Tips and tricks for multi-modality staging of oesophageal cancer - what you really need to know.

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Learning objectives

This is a quick guide to modern multi-modality imaging techniques for oesophageal cancer.

Main objectives:
- To understand the principles of multi-modality staging with MDCT, barium studies, endoscopic ultrasonography (EUS), and PET/CT
- To review the 7th edition American Joint Cancer Committee guidelines for esophageal staging and introduce the updated TNM staging criteria.
Background

Oesophageal cancer is the seventh leading cause of death due to malignancy worldwide. The majority of cases (80-85%) are diagnosed in developing countries where it is the fourth most common cancer in men and most cases are squamous cell carcinoma (SCC), although in the UK more cases are now due to adenocarcinoma. Traditionally the disease presents at a relatively advanced stage due to the late presentation of symptoms.

Endoscopy, EUS, contrast imaging, MDCT, and Positron emission tomography (PET) with 2-[fluorine-18] fluoro-2-deoxy-d-glucose (FDG) all play an important role in disease investigation. This poster gives an evidence-based, practical guide to getting the best from imaging.
Role of modern multi-modality imaging techniques

Multi-detector CT

Because of its ease of access and wide availability multi-detector CT tomography (CT) of the chest and abdomen is usually the initial test of choice for staging oesophageal carcinoma.

Multi-detector CT Tips

- Before PET it was considered the best modality to evaluate for distant metastases. CT alone has an accuracy of 50-60% for staging oesophageal cancer. It is best for hepatic and adrenal metastases but less sensitive for locoregional lymph nodes.[1] on page

- A notable limitation of CT in diagnosis involves the characterization of lymph nodes. With CT scans, size criteria are used to determine possible metastatic involvement; however, lymph nodes may be enlarged because of infectious or inflammatory etiologies. Conversely, subcentimeter lymph nodes may harbor metastatic tumor.[2] on page

- However a careful search for lymph nodes is an essential component of the interpretation. Generally a short-axis diameter exceeding 1 cm is considered abnormal for lymph nodes in all mediastinal locations except those in the subcarinal region, in which 1.4 cm is the upper limit of normal. Because lymph nodes may harbor metastases without being enlarged, noting the location of any identified lymph nodes can be important.[3] on page

- Some studies suggest that multi detector CT with 3D virtual gastroscopic imaging can yield comprehensive information about gastric ulcers, and may well be used in certain circumstances in the future.[4] on page

- CT has poor accuracy for assessment of response to neoadjuvant therapy in patients with oesophageal cancer.

Fluroscopy
Whilst the role of fluoroscopy is diminishing it is still used by radiology departments and continues to diagnose oesophageal cancer with a variety of appearances that have been well documented. Indeed, in most studies the detection of oesophageal cancer has been very high, with a sensitivity noted of 98% and a positive predictive value of 42% [5] on page , and another study showing a sensitivity of 98% [6] on page . Critically good technique is paramount. It is also good at discriminating between malignant and benign strictures [7] on page . Barium studies are most effective at looking at the contractility and functionality of the oesophagus. This is important in two respects. Firstly it often highlights cancer in patients who presented with atypical features. Secondly it is very useful for post-surgical assessment, stent placement [8] on page , and assessment of strictures.

**Fluroscopy Tips**

- A double contrast technique should be used
- It is poor at looking and lymphatic/metastatic staging, and is predominantly used to detect mucosal lesions: intraluminal, polypoid, or masslike; infiltrative; ulcerating; or varicoid.

**Case: Fluroscopy**

Figures 1 on page 12, 2 on page 12, 3 on page 13, 4 on page 14.

This patient presented to the fluoroscopy department with dysphagia and hoarseness.

**Endoscopic ultrasonography**

Endoscopic ultrasonography (EUS) provides detailed images of the oesophagus and surrounding structures, and has been used to define the layers of the oesophageal wall and thereby distinguish the depth of tumour penetration. The frequency of most endoscopic ultrasound transducers is 7.5 or 12 MHz [9] on page . It is considered the best technique for detecting loco-regional disease, and is considered better than CT in this regard.

