Single Puncture CT Guided fine-needle aspiration cytology (FNAC) and Tru-cut biopsy in Indeterminate Lung Lesions

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Abstract
Purpose
1. To establish cytological and histopathological diagnosis of indeterminate focal and diffuse lung lesions
2. Comparison of coaxial lung FNAC and trucut biopsy
3. Combined complications of coaxial lung FNAC and trucut biopsy
4. Establishment of guidelines to use FNAC or Tru-cut biopsy or both in different indeterminate lung lesions

Materials and Methods: Single puncture co-axial FNAC and biopsy was done in 76 patients referred to the department of radiodiagnosis, Indira Gandhi Medical College, Shimla who had indeterminate lung lesions on contrast enhanced CT. Role of co-axial biopsy needle in diagnosing indeterminate lesion was explored and comparison of both the techniques along with their complications was done using appropriate statistical tests.

Results: Overall sensitivity of biopsy (81.08%) was higher than FNAC (74.29%) but its specificity was low (50% versus 83.3%). Sensitivity of biopsy for benign lesion was higher than FNAC (83.3% versus 76.6%) but was comparable for malignant lesions (76.92% versus 76.6%). Hence FNAC and biopsy are complementary to each other than done alone (sensitivity 94.59%, specificity 97.22%).

Conclusion: Both the CT guided coaxial FNAC and trucut biopsy are complementary and should be done in a single sitting for a better diagnostic yield. Use of coaxial needle is more convenient for the patients rather than single biopsy needle.

INTRODUCTION
Computerized tomography (CT) guided fine needle aspiration cytology (FNAC) of lung lesions has rapidly emerged as a less-invasive, cheap, rapid and fairly accurate diagnostic tool for providing prompt classification of tumors. It has a diagnostic accuracy rate of 94% and a sensitivity rate of 95%(1), however, its diagnostic sensitivity rate in benign lung diseases is reported to be 12%(2) to 23.5%(3) only.

CT-guided Percutaneous Transthoracic Biopsy (PTB) is another diagnostic invasive modality...
which can be performed by either single needle trucut biopsy or by coaxial needle biopsy. Both techniques produce an overall diagnostic accuracy 98% for malignant lesions. The major advantage of coaxial technique is that a single pleural puncture is made, which allows multiple biopsies to be taken while a single needle biopsy technique causes two or more pleural punctures per procedure (4) hence causes inconvenience to the patient with increased risk of complications. In comparison with FNAC, core needle biopsy (CNB) achieves 90% specificity for benign lung lesions and sensitivity of 92% for malignant lung tumour with overall diagnostic accuracy of 91%, positive predictive value of 97% and and negative predictive value of 75% (5), with a risk of pneumothorax ranging from 17 to 26.6% (6) and pulmonary haemorrhage ranging from 4-27% (7).

The advantage of CNB includes the preservation of tissue architecture of the specimen, which is important in the assessment and sub-typing of some tumours and helps in applying immunohistochemical techniques (8). The tissues obtained via core biopsy allow better characterization of different cell types and is especially useful in lympho-proliferative disorders (7). CT-guided CNB is a feasible technique in acquisition of cancer tissues for EGFR gene mutation analysis. The use of CT-guided aspiration and core biopsy in a single sitting resulted in a high diagnostic yield for pulmonary nodules smaller than 1 cm. The use of the aspiration method alone is an independent risk factor associated with diagnostic failure (9) while combined use of FNAC and CNB yields better results with diagnostic accuracy of 75% for benign lesions (10). The complication rates of FNAC with the addition of a biopsy are similar to those reported in the literature for FNAC alone, hence sequential FNA and CNB improve the diagnostic yield of percutaneous CT-guided procedures in malignant lesions, especially in cases of uncertain diagnosis, without an increase in complication rate. In cases highly suggestive of a benign lesion, CNB alone may be considered as its yield is similar to that of same-session sequential CT-guided FNA and CNB procedure (11).

The aim of present study is to establish and compare the cytological and histopathological diagnosis and complications of focal and diffuse indeterminate lung lesions by use of both FNAC as well as a biopsy, in a single sitting with a single puncture, thus setting the guidelines for the use of appropriate technique in future.

