



## **Positron Emission Tomography /Computed Tomography Follow-Up in Patients with Gastrointestinal Tract Malignancies**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author AMKE designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors MAEHAED, AAAA and EMM revised the manuscript and managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** PET/CT has an increasing role in the oncology field, including GIT. The role of PET/CT is more significant in the follow-up than initial staging and diagnosis as it helps in therapy assessment and detects recurrence and metastasis. In esophageal cancer, it helps by detecting the distant metastasis and discover synchronous neoplasm. Also, it is acclaimed to help in early detection of the response of the patient to chemo and radiotherapy. In the follow-up, it may be useful to detect recurrence. PET/CT has a minimal role in gastric cancer, as it shows no superiority over C.T. alone. For Colorectal Cancer, PET/CT has a good value in cases of suspected liver or lung metastasis and local recurrence after surgery. This study aimed to evaluate the impact of PET/CT on treatment decision & follow-up of patients with gastrointestinal tract malignancies.

**Methods:** This study is a cross-sectional study and was done retrospectively by collecting data and records of 47 GIT malignancy patients who underwent PET/CT during or after treatment. At PET/CT unit, Diagnostic Radiology Department in Educational hospitals - Tanta University between July 2015 and December 2017.

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**Results:** The patients were mainly colorectal in the site and primarily adenocarcinoma in type. We found that 27.7% of cases treatment plans were influenced by the PET/CT results, the percentage is highest with colon cancer (40%) then rectal cancer (25%), and our few esophageal, gastric, intestinal malignancies cases have shown no influence which is due to a small number of cases. PET/CT seems to have the best add value in patients with colorectal cancer with metastasis with a 66.7% change in treatment plans. Six patients had inconclusive results of PET/CT due to scan limitations.

**Conclusion:** Relying on PET/CT in clinical decisions in esophageal or gastric cancer is not encouraged unless in case of clinical or imaging suspicion of recurrence. On the other hand, PET/CT is useful in detecting post-treatment metastasis and local recurrence in colorectal cancer.

*Keywords: Positron emission tomography; computed tomography; follow-up; gastrointestinal, malignancies.*

## 1. INTRODUCTION

Malignant lesions of the gastrointestinal tract are among the most common in the world. With nearly 3 million new cases diagnosed each year, colorectal, stomach, and esophageal cancers rank 3<sup>rd</sup>, 5<sup>th</sup>, and 7<sup>th</sup>, respectively, in terms of incidence worldwide. GIT tumors are a leading cause of death worldwide, accounting for 1.8 million deaths [1,2]. In Egypt, GIT malignancies represent 9.5% of whole cancer cases with 4.7% for colorectal (ranked as the 7<sup>th</sup>), gastrointestinal 3.9% (the 8<sup>th</sup>), and esophageal 0.9% (the 21<sup>st</sup>) [3, 4].

Endoscopy with biopsy is still the main tool for initial diagnosis, either regular or combined with ultrasound (EUS), and C.T. (usually with contrast) is the choice to evaluate the extent of the tumor and a common site for metastasis, MRI and PET/CT useful in some instances. Usually, a multi-modality radiological workup is the best choice for diagnosis, staging, and monitoring. Staging is generally into four grades according to the TNM (tumor, node, metastases) system [5].

The treatment of GIT malignancies can be aimed at cure or palliation. The decision on which seek to adopt depends on various factors, including a person's health and preferences and the stage of the tumor. The choice and combination of surgery, chemotherapy, and radiotherapy depending on the site, histopathology, and stage of the malignancy [6].

Approximately 40% of patients treated with the most appropriate approach will progress within the first three years. However, both recurrence and metastasis from gastrointestinal cancer can be alleviated by curative surgery or intervention. Therefore, early diagnosis and accurate staging of recurrent and metastatic gastrointestinal

cancer are essential for treatment and prognosis [7].

PET/CT has variable added value in GIT malignancies staging and monitoring. However, it has false-positive results due to high intake of glucose physiologically in some organs and pathologically non-malignant conditions, many researches which study the role of PET/CT in GIT malignancies encourage more efforts to evaluate and highlight the role to be more accurate and helpful [8,9].

This study aimed to evaluate the impact of PET/CT on treatment decision & follow-up of patients with gastrointestinal tract malignancies.

