Guidelines for radiologically guided lung biopsy

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These guidelines have been developed at the request of the Standards of Care Committee of the British Thoracic Society (BTS) and with the agreement of the Royal College of Radiologists and the British Society of Interventional Radiology, and approval of the Royal College of Pathologists in respect of the pathology recommendations and the Society of Cardiothoracic Surgeons of Great Britain and Ireland.

Lung biopsy is a relatively frequently performed procedure with considerable benefit for patient management but it may, on rare occasions, result in the death of the patient. It is a multidisciplinary procedure involving respiratory physicians, surgeons, and radiologists with an interest in chest diseases.

The aim of the group was to produce formal evidence based guidelines for subsequent use by those referring patients for the procedure and for those performing it.

The areas covered by these guidelines are as follows:

- Indications
- Complications, contraindications and precautions
- Consent
- Technique
- Staffing issues
- Patient information

The following areas are not covered by these guidelines:

- Lesions of the chest wall, pleura and mediastinum
- Bronchoscopic and open lung biopsy

FORMULATION OF GUIDELINES

Validity and grading of recommendations

The criteria for assessing the levels of evidence and grading of recommendations were based on those recommended in the Scottish Intercollegiate Guidelines Network in 1995 using the Agency of Health Care Policy and Research model used in some other BTS guidelines (tables 1 and 2).

It should be noted that there are very few randomised trials comparing the various aspects of lung biopsy and, for that reason, more detailed systems of categorisation such as that of the Scottish Intercollegiate Guidelines Network published in 2001 were not used.

The papers selected by searching PubMed and Medline were assessed by the members of the working group and decisions on levels of evidence for each paper were made by two or more members. The guidelines were sent for comment to the Royal College of Radiologists, the British Thoracic Society, the British Society of Interventional Radiology, the Royal College of Pathologists, and the Society of Cardiothoracic Surgeons.

Scheduled review of guidelines

As methods of diagnosis and tissue sampling change and new evidence comes to light, the content and evidence base for these guidelines will be reviewed.

TYPES OF LUNG BIOPSY

Percutaneous transthoracic lung biopsy

PTLB is performed with imaging guidance and most frequently by a radiologist. Usually the aim is to diagnose a defined mass. Imaging modalities are fluoroscopy, computed tomography (CT), and ultrasound. Ultrasound is useful only where the tissue mass is in contact with the chest wall since the ultrasound beam does not pass through air and, hence, the aerated lung.

Magnetic resonance imaging (MRI) currently has a limited use because of expense, difficulty accessing the patient within the magnet, the relatively poor visualisation of lung lesions, and difficulties with ferromagnetic instruments within the magnetic field.

Abbreviations: CNB, core needle biopsy; CT, computed tomography; FNA, FNAB, fine needle aspiration biopsy; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; PET, positron emission tomography; PTLB, percutaneous transthoracic lung biopsy; SCLC, small cell lung cancer
Guidelines for radiologically guided lung biopsy

The mortality rate of percutaneous lung biopsy is poorly documented. The literature contains mainly anecdotal reports. Sinner in 1975 reported no deaths in his series of 5300 biopsies but, from his knowledge, he estimated a mortality rate of 0.07%. A further series by Berquist et al reported two deaths in 430 procedures, a rate of 0.47%. Richardson et al performed a postal survey of the UK practice of lung biopsies which achieved a 61% response rate. Based on 5444 biopsies, the mortality rate was estimated at 0.15%. There is probably a tendency to under-report patient death.

**Causes of mortality**

Mortality from PTLB is generally an early event. The causes of mortality include acute massive haemoptysis or pulmonary haemorrhage, pulmonary venous air embolism leading to air within the intracerebral or coronary circulation, and large haemothorax.

**Morbidity**

**Pneumothorax**

The most common complication is pneumothorax which occurs in 0–61% of lung biopsies. Between 3.3% and 15% of all patients will require a chest drain. This large range for pneumothorax reflects both altered risk from the location of the lesion and the increased sensitivity of CT, and potentially ultrasound, to detect very small pneumothoraces which may be overlooked on the chest radiograph.

The risk of pneumothorax is related to the needle passing through aerated lung and increases significantly if the lesion is not abutting the pleura. In one series using CT guided coaxial cutting needle biopsy, the highest number of pneumothoraces occurred when the lesions were subpleural, and were 2 cm or less in depth from the chest wall. Other work has shown that perihilar biopsy is also more likely to cause pneumothoraces because of the distance of lung crossed.

Post biopsy positioning has not been found to decrease the rate of pneumothorax. Injection of autologous blood through a coaxial needle is not commonly practised and is of uncertain benefit.

Bilateral pneumothoraces have been reported in occasional patients with either unexpected lung herniation across the midline or incomplete fusion of the pleura, as well as following heart lung transplantation where there is a single pleural cavity.

**Intrapulmonary haemorrhage**

Intrapulmonary haemorrhage may occur with or without haemoptysis. Intrapulmonary haemorrhage is recorded in 5–16.9% of patients and haemoptysis in 1.25–5%. Lesion depth has been identified as the most important risk factor for haemorrhage, with an increased risk of bleeding in lesions deeper than 2 cm.

**Haemothorax**

The haemothorax rate is around 1.5%. Significant haemorrhage is rare. Haemorrhage may occur from intercostal or internal mammary arteries or veins.

**Other complications**

Case reports are noted of tumour seeding along the needle tract, cardiac tamponade, and of chest infection (pneumonia) being converted to an empyema. Patients are potentially at risk from drugs if they are administered during the procedure.

Co-existing relevant pathology should also be taken into consideration. In line with BTS guidelines on performing bronchoscopy, lung biopsy should not be performed within 6 weeks of a myocardial infarction.

**Table 1** Categories of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of evidence</th>
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<tbody>
<tr>
<td>Ia</td>
<td>Evidence obtained from meta-analysis of randomised controlled trials</td>
</tr>
<tr>
<td>Ib</td>
<td>Evidence obtained from at least one randomised controlled trial</td>
</tr>
<tr>
<td>Ila</td>
<td>Evidence obtained from at least one well designed clinical study</td>
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<tr>
<td>Iib</td>
<td>Evidence obtained from at least one type of well designed quasi-experimental study</td>
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<tr>
<td>IIa</td>
<td>Evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies, and case controlled studies</td>
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<tr>
<td>IIb</td>
<td>Evidence obtained from expert committee reports and/or clinical experiences of respected authorities</td>
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**Table 2** Grading of recommendations

<table>
<thead>
<tr>
<th>Grade</th>
<th>Type of recommendations</th>
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<tbody>
<tr>
<td>A (levels Ia, Ib)</td>
<td>Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation</td>
</tr>
<tr>
<td>B (levels Ia, Iib, IIb, III)</td>
<td>Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation</td>
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<tr>
<td>C (level IV)</td>
<td>Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality</td>
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Summary of recommendations

Mortality and morbidity
- Operators should audit their own practice and calculate their complication rates to inform patients before consent is given.
- Operators should try to achieve the lowest quoted complication rates. These should be similar to, or better than, those from the national survey: pneumothorax (20.5% of biopsies), pneumothorax requiring a chest drain (3.1%), haemoptysis (5.3%), and death (0.15%).

