Oncology
and Radiotherapy ©
Vol.16 Iss.2:30-34 • Research Article

Feasibility and therapeutic implication of computed tomography-guided TruCut biopsy in cases of recurrent adenocarcinoma lung

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SUMMARY

Introduction: Recurrence is a rule, in the case of advanced NSCLC and even patients with early-stage disease are at risk of disease recurrence. It is recommended to acquire tissue biopsy samples at recurrence, not only for the diagnosis of relapsed disease but also for additional molecular analysis. TruCut biopsy is a simple procedure, is relatively safe, rapid and a reliable technique for the diagnosis of lung lesions. But all patients may not be ideal candidates for needle biopsy at recurrence because of various tumour related and patient-related factors. This study of ours tried to find out the feasibility of image-guided transthoracic needle biopsy and compared its therapeutic implications with those who could not undergo the procedure.

Result: Overall adequacy rate of obtaining tissue samples was 89.7% (35/39). All patients who undergo needle biopsy tolerated it well. Most common complications were pneumothorax (12.8%) (5/39) and pulmonary haemorrhage (10.2%) (4/39). Two (5.1%) patients developed hydropneumothorax. The cumulative percentage of side effects was 17.9% (7/39) and no procedure-related fatality. 42.8% of patients who underwent needle biopsy were started with the second line targeted/Immunotherapy. Only 21.0% of the patients who underwent liquid biopsy instead, received targeted therapy in the second line.

Conclusion: TruCut biopsies of NSCLC'S at recurrence are feasible and are adequate in appropriately selected patients and associated with acceptable rates of complications. Rebiopsy may explore new tumour characteristics and give the opportunity to act on changes in tumour behaviour. For those patients who are not candidates for a needle biopsy, in them, liquid biopsy is a comparable alternative.

Key words: recurrent lung cancer, repeat needle biopsy, liquid biopsy

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Word count: 2472 **Table:** 03 **Figures:** 03 **References:** 13

Received: - 20 January, 2022, Manuscript No. M-51941

Editor assigned:- 22 January, 2022, PreQC No. P-51941

Reviewed:- 15 February, 2022, QC No. Q-51941

Revised:- 28 February, 2022, Manuscript No. R-51941

Published: - 10 March, 2022, Invoice NO. J-51941

INTRODUCTION

Lung cancer is one of the leading causes of cancer deaths worldwide. The common histologic types are Adenocarcinoma (ADC), Squamous Cell Carcinoma (SCC) and Small Cell Lung Cancer (SCLC). Clinical staging is performed with noninvasive diagnostic modalities, such as total body CT scan with contrast, and/or Positron Emission Tomography (PET). Diagnostic tissue biopsies may be obtained through percutaneous route with image-guided needle biopsy or bronchoscopic biopsy for endobronchial lesions or open biopsy if the former modalities could not obtain tissue. TruCut biopsy is a simple procedure, is relatively safe, rapid and a reliable technique for the diagnosis of lung lesions, particularly with the aid of a Computed Tomography (CT) scan [1]. Core biopsy not only distinguishes between benign and malignant lesions but also helps in tumour typing and molecular characterization of lung cancers, so customised targeted treatment is possible according to the tumour types. A common concept, in oncology as in microbiology, is that prolonged exposure to certain drugs can select a resistant population, either a neoplastic cell or a bacterium. Acquired resistance limits the great hopes of targeted therapies as well. The majority of patients experience it after a variable interval of time, because of a resistant clone that causes disease progression. A deeper understanding of molecular biology has made it possible in some cases to identify the specific mechanisms behind acquired resistance. So it is recommended to acquire tissue biopsy samples at recurrence, not only for the diagnosis of relapsed disease but also for additional molecular analysis [2,3]. Molecular analysis can be performed on surgical specimens, cytology cell blocks or small tissue biopsy specimens taken from the primary tumour or metastases. As needle size increases, the risk of complications also increases. Risk also depends on the location of the tumour. The most common complications include pneumothorax and bleeding. In case tissue is not obtainable, for molecular characterization of the recurrent disease, newer modalities like liquid biopsies such as Circulation Tumour Cells (CTC) or circulating tumour DNA (ctDNA) assays are promising alternatives [4,5]. So in this study, we tried to determine the feasibility and safety of CT guided lung biopsy of relapsed NSCLC and tried to determine its therapeutic implications, in comparison to where tissue biopsy was not feasible. Our aim here is to determine the feasibility and

safety of CT guided lung biopsy of NSCLC (Adenocarcinoma) at recurrence. Finer molecular characterization through next-generation sequencing and immunohistochemistry and to find out the pros and cons of image-guided lung biopsy in comparison to liquid biopsy.

