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Transthoracic Ultrasonography: Advantages and Limitations in the Assessment of Lung Cancer

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Petru Adrian Mircea

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Abstract

Lung cancer (LC) represents the leading cause of cancer-related mortality worldwide, with most of the cases being still diagnosed in advanced stages. Recently published data estimates an increase of LC deaths worldwide from 1.6 million in 2012 to 3 million in 2035. In this context, ultrasonography (US) aspires to become the method of choice that can offer essential information concerning subpleural LC. Therefore, it is an urgent need for an objective evaluation of the role of US and US-guided biopsies as an accurate diagnosis method, as until now large studies to assess this have been seldom performed. Our main aim was to perform a review over the use of US and US-guided biopsy in the assessment of LC, and our second aim was to illustrate how US is a valuable tool in the approach of patients with LC. We also compared the advantages and disadvantages of different types of biopsy needles. Other non-invasive applications of US (contrast-enhanced US and elastography) and their usefulness for LC were also evaluated. Though transthoracic US is today underused for lung cancer diagnosis, it offers multiple advantages that seem extremely useful for the efficient management of such tumours.

Keywords: biopsy, lung cancer, transthoracic, ultrasonography

1. Introduction

Lung cancer (LC) represents the leading cause of cancer-related mortality worldwide [1–3], with most of the cases being still diagnosed in advanced stages. Recently published data estimates an increase of LC deaths worldwide from 1.6 million in 2012 to 3 million in 2035 [3]. The 5-year survival of LC patients is still very low—15% even in the wealthiest countries—so urgent strategies are needed in order to facilitate early diagnosis or to improve current diagnosis techniques. Ultrasonography (US), with its multiple advantages, has an already well-established

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role in the management of tumoral and non-tumoral abdominal pathology. Though a common technique, US was less used for some organs such as the lung. Ultrasonography can assess peripheral lung tumours, offering valuable information related to the tumour structure, vascularization, the stage of parietal invasion and sometimes lymph node invasion. Moreover, US can guide the biopsy of the peripheral tumours with very good sensibility/specificity and less complications and smaller costs than computed tomography (CT). More recently, transthoracic US (TUS), US-guided biopsy and other applications (contrast-enhanced US and elastography) have gained a larger field in the management of patients with peripheral pulmonary nodules or masses. In this context, US aspires to become the method of choice that can offer essential information concerning subpleural LC [4, 5]. Therefore, an objective evaluation of the role of US and US-guided biopsies as accurate diagnosis method is necessary because until now large studies to assess this have been seldom performed.

2. Transthoracic ultrasonography for the lung cancer

2.1. Standard ultrasonography and its applications for lung cancer

Ventilated lung reflects up to 99% of the sound waves, and, consequently, the peripheral lung tumours abutting the visceral pleura can be visualized. When pleural effusions or condensate lung are present, facilitation of the ultrasound beam can also allow examination of deeper lesions.

US examination of the lung is performed with convex transducers with frequencies of 3–6 MHz. For chest wall and lung surface assessment, a higher frequencies—10–13 MHz—and linear transducers are needed. When TUS is recommended for evaluation of a lung tumour, it follows usually a radiological examination of the chest—X-ray (Rx) or computed tomography (CT)—which have detected a lesion. Otherwise, it is indicated for a localized pain or other clinical signs, so it is a guided examination of an area of the chest. Sometimes, this 'focused' US can be followed by a global US chest examination, as we must search peripheral lung, pleura or chest wall for metastasis. It is also important to scan cervical lymph nodes and at least upper abdominal organs - adrenal glands [6] and the liver for metastasis.

Normal pleuropulmonary interface is visualized as a hyperechoic line situated beneath the chest wall structure, followed by reverberation artefacts (A-lines), being mobile with respiration in real-time examination which represent the 'gliding sign'. The presence of a subpleural pulmonary lesion interrupts this hyperechoic line, appearing as a hypoechoic image with different shapes, structures and contours according somehow to the type of the disease.

When a lung tumour is identified, TUS should try to solve several issues. One of the most important problems is represented by differential diagnosis between benign and malignant lesions [7]. TUS can describe certain characteristics of a peripheral lung lesion in order to suggest benign or malignant characteristic:

—Contour of the lung surface may be irregular in LC and regular in benign lesions.

—The margins of the tumours are sharp, delineated from the ventilated lung (**Figure 1**). They can be irregular or with finger-shaped ramification into the normal lung. Benign lesions are usually less sharp delimited from normal ventilated lung.

—Destruction of the adjacent lung. LC invades the adjacent parenchyma and either destroys or displaces the bronchi and normal vessels which normally present a radial, centrifugal distribution identifiable with colour Doppler US examination (**Figure 2**). Tumour neovascularization can be seen as tortuous vessels usually situated in the periphery and calibre variations [8, 9].
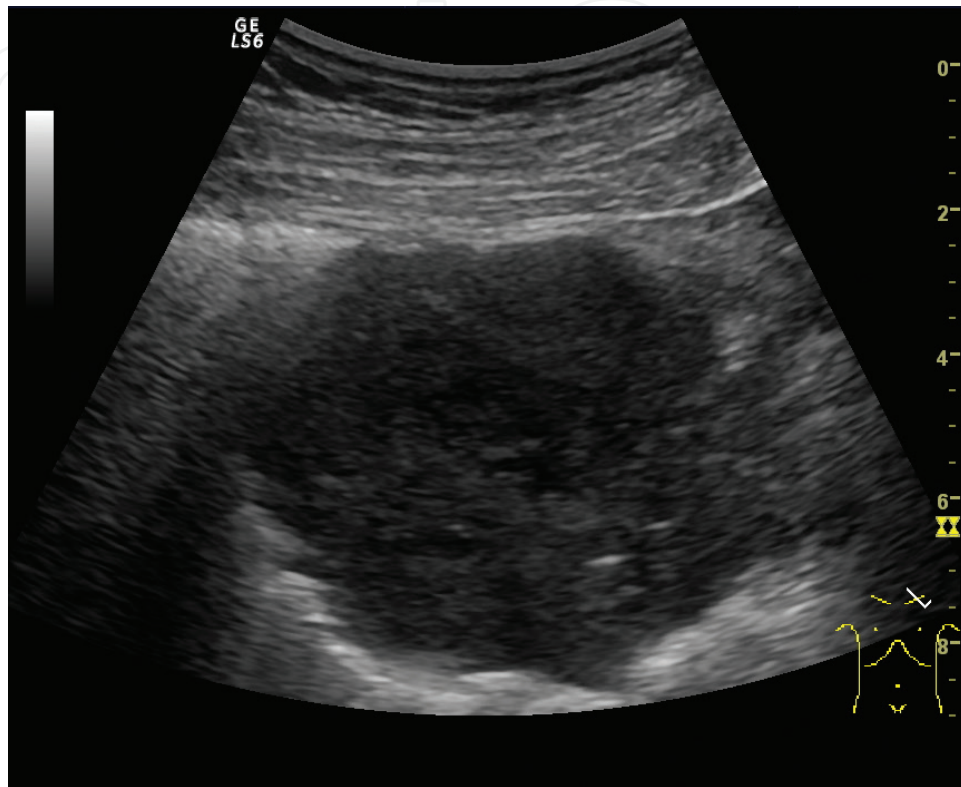

