Official Journal of the Asian Pacific Society of Respirology
Respirology

INVITED REVIEW SERIES: PLEURAL DISEASE
SERIES EDITORS: JOSÉ M. PORCEL AND Y.C. GARY LEE

# Pleural controversy: Closed needle pleural biopsy or thoracoscopy—Which first?

COENRAAD F.N. KOEGELENBERG[1] AND ANDREAS H. DIACON[1,2]

[1]*Division of Pulmonology, Department of Medicine,* [2]*Division of Medical Physiology, Department of Biomedical Sciences, University of Stellenbosch & Tygerberg Academic Hospital, Cape Town, South Africa*

## ABSTRACT

**The most efficient and cost-effective approach to the diagnosis of pleural exudates remains controversial. Important considerations include the respective diagnostic yields of thoracocentesis, closed pleural biopsy and thoracoscopy; the incremental gain in diagnostic yield when sequentially combining these investigations; and the role of various image modalities. The diagnostic yield of thoracocentesis is in the order of 60% for malignancy and >90% for tuberculosis. A second aspiration may increase the yield for malignancy, but a third is generally superfluous. Many authorities consider thoracoscopy the investigation of choice in exudative pleural effusions where a thoracocentesis was nondiagnostic and particularly when malignancy is suspected. It allows for the direct inspection of the pleura and for talc poudrage. Thoracoscopy has a diagnostic yield of 91–95% for malignant disease and as high as 100% for pleural tuberculosis. Access to thoracoscopy is, however, limited in many parts of the world, as significant resources and expertise are required. Blind closed pleural biopsy has a yield of 80% for tuberculosis and <60% for pleural malignancy. Recent studies suggest that CT and/or ultrasound guidance may improve the yield, particularly for malignancy, where it may be as high as 88% and 83%, respectively. A second thoracocentesis combined with an image-assisted pleural biopsy with either an Abrams needle or cutting needle, depending on the setting, may therefore be an acceptable alternative to thoracoscopy. With such an approach, thoracoscopy may potentially be reserved for cases not diagnosed by means of closed pleural biopsy.**

**Key words:** pleural biopsy, pleural disease, pleural effusion, thoracoscopy, ultrasound.

## INTRODUCTION

The diagnostic approach to pleural disease remains an underappreciated aspect of modern thoracic medicine, despite the fact that pleural disease affects approximately 300 subjects per 100 000 population per year world wide.[1] Diagnostic and therapeutic thoracocentesis has been the standard initial intervention since the early 19th century.[2] The first endoscopic inspection of the pleura was performed as early as 1866 and closed biopsy needles have been in use since the early 1950s.[3–7] Yet, the most efficient and cost-effective approach to pleural exudates remains uncertain and even controversial, particularly if acquisition of pleural tissue is required.

The clinician needs to consider various factors when confronted with the choice between closed pleural biopsy and thoracoscopy. These include the respective diagnostic yields of thoracocentesis, closed pleural biopsy and thoracoscopy in various clinical settings and pretest probabilities; the incremental gain in diagnostic yield when sequentially combining these investigations; and the supporting role of imagery of the pleura. Furthermore, local skill and expertise may ultimately dictate the choice. This review provides an overview of these and related issues, highlighting recent developments and controversies.

## THORACOCENTESIS BEFORE BIOPSY

### Pleural fluid analysis

Light's criteria, within clinical context, have stood the test of time as far as identifying pleural disease as the cause of a pleural effusion. Barring a few exceptions,

**The Authors:** CFN Koegelenberg (MBChB, FCP (SA), MRCP (UK)) is a specialist in Respiratory Medicine whose research interests include transthoracic ultrasound, minimally invasive transthoracic diagnostic techniques and tuberculosis. AH Diacon (MD, PhD) is an associate professor and specialist in Respiratory Medicine, whose research interests include pleural diseases and minimally invasive transthoracic diagnostic techniques and, more recently, antituberculosis drug evaluation.

Correspondence: Dr Coenraad FN Koegelenberg, Division of Pulmonology, Department of Medicine, University of Stellenbosch, PO Box 19063, Tygerberg, 7505, Cape Town, South Africa. Email: coeniefn@sun.ac.za

Received 27 January 2011; invited to revise 3 March 2011; revised 11 March 2011; accepted: 11 March 2011.




doi: 10.1111/j.1440-1843.2011.01973.x

virtually all patients presenting with pleural effusions should therefore undergo pleural aspiration to categorize effusions into transudates and exudates. This not only narrows the differential diagnosis, but also directs subsequent investigations and management.

Transthoracic ultrasound (US) guidance improves the success rate of pleural aspirations.[8–10] In fact, the success rate of US-guided thoracocentesis can be as high as 97%.[11] US detects pleural fluid septations with greater sensitivity than CT and also minimizes the risk of visceral puncture.[8,10,11] Moreover, the risk of pneumothorax following aspirations is reduced, independent of the size of the effusion.[12]

Empyema, malignancy, tuberculous effusions, chylothorax, haemothorax and rheumatoid pleurisy are important examples of diagnoses that can be definitively established on pleural fluid analysis alone.[13] Apart from routine biochemistry, pH analysis, microbiology, cell counts and cytology, specific fluid test may be indicated in certain settings, for example, triglycerides and cholesterol in case of a suspected chylothorax or adenosine deaminase (ADA), stains for acid-fast bacilli and culture for *Mycobacterium tuberculosis* in case of suspected pleural tuberculosis (TB). Pleural fluid tumour markers currently have a limited role in the routine investigation of pleural effusions.[8,14]

### Diagnostic yield

The diagnostic yield for malignancy of pleural cytology is in the order of 55–60%.[15,16] Interestingly, one study suggested a significant sequential gain of 27% from a second aspiration, although the gain of a third aspiration was only 5%.[17] It is unclear whether a larger volume of fluid is more likely yield malignant cells. Swiderek and co-workers suggested that a larger volume of fluid (60 mL) had a higher diagnostic yield than a lower volume (10 mL),[18] although others have concluded that a greater volume (>50 mL) had no increased yield.[19] Tumour type and availability of reliable immunocytochemistry may influence the yield. The cytological detection rate for adenocarcinoma is, for example, higher than that of squamous cell carcinoma, mesothelioma or lymphoma.[8]

