

Role of PET/CT in Assessment of Post Operative Colorectal Cancer

Thesis submitted in Partial fulfilment of MD Degree
In Diagnostic Radiology

Presented by

Ahmed Samy Abbas Abdalla
M.B., B.Ch, M.Sc

Supervised by

Prof. Dr. Hossam Abd El Kader Morsy
Professor of Radiodiagnosis
Faculty of Medicine - Ain Shams University

Dr. Aya Yassin Ahmed
Assistant Professor of Radiodiagnosis
Faculty of Medicine - Ain Shams University

Dr. Shaimaa El Metwally El Diasty
Lecturer of Radiodiagnosis
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University

2021

Abstract

PET/CT is developing a major role in assessing colorectal cancer. The information provided by PET/CT is likely to combine the best imaging features of both modalities and become the gold standard for staging in colorectal carcinoma. PET/CT proved significantly more accurate in restaging, and detection of metastatic as well as recurrent colorectal cancer. PET/CT is also useful in monitoring tumor response to therapy.

Keywords: Colorectal cancer; PET/CT; Recurrence; Metastasis.

Acknowledgement

First and foremost, i would like to express my deepest gratitude and thanks to **Prof. Dr. Hossam Abd El Kader** professor of radiodiagnosis, Faculty of medicine, Ain-University, for his support, guidance and care; he is my very special and dear professor.

Words could not express my great appreciation and respect to **Dr. Aya Yassin** assistant Professor of Radiodiagnosis, Faculty of medicine, Ain-University, for her assistance and concern throughout this work, providing this thesis with his scientific experience and constructive supervision.

I am also very grateful to **Dr. Shaimaa El Diasty** lecturer of Radiodiagnosis, Faculty of medicine, Ain-University, for her guidance and care.

Last, but not least, I would like to express my appreciation and thanks to my family for their understanding, patience and encouragement.

Table of Contents

	Page
Introduction and aim of work	1
Review of literature	
• Anatomy of the large intestine	5
○ Gross anatomy	5
○ Histologic anatomy	8
○ Blood supply	9
• Pathology of colorectal cancer	12
○ Risk factors	12
○ Pathological types	15
○ Tumor spread	17
○ Staging	19
○ Other tumors	21
• Physical background and technical aspects of PET/CT	24
• The role of 18F-FDG PET/CT in colorectal cancer	47
○ Diagnosis	48
○ Initial staging	49
○ Detection and restaging of recurrence	50
○ Role of PET/CT in radiotherapy planning	53
○ Monitoring tumor response to treatment	54
○ Role of PET/CT in colorectal hepatic metastasis	55
○ PET/CT colonography	59
○ Interpretation consideration of PET/CT in colorectal cancer	62
Patients and methods	65
Results	72
Cases presentation	80
Discussion	95
Summary and recommendations	104
References	107

List of Figures

<i>Figure No.</i>	<i>Title of figure</i>	<i>Page No.</i>
Figure 1	Anatomy of large intestine	5
Figure 2	Anatomy of the anal canal & rectum	8
Figure 3	Colon Layers	8
Figure 4	Blood supply of the large intestine	9
Figure 5	Venous drainage of the large intestine	10
Figure 6	Lymphatic drainage of the large intestine	11
Figure 7	Gross features of cancer colon	15
Figure 8	Spread of cancer colon	18
Figure 9	TNM staging of cancer colon	21
Figure 10	Illustrative diagram of combined PET/CT scanner components	25
Figure 11	Photograph (side view) of a hybrid PET-CT scanner	27
Figure 12	Typical imaging protocol for combined PET/CT	27
Figure 13	Positron-electron annihilation reaction	28
Figure 14	Glucose and fluorodeoxyglucose structure	29
Figure 15	Uptake of FDG by cells	30
Figure 16	Bilinear scaling function	35
Figure 17	Mean positron range and annihilation angle blurring.	36
Figure 18	Coincidence imaging	36
Figure 19	Current commercial PET/CT scanners	37
Figure 20	Normal distribution of FDG uptake by body	40
Figure 21	Physiologic muscle activity	40
Figure 22	FDG uptake by bowel	41
Figure 23	Figure showing artifacts from oral contrast medium	43
Figure 24	High-density metallic implants generate streaking artifacts	44
Figure 25	Breathing artifacts	45
Figure 26	Mis-registration artifacts	45
Figure 27	False positive uptake by intensely enhancing left axillary vein	46
Figure 28	PET/CT image demonstrates intense focal uptake in a primary sigmoid colon mass.	48
Figure 29	Midline distal left primary colon carcinoma at an unusual location..	49
Figure 30	Intense hypermetabolic activity in a cecal carcinoma primary lesion.	51
Figure 31	Focal intense radiotracer uptake in a subcentimeter left pelvic side wall lymph node is consistent with metastasis.	51
Figure 32	Diagnosis of colon carcinoma and liver metastases.	52
Figure 33	Axial fusion PET/CT demonstrates intense focal radiotracer uptake on the lateral margin of a radiofrequency ablation site in the liver.	53
Figure 34	A 33-year-old man undergoing ascending colon cancer resection two years ago.	56
Figure 35	Patient status post left hemicolectomy for colon cancer without change in CEA level.	56
Figure 36	Patient status post left hemicolectomy for colon cancer and increasing CEA level. PET was requested for restaging.	57
Figure 37	Axial contrast enhanced CT image demonstrated a tubulous polyp at the left colon flexure.	59
Figure 38	Axial contrast enhanced CT image demonstrated stenotic tumor site in the descending colon	59
Figure 39	Pie chart illustrates the distribution of cases in both sexes in our study	72
Figure 40	Column chart illustrates the indications for PET/CT examination.	74

