Staging of Colorectal Cancer

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Colorectal carcinoma remains one of the leading causes of cancer death in the United States and worldwide. In fact, the approximate average lifetime risk of colorectal cancer is a staggering 6%. For this reason, it is important that all radiology and nuclear medicine specialists are familiar with and understand how colorectal carcinoma is accurately staged and the role and benefits of PET/CT in staging this lethal disease.

Colorectal carcinoma is staged using the standardized TNM staging nomenclature. Briefly, this system uses the depth of tumor invasion (T), nodal status (N), and evidence of distant metastasis (M) to classify patients into five separate stages (**Stage 0 through 4**). Older classification schemes, such as the Dukes classification, are still in use today, however the American Joint Committee on Cancer suggests making treatment decisions based upon the TNM staging schema. Understanding how to stage patients accurately is vital, as the stage of tumor guides treatment, prognosis, morbidity and mortality.

Patients with localized disease are classified as **stage** 0 (carcinoma in situ) or **stage 1**, depending upon the depth of tumor invasion. For **stage 0**, the primary tumor invades the mucosa or lamina propria, while **stage 1 (Dukes Classification A)** disease extends into the submucosa (T1, N0, M0) or muscularis propria (T2, N0, M0). Neoplasms in these groups must not have evidence of nodal disease or distant metastasis.

In fact, depth of the primary tumor invasion is typically made at the time of biopsy and confirmed at the time of surgical resection. Imaging, such as PET/CT, simply plays a role at this point to exclude disease outside of the colon or rectum.

S**tage 2 (Dukes Classification B)** is further divided into the three subclasses, all based upon the depth of primary tumor invasion. In **stage IIA**, the primary neoplasm extends through the muscularis propria (T3, N0, M0). In **stage IIB** (T4a, N0, M0) and **stage IIC** (T4b, N0, M0), the primary neoplasm extends beyond the serosa into the visceral peritoneum or direct invasion into adjacent structures or organs respectively. Again, lesions in this stage must not have evidence of nodal disease or distant metastasis.

It is very important to differentiate between stage IIA disease and IIB or IIC disease, as patients with stage IIB or IIC disease are at increased risk for recurrence and may be offered adjunctive chemotherapy as a part of the treatment plan.

Furthermore, patients in which tumor has extended into adjacent organs may undergo more radical surgical interventions. In these patients, PET/CT can be useful modality for identifying lesions in which tumor has extended beyond the serosa (see figure 1). This includes CT findings of soft tissue infiltration beyond the expected margin of bowel, into the adjacent mesentery or direct invasion into adjacent organs, such as the prostate or urinary bladder.

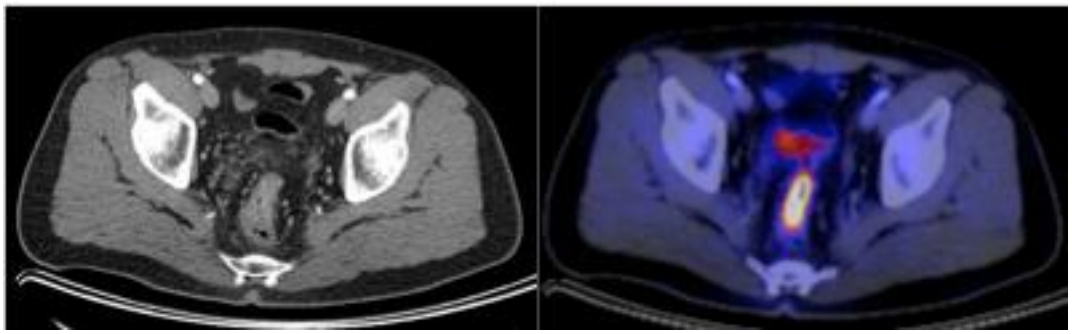

Figure 1: CT and fused PET/CT images that demonstrate eccentric sigmoid colonic wall thickening with increased metabolic activity consistent with the patient's known sigmoid carcinoma. Note on the CT images, soft tissue infiltration is seen beyond the colonic serosal margin indicating at least a **stage 2B** lesion. This case underscores the importance of evaluating both the CT and the PET images in isolation and in conjunction in order to accurately stage the patient.

