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IMAGE-GUIDED PERCUTANEOUS BIOPSY OF PERIPHERAL LUNG LESIONS: ULTRASOUND-GUIDED COMPARED TO CT-GUIDED BIOPSY

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Computed tomography (CT) guided percutaneous biopsy is well established technique used to provide tissue from the thoracic lesions, both in lung parenchyma and mediastinum. However, ultrasound (US) guided biopsy of peripheral thoracic lesions should not be underestimated because it has the advantage of real time control and the absence of radiation exposure.

In this retrospective study, which included 77 patients (59 men and 18 women) with peripheral lung lesions, we compared US and CT-guided biopsies analyzing the duration of the procedure, diagnostic accuracy, and complication rates, and we tried to determine correlation with needle diameter and lesion size.

Both techniques have successfully provided samples for histology diagnosis (95.65% with US and 90.32% with CT). There is a significantly higher rate of all complications, and especially major complications in CT-guided biopsies—22.58% versus 2.17% ($p < 0.001$). CT-guided procedure lasts significantly longer than US-guided procedure (42.48 ± 5.12 compared to 16.80 ± 3.42 minutes). There is also a significant negative correlation between lesion size and duration of the procedure in CT-guided biopsy: the smaller the lesion, the longer the duration of the procedure.

Although both techniques are very reliable and almost equally successful in obtaining samples for histopathology analysis, because of a higher rate of major complications and a longer duration of the procedure with CT guidance, ultrasound-guided biopsy should always be considered as the primary approach for peripheral lung lesions.

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Introduction

Lung cancer is recognized as a major public health issue, being the second most frequently diagnosed cancer and a leading cause of cancer-related mortality in men (1). The wider availability of CT (computed tomography) worldwide followed by an increased number of CT scans during the last two decades allowed for lung masses to be detected more frequently, but also while smaller in size, and in various locations (2). Some of these lesions are located peripherally. They remain a diagnostic challenge for pulmonologists, as flexible bronchoscopy and sputum cytology, although reliable for diagnosis of centrally located lesions, have limited value in diagnostics of peripherally located lesions (3–5). For lesions that are not accessible or remain unverified after bronchoscopy, the remaining alternatives for the acquisition of tissue samples are surgical biopsy and percutaneous biopsy. Percutaneous biopsy is certainly more popular, being minimally invasive and already proven successful and safe for several other organ systems (6), but to be precise, it has to be image-guided. Although CT is the method of choice for image guidance due to the high-resolution images it provides, it has been shown that for peripheral lesions both fluoroscopic and ultrasound-guided biopsies can provide good results (7–10). Ultrasound (US) can show masses in contact with the pleura but remains underestimated as a diagnostic method despite the fact that it has a high diagnostic value, provides real-time imaging, can be performed at the patient's bedside, and does not involve ionizing radiation (11–13).

Since there are limited data on US-guided biopsies of peripheral lung lesions, in this retrospective study we aimed to determine whether US has a role in image-guided biopsy of peripheral lung lesion comparing the results of US-guided and CT-guided transthoracic biopsy of these lesions in our institution, considering needle size (gauge), size of the lesion, duration of the

procedure, rate of complications, and success of the procedures.

Material and Methods

From January 2020 to December 2021, 107 transthoracic biopsies were performed in the Center for Radiology of the University Clinical Center of Niš, of which 46 were guided by ultrasound and 61 were guided by CT.

The criteria for inclusion in this retrospective study were the peripheral localization of the lesion in the lungs or mediastinum (which for research purposes was defined as a lesion up to 15 mm away from the pleura, or in direct contact with the pleura or with its invasion), while the exclusion criterion was the lack of imaging (previous CT examination) and accompanying medical documentation on the course of the disease before and on the course of hospitalization after the procedure.

One of the established indications suggested by guidelines for percutaneous transthoracic biopsy (14) was found in all of the patients. Before the biopsy procedure, all patients were examined for the presence of contraindications. Since there are no absolute contraindications, the medical records were reviewed and patients with image-characterized non-malignant lesions (vascular malformations, hydatid cysts, obvious inflammatory lesions) were not referred to biopsy, while on the basis of coagulation status, it was decided that some of the patients should have a coagulopathy correction.

Based on inclusion and exclusion criteria, 30 patients who underwent CT-guided biopsy were excluded from the study. Of the initial 107 subjects, 25 were not included because lesions were not peripheral, and 5 were excluded from the analysis because their records were incomplete or unavailable (as they were referred from other centers for biopsy).

