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# A direct comparison of the diagnostic yield of ultrasound-assisted Abrams and Tru-cut needle biopsies for pleural tuberculosis

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## ABSTRACT

**Background:** Tuberculous pleuritis remains the commonest cause of exudative effusions in areas with a high prevalence of tuberculosis and histological and/or microbiological confirmation on pleural tissue is the gold standard for its diagnosis. Uncertainty remains regarding the choice of closed pleural biopsy needles.
**Objectives:** This prospective study compared ultrasound-assisted Abrams and Tru-cut needle biopsies with regards to their diagnostic yield for pleural tuberculosis.
**Methods:** We enrolled 89 patients (38.7+/-16.7 years; 54 males) with pleural effusions and a clinical suspicion of tuberculosis. Transthoracic ultrasound was performed on all, whereafter patients were randomly assigned to undergo either four or more Abrams needle biopsies followed by four or more Tru-cut needle biopsies or vice versa. Medical thoracoscopy was performed on cases with nondiagnostic closed biopsies. Histological and/or microbiological proof of tuberculosis on any pleural specimen was considered the gold standard for pleural tuberculosis.
**Results:** Pleural tuberculosis was diagnosed in 66 patients, alternative diagnoses established in 20 patients and 3 remained undiagnosed. Pleural biopsy specimens obtained with Abrams needles contained pleural tissue in 81 patients (91.0%) and were diagnostic for TB in 54 patients (sensitivity=81.8%), whereas Tru-cut needle biopsy specimens only contained pleural tissue in 70 patients (78.7%, p=0.015) and were diagnostic in 43 patients (sensitivity=65.2%, p=0.022).
**Conclusions:** US-assisted pleural biopsies performed with an Abrams needle are more likely to contain pleura and have a significantly higher diagnostic sensitivity for pleural tuberculosis.

## INTRODUCTION

Approximately a third of the world's population is infected with *Mycobacterium tuberculosis* [1], and among communicable diseases, tuberculosis (TB) is the second leading cause of death.[2] Pleural TB remains a common form of extrapulmonary TB, particularly amongst Human Immunodeficiency Virus (HIV) positive individuals [3,4] and it is the commonest cause of exudative effusions in areas with a high prevalence of TB.[2,5,6]

Although a presumptive diagnosis of pleural TB is often based on elevated levels of adenosine deaminase (ADA) and interferon-gamma in pleural fluid, actual histological and/or microbiological confirmation of TB pleuritis remains the gold standard.[5,6] Pleural tissue can be harvested either by means of closed biopsies, thoracoscopy or open surgical biopsies.[5,6] Access to thoracoscopy and open surgical biopsies is limited in many parts of the world and closed biopsies are therefore the preferred initial investigation.[6]

Closed pleural biopsy needles were introduced in the mid 1950s and early 1960s and various types were utilised, including the Abrams, Cope and Vim-Silverman needles.[8-12] Of these devices, the Abrams needle was consistently shown to have a high yield and became the most widely used device. [7,12,13] In 1989 Macleod et al. described blind cutting needle (Tru-cut) biopsies as an alternative to Abrams needles in patients who present with large pleural effusions.[14] Around the same time transthoracic ultrasound (US) – assisted biopsy techniques were pioneered, and the indications were soon expanded to include cutting needle pleural biopsies.[15-18] Focal pleural abnormalities (e.g. thickening) and fluid collections could be identified by means of US, and biopsy may be aimed at these areas of interest.[19] Moreover, estimating the size of an associated effusion decreases the risk of visceral pleural lacerations, which is particularly relevant in cases with minimal pleural effusion and where pointed, cutting needle biopsy devices are employed. [19]

One small prospective study found a superior diagnostic yield for pleural TB with US-assisted Tru-cut compared to traditional Abrams needle biopsies.[17] In that study, which was performed in an area with a moderate TB prevalence, only two of ten Abrams needle biopsies were diagnostic for pleural TB. As most authors have reported diagnostic sensitivities in the order of 50-85% for Abrams needle biopsies [6,13], uncertainty remains with regards to which of these closed pleural biopsy techniques are superior for pleural TB.