METHODOLOGY

Sixty-six non-small cell lung cancer (Adenocarcinoma) patients irrespective of the stage of presentation, who were being treated in our hospital, were enrolled in the study and followed up prospectively. Over time 12 patients were lost to follow up. All of the 54 patients on follow up eventually had recurrence/progression of the disease, which was documented with contrast, enhanced CT scan. All of them were evaluated for trans-thoracic CT guided needle biopsy at progression. The feasibility of needle biopsy was studied according to the various tumour and patient-related factors and reasons for not being able to conduct needle biopsies were documented. Patients in whom, a needle biopsy was not possible for whatever reasons, were subjected to liquid biopsy. Between the liquid biopsies and needle biopsies, therapeutic implications were compared.

Pre-procedure evaluation and the procedure

Prothrombin Time (PT), International Normalized Ratio (INR), Activated Partial Thromboplastin Time (APTT), and platelet count was checked before a needle biopsy. Those patients, who were on aspirin or clopidogrel, were asked to discontinue it 5 days before the biopsy. Patients on oral anticoagulants were switched to low molecular weight heparin before 3 days, which in turn was withheld on the day of the procedure. CT studies were performed on 128 SLICE CT SCANNER [GE OPTIMA CT660] in all patients. Location of the lesions, location of fissures adjacent to the lung lesions or within the pathway of the biopsy needle trajectory, location of adjacent arteries and veins were evaluated, in order to plan the needle trajectory. The angle of entry of the needle, route of entry and distance between skin and the lesion and the length of throw was documented on the CT scan monitor. Patients were positioned either in prone, supine or lateral position depending on the skin site entry point chosen. The breath-holding technique was followed during the procedure and it was explained to the patient and was practised beforehand. Patients were asked to avoid coughing and taking deep breaths during the procedure (Figures 1-3).

Statistical evaluation

Quantitative data is represented in form of a percentage. Data analysis was done using Statistical Package for Social Sciences (SPSS) version 25.0.

RESULTS

Baseline patient and tumour characteristics are mentioned in Table 1. All of the 54 patients on follow up eventually had recurrence/progression of the disease. Forty-six (n=46) of these 54 patients had a recurrence in the lung with or without other sites of metastasis. And the rest 8 patients had recurrences at distant sites only and did not involve lung at recurrence. Out of the 46 patients who had lung lesions at recurrence, 39 patients underwent trans-thoracic needle biopsy. Among them, viable tumour tissue could be obtained for 35 patients. Among the 7 patients who did not undergo needle biopsy, 3 had a poor general condition with low oxygen saturation. For 4 patients, lung lesions were close to the great vessels, which made them unfit for needle biopsies. Patients in whom viable tissue could not be acquired through needle biopsy, or whose who could not undergo needle biopsy because of technical issues, or those who did not have a lung lesion at recurrence and other lesions were not amenable for biopsy, were subjected to liquid biopsy.

Tab. 1. Patient characteristics

Characteristics	N=54
Sex	
Male Female	32 22
Age (in years)	
Median	63(29-87)
Primary treatment	
CT+RT Palliative chemotherapy TKIs	12 20 34
Sites of disease on recurrence/progression	
Lung ± others Other sites without lung lesion	46 8
Location of the largest lung lesion	
RUL RML RLL LUL LLL	12(26%) 6(12%) 10(22%) 11(24%) 7(16%)

Tab. 2. Results of molecular analysis

	Needle biopsy at recurrence (n=35)	Liquid biopsy at recurrence (n=19)	P*
EGFR exon 19 mutation	13	9	P value not significant
EGFR exon 21 (L858R)	6	6	
EGFR Exon 20(T790M)	5	9	
PD L1	7	X	
ALK rearrangement	2	X	
ROS1	1	X	
BRAF (V600E)	2	X	

*Chi-square test

Tab. 3. Complications in rebiopsies performed in relapsed cases of Non-small cell lung cancer

Complications	(n=39)	Percentage
Pneumothorax	5	12.82%
Pulmonary Hemorrhage	4	10.25%
Hydropneumothorax	2	5.12%
No complication	32	82.05%

