National Institute for Health and Clinical Excellence

413 – Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for mediastinal masses

Consultation Comments table

IPAC date: December 14, 2007

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	British Thoracic Society (Specialist Adviser on this procedure)	**1**	I am a little reluctant with regards to the title – 'mediastinal masses';. EBUS was invented to stage and diagnose lung cancer (not lymphomas or sarcoid). At this point of time we have only 22G needle which provides cytological specimens. 21G needle is tested now as a prototype and will be available at the end of the next year - and I am sure that we would be able to broaden our indications for EBUS then.	The Committee chose not to change the title of the guidance as some of the evidence identified and reported on in the guidance also reports on the use of the procedure in the diagnosis of lymphomas and sarcoidosis. Noted, thank you.

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2	EUS users group and the Royal College of Radiologists	**1**	I agree with the comments in section 1.1. Since 2003 I have performed several hundred EBUS-TBNA procedures and I have no concerns over safety or efficacy. Please see expanded comments in the relevant sections on safety and efficacy below. With respect to training addressed in section 1.2, this is an area which needs further discussion and will be addressed further by the British Thoracic Society when they publish their updated guidelines on bronchoscopy. At present there are no formal training programmes or minimum requirements for this procedure. However, we advise that clinicians interested in starting EBUS-TBNA that they: Should be fully trained experienced bronchoscopists who have experience of performing bronchoscopy with the patient supine (ie bronchoscopist stands behind the head) and via the oral route. Contact one of the centres performing high volume (and currently there are only 3-4) and visit in order to observe procedures being performed. Attend a training course on the technique. Start with straightforward cases (eg large subcarinal masses) Gain experience interpreting the ultrasound images possibly collaborating with radiology colleagues initially. That they audit their outcomes and aim for an accuracy of around 90%.	Noted, thank you. The Committee considered the consultee's comment but made no change to the guidance.

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3	EUS users group and the Royal College of Radiologists	**2**	Further to section 2.1, I would add that while predominantly used to sample mediastinal lymph nodes, EBUS-TBNA can also be used to sample hilar lymph nodes.	Thank you. In section 2.1.1, the following sentence has been added: 'This may also be used in the investigation of hilar lymph nodes'.
			With regard to EBUS-TBNA for sarcoidosis there have been further publications since the searches performed for the draft document. E.g. Garwood S et al., Chest 2007 Oct132(4):1298-304 EBUS-TBNA will also be very useful for determining the nature of lymph nodes that have shown up positive on an FDG-PET scan.	The paper referred to by the consultee was identified in the post consultation literature search and consequently added to Table 2 of the overview.
			Please note that on page 22 of the draft document the last bullet point states that 'The NICE clinical guideline on lung cancer states that FDG-PET scanning has a central role in staging non-small cell lung cancer. When FDG-PET scanning is available, histological/cytological confirmation may not be required.' This is NOT correct and is not what the guideline states. Section 1.3.1.9 states that 'histological/cytological investigation should be performed to confirm N2/3 disease where FDG-PET is positive. This should be achieved by the most appropriate method'.	This comment refers to a statement in the overview listed under 'Issues for Consideration by IPAC'. Overview to be revised accordingly.
			With regard to the title of the document the IPAC may wish to consider modifying the title to read 'Interventional procedure overview of real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes'.	In section 2.1.1, the following sentence has been added: 'This may also be used in the investigation of hilar lymph nodes'.

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4	Australian Government	**2**	Patient population Clarify whether EBUS-TBNA is being used to investigate both of the following groups: • mediastinal masses with a suspicion of cancer • mediastinal masses without a suspicion of cancer (i.e. differential diagnosis of various benign conditions) Prior tests inclusion of a diagnostic test algorithm (as a flowchart) would assist the reader in understanding the potential place of EBUS-TBNA in UK clinical practice. Issues in regards to prior testing could be further detailed: • The procedure indication (2.1.2) clearly identifies CT +/- PET as prior tests to EBUS-TBNA. Relevant prior testing should be incorporated into the research question/selection criteria. • unclear on what basis CT +/-PET imaging is used to select patients for cytological/histological investigation in UK clinical practice. e.g. if the presence of enlarged lymph nodes on CT +/-PET is used to determine whether further cytological/histological investigation is required. • are mediastinoscopy and mediastinotomy appropriate comparators? (2.1.2). Comparators: the main comparator(s) in UK clinical practice should be stated. Evidence against the main comparator(s) should be clearly identified	Section 2.1.1 has been amended and now refers to ‘lung cancer’ alone rather than ‘non-small cell lung cancer’, IP guidance does not have the purpose of placing a procedure within a care pathway, rather to make a recommendation in regard to the procedure’s safety and efficacy. NICE IP programme’s remit precludes comparing the efficacy and safety against ‘comparator’ interventions.