The aim of this prospective study was to compare US-assisted Abrams needle biopsies to US-assisted Tru-cut needle biopsies with regards to their diagnostic yield for pleural TB.

## METHODS

### Study population

All adult patients (≥18 years) referred to the Division of Pulmonology of Tygerberg Academic Hospital with radiological evidence of a pleural effusion and clinical suspicion of pleural tuberculosis were potential candidates for this study. Our institution is a 1,200-bed academic hospital in Cape Town, South Africa. It is one of

two academic referral centres in the city and renders a tertiary service to a population of approximately 1.5 million. In 2006 the incidence of pulmonary TB in this population was 940 cases per 100,000 [1]. The Committee for Human Research of the University of Stellenbosch approved the study. Written informed consent was obtained from all subjects on enrolment and prior to any invasive procedures.

Patients referred to the division's pleural theatre were screened for indicators of a high clinical suspicion of TB, which for the purposes of the study included (1) known HIV infection, (2) persistent cough lasting >3 weeks, (3) haemoptysis, (4) weight loss >4 kg (5) intermittent fever >3 weeks and (6) drenching night sweats >2 weeks. Patients were included in the study only if transthoracic US confirmed a pleural effusion of at least 10 mm (as measured from the parietal pleura) and they had at least two clinical indicators of possible TB.

**Transthoracic ultrasound**

A consultant respiratory physician or a senior registrar under supervision performed the sonography (Toshiba Just Vision 200 SSA-320A; Toshiba Medical Systems Corporation, Tochigi-ken, Japan). The preferred patient position for the procedure was the sitting position, with the subjects arms folded across the chest and supported by a bedside table. Surveillance of the dorso-lateral thoracic wall was performed by means of a standard 3.75 MHz sector probe. The presence of an effusion was confirmed by standard means.[19] The size of the effusion was documented as follows: minimal (if the echo-free space was confined to the costophrenic angle); small (if the space was greater than the costophrenic angle but still within the range of the area covered with a 3.75 MHz curvilinear probe); moderate (if the space was greater than a one-probe range but within a two-probe range; and large (if the space was larger than a two-probe range).[19] The biopsy site was subsequently identified, with safety being a main determinant. As a rule, the aspirations and biopsies were performed in midscapular line. For minimal to moderate effusions the biopsies were taken from the site of maximum effusion as determined by US. In case of a large effusion, the puncture site was chosen to be as low as possible, but not within 25 mm of the diaphragm. All aspirations and biopsies were performed "freehand" (not under direct US guidance), and patients were requested to remain motionless during the procedures.

**Diagnostic thoracentesis**

Under sterile technique and local anaesthesia with lignocaine 1% samples were obtained for pH analysis by means of on-site blood gas analyser (Bayer Rapidlab 865 Blood Gas Analyzer, Siemens, Midrand, South Africa), chemistry, microbiology, cell counts and cytology. The chemical analyses included serum and pleural total protein, albumin, lactate dehydrogenase (LDH) and pleural fluid ADA levels. Microbiological investigations included routine gram stains and cultures, as well as stains for acid fast bacilli (Ziehl-Nielsen staining) and TB cultures (MGIT 960 liquid culture system, Becton Dickinson, Sparks, Maryland, United States of America). We defined a lymphocytic predominant effusion as one with >75 % lymphocytes and/or a lymphocyte:neutrophil ratio >0.75.[6]

**Closed pleural biopsies**

Under sterile technique and local anaesthesia, closed pleural biopsies were subsequently performed on all patients. Patients were randomly assigned (in blocks

of 6) to undergo either four or more Abrams needle biopsies followed by four or more Tru-cut needle biopsies or at least four Tru-cut needle biopsies followed by at least four Abrams needle biopsies. These biopsies were performed from the same incision site (5 mm in length) and by experienced clinicians. Abrams needle biopsies were performed according to standardised guidelines.[20,21] Biopsies were taken with the distal tip of the needle facing up to 45 degrees down in order to avoid laceration of the intercostal vessels. Cutting needle biopsies were performed by means of manually operated 14-gauge Tru-cut biopsy needles with a specimen notch of 20 mm (Allegiance, Chateaubriand, France) and technically comparable to the way described by McLeod and co-workers (figure 1).[16] Abrams and Tru-cut needle biopsy specimens were harvested until each technique yielded at least three macroscopically satisfactory specimens for histological evaluation (transported in 4% formalin) and at least one specimen for microbiological investigations (transported in 0.9% saline).

