Innovative method of Transthoracic Lung Cancer Biopsy of Parietal Lung Tumors under US Guidance after CT Pre-biopsy Planning as an Alternative to CT-Guided Biopsy

Marek Chorąży1, Marta Majcher1, Katarzyna Fedyszyn Urbanowicz1, Jędrzej Glasek2, Maciej Gawlikowicz2 and Tomasz Duniec3

1. Department of Clinical Oncology and Internal Medicine, St. Leszczyński Hospital, Katowice 40-074, Poland
2. Radiodiagnostics Department, S. Leszczyński Hospital, Katowice 40-074, Poland
3. IT Department, Leszczyński Hospital, Katowice 40-074, Poland

Received: October 08, 2014 / Accepted: October 18, 2014 / Published: October 25, 2014.

Abstract: The authors compared their earlier results of the tumor biopsies performed under computer tomography (CT) guidance against the results of their recently modified-combined method of visualization and measurement of lung tumor parameters by CT imaging followed by US guided biopsy. In 238 (6.36%) of 3,745 patients in CT examination, the lung tumor was located peripherally, and obtaining histopathological confirmation was crucial to start the proper treatment. The patients were divided into two groups, the division was based on the biopsy method. Within the first group in 118 patients, parietal lung tumor was confirmed and CT guided biopsy was performed. Within the second group, parietal lung tumor was confirmed in 120 patients and combined method of CT pre-biopsy planning and US guided biopsy were used. Pre-biopsy planning was performed using CT, measurements such as depth and distance of the tumor were made, obtained data were then saved on CT image and patient’s skin was marked. Then obtained results were analyzed using test for two proportions. The analysis of the results confirmed the higher efficacy of the combined method taking into account the number of complications ($p < 0.01$) and diagnostic histopathological results ($p < 0.001$). Suggested innovative method, involving both CT pre-biopsy planning and US guided biopsy, allows to analyze simultaneously static CT and dynamic US images and it is considered to be an easy and effective method comparing to relying on static in nature CT images only. Our method is related to a lower complication risk rate.

Key words: Parietal lung cancer diagnosis, computer tomography, ultrasound transthoracic guided fine-needle biopsy,

1. Introduction

In the clinical assessment of pathological tumor lesions, including lung tumors, we try to determine their size, location and type of histopathological pattern. To evaluate them, roentgenographic examination, computer tomography (CT) [1, 2] magnetic resonance imaging (MRI) [3, 4], positron emission tomography (PET) [5, 6], and isotopic studies [7] most frequently are applied. Fiberoptic bronchoscopy and its modifications [8] are widely used tests providing information as to the pattern of the malignant tumor. The most common is transbronchial echography combined with a biopsy endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) [9-13]. Another method which is also used is an aspiration biopsy performed under CT guidance and fluoroscopic percutaneous lung biopsy as an alternative to the
Innovative Method of Transthoracic Lung Cancer Biopsy of Parietal Lung Tumors under US Guidance 
after CT Pre-biopsy Planning as an Alternative to CT-Guided Biopsy

previous method [8, 13, 14]. There is also research concerning the identification of tumors by determining genetic markers in tumor specimens collected with the help of an aspiration biopsy [15]. It is extremely rare to use traditional ultrasonography (US) to diagnose solid lesions in lungs, because of the impenetrability of air when using ultrasounds [16].

Despite undoubted advantages of US-guided lung cancer biopsies as diagnostic procedures emphasized by biopsy operators, reports of such procedures appear sporadically in medical literature [17, 18], due to technical difficulties in obtaining adequate images of lung tumors using US only.

A conventional CT-guided transthoracic biopsy of lung tumors is well-known and a commonly used diagnostic technique that is an indispensable tool in the diagnosis of thoracic lesions [19-23]. It is most frequently used in cases when the parietal location of the tumor precludes us to obtain tissue for histopathological examination using other methods. It is considered to be minimally invasive and associated with significantly less complications. Complications arising from this method are related to the fact that samples are not collected using real time imaging but are based on the visualized images, which are static in nature, taken at the time of the CT examination.