Figure 41	Case 1	80
Figure 42	Case 2	81
Figure 43	Case 3	82
Figure 44	Case 4	83
Figure 45	Case 4	83
Figure 46	Case 4	84
Figure 47	Case 5	85
Figure 48	Case 6	86
Figure 49	Case 7	87
Figure 50	Case 7	88
Figure 51	Case 8	89
Figure 52	Case 8	90
Figure 53,54	Case 9	91
Figure 55	Case 9	91
Figure 56	Case 10	93
Figure 57, 58	Case 10	94

List of Tables

Table No.	Title	Page No.
Table 1	Dukes classification	20
Table 2	TNM Staging system for colon cancer	20
Table 3	Properties of various PET crystals	33
Table 4	Illustrates the age characteristics	73
Table 5	Illustrates the fasting blood glucose level in patients & the dose of 18-F-FDG	73
Table 6	Comparison between sensitivity, specificity, and accuracy of PET/CT and CT regarding detection of local recurrence.	75
Table 7	Comparison between sensitivity, specificity, and accuracy of PET/CT and CT regarding detection of LN metastasis.	75
Table 8	Comparison between sensitivity, specificity, and accuracy of PET/CT and CT regarding detection of hepatic metastasis.	77
Table 9	Comparison between sensitivity, specificity, and accuracy of PET/CT and CT regarding detection of peritoneal deposits.	77
Table 10	Comparison between sensitivity, specificity, and accuracy of PET/CT and CT regarding detection of pulmonary deposits.	78
Table 11	Illustrates the SUV value at the detected lesions.	79
Table 12	Comparison between CT and PET/ CT	79

List of Abbreviations

μ maps	Attenuation map
18F-FDG	¹⁸ F- FluoroDeoxyGlucose
AC/AL	Attenuation correction/Alignment
ACFs	Attenuation correction factors
CECT	Contrast enhanced computed tomography
CR	Complete Response
Cru	unconfirmed complete response
CT	Computed Tomography
ESR	Erythrocyte sedimentation rate
F 18	Fluorine 18
FDG	FluoroDeoxyGlucose
GLUT	Glucose Transporters
GSO	Gadolinium Silicate
GTD	Greatest transverse diameter
H+	Hydrogen ion
H2 (F-18)	Hydrogen fluoride
IV	Intravenous
IWC	International Workshop Criteria
KeV	Kilo electron Volt
KV	Kilo Volt
LDH	Lactate dehydrogenase
LSO	Lutetium Oxyorthosilicate
MCi	Micro Curies
MeV	Mega electron Volt
Mo	Months
MRI	Magnetic Resonance Imaging
N	Neutron,
P	Proton
PD	Progressive disease
PERCIST	PET Response Criteria in Solid Tumors
PET	Positron Emission Tomography
PET/CT	Positron Emission Tomography/ Computed Tomography
PFS	Progression Free Survival
PMTs	Photomultiplier tubes