**Immediate post-procedure care**

The incision site was re-examined by means of US immediately after the procedures for suspected pneumothoraces, and a chest radiograph was obtained if the pre- and post-procedure US findings differed and at the discretion of the attending physician. All patients were observed for at least one hour prior to discharge, and complications were noted. Patient discomfort was documented, and excessive pain was defined as any pain requiring at least a single dose of parenteral or opiate analgesics. The presence or absence of minor or major haemorrhage, as well as iatrogenic pneumothoraces was specifically documented. Major haemorrhage was defined as any haemorrhage that required additional measure above and beyond localised pressure and a single superficial suture.

**Further assessment and follow up**

All patients with a non-diagnostic closed biopsy or thoracentesis were referred for medical thoracoscopy. Those who remained undiagnosed following medical thoracoscopy were followed up for a total of six months, and the choice of further investigations was guided by the patients' attending chest physicians. These could have included observation, video-assisted thoracoscopy or open surgical procedures. Cases that remained undiagnosed after six months were deemed "undiagnosed pleural exudates". As the negative predicative value of medical thoracoscopy (when combining histology and microbiology) for TB pleuritis is practically 100%, and its sensitivity for malignancy, in combination with fluid cytology and closed needle biopsies is 97%, we decided upfront to retain these patients in the "non-tuberculous" group for statistical analysis.[6,22]

**Statistical analysis**

We expected a diagnostic sensitivity of 80% for both devices, based on our own historical data and data from Chang et al.[6,17] Utilising McNemar's test for equal proportions, it was estimated that a total sample size of 220 patients was required to prove non-inferiority (difference of less than 10%). We were, however, unsure if the diagnostic sensitivity achieved by Chang [17] in a relative small study population would be reproducible, and given the paucity of data, practical constraints as well as patient safety aspects it was decided to calculate the diagnostic yield for pleural TB of both needles after 36 months or after the inclusion of 100 patients, whichever came first. At 36 months (with 89 patients included) it became apparent that the yield

of the Abrams needle for TB was consistent with the estimate [6], but that the yield for the Tru-Cut biopsy was clearly lower than anticipated. We terminated the study, as the sensitivities for pleural TB differed significantly between the devises and subsequently analysed the all data at this point (McNemar's test for equal proportions and Chi-squared tests, with $P < 0.05$ accepted as significant). Unless stated otherwise, data are displayed as means ± standard deviation (SD). We used standard methods to calculate the sensitivity, specificity, and positive and negative predictive values.[23] For the purposes of the study, we accepted either histology compatible with tuberculosis (epithelioid granulomata with central necrosis, with or without acid fast bacilli) or microbiological proof (pleura yielding a positive culture for *Mycobacterium tuberculosis*) on any pleural specimen as the gold standard.

## RESULTS

### Patients' characteristics and transthoracic ultrasound findings

We enrolled a total of 89 patients (38.7+/-16.7 years; 54 males) over a three year period: 8 had minimal effusions, 19 had small effusions, 36 had moderate effusions and 26 had large effusions. Pleural tuberculosis was diagnosed in 66 cases (74.2%; 35.1+/-15.5 years; 35 males). Of the remaining 23 patients (49.1+/-15.9 years; 19 males), 20 (22.5%) had an alternative diagnosis and 3 (3.4%) remained undiagnosed (table 1). The HIV status of 37 patients was known at the time of enrolment: 16/26 (61.5%) of patients who were ultimately diagnosed with pleural TB were HIV positive, compared to 4/11 (36.4%, $p = 0.159$) in the group where TB was excluded.

