

## ARTICLE

# Endoscopic ultrasonography (EUS) in the staging of malignancy

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### Abstract

Since first introduced over 20 years ago, endoscopic ultrasonography (EUS) has become established as an important tool in the staging of gastrointestinal malignancies and potentially resectable non-small cell lung cancer. This review describes the current roles of EUS in staging these tumours, highlighting interventional roles, current problem areas and future developments.

**Keywords:** *Endoscopic ultrasonography; gastrointestinal malignancy; cancer; imaging.*

## Introduction

Endoscopic ultrasonography (EUS) has become established in the diagnosis, staging and, more recently, treatment of gastrointestinal and non-gastrointestinal malignancies. Like computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET), EUS technology has also progressed hugely in recent years making interpretation of older studies comparing, e.g. the accuracy of EUS with CT for tumour staging obsolete, as many of these are now of historical interest only. Many studies were also small, retrospective, poorly controlled and subject to numerous potential biases. There is also increasing recognition that studies comparing the performance of one technique against another are somewhat artificial as they are complementary in the staging algorithm of patients. Accepting these caveats, this brief review addresses the role of EUS in the staging of malignancies in 2004, highlighting recent developments and problem areas as well as potential future developments.

## Equipment and techniques

Mechanical or electronic radial instruments are most widely used and most provide a 360° image perpendicular to the long axis of the endoscope. Curved linear array echoendoscopes use an electronic transducer and provide 110–120° sector images in the same plane as the long axis of the instrument. While the learning curve for image interpretation (at least for non-radiologists) is steeper with these instruments, they offer the advantages of Doppler facilities and the ability to perform interventional procedures such as fine needle aspiration (FNA) biopsy under real-time visualisation. Echoendoscopes scan at frequency ranges of 5–12 MHz while high frequency catheter probes ('miniprobe'), which can be passed down the instrument channel of an endoscope, offer imaging frequencies of 12, 20 or 30 MHz. The latter has found increasing application in the detailed assessment of superficial mucosal lesions especially in Japan.

EUS (including FNA) is usually well tolerated under conscious sedation on an outpatient basis similar to other endoscopic procedures.

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## Oesophageal cancer

With increasing acceptance of the efficacy of neoadjuvant chemoradiotherapy<sup>[1]</sup>, albeit with increased morbidity, the concept of 'stage-directed therapy' has gained momentum. CT and/or PET continue to form the mainstay of detection of metastases but, in the absence of distant spread, the presence of T3 disease or locoregional nodal involvement (N1) is now an accepted indication for neoadjuvant therapy. Those with stage T2N0 or less generally undergo surgery alone while those with T4 disease (or bulky T3N1 disease in the presence of doubtful fitness) receive palliation. It is therefore imperative that patients are accurately staged to inform prognosis, determine therapy and to enrol patients into clinical trials.

The TNM staging system forms the basis of oesophageal cancer staging but is imperfect<sup>[2]</sup>. How best to classify true type 2 junctional tumours of the oesophagogastric junction remains unclear. Controversy also exists over how best to classify patients with involvement of distant lymph nodes. Involvement of cervical or coeliac axis nodes in patients with intra-thoracic tumours signifies a poor prognosis and unresectability and is therefore classified as M1a or M1b (Stage IV) disease depending on exact tumour location.

### Assessment of distant metastasis (M)

While limited data suggests that PET may be more accurate than combined CT and EUS-FNA for M staging<sup>[3,4]</sup>, further studies are needed and the lack of availability of PET means that CT and EUS-FNA are likely to remain the cornerstones of M staging in oesophageal cancer.

EUS can provide useful M stage information in some patients without evidence of distant metastasis on CT. Small metastasis in the left lobe of the liver can be detected and are often amenable to EUS-FNA<sup>[5]</sup>. EUS is also highly sensitive for assessing the coeliac axis for nodal involvement. The excellent sensitivity and near 100% specificity through EUS-FNA have also been demonstrated in several studies<sup>[6,7]</sup>. In one retrospective study, high quality thin slice helical CT only detected 53% of coeliac lymph nodes proven to be involved by EUS-FNA<sup>[8]</sup>. EUS can therefore play a complementary role to CT in improving the accuracy of M staging. The impact of multi-detector CT scanners on coeliac nodal staging remains to be seen but even with improved sensitivity CT relies solely on size criteria for determining the likelihood for malignant nodal involvement (short axis greater than 10 mm). EUS assesses morphological features in addition to size and offers the potential to obtain cytological proof of malignancy.