Indications for lung biopsy
- Patients with lesions on the chest radiograph should be discussed in a multidisciplinary meeting with a respiratory physician and radiologist at a minimum. [C]
- Percutaneous transthoracic lung biopsy should be considered in the following [B]:
  - New or enlarging solitary nodule or mass on the chest radiograph which is not amenable to diagnosis by bronchoscopy or CT shows it is unlikely to be accessible by bronchoscopy.
  - Multiple nodules in a patient not known to have malignancy or who has had a prolonged remission or more than one primary malignancy.
  - Persistent focal infiltrates, either single or multiple, for which no diagnosis has been made by sputum or blood culture, serology, or bronchoscopy.
  - Hilar mass. [B]

Contraindications to lung biopsy
- There are relative contraindications to PTLB and the balance of benefit against risk for the procedure should be assessed at a multidisciplinary meeting. [C]

Preoperative investigations: coagulation indices
- Prothrombin time (PT), activated partial thromboplastin time (APTT), and platelet count should be checked before percutaneous lung biopsy. [C]
- Oral anticoagulants should be stopped before a percutaneous lung biopsy in accordance with the published guidelines on perioperative anticoagulation. [C]
- Relative contraindications include:
  - Platelet count <100 000/ml
  - APTT ratio or PT ratio >1.4
  - In these situations a decision to proceed to biopsy should be made following discussion with a haematologist. [C]

Preoperative investigations: pulmonary function
- The balance of benefit against risk for PTLB should be assessed by a multidisciplinary team with a respiratory physician and radiologist as a minimum. [C]
- All patients should have recent pulmonary function tests (spirometry) before needle biopsy. [C]
- Patients with FEV1 <35% predicted should not undergo needle biopsy without further assessment by the multidisciplinary team. [C]

Preoperative investigations: chest radiography and CT scanning
- PT, APTT, platelet count, and pulmonary function tests are desirable before needle biopsy. In patients with risk factors for bleeding, PT, APTT and platelet count are required. [C]
- Recent chest radiographs and CT scans and all previous radiological investigations should be reviewed to decide if a biopsy is appropriate and must be available to the radiologist at the time of the biopsy. [C]
- CT should preferably be performed before bronchoscopy. [B]
- Repeat imaging should be performed if there has been significant change in the patient’s clinical condition, if there has been significant delay before the biopsy is performed, or if the localising CT scan at the time of the biopsy shows significant change. [C]

Biopsy procedure
- All patients should have a diagnostic CT scan of the chest and liver before a biopsy procedure. [B]
- Specific recommendations for the choice of biopsy imaging depend on the operator but, when possible, ultrasound should be used. [B]
- The decision on the type of needle used will be made by the operator and will be dependent on operator experience, available cytological support, and the position of the lesion. [B]
- Sufficient passes should be made to obtain diagnostic material (see later). [B]
Recommendations

- Operators should audit their own practice and calculate their complication rates to inform patients before consent is given.
- Operators should try to achieve the lowest quoted complication rates. These should be similar to, or better than, those from the national survey: pneumothorax (20.5% of biopsies), pneumothorax requiring a chest drain (3.1%), haemoptysis (5.3%), and death (0.15%).

INDICATIONS FOR LUNG BIOPSY

The indications for PTLB have altered substantially since the technique was developed, reflecting changes in many areas including needle technology, imaging techniques, and immunohistochemistry and cytochemistry. Further advances, particularly in positron emission tomography (PET), may alter the indications for needle biopsy and, in particular, the management of the solitary nodule.

PTLB can be used to investigate any solid or cystic lesion between the chest wall and the mediastinum which is not visible at bronchoscopy, provided it is accessible to the needle. FNAB, providing samples for cytology, can accurately diagnose malignancy, while the more recent development of cutting needles (CNB), providing histological material, has enabled a firm diagnosis of benign lesions to be made, thus improving overall diagnostic accuracy.

Although PTLB can be used to investigate interstitial lung disease (particularly in patients with focal areas of consolidation such as cryptogenic organising pneumonia), transbronchial and thoracoscopic or open lung biopsy are preferred to minimise the risk of pneumothorax and to obtain larger and more representative diagnostic samples, particularly by open lung biopsy.

Patients with lesions on the chest radiograph which require a diagnosis should be discussed with a respiratory
physician and radiologist as a minimum, preferably in a multidisciplinary meeting.24 35 Clinical and radiographic information can be reviewed and the likely diagnosis considered along with the best approach to making a diagnosis. The risks and benefits of the procedure and knowledge of the wishes of the patient will enable the management decision to be tailored to the needs of the individual.

The indications for PTLB include:

- A new or enlarging solitary nodule or mass on the chest radiograph which is not amenable to diagnosis by bronchoscopy, or CT shows it is unlikely to be accessible by bronchoscopy, when a decision has been made by the multidisciplinary team that a tissue diagnosis should be obtained.
- Multiple nodules in a patient not known to have malignancy or who has had a prolonged remission.
- Persistent infiltrates, either single or multiple, for which no diagnosis has been made by sputum or blood culture, serology or bronchoscopy.
- Hilar mass following negative bronchoscopy.

New or enlarging solitary nodule or mass on chest radiography

The most common indication for PTLB is to investigate the solitary parenchymal nodule or mass on the chest radiograph. The next radiological investigation is CT to characterise the lesion and show associated hilar or mediastinal lymphadenopathy or evidence of other abnormalities suitable for biopsy. This enables the radiologist and respiratory physician, preferably with the thoracic surgeon, to decide the most likely diagnosis and the best management thereof, avoiding bronchoscopy in those patients where CT suggests that a tissue diagnosis is unlikely to be obtained by this method.36–40 The likelihood of malignancy increases with the size of the lesion, patient age, a smoking history, and a history of haemoptysis.41–43 If the initial probability of malignancy is high, many surgeons feel that the correct approach in patients with isolated small nodules who are otherwise fit and agreeable to surgery is to carry out a diagnostic resection.44 45 Distinguishing between small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) is not an issue with these small early lesions as there is evidence of cure of SCLC in these circumstances.46 Thoracic surgery has a significant mortality (2–3% for lobectomy) and morbidity, particularly 10% of patients in all age groups.51 Accurate diagnosis of benign lesions using CNB has reduced the need for diagnostic surgery by up to 50%.29 31 44 The advent of PET scanning may also be helpful in determining the need for surgery, as a lesion which strongly takes up 18F-fluorodeoxyglucose is more likely to be malignant than benign.52–54 Patients who decline surgery or who are inoperable may be offered radiotherapy, chemotherapy, or combination treatment, but this still requires the diagnosis to be established wherever possible.

Biopsy samples can be safely taken from masses abutting the pleura under ultrasound guidance using a cutting needle which ensures an accurate diagnosis, even in patients with limited lung function, as the risk of pneumothorax is negligible when aerated lung tissue is not traversed during the procedure.55 56 Cavitating lesions are usually caused by tumours or abscesses. The clinical picture will often distinguish between these two diagnoses, but needle aspiration is helpful in providing material for bacteriology and to guide treatment in the latter.55 57

Multiple nodules in a patient not known to have malignancy or who has had a prolonged remission

Slowly enlarging or new multiple nodules on the chest radiograph may occur in a number of benign conditions including rheumatoid nodules, granulomatous diseases, Wegener’s granulomatosis, or infection (particularly fungal) in the immunocompromised patient and can be diagnosed by core biopsy.56–65 Multiple lesions of varying size are most likely to be malignant and, if the patient is known to have a primary tumour already, biopsy is unlikely to alter the presumed diagnosis of metastases.66 If there has been a prolonged remission of a tumour following initial treatment or the patient has a history of more than one primary malignancy, oncologists may want confirmation of recurrence to plan further treatment.

Persistent focal infiltrates

PTLB may be used to obtain samples of lung tissue when infiltrates persist on the chest radiograph and a diagnosis has not been made on cultures of sputum, blood, or lung lavage or other diagnostic techniques. Tissue should be cultured because, although the yield is small, the investigation is inexpensive and may increase diagnostic accuracy or guide treatment, particularly in patients who are immunosuppressed.67 68 A lesion of this type which is not resolving may be a bronchoalveolar cell carcinoma.

Hilar mass following negative bronchoscopy

Hilar masses can be accurately diagnosed by needle aspiration under CT guidance, depending on the experience of the operator for smaller lesions.51–53 70–72 Earlier work using fluoroscopic guidance for needle aspiration showed that lesions at the hilum could be diagnosed with similar accuracy to peripheral lesions and that the success of the procedure was related to the size of the lesion.