**Endoscopic ultrasonography tips**

- Eosophageal cancers can appear as hypoechoic masses that disrupt the layered ultrasonographic appearances of the oesophageal soft tissue layers.
- EUS can over and under-stage due to the limitation of ultrasonic appearances, especially in the distal oesophagus, and gastro-oesophageal junction.
- It may be difficult to perform in patients with stenotic lesions.

- EUS is crucial for the identification of celiac lymph node disease, which was considered a metastasis for proximal and mid-oesophageal tumours (AJCC 6\textsuperscript{th} edition), as it was associated with such a poor prognosis\cite{10} on page \ldots Under the latest American joint committee for cancer criteria, the 7\textsuperscript{th} edition, it is no longer considered a metastasis, but still carries a very poor prognosis. The sensitivity of detecting celiac lymph involvement, when compared to surgical findings is quite low at 66.6\%\cite{11} on page \ldots, although it is still superior to CT at 53\%\cite{12} on page \ldots

- Celiac nodes in certain cases were considered as M1A disease (metastasis) in the 6\textsuperscript{th} edition of the American Joint Cancer Committee TMN staging, however some highly selective patients can be treated and cured, and now there is a change in staging in the 7\textsuperscript{th} edition to reflect this, as described below.\cite{13} on page \ldots

-When tumours are confined to the mucosa, nodal spread is seen is less than 1\%.\cite{14} on page

**Case: Endoscopic ultrasonography**

Figures 5 on page 15, 6 on page 16, 7 on page 17, 8 on page 18

**PET-CT**

PET-CT has been shown by a recent high quality HTA (Health Technology Assessment) review\cite{15} on page \ldots to be of higher quality than CT or ultrasound in detecting distant metastases. It also showed that it was superior to CT and comparable to EUS (Endoscopic ultrasound) in the assessment or response and prognosis after neoadjuvant treatment.

A recent review has agreed that FDG-PET appears to be the best available imaging modality for assessment of neoadjuvant therapy response in oesophageal cancer\cite{16} on page \ldots. There is also some evidence that PET response is related to longer-term clinical outcomes, including disease-free survival and overall survival \cite{17} on page \ldots,\cite{18} on page \ldots,\cite{19} on page \ldots

**PET-CT Tips**
PET-CT sensitivity for early disease is limited, primarily due to its poor resolution, with sensitivity for nodal disease lying somewhere between 48-90% \[20\] on page . PET-CT is the best for detecting distant metastases (M stage) or lymph nodes (T stage), but it is less good at detecting loco-regional lymph nodes.

- It is used to determine its disease extent

- PET-CT is useful in determining recurrent disease from scar tissue.

- In addition PET-CT can play a useful role in the follow-up of patients undergoing chemotherapy and radiation therapy, allowing early treatment changes for unresponsive tumours\[21\] on page .

**Case: PET-CT**

Figures 8 on page 19, 9 on page 20, 10 on page 21

**Tumour staging**

**Comparison of the 6\textsuperscript{th} edition and the latest 7\textsuperscript{th} edition of the American joint committee on the TNM staging of oesophageal cancer.**

The latest staging criteria can be found in the AJCC (American Joint Committee on Cancer) Cancer Staging Manual (7\textsuperscript{th} edition).

Summary of changes\[22\] on page

- Tumor location is simplified, and the oesophagogastric junction and proximal five centimeters of stomach are included.

- Tis is redefined and T4 is subclassified.

- Regional lymph nodes are redefined. N is subclassified according to the number of regional lymph nodes containing metastasis.

- M is redefined.

- Separate stage groupings for squamous cell carcinoma and adenocarcinoma.

- Stage groupings are reassigned using T, N, M, and G classifications.
*(Nonmucosal cancers are not included.)*

Comparison on T stage definitions between the 6th and 7th AJCC cancer staging for oesophageal cancer[23] on page

<table>
<thead>
<tr>
<th>T stage Primary tumour</th>
<th>6th AJCC Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour invades lamina propia or submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour invades muscularis propia</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour invades adventitia</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour invades adjacent structures</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T stage Primary tumour</th>
<th>7th AJCC Guidelines 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>Tis</td>
<td>High grade dysplasia</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour invades lamina propia, muscularis mucosae or submucosa</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumour invades lamina propia, muscularis mucosae</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumour invades submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour invades muscularis propia</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour invades adventitia</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour invades adjacent structures</td>
</tr>
<tr>
<td>T4a</td>
<td>Resectable tumour invades pleura, pericardium or diaphragm</td>
</tr>
</tbody>
</table>
T4b  Unresectable tumour invading other adjacent structures such as aorta, vertebrae, body, trachea etc.  