Figure 1. Ultrasonography aspect of a lung cancer abutting the pleura—hypoechoic mass, slight inhomogeneous, with irregular surface but sharp delimited from ventilated lung.

The most difficult situations are represented by chronic pneumonia and cicatricial peripheral lesion [10] which cannot be differentiated only by imagistic methods. In these cases, the histopathological exam is decisive.

If the diagnosis of malignancy is obvious, TUS can offer elements for staging of the lung cancer too. This information (assessment of resectability) can be critical for the decision of surgical treatment or other types of therapies. Contribution of TUS for staging LC should comprise the evaluation for the invasion of the adjacent structures (T3/T4), the extension to the lymph nodes which can be examined by US—supraclavicular, axillar, and sometimes intrathoracic— and the metastases in the liver, adrenal glands (mostly left side) or other sites.

Concerning chest wall invasion US has been proven to be at least as accurate as magnetic resonance imaging (MRI) and superior to CT by many studies (**Table 1**).

There are four criteria to be checked for the diagnosis of chest wall invasion: (a) absence of the gliding sign of the tumour over the chest wall, (b) interruption of the pleuropulmonary line, (c) direct invasion of the soft structures of the wall (**Figure 3**), and (d) direct invasion of

the bony parts—mostly ribs by the tumour [14] (**Figure 4**). One of the last two criteria is diagnostic; the first two (respectively, a and b) are only suggesting invasion. A recent study also proposed a cut-off value of 4.5 cm for diameters of the LC predicting invasion of the chest wall [16]. Unfortunately, TUS is not used widely enough for these purposes, even though it has the well-known advantages over CT—availability, cost, time of examination and lack of irradiation. Invasion of the diaphragm and pericardium can be also assessed by TUS, considering the possibility of real-time evaluation to prove direct extension of the tumour and not only the contact between this and the structure of interest.
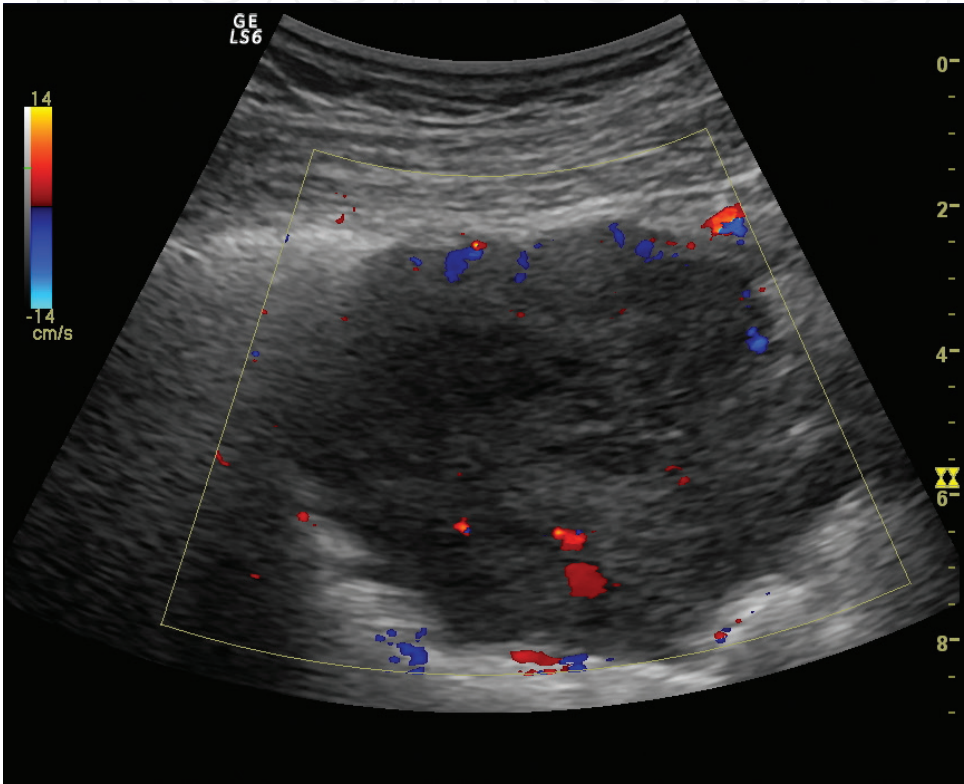

Figure 2. Colour Doppler US of a lung cancer showing hypovascularity without normal, radial distribution of vessels and bronchi (destruction of normal structure of the lung).