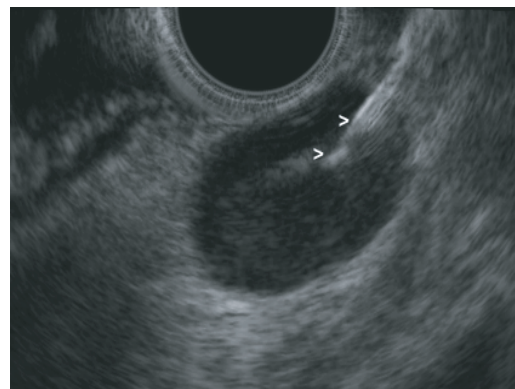
### Regional lymph node staging (N)

While less than 5% of patients with T1m tumours have nodal involvement, 60% of T2 and over 80% of

T3–T4 tumours are node-positive<sup>[9]</sup>. The presence of peritumoural nodes has a major negative impact on prognosis and cure rates with surgery alone are less than 10%. The number of nodes detected is also prognostically important and patients with more than 3 or 4 involved regional nodes fare particularly poorly<sup>[10]</sup>.

PET may be superior to CT for detection of distant lymph nodes but appears to lack accuracy for regional nodal staging. Limited spatial resolution impairs differentiation of nodal involvement from high signal in the adjacent primary tumours while reactive inflammatory nodes can lead to false positive results. Flamen *et al.*<sup>[4]</sup> reported sensitivity for detection of regional nodes (N1) of only 33% compared to 81% for EUS.

Reactive or inflammatory nodes in the mediastinum are usually flat or triangular in shape at EUS, with rather indistinct borders and an echogenic centre while malignant involvement is suggested by a size of greater than 10 mm, round shape, distinct outer border and hypoechoic echo features (Fig. 1)<sup>[11,12]</sup>. While the presence of all of these features is 80% accurate for malignant involvement, this occurs in only 25–40% of malignant nodes. Overall the sensitivity of EUS for detecting nodal involvement ranges from 50 to 75% and the accuracy is approximately 65–70%<sup>[9,13]</sup>, the latter declining with increasing distance from the primary tumour site.



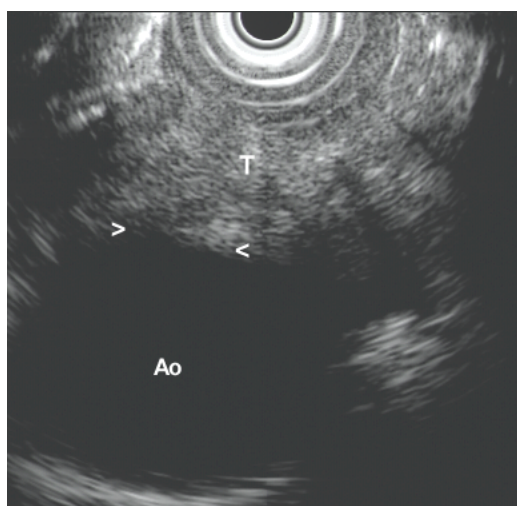
**Figure 1** EUS-guided FNA. Although this lymph node has EUS morphological features of malignancy (size  $\geq 1$  cm, round shape, echo-poor, discrete borders), EUS-FNA improves accuracy for detection of malignancy. In this case, the needle tip is clearly visible within the node (arrowheads) and cytology confirmed metastatic adenocarcinoma.

The addition of EUS-FNA improves the accuracy of lymph node staging to 85–93%<sup>[14,15]</sup>. In one retrospective study the accuracy improved from 70 to 93% with the addition of FNA. This was the result of an improvement in both sensitivity and, to a lesser extent, specificity. While safe, the addition of FNA may not be possible without traversing the primary tumour, risking contamination and false positive results. It is, however, useful if the information obtained will upstage

the patient and influence subsequent management. This is particularly relevant in the assessment of coeliac axis nodes where cytological proof of involvement usually results in a change in management to a non-surgical approach. If possible, oesophageal dilatation should be undertaken to allow adequate assessment of this area and FNA of any visualised nodes.