Table 1: Final diagnoses established in all patients (*n*=89)

| **Diagnosis** | ***n*** | ***%*** |
|---|---|---|
| Pleural tuberculosis | 66 | 74.2 |
| Bronchogenic carcinoma | | |
| - Non-small cell lung cancer | 4 | 4.5 |
| - Small cell lung cancer | 2 | 2.2 |
| Metastatic adenocarcinoma (other than lung) | 3 | 3.4 |
| Malignant mesothelioma | 2 | 2.2 |
| Sarcoma | 1 | 1.1 |
| Parapneumonic effusion (bacterial) | 7 | 7.9 |
| Sarcoidosis | 1 | 1.1 |
| Undiagnosed pleural exudates | 3 | 3.4 |

### Diagnostic thoracentesis

The pH analysis, biochemistry and microbiological results are summarised in tables 2A and 2B. In patients ultimately diagnosed with pleural TB, 90.9% had a lymphocyte predominant effusion, and 89.3% had an ADA > 50 IU/L. Combining these parameters yielded a sensitivity of 83.3%, specificity of 95.7%, positive predictive value of 98.2% and negative predictive value of 66.7% for pleural TB (table 3). Seven patients were found to have complicated parapneumonic effusions (with bacterial cultures) and malignant cells were present in 5. None of these 12 individuals had histological evidence of pleural TB.

Table 2A: Diagnostic thoracentesis results of tuberculous vs. non-tuberculous effusions: continuous variables

| | Tuberculous effusion (*n* = 66) | | | | Non-tuberculous effusion (*n* = 23) | | | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **Mean** | **SD** | **Median** | **IQR** | **Mean** | **SD** | **Median** | **IQR** |
| **pH** | 7.33 | 0.11 | 7.34 | 0.16 | 7.31 | 0.18 | 7.32 | 0.15 |
| **Lymphocytes (%)** | 76 | 23 | 84 | 23 | 47 | 35 | 49 | 77 |
| **Neutrophils (%)** | 13 | 19 | 5 | 17 | 30 | 34 | 39 | 59 |
| **Protein (g/L)** | 54.2 | 13.6 | 56.0 | 13.5 | 49.3 | 15.9 | 49.5 | 21.0 |
| **Albumin (g/L)** | 25.3 | 9.0 | 26.0 | 10.5 | 26.9 | 10.1 | 26.5 | 12.0 |
| **LDH (IU/L)** | 574 | 900 | 385 | 295 | 1675 | 2147 | 1027 | 1770 |
| **ADA (IU/L)** | 96.9 | 41.4 | 96.9 | 53 | 49.2 | 48.4 | 37.1 | 40 |

SD, Standard deviation; IQR, Interquartile range; LDH, Lactate dehydrogenase; ADA, Adenosine deaminase

Table 2B: Diagnostic thoracentesis results of tuberculous vs. non-tuberculous effusions: categorical variables

| | Tuberculous effusion (*n* = 66) | | Non-tuberculous effusion (*n* = 23) | |
|---|---|---|---|---|
| **Variable** | ***n*** | **%** | ***n*** | **%** |
| **ADA>50 IU/L** | 59 | 89.4 | 6 | 26.1 |
| **Lymphocyte predominant*** | 60 | 90.9 | 9 | 39.1 |
| **ADA>50 IU/L & Lymphocyte predominant** | 55 | 83.3 | 1 | 4.3 |
| **Culture positive for bacteria** | 0 | 0 | 7 | 30.4 |
| **AFB positive** | 0 | 0 | 0 | 0 |
| ***M tuberculosis* culture positive** | 17 | 25.8 | 0 | 0 |
| **Cytology positive for malignant cells** | 0 | 0 | 5 | 21.7 |

ADA, Adenosine deaminase; AFB, Acid fast bacilli; M, Mycobacterium
*Lymphocytic predominant effusion: >75 % lymphocytes and/or lymphocyte:neutrophil ratio > 0.75