Author	Number of patients	TUS	CT
Sugama et al. [11]	65	Acc = 77%	Acc = 39%
Suzuki et al. [12]	120	Se = 100%	Se = 68%
Nakano et al. [13]	23	Se = 76.9%, Sp = 68.8%, Acc = 72.4%	Se = 69.2%, Sp = 75.0%, Acc = 72.4%
Bandi et al. [14]	90	Se = 89%, Sp = 95%	Se = 42%, Sp = 100%
Tahiri et al. [15]	28	Se = 90.9%, Sp = 85.7%	
Caroli et al. [16]	14	Se = 88.89%, Sp = 100%	
Acc - accuracy; Se - sensibility; Sp - specificity.			

Table 1. Studies comparing diagnostic performances for chest wall invasion of LC for TUS and CT.
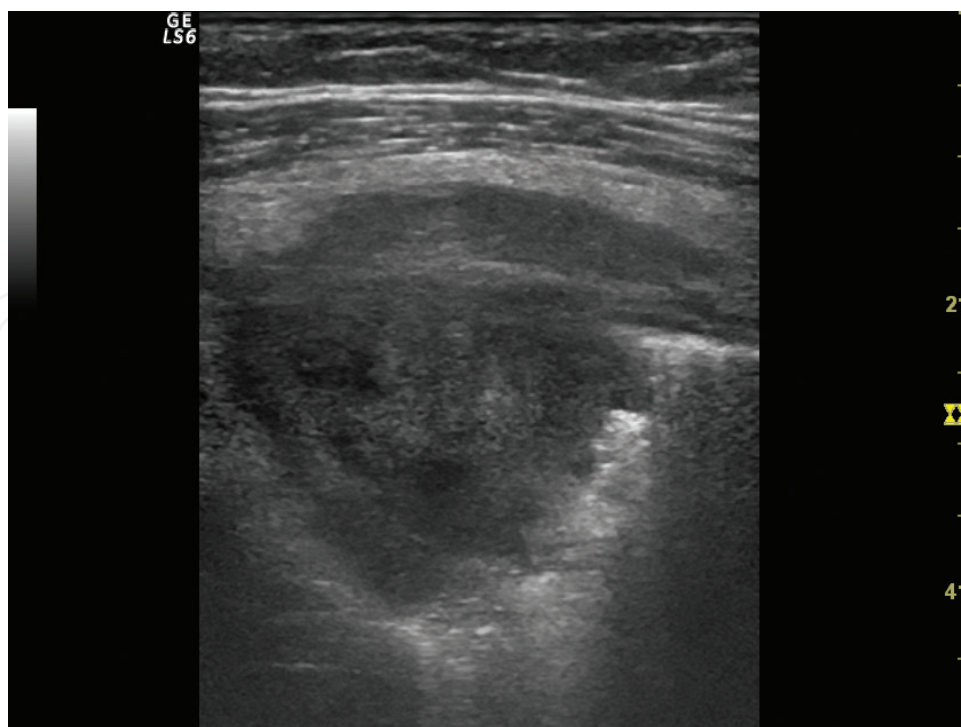
Figure 3. Peripheral hypoechoic and inhomogeneous LC with irregular contour, invading soft structures of the chest wall (extension of the tumour in the neighbouring layers of the wall).
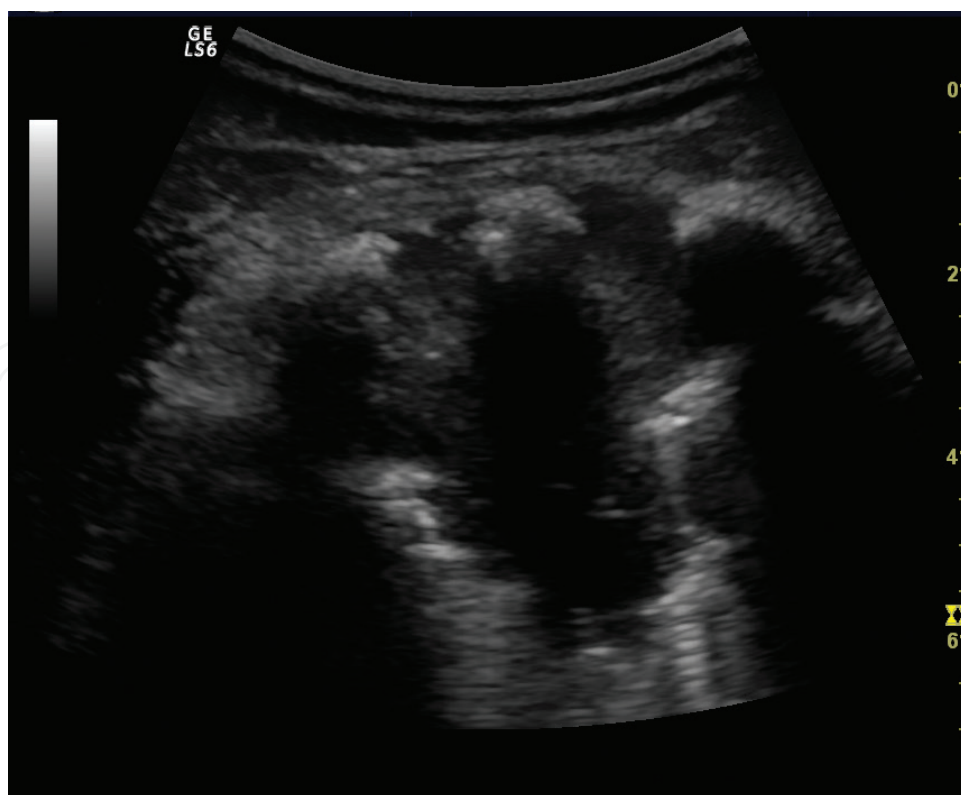

Figure 4. Peripheral hypoechoic LC invading the chest wall including ribs (three ovoid hyperechoic images with acoustic shadows partially included in the superficial tumoral area).