The usefulness of fluid analysis for pleural TB is dependent on the pretest probability for the disease, which will increase with a high local incidence of TB and high prevalence of HIV infection. In high incidence areas, more than 90% of all cases can be diagnosed following a single thoracocentesis based on the presence of a combination of a lymphocytic predominant effusion with a raised level of ADA.[20,21] Unstimulated interferon gamma levels in pleural fluid have a similar diagnostic accuracy as ADA.[22] Pleural fluid microscopy for acid-fast bacilli and pleural fluid culture for *M. tuberculosis* have poor sensitivities (<50%) for the disease.[8,20,21] The risk of false positives and overtreatment for TB in well-resourced healthcare settings is such that microbiological confirmation on pleural tissue is generally aimed for, that is, the diagnosis is not often made on pleural fluid alone, although it can be reliably excluded.[8]

Thoracocentesis has varying diagnostic yields in other settings, and clinical correlation as well as pH and glucose measurements on the pleural fluid are often required, for example, in cases of rheumatoid arthritis-associated pleural effusions.[8]

## THORACOSCOPY

### Historical perspective and technical aspects

Although Gordon described the first *in vivo* inspection of the pleura in 1866,[3] Jacobaeus is credited with firmly establishing modern thoracoscopy in 1910.[23] Medical thoracoscopy is generally performed under local anaesthesia and conscious sedation in an endoscopy suite with basic monitoring. Surgical thoracoscopy, which allows for superior visualization, complete deflation of a lung and superior access for therapeutic interventions, is significantly more invasive and expensive. It requires general anaesthesia, intubation with a double lumen endotracheal tube and more than one port of entry.[24]

There is considerable geographical variation in the use of medical thoracoscopy, even in the developed world. In Western Europe it is considered standard practice,[25] whereas only 12% of US training programmes offer medical thoracoscopy in their curriculum.[26] In the UK the procedure is still not uniformly performed, although there is growing interest. In fact, 2010 British Thoracic Society (BTS) pleural disease guideline state that thoracoscopy is the investigation of choice in exudative pleural effusions where a diagnostic pleural aspiration is inconclusive and malignancy is suspected.[8]

Medical thoracoscopy remains an invasive procedure, but complications are infrequently seen. Haemorrhage, secondary empyema and other major complications are only seen in 2–3% of cases, and death is exceedingly rare (0.4%).[8,27,28] Medical thoracoscopy has the important advantage that it may also be used therapeutically, for example, for the direct insufflation of talc in order to achieve pleurodesis and the breakdown of loculations.[8]

### Diagnostic yield

Medical thoracoscopy allows for the direct inspection of the pleura and biopsies taken under direct vision, has a diagnostic yield superior to that of blind closed pleural biopsy and thoracocentesis. The diagnostic yield is in the order of 91–95% for malignant disease and can be as high as 100% for pleural TB.[8,20,24,27–30] Of note is the fact that Loddenkemper found that the addition of ether pleural fluid cytology and blind pleural biopsy to thoracoscopy only increased the yield for malignancy by 1%.[24,29]

## CLOSED NEEDLE BIOPSY

### Historical perspective

Closed pleural biopsy needles were introduced 40 years after Jacobaeus established thoracoscopy.

Within a decade various needles were described, including the Abrams (guillotine), Cope (hook) and Vim-Silverman (puncture) needles.[4–7] Of these devices, the Abrams needle was consistently shown to have a superior yield and became the most widely used.[7,31] Cutting needle biopsy (CNB) (e.g. Tru-cut) was a relative recent addition. In 1989 Macleod described the use of blind Tru-cut needle biopsy as an alternative to Abrams needle biopsy in patients who present with large pleural effusions, which is a prerequisite for the blind use of these devices.[32]

## Technical aspects

Closed pleural biopsy requires careful local anaesthesia and should be a painless procedure. The main complication is pneumothorax. The large calibre of the Abrams needle combined with the patient's respiratory movements can allow outside air to enter the pleural space if the device is not kept closed at all times. This is often aided by falling intrapleural pressure during evacuation of pleural fluid. Pneumothorax with an underlying bronchopleural fistula can occur if the lung is punctured or otherwise injured. Although a pneumothorax may be seen in up to 15% of patients undergoing biopsies, only a small minority require intervention.[8] Other complications include site pain (1–15%), vasovagal reaction with potential syncope (1–5%), haemothorax (<2%) and site haemorrhage with haematoma formation (<1%).[8] The fall in the incidence of TB in most of the developed world over the last 50 years has led to an equally significant reduction in operator experience among respiratory physicians,[8] to the point where even experienced pulmonologists have become reluctant to utilize blind closed pleural biopsy even in settings where the anticipated diagnostic yields are high.

## Diagnostic yield: unaided closed pleural biopsies

Unaided (blind) closed pleural biopsy has a relatively modest diagnostic yield of less than 60% for pleural malignancy.[33] Of note is the fact that the overall yield for malignancy over pleural fluid cytology is only increased by 7–27%.[15,24,34] Tuberculous granulomata are far more homogenously distributed over the pleura than is the case for malignant deposits, and unaided closed biopsies are therefore more likely to be diagnostic if TB is the underlying disease. Published results vary, but yields are generally in the order of 80%.[20,35–38] Kirsch and co-workers even reported a yield of 87%, provided at least six specimens are harvested.[39]

## Image-guided closed pleural biopsies

Recent studies have proposed that image guidance may significantly increase the yield while decreasing the risk for complications. Both transthoracic US and CT scanning have been utilized.