A focus of increased 18F-FDG activity within an adjacent organ may also be the only sign of direct invasion, as many cases will show a soft tissue lesion that abuts an adjacent structure, but direct invasion is uncertain on the CT images alone.

Thus, every effort must be made to evaluate these areas carefully to ensure accurate staging. Additionally, PET/CT imaging should be used to evaluate for complications of larger primary neoplasms, such as obstruction or perforation. Although these complications do not necessarily upstage a patient, they do increase the risk of recurrence.

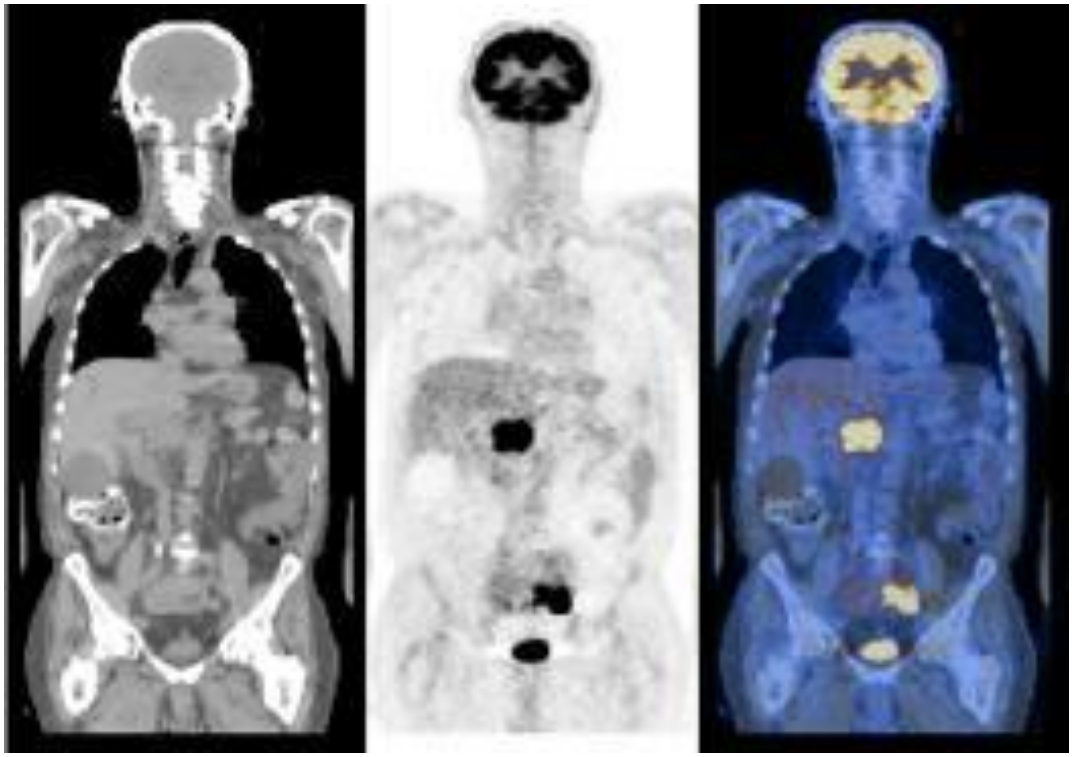

Figure 2: CT, PET and fused PET/CT images which demonstrates a sigmoid colonic mass with metastasis to enlarged retroperitoneal nodes. Given the nodal metastasis, this is at least a **stage 3** lesion.

Stage 3 (Dukes Classification C) lesions are also broken down into further subclasses, however all **stage 3** lesions share one uniting theme: lymph node metastases.

Differentiating between the subclasses within stage 3 is less important for an imaging specialist, as the treatment for all stage 3 lesions is similar, regardless of subclass.