The presence of a pleural effusion signifies a T4 stage of the disease in an LC patient [17] or M1a (according to the 7th American Joint Committee on Cancer LC classification) although in rare cases it can have other causes (lymphatic drainage dysfunction, hypoproteinemia, atelectasis) [18]. In such situation, aspiration of fluid guided by TUS followed by cytological and biochemical analysis could solve the differential diagnosis of the effusions.

In the presence of atelectasis, TUS can delineate tumoral area from atelectatic lung even better than CT scans [19] based on structure, contour and vessel disposition in targeted areas (**Figure 5**). Also large LCs, usually more than 5 cm in diameter, demonstrate central necrosis. Those structural changes can be visualized as hypoechoic or transonic areas (**Figure 6**), and when communication with the bronchial tree or infection occurs, they appear as aerated hyperechoic irregular images surrounded by a thick wall hypoechoic masses (**Figure 7**). Those necrotic changes should always be precisely identified if a transthoracic-guided biopsy is taken into account. Thus, it is surprisingly how extended can be the necrosis inside larger tumours. In these cases, the best delimitation is realized by contrast-enhanced US (CEUS) where they appear as non-enhancing areas inside a late-enhancing tumoral tissue (see also the section dedicated to CEUS).

When a central tumour becomes obstructive, it will be associated with atelectasis or recurrent pneumonitis in the same region. Consolidation of the lung tissue allows better transmission of the ultrasound beam and visualization of the tumour through the non-ventilated lung. Other signs—as vascular distribution and fluid bronchogram—can be also seen inside the consolidated non-tumoral areas.
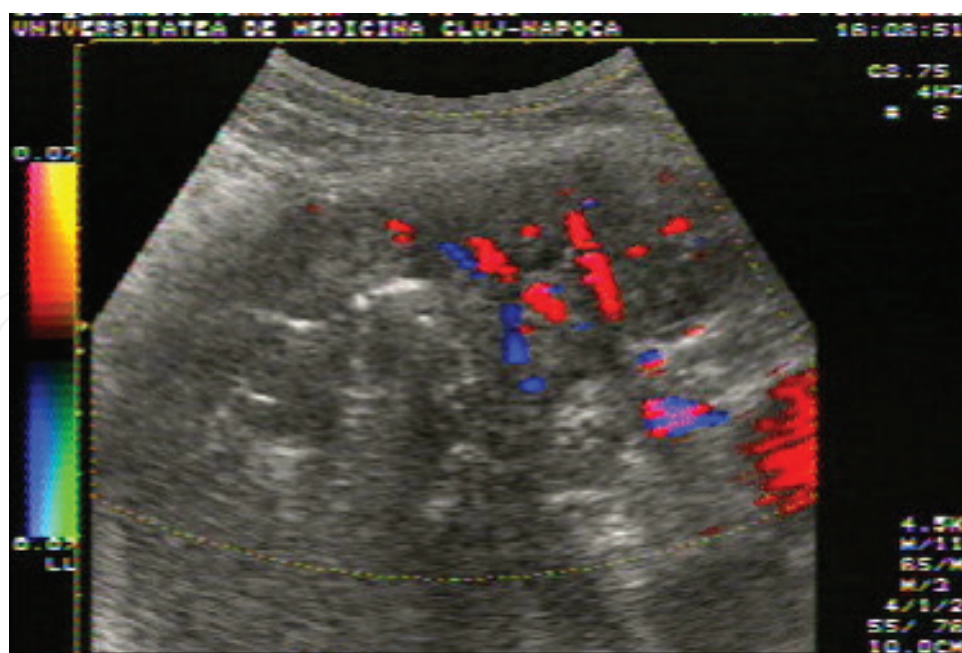

Figure 5. Large hypovascular lung cancer with central excavation containing gas (hyperechoic intratumoral images) and peritumoral atelectasis showing normal distribution of vessels (colour Doppler US examination).
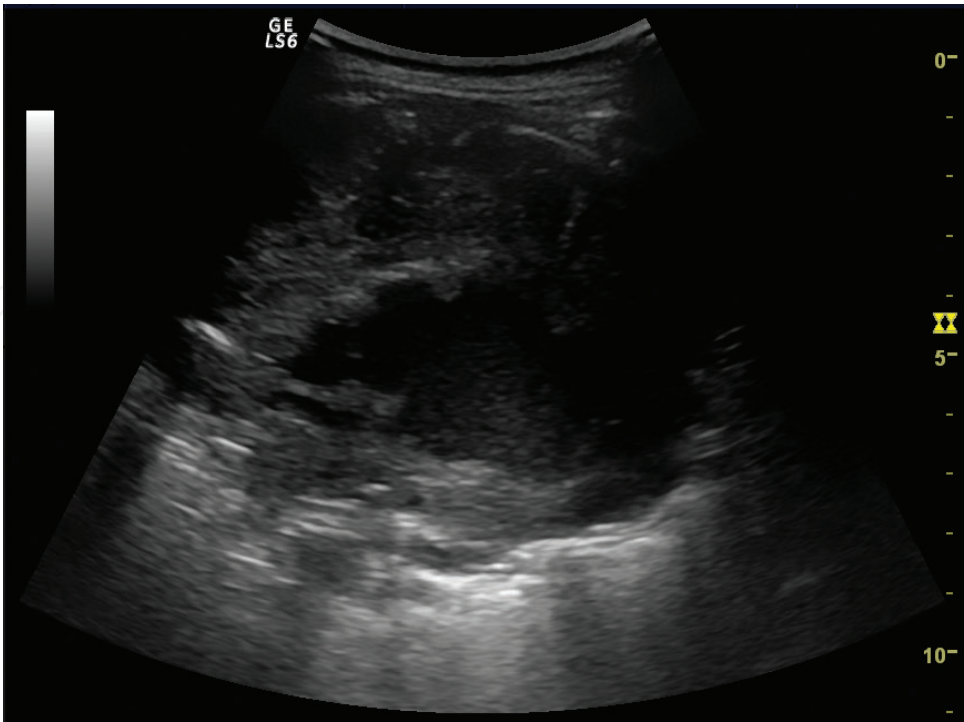
Figure 6. Large ovoid-shaped hypoechoic LC (squamous cell cancer) containing large central echo-free areas (necrosis).
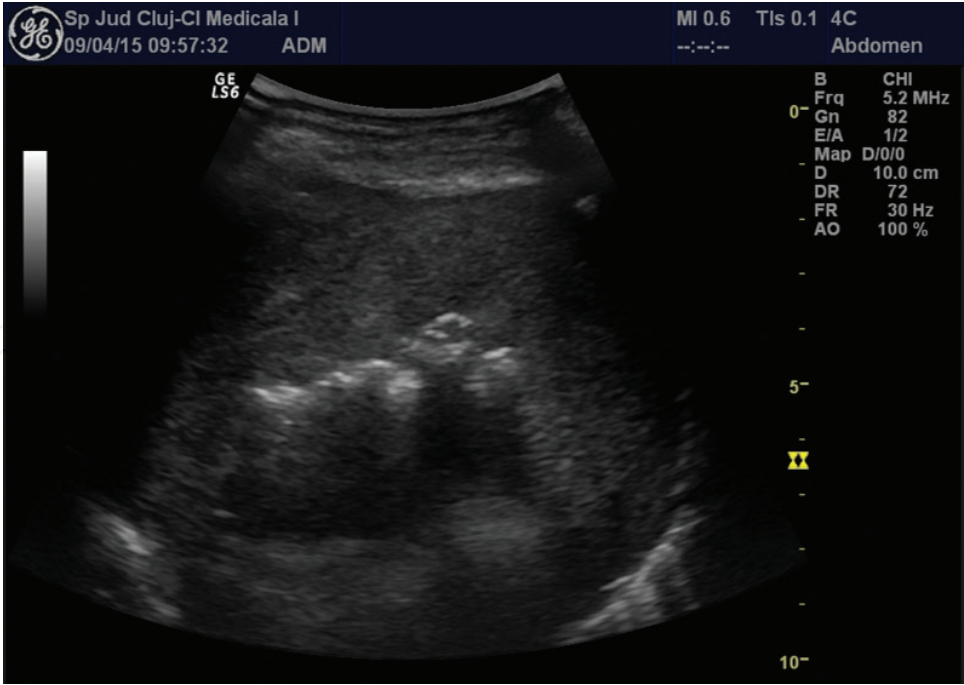