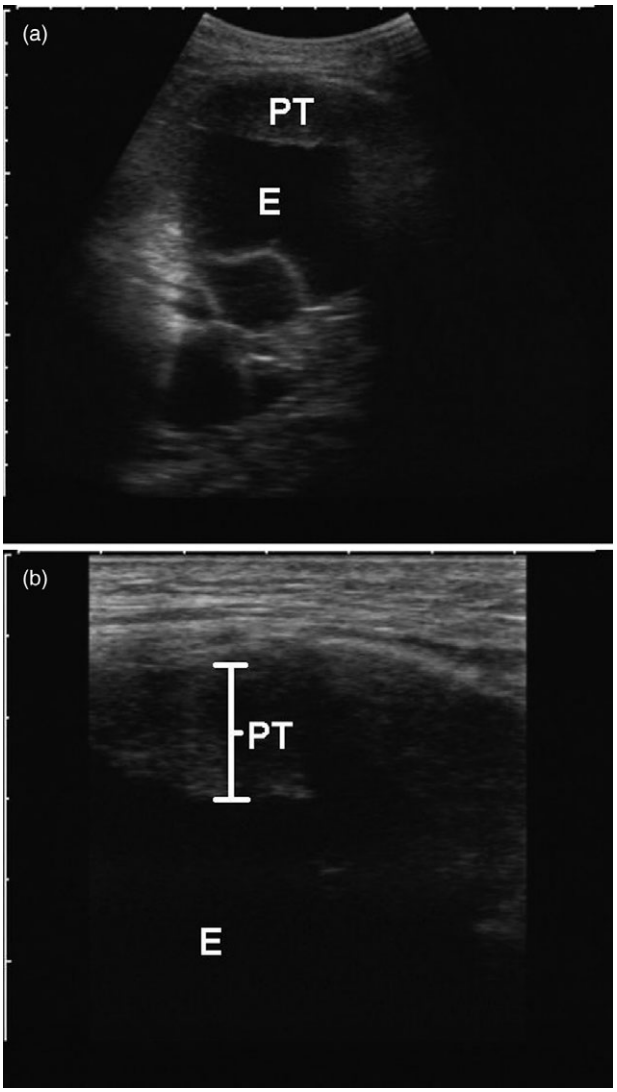


**Figure 1** Examples of pleural effusions with relevant pleural abnormalities that may be present on transthoracic ultrasound. (a) This low frequency US image shows diffuse pleural thickening (PT) with an effusion (E). (b) A high frequency image from the same patient (with better resolution but less penetration) showing pleural thickening (PT) with an effusion (E).

Transthoracic US only came to the forefront as a guide to transthoracic interventions in the late 1980s, despite the fact that diagnostic sonography dates from the 1940s.[10,40–44] Transthoracic US is an ideal aid to the clinician, given its mobility, lack of irradiation and short examination time.[10,40] US is superior to chest radiography for the visualization of pleural effusions. Moreover, the volume of fluid, the presence of septations, pleural thickening, nodules and pleural based tumours can be accurately assessed (Fig. 1).[2] Modern mobile US units are cheap and available in practically all secondary and tertiary, as well as many primary health-care facilities, even in the developing

world.[10,40–44] Basic transthoracic US can be performed by means of the most basic entry-level two-dimensional US equipment, which are more often acquired for obstetric use. A low frequency curvilinear probe (range: 2–5 MHz) is essential, whereas a high frequency linear probe (range: 5–10 MHz) is a useful addition.[40] Moreover, US-assisted pleural biopsy can be performed by a single operator with no sedation and minimal monitoring, even at the bedside.[10,40] The consumables (transmission gel, local anaesthetic, needles and syringes) are affordable. These simple yet practical considerations need to be emphasized when comparisons are made with thoracoscopy, which, despite superior diagnostic yield, is invariably performed in theatre under general anaesthesia or conscious sedation, necessitating significant expertise, resources and more costly consumables.

In a recent study, Qureshi *et al.* were able to identify 73% of malignant effusions on US appearance alone.[45] They found that pleural thickening >10 mm, pleural nodularity and diaphragmatic thickening >7 mm were highly suggestive of malignant disease.

Chang previously found the diagnostic yield of US-guided Tru-cut pleural biopsy to be as high as 87% for all pleural pathologies (77% for malignancies), irrespective of pleural thickening or nodularity.[46] For malignant mesothelioma extending at least 20 mm in any accessible dimension on US we have shown that this figure may be as high as 100%.[47]

In a recent prospective randomized study we found that US-assisted Abrams needle biopsy specimens were more likely to contain pleural tissue than specimens obtained by means of US-assisted Tru-cut biopsies (91.0% vs 78.7%, $P = 0.015$).[21] Furthermore, Abrams needle biopsies had a significantly superior yield for pleural TB compared to Tru-cut needle biopsies (81.8% vs 65.2%, $P = 0.022$), but not compared with previously reported figures for blind Abrams needle biopsies. The distribution of granulomatous inflammation in pleural TB is uniform over the pleura and visual aid therefore seemed to have offered little advantage beyond increased safety. Interestingly, and contrary to previous reports, the respective yield for both needle types for pleural malignancies was comparable and relatively high, with US-assisted Abrams needle diagnostic in 83.3%.[21] We did not utilize the US to specifically identify apparent diseased pleura, and did not limit biopsy sites to thickened pleura. One possible explanation for our relatively high yield, however, may be the fact that we utilized low biopsy sites, as the lower thoracic parietal pleura (close to the diaphragm) is more likely to contain secondary spread from visceral pleural metastases. Such an approach is possible with US assistance, but not with digital percussion as a guide (Fig. 2). Moreover, malignant disease tends to give rise to more focal pleural involvement, which may be discernable with US.

Apart from increasing diagnostic sensitivity, US may also add to patient safety. A recent survey carried out in the UK highlighted the dangers of blind pleural procedures: 67 of 101 National Health Service trusts reported at least one serious complication from intercostal drainage. In all, 47 cases of serious lung or chest wall injuries with eight deaths and six cases of intercostal drainage placement on the wrong side were described.[48] Although comparable multicentre data for unaided closed pleural biopsies do not exist, it seems plausible that similar complications can occur. Such incidents could be avoided by means of US assistance.[10,40] Recently there have been renewed