**MATERIALS AND METHODS**

In this prospective study, 76 patients from July 2014 to June 2015 underwent CT guided co-axial FNAC and trucut biopsy for indeterminate lung lesions. All patients were followed up for complications and results.

**Study technique**-

Non-contrast CT thorax was performed at 10 mm section interval [0.625 mm slice thickness, 3.3 to 5s scanning time] with a window level of 475 Hounsfield Units(HU) and window width of 1900HU using the 64-slice CT scanner (Model: VCT Xte; GE Healthcare). Patient positioning was chosen based on the location and size of the lesion as depicted on previous CT thorax. Needle path were chosen to avoid pulmonary veins, arteries, bullae and fissures. Prone position was preferred wherever possible. Supine position was used if the lesion was located anteriorly. Oblique and decubitus positions were reserved if prone and supine accessibility of lesion was not possible. A limited CT of the lesion as depicted on previous CT thorax was performed to confirm the location, size, depth, necrosis and the safe access for needle track. By choosing the appropriate CT slice location and with the help of laser light a horizontal line was marked with a marker on the skin of the patient. A grid of metallic pins was placed on this marked horizontal line and limited CT sections were again taken. The most appropriate site and depth of needle entry was chosen and a perpendicular vertical line parallel to the gantry was drawn to first marked horizontal line on the skin. The point...
of intersection of these two lines was the site of entry. The skin around the insertion site was cleaned with povidone iodine and spirit, and a sterile drape was placed. The skin, subcutaneous tissue and trajectory along the path of needle including the intercostals muscles and nerves along the ribs were anesthetised with the direct injection of 5 ml of 2% lignocaine. Five ml of this anaesthetic agent was given in the same needle path radially while withdrawing to check for entry into venous system and in the end the skin around the entry site was infiltrated with lignocaine to raise a bleb.

Coaxial biopsy needle (US Biopsy, Coaxial SABD Biopsy System) of following types was used according to the size and depth of lesion:
- 18 GauzeX9cm(Introducer 17g(1.6mm)x7cm(3.9cm),SABD-18g(1.2mm)x9cm,(15mm,20mm))
- 18 Gauze X 15cm(Introducer-17g(1.6mm)x13cm(10cm),SABD-18g(1.2mm)x15cm,(15mm,20mm))

FNAC needle of 22 G with length of 9 cm or 15 cm was used depending on the depth of the lesion.

Puncture needle/introducer with its sheath was introduced into the lesion. New axial slices were made to confirm the correct location of the needle. The puncture needle was taken out and the sheath was left in situ. FNAC needle was introduced through the sheath into the target area of the lesion. If repositioning is necessary, the needle was adjusted without exiting the lung. Teasing of tissue was done and negative pressure was applied with piston of the 20 cc syringe and aspirated sample was transferred to glass slides to make smears. Then the FNAC needle was removed and puncture needle was again introduced to avoid air entry while the loaded gun was being introduced. The puncture needle was again taken out without disturbing the sheath. Loaded biopsy gun was introduced through the sheath with notch adjusted at 1.5cm cm (for lesions<1cm) or 2.0cm (for lesions>1cm). The gun was fired and vacuum was created and then the gun was taken out. The puncture needle again inserted into the sheath to avoid air entry. Required shots were taken by slightly changing the direction of the biopsy gun depending on the material obtained.

RESULTS
A total of 76 patients of indeterminate lung lesions between the age group of 18 to 80 years (mean age of 62.3±11.5 years) were included in the study. CT guided FNAC followed by biopsy were done in all the patients in a single setting.

In our study, the results of FNAC, biopsy, combined FNAC and biopsy were calculated in terms of sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio. Benign and malignant results were taken as positive cases, and indeterminate results were negative cases. These results were compared with the clinical diagnosis which was taken as gold standard.

Clinically total number of malignant lesions were 53 (69.7%) and benign lesions were 23(30.2%). FNAC was done in all 76 patients. There were 11 (14.5%) benign lesions, 42(55.2 %) malignant lesions, and 23 (30.2%) indeterminate lesions due to inadequacy of sample obtained. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of FNAC were 74.29%, 83.33%, 98.11%, 21.74% and 75% respectively. These results are shown in table I. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of biopsy were 81.08%, 50%, 98.11%, 21.74% and 75% respectively. These results are shown in table II.