Computed tomography, and therefore PET/CT, is paramount and essentially the standard of care for the diagnosis of lymph node metastasis, especially those lymph nodes that are increased by CT size criteria or demonstrate increased 18F-FDG activity (see figure 2). However, colorectal carcinoma has a propensity to develop locoregional nodal micrometastasis, which limits the sensitivity of both CT and PET/CT, most notably due to size of the involved nodes.

For this reason, it is important to identify all adjacent pericolonic/perirectal nodes adjacent to a primary lesion, regardless of size or FDG-avidity, as they may harbor tumor and should at the very least be sampled intraoperatively (see figure 3).

In this manner, any potential lymph node metastasis can be identified allowing for appropriate surgical planning, and ultimately accurate staging.

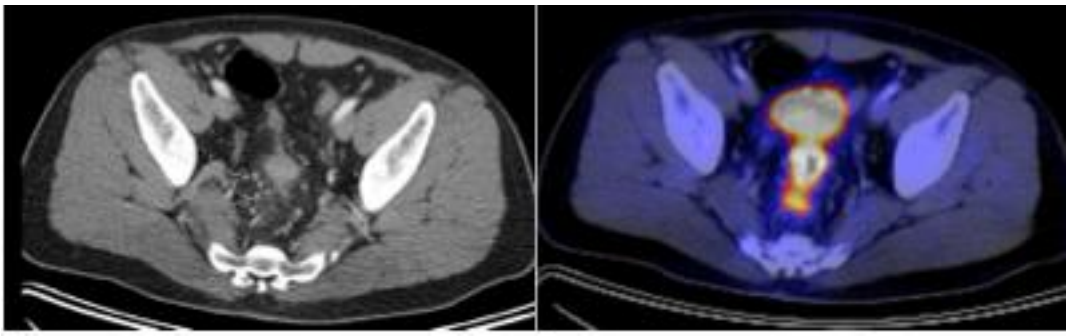

Figure 3: CT and fused PET/CT axial images from a patient with sigmoid carcinoma which demonstrates a partially visualized hypermetabolic colonic mass with adjacent small, subcentimeter pericolonic nodules (arrows on CT image). Although these nodules are below CT size criteria and below the resolution of PET, it is important to mention, as these nodules were biopsied intraoperatively and found to have micrometastasis.

Patients who have distant metastatic disease, regardless of depth of tumor invasion or nodal status, are classified as **stage 4** lesions. **Stage IVA** is defined as distant metastasis confined to a single organ or site, while **Stage IVB** indicates distant metastasis to more than one organ or to the peritoneum. Obviously, identification of distant metastatic lesions is paramount, as these patients are offered the most aggressive chemotherapy regimens, but also unfortunately have the worst prognosis.

Overall, PET/CT has a very high negative predictive value in excluding distant metastatic disease in the setting of a negative scan.

PET/CT is, however, more accurate compared to CT alone for identification of distant metastasis, specifically within the liver (most common site of colon cancer metastasis), according to Abdel-Nabi, et al.
It is important to fully evaluate the extent of hepatic tumor burden, which can be underestimated by CT alone, as some lesions are 18F-FDG avid without a definite corresponding CT abnormality (see figure 4). This is clinically important in order

accurately determine which patients are candidates for surgical resection of liver metastasis.

Furthermore, PET/CT is also useful in identifying those with early peritoneal disease or carcinomatosis. This can be suggested by the identification of FDG activity within abdominopelvic ascites, with or without frank peritoneal nodularity. In this manner, the patient can be accurately staged with PET/CT and thereby treated in the appropriate fashion.

