C. Role of PET/CT

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Learning objectives

To illustrate the role of FDG PET/CT imaging assessment of patients with thoracic oesophageal, gastro-oesophageal junction and stomach cancer. In this poster we will review the contribution of FDG PET/CT in the pre-treatment staging of this group of cancers. We will also consider the potential role of FDG PET/CT in the assessment of patients who undergo neoadjuvant chemotherapy. The aim is to provide a concise overview of the current role of FDG PET/CT in the evaluation of patients with thoracic oesophageal, gastro-oesophageal junction cancer and stomach cancer.
Is FDG PET/CT good enough for the TNM staging of thoracic oesophageal and gastro-oesophageal junction cancer?

**T stage (primary Site)**

FDG PET/CT is of limited value for T staging.

FDG PET will demonstrate the primary site in the majority of cases. It is only occasionally that the primary site is not visible on FDG PET/CT. From time to time, mucinous adenocarcinomas, especially those near or at the gastro-oesophageal junction are not visualised and high grade dysplasias which include all noninvasive neoplastic epithelia that was formerly called carcinoma in situ is beyond the resolution of FDG PET/CT.

However, FDG PET/CT cannot reliably and consistently delineate the depth of tumour extension through the oesophageal wall.

So, FDG PET/CT is not good enough for T staging and endoscopic ultrasound (EUS) remains the mainstay for imaging the primary site. FDG PET /CT is of value in the extremely unusual occasion where assessment of the primary site is considered to be inadequate following EUS and CT.

**N stage (regional lymph nodes)**

The value of FDG PET /CT is based on FDG PET studies as there are no FDG PET/CT studies.

There is considerable variation with regards to the accuracy of FDG PET for detecting regional nodal disease, from 46% to 84% (Flanagan et al. 1997, Herren 2004, Lerut et al., 2000, Meltzer et al., 2000).

The different patient cohorts studied, the different methodologies including different PET scanners and PET techniques used, and also the varying ways in which the FDG PET findings were confirmed all contribute to the conflicting FDG PET results.

The specificity of FDG PET for detecting regional nodal disease is generally high with false positive results being unusual. The low accuracy for FDG PET is due to low
sensitivity: 55% sensitivity in the study where FDG PET had an accuracy of 61%, 22% where it had an accuracy of 48% and in the study where FDG PET had an accuracy of 46%, its sensitivity was 35%. The inability of FDG PET to separately detect nodes containing tumour adjacent to the primary site contributes significantly to the false negative results.

The capability of FDG PET to detect nodal disease compared with CT and EUS is unclear. In two studies, FDG PET was found to be more accurate than CT, in one study both techniques were of similar accuracy and in yet another two studies FDG PET was less accurate. In two studies that compared FDG PET to CT and EUS, EUS was superior to FDG PET and CT although the difference did not reach statistical significance (Herren et al., 2004, Lerut et al., 2000). In the one study comparing FDG PET to CT and the combination of EUS and fine needle aspiration cytology (FNAC), there was no clear advantage of EUS over FDG or CT (Lowe et al., 2006).

It is reasonable to conclude from the literature that a positive node on FDG PET is highly likely to contain active disease, especially if it lies in the usual drainage area.

FDG PET/CT cannot, however, reliably and consistently separate the primary site from closely adjacent nodal disease and therefore distinguish between T3/4N0 and T3/4NI disease.

The available data, albeit small, indicates that the main contribution of EUS over FDG PET lies in its superior ability to discriminate between the primary tumour and peritumoural nodes (Katsoulis et al., 2007)

The assessment of prognosis is dependent on the number of lymph nodes involved (Twine et al 2009). In the revised AJCC staging, the number of regional nodes containing disease influences N stage; N1 metastasis in 1-2 regional nodes, N2 metastasis in 3-6 regional nodes, N3 metastasis in 7 or more regional nodes. This can potentially increase the contribution of FDG PET/CT as FDG PET/CT detects disease in nodes defined as normal on CT. Figure 1.

**M. stage (distant metastases)**

FDG PET/CT is accurate for detecting distant metastases. Systematic literature review showed FDG PET had a sensitivity of 67% and specificity of 91% for detecting distant metastases (van Westteenen et al., 2004).
It is more accurate than usual assessment for the detection of distant metastases. In a recent prospective study, FDG PET diagnosed additional sites of metastatic disease in 4-8% of patients when compared with standard staging techniques (Myers et. al., 2007). 

Figure 2,3.

Is FDG PET/CT good enough as the initial imaging for the pre-treatment assessment of patients with thoracic oesophageal and gastro-oesophageal junction cancer?

Or

Can FDG PET/CT substitute other imaging as initial imaging?

No studies have been directly directed at this question. But the evidence as already presented suggests that it is an attractive proposition and it is a question worth considering (Chatterton 2009). Patients (1) with definite distant metastases on FDG PET/CT may not require further imaging for planning treatment- palliative treatment (2) with bulky disease at the primary site and regional nodal disease on FDG PET/CT may also require no further imaging- neoadjuvant chemo-radiotherapy followed by surgery (3) with disease localised to the primary site and no spread on FDG PET/CT may be referred for EUS and (4) patients with equivocal results on FDG PET/CT may require other imaging which may include CT with IV contrast, MR or ultrasound (van Vliet EP et al ., 2008).

