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## Core-needle biopsy under CT fluoroscopy guidance and fine-needle aspiration cytology: Comparison of diagnostic yield in the diagnosis of lung and mediastinum tumors. Analysis of frequency and types of complications

### Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
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### Summary

#### Background:

Patients with pathological tissue mass in thoracic cage found with imaging require histopathological or cytological confirmation of malignancy before treatment. The tissue material essential for patomorphological evaluation can be acquired with fine-needle aspiration biopsies (FNAB) controlled with CT and core-needle biopsy (CNB) under real-time CT fluoroscopy guidance. The purpose of this work is to carry out a retrospective analysis of the two methods with regards to their informativity, frequency and the kind of complications.

#### Material/Methods:

From January, 2012 to May 2013, 76 core-needle biopsies of lung and mediastinum tumors were conducted and compared with 86 fine-needle aspiration biopsies (FNAB) of lung and mediastinum tumors, including 30 patients who underwent FNAB and were referred to CNB in order to specify the diagnosis.

#### Results:

Complete histopathological diagnosis was made in 91% with the use of CNB and in 37% when FNAB was the chosen method. Early complications were observed in 32% patients who underwent CNB and in group of 11% who underwent FNAB. Late complications, however, appeared in 29% patients after CNB and 13% after FNAB. In 24 cases CNB specified the complete diagnosis.

#### Conclusions:

Core-needle biopsy in comparison to fine-needle aspiration biopsy has more frequent rate of negligible complications, however, it offers higher diagnostic yield for diagnostic of lung and mediastinum neoplastic disease and allows for more precise diagnosis of focal lesions.

#### Keywords:

Core-Needle Biopsy • Fine-Needle Aspiration Biopsy • CT Fluoroscopy

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### Background

Malignant neoplasms are second most frequent cause of death in Poland. Malignant lung tumor is the most common cancer occurring in men and one of the leading cancers in women. Annually, 17,000 men and 6,000 women

die from lung cancer in Poland. It is anticipated that the number of deaths in both men and woman will increase in the following years [1]. The use of system utilizing AP and lateral imagery does not provide early diagnosis. Early and accurate diagnosis is extremely vital for subsequent and optimal treatment in patients suffering from malignant

lung tumors. Utilization of LDCT results in detection rate of focal pulmonary lesions as high as 95%. What is more, it diagnoses focal lesions with a diameter of 1–2 mm, many of which are not malignant. Several projects [2, our unpublished study in 8,650 patients] focused on the analysis of LDCT usefulness for the early detection of lung tumors. The results stated that assuming verification of lesions with a diameter of 9 mm and shorter FU of lesions with a diameter of 5–9 mm, 60% cases of lung neoplasms are in the early stages. Radical therapy was possible in 80% of cases within this group. Early and accurate identification of morphological type and individual characteristics of a tumor is crucial for further effective treatment, especially scheming the chemotherapy or resignation from surgery. Cytological confirmation of malignancy is also of immense importance. Well-differentiated tumors react to radiochemotherapy differently than poorly-differentiated tumors with high proliferative activity. Precise pathomorphological evaluation based on primary assessment (classic staining), immunohistochemistry, histological assessment and genetic trait analysis (mutations) allows for a correct and complete diagnosis [3]. Tissue samples necessary for a pathomorphological assessment may be obtained by various means: Surgical methods include open and minimally invasive procedures (mediastinoscopy and VATS), Bronchoscopy, eBUS and Transbronchial BAC, Percutaneous methods: fine-needle aspiration biopsy and core-needle biopsy, require image guidance (ultrasound, CT, CT fluoroscopy). Unlike cytologic evaluation, core biopsy tissue sample allows for a more comprehensive evaluation of pathological immunohistochemistry. However, collection of core-biopsy tissue sample requires much more aggressive approach than fine-needle aspirate. Core-needle biopsy under direct vision (x-ray, ultrasound, CT fluoroscopy and MR fluoroscopy) is the least invasive method. Nevertheless, it is also associated with a risk of certain complications, which may be related to the type of procedure monitoring and its duration. Most publications concerning the use of a CT-guided biopsy (FNAB or CNB) involve two-stage monitoring. There is a limited number of reports describing the specific advantages of a procedure performed in real-time under CT guidance. The aim of this work is the comparison of fine-needle aspiration biopsy (FNAB) and core-needle biopsy (CNB) for transdermal access in terms of informativeness, frequency and the kind of complications.

