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MINI SYMPOSIUM: PET—THE PRESENT

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PET: other thoracic malignancies

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Abstract

The vast majority of esophageal cancers are fluorodeoxyglucose (FDG) avid; the primary use for positron emission tomography (PET) in patients with esophageal cancer is in the detection of distant metastases, because known distant metastatic disease precludes surgical resection. High standardized uptake values (SUVs) may be predictive of poor prognosis. PET findings may be used to assess therapy response and evaluate for esophageal tumor recurrence after treatment. PET findings may be non-specific in different types of thymic lesions, although thymic carcinomas tend to be extremely FDG avid. PET can be helpful in detecting distant spread from invasive thymomas and thymic carcinomas. Similarly, PET may be used to assess the extent of disease in patients with malignant pleural mesothelioma, thereby facilitating optimal therapy approaches.

Keywords: *Positron emission tomography (PET); fluorodeoxyglucose (FDG); primary thoracic malignancy; standardized uptake value; therapy response; tumor recurrence.*

Introduction

Preliminary studies suggest that PET scanning is useful in evaluating patients with primary thoracic malignancies other than lung cancer. Most published work pertains to esophageal cancer, although there is some data with regard to PET findings in thymic disorders and malignant pleural mesothelioma.

Esophageal cancer

Primary esophageal cancer

Staging

Approximately 90–100% of primary esophageal cancers have been reported to be fluorodeoxyglucose (FDG) avid at positron emission tomography (PET) scanning[1]. False negative cases occasionally occur, predominantly if the tumor is small and confined to the mucosa[2]. Conversely, PET may be falsely positive in areas of inflamed esophageal wall or even in regions of normal esophagus or gastroesophageal junction[1]. Due to the poor spatial resolution of the technique (approximately 7–8 mm), PET is not useful in gauging the depth of tumor invasion and thus in determining the T stage or in diagnosing or excluding tumor involvement of regional lymph nodes adjacent to the primary tumor (Fig. 1)[1,3–6]. The dominant use for PET in patients with esophageal cancer is in the detection of distant lymph node disease (Figs 2 and 3) and other distant metastases (Fig. 4); published reports have shown approximately 70–90% sensitivity, 90% specificity, and 85–90% accuracy in this setting[1,4,6]. One small study found osseous metastases that were detected on PET but missed using bone scintigraphy[7]. The major pitfall of PET in evaluating for distant metastases is lack of sensitivity in detecting very small lesions, due to limited spatial resolution. Despite that limitation, according to published reports, PET detects previously unsuspected distant disease in approximately 10–30% of patients, thereby preventing unindicated surgery in a substantial number of patients[8].

Standardized uptake values (SUVs)

Some published reports have suggested that high SUVs of the primary tumor are predictive of poor survival[9]. One report[10] postulates that this is because patients

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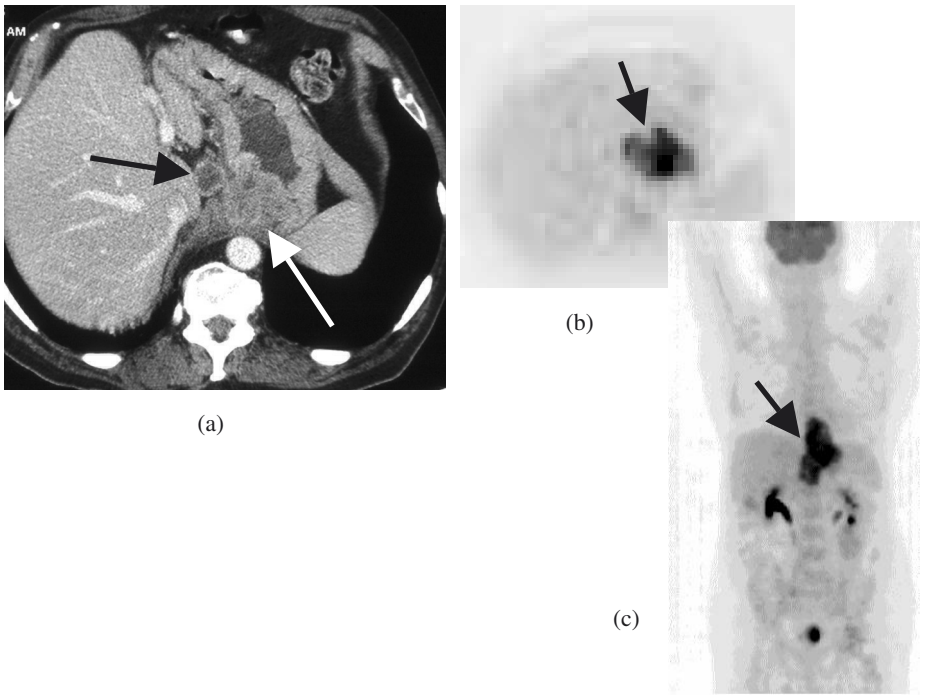


