

#### **ORIGINAL ARTICLE**

# Diagnostic accuracy of Perfusion Computed tomography (PCT) for diagnosis of colorectal carcinoma (CRC) taking histopathology as gold standard.

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**ABSTRACT... Objective:** To determine diagnostic accuracy of Perfusion Computed tomography (PCT) for diagnosis of colorectal carcinoma (CRC) taking histopathology as gold standard. **Study Design:** Descriptive, Cross-sectional. **Setting:** Department of Radiology, Allied Hospital Faisalabad. **Period:** 10<sup>th</sup> March 2022 to 9<sup>th</sup> September 2022. **Material & Methods:** A total of 451 patients with colorectal cancer suspicion and ages 50-80 years of either gender were included in the study. Patients having severe renal disease, preoperative radiation therapy or chemotherapy, no surgical intervention after CT, contrast media contraindication, pathologically benign colorectal mass, and tumor depth less than 2 cm based on CT were not included. Pre-operative perfusion CTs was performed on all patients. Dynamic perfusion CTs were performed for 65 seconds following intravenous administration of contrast media, and blood flow (BF) and blood volume (BV) in the tumor were assessed. The surgical specimens were forwarded to the hospital's pathology laboratory, where the presence of CRC was labeled according to operational definitions. CT perfusion was performed in radiology department and results of PCT were compared with that of histopathology. **Results:** Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of PerfusionComputed tomography (PCT) in diagnosing colorectal carcinoma (CRC) with histopathology being gold standard was 90.26%, 88.59%, 91.98%, 86.24% and 89.58% respectively. **Conclusion:** This study concludes that Perfusion Computed tomography (PCT) is a highly sensitive and accurate modality for the diagnosis of colorectal carcinoma.

Key words: Colorectal Cancer, Perfusion Computed Tomography, Sensitivity.

#### INTRODUCTION

CRC is a type of cancer that appears in the colon or rectum. Colorectal cancer (CRC) is the third most common cancer and the fourth major cause of cancer-related deaths, accounting for around 10% of all cases and being one of the leading causes of death worldwide.<sup>1,2</sup> CRC is China's fourth most common cancer. The most likely cause of the high frequency of colorectal cancer in the Chinese population is a high consumption of red and processed meat. There are several ways for diagnosing colorectal cancer; among them, colonoscopy & biopsy is regarded as the gold standard test for diagnosing colon cancer. However, it is an invasive procedure with a high risk of complications such as hemorrhage.<sup>2</sup> Moreover for colonoscopy sedation is required, especially

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Perfusion CT is used to assess vascular perfusion in tumors in order to better understand the functional characteristics of the neoplastic lesion. Perfusion CT's ability to measure the degree of angiogenesis in solid tumors by providing quantifiable vascular parameters is one of its most interesting features.<sup>3</sup> Perfusion CT is rapidly being used for CRC diagnosis, differentiation,

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staging, grading, and prognosis. Perfusion CT can assess tumor status by extrapolating physiological vascular parameters, enabling for in vivo assessment of tumor microvasculature.<sup>4</sup> PCT can determine tumor grade noninvasively by measuring perfusion vascular parameters such as tissue blood flow (BF), blood volume (BV), and permeability surface area product (PS) using a mathematical model. The PCT could help predict CRC grade, especially for poorly differentiated and moderately differentiated CRC. The most reliable PCT parameter that might be employed in this circumstance is the mBF.<sup>5</sup>

Omran et al. investigated the relationship between quantitative computed tomography (CT) perfusion findings and histopathological investigation in patients with colorectal thickness detected at various imaging examinations. When considering a cutoff value of 31.82 ml/100 g/min, BF exhibited 92% sensitivity and 50% specificity for identifying malignant lesions, whereas BV had 97.4% sensitivity and 75% specificity when considering a cutoff point of 1.02 ml/100g. Perfusion CT has had a significant impact on the imaging and therapy aspects of CRC management. Perfusion quantification CT measures allow for better classification and discriminating between malignant and benign tumors.<sup>6</sup>

There is a paucity of evidence in Pakistan about the association between tumor grade and perfusion CT in CRC. Histopathology, an invasive method, at current is the gold standard to diagnose CRC. Thus, the current study's goal is to assess the diagnostic accuracy (sensitivity and specificity) of perfusion CT for CRC diagnosis and to use PCT as a predictor of tumor grade. If its diagnostic accuracy is established, this noninvasive technique could be used on a regular basis in our situation.

# **Objectives & Operational Definitions**

The objective of the study was:

"To determine diagnostic accuracy of Perfusion Computed tomography (PCT) for diagnosis of colorectal carcinoma (CRC) taking histopathology as gold standard."

