Whether to Fused PET/CT or CECT in Post-Therapeutic Colorectal Cancer Assessments: A Study of the Efficacy of the Modality of Choice among Egyptian Patients

CURRENT STATUS: UNDER REVIEW

European Journal of Hybrid Imaging  Springer

Ahmed Baz
Cairo University Kasr Alainy Faculty of Medicine
ahmedbaz2012@Yahoo.com Corresponding Author

Talaat Ahmed Hassan
Cairo University Kasr Alainy Faculty of Medicine

DOI: 10.21203/rs.2.24722/v1

SUBJECT AREAS
  Laboratory Diagnostics  Nuclear Medicine & Medical Imaging

KEYWORDS
  PET-CT, CECT, Colorectal Cancer
Abstract
One of the most common cancers, colorectal cancer accounts for several tumor-related mortalities; its high recurrence rates either as a local recurrence of the disease or as a distant metastatic disease (up to 35-40%) have been reported in the treated patients within the first two years following surgery. There has been heated debate over the modality of choice for imaging the primary colorectal cancer. This study investigates the diagnostic performance of fused Positron Emission Tomography/Computed Tomography (PET/CT) in comparison to Contrast-enhanced Computed Tomography (CECT) as a follow-up and restaging imaging tool for post-therapeutic colorectal cancers. Data were collected from 84 Egyptian patients (26 females and 58 males, age ranges from 35 to 80) who were treated from colorectal cancers. They were referred to a private imaging center for evaluation of their disease recurrence by fused PET/CT. Disease recurrence was categorized as operative bed recurrence/residual (incomplete therapeutic response), nodal, and distal metastases. With reference to histopathology reports, the fused PET/CT had sensitivity, specificity, positive predictive value, negative predictive value, and an overall accuracy of 93.33%, 83.33%, 93.33%, 83.33% & 90.48% respectively as compared to CECT (73.33%, 58.33%, 81.48%, 46.67%, 69.05% respectively). Our findings indicate that fused PET/CT may be more effective than the CECT regarding the detection of operative bed recurrent disease and incomplete therapeutic responses. PET/CT may also offer a cost-effective whole-body scan for restaging the recurrent diseases through an accurate detection of the nodal and distant metastases.

Background
Colorectal cancer is one of the most common cancers that affect human beings and account for several tumor-related mortalities; high recurrence rates either as a local recurrence of the disease or as a distant metastatic disease (up to 35–40%) have been reported in the treated patients within the first two years following surgery. However, it may be potentially cured if it is early detected, and the curative measures are taken [1, 2].
Metastatic disease in colorectal carcinoma can occur anywhere in the body, but it often has nodal, hepatic, and pulmonary predilection; thus, the whole-body screening for the metastatic disease is
considered a critical step for the staging of the primary disease and restaging of the recurrent one.
Still, according to [3, 4], there is an immense debate over the modality of choice for imaging the primary colorectal cancer.

Recently, several diagnostic tools have been implemented for the follow-up of the treated colorectal cancers to assess the recurrent and the metastatic diseases: these include laboratory investigation (e.g., tumor markers and optical colonoscopy) and the conventional diagnostic imaging modalities (e.g., ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI)). However, these modalities lack high sensitivity and specificity [3, 4].

Through the assessment of the metabolic activity of the tumor tissues, functional imaging is considered a well-established imaging technique using the glucose analogue [18 F] fluorodeoxyglucose-positron emission tomography (FDG-PET) for detection of colorectal cancers and the distant metastatic deposits, yet the poor spatial resolution of FDG-PET was a limitation. To overcome this limitation, hybrid imaging techniques have emerged to provide more enhanced, anatomical details and integrated imaging modalities that may improve the detection of tumor recurrences in treated colorectal cancers and distant metastases [5–12]. The literature has presented the fused PET\CT as both cost-effective and accurate diagnostic modality for detection of the colorectal cancer recurrence [13–15].

The current study aims to investigate the diagnostic performance of fused Positron Emission Tomography/Computed Tomography (PET/CT) compared to contrast-enhanced computed tomography (CECT) in the follow-up assessment and restaging of the patients with treated colorectal cancers through measurements of the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy.

Methods

Participants

**Inclusion criteria:** Cases of colorectal malignancies who had curative (surgical or endoscopic) resection, chemotherapy, radiotherapy or any combination of them were included in the current study. However, the patients who had a benign colorectal neoplasm or had colorectal malignancy
without any previous treatment were also excluded.