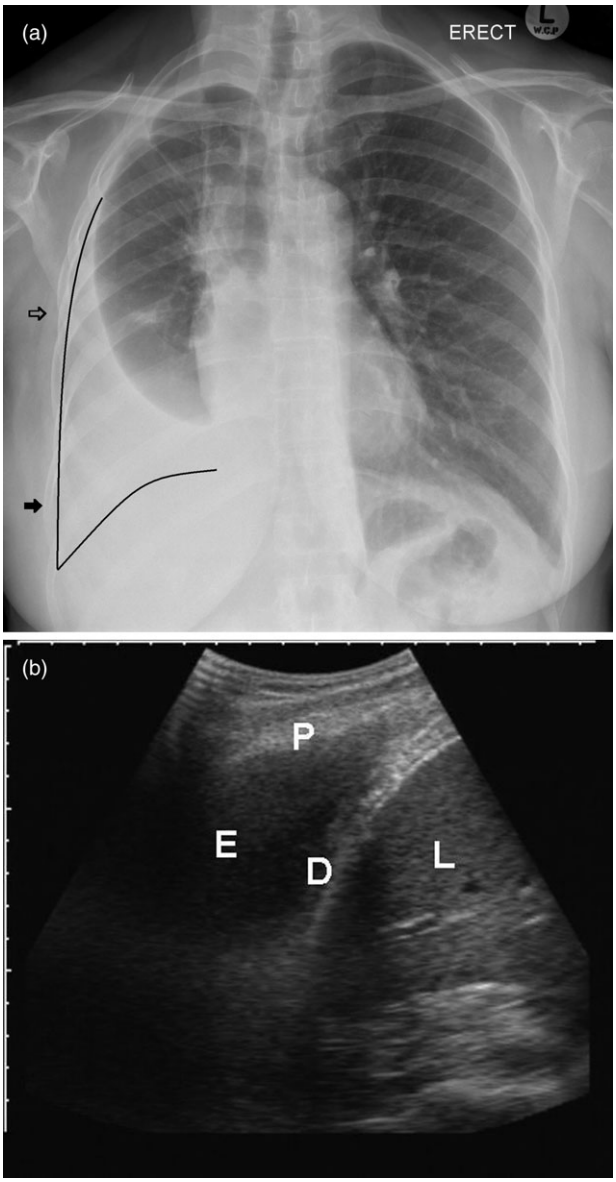


**Figure 2** (a) A relatively high biopsy site (one interspace below the spot where the percussion note becomes dull) is invariably utilized when digital percussion is used to guide blind closed pleural biopsy (hollow arrow), as the position of the diaphragm and abdominal viscera can not reliably be determined with percussion alone. With US assistance, a much lower (at least one to two interspaces above the diagram) approach is feasible and safe (solid arrow). (b) An effusion (E) with an associated pleural thickening (P) can be seen on this low frequency US image. The diaphragm (D) and liver (L) are clearly seen, allowing for the selection of a low biopsy site.

calls for formal instruction of basic transthoracic US skills to all respiratory physicians in training, and for some form of certification in basic competence in ultrasonography.[8,49,50]

The contrast-enhanced thoracic CT scan of a patient with a pleural effusion (Fig. 3) may show focal areas of abnormal thickening.[8] A study by Maskell *et al.* found that CT guidance significantly increases the diagnostic yield in the setting of pleural thickening.[51] In their study CT-guided CNB had a sensitivity of 87%, compared with unaided Abrams needle biopsy with had a sensitivity of only 44% ($P = 0.02$). Moreover, they concluded that primary use of CT-guided biopsy would avoid doing at least one Abrams biopsy for every 2.5 CT-guided biopsies undertaken, which needs to be considered where Abrams needle biopsy and CT-guided biopsy are equally accessible.[51] Adams previously found that CT-guided biopsies had a sensitivity of 93% for malignant mesothelioma.[52]

In a very recent study, Metintas and co-workers randomly assigned 124 patients with effusions not diagnosed by cytology to undergo either Abrams needle biopsy guided by CT findings or medical thoracoscopy.[53] In the CT-guided pleural biopsy group, the diagnostic sensitivity was 87.5%, compared with 94.1% in the thoracoscopy group ($P = 0.252$). CT-guided Abrams needle biopsy had a sensitivity of 95% in cases with pleural thickening $\geq$1 cm, which was on par with thoracoscopy (96%). Thoracoscopy was superior in cases with <1 cm thickening (93% vs 82%, $P = 0.42$). The cause of the effusion did not influence the sensitivities. Few complications were reported. The authors concluded that CT-guided Abrams needle biopsy should be used as the primary method of diagnosis in patients with pleural thickening or lesions observed by CT scan (as was the case in the majority of patients enrolled), but suggested that patients with only pleural fluid appearance on CT scan may still benefit from primary medical thoracoscopy.[53]

Computed tomography scanning has the added advantage of visualization and guidance in areas not discernable with US (e.g. aerated lung). As a modality, however, it lacks the mobility of transthoracic US, and the input of a specialist (interventional) radiologist is generally required.[8] In some health-care systems, waiting lists for CT-guided interventions may also favour the use of US-assisted biopsy.

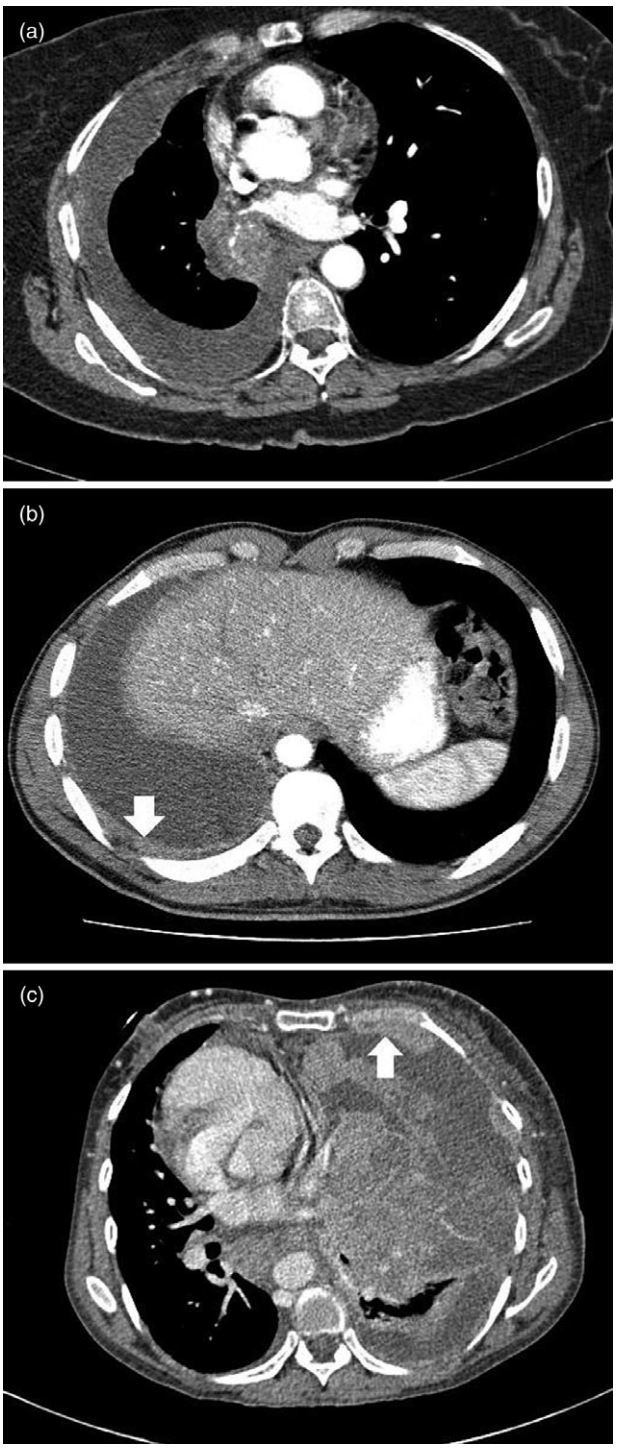


**Figure 3** The pleura may have various appearances on CT scans of patients who present with pleural exudates and may guide the choice of biopsy technique and device. Note the presence of pleural effusions in association with (a) no pleural thickening (b) pleural thickening (arrow) and (c) a pleural based mass (arrow).