### *Tumour stage (T)*

Many studies over the years have repeatedly demonstrated the accuracy of EUS for assessment of T stage in oesophageal carcinoma and overall accuracy is 80–85%<sup>[9,13]</sup>. Accuracy does vary, however, within each T stage and is generally best for T3 and T4 tumours. Accuracy is least good for T2 tumours where it ranges from 65 to 73% possibly because of difficulty detecting foci of microscopic invasion beyond the muscularis propria. EUS evidence of T4 stage is a marker of poor survival regardless of subsequent therapy and EUS is highly accurate at detecting T4 disease (Fig. 2).



**Figure 2** T4 oesophageal carcinoma. Radial imaging shows a large irregular mass (T) with invasion of the aorta (Ao, arrowheads), demonstrated by a loss of the echo-rich plane of separation.

EUS is superior to CT for T stage, as demonstrated by numerous retrospective and prospective studies<sup>[9,13]</sup>. Many of these, however, compared EUS with suboptimal, incremental CT techniques but recent studies involving high quality helical CT affirm the greater accuracy of EUS. Whether or not new multidetector CT scanning techniques will lead to improved accuracy remains to be seen.

EUS is also the only accurate technique for evaluating early (T1) carcinoma of the oesophagus. High frequency catheter probes allow careful combined endoscopic and ultrasonographic evaluation of lesions as small as a few millimetres in diameter and with increased utilisation

of endoscopic mucosal resection (EMR) or ablation techniques, accurate evaluation is essential. T1 lesions confined to the mucosa (T1m) are associated with lymph node involvement in 0–5% of cases and are therefore suitable for EMR. In contrast submucosal involvement (T1sm, Fig. 3) is associated with nodal spread in up to 25% of patients especially when deeper involvement of the submucosa is present (T1sm2 or sm3). EUS is the only existing technique capable of this degree of resolution and helps to differentiate patients suitable for EMR from those requiring surgical resection.

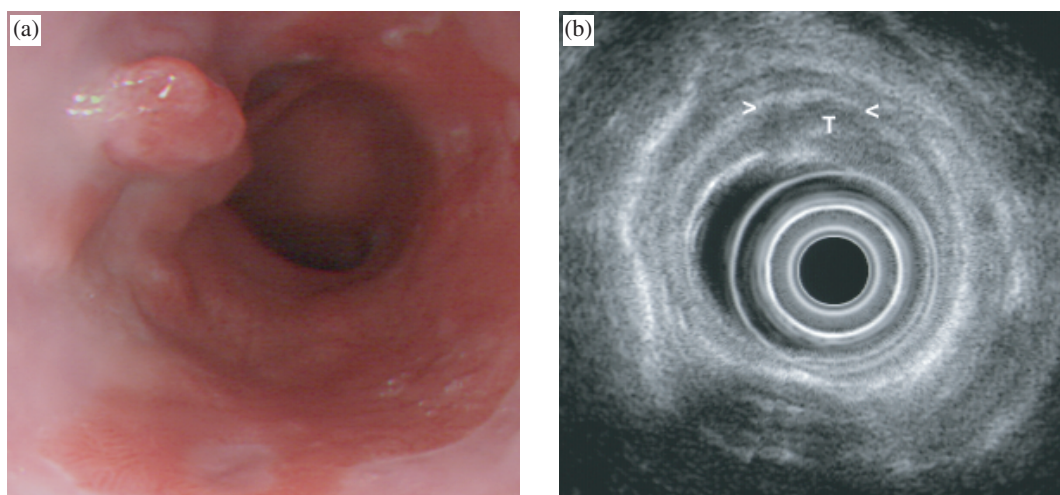
In contrast, 20–30% of patients with advanced oesophageal cancer have strictures that cannot be traversed with a standard echoendoscope yet incomplete passage is associated with significant understaging. Modern echoendoscopes are slimmer and have better video optics than earlier versions and oesophageal perforation should nowadays be rare. In a large study of 132 patients, 32% required dilatation up to 14–16 mm to complete the procedure in almost all patients and only one perforation occurred<sup>[17]</sup>. In this study advanced disease (either T4 or M1a) was detected in 19% of those undergoing dilatation. If the information gained from completing the EUS procedure is likely to impact on patient management then dilatation should be undertaken<sup>[18]</sup>. An alternative is a 7.8 mm, non-optical ‘oesophagoprobe’ (Olympus MH-908), passed over a guidewire. Several studies have reported T staging accuracy of up to 89% with this instrument.