Accordingly, 84 patients were enrolled in the period from November 2017 till July 2019; they were cases of treated colorectal cancers. They were referred to a private imaging center for their assessment by fused PET/CT and the evaluation of their treatment response. The patients’ ages ranged from 35 to 80 years with a mean age (58.73± 11.29 years). They were 26 females (31% of cases) and 58 males (69% of cases) (as shown in tables 1 and 2). Participants received one or more of the following treatment methods: the curative (endoscopic or surgical) resections, chemotherapy, and radiotherapy (See Table 5).

**Procedure**

The patients were instructed to fast for 6 hours before the examination and they were well-hydrated. Blood glucose level was measured before the examination in all patients and was within normal ranges (a maximum limit was 150 mg/dl) before [fluorine-18] fluoro-2-deoxy-d-glucose (FDG) injection. 0.22 mCi/kg (18F-FDG) was injected and then the patients relaxed for 45 minutes (considered as the uptake period). The PET/CT system using a multi-detector (sixteen detectors) CT machine (GE, Discovery IQ, USA) was employed to examine the patients. For the sake of attenuation correction and image fusion, a low dose of non-contrast enhanced CT images were taken. The examination levels were extending from the nose to the mid-thigh levels for PET scans. Before contrast media administration for the CECT examination, the serum, urea, and the creatinine levels were measured routinely in all patients. Helical CECT axial images were obtained for the head, neck, thorax, abdomen, and pelvis at intervals of 2mm after intravenous injection of the nonionic contrast media in all patients after they had completed the PET/CT examination. The total acquisition time for the integrated PET/CT scan was nearly 30 minutes.

**Statistical Methods**

Data management and analysis were performed using the Statistical Package for Social Sciences (SPSS) vs. 21. Numerical data were summarized using means, standard deviations, and ranges, as appropriate. Categorical data were summarized as numbers and percentages. The data were collected, analyzed and tabulated. The sensitivity, specificity, positive predictive value (PPV), negative
predictive value (NPV), and accuracy of the PET/CT in the diagnosis of recurrent colorectal cancers were calculated using the standard definitions [16].

**Data Analysis**

Through special workstations, the reconstruction of PET image data sets and using the CT data for attenuation correction and co-registered multiplanar images were obtained using special software. An experienced radiologist (5 years of experience in the PET/CT imaging), the CECT, PET, and the fused PET/CT images were interrogated by visual assessment that considered the hepatic parenchyma as a standard reference for the same patient, and by measuring the standardized uptake value (SUV), a semi-quantitative assessment was conducted. The histopathology reports with a correlation to the clinical and the follow-up examinations for the patients as well as the tumor markers levels (CEA) had served as the reference gold standard. SUV was then automatically calculated using the equation for SUV measurement:

\[ SUV = \frac{\text{dose in tissue}}{\text{injected dose}} \times \text{patient weight} \]

where tissue tracer activity was in microcuries per gram, injected radiotracer dose was in microcuries, and the patient weight was in kilograms [17].

**CECT Data Analysis:**

Depictions of colonic soft-tissue masses or mural thickening with or without signs of the infiltration of the surrounding peri-colonic tissues were considered as signs of malignancy. A size-based threshold of 10 mm (short axis) for the malignant lymph glands was considered. The central breaking down (necrosis) was used as a sign of malignancy; however, a preserved fatty hilum and matrix calcification of a lymph gland was considered as signs of benignity. Malignant hepatic focal lesions were reported when hypodense lesions were seen either with or without marginal contrast enhancement. For pulmonary nodules, calcification was used discriminator of benignity, where a calcified pulmonary nodule was considered as a benign nodule.

**PET/CT Data Analysis**

The colonic soft tissue masses or mural thickenings were considered as a positive recurrence if their FDG uptake was higher than the background activity. The positive hepatic focal lesions were considered if their FDG uptake was more than or equal to that of the rest of the hepatic parenchyma,
whereas negative lesions were reported if their FDG uptake was lower than that of the rest of the liver parenchyma. The pulmonary nodules that had a size of 5 mm were considered as positive for malignancy if their FDG uptake was exceeding the mediastinal blood pool, yet a metastatic disease could not be completely ruled out in the pulmonary nodules that were less than 5 mm. If the bone marrow exhibited an obvious multifocal FDG avidity, it was considered as positive for infiltration. However, a diffuse uptake pattern in reactive bone marrow hyperplasia after chemotherapy could simulate or mask a diffuse marrow infiltration; in such case, an appropriate correlation to the patient history was needed. A few weeks (3-4 weeks) after completion of the chemotherapy were enough for the physiological marrow activity to abate. The positivity of the peritoneal seeding or masses was considered when their FDG uptake was more than that of the background activity.