## Material and Methods

In the time period between January, 2012, and May, 2013, a total of 101 core needle biopsies (CNB) were performed under CT fluoroscopic guidance. These procedures included biopsy of the lung and/or the mediastinum, as well as other areas (chest wall, retroperitoneal lymph nodes, nodular changes in the kidneys, lytic foci in the bones). A total of 76 core-needle biopsies of the lung and mediastinum were analyzed. Another 56 fine-needle aspiration biopsies (FNAB/ FNAC) from a time period between May and July, 2013, were included in the analysis along with 30 FNAB performed in patients undergoing CNB for further diagnostic purposes. A total of 86 fine-needle aspiration biopsies of lung and mediastinal tumors were analyzed (Table 1).

**Table 1.** Localization of lesions, which underwent CNB and FNAC.

Location	CNB	FNAC
Mediastinum	18 (24%)	10 (12%)
Lung	58 (76%)	76 (88%)
<b>Total</b>	<b>76</b>	<b>86</b>

## Course of the procedure

**Fine needle biopsy** with a 20G or 21G needle is performed by a team consisting of a pathologist, radiologist, electro-radiology technician and a nurse. After placing the patient on the tomography table and performing the initial CT scan, radiologist determines the location (distance from laser gantry and depth) of suspicious lesions and marks the point of needle entry on the patient's skin. Next, the pathologist disinfects the skin and introduces a needle into the lesion, with no local anesthesia. Then, he inserts 20G or 21G needle into the suspicious lesion, after which a confirming CT image is performed to determine the correctness of the needle's entry. The procedure is repeated until the tip of the needle is in the proper location. Once a proper location of the needle has been confirmed, the pathologist collects the aspirate, which is then placed on glass slides and fixed with alcohol. After the procedure is completed, wound dressing is applied over the needle puncture site. Then, a follow-up CT imaging is performed in order to identify potential early complications. During this process real-time visualization of the needle's location is not utilized, as opposed to the procedure of CT fluoroscopy.

**Core needle biopsy** with CT fluoroscopy guidance is performed by a team consisting of a radiologist, technician and a nurse. Prior to core-needle biopsy, the patient is premedicated to reduce the pain, intravenous access is established and coagulation parameters are measured. Following a scan of the area containing the lesion, radiologist selects a position which provides the best view and the easiest and safest access to the lesion. Insertion site of the biopsy needle is marked on the monitor along with the distance in relation to laser guidelines originating from the CT gantry. Then, the depth of the lesion from the surface of the skin is measured and needle puncture site is marked on the patient's skin. Radiologist selects the appropriate length (9–20 cm) and thickness of the biopsy needle (14–20 G). Once a sterile field (sterile drape cover, skin disinfection) has been created, radiologist administers a local anesthetic and after a period of about 2 minutes, incises the skin with a scalpel and inserts the biopsy needle under CT fluoroscopy guidance with real-time tracking and collects tissue sample. The range of CT fluoroscopy scan is 1.5 cm (3 layers, each 5 mm thick). The images are created at a rate of 1/s. Imaging parameters are set: 120 kV voltage, initially at 15 mA current. Once the biopsy needle has been properly positioned, sample material is collected. It is visually inspected for quality, placed in a container with formalin and transported to the Department of Pathology where it is immersed in a paraffin block. The insertion would be repeated should there be no or little sample obtained or lack of tissue (fluid, necrosis) acquired. After

**Table 2.** Types of diagnoses made after CNB and FNAC with their percentage distribution.

Type of diagnosis	CNB	FNAC
Group I – nondiagnostic material		
Technical difficulty, lack of specimen, bloodstained, insufficient, necrosis	5 (7%)	5 (6%)
Group II – partially diagnostic material		
Cellulae suspectae	0 (0%)	2 (2%)
Cellulae carcinomatosae (no type)*	2 (3%)	47 (55%)
Group III – complete diagnosis		
Malignant tumor, without immunohistochemical diagnosis*	31 (41%)	0 (0%)
Complete diagnosis of a malignant tumor with immunohistochemical diagnosis*	19 (25%)	0 (0%)
Negative result (cancerous cells were not found)*	10 (13%)	26 (30%)
Benign proliferative change	1 (1%)	0 (0%)
Inflammatory change	8 (11%)	6 (7%)
<b>Total</b>	<b>76 (100%)</b>	<b>86 (100%)</b>

\* Statistically significant differences.

the procedure, the nurse applies a dressing. Follow-up CT scan is performed after 2–5 minutes to rule out any early complications.