Recommendations

- Patients with lesions on the chest radiograph should be discussed in a multidisciplinary meeting with a respiratory physician and radiologist at a minimum. [C]
- Percutaneous transthoracic lung biopsy should be considered in the following [B]:
  - New or enlarging solitary nodule or mass on the chest radiograph which is not amenable to diagnosis by bronchoscopy or CT shows it is unlikely to be accessible by bronchoscopy.
  - Multiple nodules in a patient not known to have malignancy or who has had a prolonged remission or more than one primary malignancy.
  - Persistent focal infiltrates, either single or multiple, for which no diagnosis has been made by sputum or blood culture, serology, or bronchoscopy.
  - Hilar mass. [B]

CONTRAINDICATIONS TO LUNG BIOPSY

There are several relative contraindications to PTLB. Patients should not undergo the procedure without adequate pre-biopsy assessment or if they plan to fly within 6 weeks of the procedure. The risk is increased by abnormalities of lung function, respiratory failure (including mechanical ventilation), arterial and venous pulmonary hypertension, and coagulation abnormalities (see preoperative investigations).35 The balance of benefit against risk for the procedure should
be assessed at a multidisciplinary meeting. The role of needle biopsy is to establish a diagnosis to enable appropriate treatment to be given. Failure to obtain informed consent from a patient is a contraindication, and management should be reconsidered in these circumstances.

Previous pneumonectomy is an exclusion criterion for needle biopsy in many series. However, if the lesion in the remaining lung is pleural based and is accessible without traversing any lung tissue, it may not be considered an absolute contraindication as the risk of pneumothorax is low. 24

Mechanical ventilation will make the process of biopsy more difficult but, if the lesion is visualised by ultrasound, it may be undertaken. Biopsy samples of intrapulmonary lesions can be taken by experienced operators under CT guidance while ventilation is controlled during the procedure, but this is difficult because of the limited space as well as access of medical and nursing staff during radiation exposure.

Vascular lesions, either aneurysms or arteriovenous malformations, should have been identified by CT and should not be subjected to biopsy. This diagnosis should be considered before the biopsy procedure at a multidisciplinary meeting. Biopsy of an unsuspected vascular lesion may lead to an increased risk of haemorrhage.

Pulmonary arterial and venous hypertension may increase the risk of haemorrhage but there are no data to support this. If the hypertension is significant, this would be a contraindication to surgery; the risk of the diagnostic procedure needs to be considered against the benefit of having an answer on patient management.

The uncooperative patient

It is essential that the patient is cooperative during percutaneous lung biopsy. A sudden or unexpected movement while the biopsy needle is in the lung parenchyma may lead to a tear and subsequent intrapulmonary bleeding and/or pneumothorax. If the patient is frightened despite careful explanation and reassurance, an anxiolytic drug may be helpful. If the patient remains uncooperative after these measures, the management should be reconsidered.

Recommendations

- There are relative contraindications to PTLB and the balance of benefit against risk for the procedure should be assessed at a multidisciplinary meeting. [C]

Abnormal coagulation indices and lung function

These are discussed in more detail in the next section.

PREOPERATIVE INVESTIGATIONS

Coagulation indices

Fortunately, significant bleeding rarely complicates percutaneous lung biopsies. Quoted complication rates for local pulmonary haemorrhage range between 5% and 16.9% and haemoptysis between 1.25% and 5%. 73 Deaths from bleeding following percutaneous lung biopsy are reported although fewer than 10 cases have been described. 71-73

Certain patient groups are known to be at increased risk of bleeding. These include those who have haemophilia, pulmonary hypertension, liver disease, coagulation disorders or thrombocytopenia. 76 Patients with haemophilia should be given DDAVP (desmopressin acetate).

Although complication rates for pneumothorax are similar for FNAB and automated biopsy devices, a slightly higher, but not significant, incidence of pulmonary bleeding with haemoptysis is reported in series using automated biopsy devices. 79

There is no specific guidance in the literature regarding the value of routine clotting studies before performing percutaneous lung biopsy. Many studies have found that preoperative screening for coagulopathies not suspected on the basis of detailed clinical examinations is unnecessary. 79-81 In these situations, however, operations and biopsies are performed under direct vision. This is not the case in percutaneous lung biopsy. In the absence of specific evidence, routine clotting studies are justifiable and should be performed in order to minimise the risk of the procedure. In accordance with the British Thoracic Society guidelines on diagnostic flexible bronchoscopy it is therefore recommended that the platelet count, prothrombin time (PT), and activated partial thromboplastin time (APTT) should be checked before performing percutaneous lung biopsies. 82

There is no information as to what constitutes a “safe” level for clotting before the biopsy procedure. In transbronchial biopsies platelet counts below 50 000/ml have been shown to be associated with a significant risk of bleeding. 83 Opinion in the world literature suggests that a PT or international normalised ratio (INR) or APTT ratio of more than 1.4 and a platelet count below 100 000/ml should be relative contraindications to percutaneous lung biopsy. 84 Haematological advice in these circumstances should be sought before the biopsy is performed. In patients with a haemoglobin level of less than 10 g/dl the procedure should be carefully considered, although there is no evidence to support a particular figure and there are reports of successful procedures in anaemic patients.

If the patient is taking oral anticoagulants, published guidelines for the management of anticoagulation in the perioperative period are relevant. 85 These state that oral anticoagulation should be stopped before surgery and, depending on the thrombotic risk of the condition for which the patient is receiving anticoagulant therapy, the INR can be measured and, if necessary, heparin instituted once the INR is below the therapeutic range. It is worth noting that, after warfarin is stopped, it takes 4 days typically for the INR to reach 1.5 and therefore oral anticoagulants should be stopped at least 4 days before a percutaneous lung biopsy is performed. 85 There is no evidence to support stopping antiplatelet drugs before the procedure.

Recommendations

- Prothrombin time (PT), activated partial thromboplastin time (APTT), and platelet count should be checked before percutaneous lung biopsy. [C]

- Oral anticoagulants should be stopped before a percutaneous lung biopsy in accordance with the published guidelines on perioperative anticoagulation. [C]

- Relative contraindications include:
  - Platelet count <100 000/ml
  - APTT ratio or PT ratio >1.4
  - In these situations a decision to proceed to biopsy should be made following discussion with a haematologist. [C]

Pulmonary function

The most common complication of lung biopsy is a pneumothorax, and it is essential to assess whether the patient can safely withstand the procedure, particularly as many patients being investigated in this way will have smoking related lung disease in addition to any changes in lung function caused by the lesion under investigation. Measurement of lung function is used to assess this and also suitability for surgery if appropriate. Data from several
retrospective studies using spirometry are conflicting. Several studies found no relation between forced expiratory volume in 1 second (FEV₁) and the incidence of pneumothorax, while both Poe et al. and Vitulo et al. suggested that this was related to the presence of hyperinflation. However, Anderson et al. and Fish et al. found that patients with airflow obstruction were significantly more likely to require tube drainage if a pneumothorax occurred.

Garcia-Rio et al. carried out a prospective study of 51 patients and were able to show that the mean FEV₁ % predicted, FVC (forced vital capacity) % predicted, and the FEV₁/FVC ratio were significantly lower in patients who developed pneumothoraces, the closest correlation being with FEV₁ % predicted. They estimated that the risk of a pneumothorax was 35.6% in patients with an FEV₁ reduced to 70% predicted. No figures are suggested for the minimum FEV₁, at which the procedure is contraindicated, although most practising physicians and radiologists use a cut-off of 1 litre. However, this could overestimate the risk of severe respiratory embarrassment with a large pneumothorax in a small patient while underestimating the risk in a very tall man. It is therefore suggested that the percentage predicted should be used. An absolute figure of an FEV₁ of 1 litre is approximately 35% predicted for a white man of 70 years and 1.73 metres height. This approach is in line with that adopted in the recently published guidelines on the selection of patients with lung cancer for surgery, where an absolute figure of a minimum FEV₁ of 1.5 litres is suggested for lobectomy but a figure including percentage predicted is used for borderline cases. In cases of poorer lung function where the risk of pneumothorax is less—for instance, where the lesion abuts the pleura—biopsy may be possible.