Figure 7. Large round-shaped hypoechoic LC (squamous cell cancer) containing hyperechoic central images corresponding to excavated necrotic core.

Colour Doppler examination of the neoplastic lung lesions reveals a reduced vascularization and disruption of normal vessel architecture [8, 9, 20]. In neoplastic lesions invasion of pulmonary arteries occurs in 56–87% of cases [21, 22], and vascularization is based mainly on neoangiogenesis originating in bronchial artery [23]. Moreover, central areas of the tumours are hypovascular due to stenosis/occlusions of pulmonary arteries. Duplex Doppler evaluation of impedance indices reveals monophasic low-resistance flow in the arterial vessels of the tumours [9] compared to high resistivity indices in pulmonary arteries present in benign lesions. Neoangiogenetic vessels can be suspected if they present a variable and convoluted/irregular position (**Figure 8**), variable flow direction and near-constant flow with reduced systolic-diastolic variations. It is important to know that almost 50% of the lung lesions present more than one type of vascularization [24] underlining the complexity of vascular distribution.
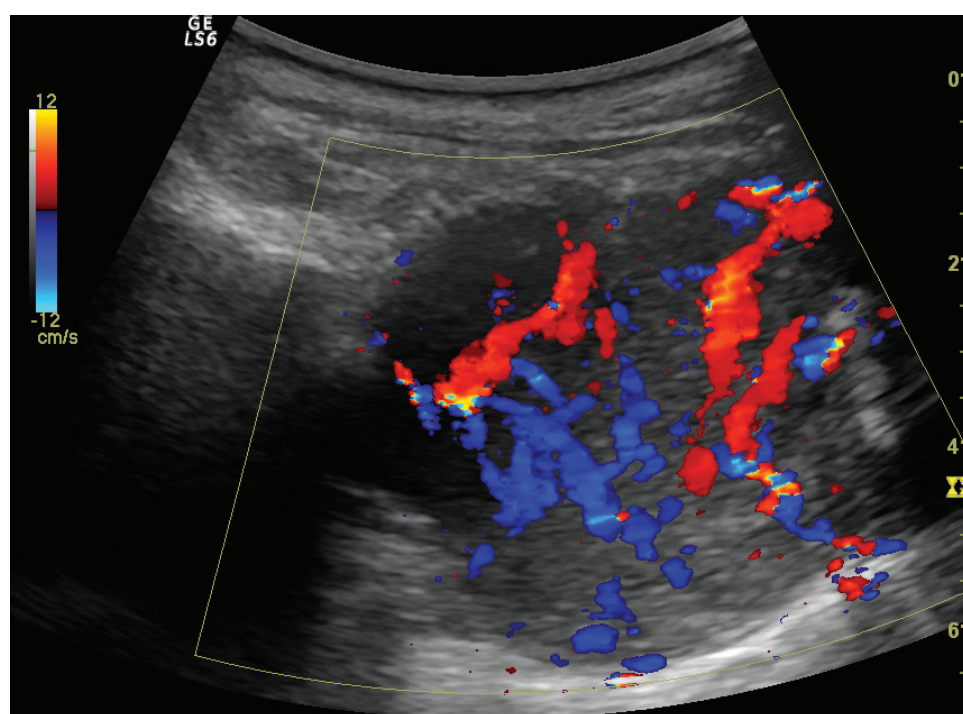

Figure 8. Hypervascular peripheral round-shaped hypoechoic LC with neovascularization—tortuous vessels with variable flow direction.