Figure 1 **Primary distal esophageal adenocarcinoma (white arrow) with adjacent, regional lymph node metastases (black arrow) on CT (a). Lymph node metastases are indistinguishable from the adjacent primary tumor on PET images (black arrow, b and c).**

with tumors showing high SUV generally have metastatic disease, and therefore the tumors are not resected. On the other hand, tumors with low SUV tend to be localized and do undergo resection; increased survival in this group may be due to surgery, rather than related to the low metabolic rate of the primary neoplasm. In the study of Hong *et al.*[11], baseline SUVs (before treatment) did not correlate with overall survival or disease free survival in 47 patients, all of whom underwent neoadjuvant chemoradiotherapy followed by surgery.

Radiation therapy planning

One recent study evaluated the impact of PET findings on radiation therapy treatment planning[12]. These authors found that PET information, co-registered with treatment planning computed tomography (CT), led to substantial increase or decrease in the estimated gross tumor volume (GTV) in 6 of 34 patients. Overall, modifications of the GTV changed the treatment plan in 18 of 34 patients, and affected the percentage of total lung volume receiving >20 Gy in 25 of 34 patients.

Evaluating response to therapy

Small published studies have indicated that resolution of PET abnormalities or decrease in SUV following neoadjuvant chemotherapy, with or without concurrent radiation therapy, correlates well with pathological response and with disease free survival and overall survival[13–15]. Furthermore, PET scanning during administration of therapy has the potential to differentiate non-responders from responders, thereby minimizing the toxicity of therapy and directing non-responders towards alternative therapies[14]. However, Song and colleagues[16] reported that metabolic response after neoadjuvant chemoradiotherapy correlated with pathologic response only in tumors with an initially high SUV (≥ 4); this relationship was not observed in tumors with an initially low SUV (<4).

Comparison between PET and other modalities

A cost effectiveness study comparing CT, endoscopic ultrasound with fine needle aspiration biopsy (EUS-FNA), PET and thoracoscopy/laparoscopy in patients with esophageal cancer found that the combination of CT and EUS-FNA was the most inexpensive strategy and offered more quality adjusted life-years, on average, than all other strategies except for PET and EUS-FNA. The latter strategy, although slightly more effective, was also more expensive. The authors recommended use of PET and EUS-FNA unless resources are scarce or PET is unavailable[17].

Recurrent esophageal cancer

There is some evidence suggesting that PET is helpful in evaluating for recurrent esophageal cancer, after