#### Classification of biopsy results

Data obtained from CNB and FNAC was divided into three groups according to its value.

- Group I – nondiagnostic material** – included all cases of unsuccessful biopsy (technical difficulties – inability to reach the lesion, lack of specimen in the needle despite repeated collection attempts, bloodstained material, insufficient and necrosis – preventing establishment of a diagnosis).
- Group II – partially diagnostic material**, i.e. one that did not facilitate the establishment of a diagnosis and the initiation of proper therapy. This group included cellulae suspectae and cellulae carcinomatosae.
- Group III – diagnostic material**, on the basis of which a complete and reliable identification of a benign or malignant lesion was possible.

#### Analysis of complications

After completion of biopsy, patients were evaluated for the presence of complications arising during or immediately after the procedure, as well as late complications assessed clinically and radiographically at the Department of Thoracic and Oncologic Surgery a few hours after the procedure. Complications, which can be accredited to CNB and FNAC can be divided into two groups: early complications, which can occur during the procedure of biopsy or directly afterward, and late complications, which can be observed within several hours after the procedure. The following complications were included: pneumothorax not requiring drainage, subcutaneous emphysema, pneumothorax requiring drainage, interstitial hematoma, pleural hematoma,

hemoptysis, airway hemorrhage requiring intervention, pain, cough, air embolism, death.

Statistical analysis was performed using Statistica software. Normality of parametric variables' distribution was analyzed with Saphiro-Wilk test. Test Chi<sup>2</sup> was used in order to compare the distribution of age and gender and to analyze the frequency of complications. Differences in the lesions was performed with test t.

#### Results

CNB was performed in 37 women and 39 men, ages 19–82 (mean age 59 years), FNAC was performed in 29 women and 57 men, ages 21–87 (mean age 62 years). No significant differences in age distribution were found, however, FNAC was conducted in men significantly more frequently than in women. Samples obtained with the use of CNB were acquired from lesions with diameter of 12 to 292 mm, in FNAC they were of 13 to 136 mm ( $p > 0.05$ ). The average of needle insertion for each CNB session was 2,7. The most frequently used gauge of the needle were 18 and 16 G.

Table 2 presents data and percentage distribution of diagnoses acquired with CNB and FNAC. An essential difference between the scope of obtaining full patomorphological diagnosis of the cancer was stated.

Table 3 shows numerical data and percentage distribution of diagnoses obtained from CNB and FNAC. Early complications occurred essentially more frequently after CNB than after FNAC (24 vs. 9) and mainly resulted in interstitial hematoma and hemoptysis. After both CNB and FNAC, there were no occurrences of complications requiring urgent intervention (haemorrhage, pneumothorax requiring drainage, air embolism, death). In once case, around the third minute of biopsy, the female patient lost consciousness accompanied by clenched jaw and right eye deviation.

**Table 3.** Types of early complications and their frequency according to the biopsy method.

Type of complication	CNB (n=76)	FNAC (n=86)
Pneumothorax not requiring drainage	8 (11%)	6 (7%)
Pneumothorax requiring drainage	0 (0%)	0 (0%)
Subcutaneous emphysema	1 (1%)	0 (0%)
Interstitial hematoma*	10 (13%)	3 (4%)
Hemoptysis*	4 (5%)	0 (0%)
Pleural hematoma	0 (0%)	0 (0%)
Hemorrhage	0 (0%)	0 (0%)
Pain	0 (0%)	0 (0%)
Air embolism	0 (0%)	0 (0%)
Cough	1 (1%)	0 (0%)
Death	0 (0%)	0 (0%)
<b>Total</b>	<b>24 (32%)</b>	<b>9 (11%)</b>

\* Statistically significant differences.