PR	Partial Response
SD	Stable disease
RECIST	Response Evaluation Criteria in Solid Tumors
SLL	Small-cell lymphocytic lymphoma
SPD	Sum Of The Products Of The Greatest Diameters
β-	Electron
β+	Positron
SUV	Standardized Uptake Value
SUVavg	Average Standardized Uptake Value
SUVmax	Maximum Standardized Uptake Value
US	Ultrasound
WBC	White blood cells
WHO	World Health Organization
Wt	Weight
XRT	Radiotherapy
Γ	Photon

Introduction

Colorectal cancer is the third leading cause of cancer worldwide; it accounts for a large number of tumor related deaths. As with all types of cancer, early diagnosis of colorectal cancer is the key for its cure. If diagnosed early, before it has metastasized, the disease is considered curable. If the cancer has already spread to distant organs, the long term survival is much lower (***Patrick et al.,2005***).

Determining the stage of colorectal cancer often requires multi-modality, multi-step imaging approach. Optical colonoscopy represents the reference standard in terms of cancer detection and tissue sampling. However optical colonoscopy only offers an endo-luminal view. Complete "conventional" staging concepts require additional imaging procedures to assess potential metastatic spread to lymph nodes and solid organs (***Cohade C et al.,2003***).

Of these conventional imaging procedures, contrast enhanced computed tomography (CT) is the most common for both the abdomen and pelvis. However, CT offers only morphological data for the evaluation of tumor stage. Glucose analogue [18 F] fluorodeoxyglucose-positron emission tomography (FDG-PET) can display functional information and has been found to be accurate in the detection of colorectal cancer and its distant metastasis. However, based on its limited spatial resolution, FDG-PET often makes exact anatomical localization and demarcation of the lesion difficult (***Cohade C et al.,2003***).

A limitation of CT and other radiological imaging procedures pertains to their lack of functional data, which may render determination of lesion size, potential infiltration of adjacent organs or involvement of loco-regional lymph nodes difficult. [18F] fluoro-deoxyglucose (FDG)PET, on the other

hand, is highly accurate when staging primary and recurrent colorectal cancer (***Kantorova I et al.,2003***).

The functional data of fluorine 18 (18F) fluorodeoxyglucose (FDG) positron emission tomography (PET) have been reported to have an important complementary role in the detection of distant metastases and local recurrence and in the differentiation of tumoral and nontumoral masses in patients with colorectal cancer (***Kalff et al.,2003***).

Thus fusion of functional with morphological data may be of benefit for tumor staging. As a consequence, combined PET/CT scanner has been introduced into clinical practice. Its ability to detect and characterize malignant lesions, with advantages over morphology and function alone, has been documented for different tumours including colorectal cancer (***Valk PE et al.,1999***).

Whole-body PET/CT with integrated colonography is technically feasible for whole body staging in patients with colorectal cancer. This integrated protocol may be of substantial benefit in staging patients with colorectal cancer, focussing on patients with incomplete colonoscopy and those with small synchronous bowel lesions. (***Patrick et al.,2005***).

Recurrence of colorectal cancer occurs in about one-third of patients within the first 2 years after surgery. Before PET was introduced, it was extremely difficult to monitor for suspected recurrence. The other techniques available for staging and assessment of potential recurrences lack sensitivity and precision. Moreover, frequent non-conclusive investigations result in diagnostic and therapeutic delay. In many colorectal cancer patients, pelvic CT will demonstrate a suspicious mass, but cannot distinguish mass tumor recurrence from post-operative or post-radiation scar (***Kamel IR et al.,2004***).

Computed tomography (CT) and positron emission tomography (PET) are both well-established methods for the evaluation of patients with suspected recurrence. The results of CT depend on the site of recurrence, size and morphological appearance of the lesion. Because of the well-known high uptake of 18F-FDG in primary colorectal carcinomas and their recurrences, FDG-PET provides accurate information about changes in glucose metabolism; however, it is of limited value for anatomical localization and morphological depiction. Integrated imaging using both modalities improves the detection of recurrence. **(Jana et al.,2006).**

In post-operative patients, an elevated serum carcinoembryonic antigen (CEA) level suggests recurrent and/or metastatic disease. Resection of isolated metastases is associated with improve survival while multifocal metastatic lesions are associated with less favorable prognosis **(H. Jadvar and JA Parker.,2005).**