Illustration shows T stages of oesophageal malignancy on page 22 (Figure 12)

Comparison on N stage definitions between the 6th and 7th AJCC cancer staging for oesophageal cancer[24] on page

<table>
<thead>
<tr>
<th>N stage</th>
<th>Regional lymph nodes 6th AJCC Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastasis</td>
</tr>
</tbody>
</table>

N stage Regional lymph nodes 7th AJCC Guidelines

<table>
<thead>
<tr>
<th>N stage</th>
<th>Regional lymph nodes cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastases involving 1-2 nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Regional lymph node metastases involving 3-6 nodes</td>
</tr>
<tr>
<td>N3</td>
<td>Regional lymph node metastases involving 7 or more nodes</td>
</tr>
</tbody>
</table>

Comparison on M stage definitions between the 6th and 7th AJCC cancer staging for oesophageal cancer[25 on page]

<table>
<thead>
<tr>
<th>M stage</th>
<th>Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>MX</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
</tbody>
</table>

6th and 7th AJCC Guidelines
For the 7th AJCC TNM staging guidelines there is no longer categorisation of M1a and M1b tumours. For example cervical lymphadenopathy for upper thoracic tumours and celiac lymphadenopathy for lower oesophageal tumours used to be considered as M1a disease according to the 6th AJCC guidelines. Now, in these circumstances, they are considered regional lymph nodes.

**Explanation of changes in the 7th American joint cancer committee.**

- The 7th edition of the American joint committee [26] on cancer includes non-anatomic cancer characteristics: histologic cell type (either adenocarcinoma or squamous cell carcinoma); histologic grade - from G1 (well differentiated) to G4 (undifferentiated); and cancer location - upper, middle, or lower thoracic or oesophagogastric junction. This has been shown to improve correlation of staging with prognosis.[27] on page

- In the future PET results pre-and post imaging will likely have an increasingly important part of predicting prognosis and staging will involve a metabolic component as well as an anatomical component.

- Crucially celiac nodes for mid and upper squamous cell cancers used to be considered metastases (M1a). Although they are still considered to be associated with very poor prognosis they are now treated as if they are just regional lymph nodes regardless of the primary tumour location or histology.[28] on page

- A simplification of tumor location and inclusion of tumors at the oesophagogastric junction and proximal 5cm of the stomach that extend into the EGJ or oesophagus (the so-called Siewert III EGJ tumors). Tumors arising in the cervical, thoracic oesophagus, or abdominal oesophagus, including those that arise within the cardia of the stomach within 5 cm of the oesophago-gastric junction now share the same criteria for T stage designation. [29] on page

- Redefinition of Tis as high-grade dysplasia, which includes all noninvasive neoplastic epithelia that was formerly called "carcinoma in situ", a diagnosis that is no longer used for columnar mucosa anywhere in the GI tract.[30] on page

- Subclassification of T4 disease based upon potential resectability of adjacent involved organs/structures.[31] on page T4a means that the cancer has grown into the pleura, the pericardium, or the diaphragm. T4b means that the cancer has spread into other nearby structures such as the trachea, vertebra or a major blood vessel (the aorta).[32] on page
- There is now subclassification of nodal (N) status according to the number of regional nodes containing metastases, which correlates to survival.[33] on page

**Practice Case**

Figures 13 on page 23, 14 on page 24, 15 on page 25

**Practice Case**

Figures 16 on page 26, 17 on page 27

**Final case**

All imaging modalities are used to assess a potential tumour.

Fig. 0: Barium swallow shows an abnormality (arrow) of the proximal oesophageal mucosa.

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**Fig. 0:** Closer examination allows a more detailed depiction of the lesion (arrow) which shows a large constricting lesion with extravasation of contrast into an ulcerated mass.

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Fig. 0: The upper oesophageal tumour (arrow) is further visualised on this sagittal CT.