Patients admitted to hospital as emergencies who are found to have an incidental lesion on the chest radiograph should have their underlying condition stabilised before referral to a multidisciplinary team consisting of a respiratory physician and a radiologist as a minimum. Patients with respiratory failure, in particular, should not undergo a biopsy procedure without careful assessment.

**Recommendations**

- The balance of benefit against risk for PTLB should be assessed by a multidisciplinary team with a respiratory physician and radiologist as a minimum. [C]
- All patients should have recent pulmonary function tests (spirometry) before needle biopsy. [C]
- Patients with FEV₁ <35% predicted should not undergo needle biopsy without further assessment by the multidisciplinary team. [C]

**Chest radiography**

A chest radiograph will usually have been performed at the initial assessment of the patient. Alternatively, the lesion may have been found incidentally on a chest radiograph or CT scan performed for some other reason. All imaging should be reviewed at a multidisciplinary meeting to decide if a biopsy is appropriate. If there is anything to suggest that the patient’s condition has changed at the immediate pre-biopsy clinical assessment, the patient should have a repeat chest radiograph. If there has been a substantial change such as new collapse or consolidation, it may be necessary to reconsider if the biopsy should be performed.

With the current emphasis on speedy investigation, the chest radiograph is unlikely to be significantly out of date and the lesion will be further assessed at the time of biopsy.

**Computed tomography (CT)**

Most patients thought likely to have a lung carcinoma will require imaging with CT to determine the stage of their disease and to help determine any appropriate treatment such as resection, radiotherapy, or palliative interventions. There are advantages in performing a CT scan before any further intervention in patients thought likely to have a lung carcinoma. A CT scan performed before fibreoptic bronchoscopy (FOB) has been shown to increase the diagnostic yield of FOB by directing the bronchoscopist to the site most likely to give a diagnosis. Bronchoscopy and biopsy itself may alter the appearance of the CT scan as a result of local haemorrhage. It can also show carcinomas not visible on bronchoscopy, and may direct the clinician to a more appropriate method to obtain histological specimens such as mediastinoscopy or biopsy of a lesion outside the chest. There is no need to perform routine FOB in patients thought to have resectable disease in whom tissue has been obtained by CT biopsy with no preoperative FOB.

A staging CT scan may be performed before biopsy on a separate occasion. Alternatively, the patient may attend for a staging CT scan and the decision to proceed directly to biopsy may be made while the patient remains in the CT department or even on the CT table. The second approach may have some advantages in terms of patient convenience as only one visit to the department is required, but special care with this approach is necessary, particularly with patient consent. In addition, there are organisational problems, particularly in units where care after the biopsy must be organised in advance.

**Delay since investigation**

At the time of biopsy a CT chest scan is performed to assess the best site to biopsy, the most appropriate route, and therefore the most appropriate patient position. This may be a limited unenhanced study to localise the mass. If there has been a significant delay between the original staging CT scan and the biopsy procedure, there is a risk that the tumour may have grown and increased in stage. It is imperative that the radiologist performing the procedure is fully aware of all previous investigations and so can compare the imaging at the time of the biopsy with previous imaging and consider if a repeat staging CT scan may be necessary. In addition, the reason for the biopsy and its relevance to the patient’s management must be clear so that any change in the patient’s condition or imaging can be taken into account to decide if the biopsy is still appropriate.

**Recommendations**

- PT, APTT, platelet count, and pulmonary function tests are desirable before needle biopsy. In patients with risk factors for bleeding, PT, APTT and platelet count are required. [C]
- Recent chest radiographs and CT scans and all previous radiological investigations should be reviewed to decide if a biopsy is appropriate and must be available to the radiologist at the time of the biopsy. [C]
- CT should preferably be performed before bronchoscopy. [B]
- Repeat imaging should be performed if there has been significant change in the patient’s clinical condition, if there has been significant delay before the biopsy is performed, or if the localising CT scan at the time of the biopsy shows significant change. [C]
THE BIOPSY PROCEDURE

Protective clothing
The procedure should be performed using standard universal precautions. Protective gloves should be worn. If possible, non-powdered latex gloves or non-latex gloves should be used.144

Patient positioning and instruction
The patient should be positioned prone or supine dependent on the skin entry site chosen. Biopsy specimens should not be taken with the patient in a seated position because of the potential small risk of air embolus105 or fainting during the procedure. It is difficult for patients to maintain a consistent decubitus position and this should be avoided if possible. The breathing technique required during the procedure should be explained to the patient and practised beforehand. Deep breaths and coughing should be avoided during the biopsy procedure.

Imaging techniques
The decision on the most appropriate imaging modality used for biopsy is made on reviewing the pre-biopsy CT scan. Fluoroscopy, CT, and ultrasound may all be used for imaging guidance, and familiarity of the operator with all three modalities is helpful in choosing the most appropriate technique.35 76

The imaging technique chosen is dependent on the size and position of the lesion, its visibility on plain radiographs, its relation to other structures such as fissures, vessels and bullae, equipment availability, and operator preference.15 78 106 107

Whenever possible, PTLB should be performed under ultrasound guidance as this is the safest, quickest, and least expensive method.106 For lesions not suitable for ultrasound guided biopsy, CT is now the preferred imaging modality.20 31 35 78 106

Fluoroscopic guidance may also be used for larger lesions visualised on a posteroanterior and lateral chest radiograph.109 110

If the biopsy is to be performed using fluoroscopy, the best results are usually obtained with C-arm screening (or, if available, bi-plane) with vertical or horizontal needle insertion.106 109 110 The correct depth of needle insertion may be estimated from the pre-biopsy CT scan. If using ultrasound, needle entry into the lesion should be directly visualised and biopsy sites away from identified areas of cavitation or necrosis chosen.107 131–133

If using CT, a needle entry site which avoids crossing fissures, bullae and large vessels should be chosen if possible to reduce the incidence of pneumothorax and haemorrhage.

Biopsy technique
The skin entry site should be sterilised with standardised antiseptic solution and the cutaneous and subcutaneous tissue infiltrated with lidocaine (lignocaine) up to a maximum dose of 20 ml of a 2% solution. The pleura should not be anaesthetised directly as this increases the risk of pneumothorax before the biopsy itself.

When the biopsy needle is being advanced or withdrawn the patient should suspend respiration. Most patients find it more comfortable to hold their breath after a submaximal inspiration. For lesions at the lung bases a breath held on gentle expiration may make the biopsy procedure easier. Wherever possible a needle entry site immediately cephalad to a rib should be chosen to avoid intercostal vessel puncture.114 Care should be taken to avoid the internal mammary vessels if the biopsy is performed adjacent to the central cartilages and sternum.115

In all instances the biopsy needle should be advanced or withdrawn only during suspended respiration. The patient may breathe gently with the needle in place. If an aspiration biopsy is performed, the central stylet is removed and a 10 ml syringe attached. Suction should then be applied while rotating and moving the needle to and fro during suspended respiration.114 117

Instillation of autologous blood along the needle track has been reported to be of benefit in some reports but is not commonly used and its routine use is probably not warranted.118–120

A coaxial technique may be used to allow multiple passes and to reduce the number of pleural punctures.20 75

If a CNB is performed, it is important to confirm before the procedure that either the tip of the needle remains within the lesion once fired or stops in a safe place.

Type of needle and number of passes
The number of passes needed per procedure has not been defined. Most operators perform at least two. Variables to consider are: the difficulty of the procedure, complications arising from each biopsy, the quality of the specimen obtained, the characteristics of the lesion biopsied, and the need for specimens for cytological, histological and microbiological examination. The presence of an on-site cytologist or technician may reduce the number of passes required.120–125

When deciding whether to use FNAB or a cutting needle biopsy (CNB), it is important to be aware of the accuracy of the technique as well as its complications.