Informed consent was acquired from all patients, after detailed informing on the procedure algorithm, possible complications and treatment. The records of the included patients were reviewed retrospectively.

The pre-procedural thoracic CT scans of 77 patients (46 for US-guidance, 31 for CT-guidance) and the size of the targeted lesions (the largest diameter was recorded) were reviewed. The lesions were divided into three groups based on the largest diameter (group I—SMALL ≤ 25 mm, group II—MEDIUM 26−50 mm, and group III—LARGE ≥ 51 mm).

All biopsies were performed by two interventional radiologists—CT-guided procedures on a GE multidetector computed tomography system—GE 64, while US-guided procedures were performed on a GE LOGIQ 7 ultrasound machine.

Patients were positioned regarding the location of the target lesion.

CT scanning was performed prior to biopsy, followed by measuring distances and determining the point of puncture.

An ultrasound-guided biopsy followed the analysis of the previously performed CT examination to determine the localization of the change, which was confirmed by an ultrasound examination of the pleural space and lungs with the use of a probe with a sterile sheath, and the puncture site was determined.

After cleaning and sterilizing the skin, and applying a local anesthetic, a minimal incision was made to ensure the passage of the needle. Needles with a diameter of 14 G, 16 G and 18 G were used (grouped into two groups—needles with a large gauge of 14 G and needles with a small gauge of 16 G and 18 G), which were introduced towards the lesion. Samples were taken by the automated BARD MAGNUM Multiple CORE Biopsy System (C. R. Bard, Inc. Bard Medical, Covington, Georgia) with appropriate CORE biopsy needles (C. R. Bard, Inc. Bard Medical, Covington, Georgia)—three samples per patient, if it was possible.

In the case of CT-guided biopsy, the needle was introduced, positioned and a control scan was performed until a satisfactory position was achieved, while in US-guided biopsy the needle was introduced under continuous control of the position in real-time. Immediately after the CT-guided biopsy procedure, control CT scans were performed, while after the US-guided biopsy, a US examination was performed.

The duration of the procedure was noted in the reports (measured in minutes from the moment the doctor approached the patient until the end of the procedure).

Control X-ray of the chest 4 hours after the procedure. Complications were noted in the reports.

Complications (pneumothorax, bleeding, hemoptysis, etc.) and interventions necessary for treatment were recorded. Depending on the presence of complications, they were divided into three groups: without complications, minor complications (hemoptysis, pulmonal hemorrhage, minimal pneumothorax) and major complications (pneumothorax requiring drainage, hemorrhage requiring blood transfusion).

The procedure was considered successful if the obtained samples allowed a histopathological diagnosis to be made.

Results

Transthoracic biopsy using the CORE biopsy system with an automatic gun was performed in 77 patients, for whom complete records were available. The average age of the patients was 62.50 ± 4.65 years; 18 of them (23.3%) were women and 59 (66.67%) were men. The longest axial diameter of the target lesions varied from 20 mm to 95 mm.

Tissue samples after transthoracic biopsy were obtained in all 77 patients (100%), of which the results were diagnostic in 72 (93.50%). Pathology results were non-diagnostic in 5 patients (6.49%).

Differences between CT- and US-guided biopsy were tested using the chi-square test. There were significant differences in needle diameter and complication rates between CT-guided and US-guided transthoracic biopsies of peripheral lung lesions (Table 1). Ultrasound-guided procedures allowed for larger gauge needles to be used (73.91% compared to 22.58% for CT-guidance) (and therefore larger samples) with a significantly lower rate of complications (15.21% compared to 54.84% for CT guidance). No complications were recorded in 84.79% of US-guided biopsies.

The difference in duration was tested by t-test (Table 2). The Kolmogorov Smirnov test confirmed normality in each procedure separately. The CT-guided procedure lasts significantly longer (42.48 ± 5.12 min compared to US-guided 16.80 ± 3.42 min).

The correlation was tested with the Spearman correlation coefficient (Table 3).

In CT-guided procedures, there was a significant negative correlation between the duration of the procedure and the size of the lesion (Rs = -0.846, sig = 0.000) - the smaller the lesion, the longer the procedure.

In the US-guided procedure, there was a significant negative correlation between the duration of the procedure and the size of the lesion (Rs = -0.841, sig = 0.000) - the larger the lesion, the shorter the duration of the procedure.