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**Fig. 0:** PET-CT demonstrates raised standard uptake value within the primary tumour (crosslines) indicating oesophageal cancer

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**Fig. 0:** Barium swallow showing an annular cavitating stricture of the mid oesophagus, consistent with a malignancy (arrow).

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Fig. 0: A contrast enhanced CT showing an annular soft tissue mass of the mid oesophagus effacing the soft tissue plains of the aorta (*) and the pleura (arrow)

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Fig. 0: An endoscopic ultrasound image showing the full thickness tumour of the oesophagus with tumour growth out to the left pleura (arrow) and abutting the anterior aspect of the aorta (arrowhead)

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Fig. 0: A PET CT fusion image of the mid oesophagus, showing added activity relating to the oesophageal primary and tumour growth to the left pleura and aorta

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Fig. 0: CT image demonstrating the ill-defined tumour of the gastro-oesophageal junction, infiltrating the cardia (Siewert 2 tumour)

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**Fig. 0:** PET CT image shows a primary with infiltration into the stomach consistent with a Siewert 2 tumour (arrows).

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Fig. 0: PET CT image showing incidental right subscapularis metastasis and primary tumour with gastric infiltration (arrows)

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**Fig. 0:** Stages of esophageal malignancy. T1 lesion involves mucosa (m) or submucosa (s), T2 lesion invades muscularis propria (mp), T3 lesion invades adventitia (a), and T4 lesion involves adjacent organ (A). N indicates metastatic lymph node.

**Fig. 0:** CT shows a thickening of the gastro-oesophageal junction (arrow), which would now use the normal tumour (T) stage classification according to the new 2010 American Joint Cancer Committee.

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**Fig. 0:** Endoscopic ultrasound. The lesion (arrow) can be seen at 40cm from the incisors.

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**Fig. 0:** There is moderate linear increased uptake of activity in a section of the distal oesophagus just proximal to the gastro-oesophageal junction (cross-lines). This extends over a sagittal length of approximately 4 cm. There were no FDG avid local nodes.

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**Fig. 0:** CT shows a large tumour (arrow) at the Oesophago-gastric junction.

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Fig. 0: PET-CT shows a large mass (arrow and cross-lines) expanding the lower oesophagus and extending into the stomach, with axial diameter of 4.9 cm and supero-inferior dimension of 7.5 cm. It is active with an standard uptake value of 16.4. Below the diaphragm there are several lymph nodes around the coeliac axis the largest 2 cm in diameter with an SUV of 12.1. Prior to the 2010 American joint committee on cancer's reappraisal of oesophageal cancer this would have been a M1a lesion, however it is now an MO lesion (in the absence of any other metastasis).

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**Fig. 0:** Oblique fluoroscopic images of a barium swallow series demonstrate a well defined filling defect in the lateral wall of the oesophagus (arrow) which has a smooth contour forming an oblique angle with the oesophageal wall. Despite the apparently benign features there is subtle mucosal ulceration that is unusual for benign pathologies.

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Fig. 0: Contrast enhanced CT thorax reveals focal wall thickening (arrow) of the upper oesophagus correlating with the barium swallow appearances.

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**Fig. 0:** The EUS image demonstrates a hypoechoic mass (arrow) indistinguishable from muscularis propria. The mass is therefore intrinsic to the oesophageal wall.

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Fig. 0: Axial and sagittal PET CT images demonstrating an area of high FDG uptake involving the upper oesophagus corresponding to the previously described abnormality. Appearances confirm an upper oesophageal malignancy. PET-CT did not reveal any metastasis.

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Conclusion

The education has offered practical guidance on the multi-modality staging of oesophageal cancer to illustrate how to avoid potential pitfalls. It has demonstrated the important uses for all the modern imaging modalities, and has given an updated account of the modern TNM staging classification according to the 7th American Joint Commission of Cancer.
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Medscape hybrid imaging


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Medscape hybrid imaging


[23] Tables adapted from:


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[25] Ibid.


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[30] Ibid.

[31] Ibid.

[33] Salzman, J; Gibson, M. Diagnosis and staging in oesophageal cancer. In: UpToDate; Ed. Howell, Douglas, UpToDate, Waltham, MA, September 2010.