Blood pressure 120/80 and pulse 72/min. An anesthesiologist was called. Despite clenched jaw, the patient was breathing on her own through an oropharyngeal tube, but failed to regain consciousness in the first few minutes. Follow-up chest CT performed 15 minutes after the puncture revealed subcutaneous emphysema, 10 mm pneumothorax and small pleural interstitial hematoma. CT scan of the head performed due to suspicion of a right-sided stroke or air embolism revealed no suspicious changes. The patient was transported for a neurology consult at another hospital. Consultation indicated seizure as the cause of loss of consciousness and other neurological symptoms. Three deaths were recorded the day following CNB. Multiple organ failure due to advanced cancer was diagnosed.

Table 4 presents types of late complications and their frequency according to the biopsy method. Besides a significantly higher incidence of pain in patients undergoing CNB as compared to FNAC (10 vs. 2), no significant difference was observed in the incidence of late complications.

## Discussion

The purpose of pathological evaluation of FNAC is to determine whether the collected cells are cancerous or not. In case of a positive result, the specimen is evaluated according to three categories: sarcoma, carcinoma, lymphoma. Cancer is evaluated whether it is a small cell or non-small cell carcinoma. Immunohistochemical analysis is not routinely performed. Modern standards of management require a more detailed pathological assessment with precise subtyping based on histological molecular evaluation and gene expression. On this basis, proper therapy is implemented to reduce the severity of the disease and enable a more radical management. Precise pathomorphological evaluation based on a primary assessment (classical

**Table 4.** Types of late complications and their frequency according to the biopsy method.

Type of complication	CNB (n=76)	FNAC (n=86)
Pneumothorax not requiring drainage	4 (5%)	2 (2%)
Pneumothorax requiring drainage	4 (5%)	4 (5%)
Pain*	9 (12%)	2 (2%)
Other	4 (5%)	2 (2%)
Cough	1 (1%)	1 (1%)
<b>Total</b>	<b>22 (29%)</b>	<b>11 (13%)</b>

\* Statistically significant differences.

staining), immunohistochemistry and histological analysis of genetic traits (mutations), allows for making a correct diagnosis. It is obvious, that material obtained through CNB allows for more thorough analysis required to undertake adequate decision about therapy.

The insertion of the needle under CT fluoroscopy increases certainty of obtaining material from different areas of focal lesion, it also decreases the time of puncture (similarly to echography). Significantly shorter procedure time in case of CT fluoroscopy, theoretically allows for repeat specimen collection from different parts of the lesion and significantly reduced risk of obtaining bloody specimen. The available literature provides only a few studies evaluating the effect of real-time puncture monitoring of focal lesions in the lungs [4–6].

The aim of this work is the comparison of fine-needle aspiration biopsy (FNAB) and core-needle biopsy (CNB) for transdermal access in terms of informativeness, frequency and the kind of complications. CT guidance of biopsy is possible in two fundamentally different ways. Classic variant consists of planning access to the lesion and inserting the needle with no visual guidance, as in FNAB performed by pathologists in cooperation with a radiologist. CT fluoroscopy allows for direct visual guidance in near real-time, similar to sample collection under ultrasound guidance. The term “near real-time” refers to a short delay of the projected image in relation to performed activity. This time lag lasts about 1s and results primarily from the processing of scanned data. In the remainder of this publication, we ignore this delay and refer to the preview as “real-time”.

In case of both, CNB and FNAC, the radiologist determines the patient's position on a CT table (supine, prone, lateral), to facilitate the best access to the lesion (shortest needle path, avoid bones, minimize the risk of complications related to the vicinity from large vessels, bronchial and mediastinal structures). Comparison of the 2 procedures clearly shows a difference in their duration. In case of FNAC, the need for an additional CT scan to locate the needle prolongs the procedure. FNAC also requires the presence of a pathologist, however coagulation parameters are not routinely measured, nor is local or intravenous anesthesia used. Significant difference concerning x-ray exposure should also be noted. Only

patient is exposed during FNAC, whereas in case of CNB-CT fluoroscopy, the patient, the radiologist performing the procedure and the assisting nurse are all exposed to x-rays. Assessment of the level of patient and staff x-ray exposure requires further studies. In order to reduce x-ray exposure by staff, some centers utilize custom tools to hold the biopsy needle during the exposure [7]. In the reviewed literature [4–6] the reported voltage was 120–130 kV with a 20–50 mAs current. However, exposure conditions during CT fluoroscopy, at our facility, are constant, 15 mAs/120 kV. The use of lower parameters did not result in any difficulties in locating or monitoring of the puncture, it was advantageous to use lower doses without affecting the quality of the procedure.