Based on these facts, the authors decided to find out whether using combined method of US guided biopsy preceded by CT pre-biopsy planning would improve the diagnostic results and decrease the number of complications.

Having vast experience in performing biopsies (including transthoracic biopsies) [24-27], the authors compared their earlier results of the tumor biopsies performed under CT guidance against the results of their recently modified-combined method of visualization and measurement of lung tumor parameters by CT imaging followed by US guided biopsy.

2. Materials and Methods

The research was conducted from January 1997 to December 2012. CT results of 3,745 patients, who had a CT examination performed to diagnose lung cancer were analyzed. There were 2,177 (58.1%) men and 1,568 (41.9%) women.

In 238 (6.36%) of the 3,745 patients, a lung tumor was located parietally. All 238 patients were referred for transthoracic biopsy as a way of obtaining histopathological confirmation which was crucial to start the proper treatment.

The patients were referred for the procedure to the Oncology Outpatient Clinic. All biopsies were performed in the Biopsy Room of the Department of Clinical Oncology and Internal Medicine.

All patients were given an explanation of the nature and purpose of the procedure and a consent form was signed by each patient before undertaking the procedure.

There were several pre-biopsy requirements which included: informed consent, prothrombin activity greater than 70%, a platelet count higher than 80,000/μL and 12 h of fasting before the procedure. The procedure was performed under local anesthesia.

The analyzed patients were divided into two groups based on the biopsy method.

The first group was diagnosed between January 1997 and August 2006; 1801 patients had thoracic CT scans done, in 118 of them, a parietal lung tumor was confirmed and in 113 of the patients, a CT guided biopsy was performed.

The location of the tumor was established during a CT examination. A CT was performed with the use of a Siemens Somatom ARTX and Siemens Somatom Sensation Open Scanner. The procedure consisted of direct measurement of the distance between the tumor and the anatomical/topographical landmarks (i.e., the anterior or posterior median line or the jugular notch of the sternum) as well as the exact measurement of the angle and depth of the biopsy needles insertion (Figs. 1 and 2). The specimens were taken with 90 × 1.2 mm diameter Bolton biopsy needles. The needle insertion was performed only once trying to collect 2-4
Innovative Method of Transthoracic Lung Cancer Biopsy of Parietal Lung Tumors under US Guidance after CT Pre-biopsy Planning as an Alternative to CT-Guided Biopsy

The second group was diagnosed between July 2006 and December 2012 and consisted of 1944 patients with lung cancer. Within that group, a parietal lung tumor was confirmed in 120 of the patients. In 113 of 120 patients, a transthoracic biopsy was performed. Contrary to the first group, an innovative, combined-method of CT pre-biopsy planning and biopsy under US guidance was used. A CT pre-biopsy planning was performed using the Siemens Somatom Sensation Open Scanner, measurements such as depth and distance of the tumor were made, the obtained data was then saved on CT images and the needle insertion site was marked on each patient skin.

Initially, CT images obtained during pre-biopsy planning were transferred to the ultrasound room on removable storage media (CD Flash Drive) and displayed on a monitor placed near the ultrasound monitor. Currently, all of the gathered metric data were then saved in DICOM format and exported to Picture Archiving and Communication Systems (PACS) which is a part of the integrated hospital information system introduced in our hospital in 2011 by PIXEL Technology Company [28]. The achieved results were available in the biopsy room allowing the biopsy operator to visualize and compare simultaneously both images: a static CT image made during pre-biopsy planning, consisting of all data and measurements plotted in the CT image and the real-time US images. As the operator’s assistant maintained the probe steadily, the biopsy needle was inserted at the marked position on the skin during the CT pre-biopsy planning spot and US imaging was used to track the manually inserted needles path in real-time. (Figs. 3 and 4). Then it was displayed in a given area with the help of ultrasound examination (Fig. 5). The biopsy operator being able to view static images of the lesion taken during CT pre-biopsy planning (Fig. 2) introduced the needle into the lesion (Fig. 6) under the control of US in real-time. The
accuracy of the procedure was dependent on the visibility of the needle tip within the lesion. US Hitachi EUB 515 and Logiq C5 with a Convex 3.5 MHz transducer were used to visualize the lesions. For specimen collection, biopsy needles (size 90 \times 1.2 mm) were used. During each procedure, 2-4 punctures of the tumor were made in order to obtain samples from the most representative sites of the tumor visualized by the US and collected tissue samples were then sent for histopathological analysis.