## 2. PATIENTS AND METHODS

This study is a cross-sectional study and was done retrospectively by collecting data and records of patients at PET/CT unit, Diagnostic Radiology Department in Educational hospitals - Tanta University between July 2015 and December 2017. Patients were referred from in Educational hospitals - Tanta University and Oncology committee at Insurance Hospital in Tanta.

Patients with diagnosed gastrointestinal tract malignancies with at least one PET-CT study during the period of follow-up were included in the study with no age restriction.

The exclusion criteria were patients in diagnosis or staging stage and with concurrent primary tumors or a second primary cancer.

The study was performed on a dedicated PET/CT scanner (Philips Gemini NM), complete clinical history was taken from all patients. All of them were subjected to complete physical

examination and Kidney Functions Tests. Patients were fasting 6 hours before the time of injection, and their weight, height, and blood glucose level were measured before FDG injection

### 2.1 PET Acquisition

Image acquisition was started 45-60 minutes following injection of 3.7 MBq/kg 18 F-FDG. During this period, the patient was isolated in a semi-dim quiet room, resting on a semi-setting recliner with no movement.

Field of imaging:

- Whole-body scans: from the feet to the vault of the skull
- Torso scans: acquired from Base of the skull to mid-thigh

Acquisition time: 2 minutes per bed position.

Standard uptake value (SUV) was done for any suspected lesion.

### 2.2 C.T. Scan

Two types of scans were used; Low dose non-contrast C.T. scan (from the vault of the skull to the foot, 50 kV, 50 mA) and Diagnostic (High dose) C.T. scan (from skull base to mid-thigh, 1-2 mL/ kg of a low-osmolarity iodinated CM at a rate of 4 ml /sec, 130 kV, 100 mA) both with 1-s tube rotation, 4-mm slice collimation, and bed speed of 8 mm/s.

## 3. RESULTS

The study included 47 patients' data and records. According to patients' basic data mean age was

57.4. years and male patients present the majority with 70.2%, which is supposed to be less compared to worldwide incidences. The colon is the most frequent site for primary tumor with 19 cases (40.4%). Overall colorectal cancers represent most cases with 38 patients (80.8%); adenocarcinoma is the most frequent (87.2%) pathological type of GIT malignancies.

Spread to local lymph nodes was the most frequent and was reported in the history of 57.4% of cases. Fifteen cases (31.9 %) had a history of distant metastasis, and six patients had a history of local invasion to surrounding organs (12.8%).

Underwent surgery then receiving chemotherapy was the most frequent management plan (22 cases; 46.8%) and mainly planned for colon cancer patients. The second most frequent is adjuvant Chemoradiotherapy, then surgery, then chemotherapy for cancer rectum (9 cases, 19.1%). Besides the basic treatment, three patients underwent Radiofrequency ablation for hepatic focal lesion, and one patient receiving Imintab for GIST (Table 1).

Most patients were referred to after finishing their treatment (72.4%). Only 13 cases (27.6%) came during the treatment before completing all management plan steps.

Comparing to known confirmed malignant lesions, 27 cases (53.4%) showed new metabolically active lesion/s, which in relation to the primary tumor site was distributed as local, distant. L.N.s. The significant increase in the size of the known lesion was considered a new lesion. It should consider that not all active lesions were deemed to be malignant.

**Table 1. Management plan**

Management plan	Total (n=47)	
	n	%
<b>Main management plan</b>		
Surgery	3	6.4
Surgery then chemo	22	46.8
Surgery then chemo & radio	4	8.5
Chemo +/- surgery	7	14.9
Chemo and radio then surgery then chemo	9	19.1
Chemo then surgery then chemo	1	2.1
Surgery then rad	1	2.1
<b>Other management</b>		
No	43	91.5
Radiofrequency ablation for HFL	3	6.4
Imintab	1	2.1

In 6 cases, PET/CT, due to its limitations, can't add new significant information and was inconclusive. About half of the rest, 41 cases found to be in complete remission (21 cases), 4 patients were found to have a recurrence after a period of complete remission, and 12 show a progressive course of residual malignancy. About half of the patients (17 of 36) who was sent to assess the therapy shows the good response with complete or partial remission and recurrence was detected in a quarter of patient who was suspected of having it (Table 2). After PET/CT; 13 cases of 47 who was included in the study, their management was influenced by PET/CT outcome and findings, which represent 27.7% (Table 3).

