (53.6%)		
T staging				
Phase 1/2	5 (29.4%)	8 (28.6%)		
Phase 34	12 (70.6%)	20 (71.4%)		
Lymph node metastasis				
Yes	7 (41.1%)	12 (42.9%)		
No	10 (58.9%)	16 (57.1%)		
Distant metastasis (m)				
Yes		2 (7.1%)		
No	17 (100%)	26 (92.9%)		
SDCT parameters				
40-keV VMI	180.53 ± 44.03	143.07 ± 17.72	0.001	
70-keV VMI	79.76 ± 12.65	76.86 ± 11.86	0.373	
100-keV VMI	57.53 ± 6.00	55.18 ± 5.14	0.244	
VMI Slope	3.16 ± 0.80	2.63 ± 0.36	0.008	
AP-IC	0.74 ± 0.43	1.11 ± 0.42	0.005	
VP-IC	1.51 ± 0.060	1.64 ± 0.42	0.286	
Z effect	8.13 ± 0.30	8.20 ± 0.20	0.313	

p < 0.05 indicates statistical significance. Values are the mean \pm SD.

AP-IC = arterial phase iodine concentration; VMI = virtual monoenergetic image; VP-IC = venous phase iodine concentration; SDCT = spectral detector computed tomography.

www.ejcma.org

abundant blood supply from the decrease in density based on the enhanced image, which is difficult for conventional CT. In the high-energy-level imaging of 100-keV VMI, the HU value of the lesion is concentrated at 40 to 60 HU (no statistical difference), which led to the correlation between VMI Slope and Ki-67 in the Spearman test; however, VMI Slope was still eliminated as a confounding factor by the multivariate logistic regression.



Fig. 2 ROC curves of the various parameters of spectral detector computed tomography for preoperative prediction of Ki-67 in patients with colorectal cancer. AUC = area under curve; IC = iodine concentration; ROC = receiver operating characteristic curve; VMI = virtual monoenergetic image.

613

Wang et al.

J Chin Med Assoc



Fig. 3 A 70-y-old female patient with ascending colon cancer (yellow arrow). A, The 40- 200-keV Hounsfield unit (HU) attenuation plot. B1, Routine plain scan. B2, Arterial phase-enhanced scan. B3, Venous phase-enhanced scan. C1, The effective atomic number can measure the effective atomic number of the lesion. C2, Arterial phase iodine concentration has poor resolution, but it can quantitatively analyze the iodine concentration in the lesion. C3, The 40-keV virtual monoenergetic image based on venous phase-enhanced reconstruction can not only perform a more detailed analysis of the lesion but also improve the contrast compared to traditional venous phase-enhanced images (B3). ROI = region of interest.

In the study by Yang et al, the imaging parameters of spectral CT (including IC, normalized iodine concentration, and the slope of the spectral HU curve) were significantly improved compared to traditional 70-keV CT for evaluating the degree of differentiation in colon cancer.²⁴ Our research also reached a similar conclusion; ie, the iodine concentration in the arterial phase is relevant to the judgment of colorectal cancer. As the Ki-67 index increases, the IC value will also increase. Our results differ from the research conclusions of Fan et al, who used DECT in their study and confirmed that the iodine concentration value can not only be used to evaluate the Ki-67 index of colorectal cancer but also to distinguish between the arterial phase and the venous phase. In our study, only the iodine concentration at AP reacted to the content of Ki-67, and the iodine concentration at VP had no correlation. This shows that the iodine concentration is dependent on the Ki-67 index in patients with colorectal cancer. However, compared with the IC value of the venous phase, only the IC value of the arterial phase is dependent on Ki-67 expression. This change

may be related to the tumor microenvironment. It is generally believed that this may be because as the malignancy of colorectal cancer increases, the blood supply required by the tumor also increases. In the arterial phase, because the IC value is mainly affected by the blood supply of the tumor, during the early stage of enhancement, the level of malignancy can be clearly distinguished statistically. However, this performance was not reflected in the intravenous phase in this study. This phenomenon may be due to the changes in the microenvironment within the tumor, which may be due to the following two reasons: (1) the localized expansion of the microvessels leads to the accumulation of contrast agent and increase in the iodine concentration; (2) due to differences in the circulatory function of patients (especially the elderly), the rate of passage of the contrast agent is reduced. Compared with the DECT-only study on the Ki-67 index of colorectal cancer, this study distinguished between the different periods of enhancement and concluded that only the IC value of the arterial phase is affected by the Ki-67 index.18