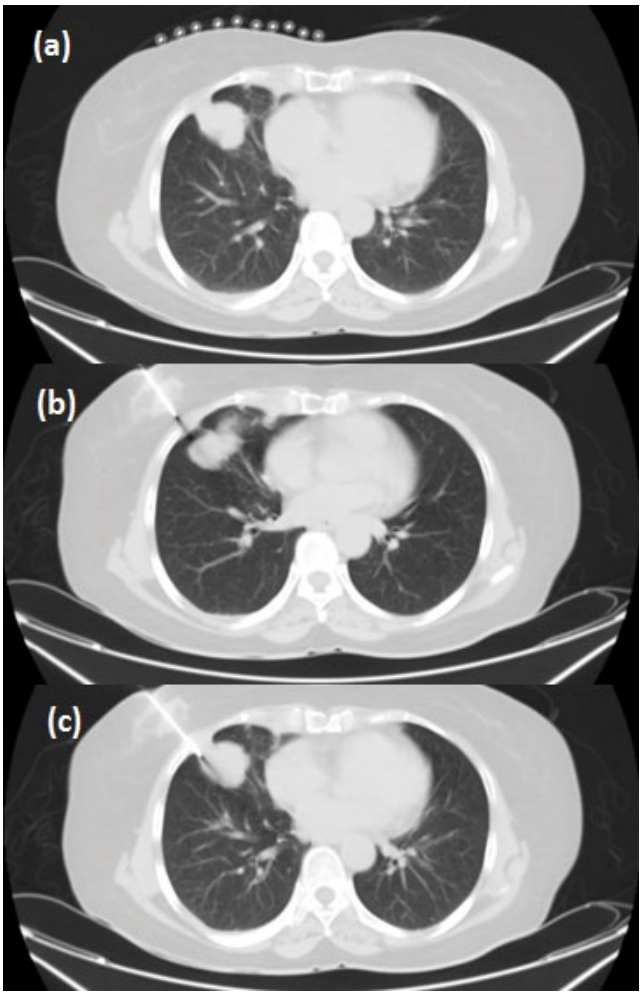

Fig. 1. Representative case of percutaneous transthoracic core needle biopsy in a Relapsed NSCLC patient. Axial CT image (lung window) (5 mm section thickness) shows a mass in the right middle lobe; (a): Surface Markers; (b): Coaxial needle approach; (c): Advancement to lesion-Repeat CT scan obtained after needle insertion ensures that the needle tip (arrow) is located within the target mass

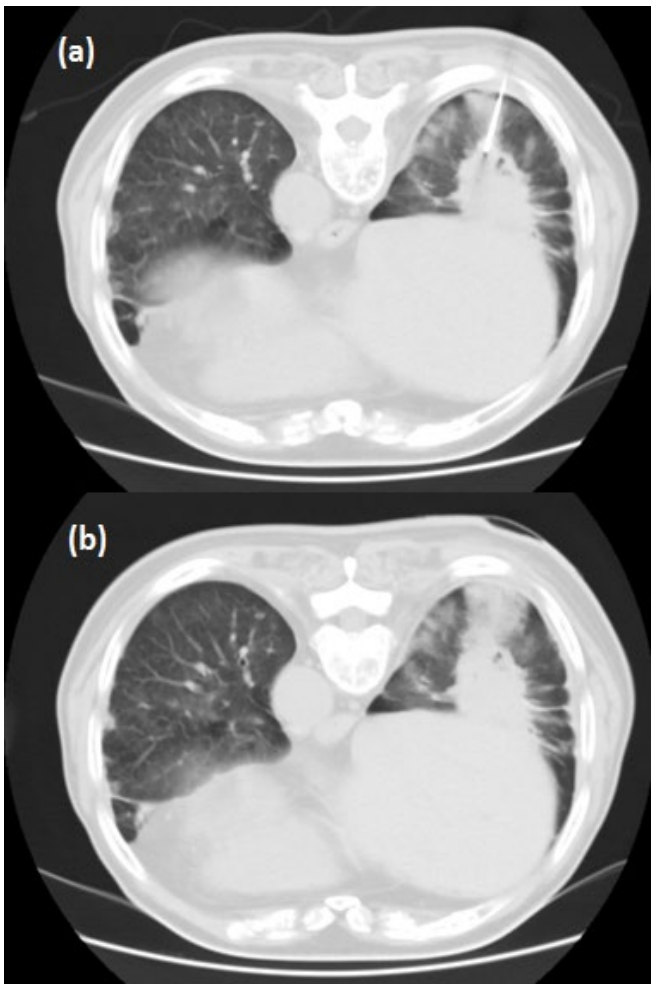

Fig. 2. Representative case of percutaneous transthoracic core-needle biopsy in a Relapsed NSCLC. Patient. Axial CT image (lung window) (5 mm section thickness) shows mass in the right lower lobe; (a): Repeat CT scan obtained after needle insertion ensures that the needle tip (arrow) is located within the target mass; (b): Post Procedure-Pulmonary Hemorrhage