Test result for two proportions is associated with the number of results obtained.

Unfortunately, in 12 cases (five in the first and seven in the second group), the biopsy was withdrawn due to an inaccessible location of the tumor behind anatomical structures such as bones (Fig. 7)

3. Results

The starting point of the study was the observation that in the majority of cases, conventional US images of lung masses are inconclusive and could only suggest the presence of suspicious lesions in the lungs while using both US imaging supported by static CT scans obtained during pre-biopsy planning gives the opportunity to control biopsy needle path in real-time under US guidance. In addition, during CT pre-biopsy planning, a mark is made on the skin where the needle is to be inserted helping the biopsy performer to localize needle entry site and perform the procedure.

The main purpose of the study was to find out if simultaneous use of two forms of lung tumor imaging (CT and US) while performing biopsy has advantages over blind CT-guided biopsy and to compare its influence on histopathological results.

The other goal of the study was to compare the number of complications (such as haemoptysis, pneumothorax) of our innovative, combined method of US-guided biopsy preceded by CT pre-biopsy planning to number of complications after conventional CT-guided biopsy.

For this purpose, patients were divided into two groups:

The first group consisted of 118 patients who underwent thoracic CT scans between 1997 and 2006, which confirmed a parietally located lung tumor. One hundred thirteen of the 118 patients had a CT guided biopsy of which 98 cases (86.72%) allowed us to obtain an unambiguous histopathological diagnosis. In the remaining five cases, a diagnosis was not established as inadequate or necrotic material was obtained.

The consecutive group of 120 patients was referred for a transthoracic biopsy of the peripherally located tumors between July 2006 and December 2012. The procedure, performed in 113 of the patients, was modified-performed under US guidance and after establishing the exact location of the tumor as well as the place and depth of needle insertion during CT pre-planning biopsy. Correct histopathological diagnosis was obtained in 111 of the patients (98.23%).
Analysis of all biopsy results revealed statistically significant difference among the numbers of accurate histopathological results of biopsies performed using our innovative, combined method as compared to CT guided biopsy results (test for two proportions). However, analyzing histopathological results of samples obtained from different regions of the lungs showed no significant statistical difference which is probably related to small number of cases in each group (Table 1).

In the first group, five patients did not undergo the procedure as the lesion was inaccessible for needle insertion due to location behind the scapula or ribs. A similar situation occurred in the second group in seven cases.

The most common biopsy-related complications included pneumothorax and haemoptysis. An analysis of these complications revealed significantly lower incidence of pneumothorax in patients who underwent US guided biopsy preceded by CT pre-biopsy planning as compared to the complications rate in patients referred for CT guided biopsy only. There was also statistically significant difference between these two groups for total number of all complications (Table 2).

In all cases, complications relieved themselves spontaneously and did not require any additional interventions.

The most common tumor was squamous cell carcinoma (49%) followed by adenocarcinoma (28%) and small cell carcinoma (23%) (Table 3).

The obtained histopathological results subdivided themselves similarly in both groups in accordance with the frequency of occurrence of lung cancer. There was no correlation between the localization of the tumor and histopathological pattern.

In both groups, tumor size varied between 3 and 8 cm.