This study did not find Ki-67 expression to be correlated with the Z effect in patients with colorectal cancer. Although many studies have shown that the Z value can be used to distinguish high- or low-grade intestinal tumors,²⁵ it seems that the Z effect is not as significant as the expression of the more refined tumor index Ki-67. This result may be because in their study only 8 patients were compared with Z effect, and only because of the classification of the high and low levels of colorectal cancer was it not subdivided based on Ki-67 expression. In terms of clinical application, this technology mainly uses pseudo color images to intuitively reflect the difference in effective atomic number of lesions in the area, which leads to differences in visualization, allowing the doctors to detect lesions. At present, it has a good application in determining the scope of pulmonary embolism and detecting negative stones in the gallbladder (Supplementary Fig. 1, http://links.lww.com/JCMA/ A134). In this study, the more subtle judgments on the pathology of colorectal cancer did not seem to be as accurate as the other quantification indexes.

In fact, an increasing number of studies have found no significant difference in the accuracy of colorectal cancer research when DECT versus MRI is used.²⁶ SDCT has further improved the imaging quality and accuracy. Compared with MRI, SDCT shows a significant improvement in terms of the spatial resolution of soft tissue. While providing more information about lesion parameters, it also confers the traditional advantages of CT, namely, high-resolution, fast scanning speed, and reduced motion artifacts. In addition, it is less expensive than MRI, which facilitates screening and reduces the burden on patients. The parameters and imaging methods of DECT play a significant role in applications such as detecting gastrointestinal tumors, distinguishing tumor from normal tissues, identifying excretions in the gastrointestinal tract, and evaluating lymph node metastasis. In the study by Najami et al, a more detailed analysis of the lymph nodes around the tumor revealed that the use of dual-energy CT can even identify lymph nodes that are affected by tumor metastasis.27 A similar conclusion was reached in the study by Sato et al, in which the IC value of metastatic lymph nodes was significantly reduced.²⁸ In addition to the IC value, Sun et al found that the Z effect is also significantly correlated with lymph node metastasis in rectal cancer. In the study of colorectal cancer liver metastasis, DECT can not only identify the lesions effectively but also yields higher quality images. At the same time, the dual-energy iodine map has a very significant effect on distinguishing benign and malignant tumors and improving the screening rate.29 In patients with colorectal cancer after radiotherapy and chemotherapy, multiple studies have found that the HU value, IC value, and Z effect in DECT are significantly reduced.^{30,31} As an upgraded version of DECT, we have a reason to believe that SDCT can play a greater role in disease detection.

This study has some limitations, such as an insufficient sample size and no patient prognostic information. In this study, we could only identify a correlation between the parameters of SDCT and the expression of Ki-67 in colorectal cancer. With a more sufficient sample size and a longer follow-up time, we hope to construct a reliable nomogram to evaluate the malignancy and survival time of patients with colorectal cancer before surgery in the future. In addition, the one-to-one correspondence of lesions in pathology imaging allows us to more accurately understand the relationship between the pathology and imaging of colorectal cancer. It can also help doctors better serve patients by formulating more accurate treatment and prognosis plans before surgery.

In conclusion, our study found that the 40-keV VMI and AP-IC values of SDCT are correlated with the Ki-67 index in colorectal cancer.

J Chin Med Assoc

ACKNOWLEDGMENTS

()

This study is supported by a grant from Clinical Research Project of Shenzhen Second People's Hospital, China (No. 20203357036). Thanks to Siling Gu and Lin Wang for their help in this research.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://links.lww.com/JCMA/A134.