**Results**

Recurrent disease was present in 60 patients out of 84 (71.4%) (See Figs. 1, 4 & 6) but did not occur in the other 24 patients (28.6%) figures (2, 3 & 5). Recurrent disease was categorized as operative bed recurrence/residual (Fig. 1), metastatic lymph nodes (Fig. 4), and distant metastatic lesions (Table 3) (Figs. 1, 4 & 6). The site of the tumor recurrence was predominantly seen in the rectosigmoid region in 31 patients (36.9%), followed by the ascending colon where it was present in 13 patients (15.4%), then the transverse colon as depicted in 9 patients (10.7%); The descending colon recurrence was noted in 6 patients (7.1%), and the cecal recurrence existed in only one patient (1.3%) as presented in table 4. The reference gold standard in our study was the histopathology results with a correlation to the clinical and the radiological follow-up assessments as well as the tumor markers (CEA) if they were available. With reference to the gold standard, the fused PET\CT (for the tumor recurrence\residual) had sensitivity, specificity, positive predictive value, negative predictive value and an overall accuracy of (93.33%, 83.33%, 93.33%, 83.33% & 90.48%) respectively with 95% confidence interval (95% CI) (83.8% to 98.15%, 62.62–95.26%, 85.09–97.17%, 65.61–92.91% & 82.09–95.80%) respectively, while the CECT for the tumor recurrence\residual had sensitivity, specificity, positive predictive value, negative predictive value and an overall accuracy of (73.33%, 58.33%, 81.48%, 46.67%, 69.05%) respectively with 95% CI (60.34% to 83.93%, 36.64–
77.89%, 72.79–87.86%, 33.80–60.0% & 58.02–78.69%) respectively (As shown in tables 6–8).

Discussion

Colorectal cancer is the third leading cause of death worldwide with a relatively high recurrence rate that has been reported in up to one-third of the treated cases; nevertheless, the recurrence patterns could be a loco-regional, nodal or distant metastatic disease. As the recurrent disease is potentially curable in certain cases, the restaging of the recurrence was mandated, and a highly sensitive imaging modality was chosen [18–20].

The follow-up methods are quite variable including laboratory studies (tumor markers), endoscopy, and the conventional imaging studies like CT and MRI; however, the lack of a standardized imaging protocol and the reported low sensitivity in the differentiation between the tumor tissue and the postoperative sequelae of intervention has greatly limited the use of such modalities. Moreover, a certain size of the tumor recurrence is required to be assessable and measurable by using these modalities [21, 22].

As the conventional CECT may provide useful data about the anatomical and the morphological aspects of the tumor recurrence, the metabolic activity of the tumor cells could also be assessed by FDG PET, thus an integration of their images as fused PET\CT system allows an optimum co-registration of the images with more accurate results than side by side interpretation [5–12, 23].

In line with the findings of previous studies [24–26], we have reported tumor recurrences in the operative bed; nodal metastases, distant organ metastases, and peritoneal seeding as shown in table 3 (See Figs. 1, 4 &6). Ries et al described the rectosigmoid region as the commonest location for operative bed recurrence [27], which matches our findings where the rectosigmoid region being affected in 31 patients (36.9%). As we have reported the disease recurrence in three categories, the operative bed recurrence is present in 60 patients (71.4%), nodal metastases present in 30 patients (35.7%), and distant metastases in 26 patients (30.9%); these findings match those of studies conducted by Chiewvit et al and Hussein and Nassef, who documented a recurrence rate of over 70% [26, 28].

In reference to the histopathology results, clinical and radiological follow-up assessments and the
tumor markers (if available), the accuracy measures in our study are in a concordance with those by the studies [25, 26, 29, 30].

The false-positive results given by the CECT may lead to a clinical conflict, especially if the patient's laboratory findings are discordant, necessitating a biopsy for the suspicious soft tissue masses. In this way, the fused PET\CT adds great value in this regard and could mitigate the issue (the negative predictive value was 83.33% in our study) as it assesses the metabolic activity in the soft tissue masses for detection of the viable tumor cells with high metabolic activity and the sterile masses with no tumor activity that may represent otherwise scar or operative bed granulation tissues (See Fig. 4).