### **Current issues for EUS in oesophageal cancer staging**

#### *Can the accuracy of nodal staging be improved?*

It is essential to improve on the modest accuracy rates of EUS imaging alone. One retrospective study assessed the impact of EUS-FNA in 64 patients<sup>[16]</sup>. The addition of FNA increased the accuracy of nodal staging to 93% largely by increasing the sensitivity and, to a lesser degree, specificity.

One continuing problem area is the detection of micrometastases in small nodes, which are often isoechoic with surrounding tissues. In a retrospective study of EUS-FNA of coeliac lymph nodes, 89 such nodes were resected from 14 patients in whom EUS of the coeliac axis had been negative. Thirty-nine of these nodes (44%) were involved, of these 39% had only microscopic involvement (tumours focus 1 mm) and the median size of all 89 lymph nodes was 5 mm<sup>[7]</sup>. At present it is difficult to envisage how advances in technology will improve this rate-limiting step in the performance of both EUS and all other modalities.



**Figure 3** (a) Early polypoid Barrett's adenocarcinoma of the oesophagus. (b) Radial EUS (7.5 MHz) demonstrates the lesion as a hypoechoic thickening with attenuation of the echo-rich third layer (submucosa, arrowheads) indicating invasion (stage T1sm, confirmed at surgery).

### *Does EUS have an impact on clinical outcome?*

Properly designed outcome studies in this area are relatively few. A prospective UK study of 100 consecutive patients found that three oesophagogastric surgeons deemed EUS useful in 87, 65 and 63% of cases. Agreement on management was lowest without EUS and the number of concordant treatment plans rose from 53 to 62% following addition of EUS information, mostly the result of more decisions to opt for non-surgical palliation<sup>[19]</sup>.

Giovannini *et al.*<sup>[20]</sup> reported that EUS demonstrated distant lymphadenopathy in 40 of 198 patients (20%) with oesophageal cancer. EUS-FNA of these nodes (sensitivity 97%, specificity 100%) led to a change in treatment in 77.5% of this subgroup of patients (i.e. 16% of all patients). Other studies have demonstrated a similar impact on management<sup>[21]</sup>.

### *Is EUS useful for restaging after neoadjuvant therapy?*

EUS restaging after neoadjuvant chemoradiotherapy cannot reliably differentiate residual tumour from inflammatory or fibrotic changes. Alternatively, documenting a reduction in maximal tumour cross-sectional area may be a promising means of predicting response to therapy. Several small studies have reported that a 50% or greater reduction in cross-sectional area reasonably accurately predicts response<sup>[22,23]</sup>. Whether or not the use of 3-D EUS imaging to estimate tumour volumes will be of value in assessing treatment responses is unknown.

## **Gastric cancer**

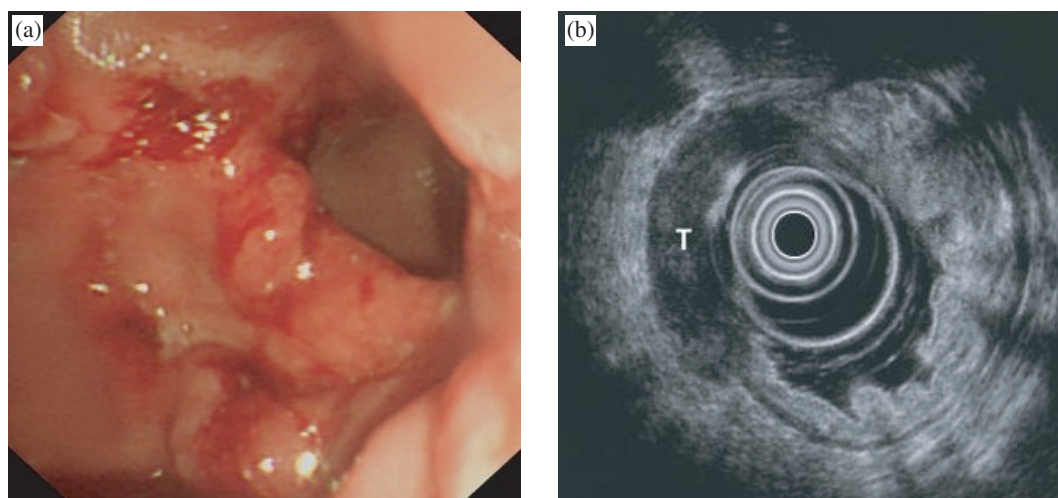
Cancers of the cardia and oesophagogastric junction usually undergo EUS staging as for oesophageal carcinoma. In Japan and other countries where the incidence of this disease is higher, and screening programmes frequently detect early disease, miniprobe EUS is highly accurate in differentiating mucosal from submucosal involvement and therefore suitability for EMR. Depressed or ulcerated lesions, however, may be associated with significant inflammation or fibrosis leading to potential overstaging.