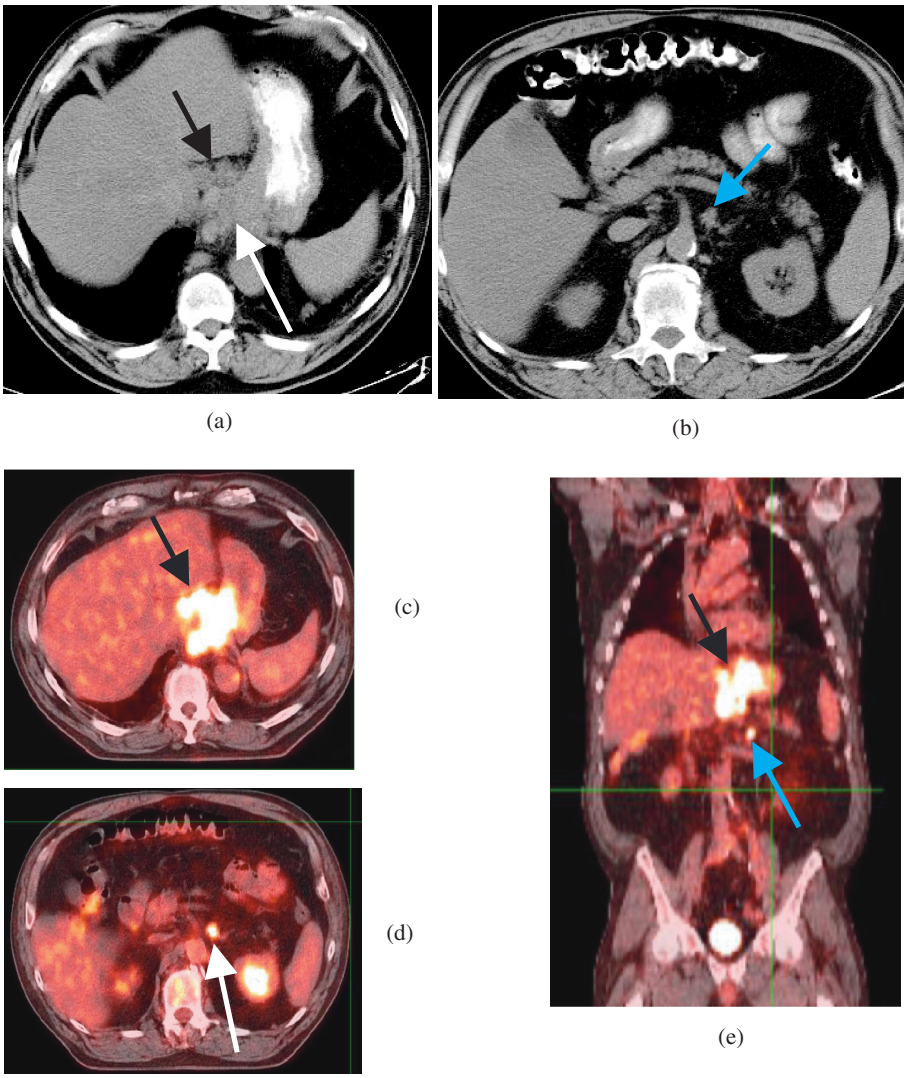


Figure 2 **Primary distal esophageal adenocarcinoma with regional and distant lymph node metastases. CT shows thickening of the distal esophagus (white arrow) with adjacent enlarged, regional lymph nodes (black arrow) (a) and a small lymph node adjacent to the superior mesenteric artery (distant lymph node) (blue arrow, b). FDG uptake is seen not only within the primary tumor and adjacent lymph nodes (black arrow, c and e), but also within the small distant lymph node (blue arrow, d) on the fused PET-CT images; distant lymph node disease contraindicated surgical resection.**

treatment[1,18]. PET may help to support or negate the suspicion for malignancy in areas of CT abnormality (Fig. 5), may detect additional, previously unsuspected sites of disease, and may assist in locating the easiest site to biopsy, in order to prove recurrence of cancer. False positive scans sometimes occur in tissue with an active inflammatory component, for example related to post-operative healing or benign anastomotic strictures.

Thymic lesions

Thymic lesions, including hyperplasia, thymoma, carcinoid, thymic carcinoma, lymphoma, and germ cell tumors, are frequently FDG avid, and therefore PET may be useful in differentiating between the normal and the abnormal thymus[19–21]. However, increased thymic uptake may occur in children and young adults without thymic disease, and this is particularly problematic in assessing for lymphomatous involvement of the thymus in patients with a history of lymphoma[20]. Other FDG avid benign entities, such as thymic sarcoidosis, may also be seen occasionally[22]. Although it has been suggested that thymic carcinomas (Fig. 6) tend to show higher SUVs compared to thymomas (Fig. 7) and thymic hyperplasia, the latter two entities occasionally also show intense uptake[23]; therefore, PET is generally unhelpful in distinguishing among these entities. However, if distant