Ideally, the technique must not only be able to diagnose malignancy but also to make a definite diagnosis if the lesion is benign. Different populations have different ratios of benign to malignant disease and this can affect reported positive and negative predicted values.126

FNAB has an accuracy of up to 95% for malignant lesions127 but the yield for benign lesions is lower (10–50%).32 128–131 Cytology is reported to be less reliable than histology in determining the cell type in malignant lesions,38 129 132 although Stewart and Stewart133 were able to diagnose correctly small and large cell carcinomas in their series.

There is wide variation in reported diagnostic accuracies of FNAB between different institutions, ranging from 64% to 97%.10 134 A high diagnostic accuracy is best achieved with large nodules106–108 and a cytopathologist present to evaluate the adequacy of the specimens.106 A cytopathologist is not available in many centres and this factor may persuade the operator to use a cutting needle, particularly for small nodules.11 80 The high diagnostic figures reported from some American studies may be achieved after repeated biopsies over a short period (2 or 3 hours) rather than a single episode.

Several recent studies have advocated the use of 18 and 20 gauge cutting needles as well as coaxial techniques to improve the diagnostic yield and have achieved diagnostic accuracies for malignancy of 74–95%.9 137 138 Others19 20 have found the diagnostic yield for malignancy with CNB to be lower than with FNAB. Charig and Phillips135 found the diagnostic accuracy of CNB to be similar to FNAB with an on-site cytopathologist. Their accuracy was in line with those reported from other core biopsy studies.

Using a 21 gauge CNB needle and frozen section, Stewart and Stewart133 achieved a specific diagnosis in 77% of benign lesions; in other studies CNB improved the diagnostic yield compared with cytology from 10% to 40%128 and from 16.7% to 81.7%.12 The reported specific diagnosis in cases of benign disease varies from 78.3%11 12 to 91%,9 although this may reflect the local populations.

The false negative results for malignancy may be due to a variety of factors including the patient’s inability to cooperate, overlying bone which may contribute to missing the lesion completely, obtaining only necrotic tissue, or sampling pneumonitis distal to an obstructing lesion.92 136 These factors
are the same irrespective of the choice of needle, but the false negative rate has been shown to be significantly lower with cutting needles.\(^{100}\)

False positive rates of 0.8\% have been reported with FNAB\(^{104}\) but no false positive cases have been reported using CNB.

Complications

Historically, cutting needles have been associated with a relatively high incidence of complications but many of these data are based on large calibre, non-automated needles using fluoroscopic guidance. Recent studies using small gauge cutting needles have shown complication rates comparable to, or only slightly higher than, those using FNAB.\(^{70\ 101}\) The most common complication following lung biopsy is pneumothorax, with reported rates of 0–61\% for FNAB and 26–54\% for CNB, requiring chest drain insertion in 1.6–18\% and 3.3–15\% of cases, respectively.\(^{7\ 13}\) However, the pneumothorax rate is negligible if the lesion biopsied is peripheral and abuts the pleural surface.\(^{77}\)

There is no correlation between the size or type of needle and the incidence of pneumothorax, although there is a non-significant trend towards increased haemorrhagic complications with cutting needles.\(^{11\ 140\ 142\ 144}\) Reports show that there is no correlation between the number of passes made with the biopsy needle or chest drain placement and the rates of pneumothorax.\(^{11\ 140\ 142\ 144}\) Although this is counterintuitive to most operators’ experience.

In conclusion, the literature indicates that cutting needles have the same sensitivity in the diagnosis of malignancy as FNAB with an on-site cytopathologist (see later), are better able to produce a specific benign diagnosis, have a significantly lower false negative rate and, by providing a histological core, should have a negligible false positive rate. The complication rate is not associated with needle type or size.

Recommendations

- All patients should have a diagnostic CT scan of the chest and liver before a biopsy procedure. [B]
- Specific recommendations for the choice of biopsy imaging depend on the operator but, when possible, ultrasound should be used. [B]
- The decision on the type of needle used will be made by the operator and will be dependent on operator experience, available cytological support, and the position of the lesion. [B]
- Sufficient passes should be made to obtain diagnostic material (see later). [B]

SEDATION

The cooperation of the patient is paramount during the biopsy procedure, particularly in suspending respiration. As such, virtually all biopsies should be performed without sedation. Adequate explanation before the procedure and adequate local anaesthesia during the procedure renders sedation unnecessary for the majority of patients. An oral anxiolytic drug can occasionally be helpful.

Recommendation

- Biopsies should be performed without sedation whenever possible. [C]

INFORMED CONSENT

Informed consent should be obtained in writing before the biopsy procedure in accordance with individual hospital policies. Verbal and understandable written patient information before diagnostic procedures improves the patient’s tolerance of the procedure, as has been shown in bronchoscopy.\(^{145\ 146}\)

Valid consent as defined by the Department of Health\(^{147}\) ‘must be given voluntarily by an appropriately informed person who has the capacity to consent to the intervention in question. Acquiescence where the person does not know what the intervention entails is not ‘consent’’. The capacity of the patient to give consent and the circumstances in which it should be given are also set out in the document. Sufficient information should be provided as to the nature and purpose of the procedure and ‘any misrepresentation of these elements will invalidate consent’.

In considering what information to provide, the health professional should try to ensure that the patient is able to make a balanced judgement on whether to give or withhold consent.

Specific risks to be mentioned

From the above it can be concluded that the common complications such as pneumothorax with, for example, the possibility of chest drainage and haemoptysis should be discussed and the local complication rates for these problems mentioned. Death is extremely uncommon as a consequence of lung biopsy and its inclusion in the discussion of the procedure may be regarded as likely to cause unnecessary anxiety to the patient, but a complete explanation of all risks is advocated by the General Medical Council.\(^{148}\)

The NHS Litigation Authority has published some standards aimed at managing clinical risk.\(^{149}\) These state that, before starting any treatment, doctors must ensure that they have established:

- what the patient wants to know;
- what the patient ought to know;
- that the patient understands the information which has been given;
- that the patient consents to the treatment;
- proposals for treatment should be supported by written information.

Who should obtain consent?

The clinician performing the investigation is responsible for ensuring that the patient has given valid consent before treatment begins. The task of seeking consent may be delegated to another health professional provided that professional is suitably trained and qualified.\(^{147}\)

The physician or surgeon who is looking after the patient should explain how the biopsy fits into the overall management and discuss the alternatives. These might range from doing nothing to excision biopsy. Most lung biopsies will be performed by radiologists who will be in a less appropriate position to do this.

The patient should receive an appropriately written pamphlet either at the time of discussion of options in the clinic or with the appointment. In some units it is proposed that the patient signs each part of the information sheet to show that they have read it.

The operator performing the biopsy will then be able to deal with any last minute questions and obtain written consent. Patients should not be expected to make up their mind about the biopsy when they arrive for the procedure as there is nearly always an interval of several days from the initial suggestion of the biopsy to the actual event.

The patient should understand:

- the nature of the proposed procedure;
- the reason for the procedure;
- the benefits of the procedure;
• the risks and complications;
• alternatives to the procedure (including an assessment of the relative risk/benefit ratios);
• the nature of the anaesthetic to be employed and the imaging modality.

Patient information
It has been strongly recommended by several bodies that it is good practice to provide written information to patients. Various pamphlets are available and these can be used directly or adapted to local circumstances. The Royal College of Radiologists produces a series for several interventional procedures which were developed with the help of patient representatives. Examples of a patient information sheet and biopsy request proforma are given in Appendices 1 and 2. Patient understanding and retention of the risks can be increased by encouraging them to recite the procedure risks before the biopsy.

Recommendations
• Written information should be given to all patients before the procedure. [C]
• Informed consent should be obtained in a written form from all patients. [C]

STAFFING ISSUES
All interventional procedures require the involvement of a team to ensure patient comfort and safety and the technical success of the procedure. Lung biopsy has not been addressed specifically, but two reviews of interventional procedures which were developed with the help of patient representatives, and the Royal College of Radiologists (RCR) and the Royal College of Nursing (RCN). NCEPOD indicates that:

• the patient should be under the care of the appropriate specialist;
• the radiologist should have sufficient expertise to perform the procedure safely and to deal with any complications that may arise;
• there should be sufficient staff to perform the procedure safely;
• monitoring of the patient should be performed during all interventional radiological procedures and this should be done by someone other than the radiologist performing the procedure.