Early detection of recurrent colorectal carcinoma has become more important in the past decade, as the treatment options for localized disease have improved significantly. However, aggressive locoregional interventions (e.g. partial liver resections, radiofrequency ablation (RFA) of liver metastases, resections of pulmonary metastases) are as of yet considered futile in the presence of metastases elsewhere [1]. Therefore, detection of tumour sites throughout the body is needed with high sensitivity and specificity **(Vogel,et al.2005).**

Whole body PET/CT imaging is said to be the most accurate diagnostic test for detection of recurrent colorectal cancer, and is a cost effective way to differentiate resectable from non-resectable disease **(Kantorova et al.,2003).**

¹⁸F-FDG PET has been shown to be highly accurate in the detection of recurrent and metastatic colorectal cancer. A PET scan has comparable sensitivity to a CT scan for the detection of colorectal liver metastases but has superior sensitivity in the detection of extrahepatic disease, compared with CT, and changes the estimation of disease extent in over one third of patients. Several reports also indicate that PET can influence the management of patients with metastatic colorectal cancer (**Scott A.M et al,2008**).

Interpreting fused images provided more accurate diagnosis than interpreting CT, PET, or PET + CT images. This method of manually fusing separately obtained PET and CT images increased the diagnostic certainty for detecting colorectal cancer recurrence and decreased the number of equivocal cases.(**Yuji et al.,2007**).

Aim of work:

- The aim of this study is to highlight the role of PET/CT in evaluation of post operative colorectal cancer, hence guiding the clinician to the proper management strategy.

Colorectal anatomy

The large intestine extends from the end of the ileum to the anus. It is about 1.5 meters long. It differs from the small intestine in its greater caliber, its more fixed position, its sacculated form, and in possessing certain appendages to its external coat, the appendices epiploicae. Further, its longitudinal muscular fibers do not form a continuous layer around the gut, but are arranged in three longitudinal bands. The large intestine is divided into the cecum, colon, rectum, and anal canal (**Henry Gray 2004**).

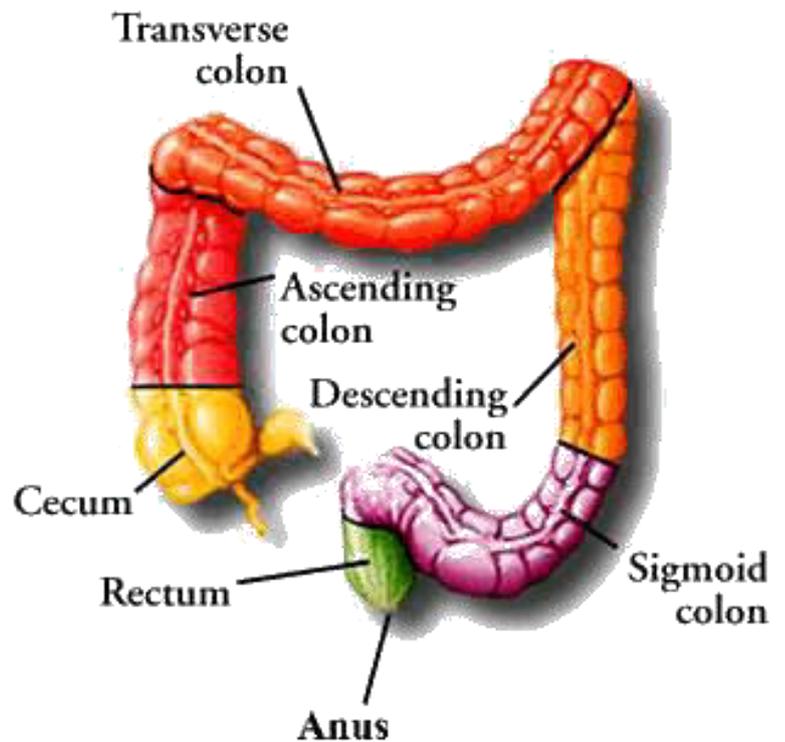


Fig1: large intestine (Brewer C,2004).

I-The Cecum:

It is attached to the ileum and extends approximately two and one-half inches below it. The cecum in an adult usually is adherent to the posterior wall of the peritoneal cavity and has a serosal covering on its anterior wall only. The cecum forms a blind pouch from which the appendix projects (**Henry Gray 2004**).