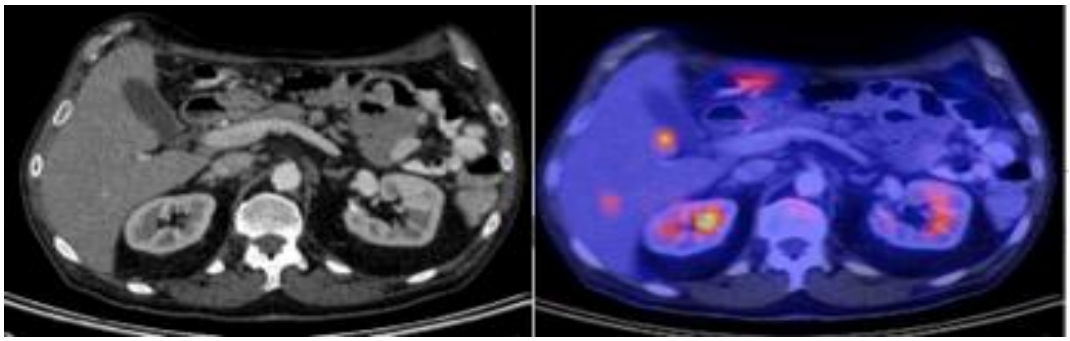

Figure 4: CT and fused PET/CT images of a patient with colonic mass with two hypermetabolic foci within the liver without definite corresponding CT abnormality very worrisome for hepatic metastasis. This case demonstrates the advantage of PET/CT over CT alone in the imaging of distant colonic metastasis.

PET/CT also plays a crucial role in the evaluation for recurrent disease and **restaging** of patients with colorectal carcinoma. In fact, according to Staib, et al, PET/CT altered surgical management in patients with recurrent colorectal cancer in approximately 60% of patients compared to CT, ultrasound and CEA levels. This is not surprising given the propensity of colon cancer to recur more commonly within the liver and abdomen, compared to the original site, and the power of 18F-FDG PET/CT in the identification of distant metastatic disease. According to a meta-analysis, PET/CT is 97% sensitive in the evaluation of recurrent colorectal carcinoma.

This is especially true in the ability of PET/CT to distinguish between recurrent tumor and post-treatment scar based upon metabolic activity, which is limited on other imaging modalities (see figure 5).

However, it must be stated that the sensitivity for PET/CT is decreased in tumors with high mucinous content, presumably due to decreased cellular activity. Nevertheless, ^{18}F-FDG PET/CT remains a mainstay in the evaluation of recurrent colorectal carcinoma.

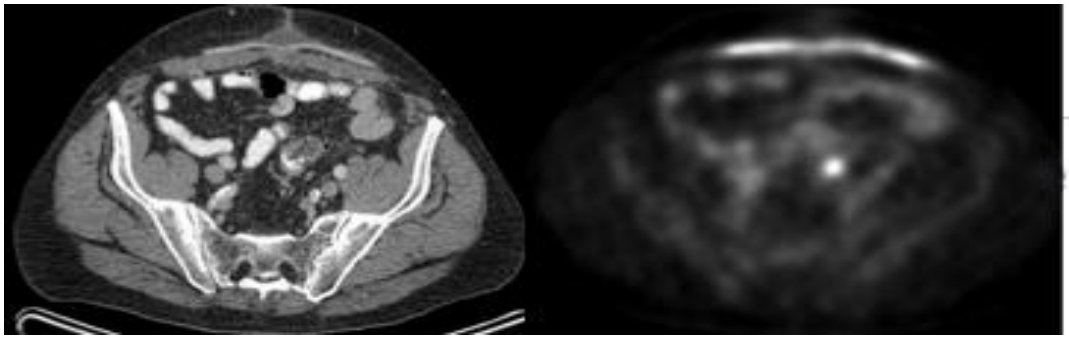

Figure 5: PET and CT images of a patient with colon cancer status post resection with reanastomosis. The patient developed a new focus of increased metabolic activity at the anastomotic site without a definite corresponding CT abnormality. This region was resected and found to harbor recurrent tumor upon pathology, further illustrating the power of PET imaging in colon cancer surveillance, especially at the surgical site.

Accurate **staging** is one of the key roles imaging specialists play in diagnosis and treatment of colorectal carcinoma. It is necessary to understand how this deadly cancer is staged in order to identify the salient findings on an examination, especially those that alter clinical management. It is these features that must be scrutinized on every exam to ensure accurate staging.

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