The RCR and RCN also regard the trained radiology nurse as part of the interventional team, both to allay patient anxiety and to ensure careful monitoring of the patient during and immediately after the procedure during recovery. In some circumstances there is also a role for the nurse in the pre-assessment of the patient by instigating or checking investigations according to agreed protocols and pathways. There should be sufficient nurses to fulfil these requirements, although the number may vary according to the activity of the department.

Recommendations
• Staffing should be adequate to enable the patient to be monitored for signs of distress during and after the procedure. [C]

Experience of the operator
Lung biopsies are almost always performed by or under the close supervision of an experienced consultant. The number of pneumothorax complications may decrease with operator experience.

SAMPLE EXAMINATION AT THE TIME OF BIOPSY
Macroscopic appearance
Macroscopic examination (visual inspection) of the biopsy specimen may also enable an estimate of the likelihood of achieving a diagnosis per procedure, and most radiologists perform this practice.

Immediate pathological examination
For FNAB, there have been a number of reports of the value of having a cytologist or cytopathologist present at the time of the biopsy procedure. It is likely that immediate microscopic examination reduces the number of biopsy specimens required to achieve a diagnosis, but for most centres this is not a realistic option.

There are no data on the immediate assessment of core adequacy following CNB, and visual inspection to confirm an adequate tissue sample seems an appropriate practice. It is possible to perform touch preparation imprints on core biopsy specimens to obtain cytology and these appear to offer a similar accuracy to cytological examination.

EXPECTED ACCURACY OF SAMPLING
Over a 10 year period in one US laboratory the annual number of lung FNA samples increased from 13 to 206. As it has gained in popularity, the accuracy of lung FNA has come under scrutiny. Audit has shown that this technique has a higher rate of positivity for malignancy than any form of endoscopic bronchial sampling. Problems, where they exist, revolve mainly around adequacy and, to a lesser extent, accuracy of cell typing, but overall the technique has proved extremely successful and is continually being further refined.

Core CNB does not necessarily confer any significant diagnostic advantage over FNA in the diagnosis of malignancy, although some authors advocate it for benign lesions.

Sensitivity, specificity, and adequacy
Several large studies of the accuracy of lung FNA have been reported and sensitivity, specificity, and adequacy of over 90% are achievable. The false positive rate is usually less than 1%, and the false negative rate is generally under 10%. Diagnostic accuracy is dependent on the size and site of the lesion, operator experience, needle type, choice of biopsy technique, and availability of cytopathology expertise.

Larger lesions are more likely to enable a positive diagnosis of malignancy, although some operators have reported no significant difference in lesions more or less than 2 cm. The reports from lung cancer screening programmes also support the ability to achieve an accurate diagnosis in lesions of less than 1 cm. Accuracy may be further improved by reducing the number of inadequate samples by using new techniques.

Some authors expound on the value of on-site technical assistance with smear preparation and immediate reporting to enhance the adequacy rate.

Cell typing
To provide clinically useful cytology reports in terms of appropriate treatment, accurate cell typing is required. FNA can reliably distinguish small cell carcinoma from non-small cell carcinoma. The highest accuracy is obtained with a diagnosis of small cell carcinoma with lower accuracy for diagnosing squamous carcinoma and adenocarcinoma. Interobserver variation studies suggest that diagnosis by cytology is almost as reproducible as by histology.

Areas of difficulty in cell typing include the distinction of...
small cell carcinoma from poorly differentiated non-keratinising squamous cell carcinoma, small cell carcinoma from malignant lymphoma, and combined small cell carcinoma from non-small cell carcinoma. A59 Accurate cell typing is reported in the setting of a small hospital, A60 but specialist cytopathology training is recommended. A61

Immunocytochemistry
As an aid to diagnosis, immunocytochemistry may be undertaken in a minority of cases. Using a panel of antibodies can assist in identifying metastatic lesions and confirming a pulmonary origin for some adenocarcinomas. A131 Immunocytochemistry of FNA samples can deliver comparable results to those obtained from biopsy material, A167 although it is rarely feasible to perform more than a small panel of immunostains on an FNA sample. Liquid-based cytology has much to recommend it, even for the preparation of smear preparations. A172 Instead of, or as well as, making smears, the sample is washed into a preservative solution. Good fixation is ensured and it is simple to make multiple preparations for immunocytochemistry. It is at least as accurate as smear preparations and, by removal of red cells, the slides are quicker and easier to read. It does, however, involve extra technical work and cost.

“Suspicious for malignancy” and “negative for malignancy” diagnoses
The diagnostic category “suspicious, but not diagnostic of malignancy” usually comprises 4–13% of results. A124 164 This can affect the sensitivity of the test as some calculations of sensitivity include and others exclude these from the malignant category. Certainly, on follow up of FNA samples classified as suspicious, a high proportion of the lesions turn out to be malignant. A164 Long term follow up of patients with negative FNA samples shows a significant proportion finally have a diagnosis of malignancy. A161 172

Factors affecting diagnostic accuracy
The reported diagnostic accuracy rate is dependent on the size of the lesion, A10 26 33 35 78 136 163 164 the location of the lesion, operator experience, A114 type of needle used (FNA or CNB), A20 26 35 78 135 the choice of biopsy technique, A26 35 78 133 136 163 164 the pretest probability of malignancy, A126 174 and the expertise of the reporting pathologist. A174 Larger lesions are more likely to allow a positive diagnosis of malignancy to be made, A10 31 134 136 165 although some operators have reported no significant differences in results between lesions more or less than 2 cm. A134 The reports from lung cancer screening programmes also support the ability to achieve an accurate diagnosis in lesions of less than 1 cm. A166

Accuracy may be further improved by reducing the number of inadequate samples using new techniques. A174 175

Recommendations
- False positives should be less than 1%. [C]
- Adequacy of sample should be over 90%. [C]
- Sensitivity for malignancy should be within the range of 85–90% in lesions over 2 cm. [C]
- Standards should be set and outcomes audited.

POST BIOPSY OBSERVATION
Most complications occur immediately or within the first hour of a PTLB. One hour following the biopsy procedure, most pneumothoraces are detectable on a chest radiograph. A15 87 176 Perlmutt et al, A177 in a series of 673 biopsies, detected 98% of pneumothoraces on radiographs taken either immediately after the procedure or at 1 hour. More recent literature documents delayed pneumothoraces presenting 24 hours after biopsy, despite normal 1 and 4 hour post biopsy radiographs. A178

No specific monitoring is required following an uncomplicated biopsy procedure, but patients should remain in hospital for at least 1 hour, or longer if further radiographs are required to monitor a pneumothorax. Patients should be in a supervised area so staff can be alerted if they develop shortness of breath, chest pain, or other symptoms.

Recommendations
- An erect chest radiograph should be performed 1 hour after the biopsy and is sufficient to detect the majority of post biopsy pneumothoraces. [B]
- Patients should be informed of the risks of delayed pneumothoraces. [B]
- No specific observations are necessary after the biopsy procedure, but patients should remain in a place where staff can be alerted if new symptoms develop in the first hour. [C]
- The chest radiograph should be reviewed by a suitably qualified member of staff. [B]
- If a pneumothorax has developed, the clinical condition of the patient and their home circumstances should be considered before deciding on further management. [B]

The British Thoracic Society guidelines state that a patient should not travel by air within 6 weeks of thoracic surgery or resolution of a spontaneous pneumothorax. A179

MANAGEMENT OF ACUTE COMPlications
Pneumothorax
A pneumothorax complicates up to 61% of all lung biopsies. A8 9 174 180 183 Acutely symptomatic pneumothoraces may develop at the time of the lung biopsy procedure and require immediate drainage. Smaller or better tolerated pneumothoraces will be detected on post biopsy chest radiographs.