22 cases came for PET/CT scan in complete remission, 4 cases of them diagnosed in recurrence by the scan, which changed their management, and that represent 18.2% of them. Of the 25 cases that came with residual malignancy, 9 changed their management (36%). However, 12 cases of the 25 were found to have a progressive course; only 8 of them had changes in their plans.

15 patient came with the M1 stage with a history of metastasis in the liver, lung, and peritoneum; 8

of them changed their management (53.3%) (Table 4)

All cases that changed their management are colon and rectum cases, with 9 cases for colon (40.9% of all colon cases) and 4 cases for rectum (25 % of all rectum cases). The change in management was sometimes modification in the same treatment (change chemotherapy protocol or change extension and the intention of surgery), avoiding unnecessary treatment (stopping chemotherapy or canceling planned surgery) or start/ recurrent new treatment. (Table 5)

#### 4. DISCUSSION

All the influenced cases in our result had colon or rectal cancer as esophageal and gastric cancer patient treatment influence with PET/CT result after surgery showed to seem very low. PET/CT scan usage in follow up during and after treatment of esophageal and gastric cancer is still controversial and needs more specification before, and after surgery, hence the guidelines do not recommend routine PET/CT scans as it has a low impact in the presence of other less expensive modalities with close accuracy.

**Table 2. PET/CT scan final outcome in relation to the cause of referral**

PET/CT outcome	Total (n=47)	
	n	%
<b>Assess the therapy (n=36)</b>		
Not conclusive	4	11.1%
Complete remission	15	41.7%
Recurrence	2	5.6%
Stationary	1	2.8%
Partial remission	2	5.6%
Progression	12	33.3%
<b>Suspect recurrence (n=8)</b>		
Not conclusive	1	12.5%
Complete remission	5	62.5%
Recurrence	2	25.0%
<b>Search metastasis (n=3)</b>		
Not conclusive	1	33.3%
Complete remission	1	33.3%
Local progression	1	33.3%

**Table 3. Change in management protocol induced by PET/CT scan outcome**

Management change	Total (n=47)	
	n	%
Non conclusive	6	12.8
No change	28	59.6
Change	13	27.7

In esophageal cancer; PET/CT role after starting the treatment is not settled yet [10-12] as it has a low influence on management [13] and low or no positive impact on survival rate, which doesn't encourage to relayed on PET/CT for clinical evaluation during chemo or radiotherapy or routinely after surgery [10,11,14-16]. As the ability of PET/CT to detect local lesions regress markedly after treatment [17]. Some studies suggest that it may be helpful in the presence of strong clinical or imaging suspicion due to its high positive predictability. Still, Goense and colleagues found no difference between routine scans and those which were done for suspected cases of recurrence or metastasis. [18] many studies try to search using SUVmax as a tool to follow-up tumor response to therapy. Cremonsi et al., in their systematic review, found that eight studies showed an association between a decrease of SUVmax and tumor response to treatment. In comparison, five studies did not find any association. So they concluded that the rely on clinical decisions on PET/CT is not supported [19].

PET/CT is not recommended to be used in follow up in gastric cancer detection of recurrence as however its mildly more sensitive than C.T. it has less specificity [20-22], However, some studies advocate the usage of PET/CT in follow up especially in the presence of suspicion of recurrence or metastasis [23-26] but low specificity make it unreliable, in Sim et al study clinical decisions that made in depend on PET/CT and in contraindication with C.T. show only 42% accuracy [27], and Blencowe et al found that also local recurrence after surgery at the site of anastomosis can't be detected due to sustained chronic inflammation [28]. In our study, the low impact in cases of esophageal and

gastric cancer would be expected as 85 % of them underwent PET/CT scans without clinical or imaging suspicion.