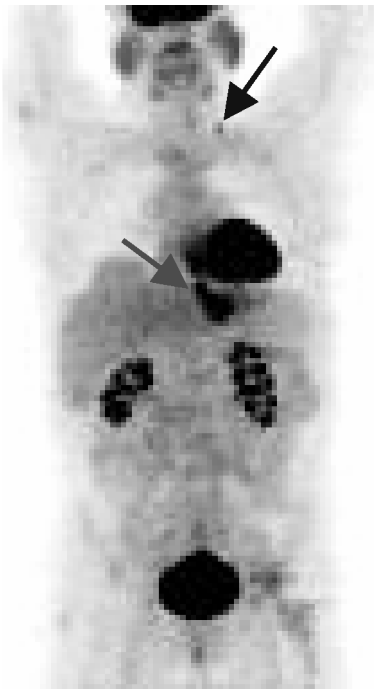


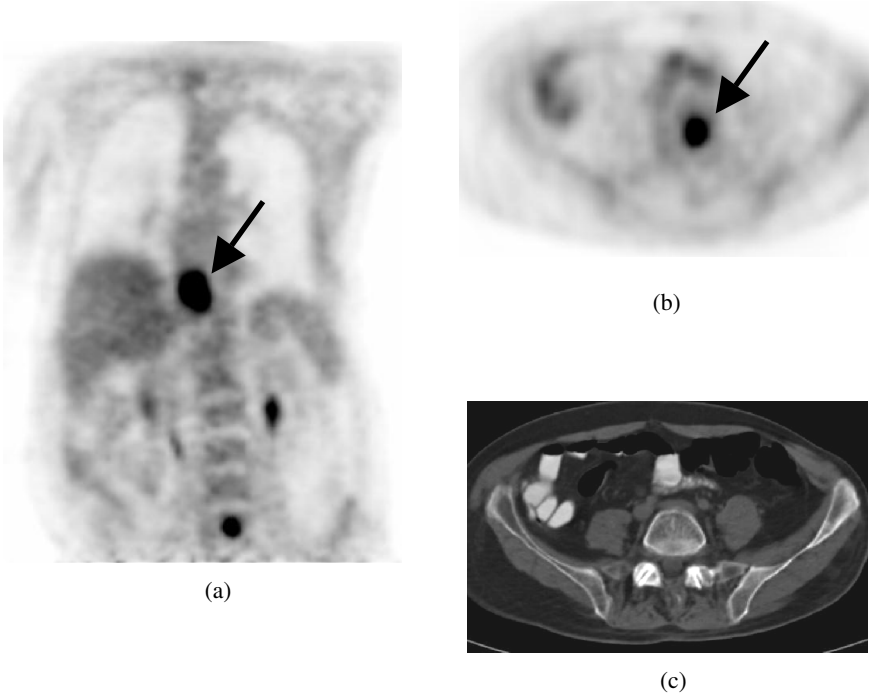
Figure 3 **PET scan shows FDG avid primary distal esophageal adenocarcinoma (red arrow). Uptake within a left supraclavicular lymph node (black arrow) represents a distant lymph node metastasis, indicating unresectable disease.**

foci are identified at PET, then invasive thymoma or carcinoma is suspected. PET has also occasionally been used to evaluate for recurrent thymic neoplasm after resection or chemotherapy[22,24].

Malignant pleural mesothelioma

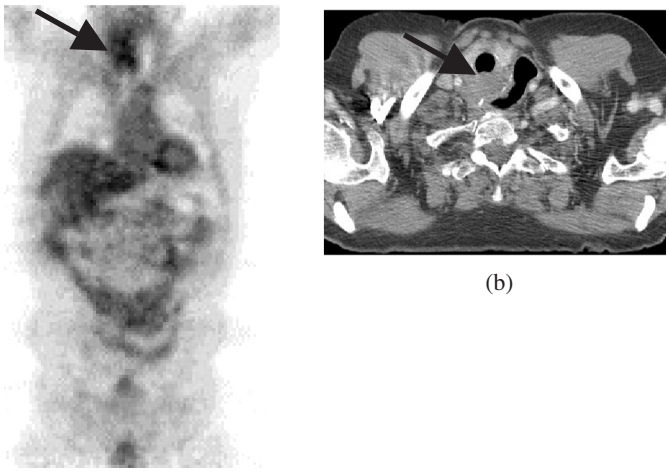
FDG PET is helpful in distinguishing benign from malignant pleural diseases, although not infallible. Empyemas and inflammatory processes (including pleural reaction after talc pleurodesis) may be extremely FDG avid, and falsely positive at PET scanning[25]. False negative cases may occur with small and/or low grade pleural malignancies; a case of an FDG negative, slowly growing malignant fibrous tumor of the pleura is reported in the imaging literature[26]. In a patient with suspected malignant pleural mesothelioma (MPM), PET may be used to select the location with the highest metabolic activity for tissue sampling.