In locally advanced cancers, the role of EUS is more restricted. Laparoscopy will more often yield important findings such as peritoneal deposits or small volume ascites and is usually the next investigation after CT. Furthermore, nodal staging depends on the *number* of involved lymph nodes and EUS cannot image all the lymph node drainage groups of the stomach. Finally, the majority of patients undergo resection whether for cure or palliation and EUS findings do not generally influence the decision to resect. Occasionally it is difficult to determine whether or not there is pancreatic invasion on CT or laparoscopy and EUS can help in this setting.

The role of EUS in the evaluation of submucosal lesions (e.g. gastrointestinal stromal tumours (GISTs)) is beyond the scope of this article but the development of EUS-guided core biopsy needles and the importance of immunohistochemical staining for *c-kit* mutations has emphasised the importance of EUS in the management of these lesions.

## **MALToma and primary gastric lymphoma**

The majority of extranodal non-Hodgkin's lymphomas arise from mucosa-associated lymphoid tissue (MALT)



**Figure 4** (a) Endoscopic view of a primary gastric lymphoma. (b) Radial EUS demonstrates hypoechoic thickening through the gastric wall and loss of normal wall layer structures (T). Note the normal wall layers on the lower right of the image.

and the stomach is the most common site. EUS is the most accurate modality for assessing and staging infiltrative lesions of the gastric wall with accuracy for depth of invasion approaching 95%<sup>[24]</sup>. EUS is able to resolve the normal five layer structure of the gastric wall, can estimate wall thickness and also image adjacent organs and lymph nodes (Fig. 4). Several studies have demonstrated the ability of EUS to predict the likelihood of remission after *Helicobacter* eradication therapy in those with disease limited to the first three layers (submucosa). In contrast patients with deeper infiltration are unlikely to respond without additional therapy and those with ongoing gastric wall thickening after therapy are more likely to have persistent lymphoma even when endoscopic mucosal biopsies are negative. For these reasons EUS has earned a pivotal place in the assessment and follow-up of this disease.

## Pancreatic carcinoma

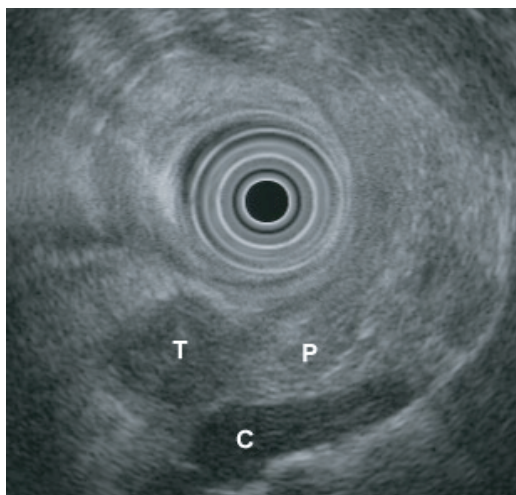
### *Role in diagnosis and staging of pancreatic carcinoma*

Overcoming the limitations of transabdominal ultrasound by placing an ultrasound transducer on the tip of an endoscope that could be inserted into the duodenum, close to the head of the pancreas, was a major driver for the development of EUS. It is ironic therefore that the greatest controversy surrounding EUS has been in relation to its role in patients with suspected pancreatic carcinoma.