Such an imaging pathway will mean that some patients will require fewer investigations before starting treatment, and improve the patient experience. It can also translate into some financial saving for the health provider.

Synchronous Cancer

When FDG PET CT is used for the staging and restaging of oesophageal cancer other primary cancers are detected (van Westreenen et al., 2005). The incidence of synchronous head and neck and lung tumours in patients with oesophageal cancer is 2-3% (Wong, Chambers, 2008); tobacco and alcohol consumption link these tumours. Unexpected lung cancers are revealed more often than head and neck cancers, since the latter are usually apparent clinically. FDG PET CT also detects other asymptomatic synchronous tumours, the most common being colo-rectal cancer. It is perhaps important to remember that benign polyps and diverticular disease also cause focal areas of increased FDG uptake and mimic malignant lesions (van Westreenen HL et al. 2007) Figure 4.
Is FDG PET/CT good enough for detecting residual disease following neo-adjuvant chemotherapy in patients with thoracic oesophageal and gastro-oesophageal cancer?

OR

Is FDG PET/CT good enough to identify complete histological responders and hence obviate the need for surgery?

FDG PET/CT cannot reliably detect residual disease. In a recent study of 50 patients FDG PET failed to detect residual disease in 13 of 20 patients (Mc Loughlin et.al., 2008).

No residual disease on FDG PET/CT cannot obviate the need for definitive surgery (Klaeser B et al., 2009)

Is FDG PET/CT response good enough to help tailor treatment in patients with thoracic oesophageal and gastro-oesophageal cancer?

Yes, potentially. Several well designed studies have shown that decrease of 35% or more in SUV (maximum) between the FDG PET CT pre-treatment and 14 days after start of cisplantium based chemotherapy is an accurate predictor of final outcome (>90% sensitivity) (Weber etal., 2001, Ott et al., 2006, Lordick et al., 2007). Figures 5, 6, 7.

A recent study demonstrated that treatment pathways which include using FDG to assess early response are feasible and that it may contribute to overall improved outcome (Lordick., 2007). Figure 7.

 Awaited are multi-centre prospective validation and randomised studies using FDG PET/CT as suggested by Weber and his colleagues recently. Figure 8.

FDG PET/CT can potentially avoid costly and ineffective treatments, affording benefits to health providers and patients alike.

Is FDG PET/CT good enough for the assessment of gastric cancers?

The role of FDG PET/CT in this cancer is evolving. What is clear is that signet ring and mucinous carcinomas show low FDG uptake. Also, diffuse FDG uptake is a feature of gastritis including Helicobacter pylori gastritis and lymphoma.
When should FDG PET/CT currently be considered in our patients with thoracic oesophageal and gastroesophageal junction cancer?

In all patients prior to embarking on treatment with curative intent and especially if they are at high risk of disseminated disease.
Fig. 0: FDG PET/CT shows the primary upper thoracic oesophageal cancer and a right supraclavicular nodal mass. In addition, FDG PET/CT demonstrates the para-oesophageal node which is normal by CT criterion

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Fig. 0: FDG PET/CT shows the primary distal thoracic oesophageal cancer. It also shows disease within a lymph node in the inter aorto-caval region and adjacent to the coeliac axis. FDG PET/CT detection of unexpected lymph nodal disease in the retroperitoneum changed stage of disease from T3N0M0 to T3N0M1 and altered management plan from treatment with curative intent to palliative treatment.

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**Fig. 0:** FDG PET/CT shows the thoracic oesophageal primary site and left supraclavicular nodal disease. It also shows the small unsuspected left adrenal deposit. FDG PET/CT findings changed stage of disease from M0 to M1 and management from treatment with curative intent to palliative treatment

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Fig. 0: FDG PET/CT shows the primary gastro-oesophageal junction cancer and the unexpected caecal cancer (within cross hairs).

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**Fig. 0:** A decrease of 35% or more in SUV (maximum) between the FDG PET CT pre-treatment and 14 days after start of cisplantium based chemotherapy is an accurate predictor of final outcome

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**Fig. 0:** A recent study which demonstrated that treatment pathways which include using FDG to assess early response is feasible and that it may contribute to overall improved outcome

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Fig. 0: Suggested algorithm for incorporating FDG PET/CT into "early therapeutic response to treatment" studies.

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**Fig. 0:** FDG PET/CT shows FDG uptake in the stomach due to *Helicobacter pylori*.

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**Fig. 0:** FDG PET/CT shows diffuse FDG uptake in the stomach and in upper abdominal lymph nodes due to diffuse large B cell lymphoma.

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28. The assessment of prognosis of surgically resected oesophageal cancer is dependent on the number of lymph nodes examined pathologically. Histopathology. 55(1):46-52


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