## Image-guided biopsy of mass lesions associated with pleural effusions

Although technically not within the realms of closed pleural biopsy, image-guided transthoracic fine needle aspiration (TTFNA), preferably with rapid on-site evaluation and image-guided CNB of mass lesions associated with pleural effusions are well-validated modalities with diagnostic yields higher than closed pleural biopsy.[47,54–58] Pleural based solid metastases and malignant effusions are both considered M1a disease according to the 2009 International Association for the Study of Lung Cancer staging system.[59] Serious consideration should therefore be given to using an US-assisted biopsy procedure in the setting of a pleural effusion with an apparent pleural

based solid metastasis.[54–58] TTFNA are generally performed under local anaesthesia with a 22-gauge injection-type or spinal needle. CNB follow the same principles as TTFNA. The devices harvest tissue suitable for histological evaluation, but are more invasive and carry the higher risk of vascular or visceral trauma.[40] We previously found that US-assisted TTFNA and CNB had a combined yield of 89%.[54] US-guided TTFNA was significantly superior to CNB in confirming a diagnosis of bronchogenic carcinoma (95% vs 81%, $P = 0.006$), whereas CNB was superior in cases of non-carcinomatous tumours and non-malignant lesions.[54]

## IMAGE-GUIDED CLOSED NEEDLE PLEURAL BIOPSY VS MEDICAL THORACOSCOPY

### General practical considerations

The estimated incremental gains in the diagnostic yields, respectively, for pleural malignancy and tuberculous pleuritis when sequentially combining pleural fluid analysis, image-guided closed pleural biopsy and medical thoracoscopy are summarized in Figure 4.

Many authorities on the subject, including the BTS Pleural Disease Guideline Group, favour thoracoscopy as the investigation of choice in exudative pleural effusions where a thoracocentesis was nondiagnostic and particularly when malignancy is suspected.[8,24,29] Protagonists of this approach will point out the superior diagnostic yield (Fig. 4), relative safety and the ease of talc poudrage under direct vision.[8] Medical thoracoscopy, however, requires some degree of expertise and is often not offered at a District hospital level, necessitating referral to a centre with the capacity and experience to perform it.

Image-assisted closed biopsy, on the other hand, can potentially be performed in most medical facilities, provided the operator is competent in imaging (CT and/or US) and closed pleural biopsy techniques, and offers a more rapid, more accessible and cheaper alternative,[10,21] albeit at the cost of a marginally lower yield. Local expertise, availability, cost constraints and the potential need to perform the biopsies outside of a radiology unit will likely dictate the choice between CT and US as the imaging modality. The pretest probability for malignancy or TB and image findings should also influence the choice of biopsy technique. Image-assisted biopsy is more likely to be diagnostic in the presence of pleural thickening >10 mm, pleural nodularity, pleural based mass lesions of >20 cm and solid pleural tumours.[11,45,47,53,54] Utilizing a relatively low supra-diaphragmatic biopsy site (Fig. 2) and acquiring at least six biopsy specimens may also increase the yield.[21,39] There is undoubtedly a need for large prospective studies to better define the role of image-assisted pleural biopsy, particularly for the diagnosis of pleural malignancy.

Taking all of the above evidence into account, a case can be made for offering medical thoracoscopy as the principal investigation in health-care settings with little financial constraints and rapid access to the modality. This is in fact the current suggestion by the BTS, although only based on level C evidence.[8] In other settings (which arguably include most regions outside of Western Europe) a strong case can be made for offering a second image-assisted thoracocentesis and image-assisted closed biopsy to a patients with an exudative pleural effusion where the initial thoracocentesis was nondiagnostic, and to reserve thoracoscopy for those who remain undiagnosed.

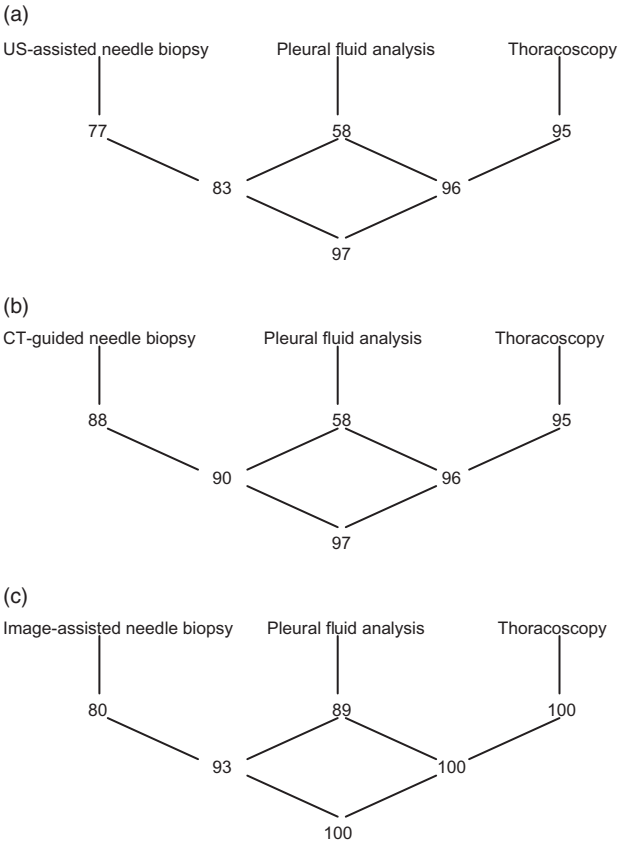


**Figure 4** The incremental gains in the diagnostic yields when thoracocentesis, image-guided closed pleural biopsy and medical thoracoscopy are performed in sequence. (a) Sensitivity (%) of ultrasound (US)-assisted pleural biopsy and thoracoscopy in the diagnosis of malignant pleural effusions, with cytological and histological results combined.[8,11,16,21,29,46,51,52] Note that the combined yield of pleural fluid analysis (on two pleural aspirates) and image-assisted closed biopsy is currently only and estimate based on a small case series.[21] (b) Sensitivity (%) of the CT-guided pleural biopsy and thoracoscopy in the diagnosis of malignant pleural effusions, with cytological and histological results combined.[16,53] Note that the combined yield of pleural fluid closed biopsy is only an estimate. (c) Sensitivity (%) of the different biopsy techniques in the diagnosis of tuberculous pleural effusions, with pleural fluid analysis (including ADA and differential cell counts) and histological results combined[8,16,20,21] (Adapted and updated from Loddenkemper *et al.*[16]).