Table 3: Diagnostic accuracy of pleural fluid analysis

| **Parameter** | **Sensitivity** | **Specificity** | **PPV** | **NPV** |
|---|---|---|---|---|
| **ADA (IU/L)** | 89.4% | 73.9% | 90.8% | 70.8% |
| **Lymphocyte predominance*** | 90.9% | 60.9% | 87.0% | 70.0% |
| **ADA>50 IU/L & Lymphocyte predominant** | 83.3% | 95.7% | 98.2% | 66.7% |
| ***M tuberculosis* culture positive** | 25.8% | 100% | 100% | 31.9% |

PPV, positive predictive value; NPV, negative predicative value ADA, Adenosine deaminase; M, *Mycobacterium*
*Lymphocytic predominant effusion: >75 % lymphocytes and/or lymphocyte:neutrophil ratio > 0.75

## Closed needle biopsies – diagnostic yield

Pleural tissue was present at histology of Abrams needle biopsies in 91.0% and Tru-cut biopsies in 78.7% (p = 0.015) (table 4). Abrams needle biopsies had a yield for all diagnoses of 78.7% compared to 62.9% observed with Tru-cut needles (p = 0.014). Amongst the 66 patients that were diagnosed with pleural TB, Abrams needle biopsies provided proof in 81.8%: 77.3% had histological evidence of TB and biopsies from 63.6% were culture positive for *Mycobacterium tuberculosis*. Tru-cut needles yielded evidence of pleural TB in 65.2% (p = 0.022): 60.6% patients had histological evidence of TB (p = 0.029) and biopsies from 39.4% were culture positive (p < 0.001). Two of the twelve cases that escaped a histological diagnosis of TB with Abrams needles were diagnosed on specimens harvested with Tru-cut needles (a total of 56 patients were thus diagnosed with pleural TB on the basis of closed pleural biopsies).

Table 4: Diagnostic yield of Abrams and Tru-cut needle biopsies (*n*=89)

| Parameter | Abrams | Tru-cut | Significance |
|---|---|---|---|
| **Pleural tissue present at histology (n=89)** | 81 (91.0%) | 70 (78.7%) | p = 0.015 |
| **All diagnoses (n=89)** | 70 (78.7%) | 56 (62.9%) | p = 0.014 |
| **Pleural tuberculosis (n=66)** | 54 (81.8%) | 43 (65.2%) | p = 0.022 |
| - Histological evidence | 51 (77.3%) | 40 (60.6%) | p = 0.029 |
| - AFB positive | 29 (43.9%) | 25 (37.9%) | p = 0.423 |
| - Culture positive | 42 (63.6%) | 26 (39.4%) | p < 0.001 |
| **Alternative diagnoses (n=23)** | 16 (69.6%) | 13 (56.5%) | p = 0.450 |
| - Malignancy (n=12) | 10 (83.3%) | 8 (66.7%) | p = 0.683 |
| - Benign pathology (n=8) | 6 (75.0%) | 5 (62.5%) | NA |
| - Undiagnosed exudates (n=3) | 0 | 0 | NA |

AFB = Acid fast bacilli; NA = Not applicable

Malignant pleural effusions were diagnosed in 12 patients. All had at diagnostic closed pleural biopsies: Abrams needle biopsies yielded histological confirmation in 10 (83.3%) and Trucut needle biopsies in 8 (66.7%) respectively. Two cases not diagnosed with Abrams needles were both diagnosed on specimens obtained with Trucut needles, and the four cases with false negative Tru-cut biopsies (for malignancies) had positive Abrams needle biopsies. With regards to patients diagnosed with parapneumonic effusions (all with positive gram stains and cultures for bacteria on pleural fluid), acute pleuritis and/or non-specific inflammation were present on 6 specimens obtained by Abrams needles and 5 obtained by Trucut needles.

**Closed pleural biopsies – Complications**

The procedures were generally well tolerated and no pneumothoraces or major haemorrhage were documented. Two patients required parenteral analgesics: one patient complained of severe pain following Abrams' needle biopsies and one following Tru-cut biopsies (on both occasions the analgesics were administered following the second procedure). Two female patients (aged 20 and 22) experienced syncope following Abrams needle biopsies – both recovered fully within 60 seconds (neither required any specific medical intervention). No procedure was abandoned due to complications.