On the other hand, the impact of PET/CT in the colon and rectal cancers in our study is significant. PET/CT scan induce a change in the treatment of 40.9% of colon cancer cases (9 of 22 cases) and of 25% of rectal cancer cases, which make the result for colorectal cancers 34.2%. In Marcus and colleagues' retrospective study, patients in remission and was not on treatment who PET/CT scans led to the initiation of new therapy was represent 35.2% of cases. patients who were on treatment before the scan, 30.1% of scans led to change in treatment, and treatment was stopped following 8.4% of scans [29]. Artiko et al. reported after a prospective study on 75 patients that 18F-FDG PET/CT had influenced treatment decisions by 40%, and this influence prolonged survival by 25% [30]. A meta-analysis by Maffione et al. suggested that 18F-FDG PET/CT has less, but still valuable, impact (ranging between 15%-42%) on patients with colorectal cancer and liver metastases [31]. Georgakopoulos et al. and Kochhar et al. reported results at the same range (31.4% and 33.8% respectively) [32,33].

Fifteen cases in our study came in the M1 stage; the PET/CT scan influenced the management in 8 cases (53.3%), the percentage is higher with colorectal patients, as all the 8 are colorectal patients out of 12 cases with a percentage of 66.6%, Artiko et al. in the same mentioned study showed a large proportion of patients with colorectal cancer and liver metastases with altered treatment regime. However, their results showed that local recurrence diagnosed by PET/CT was significantly associated with more

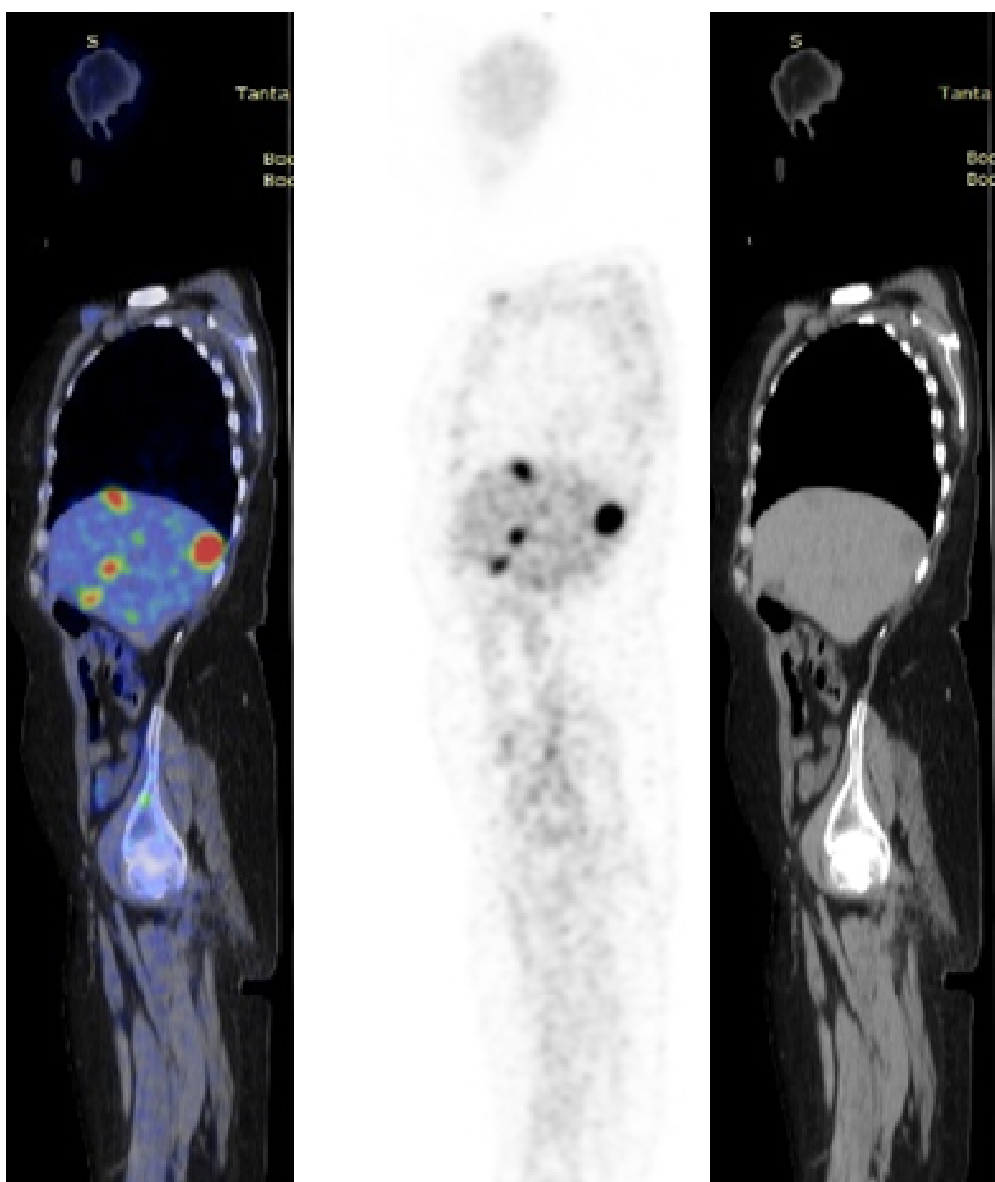
**Table 4. Change in management in relation of case of the patient's tumor**