#### **Operational Definitions**

- 1. Diagnostic accuracy: was measured as
- a. Sensitivity: Ability of PCT to correctly identify patients having CRC.
- b. Specificity: Ability of PCT to correctly identify patients not having CRC.
- c. PPT: Proportion of positive patients of PCT among all positive cases.
- d. NPV: Proportion of negative patients of PCT among all negative cases.
- 2. True Positive: Presence of CRC on both PCT as well as on histopathology
- 3. True negative: Absence of CRC on both PCT as well as on histopathology
- 4. False Positive: Presence of CRC on PCT but absence on histopathology
- 5. False negative: Absence of CRC on PCT but Presence on histopathology
- 6. Perfusion CT: Dynamic perfusion CT scans was performed at the mid-portion of the tumor.
- Histopathological assessment: All the tumors will undergo postoperative histopathological assessment and presence of irregular tubular cells originating from epithelial cells and invading muscularis mucosal and submucosal layers was labeled as malignant CRC.
- Correlation of CT Perfusion and Histopathology: Results of histopathology were correlated to CT perfusion parameters at cut off values of 68.45 for blood flow and 4.27 for blood volume.

### **MATERIAL & METHODS**

#### **Study Design**

This Descriptive, Cross-sectional study was conducted at Department of Radiology, Allied Hospital Faisalabad from 10t<sup>h</sup> March 2022 to 9<sup>th</sup> September 2022. The Sample Size was conducted as following:

Confidence level	95%
Expected Sensitivity6	97.4%6
Expected Specificity6	75%6
Prevalence of disease (p)	5%1
Final Sample size	451

The Sample Technique was Non-probability, consecutive sampling.

### a. Inclusion Criteria

50 -80 years age group Both Male and female Patients suspected for colorectal carcinoma with complaints of abdominal pain or constipation.

## **b. Exclusion Criteria**

Patients were excluded if they had Severe renal failure Preoperative radio chemotherapy No surgical procedure after CT Contrast media contraindication No biopsy results Benign colorectal lesions on biopsy Less than 2 cm deep lesions on CT.

### **Data Collection Procedure**

After taking approval from institutional ethical review committee (CPSP/REU/RAD-2019-3028) the study was started. After providing detailed information about the trial, each patient provided written informed permission. Patients with CRC who were diagnosed preoperatively by endoscopy were included in the trial. The location of tumors was determined using CT scans and confirmed using endoscopy. All patients had pre-operative perfusion CT scans. Dynamic perfusion CTs were done for 65 seconds following intravenous administration of contrast media, and blood flow (BF) and blood volume (BV) in the tumor were assessed. The surgical specimens were forwarded to the hospital's pathology laboratory, where the existence of CRC was labeled according to operational standards. CT perfusion was done in the radiology department, and PCT results were compared to histopathology. PCT sensitivity and specificity were estimated using a 2/2 table.

### **Data Analysis Procedure**

SPSS software (version 25.0) was used to enter the gathered data. Mean ± SD were computed for quantitative variable i.e., age, blood flow, blood volume. Qualitative variables were presented as frequency and percentage e.g. sex, site of lesion, TP, TN, FP, FN. Effect modifiers such as age, gender, site of lesion were controlled by stratification. For CRC, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and PCT accuracy were assessed using histopathology as the gold standard. (using

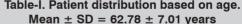
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		Histopathology		Total		
		Positive	Negative	Iotai		
PCT	Positive	TP	FP	TP+FP		
PCI	Negative	FN	TN	FN+TN		
Total		TP+FN	TN+FP	Ν		
	Sensitivity: TP / (TP+FN) * 100					
Specificity: TN / (TN+FP) * 100						
PPV: TP / (TP+FP) * 100						
NPV: TN / (TN+FN) * 100						
Diagnostic accuracy:						
TP+TN						
TP+FP+TN+FN						

### RESULTS

The age range in this study was from 50 to 80 years, with a mean age of  $62.78 \pm 7.01$  years. Most of them, 320 (70.95%), were between the ages of 50 and 65. (Table-I). The male to female ratio was 1.3:1 (Figure-1), with 256 males (56.76%) and 195 females (43.24%). Histopathology revealed that 241 PCT positive patients (True Positive) had colorectal cancer and 21 patients (False Positive) did not. Table-II shows that among 189 PCT negative patients, 26 (False Negative) developed colorectal cancer on histopathology while 163 (True Negative) did not (p=0.0001). The mean blood volume was 70.33  $\pm$  6.32, and the mean blood flow was 5.43  $\pm$  3.21. Table-III illustrate the stratification of diagnostic accuracy by age group 50 to 65. Table-IV and V indicate a stratification of diagnostic accuracy based on lesion location.