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5	British Thoracic Society	**2.1**	It should be ... 'of staging of lung cancer'; -(not only non-small cell, this procedure is good enough for small cell as well). I am not sure that there is enough data to support the statment that EBUS is good for sarcoidosis - a BIOPSY specimen not FNA is required to diagnose sarcoid comfortably. With EBUS specimens we can say that cytology is consistent with clinical picture of sarcoidosis and that there were no malignant cells but I would be quite critical on diagnosis sarcoid on cytology (here in Edinburgh we had one case diagnosed as sarcoidosis on EBUS which retrospectively (4/12 later) turned up to be adenocarcinoma on second EBUS specimen and when we analysed the first specimen retrospectively).	Section 2.1.1 has been amended and now refers to 'lung cancer' alone rather than 'non-small cell lung cancer', Evidence about use of this procedure for diagnosis of sarcoidosis was presented, and additional evidence accrued since. See comment No 3. Specificity and sensitivity are not 100%.
6	Australian Government	**2.2**	Index test The difference between linear probe EBUS-TBNA and radial probe EBUS-TBNA should be discussed. The current draft guidance presents studies of linear EBUS-TBNA as primary evidence and studies of radial EBUS-TBNA as supportive evidence and the justification for this distinction needs to be clearly stated. • If expert advice indicates that only studies of linear EBUS-TBNA are clinically useful it may be appropriate to limit the review to linear EBUS-TBNA and reflect this throughout the document • If expert advice indicates that both studies of linear EBUS-TBNA and radial EBUS-TBNA are clinically useful it may be more appropriate to divide the primary and supportive evidence on the basis of comparative and non-comparative evidence respectively.	This comment relates to the use of 'real-time' or 'non-real' time devices. It is customary for the IP Programme to consider ultrasound-guided interventions together for both 'real time' and 'non-real time' modalities (e.g. recent example, US-guided visualisation of epidural space). In the team's opinion this is appropriate.

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7	Royal College of Radiologists	**2.2**	Please note that in the draft document there is in places, some confusion between real-time EBUS-TBNA and non real-time EBUS-TBNA. Prior to the advent of the real-time linear EBUS-TBNA bronchoscope (BF-UC260F-OL8) the only method of performing EBUS was to use a radial ultrasound probe or radial miniprobe introduced through a standard bronchoscope. While allowing visualisation of potential targets these devices do not allow real-time needle aspiration guidance to be performed. Following ultrasound localisation a separate biopsy needle has to be inserted down the bronchoscope and biopsy performed but it is not done under real-time guidance. It should be noted that this procedure is best performed with the patient supine and the bronchoscopist standing behind the patient's head and using the oral route.	See response to comment no. 6.
8	British Thoracic Society	**2.3**	You may want to include my last abstract publication: Minimally invasive staging in lung cancer by real-time endobronchial ultrasound (EBUS): Chest 2007;132(4):591S. 300 procedures for staging and diagnosis of lung cancer with sensitivity of 94% and accuracy 96%.	Thank you for bringing this to our attention. In the IP Programme abstracts are not normally selected for presentation to the Committee unless they provide new safety information relating to serious adverse events. (See the IP Programme Methods Guide for further details: www.nice.org.uk)
9	Australian Government	**2.3**	Outcomes The draft guidance clearly states the weaknesses of the reported diagnostic accuracy estimates in the included studies due to the potential for false positives. Of considerable concern are the measures of specificity and this weakness should be mentioned in all summaries of results or measures of specificity should be removed from these summaries. Quality and Applicability The draft guidance presents brief comments on quality and applicability issues for the included studies, however the impact of these issues could be further discussed.	The team believes the consultee is referring to bullet point 2 of the Validity and Generalisability section in the overview (not the draft guidance as stated).

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10	EUS users group and the Royal College of Radiologists	**2.3**	Most of the document and reviewed papers refer to real-time linear EBUS-TBNA using the BF-UC260F-OL8 device (or a prototype). Section 2.3.7 above and Reference 7 in the draft document (Herth F, Conventional versus endobronchial ultrasound-guided transbronchial needle aspiration: a randomized trial. Chest 125 (1) 322) uses radial EBUS and not linear EBUS-TBNA although they do use the term EBUS-TBNA in the title and the text. This is rather confusing. In appendix A of the draft document (also listed as table 2 – which I think is a typo) the papers by Herth FJ (2003 and 2005), Kanoh K (2002 and 2005) and the paper by Shannon JJ refer to radial EBUS. All the others refer to linear EBUS. Members of the IPAC may wish to consider whether they intend to keep the document dealing purely with linear real-time EBUS-TBNA or also include radial EBUS. If they wish to do the latter, then the document will need to be modified to reflect this fact and clearly explain the difference between the two approaches. To my knowledge there is no one in the UK currently using radial EBUS.	See response to comment no. 6.

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11	EUS users group and the Royal College of Radiologists	**2.4**	In our hands linear real-time EBUS has been a very safe technique and the side-effects are really no different to standard bronchoscopy. You may wish to point out that if a patient is fit for a standard bronchoscopy (lying supine) then they should be fit for EBUS-TBNA. We have had one or two patients (out of several hundred) with post-procedure fever and one patient who developed atrial fibrillation during the procedure which spontaneously reverted to sinus rhythm post-procedure. I agree with the comments of the specialist advisers other than the one about significant bleeding. Does he mean within the airway? We have never had anything other than minor bleeding at the needle puncture site. Theoretically, one could get more serious bleeding if one tore a vein within the mediastinum or hilar regions during aspiration. It should be noted that puncture of a suspected mediastinal cyst is contra-indicated as this could lead to mediastinitis.	Significant bleeding was a theoretical adverse event listed by one of the Specialist Advisers in their advice, seen by the Committee when it made its recommendations.
12	Australian Government	**2.5**	A comment on the other major application of the EBUS procedure EBUS-TBBX for the diagnosis of peripheral lung lesions could be added. However this technology is outside the scope of the NICE draft guidance and would require a separate appraisal.	EBUS-TBBX is not within the scope of this procedure. The IP Programme has requested that the consultee notify this procedure if deemed appropriate.
13	EUS users group and the Royal College of Radiologists	**2.5**	The committee noted that some patients reported pain during EBUS-TBNA. This is not actually mentioned in the draft document and we have not come across this in our experience. However, I agree that attention should be paid to analgesia during the procedure.	This committee comment refers to several comments about pain during the procedure submitted by patients in their commentary to the committee while it was formulating its recommendations.