PET/CT findings	Total (n=47)		Changed management	
	n	%	n	%
<b>Patients in complete remission (n=22)</b>			4	18.2
Not conclusive	4	8.5	0	0
Complete remission	14	29.8	0	0
recurrence	4	8.5	4	100
<b>Patients with residual Lesion/-s (n=25)</b>			9	36%
Not conclusive	2	4.3	0	0
Complete remission	7	14.9	0	0
Stationary	1	2.1	1	1
Partial remission	3	6.4	0	0
Progression	12	25.5	8	66.6

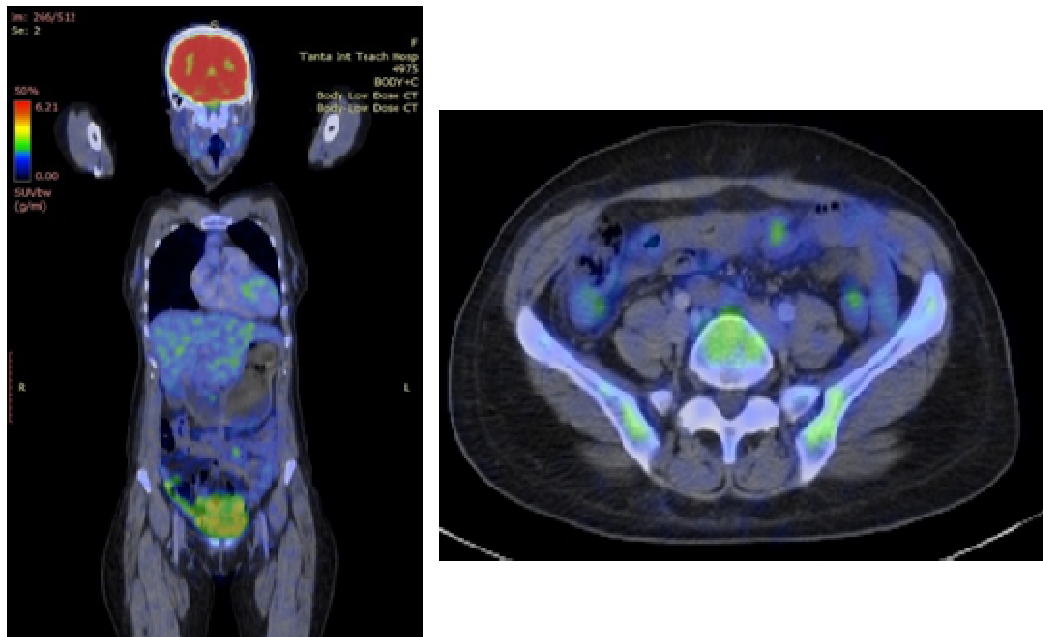
**Table 5. Types of change in management protocol induced by PET/CT Findings**

The change induced	Total (n=13)	
	n	%
Not closing colostomy and recurrent chemo	6	46.2
Starting treatment plan for recurrence	1	7.7
Avoid useless metastectomy	1	7.7
Change the chemotherapy protocol	2	15.4
Change extension and type of surgery	1	7.7
Change from chemotherapy to palliative	2	15.4