One of the most difficult diagnostic problems is represented by the peripheral adenocarcinoma with lepidic growth, which looks similar to a benign consolidation. The tumour can also preserve the normal bronchial tree and pseudo-normal distribution of vasculature (**Figure 9**) mimicking almost perfect pneumonic areas [25]. Minimal changes suggesting malignancy can be represented by irregular lung surface. In these cases, transthoracic US-guided biopsy refines the diagnosis.

In some cases, TUS can prove the extension of LC to hilar or mediastinal vessel. The invasion of pulmonary vessels can be visualized through the condensed or neoplastic lung in advanced cases. In these cases, TUS can also visualize metastatic hilar or mediastinal

lymph nodes, which are commonly impossible to assess by this method. The superior vena cava should be examined in order to diagnose compression or thrombosis of the locally advanced LC.
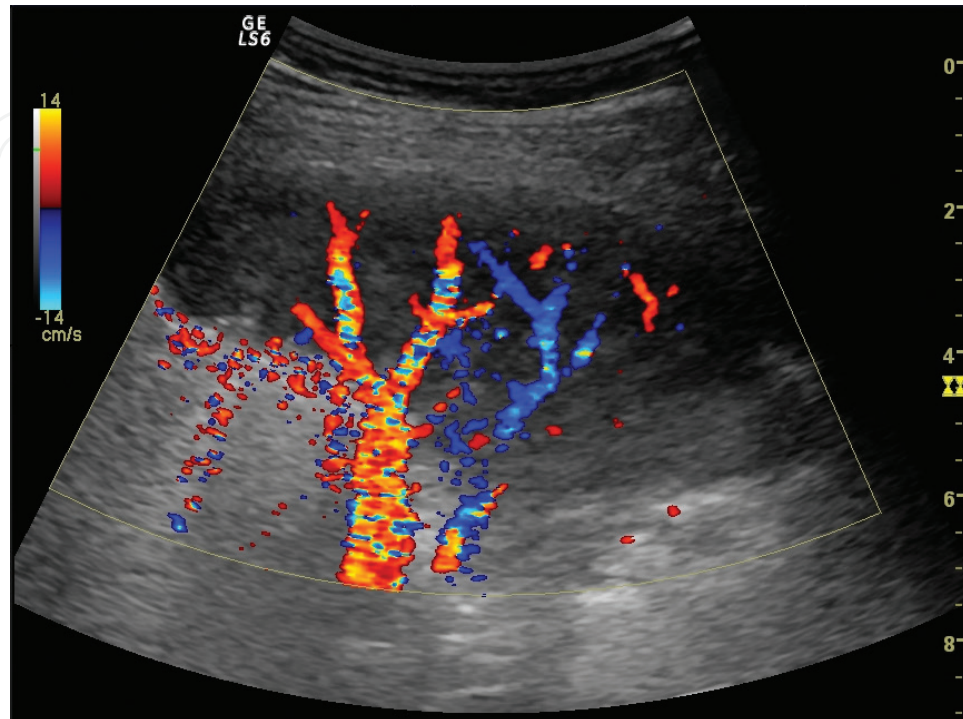

Figure 9. Adenocarcinoma with lepidic growth mimicking benign consolidation (pneumonia-like) with triangular-shaped and pseudonormal distribution of vascularization.

Another important component of US evaluation of an LC patient should include screening for the metastatic lymph nodes which cannot be clinically assessed with good accuracy— mainly supraclavicular stations. Metastases in cervical and supraclavicular nodes are present in 16–26% of cases, and US improves the identification of these affected stations with 31% [26, 27]. It surpasses three times the palpation performances and also CT scan with identification of 18–36% more cases of metastasis.

For the next step—histopathological diagnosis—TUS offers the possibility of guiding the percutaneous biopsy of the peripheral LC, with many advantages over radiological methods which were classically used. US guidance for transthoracic biopsies was done firstly more than four decades in the past, and since then, it has been successfully performed with various needle types [28, 29]. Indications and contraindications for percutaneous lung biopsy are according to the guidelines [30]. Most contraindications of transthoracic needle biopsy (TNB) are relative (platelet count < 100.000/ml, activated partial thromboplastin time (APTT) ratio or prothrombin time (PT) ratio > 1.4, contralateral pneumonectomy, Forced expiratory volume in the first second (FEV_1) < 35% or 1 l) and should be discussed in a multidisciplinary team [30]. Besides the contraindications, there are some limitations or particular situations such as the patients with pneumonectomy and nodule (either multiple or single) in

the remaining lung [31]. Not seldom we encounter patients presenting multiple comorbidities that affect respiratory and/or circulatory systems such as chronic heart failure, chronic respiratory failure or association of the two. In patients with such severe disease, oxygen therapy during the procedure might be essential, since the approach of the lesions requires the patient to lay down either in dorsal or even in ventral decubitus in order to perform the biopsy.

Complications of TNB are theoretically numerous (chest wall haematoma, parietal pain, pneumothorax, haemoptysis, intrapulmonary haemorrhage, haemothorax, air embolism, empyema—mostly for infected lesions, tumour seeding along the needle tract, death (0.15%)) [30]. Among those two are more important: haemoptysis and pneumothorax. Haemoptysis is most of the time self-limited (in less than 1% significant) and not life-threatening. It appears seldom after US guidance—under 3% than under CT guidance, 5.3–15% [32]—also due to deeper lung tumour approach by CT. The risk of pneumothorax after US-guided TNB is significantly lower (1–3%) than after CT-guided biopsy (up to 20.5–25%), due to the real time visualization and direct approach of the tumors abutting the pleura during the US-guided biopsies. It is increased in the presence of emphysema and larger needle calibre [32]. The presence of pneumothorax must be routinely checked after TNB, and the presence of clinically significant pneumothorax must be followed by percutaneous drainage which can be done also under US guidance [30].