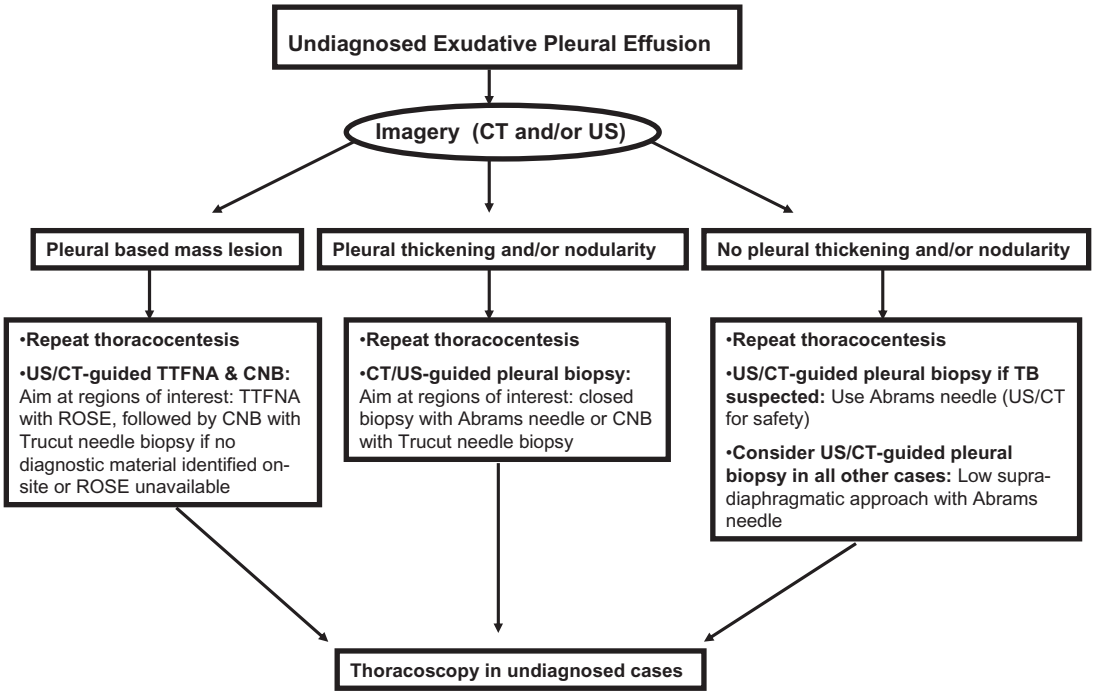


**Figure 5** A suggested diagnostic approach to an exudative pleural effusion and a nondiagnostic thoracocentesis. Either CT or US findings may be used to guide the choice between various biopsy devices and techniques (see text for details). CNB, cutting needle biopsy; ROSE, rapid on-site evaluation; TB, tuberculosis; TTFNA, transthoracic fine needle aspiration; US, ultrasound.

The added benefit of thoracoscopic talc poudrage during thoracoscopy, which is considered by some to be superior to tube thoracostomy and talc slurry, is often used to justify medical thoracoscopy in patients who present with large pleural effusions with a high pretest probability for malignancy.[8,60–62] In the largest study in the field, however, Dresler and co-workers found both methods of talc installation to be similar in efficacy.[63] Their data suggested no overall difference in the percentage of patients with successful 30-day outcomes following thoracoscopy with talc insufflation compared with thoracostomy and talc slurry instillation (78% vs 71%). The subgroup of patients with primary lung or breast cancer had higher success with thoracoscopy (82% vs 67%), but at a price of higher respiratory complications (14% vs 6%).

### A proposed practical approach

A suggested approach to the patient with an exudative pleural effusion and a nondiagnostic thoracocentesis is summarized in Figure 5. Based on initial imaging, a patient may either have: (i) a mass lesion with an interface of at least 1 cm in two dimensions; (ii) diffuse pleural thickening (>10 mm) and/or nodularity; or (iii) insignificant pleural thickening.

Pleural based masses are ideally suited for US-assisted TTFNA, preferably with rapid on-site evaluation and US-assisted CNB.[47,54,59–62] In the absence of a pleural based mass lesion, the choice of biopsy device and technique is best guided by the clinical setting. If the pretest probability for TB is high, an Abrams needle should be utilized (irrespective of pleural thickening),[21] and imaging should be used to improve safety.[10] In the presence of pleural thickening or nodularity, CT- or US-guided biopsy with either Tru-cut or Abrams needle of these areas of interest should be performed.[21,51,52] In the absence of overt pleural abnormalities, clinical context and local expertise should dictate whether an image-assisted biopsy should be used before thoracoscopy, as the value of image-assisted biopsy is less well defined in this setting (with the exception of suspected pleural TB). If utilized, an image-assisted low supra-diaphragmatic biopsy with an Abrams needle is suggested, as it is more likely to harvest pleura.[21] Cases that remain undiagnosed after thoracocentesis and closed biopsy warrant thoracoscopy. It should be emphasized that these suggestions are not based on large multicentre prospective studies, but small single centre trials and expert opinion,[10,17,20,21,31,39,40,47,51–54] and that local expertise and ease of access to image modalities should dictate the approach.

## CONCLUSIONS

Thoracoscopy has a superior diagnostic yield for pleural malignancy and TB, and is therefore considered by many to be the investigation of choice in

exudative pleural effusions where a thoracocentesis was nondiagnostic and particularly when malignancy is suspected. Furthermore, it allows for the direct inspection of the pleura and for the potential direct application of talc pleurodesis when required. Access to thoracoscopy is, however, limited in many parts of the world, as significant resources and expertise are required.