We had false-positive results by fused PET\CT for operative bed recurrent tissues in four of our cases (4.7%) as negative for tumor cells by the histopathology examination (the gold standard reference in the study for the operative bed recurrence); however, the tumor markers and the follow-up studies for these cases supported the pathology results in terms of the decline in the tumor marker levels, and the metabolic activity in the suspected lesion was no longer seen in the follow-up imaging; these findings align with those by Rodríguez-Vigil et al and other studies, which indicate that the 18F-FDG could be taken up by both malignant and inflammatory cells [31–33].

However, the accuracy measures for the detection of the nodal and the distant metastases were not conducted in the current study as the histopathology reference was not available for the nodal and the metastatic lesions, and therefore their assessment was based on the morphological and the metabolic activity for any suspicious lesion as well as its therapeutic response on the follow-up studies and the decline in the CEA levels. The reference standard for the nodal and distant metastatic lesions were the clinical, radiological follow-up and the tumor marker levels as the need for a biopsy from a metastatic lesion is not accepted in the clinical practice except if there was an absolute indication [25, 26].

For the nodal metastasis, our study has revealed that nodal affection by PET\CT in 30 cases (35.7%) that were predominantly abdominal in location (22 cases; 26.2%) followed by the mediastinal nodes (6 cases; 7.14%) then by the cervical nodes (3 patients; 3.6%) (See Fig. 4). Such findings agree with those from Hussein and Nassef’s study as well as those from Taha Ali’s study regarding the detection
of the metabolically active lymph glands (as shown by follow-up and by the tumor markers) as malignant nodes with a therapeutic response to the chemotherapy. Hence, the fused PET\CT adds a diagnostic value for detection of the metabolically active lymph glands with a better anatomical localization than the size-based CT detection when used solely.

Regarding the distant metastases, they were ordered sequentially as hepatic, pulmonary, peritoneal, bone, and atypical site metastasis (22, 11, 3, 2 & 1 cases respectively) (See Figs. 1, 4 & 6) as presented in Riopel et al study that also describes the incidence of the osteolytic metastatic lesions with the rectal rather than the colonic carcinoma. Riopel et al offer a rationale for this pattern of metastases where the venous plexus (Batson’s plexus) being considered as the route of tumor spread as well [34]. Regarding the detection of the distant metastatic lesions and the peritoneal seeding by the PET\CT, a concordance with the findings from Chen et al and Choi et al studies is present [35, 36], those from Hussein and Nassef [25] as well as Taha Ali [26].

Through the assessment of the FDG avidity, hepatic metastases were excluded in some of the cases as well as the pulmonary nodules (See Figs. 3 & 5) and a detection of such FDG avidity may show a metastatic affection (See Figs. 1, 4 & 6), which was correlated to the clinical, radiological follow-up studies and to the tumor marker levels as well. This finding matches those from [25, 26, 35, and 36] that have highlighted a high sensitivity of the fused PET\CT for depiction of distant metastatic diseases and peritoneal seeding. Still, one caveat is that false-positive nodal affection could occur due to inflammatory process.

The atypical distant metastasis was present in only one case (1.2%) of our study, seen in the left adrenal gland (As shown in Fig. 4). This finding concurs with those from Ouchi et al who describe atypical sites of metastases that are infrequently depicted like metastases to the spleen, biliary system, pancreatic, peripancreatic LN, adrenals, mammary, gonadal, cutaneous, umbilical, oral and the vagina cavities [36].

**Conclusion**

In summary, the current study has shown that fused PET\CT may be more effective than CECT regarding the detection of operative bed recurrent disease and incomplete therapeutic responses
(residuals). Besides, PET/CT could offer a cost-effective whole-body scan to restage the recurrent diseases through a precise detection of the nodal and distant metastases with a potentiality to be the modality of choice.

Abbreviations
PET/CT
positron emission tomography/computed tomography.
CECT
contrast-enhanced computed tomography.
SUV
standardized uptake value.
FDG
fluoro-2-deoxy-d-glucose.

Declarations

Ethics approval & Consent to participate
- The protocol was reviewed and approved by the local ethics committee of the radiology department, Kasr Alinyy hospital, Cairo University.
- The reference number was not applicable
All patients had given their written consents to participate in this work

- Consent for publication
All patients had given their written consents for publication of this work

- Availability of data and material
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

- Competing Interest:
The authors declare that they have no competing interests

- Funding
All authors had no fund for this research and had no competing interests.