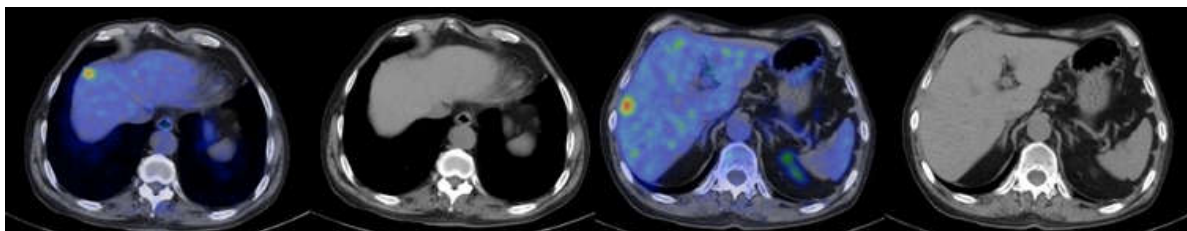
*Examples of our cases are shown in Figs. 1-5*



**Fig. 1. A female (60y) with infiltrative transverse colon adenocarcinoma with omental deposits and underwent colectomy with partial gastrectomy and chemotherapy. Triphasic CT showed multiple focal lesions in liver. PET/CT scan showed new multiple active hepatic focal lesions and also enlarged active retro-pancreatic nodule indicate progressive course of the case. Chemotherapy protocol was changed**



**Fig. 2. A female with high risk GIST at small intestine underwent surgical resection of the tumor. C.T. follow-up showed suspicious irregular mural thickening at the site of anastomosis. PET/CT showed that the site of anastomosis had low metabolic activity denying recurrence**



**Fig. 3. A male with ileo-cecal adenocarcinoma who underwent right hemicolectomy with colostomy then received chemotherapy. Follow-up CT showed clear operative bed and no L.N.s or distant metastasis and patient was sent to PET/CT for assessment before closure of colostomy. PET/CT showed multiple metabolically active hepatic focal lesions highly suspected to be metastatic which contraindicated colostomy closure**

treatment alterations as compared to recurrent metastatic cancer, which doesn't compile with ours, as we have got 41.7% alteration of management with local recurrence and 58.3% for found new metastasis.

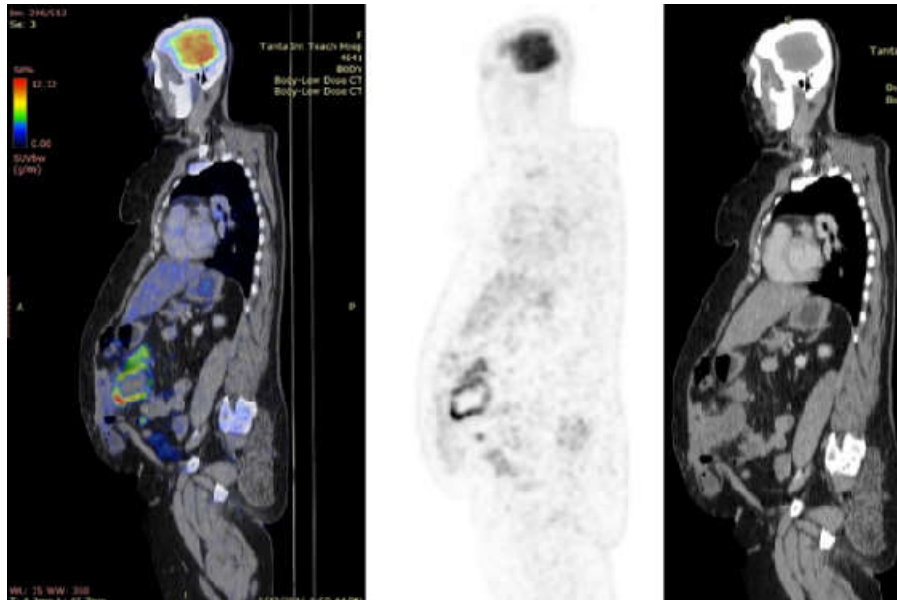
In relation to the cause of referral, the percentage of changed treatment was higher for patients who were sent for therapy assessment than who had suspected recurrence (30% and 25%, respectively). In relation to tumor condition before the scan, cases who were supposed to be in complete remission showed change in 18.2% of cases due to recurrence (4 of 22 cases) while patients with residual tumor, L.N.s, or metastasis showed a change in 36% due to progression and not responding to therapy (9 of 25 cases), the percentage for colorectal only is insignificantly

higher (23.5 and 40.9%), that may indicate that usage of PET/CT is more efficient with in follow-up patients in advanced stages and with residual disease.