### Table 1 Results of the biopsies of peripheral lung tumors.

<table>
<thead>
<tr>
<th>Biopsy method</th>
<th>Number of cases</th>
<th>Number of biopsies performed</th>
<th>Number of results obtained</th>
<th>Test results for two fractions*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total number of biopsies performed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>118</td>
<td>113 (95.8%)</td>
<td>98 (87.73%)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>CT + US</td>
<td>120</td>
<td>113 (94.16%)</td>
<td>111 (98.23%)</td>
<td></td>
</tr>
<tr>
<td><strong>Lung apex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>32 (27.11%)</td>
<td>28 (24.77%)</td>
<td>27 (28.12%)</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>CT + US</td>
<td>34 (28.33%)</td>
<td>31 (27.43%)</td>
<td>30 (27.02%)</td>
<td></td>
</tr>
<tr>
<td><strong>Anterior part of the thorax</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>22 (18.64%)</td>
<td>22 (19.46%)</td>
<td>19 (19.38%)</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>CT + US</td>
<td>20 (16.67%)</td>
<td>19 (16.81%)</td>
<td>19 (17.12%)</td>
<td></td>
</tr>
<tr>
<td><strong>Posterior part of the thorax</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>41 (34.74%)</td>
<td>40 (35.39%)</td>
<td>35 (35.71%)</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>CT + US</td>
<td>44 (36.67%)</td>
<td>41 (36.28%)</td>
<td>40 (36.04%)</td>
<td></td>
</tr>
<tr>
<td><strong>Lung base</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>23 (19.49%)</td>
<td>23 (20.35%)</td>
<td>17 (17.34%)</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>CT + US</td>
<td>22 (18.33%)</td>
<td>22 (19.47%)</td>
<td>22 (19.82%)</td>
<td></td>
</tr>
</tbody>
</table>

*Test result for two proportions is associated with the number of results obtained.

Test results for two proportions used for comparison of the fraction (percentage) of the obtained results (in relation to the number of biopsies taken) in both treatment groups (86.73% and 98.3%) indicates that this fraction is statistically higher in the group when the combined method of CT + US was used (p < 0.001). Comparisons of fraction results obtained after analyzing location did not show statistical significance (all p > 0.05). Only the total score shows the difference discussed above.

### Table 2 Post-procedure complications in both groups.

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>CT guided biopsy (n = 113)</th>
<th>US guided biopsy supported by CT pre-biopsy planning (n = 113)</th>
<th>Test result for two fractions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax</td>
<td>18 (16%)</td>
<td>8 (7.07%)</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>6 (5.3%)</td>
<td>3 (2.65%)</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>11</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

The difference in the incidence of pneumothorax (p < 0.05) was significant, no significant difference (p > 0.05) in the incidence of hemoptysis was noted. However, differences in the incidence of total complications (p < 0.01) was found highly statistically significant.
Innovative Method of Transthoracic Lung Cancer Biopsy of Parietal Lung Tumors under US Guidance after CT Pre-biopsy Planning as an Alternative to CT-Guided Biopsy

Table 3  Histopathological results.

<table>
<thead>
<tr>
<th>Histopathological pattern</th>
<th>Biopsy results obtained using CT guided biopsy n = 98</th>
<th>Biopsy results obtained using US guided biopsy supported by CT pre-biopsy planning n = 111</th>
<th>In total : n = 209</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell carcinoma</td>
<td>n = 46 (46.93%)</td>
<td>n = 54 (48.64%)</td>
<td>n = 100 (47.84%)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>n = 27 (27.56%)</td>
<td>n = 31 (27.93%)</td>
<td>n = 58 (27.75%)</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>n = 25 (25.51%)</td>
<td>n = 26 (23.43%)</td>
<td>n = 51 (24.41%)</td>
</tr>
</tbody>
</table>

The most common tumor was squamous cell carcinoma (49%) followed by adenocarcinoma (26%), small cell carcinoma (20%) and large cell carcinoma (5%).

The incidence of various types of lung cancer located parietally does not differ from the general statistics of tumors in the lungs.

4. Discussion

The analysis clearly indicates a statistically significant greater number of correct biopsy results obtained thanks to innovative, combined-method of US guided biopsy supported by CT pre-biopsy planning as compared to CT-guided biopsy only. No significant difference in the effectiveness of the biopsy in relation to tumor location was noted (Table 1). In most cases, it is impossible to detect parietally located lung tumors and qualify patients for transthoracic biopsy using US visualization only. Detecting pathological lesions in the lungs by US examination supported by CT images acquired during pre-biopsy planning seems to be a reliable and easy way to access the pathological mass as long as no barriers such as collection of air in the pleural space or anatomical structures like ribs, vertebra or scapula occur.