- Authors' Contributions:
AAB: the corresponding author had contributed by data collection and some interpretation of the
image studies in the research work and in the editing of the manuscript and reference collections had introduced the idea of the current study and helped in the image selection and in the final revision of the submitted version.

-Authors' information:
Ahmed A. Baz, MD, Radiology Department, Faculty of Medicine, Cairo University. Email: ahmedbaz2012@yahoo.com
Talaat A. Hassan, MD, Radiology Department, Faculty of Medicine, Cairo University. Email:talaathassan38@yahoo.com

-Acknowledgments.
Not applicable; as all authors are co-authors for this research.

References
[1] Elias D, Sideris L, Pocard M, Ouellet JF, Boige V, Lasser P, et al. Results of R0 resection for colorectal liver metastases associated with extrahepatic disease. Ann Surg Oncol 2004;11:274–80. http://dx.doi.org/10.1245/ASO.2004.03.085.
[2] Chen LB, Tong JL, Song HZ, Zhu H, Wang YC. (18)F-DG PET/ CT in detection of recurrence and metastasis of colorectal cancer. World J Gastroenterol 2007;13:5025–9. http://dx.doi.org/10.3748/wjg.v13.i37.5025.
[3] Pfannschmidt J, Bischoff M, Muley T, Kunz J, Zamecnik P, Schnabel PA, et al. Diagnosis of pulmonary metastases with helical CT: the effect of imaging techniques. Thorac Cardiovasc Surg 2008;56:471–5.
[4] Wiering B, Ruers Tj, Krabbe PF, Dekker HM, Oyen Wj. Comparison of multiphase CT, FDG-PET and intra-operative ultrasound in patients with colorectal liver metastases selected for surgery. Ann Surg Oncol 2007;14:818–26.
[5] Arulampalam T, Costa D, Visvikis D, et al. The impact of FDG-PET on the management algorithm for recurrent colorectal cancer. Eur J Nucl Med 2001;28:1758–65.
[6] Heusner T, Hahn S, Hamami M, Kim UH, Baumeister R, Forsting M, et al. Gastrointestinal 18F-FDG accumulation on PET without a corresponding CT abnormality is not an early indicator of cancer
development. Eur Radiol 2009;19:2171–9.

[7] Terezakis S, Yahalom J. PET-computed tomography for radiation treatment planning of lymphoma and hematologic malignancies. PET Clin 2011;6:165–75.

[8] Engledow H, Bond-Smith G, Francis D, Pakzad F, Bomanji J, Groves A, et al. The incremental value of dual-modality PET/CT imaging over PET imaging alone in advanced colorectal cancer. Indian J Surg 2009;71:63–8.

[9] Endo K, Oriuchi N, Higuchi T, Iida Y, Hanaoka H, Miyakubo M, et al. PET and PET/CT using 18F-FDG in the diagnosis and management of cancer patients. Int J Clin Oncol 2006;11:286–96.

[10] Schulthess GK, Steinert HC, Hany TF. Integrated PET/CT: current applications and future directions. Radiology 2006;238:405–22.

[11] Ell PJ. The contribution of PET/CT to improved patient management. Br J Radiol 2006;79:32–6

[12] Kantorova I, Lipska L, Belohlavek O, Visokai V, Trubac M, Schneiderova M. Routine (18)F-FDG PET preoperative staging of colorectal cancer: comparison with conventional staging and its impact on treatment decision making. J Nucl Med 2003; 44: 1784–8.

[13] Scott AM, Gunawardana DH, Kelley B, et al. PET changes management and improves prognostic stratification in patients with recurrent colorectal cancer: results of a multicenter prospective study. J Nucl Med 2008; 49:1451-1457

[14] Brush J, Boyd K, Chappell F, Crawford F, Dozier M, Fenwick E, et al. The value of FDG positron emission tomography/computerised tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation. Health Technol Assess 2011;15:1–192. http://dx.doi.org/10.3310/hta15350.

[15] Kapoor V, Mc Cook BM, Torok FS. An introduction to PET/CT Imaging. Radio Graphics 2004; 24: 523-54.

[16] Galen RS: Predictive values and efficiency of laboratory testing. Pediat J Clin North Am, 1980 27:861-69.