**Further assessment and follow up**

Thoracocentesis and closed pleural biopsy established aetiological diagnoses in 75 of the 89 patients. Diagnostic medical thoracoscopies were performed in 14. Aetiological diagnoses were subsequently made in a further 11 patients (10 cases of pleural TB and one of sarcoidosis). Three male patients aged 18, 51 and 63 years respectively remained undiagnosed. All were HIV negative, had minimal (n=1) or small (n=2) effusions, and specimens obtained during thoracoscopy either showed non-specific pleuritis (n=2) or pleural fibrosis (n=1). A complete radiological recovery was documented in all three cases, and all three were asymptomatic at six months follow-up.

## DISCUSSION

This is to the best of our knowledge the largest prospective and the first randomised study performed to compare ultrasound-assisted Abrams needle biopsies to ultrasound-assisted Tru-cut needle biopsies with regards to their diagnostic yield for pleural TB. We enrolled a relatively large population with a moderate to high pre-test probability for pleural TB, and randomised patients to undergo either biopsy technique first, in order not to disadvantage either needle. Abrams needle biopsies were more likely to contain pleural tissue ($p = 0.015$) and to confirm the diagnosis of TB ($p = 0.022$) than pleural biopsies obtained with Tru-cut needles.

We found US-assisted Abrams needle biopsies to have an overall diagnostic yield of 81.8% for TB pleuritis in a study population with a high pre-test probability for the disease. We previously found medical thoracoscopy to have a diagnostic sensitivity of 100% for pleural TB. [6] The present study establishes ultrasound-assisted Abrams needle biopsies as the principle technique to obtain pleural tissue in patients with suspected TB pleuritis, with medical thoracoscopy being reserved for the minority of cases that escape diagnosis by means of closed biopsies.

In general, blind Abrams needle biopsies have a yield of 50-85% for TB pleuritis.[6,24-28] Valdés and co-workers reported a diagnostic sensitivity of 79.8%, when they analysed the case histories of 254 patients with conformed pleural TB in a Spanish university hospital.[27] Diacon et al. previously found Abrams needle to have a diagnostic yield of 79% in patients from with undiagnosed exudative pleural effusions who presented to our institution.[6] We specifically enrolled patients with at least a moderate pre-test probability of TB, which may account for the relatively high sensitivity. The use of US prior to closed pleural biopsies is currently advocated [19,29,30], both as a safety measure and to detect localised pleural thickening and other abnormalities.[29,30 Pleural TB is a diffuse disease process [25], and it can therefore be postulated that the addition of US prior to the Abrams needle biopsies is unlikely to affect the sensitivity. Although we did not specifically employ the US to detect localised abnormalities, our findings certainly support this.

Tru-cut biopsies yielded pleural tissue in 78.7% of patients enrolled onto this study, and it had diagnostic sensitivity of 65.2% for pleural TB and 66.7% for malignancy. Chang et al. conducted the only other prospective study that specifically compared the diagnostic yield of US-guided pleural biopsy with a Tru-cut needle and (blind) pleural biopsy with an Abrams needle.[17] They enrolled 49 patients with unilateral pleural effusion: 24 underwent pleural biopsy with an Abrams needle and 25 with US-guided pleural biopsy with a Tru-cut needle. Only 17 patients had pleural TB. Abrams needle biopsies were diagnostic in 20% (2/10), whereas Tru-cut needle biopsies were diagnostic in 86% (6/7). The diagnostic yields for malignancies were 44% and 77% respectively. Four major differences in the studies should be highlighted: We enrolled almost four times as many patients with pleural TB, performed thoracic US prior to all biopsies, utilised both biopsy needles in all cases and specifically reported the presence of pleural tissue at histology. Furthermore, we utilised liquid culture media, which has a proven superior yield for pleural biopsies.[31,32]