REFERENCES

- 1. Sivrioglu AK, Aribal A, Onder H, Onol SD. Utility of MR imaging in the evaluation of colon cancer. *Jpn J Radiol* 2017;35:404–5.
- Wu XL, Yang ZW, He L, Dong PD, Hou MX, Meng XK, et al. RRS1 silencing suppresses colorectal cancer cell proliferation and tumorigenesis by inhibiting G2/M progression and angiogenesis. *Oncotarget* 2017;8:82968–80.
- Pap Z, Ilyés IÁ, Mocan SL, Dénes L, Muică Nagy-Bota MC, Pávai Z, et al. Changes in immunoexpression of p53, Ki-67, Ets-1, APAF-1 and PTEN in serrated and conventional colon adenomas. *Rom J Morphol Embryol* 2015;56:1389–96.
- Yoshikawa K, Shimada M, Higashijima J, Nakao T, Nishi M, Takasu C, et al. Ki-67 and survivin as predictive factors for rectal cancer treated with preoperative chemoradiotherapy. *Anticancer Res* 2018;38:1735–9.
- Jafarian AH, Kermani AT, Esmaeili J, Roshan NM, Seilanian-Toosi M, Omidi AA, et al. The role of COX-2 and Ki-67 over-expression in the prediction of pathologic response of rectal cancer to neoadjuvant chemoradiation therapy. *Indian J Cancer* 2016;53:548–51.
- Hotta K, Shimoda T, Nakanishi Y, Saito D. Usefulness of Ki-67 for predicting the metastatic potential of rectal carcinoids. *Pathol Int* 2006;56:591–6.
- Liu LH, Lv H, Wang ZC, Rao SX, Zeng MS. Performance comparison between MRI and CT for local staging of sigmoid and descending colon cancer. *Eur J Radiol* 2019;**121**:108741.
- Kim C, Kim SY, Kim MJ, Yoon YS, Kim CW, Lee JH, et al. Clinical impact of preoperative liver MRI in the evaluation of synchronous liver metastasis of colon cancer. *Eur Radiol* 2018;28:4234–42.
- Meng X, Xia W, Xie P, Zhang R, Li W, Wang M, et al. Preoperative radiomic signature based on multiparametric magnetic resonance imaging for noninvasive evaluation of biological characteristics in rectal cancer. *Eur Radiol* 2019;29:3200–9.
- Meyer HJ, Höhn AK, Woidacki K, Andric M, Powerski M, Pech M, et al. Associations between IVIM histogram parameters and histopathology in rectal cancer. *Magn Reson Imaging* 2021;77:21–7.
- Surov A, Meyer HJ, Höhn AK, Behrmann C, Wienke A, Spielmann RP, et al. Correlations between intravoxel incoherent motion (IVIM) parameters and histological findings in rectal cancer: preliminary results. *Oncotarget* 2017;8:21974–83.
- Sun Y, Tong T, Cai S, Bi R, Xin C, Gu Y. Apparent diffusion coefficient (ADC) value: a potential imaging biomarker that reflects the biological features of rectal cancer. *PLoS One* 2014;9:e109371.
- Ommen FV, Jong HD, Dankbaar JW, Bennink E, Leiner T, Schilham A. Dose of CT protocols acquired in clinical routine using a duallayer detector CT scanner: a preliminary report. *Eur J Radiol* 2019;112:65–71.
- Li B, Pomerleau M, Gupta A, Soto JA, Anderson SW. Accuracy of dualenergy CT virtual unenhanced and material-specific images: a phantom study. AJR Am J Roentgenol 2020;215:1146–54.
- Hua CH, Shapira N, Merchant TE, Klahr P, Yagil Y. Accuracy of electron density, effective atomic number, and iodine concentration determination with a dual-layer dual-energy computed tomography system. *Med Phys* 2018;45:2486–97.
- 16. Nadjiri J, Kaissis G, Meurer F, Weis F, Laugwitz KL, Straeter AS, et al. Accuracy of calcium scoring calculated from contrast-enhanced coronary computed tomography angiography using a dual-layer spectral CT: a comparison of calcium scoring from real and virtual non-contrast data. PLoS One 2018;13:e0208588.
- 17. Ananthakrishnan L, Duan X, Xi Y, Lewis MA, Pearle MS, Antonelli JA, et al. Dual-layer spectral detector CT: non-inferiority assessment compared to dual-source dual-energy CT in discriminating uric

www.ejcma.org

Wang et al.

acid from non-uric acid renal stones ex vivo. *Abdom Radiol (NY)* 2018;43:3075-81.