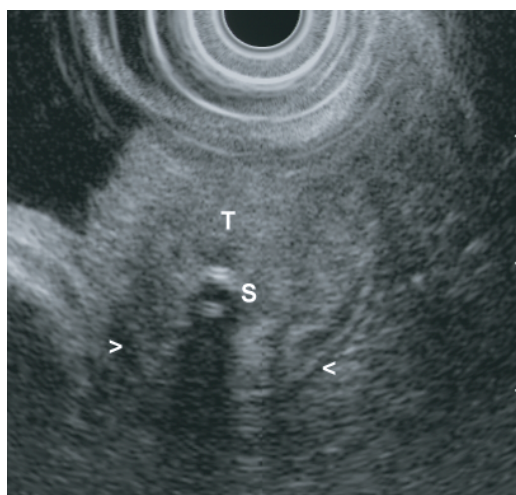
While endosonographers were hard at work evaluating the potential of EUS, the advent of helical pancreatic CT scanning protocols and recently multi-detector CT

has made it difficult to draw useful conclusions. In good hands both EUS and helical CT are highly accurate at detecting pancreatic malignancy and there is little to choose between them in terms of performance with accuracies of over 90%<sup>[25,26]</sup>. In a similar way, early studies reported that T and N staging accuracy of EUS was superior to CT particularly for the detection of vascular invasion of the mesenteric vessels<sup>[27,28]</sup> but more recent studies have been less optimistic and again EUS and dedicated helical CT seem to be of equivalent accuracy in determining resectability. In a French study the accuracy of EUS for predicting resectability was 89% while that of CT was 92%<sup>[25]</sup>; EUS was more sensitive for detecting hepatic artery involvement while CT was more sensitive for superior mesenteric artery involvement, a finding confirmed in other studies. In contrast, the majority of studies have found that EUS is significantly more accurate than CT for the detection of distant lymph node involvement with approximate figures of 74–86% for EUS, compared to 65–77% for CT<sup>[29,30]</sup>. Thus, CT and EUS appear to provide complementary information and when used together have the potential to enhance staging accuracy even further. Few if any studies to date have compared EUS with multi-detector CT or PET and equally scarce are studies on EUS and laparoscopic ultrasonography.

There may still be a slight advantage in favour of EUS for the detection of lesions smaller than 2 cm (Fig. 5) and EUS is the imaging modality of choice for staging ampullary and periampullary tumours, where it is possible to detect lesions not seen on CT and to determine whether or not there is invasion through the duodenal muscularis into the pancreas (Fig. 6).



**Figure 5** Pancreatic carcinoma (1.5 cm) seen as a hypoechoic mass (T) arising from the neck of the pancreas (P). The lesion is close to, but does not involve the splenoportal confluence (C).



**Figure 6** Small (1 cm) ampullary adenocarcinoma (T) with plastic biliary stent (S) *in situ*. The lesion is confined to the ampulla with no invasion through the duodenal muscularis propria (MP) into the pancreas. The lesion is suitable for local resection.

#### *Tissue diagnosis in pancreatic carcinoma*

EUS-FNA is safe and has a relatively high diagnostic yield and accuracy, although lesions in the uncinata process are often difficult to biopsy<sup>[14,15,31]</sup>. Overall sensitivity rates of 85% and specificity of 100% are reported, even in patients in whom cancer is suspected but previous attempts at percutaneous biopsy have been negative. There are a number of theoretical advantages in favour of EUS-FNA over other biopsy methods, particularly safety and minimisation of the potential for needle track seeding as this is usually contained within any subsequent resection specimen. Complications are

rare (<1%) but, like other methods, pancreatitis and bleeding have been reported<sup>[14,15,31,32]</sup>. The accuracy of EUS-FNA using 21–22G needles is limited by small sample size and the low cellularity of some lesions. To overcome this spring-loaded 19G core biopsy needles have been developed and show promise<sup>[33]</sup> although larger studies are awaited.

#### *Interventional role of EUS*

As non-invasive imaging continues to improve, it is likely that EUS, analogous to endoscopic retrograde cholangiopancreatography (ERCP), will become an increasingly interventional procedure. In addition to providing a tissue diagnosis from the primary lesion itself or confirming involvement of metastatic lymph nodes, coeliac plexus neurolysis for pain relief is safe, effective and straightforward under direct EUS guidance<sup>[34]</sup>. There are also potentially exciting future roles for interventional EUS and case reports of EUS guided therapy (e.g. photodynamic therapy or radiofrequency ablation) are beginning to appear.