We encountered a number of unexpected results. All pleural malignancies were diagnosed by means of either the Abrams or Tru-cut needles, and the combined

diagnostic yield was therefore 100%. Although this study was not designed to specifically address this issue, this figure is significantly higher than reported figures.[33,33] Malignant disease tends to give rise to focal involvement [25], and the lower thoracic and diaphragmatic parietal pleura are more likely to contain secondary seeding from visceral pleural metastases.[34,35] We aimed to utilise relatively low (supra-diaphragmatic) biopsy sites, which may partially explain the relatively high yield observed in our study. Moreover, we harvested at total of at least 6 specimens for histology per patient, and it is known that the yield of closed biopsies increases with increasing number of biopsies.[25] We did not specifically evaluate the role of US in predicting pleural malignancies, as recently reported by Qureshi and co-workers.[36] In their study, US correctly identified 73% of malignant effusions on appearance alone.[36] The yield of US-assisted closed pleural biopsies in experienced hands may be much higher than previously believed and certainly deserves to be studied prospectively.

We found the Abrams needle to have a statistically significant superior yield for all diagnoses, and our data even suggested a comparable yield for pleural malignancy. Tru-cut pleural biopsies can safely be perform in the presence of very little pleural fluid and has a diagnostic yield for pleural malignancy that is generally reported to be superior to that of Abrams needle biopsies. [17,19,26,30] Maskell and co-workers previously found CT-guided Tru-cut pleural biopsies to have a superior sensitivity of 87% for pleural malignancies compared to 47% of unaided Abrams needle biopsies.[33] Local disease prevalence may therefore dictate the choice of biopsy needle, and the Tru-cute needle may still be the needle of choice in patients with suspected pleural malignancy.

Kitinya et al. found that the HIV status of a patient impacted on pleural biopsy results.[37] Their data suggested that granulomata were less likely to be observed, whereas pleural tissue from HIV positive patients was more likely to be culture positive. Yet, in our study population the majority of patients diagnosed with pleural TB by means of closed pleural biopsies had granulomata on histology, and the addition of TB culture only marginally increased the overall diagnostic yield.

Our data confirm previous findings on the very high specificity of an ADA >50 IU/l in the presence of a lymphocyte predominant effusion.[6,38] We found specificity of 95.7% and a positive predictive value of 98.2%. More important was the observation that in a population with a high pre-test probability for TB, pleural TB could be diagnosed in the majority of cases without the need for a pleural biopsy.

After three years it became evident that we had to abandon the original non-inferiority design, as the sensitivity of the Tru-cut biopsies was significantly lower than the original estimation at this point. While this certainly could be viewed as a weakness in the original study design, we strongly believe that this had no impact on the conclusion of the study. We collected robust data with complete follow-up. The end points used were dichotomous, objective laboratory parameters which are not subject to random variation. Furthermore the study design was on par with other studies in the field and the achieved sample size on the higher end of the spectrum. [6,14,17,18,33]

In conclusion, US-assisted pleural biopsies performed with an Abrams needle are more likely to contain pleura and have a significantly higher diagnostic sensitivity for pleural TB. The Abrams needle should be the needle of choice for closed pleural biopsies in the setting of probable tuberculous effusions.

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**COMPETING INTEREST**

None

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**FIGURE LEGEND**

**Figure 1:** Cross section through an intercostal space, showing the position of the open Tru-cut needle immediately prior to harvesting a specimen. The Tru-cut needle is cautiously introduced through an incision at 45 degrees to the skin in the direction of the chosen intercostal space above the lower rib. Adjacent areas of pleura are then sampled. A distinct "give" indicate entry into the pleural space, which is confirmed by the ease of advancement of the inner stylet. The whole Tru-cut needle as is then angled towards the skin (position A to B), allowing the inner stylet to be advanced along the inner aspect of the thoracic wall and away from the lung. The outer cutting sheath is subsequently advanced over the inner stylet, yielding biopsy samples of up to 2 cm of parietal pleura and intercostal muscle. (Adapted from reference 14)

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