Between the size of the lesion and complications, there was no significant influence either with CT (sig = 0.177) or with US (sig = 0.618).

In CT-guided procedures, there was a significant negative correlation between the size of the lesion and the diagnosis (Rs = -0.395, sig = 0.028) - the larger the lesion, the lower the chance of diagnosis.

In US-guided procedures, there was a significant correlation between needle gauge and diagnosis (Rs = 0.359, sig = 0.014) – the larger the needle, the greater the chance of diagnosis.

Table 1. Relationship of US and CT guided biopsy with needle size, lesion size, complication rate and success of the procedure.

		IMAGE GUIDANCE		Total	Chi2	sig
		CT	US			
NEEDLE SIZE	LARGE BORE	7 (22.58%)	34 *(73.91%)*	41 (53.25%)	19.602a	.000
	SMALL BORE	24 (77.42%)	12 (26.09%)	36 (46.75%)		
LESION SIZE (mm)	SMALL	6 (19.35%)	4 (8.7%)	10 (12.99%)	1.942a	.379
	MEDIUM	14 (45.16%)	22 (47.83%)	36 (46.75%)		
	LARGE	11 (35.48%)	20 (43.48%)	31 (40.26%)		
COMPLICATIONS	NO	14 (45.16%)	39 *(84.78%)*	53 (68.83%)	14.937a	.001
	MINOR	10 *(32.26%)*	6 (13.04%)	16 (20.78%)		
	MAJOR	7 *(22.58%)*	1 (2.17%)	8 (10.39%)		
HP DIAGNOSIS	NO	3 (9.68%)	2 (4.35%)	5 (6.49%)	.866a	.352
	YES	28 (90.32%)	44 (95.65%)	72 (93.51%)		

Table 2. Comparison of US and CT guided biopsy procedure duration

		N	Mean	Std. Deviation	t	sig
PROCEDURE DURATION (min)	CT	31	42.48	5.12	24.489	.000
	UZ	46	16.80	3.42		

Table 3. Correlation of needle and lesion size with procedure duration and complication rate for US and CT guided biopsy.

			PROCEDURE DURATION	COMPLICATIONS	HP DIAGNOSIS
CT	NEEDLE GAUGE	Rs	-.635**	.084	-.345
		sig	.000	.655	.057
	LESION SIZE	Rs	-.846**	-.288	-.395*
		sig	.000	.117	.028
US	NEEDLE GAUGE	Rs	-.009	.251	.359*
		sig	.951	.092	.014
	LESION SIZE	Rs	-.841**	-.076	-.232
		sig	.000	.618	.120

Discussion

Determining adequate image modality for biopsy guidance of peripheral lung lesions is a very important issue for any specialist performing them since it can influence the outcome, success of the procedure and probability of complications. Our results demonstrate that ultrasound should be assessed and can be used as a reliable guiding modality in cases where the targeted lesion can be visualized by it (as in lesions in contact with or affecting the pleura). We confirmed that ultrasound is safer, less time-consuming, and equally (or even more) reliable than CT for peripheral lesions.

In our study, all lesions were 20 mm or larger (in measured diameter). The overall diagnostic reliability was noted to be very high with 2–3 samples obtained during each biopsy (15), totaling 93.51%. In 6.49% of our cases, the tissue samples were not diagnostic, the reasons for which were considered to be sampling errors—missed lesions, taking samples from the necrotic center or peritumoral inflammatory zones. In different studies the reported reliability for US-guided biopsies varies from 64% to 97% (10, 12, 13, 16, 17) compared to CT-guidance varying from 80% to 95% (7, 8, 9). Our results are in accordance with literature data, and we confirmed that as an imaging modality used for guidance, US (95.65%) was slightly more reliable than CT (90.32%). This can also be explained by the possibility of using large diameter needles when guiding the procedure with ultrasound (73.91%) (since lesions were adjacent to pleura) compared to CT (22.58%).

By comparative analysis of US- and CT-guided biopsies, we concluded that the total number of all complications, especially major ones, is significantly higher in CT-guided biopsies, up to 22.58% (compared to 2.17% in US-guided biopsies—this is somewhat expected because in our study CT-guided punctures targeted both peripheral lesions that are pleural-based and those not in direct contact with the pleura but within 15 mm distance from pleura, which in itself increases the risk of complications). The rate of pneumothorax is significantly lower in the literature, ranging from 1% to 5% (9, 13), compared to ours (overall 10.39%). This can be explained by our technique that is not based on coaxial introducers and by our use of larger gauge needles compared to others (18, 19). The total number of major complications in our study was 8 (10.38%), and all patients with major complications had a massive pneumothorax that was drained and therefore prolonged hospitalization, but of all these patients, only one underwent US-guided biopsy.