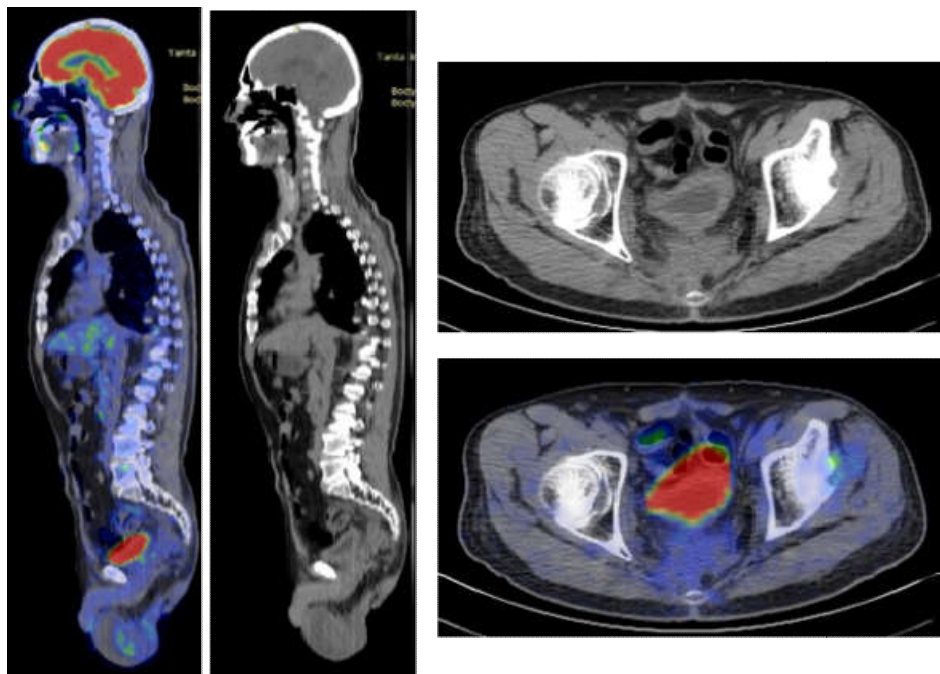
Our study had some limitations; The study was a retrospective study and can have the possibility of inherent errors of confounding when the exposure is not controlled. The number of patients was overall few for the wide-scale of organs and pathological types, also for a retrospective study. The clinical cause of referral of the study was retrospectively examined from medical records and the PET/CT reports. The exact perspective of the clinician ordering the study was not collected prospectively, and we may have underestimated the clinical suspicion prior to the scans. This may have overestimated

the number of studies we classified as therapy assessment scans. Our patients had been sent after a wide variation of time since the start or

end of the therapy, so we can't standardize a specific time interval.



**Fig. 4.** A female with transverse colon cancer who underwent tumor resection and received chemotherapy. C.T. and MRI follow-up suspected local recurrence at the site of anastomosis. PET/CT showed metabolic activity confirmed malignancy of the lesion and recurrence. Colostomy wasn't closed, and the patient received chemotherapy



**Fig. 5.** A male (60y) with lower esophageal adenocarcinoma underwent partial esophagogastrectomy and received radiotherapy. After two years, A follow-up C.T. showed post gastric pull up and suspected recurrence at the site of anastomosis. PET/CT showed a metabolically active gastric wall (SUVmax = 4.9) at the operative bed but with a pattern suggested to be an inflammatory process, which was proved by endoscopy



## 5. CONCLUSION

PET/CT has a significant add-value in the oncology field; however, it has not satisfying impact on patient management when routinely used in esophageal and gastric cancer after starting the treatment. On the other hand, it is useful in colorectal cancer after surgery in surveillance for metastasis and differentiates between postoperative fibrosis and local recurrence, which lead to valuable changes in patients' treatment

## CONSENT

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

The study was approved by the Ethics Committee of Faculty of Medicine, Tanta University.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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