Age (in years)	Number of Patients	%age	
50-65	320	70.95	
66-80	131	29.05	
Total	451	100.0	
Table 1. Detient distribution based on any			



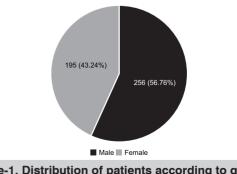


Figure-1. Distribution of patients according to gender (n=451).

	Histo-pathology Proven Positive Results	Histopathology Proven Negative Results	P- Value
Positive result on PCT	241 (TP)*	21 (FP)**	0.0001
Negative result on PCT	26 (FN)***	163 (TN)****	0.0001

 Table-II. Diagnostic accuracy of Perfusion Computed tomography (PCT) for diagnosis of colorectal carcinoma (CRC) using histopathology as the gold standard.

\*TP=True positive \*\* FP=False positive \*\*\* FN=False negative \*\*\*\* TN=True negative

Sensitivity: 90.26%, Specificity: 88.59%, Positive predictive value (PPV): 91.98%, Negative predictive value (NPV): 86.24%, Diagnostic accuracy: 89.58%

	Histopathology Proven Positive Results	Histopathology Proven Negative Results	P-Value	
PCT diagnosed positive results	172 (TP)	18 (FP)	0.001	
PCT diagnosed negative results	20 (FN)	110 (TN)	0.001	

Table-III. Stratification of diagnostic accuracy with respect to age 50-65 years (n=320).

Sensitivity: 89.58%, Specificity: 85.94%, Positive predictive value (PPV): 90.54%, Negative predictive value (NPV): 84.62%, Diagnostic accuracy: 88.13%

	Histopathology Proven Positive Results	Histopathology Proven Negative Results	P-Value
PCT diagnosed positive results	174 (TP)	12 (FP)	0.001
PCT diagnosed negative results	23 (FN)	118 (TN)	0.001

Table-IV. Diagnostic accuracy stratification in relation to colon lesion (n=327).

Sensitivity: 88.32%, Specificity: 90.77%, Positive predictive value (PPV): 93.55%, Negative predictive value (NPV): 83.69%, Diagnostic accuracy: 89.30%

	Histopathology Proven Positive Results	Histopathology Proven Negative Results	P-Value
PCT diagnosed positive results	67 (TP)	09 (FP)	0.001
PCT diagnosed negative results	03 (FN)	45 (TN)	0.001
			(

Table-V. Diagnostic accuracy stratification in relation to rectum lesion (n=124).

Sensitivity: 95.71%, Specificity: 83.33%, Positive predictive value (PPV): 88.16%, Negative predictive value (NPV): 93.75%, Diagnostic accuracy: 90.32%

### DISCUSSION

Colorectal cancer is extremely frequent, accounting for the fourth leading cause of cancer death and the world's second most common cancer, with around one million new cases diagnosed each year.7,8 More than one-third of all colorectal cancer cases are rectal cancer, with more than 40% occurring within 6 cm from the anal verge.9 While colonoscopy and biopsy are gold standard diagnostic techniques to initially diagnose rectal cancer and will continue to be so, traditional radiologic imaging techniques are essential for both local and distant spread of disease (local & distant staging). Diagnostic imaging is unquestionably important in accurate distant staging, with multidetector computed tomography, magnetic resonance imaging & positron emission tomography all helpful for identifying the three most common sites of distant

metastatic disease; liver, lungs, and distant lymph nodes.<sup>8,10</sup>

This study was conducted to evaluate the diagnostic accuracy of Perfusion Computed Tomography (PCT) to diagnose colorectal cancer (CRC) using histopathology as the gold standard. In my study, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of Perfusion Computed Tomography histopathology (PCT) using as the gold standard to diagnose colorectal cancer (CRC) were 90.26%, 88.59%, 91.98%, 86.24%, and 89.58%, respectively. Omran et al. investigated the relationship between quantitative computed tomography (CT) perfusion findings and histopathological investigation in patients with colorectal thickness detected at various imaging examinations. When considering a threshold value of 31.82 ml/100 g/min, BF exhibited 92% sensitivity and 50% specificity for identifying malignant lesions, whereas BV had 97.4% sensitivity and 75% specificity when considering a cutoff point of 1.02 ml/100 gm.<sup>6</sup>