An original study that compared CT-guided biopsy versus US-guided biopsy concluded that US is a valuable option to CT for guidance of transthoracic biopsies [33]. Authors found that US guidance provided diagnosis in 91% cases, while CT in 71%. In the same study analyzing the average time for biopsy and the average time per passage, results indicated that they were both statistically significantly shorter for US guidance than for CT guidance of the biopsy ($P < 0.05$) [33]. Results obtained by Sconfienza et al. [34] also favour US for biopsy guidance, the authors reporting successful biopsies using US guidance in 97.1% versus the CT-guided biopsies in which technical success was obtained in 96.5%. Also, there was a statistically significant lower rate of pneumothoraxes ($P = 0.025$) and a shorter median time per intervention for US compared to the CT-guided biopsy [34]. A review published in 2015 [35] revealed important aspects summarizing data regarding US, CT and electromagnetic navigational-transthoracic needle aspiration. In this review data from 75 studies was analyzed with authors finding that the rate of post procedure pneumothorax was higher in CT (20.5%) than in US-guided biopsy (4.4%). The authors underline also the paucity of data regarding US-guided biopsy since they have found just ten studies that assessed it and forty-eight that have performed CT-guided biopsy. Authors have determined an overall pooled diagnostic accuracy for CT to be 92.1% and for US 88.7% with similar sensitivies for the detection of malignancies—92.1% for CT and, respectively, 91.5% for US [35].

Some authors did not found a statistically significant difference in the diagnostic yield of fine-needle aspiration (FNA) versus core biopsy or FNA + core biopsy ($P = 0.96$) [36]. Other authors found that cutting-needle biopsies are more sensitive than fine-needle aspiration for the diagnosis of malignancies including mesothelioma [37, 38]. It is considered now that there are some advantages for the cutting needles over fine needle consisting in a superior diagnostic

accuracy, a better differentiation of LC subtypes and a better sensibility for the diagnosis of lung benign lesion [39].

An older study compared a cutting needle (Trucut) versus an aspiration needle (Surecut—a modified Menghini) concluding that US-guided needle biopsy was accurate and safe while providing an adequate histological specimen with a diagnostic yield comparable for both of the needles [40]. An important study regarding the types of needle is the study performed by Tombesi et al. [41]. The authors compared Trucut-type and a Menghini-modified needles. They found that the Trucut needle was superior, as it achieved a correct diagnosis more than the Menghini modified results that reached statistical significance (P = 0.0041). The authors also compared the diagnostic yield and found that the Trucut improved the diagnostic yield significantly statistic for smaller lesions ≤2 cm (P = 0.0139). Also, the Trucut needle provided a lower number of inadequate specimens [41].

Comparison the data concerning biopsy needle diameter indicated that a larger diameter does not have a significantly higher benefit [38, 42, 43].

The size of the lesion is not a problem for US guidance, even small tumour (less than 2 cm) being amenable for this approach [36, 44].

For optimization of the biopsy accuracy, various strategies have been proposed regarding [45] the approach and incidence of the needle, the orientation of the probe or the use of probes which allow guidance by a central orifice [28, 46].

It is well known that US guidance of the transthoracic biopsy of neoplastic lesions improves the overall performance, even in the presence of the necrosis [47]. Necrotic areas in larger tumours can lower the accuracy of TNB with 9–26% [48, 49]. Contrast-enhanced US (CEUS) can solve this issue, by revealing the non-enhancing areas corresponding to necrosis [50].

Regarding the factors that affect diagnostic yield in US-guided transthoracic biopsy, Jeon et al. found that the only statistically significant factor was the lesion-pleura contact arc length [51]. Some authors have not found statistically significant correlations between the size of the pleural surface of the lesion and the outcome—an adequate biopsy specimen (P = 0.106) or the incidence of complications (P = 0.23) [52].

Fontalvo et al. [52] analyzed the US-guided biopsy performed in children and found that this technique is safe and adequate for sampling of lung tissue.

Though the rate of complications is low, constant efforts are made to optimize the US guidance of biopsies [45] as well as for training specialists [53, 54]. Still, there are discrepancies even when comparing data from studies; in some of the studies, biopsies were performed using the free-hand technique which is more operator dependent and other studies using automatized systems for guidance. Using a guidance system allows a more predictable path of the needle, as well as a shorten time for performing the biopsy [55]. The free-hand approach has also certain advantages, providing more freedom to the operator, and reduces the costs associated with the use of various systems for various transducers. Those advantages have led some authors and centres to prefer free-hand guidance [55]. Also, in our centre, we prefer and perform the free-hand approach.

After the complete diagnosis, the results of the chosen therapy (assessment of response and recurrence) can be followed up precisely by TUS and can save a lot of resources and irradiation for the patients with peripheral LC.

2.2. Newer ultrasonography techniques for lung diseases

2.2.1. Contrast-enhanced ultrasonography (CEUS)

The first results of the application of CEUS in lung tumours were represented by a better identification of necrotic areas in order to improve the performance of percutaneous US-guided biopsy [50]. The authors reported a successful percutaneous biopsy after using a contrast agent in a case with previous non-diagnostic US-guided biopsy. In recent studies, another authors showed much more frequent identification of necrosis in patients with tumours when they used CEUS (43.9%) compared with standard US (6.7%) and an improvement in diagnostic performance of biopsies after CEUS (93.6% compared to 80%) [56, 57].

Benign lung lesions have dual arterial supply (pulmonary and bronchial) compared to LC that usually has just a single arterial supply (bronchial). This peculiarity of LC perfusion can be demonstrated with the use of intravascular contrast agents. CEUS has added diagnostic value to standard US examination [58, 59] of the pleural-based lesions. The contrast substance commonly used is the second-generation agent hexafluoride sulphur (Sonovue®, Bracco Imaging srl, Milano, Italy). One of the preliminary studies using CEUS for the diagnosis of peripheral lung lesions (60 cases) has offered a sensitivity of for CEUS 95.0% compared with CT 96.66%, B-mode ultrasound 83.33% and conventional radiology 86.66% [60]. They found three signs suggesting neoplastic lesion (inhomogeneous enhancement, absence of pulmonary arteries and wash-out within the first 120 s) in 88.8% of cases [60]. Other studies (95 cases) proved that LC has a later enhancement—more than 2 s delay from normal lung or benign lung lesions [61]—or synchronous with the chest wall and a variable extent of enhancement (non-homogenous, with non-enhancing areas corresponding to necrosis). Also, these authors have proposed an arbitrary score of enhancement and wash-out parameters after contrast administration that has also offered significant sensibility (Se = 98.1%, Sp = 95.1%) [61].