Blind closed pleural biopsy has a modest yield. Recent studies suggest that image guidance improves the yield, particularly for malignancy. An image-assisted second thoracocentesis combined with an image-assisted pleural biopsy with either an Abrams needle or cutting needle (depending on the clinical setting and imagery) may therefore be an acceptable alternative to thoracoscopy, particularly when there is a high probability of pleural TB. Cases that remain undiagnosed warrant thoracoscopy.

## REFERENCES


1 Du Rand I, Maskell N. Introduction and methods: British Thoracic Society pleural disease guideline. *Thorax* 2010; **65**(Suppl. 2): ii1–3.
2 Bowditch H. On paracentesis thoracis. *Boston Surg. J.* 1857; **56**: 348–54.
3 Gordon S. Clinical reports of rare cases. *Dubl. QJ Med. Sci.* 1866; **41**: 83–99.
4 Abrams LD. A pleural biopsy punch. *Lancet* 1958; **i**: 30–1.
5 Cope C. New pleural biopsy needle. *JAMA* 1958; **167**: 1107–8.
6 Kettle LJ, Cugell DW. Pleural biopsy. *JAMA* 1967; **200**: 317–20.
7 Schools GS. Needle biopsy of parietal pleura: current status. *Tex. J. Med.* 1963; **59**: 1056–65.
8 Hooper C, Lee YC, Maskell N. Investigation of a unilateral pleural effusion in adults: British Thoracic Society pleural disease guideline 2010. *Thorax* 2010; **65**(Suppl. 2): ii4–17.
9 Diacon AH, Brutsche MH, Solèr M. Accuracy of pleural puncture sites: a prospective comparison of clinical examination with ultrasound. *Chest* 2003; **123**: 436–41.
10 Koegelenberg CFN, Bolliger CT, Diacon AH. Pleural ultrasound. In: Light RW, Lee YC (eds) *Textbook of Pleural Disease*, 2nd edn. Hodder & Stoughton, London, 2008; 275–83.
11 Yang PC, Kuo SH, Luh KT. Ultrasonography and ultrasound-guided needle biopsy of chest diseases: indications, techniques, diagnostic yields and complications. *J. Med. Ultrasound* 1993; **1**: 53–63.
12 Barnes TW, Morgenthaler TI, Olson EJ *et al*. Sonographically guided thoracentesis and rate of pneumothorax. *J. Clin. Ultrasound* 2005; **33**: 442–6.
13 Sahn SA. Diagnostic value of pleural fluid analysis. *Semin. Respir. Crit. Care Med.* 1995; **16**: 269–78.
14 Porcel M, Vives M, Esquerda A *et al*. Use of a panel of tumour markers (carcinoembryonic antigen, cancer antigen 125, carbohydrate antigen 15-3 and cytokeratin 19 fragments) in pleural fluid for the differential diagnosis of benign and malignant effusions. *Chest* 2004; **126**: 1757–63.
15 Nance KV, Shermer RW, Askin FB. Diagnostic efficacy of pleural biopsy as compared with that of pleural fluid examination. *Mod. Pathol.* 1991; **4**: 320–4.
16 Loddenkemper R, Boutin C. Thoracoscopy: present diagnostic and therapeutic indications. *Eur. Respir. J.* 1993; **6**: 1544–55.
17 Garcia L. The value of multiple fluid specimens in the cytological diagnosis of malignancy. *Mod. Pathol.* 1994; **7**: 665–8.
18 Swiderek J, Marcos S, Donthireddy V *et al*. Prospective study to determine the volume of pleural fluid required to diagnose malignancy. *Chest* 2010; **137**: 68–73.
19 Abouzgheib W, Bartter T, Dagher H *et al*. A prospective study of the volume of pleural fluid required for accurate diagnosis of malignant pleural effusion. *Chest* 2009; **135**: 999–1001.
20 Diacon AH, Van de Wal BW, Wyser C *et al*. Diagnostic tools in tuberculous pleurisy: a direct comparative study. *Eur. Respir. J.* 2003; **22**: 589–91.
21 Koegelenberg CF, Bolliger CT, Theron J *et al*. Direct comparison of the diagnostic yield of ultrasound-assisted Abrams and Tru-Cut needle biopsies for pleural tuberculosis. *Thorax* 2010; **65**: 857–62.
22 Greco S, Girardi E, Masciangelo R *et al*. Adenosine deaminase and interferon gamma measurements for the diagnosis of tuberculous pleurisy: a meta-analysis. *Int. J. Tuberc. Lung Dis.* 2003; **7**: 777–86.
23 Jacobaeus HC. Über die möglichkeit die Zystosopie bei untersuchung seröser höhlungen anzuwenden. *Munch. Med. Wochenschr* 1910; **57**: 2090–2.
24 Loddenkemper R. Thoracoscopy—state of the art. *Eur. Respir. J.* 1998; **11**: 213–21.
25 Dijkman JH, Martinez Gonzales del Rio J, Loddenkemkper R *et al*. Report of the working party of the 'UEMS Monospeciality Section on Pneumology' on training requirements and facilities in Europe. *Eur. Respir. J.* 1994; **7**: 1019–22.
26 Pastis NJ, Nietert PJ, Silvestri GA. Variation in training for interventional pulmonary procedures among US pulmonary/critical care fellowships: a survey of fellowship directors. *Chest* 2005; **127**: 1614–21.
27 Hansen M, Faurschou P, Clementsen P. Medical thoracoscopy, results and complications in 146 patients: a retrospective study. *Respir. Med.* 1998; **92**: 228–32.
28 Lee P, Hsu A, Lo C *et al*. Prospective evaluation of flex-rigid pleuroscopy for indeterminate pleural effusion: accuracy, safety and outcome. *Respirology* 2007; **12**: 881–6.
29 Loddenkemper R, Grooser H, Gabler A *et al*. Prospective evaluation of biopsy methods in the diagnosis of malignant pleural effusions. Inpatient comparison between pleural fluid cytology, blind needle biopsy and thoracoscopy. *Am. Rev. Respir. Dis.* 1983; **127**(Suppl. 4): 114.
30 Sakuraba M, Masuda K, Hebisawa A *et al*. Diagnostic value of thoracoscopic pleural biopsy for pleurisy under local anaesthesia. *Aust. N Z J. Surg.* 2006; **76**: 722–4.
31 Kirsch CM, Kroe DM, Jensen WA *et al*. A modified Abrams needle biopsy technique. *Chest* 1995; **108**: 982–6.
32 McLeod DT, Ternouth I, Nkanza N. Comparison of the Tru-cut biopsy needle with the Abrams punch for pleural biopsy. *Thorax* 1989; **44**: 794–6.
33 Tomlinson JR. Invasive procedures in the diagnosis of pleural disease. *Semin. Respir. Med.* 1987; **9**: 30–60.
34 Prakash UB, Reiman HM. Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: analysis of 414 cases. *Mayo Clin. Proc.* 1985; **60**: 158–64.
35 Seibert AF, Haynes J Jr, Middleton R *et al*. Tuberculous pleural effusion. Twenty-year experience. *Chest* 1991; **99**: 883–6.
36 Jiménez D, Pérez-Rodriguez E, Diaz G *et al*. Determining the optimal number of specimens to obtain with needle biopsy of the pleura. *Respir. Med.* 2002; **96**: 14–17.
37 Valdés L, Alvarez D, San José E *et al*. Value of adenosine deaminase in the diagnosis of tuberculous pleural effusions in young patients in a region of high prevalence of tuberculosis. *Thorax* 1995; **50**: 600–3.
38 Valdés L, Alvarez D, San José E *et al*. Tuberculous pleurisy: a study of 254 patients. *Arch. Intern. Med.* 1998; **158**: 2017–21.
39 Kirsch CM, Kroe DM, Azzi RL *et al*. The optimal number of pleural biopsy specimens for a diagnosis of tuberculous pleurisy. *Chest* 1997; **112**: 702–6.
40 Koegelenberg CFN, Diacon AH, Bolliger CT. Transthoracic ultrasound of the chest wall, pleura, and the peripheral lung. In: Bollger CT, Herth FJF, Mayo PH *et al*. (eds) *Progress in Respiratory Research. Clinical Chest Ultrasound*. Karger, Basel, 2009; 22–33.