[17] Jadvar H & Parker J. PET Physics and Instrumentation. In: Clinical PET and PET/CT, Jadvar H & Parker J eds. Springer-Verlag London Limited 2005, 1:1-44.
[18] Hillner BE, Siegel BA, Liu D, et al. Impact of PET/CT and positron emission tomography (PET) alone on expected management of patients with cancer: initial results from the national oncologic PET registry. J Clin Oncol. 2008;26:2155–2161

[19] Khatri VP, Chee KG, Petrelli NJ. Modern multimodality approach to hepatic colorectal metastases: solutions and controversies. Surg Oncol. 2007;16:71–83.

[20] Herbertson RA, Scarsbrook AF, Lee ST, Tebbutt N, Scott AM. Established, emerging and future roles of 18FDG PET-CT in the management of colorectal cancer. Clin Radiol 2009;64:225–37.

[21] Kamel IR, Cohade C, Neyman E, Fishman EK, Wahl RL. Incremental value of CT in PET/CT of patients with colorectal carcinoma. Abdom Imaging 2004;29:663–8.

[22] Poeppel T, Krause B, Heusner T, et al. PET/CT for the staging and follow-up of patients with malignancies. European Journal of Radiology 2009; 70: 382–392.

[23] William E and Clyde A. Fundamentals of diagnostic radiology. Book(2007); p: 850-856

[24] Taha Ali, T. Usefulness of PET–CT in the assessment of suspected recurrent colorectal carcinoma. The Egyptian Journal of Radiology and Nuclear Medicine, 2012; 43(2), pp.129-137.

[25] Hussein, A. and Nassef, M. Assessment of postoperative local and distant recurrence in colorectal cancer patients: Comparison between PET/CT and CECT. The Egyptian Journal of Radiology and Nuclear Medicine, 2016; 47(2), pp.431-438.

[26] Ries LAG, Young JL, Keel GE, et al., editors. SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute; 2007. SEER Program.

[27] Chiewvit S, Jiranantanakorn T, Apisarnthanarak P, Kanchaanapiboon P, Hannanthawiwat C, Ubolnuch K, et al. Detection of recurrent colorectal cancer by 18F-FDG PET/CT comparison with contrast-enhanced CT scan. J Med Assoc Thai 2013;96(6):703–8.

[28] Chowdhury FU, Shah N, Scarsbrook AF, et al. [18F]FDG PET/ CT imaging of colorectal cancer: a pictorial review. Postgrad Med J 2010;86:174–82.

[29] Hebertson RA, Scarsbrook AF, Lee ST, et al. Established, emerging and future roles of PET/CT in the management of colorectal cancer. Clin Radiol 2008;64:225–37.
[30] Rodriguez-Vigil B, Gomez-Leon N, Pinilla I, et al. PET/CT in lymphoma: prospective study of enhanced full-dose PET/CT versus unenhanced low-dose PET/CT. J Nucl Med 2006; 47:1643-1648.

[31] Gutman F, Alberini J, Wartski M, Vilain D, Le Stanc E, Sarandi F, et al. Incidental colonic focal lesions detected by FDG PET/CT. AJR Am J Roentgenol 2005;185:495–500.

[32] Konishi J, Yamazaki K, Tsukamoto E, Tamaki N, Onodera Y, Otake T, et al. Mediastinal lymph node staging by FDG-PET in patients with non-small cell lung cancer: analysis of false-positive FDG-PET findings. Respiration 2003;70:500-6.

[33] Riopel M, Klimstra T, and Godellas CV. Intra-biliary growth of metastatic colonic adenocarcinoma. A pattern of intra-hepatic spread easily confused with primary neoplasis of the biliary tree. Am. J. Surgical Pathology; (1997). 21:1036.

[34] Chen LB, Tong JL, Song HZ, Zhu H, Wang YC. (18)F-DG PET/CT in detection of recurrence and metastasis of colorectal cancer. World J Gastroenterol 2007;13:5025-9.

[35] Choi EK, Yoo LR, Han EJ, Oo JH, Kim SH, Chung SK. Value of surveillance F-18 FDG PET/CT in colorectal cancer: comparison with conventional imaging studies. J Nucl Med 2010;51(2 Suppl):1208 [abstract].

[36] Ouchi K, Sugawara T and Ono H. Histologic features and clinical significance of venous invasion in colorectal carcinoma with hepatic metastasis. Cancer; (1996).78: 2313.