2.2.2. Ultrasonographic elastography in lung cancer

There are few studies published assessing US elastography for lung tumours. One of them used colour-coded strain elastography on 95 patients, of which 61 have been diagnosed with lung cancer and the other 34 with pneumonic condensations [62]. The authors found that LC has a significantly statistic (P < 0.001) higher rigidity and high elastographic Itoh's score (of 4–5) [63] comparing it to pneumonia and lymphoma which demonstrated lower scores (≤3) [62]. Considering score 4 as a cut-off value for colour-coded elastography (in a scale of 0–5), this value has a sensibility of 87% and specificity of 99% for diagnosis of lung cancer. Also, squamous LC had the highest score, almost 5. These possibilities of differentiation malignant from benign lung lesions based on the elastography properties can be a useful adjunct for US method.

Another group tried to visualize through elastographic approach in pulmonary metastasis without pleural contact (invisible otherwise by US), and they succeed in a preliminary study

to identify all lesions situated within 2.5 cm from the pleural space [64] in 18 patients. This new application tries to push further the borders of TUS application into a new area [65], and data presented by Adamietz et al. [64] proved its tremendous potential. The time will probably show if the peripheral tumours without pleural contact will be investigated by elastographic methods, but further rigorous studies to assess a greater number of patients to prove that the technique is reproducible are mandatory.

3. Advantages of transthoracic ultrasonography

Firstly, there are general advantages of US examination compared with other radiological examinations, considering availability, cost, time, lack of irradiation and bedside examination in critical patients. Careful and complete examination of a lung lesion by TUS can provide a lot of information for its benign or malignant character. For malignant lesions TUS provides very important details concerning size, local extension, association of atelectasis, necrosis, vascular invasion and sometimes intrathoracic lymph node metastasis. It can also diagnose pleural effusions with the highest sensitivity compared to other radiological methods. Also, for some information provided by TUS, accuracy is superior to that of CT scans and at least comparable to MRI. For example, diagnosis of chest wall invasion of LC by TUS has been already proven by many studies [14, 19, 66] to be more precise than those provided by CT. Being a dynamic exploration, TUS has advantages over CT scans, allowing a real-time examination of the pleuropulmonary interface during spontaneous respiration or cough.

Introduction of second-generation contrast agents for US added the possibility of perfusion analysis of lung lesion, with much less adverse reaction compared to other contrast agents used with CT (especially allergic, nephrotoxicity, etc.). CEUS improves the differential diagnostic between benign and malignant lesions, provides a better delineation of necrotic areas inside the tumours improving also the performance of US-guided lung biopsy. In the patients with allergic reaction or contraindications for administration of contrast agents, elastography can be used, and colour-coded information show a higher rigidity of the tumours compared to benign lesion (pneumonia being most studied). Also, we mentioned that, among cancers, squamous type showed the highest rigidity.

There are certain advantages for the US-guided biopsy over CT-guided biopsy:

—Comparable sensitivity and specificity with lower costs

—Less complications

—Less time

—No irradiation.

In patients with lung cancer US has to assess also extrathoracic lymph nodes, cervical, supraclavicular and eventually axillary, and at least the upper abdominal organ commonly affected by metastatic disease, the liver, adrenal glands (mainly left) and lymph nodes.

4. Limitations of transthoracic ultrasonography

TUS allows the assessment of pleural-based masses, providing information proportionally with the dimension of the contact of the tumour with the chest wall. When the pleural abutting is very small, only a part of the tumour can be seen even if it is large, but when the cancer invades the parietal pleura or the chest wall on large front, it can be characterized completely by TUS. Interposition of bony parts of the thorax and shoulder can also limit the visibility of some peripheral lesions (paravertebral, retroscapular, some apical tumours) by TUS and, consecutively, also the possibility of US-guided biopsy. Another limitation of TUS is the presence of chest wall pathology above the pulmonary region of interest—hematoma, fractures and parietal tumours—or pleural disease like calcifying pleuritis or fibrothorax which doesn't allow a proper examination of subsidiary lung areas. But fortunately, those situations are uncommon.

Contact of a tumour with the heart can be a limitation for TNB due to movement of the lesion. Limited pleural contact of an LC in patients with comorbidities and dyspnoea can increase the risk of post-TNB complications.

A problem for all imagistic methods is the differential diagnosis of primary LC from metastases. When metastases are abutting the visceral pleura, they can be visualized by TUS as rounded or ovoid hypoechoic lesions without aeric alveolograms. Their surfaces are sharp delineated from the surrounded lung with regular or irregular contours, and the vessels are usually displaced into the periphery. Single metastasis cannot be differentiated from primary LC, but when they are multiple or in a suggestive clinical context (other primary lesion diagnosed), they should be suspected.

5. Conclusions

Considering all advantages and limitations, TUS represents an essential investigation not only for the characterization of lung tumours, mainly subpleural, but also for guidance of various interventional procedures. It offers many advantages over CT including a better accuracy for identification of tumour necrosis, atelectasis, chest wall invasion and fewer complications after transthoracic US-guided biopsy with same accuracy as CT-guided biopsy.

Abbreviations

APTT	Activated partial thromboplastin time
CEUS	Contrast-enhanced ultrasonography
CT	Computed tomography
FEV_1	Forced expiratory volume in the first
FNA	Fine-needle aspiration
MRI	Magnetic resonance imaging

PT	Prothrombin time
SQC	Squamous cell lung carcinoma
TNB	Transthoracic needle biopsy
TUS	Transthoracic ultrasonography

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