Presentation
Acute presentation is usually with acute ipsilateral chest pain and dyspnoea. Clinical findings may be minimal or may include diminished breath sounds and mediastinal shift. In a tension pneumothorax the patient may become tachycardic and hypotensive and develop cyanosis. Monitoring of oxygen saturation is advised, together with the administration of oxygen as necessary. In an acutely unwell patient a chest radiograph or CT scan can be used to identify whether symptoms relate to pulmonary haemorrhage or pneumothorax. In a supine patient a pneumothorax may accumulate inferiorly, producing a deep radiolucent costophrenic sulcus on the chest radiograph.
Timing of chest radiography

Several studies have shown that most significant pneumothoraces will be detected on a chest radiograph performed 1 hour after the procedure, although they may not be visible on radiographs taken immediately after the procedure. Ultrasound and CT guided biopsies enable detection of very small pneumothoraces, but will still require follow up chest radiography to assess progression. Occasional delayed pneumothoraces have been reported more than 24 hours after biopsy, despite the absence of a pneumothorax on chest radiographs taken 4 hours after biopsy.

Management options

Where a pneumothorax is detected following a biopsy procedure, the management options include observation, aspiration, or drain insertion. This decision will be affected by factors such as the size of pneumothorax, co-existent lung pathology such as emphysema affecting respiratory reserve, and pain suffered. BTS guidelines on the management of pneumothorax suggest initial treatment by aspiration, with subsequent drainage if a leak and significant pneumothorax persist. A small gauge drain is usually adequate.

Chest drains are required in 3.3–15% of all patients undergoing lung biopsy. In the UK most clinicians attach drains to an underwater seal, but the Heimlich one way flutter valve is an alternative. This valve allows prolonged drainage for a pneumothorax and outpatient management. If the pneumothorax continues to enlarge or the patient develops surgical emphysema, the flutter valve can be replaced by a system attached to an underwater seal.

Pulmonary haemorrhage or haemoptysis

Pulmonary haemorrhage may occur with or without haemoptysis. Haemorrhage is recorded in 5–16.9% and haemoptysis in 1.25–5% of patients. Lesion depth has been identified as the most important risk factor for haemorrhage. An increased risk of bleeding occurs in lesions deeper than 2 cm.

Pulmonary haemorrhage in the absence of haemoptysis is usually minor and often asymptomatic but, if larger, it may present with the patient becoming confused from hypoxia or shocked. The differential diagnosis includes pneumothorax, haemothorax, or an air embolism. Initial treatment should include oxygen and general resuscitation. A chest radiograph is useful to identify a pneumothorax or pleural collection. The clinical team should be contacted.

Haemoptyses are usually self-limiting. Patient reassurance and being placed in a lateral position with the biopsy side down will often be adequate. If there is a more significant haemorrhage, patient resuscitation and oxygen should be administered and the clinical team contacted. In some centres there may be an option of selective bronchial intubation or of performing a rigid bronchoscopy to protect the opposite lung in patients with severe haemorrhage.

Air embolism

The incidence of air embolism is unknown. There are single case reports of fatalities and some survivors. The complication may be overlooked if there is a fatality, unless the pathologist has been alerted to the possibility.

Air embolism may lead to gas within the intracerebral or coronary circulation. This may occur because of a bronchovenous fistula created at the time of the biopsy procedure or because, on removal of the needle stylet, air is inadvertently aspirated through the needle lumen into the pulmonary vein. Lung biopsies should be performed with the patient prone or supine so that, in the event of an air embolism, air is less likely to travel to the cranial circulation.

Presentation may be with cardiac or neurological symptoms and signs: chest pain or rapid circulatory collapse, generalised seizures or focal neurological defects. Patient outcome is variable but is usually fatal, although the incidence is unknown. Fatal dysrhythmias may occur from a small volume of air, or air may dissolve and symptoms subside within minutes. In some cases intravascular air has been identified up to 48 hours after the biopsy procedure.

The diagnosis may be confirmed on the CT scan by identifying gas within the intracranial or coronary circulation. Fundoscopy may show the presence of frothing blood in retinal vessels.

Treatment is to administer 100% oxygen and anticonvulsants where necessary. The patient should be placed in the Trendelenburg position or in a left lateral decubitus position in case of a residual gas collection within the left heart. Steroids and aspirin are also recommended. Hyperbaric oxygen therapy has been used with a successful outcome in one case report.

Haemothorax

Significant haemothorax is rare but may develop from biopsy procedures through the intercostal or internal mammary arteries. When a large haemothorax develops, the patient should be given supportive care and the clinical team contacted. Signs of this are usually evident within the first hour. Assistance from general or thoracic surgeons and interventional vascular radiologists may be needed.

Recommendations

- The operator should be able to identify and appropriately manage the complications of lung biopsy procedures. Resuscitation facilities and chest drain equipment should be immediately available. [B]
- When a complication has occurred, the pulse, blood pressure and oxygen saturations should be monitored and recorded in a severely unwell patient. [C]

OUTPATIENT AND DAY CASE BIOPSIES

Delayed pneumothorax is a rare but recognised complication following lung biopsy. Dennie et al studied 506 patients undergoing PTLB. Patients were discharged after a 30 minute post biopsy chest radiograph if there was no pneumothorax and after a 60 minute radiograph if they had a stable asymptomatic pneumothorax. Symptomatic or enlarging pneumothoraces were treated with pigtail catheter insertion attached to a Heimlich valve and discharged. Seven (1.4%) patients developed a symptomatic pneumothorax after discharge and all required treatment. There were no deaths or other major complications. Catastrophic haemorrhage following biopsy has been reported as a cause of death following PTLB. This has occurred swiftly in each case. There are no reports in the literature of delayed haemorrhage causing death or serious morbidity.

There is no specific guidance in the literature on the choice of patients for day case biopsy. High risk patients—that is, those with borderline lung function (see earlier) and those with significant co-morbid pathology or inadequate home support—should not have a biopsy performed as a day case. Following an outpatient biopsy, patients should be given verbal and written instructions to telephone or return to the hospital if they develop breathlessness, chest pain, or haemoptysis.

Outpatient biopsies do not affect outcome either in terms of complication rate or diagnoses achieved. All studies report a comparable diagnostic rate for biopsies performed on inpatients. There are economic advantages to outpatient biopsies. One study estimated a reduction in costs of...
27% in an uncomplicated procedure. There is a reduction in variability due to bed shortages may be prevented.

Recommendations
- Percutaneous lung biopsies can be performed safely on an outpatient basis. [B]
- “High risk” patients should not have a biopsy performed as a day case procedure. [C]
- A post biopsy erect chest radiograph should be performed at least 1 hour after the procedure and a decision should be made at that time regarding further management if a pneumothorax is present. [B]
- Patients should be warned of delayed complications and given verbal and written instructions to return if symptomatic. [C]
- When biopsies are performed on an outpatient basis, patients should live within 30 minutes of a hospital, have adequate home support, and have access to a telephone. [C]

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C Clelland, Royal College of Pathologists
A Manhire, M Charig, F Gleeson, H Moss, K Pointon, British Society of Chest Radiologists

REFERENCES
Guidelines for radiologically guided lung biopsy


60 Fekele PS, Campbell WG, Bernardino ME. Transthoracic needle aspiration biopsy in Wegener’s granulomatosis. Morphologic findings in five cases. Acta Cytol 1993;35:280–1. [Ib]


Royal College of Radiologists. Lung biopsy information 2000. (available at www.rcr.ac.uk)