Biopsy showed 20(26.3%) cases having benign lesions and 40(52.7%) as malignant lesions. In 16 patients (21.0%) biopsy yielded indeterminate results due to insufficient samples. The sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy of biopsy were 81.08%,50%,98.36%,6.67%,80.2% respectively (Table I). The sensitivity and specificity for
malignant lesions were 76.92% and 100% (Table-II), and for benign lesions were 83.33% and 100% respectively (Table-III). The overall sensitivity, positive predictive value, diagnostic accuracy of both FNAC and biopsy were 90.38%, 100%, and 92% respectively (Table-I). The sensitivity and specificity for malignant lesions were 90.38% and 100% respectively (Table-II) and for benign lesions were 90% and 60% respectively (Table-III).

Table I-Performance in all lesions

|                     | FNAC     | Biopsy   | FNAC+Biopsy |
|---------------------|----------|----------|-------------|
| Sensitivity         | 74.29%   | 81.08%   | 94.59%      |
| Specificity         | 83.3%    | 50%      |             |
| Positive Likelihood Ratio | 4.46     | 1.62     | 0.95        |
| Negative Likelihood Ratio | 0.31     | 0.38     |             |
| Positive Predictive Value | 98.11%   | 98.36    | 97.22%      |
| Negative Predictive Value | 43.48%   | 6.67     | 0%          |

Table II-Performance in malignant lesions

|                     | FNAC     | Biopsy   | FNAC+Biopsy |
|---------------------|----------|----------|-------------|
| Sensitivity         | 76.36%   | 76.92%   | 90.38%      |
| Specificity         | 100%     | 100%     | 100%        |
| Positive Likelihood Ratio | -        | -        | -           |
| Negative Likelihood Ratio | 0.24     | 0.23     | 0.10        |
| Positive Predictive Value | 100%     | 100%     | 100%        |
| Negative Predictive Value | 43.48%   | 25%      | 16.67%      |

Table III-Performance in benign lesions

|                     | FNAC     | Biopsy   | FNAC+Biopsy |
|---------------------|----------|----------|-------------|
| Sensitivity         | 47.62%   | 83.33%   | 95%         |
| Specificity         | 92.31%   | 100%     | 60%         |
| Positive Likelihood Ratio | 6.19     | -        | 2.37        |
| Negative Likelihood Ratio | 0.57     | 0.17     | 0.08        |
| Positive Predictive Value | 90.91%   | 100%     | 90.48%      |
| Negative Predictive Value | 52.17%   | 75%      | 75%         |

Among malignancies, maximum number of cases were of adenocarcinoma and among benign lesions tuberculosis was the commonest (Table IV).

Table IV-Distribution of Lesions

| MALIGNANT LESIONS           | FNAC | BIOPSY |
|-----------------------------|------|--------|
| Adenocarcinoma              | 12   | 14     |
| Squamous cell carcinoma     | 8    | 10     |
| Small cell carcinoma        | 8    | 5      |
| Non small cell carcinoma    | 9    | 2      |
| Bronchoalveolar carcinoma   | 0    | 2      |
| Unclassified carcinoma      | 4    | 3      |
| Metastases                  | 2    | 2      |
| Lymphoma                    | 0    | 1      |
| BENIGN-LESIONS              |      |        |
| Pulmonary TB                | 2    | 3      |
| Thymoma                     | 0    | 2      |
| Hamartoma                   | 1    | 1      |
| Purulent infection          | 1    | 0      |

Out of 76 patients, 18 patients (23.7%) developed pneumothorax (Table V). Out of these patients only 2 (11.1%) patients required chest tube insertion.
Only 9 patients (11.8%) developed haemorrhage along tract (Table VI). Only one patient developed mild haemoptysis (1.3%).