MPM may be treated with extrapleural pneumonectomy, chemotherapy and/or radiation therapy. The tumor is generally considered unresectable if there is evidence of tumor spread to mediastinal lymph nodes or direct spread to the upper abdomen; extensive/diffuse chest wall involvement and distant metastases would also preclude resection. Approximately one-quarter of patients with MPM have unresectable disease at exploratory thoracotomy, after preoperative imaging with conventional modalities such as CT or magnetic resonance (MR)[27]. Preliminary reports suggest that preoperative FDG PET is superior to CT and MR in staging the tumor, and



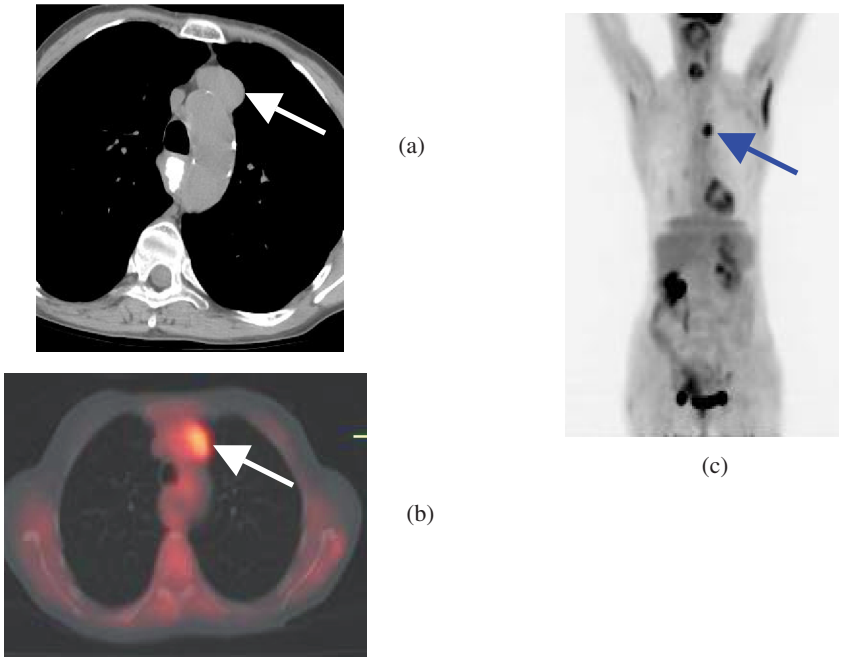
(a) (b) (c)

Figure 4 **PET scan shows FDG avid distal esophageal adenocarcinoma (arrow, a) with previously occult distant metastasis to vertebral body (arrow, b), not visible at CT (c).**



(a) (b)

Figure 5 **FDG avid, peri-anastomotic recurrent esophageal carcinoma (arrow) at PET (a) and CT (b), 4 years following esophagectomy and gastric pull through.**



(a) (b) (c)