### Tables

Table (1): demonstrating the range of age in years.

| Age       |          |
|-----------|----------|
| Mean      | 58.73    |
| Standard Deviation (SD) | 11.29    |
| Minimum   | 35       |
| Maximum   | 80       |
Table (2): demonstrating the distribution according to sex.

| Sex    | Frequency | Valid Percent |
|--------|-----------|---------------|
| Female | 26        | 31%           |
| Male   | 58        | 69%           |
| Total  | 84        | 100%          |

Table (3) Patterns of tumor recurrence/ residual, lymph nodes (nodal), and distant metastasis (mets.) in the study by PET\ CT with their number (No.) and percent (%).
Table (4) showing the site of tumor recurrence with a demonstration of the number (No.) and the percent (%) for each site.
| Site                  | No. of patients | % of patients |
|----------------------|-----------------|---------------|
| Recto-sigmoid        | 31 patients     | 36.9%         |
| Ascending colon      | 13 patients     | 15.4%         |
| Transverse colon     | 9 patients      | 10.7%         |
| Descending colon     | 6 patients      | 7.1%          |
| Cecum                | 1 patient       | 1.2%          |

Table (5) showing the treatment methods for the patients in the study with a demonstration of their number (No.) and percent (%).

| Treatment method(s)                                               | No. of patients | % of patients |
|-------------------------------------------------------------------|-----------------|---------------|
| Operative and/or endoscopic intervention (Only)                   | 24 patients     | 28.6%         |
| Chemotherapy (Only)                                              | 18 patients     | 21.4%         |
| Radiotherapy (Only)                                              | None            | 0 %           |
| Operative and/or endoscopic intervention in addition to chemotherapy and radiotherapy | 12 patients     | 14.3%         |
| Operative and/or endoscopy in addition to chemotherapy            | 36 patients     | 43.0%         |
| Chemotherapy and radiotherapy                                     | 4 patients      | 4.7%          |

Table (6) Patterns of tumor recurrence/residual with reference to the gold standard, by PET/CT in comparison to CECT with a demonstration of the number (No.), percent (%) of the patients.
| Operative bed residual \ recurrence | Positive by the gold standard | Negative by the gold standard |
|------------------------------------|------------------------------|-----------------------------|
| I) by PET\CT                       |                              |                             |
| Positive                           | 56 patients 66.6%            | 4 patients                  |
| Negative                           | 4 patients 4.7%              | 20 patients                 |
| II) by CECT                         |                              |                             |
| Positive                           | 44 patients 52.4%            | 10 patients                 |
| Negative                           | 16 patients 19.05%           | 14 patients                 |

Table (7) Accuracy measures for operative bed residual\recurrence as detected by PET\CT with a demonstration of the 95% confidence interval (CI).  

| Statistical parameter     | value       | 95% CI               |
|---------------------------|-------------|----------------------|
| Sensitivity               | 93.33%      | 83.8% to 98.15%      |
| Specificity               | 83.33%      | 62.62% to 95.26%     |
| Positive predictive value | 93.33%      | 85.09% to 97.17%     |
| Negative predictive value | 83.33%      | 65.61% to 92.91%     |
| **Accuracy**              | **90.48%**  | **82.09% to 95.80%** |

Table (8) Accuracy measures for operative bed residual\recurrence as detected by CECT with a demonstration of the 95% confidence interval (CI).
| Statistical parameter          | value  | 95% CI                  |
|-------------------------------|--------|-------------------------|
| Sensitivity                   | 73.33% | 60.34 % to 83.93%       |
| Specificity                   | 58.33% | 36.64% to 77.89%        |
| Positive predictive value     | 81.48% | 72.79% to 87.86%        |
| Negative predictive value     | 46.67% | 33.80% to 60.0%         |
| **Accuracy**                  | **69.05%** | **58.02% to 78.69%**    |