#### *Which patients with solid pancreatic masses should undergo EUS?*

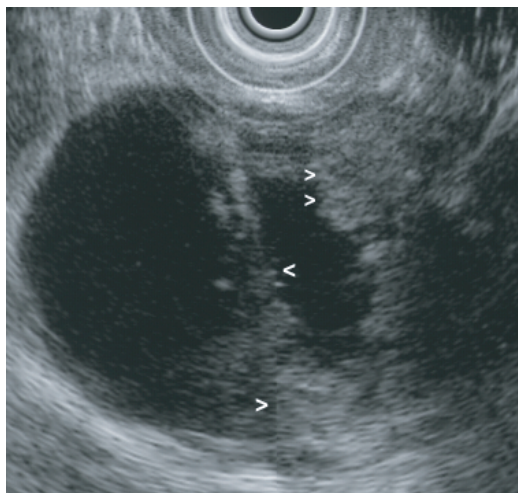
The fortunate few who are fit and have a small resectable mass on CT should probably be referred directly for consideration of surgery. Similarly, frail or unfit patients with an unresectable mass on CT and for whom palliation is the treatment of choice are unlikely to benefit from EUS. In contrast, if there is doubt about resectability on CT, if there is a clinical suspicion of pancreatic cancer but a negative or equivocal CT, or if it is unclear whether a pancreatic lesion is neoplastic or inflammatory, then EUS is often useful.

As for EUS-FNA, again patients with small resectable lesions should probably not undergo attempts at biopsy given the small theoretical risks of seeding and biopsy related pancreatitis which could make surgery more difficult. Similarly, FNA is unlikely to help frail patients with advanced disease who require palliation. In cases where there may be 'surgical uncertainty' or borderline surgical fitness, in rare cases where an alternative diagnosis such as lymphoma or metastasis to the pancreas are being considered and in unresectable patients who are candidates for chemotherapy or trial protocols, EUS-FNA is generally appropriate.

#### **Pancreatic cystic lesions**

Cross-sectional imaging demonstrates these lesions well but is unable to distinguish mucinous from non-mucinous cysts accurately. EUS can provide additional information not seen on CT such as microcystic nature,

focal wall thickening or papillary projections, septations (Fig. 7) and the presence of an adjacent mass lesion or lymphadenopathy. Early studies reporting that such features were highly accurate at detecting potential malignancy have not been borne out. In a prospective multicentre study of 112 surgically resected cystic lesions, the relative accuracies of EUS morphology, EUS-FNA cytology and CEA analysis were evaluated. The accuracy of CEA measurement for differentiating mucinous from non-mucinous lesions was 79% compared to 51% for EUS morphology and 59% for cytology<sup>[35]</sup>. No combination of these was better than CEA alone but this study did show that EUS-guided aspiration of pancreatic cysts is feasible and safe. Further studies involving newer tumour markers and long-term follow-up are awaited but, in our Unit, cystic lesions detected on CT are discussed by the pancreaticobiliary multidisciplinary team and, if appropriate, EUS is performed under antibiotic prophylaxis with FNA for cytology, mucin analysis, carcinoembryonic antigen (CEA) and amylase measurements.



**Figure 7** Radial imaging shows this 3 cm cystic lesion of the pancreatic tail to have solid papillary wall components (arrowheads) consistent with a cystic neoplasm. Surgical resection confirmed a mucinous cystadenoma.

#### *Pancreatic neuroendocrine tumours (NET)*

EUS, with its ability to detect lesions as small as 3–4 mm, is a sensitive and accurate tool for detecting and localising neuroendocrine tumours of the pancreas but again much of the available data compared EUS with non-helical CT and few modern comparative studies have been reported. For gastrinomas, however, somatostatin receptor scintigraphy remains the most sensitive method of localisation. EUS does offer the ability to perform FNA for confirmation or guided injection of India ink to aid subsequent intraoperative localisation.