Apart from described and reported safety benefits of US guidance, our study determined that CT-guided procedures last significantly longer than US-guided procedures (42.48 ± 5.12 min versus 16.80 ± 3.42 min, respectively), which can be explained by the depth of the lesions but above all by the imaging capabilities of monitoring the US-guided procedure in real-time. The literature also reports a shorter duration of US-guided procedures (13), with time-saving effects varying from 20% to 42% (13, 20, 21). It seems that in our study the time-saving effect was higher, but it was not calculated, and it was probably based on previous CT existing in every patient, which allowed for faster US localization of the lesion.

Our results showed a statistically significant correlation of complications (major pneumothorax requiring drainage) with CT-guided biopsies (Table 1) and a correlation of procedure duration with lesion size (Table 2), suggesting that smaller diameter lesions require longer procedure time when using CT guidance. Heerink et al. (22) also found that with the growth of the lesion, the probability of obtaining a diagnostic sample is lower due to the high probability of necrotic parts of the change, which was confirmed by our study (Table 3).

Conclusion

Our study shows that the diagnostic reliability of ultrasound-guided biopsy of peripheral lung lesions is approximately equal to the reliability of CT-guided biopsy, with a significantly lower complication rate and significantly shorter procedure duration. Since it is performed without ionizing radiation, it has a shorter overall procedure duration, and is equally (or more) accurate, ultrasound-guided lung biopsy should be considered as a standard procedure and a viable, even more favourable alternative to CT-guided biopsy for peripheral lesions that affect pleura, in case there is a specialist who can perform it and if the lesion is easily visualized by ultrasound.

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PERKUTANA BIOPSIJA PERIFERNIH LEZIJA PLUĆA VOĐENA SLIKOM: POREĐENJE BIOPSIJE VOĐENE ULTRAZVUKOM I BIOPSIJE VOĐENE KOMPJUTERIZOVANOM TOMOGRAFIJOM

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Perkutana biopsija vođena kompjuterizovanom tomografijom (engl. *computed tomography* – CT) dobro je ustanovljena tehnika za pribavljanje uzoraka iz promena grudnog koša, pluća i medijastinuma. Međutim, zbog prednosti koje ultrazvučno vođena biopsija ima u kontroli procedure u realnom vremenu i odsustva jonizujućeg zračenja, ne treba je potcenjivati. Cilj ove studije, koja je obuhvatila 77 bolesnika (59 muškaraca i 18 žena) sa perifernim promenama pluća, bio je da utvrdi odnos ultrazvučno vođene biopsije i biopsije vođene CT-om upoređivanjem trajanja intervencije, dijagnostičke uspešnosti i stope komplikacija, kao i ispitivanjem njihove povezanosti sa veličinom promena i prečnikom igle.

Histološka dijagnoza je uspešno postavljena obema tehnikama (95,65% kod ultrazvuka (UZ), odnosno 90,32% kod CT-a). Postoji statistički značajna razlika između stope komplikacija i načina vođenja procedure; evidentiran je značajno veći broj svih, a posebno teških komplikacija, kod biopsija vođenih CT-om – 22,58% spram 2,17% ($p < 0,001$). Procedura vođena CT-om traje znatno duže od one vođene UZ-om (42,48 minuta ± 5,12 minuta naspram 16,80 minuta ± 3,42 minuta). Utvrđeno je da postoji značajna negativna korelacija između veličine lezije i trajanja procedure kod biopsije vođene CT-om: što je manja lezija, to duže traje procedura.

Iako su obe tehnike veoma pouzdane i skoro jednako uspešne u obezbeđivanju adekvatnih uzoraka za postavljanje histološke dijagnoze, s obzirom na veću stopu teških komplikacija i duže trajanje procedure prilikom vođenja CT-om, kod perifernih promena u plućima uvek treba prvo razmotriti biopsiju vođenu UZ-om.

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***Ključne reči**: ultrazvuk, kompjuterizovana tomografija, torakalna biopsija, biopsija pluća*