- 18. Fan S, Li X, Zheng L, Hu D, Ren X, Ye Z. Correlations between the iodine concentrations from dual energy computed tomography and molecular markers Ki-67 and HIF-1α in rectal cancer: a preliminary study. *Eur J Radiol* 2017;96:109–14.
- Große Hokamp N, Gilkeson R, Jordan MK, Laukamp KR, Neuhaus VF, Haneder S, et al. Virtual monoenergetic images from spectral detector CT as a surrogate for conventional CT images: unaltered attenuation characteristics with reduced image noise. *Eur J Radiol* 2019;117:49–55.
- 20. Nagayama Y, Iyama A, Oda S, Taguchi N, Nakaura T, Utsunomiya D, et al. Dual-layer dual-energy computed tomography for the assessment of hypovascular hepatic metastases: impact of closing k-edge on image quality and lesion detectability. *Eur Radiol* 2019;**29**:2837–47.
- Zhang XP, Wang ZL, Tang L, Sun YS, Cao K, Gao Y. Support vector machine model for diagnosis of lymph node metastasis in gastric cancer with multidetector computed tomography: a preliminary study. *BMC Cancer* 2011;11:10.
- 22. Taguchi N, Oda S, Imuta M, Yamamura S, Yokota Y, Nakaura T, et al. Dual-energy computed tomography colonography using dual-layer spectral detector computed tomography: utility of virtual monochromatic imaging for electronic cleansing. *Eur J Radiol* 2018;**108**:7–12.
- Kalender WA, Klotz E, Kostaridou L. An algorithm for noise suppression in dual energy CT material density images. *IEEE Trans Med Imaging* 1988;7:218–24.

 Yang CB, He TP, Duan H, Jia YJ, Zhang XR, Ma GM, et al. Quantitative assessment of the degree of differentiation in colon cancer with dualenergy spectral CT. *Abdom Radiol* 2017;42:2591–6.

J Chin Med Assoc

- Al-Najami I, Mahmoud Sheta H, Baatrup G. Differentiation between malignant and benign rectal tumors by dual-energy computed tomography - a feasibility study. *Acta Oncol* 2019;58(Suppl 1):55–9.
- Al-Najami I, Lahaye MJ, Beets-Tan RGH, Baatrup G. Dual-energy CT can detect malignant lymph nodes in rectal cancer. *Eur J Radiol* 2017;90:81–8.
- 27. Al-Najami I, Beets-Tan RG, Madsen G, Baatrup G. Dual-energy CT of rectal cancer specimens: a CT-based method for mesorectal lymph node characterization. *Dis Colon Rectum* 2016;**59**:640–7.
- Sato K, Morohashi H, Tsushima F, Sakamoto Y, Miura T, Fujita H, et al. Dual energy CT is useful for the prediction of mesenteric and lateral pelvic lymph node metastasis in rectal cancer. *Mol Clin Oncol* 2019;10:625–30.
- Sun K, Han R, Han Y, Shi X, Hu J, Lu B. Accuracy of combined computed tomography colonography and dual energy iiodine map imaging for detecting colorectal masses using high-pitch dual-source CT. Sci Rep 2018;8:3790.
- Sauter AP, Kössinger A, Beck S, Deniffel D, Dapper H, Combs SE, et al. Dual-energy CT parameters in correlation to MRI-based apparent diffusion coefficient: evaluation in rectal cancer after radiochemotherapy. *Acta Radiol Open* 2020;9:2058460120945316.
- 31. Al-Najami I, Drue HC, Steele R, Baatrup G. Dual energy CT a possible new method to assess regression of rectal cancers after neoadjuvant treatment. *J Surg Oncol* 2017;**116**:984–8.

www.ejcma.org

616

۲