## Rectal cancer

Transrectal ultrasound using either rigid ultrasound probes or flexible echoendoscopes is the most accurate modality for assessment of locally invasive rectal cancer and detection of perirectal lymph node involvement. Accurate preoperative staging determines both the type of surgery performed and the decision to use preoperative chemoradiation. Overall, EUS accuracy for T staging is approximately 83% while the corresponding figure for N staging is 75%<sup>[36,37]</sup>. Inaccurate staging tends to result from overstaging because of associated peritumoural inflammation and the difficulty distinguishing malignant from benign reactive lymphadenopathy. In addition, tumour stenosis prevents full staging in approximately 14% of patients. Comparative studies have demonstrated that EUS is superior to CT in staging accuracy and equivalent to MRI for T and N staging<sup>[38]</sup>. Endorectal coil MRI improves accuracy but remains equivalent to EUS and the latter offers the potential for FNA sampling of perirectal lymph nodes or masses. EUS is also accurate at detecting early post-operative recurrence.

## Lung cancer

In the absence of distant metastases, mediastinal lymph node metastases in non-small cell lung cancer (NSCLC) are critical determinants of management and prognosis, being present in up to 38% of patients<sup>[39]</sup>. Ipsilateral mediastinal and subcarinal lymph nodes are designated as N2 nodes and generally signify inoperability as does contralateral lymph node involvement (N3).

Detection of nodal metastases by CT is based on size alone with a short axis diameter of 10 mm used as a cut-off value yet mediastinal node involvement may occur in 15–20% of patients who do not meet this size criterion<sup>[40]</sup>. Conversely, up to 37% of mediastinal lymph nodes with a diameter of 2–4 cm in patients with known lung cancer are benign and presumably reactive. Recent data for helical CT indicate sensitivity, specificity and accuracy rates of 57%, 74% and 67%, respectively, for detecting malignant nodal involvement<sup>[41]</sup>. It was hoped that PET would resolve these problems but it is often not possible to identify accurately which groups of lymph nodes are involved, with potential therapeutic consequences. False positive results with PET have also been reported in a number of benign diseases including tuberculosis, sarcoidosis and fungal infections, confirming that tissue is still essential to confirm lymph node metastases.

Trans-bronchial needle aspiration (TBNA) of lymph nodes identified by CT is relatively 'blind' and even in the best series sensitivity is only 70%. Mediastinoscopy and thoracoscopy, are expensive, invasive, require a general anaesthetic and have a significant (1–3%) complication rate. EUS-FNA, in contrast, is safe, simple and highly

accurate in detecting and confirming nodal metastases and has been increasingly used for staging of potentially resectable NSCLC. EUS can visualise the posterior and inferior nodal stations 9, 8, 7 and 5 and also sometimes level 4 (paratracheal) but cannot image anterior mediastinal nodes because of interposed airways. The left lobe of the liver and the left adrenal gland can also be studied and sampled for metastases if abnormalities are found. Transoesophageal EUS-FNA samples have a sensitivity of 87% for detecting malignant nodal involvement<sup>[42–44]</sup>. Morbidity from this technique is almost nil and even patients with poor lung function tolerate it well. Whether newly available 19G core biopsy needles will improve sensitivity further by overcoming the problem of micrometastases in small nodes remains to be seen. Prototype linear array instruments for bronchoscopic ultrasound-guided FNA (BUS-FNA) are now being tested and early results are promising, allowing trans-bronchial FNA of anterior and superior mediastinal nodes under real-time guidance<sup>[45]</sup>.

### Future developments

Echoendoscope technology continues to develop and the introduction of 360 degree electronic radial instruments will hopefully improve staging performance further. Improved software now allows real-time 3-D reconstruction of tumours in the oesophagus or biliary tree, from which volume sets can be determined and a clearer idea of tumour anatomy obtained. Whether or not estimated tumour volumes correlate with TNM stage or prognosis remains to be seen as does the possibility that reductions in tumour volume after chemoradiotherapy might correlate with tumour response. The potential use of second generation ultrasound contrast agents in combination with EUS is still largely unexplored. Lastly, it seems likely that, as non-invasive imaging techniques continue to improve, EUS will become an increasingly interventional tool to acquire tissue and, hopefully, to deliver therapies such as radiofrequency ablation, photodynamic therapy or injection of antitumour agents. Much of this is speculative but what is certain is that this area will progress rapidly, rendering this review outdated before long.

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