Unfortunately, despite numerous studies conducted over the last 15 years to establish PCT as a tool for local rectal cancer staging, the findings have been inconclusive.8 According to a 2009 study by Juchems et al., PCT was unable to discriminate cancers that required neoadjuvant therapy from lesions that could be directly surgically removed.<sup>11</sup> Another study published during 2007 revealed that PCT showed a low accuracy to see involvement of the mesorectal fascia by tumor cells.12 However, Kanamoto et al. reported in 2007 that the sensitivity/specificity for T1 and T2 tumors was 93.9%/94.3%, whereas T3 tumors had a sensitivity/specificity of 93.8%/94.3%. Taylor et al, discovered in 2007 that the accuracies of PCT and MRI for CRM involvement were frequently comparable.<sup>13,14</sup> While individual data many years ago showed variable results, with some studies showing acceptable T-staging and accuracies for the involvement of CRM, a large meta-analysis by Kwok et al. examining nearly 500 patients detected that PCT had a sensitivity of only 78% for tumor extension through the rectal wall (with an accuracy of only 73%), as well as a sensitivity of 52% and specificity of 78% for metastasis to the mesorectal lymph nodes.<sup>15-17</sup> Overall, there is little uncertainty that MDCT should not be used as a first-line imaging technique for local staging of rectal cancer, particularly T-staging and to detect CRM involvement.<sup>18</sup>

Because of its wide availability and low scanning periods, PCT is frequently employed as the initial staging modality for rectal cancer. PCT can evaluate both local staging and distant metastases in a single examination of the abdomen, pelvis, and chest.<sup>19</sup> T staging accuracy rates of 79%-94% were reported in preliminary trials utilizing conventional CT to assess locally advanced rectal tumors (i.e., T3).<sup>20-22</sup> Advances in multi-detector CT (PCT) technology have improved spatial resolution and accuracy rates to more than 90% using thin-collimation scanning and

multi-planar reformation.<sup>23</sup> Nonetheless, PCT has little utility in distinguishing T1 and T2 lesions that are restricted to the rectal wall; however, these early stage lesions are better examined using EUS. Furthermore, low resolution of PCT makes it difficult to detect lavers of the rectal wall and to distinguish between desmoplastic or peritumoral inflammatory reactions and tumor infiltration into the perirectal fat.<sup>24</sup> Because of these shortcomings, PCT has a tendency to over stage T1 or T2 lesions as T3 tumors. Size of the LN is the major criteria for its staging however, morphology of these lymph nodes is also a minor criteria. According to one study, LN with an axis more than 4.5 mm in diameter favors malignancy; nevertheless, such size criteria have lower accuracy.25 Because there is no definite cut-off value of diameter for detecting whether a LN is metastatic, there is a wide range of sensitivity and accuracy for LNstaging using CT, with rates ranging from 25% to 86% and 35% to 84%, respectively.<sup>25</sup> Furthermore, even with enhanced PCT resolution, appropriate assessment of nodal status remains challenging since CT cannot detect microscopic metastases in normal-sized LNs. In a multicenter trial of 250 patients, for the assessment of CRM involvement in mid to upper rectal cancer, PCT demonstrated overall sensitivity and specificity rates of 76% and 96% respectively.26 This finding suggests that CT, rather than MRI, could be utilized to predict CRM involvement in such patients. In lower rectal cancer, CT is less reliable and inconsistent in determining CRM involvement.27,28

A few recent studies have found that computed tomography (CT) staging in rectal cancer is extremely accurate in assessing disease extent and effective in rectal cancer treatment planning.<sup>29,30</sup> CT scans are used to stage rectal carcinomas prior to therapy, to stage recurrent disease, and to detect distant metastases following surgery. As part of presurgical planning, CT is used to assess the tumor and involvement of adjacent structures such as fat and pelvic side walls including pelvic musculature.<sup>29-31</sup> One study determined that the percentage of colon carcinoma was 60%, and the accuracy of detecting CRC in unprepared bowel on CT was assessed to be 80%, with sensitivities of 75%-100% and specificities of 86%-96%.<sup>32</sup>

## CONCLUSION

According to the findings of this study, Perfusion Computed Tomography (PCT) is a highly sensitive and accurate method for identifying colorectal cancer, and that it not only improves our ability to diagnose colorectal carcinoma patients, it also enhances patient care by offering prompt and appropriate surgical therapy, thereby reducing complications. As a result, we suggest that all colorectal cancer patients should be assessed by Perfusion Computed Tomography (PCT) for early diagnosis, which will aid surgeons in preoperative planning and give adequate and timely management of neoadjuvant therapy to these patients for a better prognosis.

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