APPENDIX 1: EXAMPLE OF PATIENT INFORMATION SHEET

<table>
<thead>
<tr>
<th>PATIENT INFORMATION: HAVING A LUNG BIOPSY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your doctor has advised that you need a test called a lung biopsy. This leaflet explains a bit more about it.</td>
</tr>
<tr>
<td><strong>What is a lung biopsy?</strong></td>
</tr>
<tr>
<td>A lung biopsy is a way of getting a sample of tissue from the lungs using a small needle. It helps us to find out what is wrong.</td>
</tr>
<tr>
<td><strong>Will I need a general anaesthetic?</strong></td>
</tr>
<tr>
<td>No. A lung biopsy is done under local anaesthetic – a small injection is used to numb the skin.</td>
</tr>
<tr>
<td><strong>What happens now?</strong></td>
</tr>
<tr>
<td>You will receive a letter or phone call telling you when and where to report. The biopsy will normally be done within 2 weeks.</td>
</tr>
<tr>
<td><strong>Can I eat and drink before the test?</strong></td>
</tr>
<tr>
<td>You may have a light breakfast before the test – some tea and toast for example.</td>
</tr>
<tr>
<td><strong>Do I take my tablets on the day of the test?</strong></td>
</tr>
<tr>
<td>Yes, generally. The doctor you saw in the clinic will have checked your medicines with you. Please ask if you are to take them. You should not be taking warfarin or certain medications for diabetes.</td>
</tr>
<tr>
<td><strong>What happens next?</strong></td>
</tr>
<tr>
<td>The doctor who performs the test is an x-ray specialist, called a radiologist. An x-ray, CT, or ultrasound machine is used to let the doctor know exactly where to take the samples from. The doctor then gives a local anaesthetic and passes a small needle into the relevant area in the lung and takes some tiny samples of tissue. The samples are then sent to the laboratory and are examined under the microscope by a specialist called a pathologist.</td>
</tr>
<tr>
<td><strong>Will it hurt me?</strong></td>
</tr>
<tr>
<td>It shouldn’t be painful at the time. Some people have a bit of pain afterwards once the anaesthetic has worn off. If you do have any pain you can take a painkiller like paracetamol (up to 2 tablets, 4 times a day)</td>
</tr>
<tr>
<td><strong>How long does it take?</strong></td>
</tr>
<tr>
<td>It is usually a quick procedure, but may take up to 45 minutes.</td>
</tr>
<tr>
<td><strong>Can I go home after the procedure?</strong></td>
</tr>
<tr>
<td>Most people are able to go home after a few hours, but there must be someone to stay with you overnight. You may be admitted to hospital the day before. Please bring an overnight bag with you.</td>
</tr>
<tr>
<td><strong>What are the risks of having a lung biopsy?</strong></td>
</tr>
<tr>
<td>It is quite common for a little air to escape into the space around the lung during the biopsy. This may cause the lung to partially collapse. We call this a pneumothorax. Recent research shows this may happen in around 1 in 5 of procedures. Usually a pneumothorax is small and does not cause any problems. Rarely, (in up to 3 out of 100 procedures), a lot of air leaks out and causes a big pneumothorax. If that were to happen then we would treat it by either sucking the air out again with a needle (this is called aspiration) or by putting in a tube to let the air out (the tube is called a chest drain). If this happened you would probably have to stay in hospital for a day or two.</td>
</tr>
<tr>
<td>It is quite normal to cough up some streaks of blood at the time or for a day or two after the procedure. Very rarely a more significant bleed can occur, in which case you should contact your GP or the assessment unit at the hospital.</td>
</tr>
<tr>
<td><strong>Will there be any side effects after the biopsy?</strong></td>
</tr>
<tr>
<td>Most people have no problems. If you suddenly become short of breath or have severe chest pain, this may mean that there has been an air leak (a pneumothorax). You should contact the assessment unit at the hospital straight away to arrange to be seen and have another chest X-ray. (Tel: )</td>
</tr>
<tr>
<td><strong>Can I drive after the biopsy?</strong></td>
</tr>
<tr>
<td>Someone else must drive you home after the test. You should be able to drive again the next day if you feel well.</td>
</tr>
<tr>
<td><strong>Are there any problems flying in an aircraft after a biopsy?</strong></td>
</tr>
<tr>
<td>You should normally not fly for 6 weeks. If you wish to fly in less than 6 weeks please discuss this with your hospital doctor.</td>
</tr>
<tr>
<td><strong>When can I go back to work?</strong></td>
</tr>
<tr>
<td>You should be able to go back to work the day after the lung biopsy unless advised otherwise.</td>
</tr>
<tr>
<td><strong>When will I get the results?</strong></td>
</tr>
<tr>
<td>It can take up to a week for the results to come back to the doctor who asked for the test. You should have been given an appointment to see the doctor again. If you have not heard from the hospital within 10 days of the biopsy you should telephone the consultant’s secretary to make another appointment.</td>
</tr>
<tr>
<td><strong>Please now ask any questions you have and then sign the form to confirm you have understood the information</strong></td>
</tr>
<tr>
<td>Thank you.</td>
</tr>
<tr>
<td>Please sign below if you have read and understood “Patient Information: Having a Lung Biopsy” and have had the opportunity to ask further questions.</td>
</tr>
<tr>
<td>Name ______________________ Signed ___________________ Date ____________</td>
</tr>
</tbody>
</table>
APPENDIX 2: EXAMPLE OF BIOPSY REQUEST AND ADMISSION PROFORMA

RESPIRATORY MEDICINE

Transthoracic Needle Biopsies
Request and admission (R&A) form

To be completed in clinic for all patients.
No further clerking is required if patient's condition has not altered since clinic visit.

<table>
<thead>
<tr>
<th>Date</th>
<th>Surname</th>
<th>Forename</th>
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<tr>
<th>Consultant</th>
<th>Hospital No</th>
<th>D.O.B.</th>
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<table>
<thead>
<tr>
<th>Requested by</th>
<th>Address</th>
<th>(affix patient label)</th>
</tr>
</thead>
<tbody>
<tr>
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</table>

<table>
<thead>
<tr>
<th>Indication</th>
<th>Lesion side</th>
<th>Suggested imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung mass</td>
<td>Left</td>
<td>Fluoroscopy</td>
</tr>
<tr>
<td>Mediastinal mass</td>
<td>Right</td>
<td>CT</td>
</tr>
<tr>
<td>Pleural mass</td>
<td>Bilateral</td>
<td>Ultrasound</td>
</tr>
<tr>
<td>Suspected infective lesion</td>
<td>Comments</td>
<td></td>
</tr>
<tr>
<td>Other (specify)</td>
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Relevant Past Medical History

FEV1
Information sheet completed by patient? Y/N
Can biopsy be done as a day case? Y/N
Clinical condition satisfactory for biopsy? Y/N

Telephone No for short notice contact

Can a carer stay with patient overnight? Y/N

Clotting results:
INR
APTT ratio
Platelets
Signed

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Screening</th>
<th>Fluoroscopy</th>
<th>Y/N</th>
<th>Needle aspiration</th>
<th>Y/N</th>
<th>FNA cellular?</th>
<th>Y/N</th>
<th>Needle size, type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
<td>Y/N</td>
<td></td>
<td></td>
<td>Core biopsy</td>
<td>Y/N</td>
<td>No. of passes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>Y/N</td>
<td></td>
<td></td>
<td>Histology</td>
<td>Y/N</td>
<td>Microbiology</td>
<td>Y/N</td>
<td></td>
</tr>
<tr>
<td>Time of CXR(s)</td>
<td>1 hour</td>
<td>4 hours</td>
<td>24 hours</td>
<td>Other (specify)</td>
<td></td>
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Complications
Pneumothorax Y/N
Haemoptysis Y/N

Chest drain Y/N
Haemoptysis >100ml Y/N

<table>
<thead>
<tr>
<th>Aspiration</th>
<th>Y/N</th>
<th>Requires O/N stay</th>
<th>Y/N</th>
</tr>
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Has patient's condition deteriorated since clinic visit? If yes specify below and contact senior colleague to discuss BEFORE biopsy Y/N

Date Admitted

Date Discharged

If not discharged same day as biopsy specify reason

Patients with a pneumothorax should be reviewed by the respiratory team. If a pneumothorax is seen a follow up CXR is required in 4 hours. No patients with pneumothoraces should be discharged if they are alone at home. If in doubt request senior review.