41 Beckh S, Bolcskei PL, Lessnau KD. Real-time chest ultrasonography: a comprehensive review for the pulmonologist. *Chest* 2002; **122**: 1759–73.
42 Diacon AH, Theron J, Bolliger CT. Transthoracic ultrasound for the pulmonologist. *Curr. Opin. Pulm. Med.* 2005; **11**: 307–12.
43 Mayo PH, Doelken P. Pleural ultrasonography. *Clin. Chest Med.* 2006; **27**: 215–17.
44 Evans AL, Gleeson FV. Radiology in pleural disease: state of the art. *Respirology* 2004; **9**: 300–12.
45 Qureshi NR, Rahman NM, Gleeson FV. Thoracic ultrasound in the diagnosis of malignant pleural effusion. *Thorax* 2009; **64**: 139–43.
46 Chang BD, Yang PC, Luh KT *et al*. Ultrasound-guided pleural biopsy with Tru-Cut needle. *Chest* 1991; **100**: 1328–33.
47 Diacon AH, Schuurmans MM, Theron J *et al*. Safety and yield of ultrasound assisted transthoracic biopsy performed by pulmonologists. *Respiration* 2004; **71**: 519–22.
48 Harris A, O'Driscoll BR, Turkington PM. Survey of major complications of intercostal chest drain insertion in the UK. *Postgrad. Med. J.* 2010; **86**: 68–72.
49 Kaplan A, Mayo PH. Echocardiography performed by the pulmonary/critical care medicine physician. *Chest* 2009; **135**: 529–35.
50 Mayo PH, Beaulieu Y, Doelken P. American College of Chest Physicians/La Société de Réanimation de Langue Française statement on competence in critical care ultrasonography. *Chest* 2009; **135**: 1050–60.
51 Maskell NA, Gleeson FV, Davies RJ. Standard pleural biopsy versus CT-guided cutting-needle biopsy for diagnosis of malignant disease in pleural effusions: a randomised controlled trial. *Lancet* 2003; **361**: 1326–30.
52 Adams RF, Gleeson FV. Percutaneous image-guided cutting needle biopsy of the pleura in the diagnosis of malignant mesothelioma. *Chest* 2001; **120**: 1798–802.
53 Metintas M, Ak G, Dundar E *et al*. Medical thoracoscopy vs CT scan-guided Abrams pleural needle biopsy for diagnosis of patients with pleural effusions: a randomized, controlled trial. *Chest* 2010; **137**: 1362–8.
54 Diacon AH, Theron J, Schubert P *et al*. Ultrasound-assisted transthoracic biopsy: fine-needle aspiration or cutting-needle biopsy? *Eur. Respir. J.* 2007; **29**: 357–62.
55 Koegelenberg CF, Bolliger CT, Plekker D *et al*. Diagnostic yield and safety of ultrasound-assisted biopsies in superior vena cava syndrome. *Eur. Respir. J.* 2009; **33**: 1389–95.
56 Koegelenberg CFN, Bolliger CT, Irusen EM *et al*. The diagnostic yield and safety of ultrasound-assisted transthoracic fine needle aspiration of drowned lung. *Respiration* 2011; **81**: 26–31.
57 Koegelenberg CF, Diacon AH, Irusen EM *et al*. The diagnostic yield and safety of ultrasound-assisted biopsy of mediastinal masses. *Respiration* 2011; **81**: 134–41.
58 Schubert P, Wright CA, Louw M *et al*. Ultrasound-Assisted Transthoracic Biopsy: Cells or Section? *Diagn. Cytopathol.* 2005; **33**: 233–7.
59 Detterbeck FC, Boffa DJ, Tanoue LT. The New Lung Cancer Staging System. *Chest* 2009; **136**: 260–71.
60 Tan C, Sedrakyan A, Browne J *et al*. The evidence on the effectiveness of management for malignant pleural effusion: a systematic review. The evidence on the effectiveness of management for malignant pleural effusion: a systematic review. *Eur. J. Cardiothorac. Surg.* 2006; **29**: 829–38.
61 Tschopp JM, Schnyder JM, Astoul P *et al*. Pleurodesis by talc poudrage under simple medical thoracoscopy: an international opinion. *Thorax* 2009; **64**: 273–4.
62 Stefani A, Natali P, Casali C *et al*. Talc poudrage versus talc slurry in the treatment of malignant pleural effusion. A prospective comparative study. *Eur. J. Cardiothorac. Surg.* 2006; **30**: 827–32.
63 Dresler CM, Olak J, Herndon JE *et al*. Phase III intergroup study of talc poudrage vs talc slurry sclerosis for malignant pleural effusion. *Chest* 2005; **127**: 909–15.