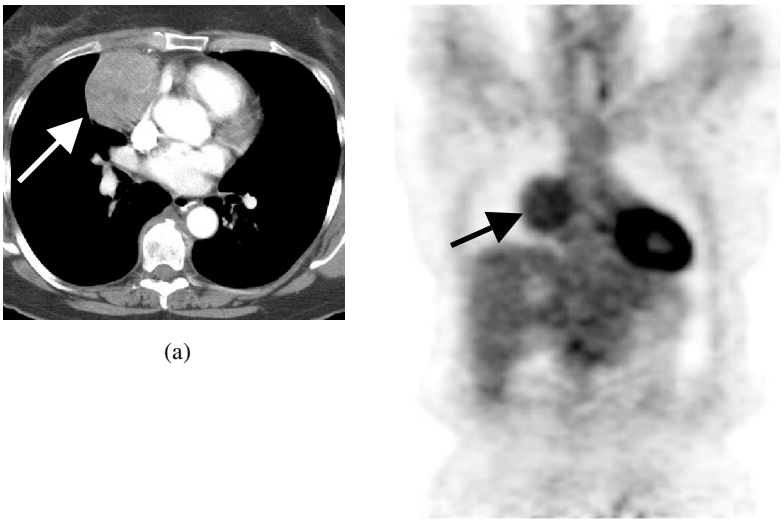
Figure 6 **Small cell carcinoma of the thymus (arrow) shown on CT (a), fused PET-CT image (b) and frontal PET image (c). The cancer is extremely FDG avid.**

may show additional sites of disease that are not evident on conventional imaging, thus precluding unnecessary surgery[28–30]. The limited spatial resolution of PET, however, leads to difficulty in distinguishing pleural disease from possible adjacent disease in or below the diaphragm or in the mediastinum or chest wall (Fig. 8).

Preliminary studies suggest that high SUV in primary MPMs is associated with poor survival[27]. Other uses for PET scanning in MPM include evaluating for therapy response and for recurrence after treatment[31].

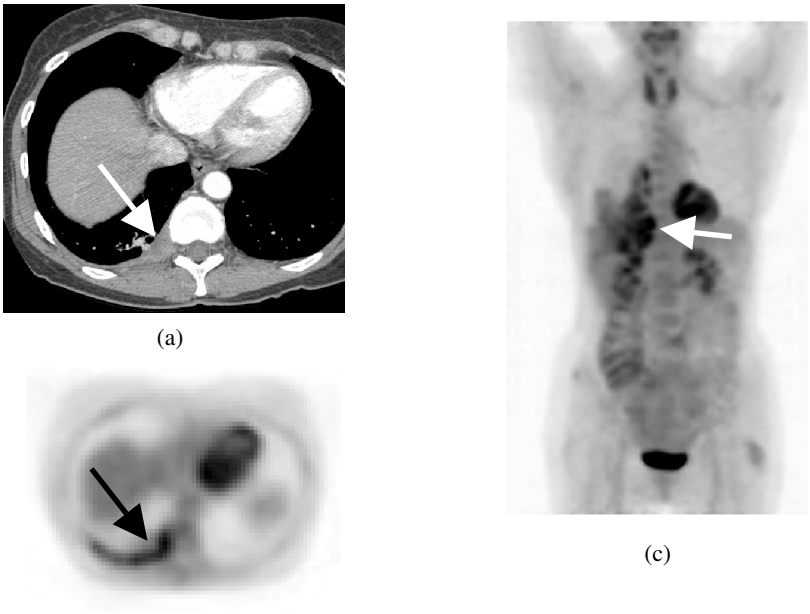
Conclusions

The use of FDG PET scanning in the evaluation of patients with non-lung primary thoracic neoplasms is becoming increasingly common. There is a growing body of data suggesting that PET is helpful in patients with new, treated or recurrent esophageal cancer. In addition, preliminary reports suggest that PET may also add useful information in patients with thymic lesions and known or suspected MPM.



(a) (b)

Figure 7 **Minimally invasive thymoma (arrow) on CT (a) and PET (b). The tumor is moderately FDG avid (first published as Fig. 12 in Cancer Imaging 2005; 5: 139–149).**



(a) (c)

(b)

Figure 8 **Malignant pleural mesothelioma. Right pleural thickening on CT (white arrow, a) that shows FDG avidity on the corresponding axial PET image (black arrow, b). The frontal, projection PET image shows ill defined, poorly localized activity in the region of the diaphragm (white arrow, c). Exploratory laparatomy revealed a small tumor implant on the peritoneal surface of the diaphragm, contraindicating full surgical resection.**

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