Table VI - Haemorrhage along tract

| Haemorrhage along tract | Frequency | %  |
|-------------------------|-----------|----|
| Present                 | 9         | 11.8|
| Absent                  | 67        | 88.2|

**DISCUSSION**

CT guided transthoracic needle biopsy has emerged as one of the leading procedures for the diagnosis of indeterminate pulmonary and mediastinal lesions. When successful, this method may obviate the need for more invasive diagnostic approaches such as thoracoscopy, mediastinoscopy or thoracotomy. Fine-needle aspiration (FNA) provides a sample that is usually adequate for cytological and microbiological examinations, but not for a histological evaluation. The larger volume of tissue obtained by percutaneous core-needle biopsy (CNB) enables histopathological diagnosis and more sophisticated laboratory analysis. The optimal technique for the diagnosis of intrathoracic lesions has not yet been recommended (11,12). FNA or CNB are commonly used, while single puncture FNAC with trucut biopsy is not yet the trend.

Only a few studies are available in the literature in which both CT guided FNAC and biopsy were performed sequentially with a single puncture using coaxial approach. Our study is in concordance with Aviram et al (11) who showed that using sequential FNA and CNB improves specimens adequacy (95%) and hence the rate of precise diagnosis (94.5%). However, in their study the patient was subjected to two punctures, one for FNAC and the next for coaxial biopsy as opposed to our approach of giving single puncture to the patient for both FNAC and biopsy. There was also presence of on-site cytologist in their study but not in ours.

Our results were also in agreement with Yamagami et al (13) who performed both CT guided FNAC and biopsy under CT Fluoroscopy and the combined results (94.2%) were better than either performed alone (79.7% for FNAC and 89.1% for biopsy). CT guided fluoroscopy is a real time procedure, however it is not available in many centres and is associated with high radiation exposure.

Schoellnast et al (3) concluded that CT-guided biopsy of a lesion of the lung with FNA, and without an on-site cytopathologist, did not yield higher sensitivity or specificity compared to CNB alone. The result of this study was opposite to our study, which showed definite improvement in results by combining FNAC and biopsy. Our study emphasised the use of coaxial needle for performing the CT guided FNAC and biopsy of indeterminate lung lesions.

In a study performed by Wu et al (4) on the use of single or coaxial biopsy needles the results showed that both techniques yielded an overall diagnostic accuracy of 98% for malignant lesions with similar sensitivity (single needle: 96.9% vs. coaxial: 96.4%) and specificity (single needle: 100% vs. coaxial: 100%). The major disadvantage of performing single needle transthoracic biopsy is that the correct needle positioning has to be made each time a pleural puncture is performed, hence
more time consuming. In comparison, the coaxial system would allow multiple numbers of tissue extractions with single pleural puncture, which is more convenient, relatively easy and gives less radiation dose to the patient as sheath position is to be checked only once by CT. However, the coaxial system may be more costly approximately 21% higher than that of single needle technique per procedure. Secondly, results showed that using single needle technique does not take longer duration, in fact shorter than that of the coaxial technique when performing cutting needle biopsy. These suggest that a single needle technique may have value when considering which of techniques to use to perform transthoracic biopsies. The disadvantage of the single needle technique is that each time the needle is introduced into the lesion; image guidance is required, resulting in increased procedure time. Moreover, intervening structures are traversed each time, resulting in increased risk of complications. While a coaxial technique offers many advantages, larger caliber guiding needles are required to puncture the pleura. In the presence of a prominent internal air-bronchogram or open-bronchus sign in the lesion, a coaxial technique should be used more carefully as there is an increased risk of air embolism.

CONCLUSION
In our study 76 patients had undergone CT guided coaxial FNAC and trucut biopsy in a single sitting. The sensitivity and diagnostic accuracy of biopsy were better than FNAC for both benign as well as malignant lesions. The sensitivity, positive predictive value and diagnostic accuracy of combined FNAC and biopsy were much higher than either FNAC or biopsy alone. The coaxial needle was also more compliant for the patients. Thus, the inference of our study is that both the CT guided coaxial FNAC and trucut biopsy of indeterminate lung lesions should be done for a better diagnostic yield, thus both modalities are complementary to each other and the use of coaxial needle is more convenient for the patients rather than single biopsy needle.

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