Most of complications occurring after biopsies are of light nature and are possible to alleviate without any essential clinic consequences. According to literature, the most frequently appearing early complications are emphysemas (29–34%) and interstitial hemorrhage (25–29%). [5,8–10] In the course of our studies, we did not approach any serious complications like air embolism or death.

The recommendations of the BTS (British Thoracic Society) state that the acceptable incidence of deaths is 0,15% [11], which confirms that it might occur. The late complications after CNB and FNAC are chiefly pneumothoraxes (some of which require drainage) and pain sensed by the patient near the punctured area.

Real-time techniques reduce the time necessary to obtain the specimen, while the use of semi-automatic biopsy needles eliminates the step necessary to release the cells, as required during fine needle biopsies. Repeated passage of the needle through the tumor and the surrounding lung parenchyma may increase the risk and size of pneumothorax and hematoma, although this occurrence was not uniformly recorded [4,6,9,12]. The diameter of the needle is similarly important, the larger the needle, the greater the risk of tissue damage and the development of pneumothorax and hematoma. Although, this occurrence was not uniformly recorded [4,6,9,12]. In our study, the average number of punctures during a single CNB procedure was 2.7 (1–6). A similar number of specimen collection has been published by Hiraki T et al. [4]. It results from the fact that a macroscopic evaluation leads to frequent repeats of the procedure, as deemed necessary by the radiologist.

Guidelines regarding the frequency of complications and the process of performing a lung biopsy have been developed [11]. According to these recommendations, the operator should strive for the lowest number of complications and not exceed their prevalence: for pneumothorax 20.5%,

pneumothorax requiring drainage 3.1%, bleeding 5.3% and mortality 0.15%. In a large meta-analysis [8] reviewing 11 studies concerning CNB and FNAC, the frequency of complications has been reported as follows: pneumothorax 0–35.5% for CNB and 7.9–35.8% for FNAC, pneumothorax requiring drainage 2–3.8% for FNAC and 2–4.1% for CNB. The use of smaller needles (19G) reduces the risk of edema as compared to larger needles (18G) [13]. What is more, there is increased risk of pneumothorax with advancing age (higher risk in individuals over 60 and 70 years of age) [13]. The reported incidence of bleeding is in the range 1.1–13.6% for FNAC and 0–28.6% for CNB. In our study, the occurrence of pneumothorax immediately after the puncture was reported in 10.5% of patients managed with CNB and in 7% of those with FNAC. Despite the use of an algorithm recommending numerous punctures of the lesion, this result does not differ from other published documents.

In case of FNAC, it was confirmed that accuracy increases with the number of specimen collections, decreases with longer distance to the lesion, is higher for thicker needles (16–18G) than thinner needles (20–22G), increases with a size of the lesion and is dependent on the experience of the individual performing the biopsy [12]. The cited literature reports accuracy of 90–100% for lesions over 10 mm, 52–88% for lesions under 10 mm. In our case, the size of the biopsied lesion was no lower than 1 cm, but other authors [14] report high success rate of a CNB with an 18G needle on lesions smaller than 1 cm. Interestingly, authors of the publication did not perform a follow-up CT scan after the biopsy, arguing that although small pneumothorax can be seen on a CT, it is not clinically significant, while those that have clinical significance can be seen on an x-ray performed 2 hours after surgery. At our medical center, patients undergoing CNB or FNAC are hospitalized. While patients in the article [10] were biopsied on an outpatient basis and remained under observation for 4 hours. Asymptomatic patients or those with small pneumothorax were discharged home. Such proceeding is allowed by the recommendations of the BTS (British Thoracic Society) [11], except for high-risk. In case of low-risk patients, chest x-ray should be performed and decision on the management of pneumothorax should be made. Patient discharged home should remain within 30 minutes from the hospital, have appropriate care at home and access to a telephone.

## Conclusions

Despite an increased risk of some minor complications, core-needle biopsy is highly useful in the diagnosis of cancer of the lungs and mediastinum, and helps precisely diagnose focal lesions.

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