The main disadvantage of using CT guided biopsy is the inability to track the biopsy needle in real-time and visualizing the needle tip in the lesion.

Moreover, in cases of necrotic tumors or in situations when the majority of the tumor mass is located behind anatomical structures such as bones, the risk of obtaining incorrect tissue samples increases, therefore increasing the risk of misdiagnosis due to the fact that the final step is performed blindly, using static images.

In our method, the order of the biopsy procedure was as follows: the location of the lung tumor and the planned needle path were established during CT pre-biopsy planning (Fig. 8), then the lung tumor was visualized thanks to US (Fig. 9) and subsequently the biopsy needle was inserted under direct vision (Fig. 10) in order to collect samples.

One example supporting the advantage of our innovative method is the case of a patient with a lung tumor in the lung apex where the needle path was initially planned during CT pre-biopsy planning choosing the shortest way through the muscles and soft tissues (Fig. 11), but the presence of blood vessels did not allow us to use the shortest way. Eventually, the lung tumor was visualized by the US from the axillary fossa increasing the safety of the procedure (Fig. 12).
Another problem we encountered were cases when the lung tumors were situated behind natural barriers such as ribs, the spine or scapula. That situation occurred in 12 cases in both groups which stands for 5% of all cases and made performing the biopsy impossible. All 12 patients were referred for thoracic surgery.

Therefore, we doubt the results of other researchers indicating the effectiveness of CT guided biopsy of more than 93% [20-22], as only the location of the lung tumor makes the biopsy impossible in more than 5% of cases. Probably other criteria were applied to include patients for the procedure.

Another problem while performing CT guided biopsy is the selection of the puncture site. The innovative authors’ method enables us to choose a place where we least expect necrosis or inflammation due to real-time visualization.

There was also a statistically significant difference in the total number of complications after the procedure, which could be seen mainly in the incidence of pneumothorax. No significant difference in severe haemoptysis was probably related to a small number of cases presenting this complication.

In the first analyzed group, pneumothorax occurred in 18 (16%) of cases and haemoptysis in 6 (5.3%).

In the second group, pneumothorax occurred in 8 (7.07%) and haemoptysis in 3 (2.65%) (Table 3). The lower rate of complication is probably related to the biopsy operator being able to guide the needle in real time which does not cause any unnecessary damage to pleura in order to collect tissue for diagnosis. Simultaneous observation of CT and US images allows to bypass natural obstacles (such as nerves, and blood vessels from the axillary fossa) (Fig. 11) that cannot be visualized by US only which undoubtedly lowers the number of complications.

Based on the obtained results, the authors came to the conclusions that for patients with parietal lung tumors, which occur in approximately 6.36% of all patients with newly diagnosed lung cancer, transthoracic needle aspiration is the only way to obtain material for histopathological examination. Innovative method suggested by the authors involving both CT pre-biopsy planning and US guided biopsy provides the ability to analyze simultaneously static CT and US dynamic images and is considered to be an easy and effective method compared to relying on CT guided biopsy only. It is also related to a lower complication risk rate. In this method, only in 5% of cases, it is impossible to perform the procedure due to the inaccessible location of the tumor (behind the bones).

5. Conclusions

The analysis of the results confirmed the higher efficacy of the combined method taking into account the number of complications ($p < 0.01$) and diagnostic histopathological results ($p < 0.001$). Innovative method suggested by the authors involving both CT pre-biopsy planning and US guided biopsy provides the ability to analyze simultaneously static CT and US dynamic images and is considered to be an easy and effective method compared to relying on CT guided biopsy only.

References


M. Chorząży, D. Jabłońska, E. Skrzypek, A. Nasiek-Palka. Several years’ observation of a suppurring pancreatic cyst, which eventually turned out to be a cancer-case study, Contemp Oncol (Pozn) 13 (2) (2009) 102-107.

M. Chorząży, M. Majcher, K. Fedyszyn-Urbanowicz, G. Bierzyńska-Macyszyn, R. Kwiatkowski, Atypical dissemination of lung cancer to the adrenal gland and to
the spleen, Contemp. Oncol. (Pozn)/Współcz Onkol 16 (5) (2012) 444-446.