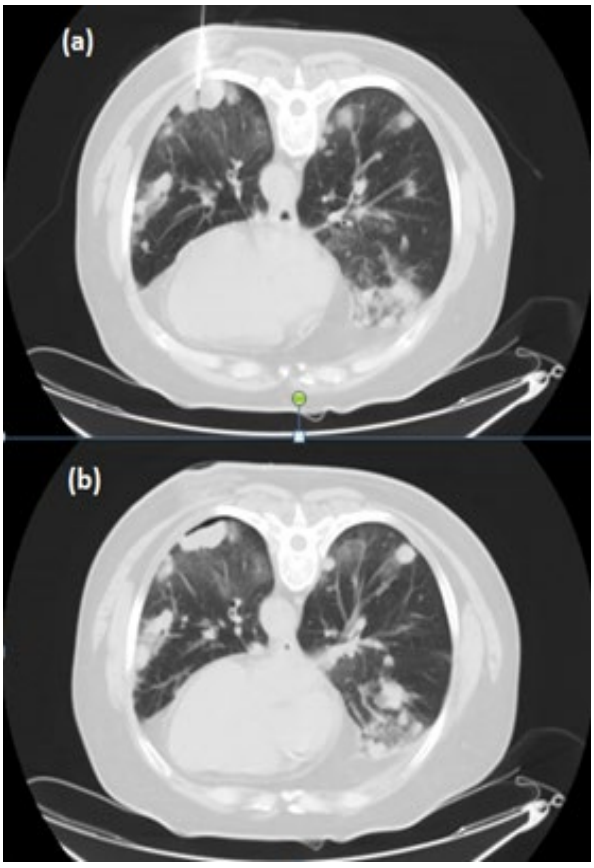

Fig. 3. Representative case of percutaneous transthoracic core needle biopsy in a Relapsed NSCLC patient. Axial CT image (lung window) (5 mm section thickness) shows a mass in the left lower lobe (a case of multicentric recurrence); (a): Repeat CT scan obtained after needle insertion ensures that the needle tip (arrow) is located within the target mass; (b): Post Procedure-Minimal Pneumothorax.

DISCUSSION

The study was conducted with the objective to determine the feasibility and safety of CT guided TruCut biopsy in recurrent NSCLC (adenocarcinoma) patients. Out of 46 patients who had lung lesions at recurrence, rebiopsy was performed in 39(84.7%) patients, 7(15.3%) patients did not undergo biopsy due to the limiting factors such as poor performance status and difficult location of the tumour. Out of 39 patients who underwent needle biopsy, adequate tumour tissue could not be obtained in 4(10.3%) patients. So the adequacy rate of obtaining tissue samples was 89.7% (35/39). All patients who underwent needle biopsy tolerated well, cumulative percentage of side effects was 17.9% (7/39) and no procedure-related fatality (Tables 2 and 3) (Figures 2 and 3). According to studies, pneumothorax has been reported to be the most common complication of needle biopsy of the lung lesions and is reported to occur in 17%-27% of patients; pulmonary haemorrhage is the second most common complication, with reported frequencies ranging from 4%-27% [6-10]. Our complication rates for pneumothorax (12.82%) and pulmonary haemorrhage (10.25%) were comparable to the above-mentioned studies. Patients treated with EGFR-TKIs, frequently leads to the appearance of drug-resistant mutations within the target kinase [11-13]. A few of these new mutations are targetable, so the molecular characterisation of the additionally acquired mutations is the need of the hour. In our study, there was no statistically significant difference in the probability of finding a driver mutation or a resistance causing mutation like T790M, between needle biopsy and liquid biopsy. But in comparison to the liquid biopsy, a needle biopsy can procure tissue for histopathologic examination and IHC, so can detect histologic transformations or second primary if any, as well (Table 2). 42.8% (15/35) of patients who underwent needle biopsy were started with the second line targeted/ Immunotherapy. Only 21.0% (4/19) of the patients who underwent liquid biopsy instead, received targeted therapy in the second line.

CONCLUSION

Rebiopsy and mutational analysis of NSCLC'S are feasible and are adequate in appropriately selected patients and associated with acceptable rates of complications. Rebiopsy may explore new tumour characteristics and give the opportunity to act on changes in tumour behaviour. Rebiopsy can be used to predict therapeutic resistance and consequently redirect targeted therapies. Thus changes in treatment facilitate better tumour control. For those patients who are not candidates for a needle biopsy, in them, liquid biopsy is a comparable alternative.

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