**Figures**

**Figure 1**

Axial CECT and fused PET-CT images of A 62-years old female patient presented with a history of cancer rectum for which she had an operation followed by chemotherapy. The baseline study was in 9/2018: Images A and B showed an operative bed deep pelvic left side ill-defined soft tissue lesion (red arrow) measuring 4.5x3.5cm. In CT, it might represent postoperative scarring or recurrent neoplastic mass lesion, but it showed an increased FDG
uptake with SUV max= 6.1 denoting a recurrent neoplastic lesion, and this was confirmed by histopathological examination. Images C and D showed a hypermetabolic metastatic left external iliac lymph node (yellow arrow) measuring 1.6 cm and showed SUV max=8.1, moreover, a metastatic sacral metabolically active osteolytic lesion (blue arrow) that was measuring 6x4 cm with SUV max=14 was also demonstrated. The follow-up study was in 12/2018: Images E and F showed a morphological and metabolic regression of the operative bed hypermetabolic recurrent soft tissue lesion (red arrow) showing SUV max 4.1. Images G and H showed morphological and metabolic regression of the metastatic left external iliac lymph node (yellow arrow) showing SUV max 2. Images G and H showed marked metabolic regression of the sacral osteolytic lesion (blue arrows) with SUV max = 3.6. It also showed a regressive morphologic course with evident sclerosis (healing) and decreased extra-osseous pre-sacral soft tissue component as well as the intra-sacral component
Axial CECT and axial and coronal fused PET-CT images for a 50-year old female patient presented with a history of sigmoid colon cancer for which she had an operation followed by chemotherapy. The baseline study was in 6-2018: Images A and B showed no evidence of metabolically active loco-regional residual/ recurrent lesions. Image C showed no distant metastatic lesions. The follow-up study in 9-2018: Images D and E showed a rather stationary course and still no metabolically active loco-regional residual/ recurrent lesions.

Image C showed a stationary course and still no distant metastatic lesions.
Axial and coronal CECT and fused PET-CT images for a 70-year old male patient presented with a history of sigmoid cancer colon, for which he had sigmoidectomy with pathological diagnosis of infiltrating adenocarcinoma grade II, then he had received chemotherapy. Images A, B, C, and D showed clear colectomy (yellow arrow) and colostomy (red arrow) operative bed with no abnormal FDG uptake denoting no residual or recurrent loco-regional neoplastic lesions. Images E, F, G, and H showed few right hepatic lobe hypodense focal lesions that were suggestive of the metastatic process in CT. Yet, they showed no significant FDG uptake denoting the absence of tumor activity. The largest lesion is seen in segment VI and was measuring about 12 mm.
Axial CECT, PET, and fused PET-CT images for a 75-years old male patient with a history of the anorectal tumor. The patient underwent surgical resection and received chemotherapy.

Images A, B, and C showed irregular pre-sacral soft tissue density in the operative bed suggesting a tumor recurrence; yet, it shows no gross FDG uptake denoting a postoperative scarring (red arrow). Image D showed metabolically active metastatic left adrenal mass lesion (green arrow) measuring 6.3cm in its maximum dimensions with SUV max=9.6. Image D showed metabolically active metastatic right retro-crural lymph node (white arrow) measuring 14x19mm in its maximum dimensions with SUV max= 3.2. Image E showed hypermetabolic metastatic right upper lobar posterior segment subpleural pulmonary mass (yellow arrow) measuring 2.8x3.7cm with SUV max=11.6. Image F showed metabolically active metastatic left supra-clavicular nodal mass (blue arrow) measuring 5cm in its maximum dimension with SUV max= 7.7.
Coronal and axial CECT and fused PET-CT images for a 50-year old male patient diagnosed with colonic hepatic flexure infiltrating adenocarcinoma for which he had a right hemicolecotony followed by chemotherapy. Images A and B showed a clear operative bed
with no gross hypermetabolic mass lesions (red arrows). Images C and D showed a right hepatic lobe (segment VIII) hypodense focal lesion that was noted in CT but showed no FDG uptake denoting the absence of tumor activity (yellow arrows). Images E and F showed a left lung pulmonary nodule that was noted in CT but showed no FDG uptake denoting the absence of tumor activity (green arrows).

Figure 6
Axial CECT, PET, and fused PET-CT images for a 52-years old male patient presented with transverse colon cancer. He underwent surgical resection and then received chemotherapy. The baseline study was in 8/2018: Images A, B, and C showed increased FDG uptake (SUV max 6) by thin soft tissue sheet related to the greater curvature of the stomach (red arrows), denoting a peritoneal deposit. It was missed in CT. Images D, E, and F showed increased FDG uptake (SUV max 6.9) by small soft tissue nodule that was related to the sigmoid colon (yellow arrows) denoting a peritoneal deposit. It was also missed in CT. The follow-up study was in 12/2018: G, H, and I showed the metabolic and morphological course of the peritoneal deposit that was related to the greater curvature of the stomach (green arrows) showing SUV max 10.2. Images J, K, and L showed the metabolic and morphological course of the peritoneal deposit that was related to the sigmoid colon (blue arrows) showing SUV max 14.9.