Review

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Contrast enhanced ultrasound guidance: a new tool to improve accuracy in percutaneous biopsies

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Abstract

The performance of percutaneous echoguided biopsy in the tumoral diagnosis is limited by several factors, among which tumor characteristics such as tumor type, size and location play an important role. With all the advantages offered by the ultrasound guidance, the overall sensitivity of this method in the tumoral diagnosis of tumor has remained around 90%.

Contrast enhanced ultrasound guided percutaneous biopsy is a new developed technique aimed to increase the acurracy of percutaneous biopsies. With new ultrasound devices with split-screen mode, which displays both the CEUS and background B-mode US image simultaneously, on a single monitor, the procedure is technically feasible. CEUS guided percutaneous biopsy should be applied in large tumors with consistent necrosis, in hypovascular tumors or in those invisible or poorly visible to conventional ultrasound. The increased accuracy was demonstrated in liver tumors and in prostate adenocarcinoma.

Keywords: abdominal tumors, percutaneous echoguided biopsy, contrast enhanced ultrasound

Rezumat

Performanţele puncţiei biopsie ecoghidate în diagnosticul tumoral sunt limitate de mai mulţi factori între care caracteristicile tumorii (tip histologic, mărime şi localizare) ocupă un loc central. Cu toate avantajele oferite de ghidarea ecografică, în diagnosticul tumoral sensibilitatea metodei a rămas în jur de 90%. Puncţia percutană ghidată prin ecografie armonică cu contrast (PB-CEUS) este o metodă nouă, dezvoltată cu scopul creşterii acurateţii diagnostice a puncţiei percutane. Folosind ecografe ce permit împărţirea ecranului şi redarea atît a imaginii armonice cu contrast cât şi a celei în mod B , metoda este tehnic fezabilă. Puncţia biopsie ghidată prin CEUS trebuie folosită în cazul tumorilor mari cu necroză, a celor hipovasculare sau pentru cele invizibile sau slab delimitabile în ecografia convenţională.

Cuvinte cheie: tumori toracoabdominale, punctie biopsie ecoghidată, ecografie armonică cu contrast

Current state of knowledge

In patients suffering from neoplasia (particularly those with advanced forms) detailed information on the tumor histology is necessary to offer the elements supporting the decision of a proper treatment such as chemotherapy. This becomes even more important when initiating certain new molecular or genic oncological therapies. In such cases, the tumor diagnosis is based on the histological data offered by the tumor fragment, sampled usually by means of a percutaneous needle biopsy. In many cases, the distinctive features of certain tumors impose a different approach (e.g. the systematic biopsies for the diagnosis of prostate cancer).

In spite of the dramatic improvement in imaging and tumoral markers diagnosis in oncology over the last years, percutaneous biopsy continues to be used for tumor diagnosis. With all the advantages offered by ultrasound guidance, the overall sensitivity of this method in the tumoral diagnosis of the tumor has remained around 90%. Consistent progress has been made in the last years in terms of needle design [1] or ultrasound methods with

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complementary role in guidance (Color or Power Doppler, 3D/4D ultrasound, navigation systems) [2-4].

The performance of percutaneous guided puncture biopsy in the tumoral diagnosis is limited by several factors, among which tumor characteristics such as tumor type, size and location play an important role. Such performances are lower for large tumors due to the existence of tumoral necrosis or fatty changes. Necrotic tissue cannot be identified on B-mode sonography, especially before liquefaction has occurred, possibly leading to an unsuccessful biopsy or a false-negative diagnosis [5]. In larger lesions biopsy is performed therefore in the peripheral zone or a hypervascular area of the tumors.

Due to difficulties of visualization and targeting, small lesions represent another cause of false negative result of percutaneous biopsy. Lesions deep located or in risky locations (i.e. near major vascular structures, gallbladder, colon or pancreas) and those with low visibility on B mode ultrasound are other factors responsible for failures or the increased complication rate [5,6].

Peculiarities of tumors, where lesions are often invisible in B mode ultrasound (often multifocal lesions of adenocarcinoma of the prostate, small liver metastasis) or their distribution is unequal (i.e. in tumoral nodes) require the use of special techniques, which require multiple, systematic passages with the scanning of the whole parenchyma. This approach inevitably increases labor costs, risk of complications and degree of acceptance by the patient.

Contrast harmonic ultrasound

Ultrasound harmonic imaging with 2nd generation contrast agents (SonoVue) (CEUS) has the capacity of emphasizing the macro and above all the microvascularization of various parenchyma and tumors. Beside the well accepted use in detection and characterization of various tumors, especially those located in the liver, the use of this technique has enabled the delimitation of the avascular, necrotic areas from the viable, active, vascularized regions of the tumors. The differentiation of viable from necrotic tumor areas is possible by depicting ring like enhancement or bolus enhancement in the arterial phase and contrast material washout in the portal or parenchymal phase. The necrotic areas usually present no enhancement in all vascular phases of CEUS and may appear echo free or slightly hypoechoic in the background of enhanced liver parenchyma.

The first data published in literature have reported that by using CEUS it may be possible to increase the accuracy of percutaneous needle biopsy in the tumoral diagnosis by targeting hyperperfused tumoral areas or by increasing the conspicuity of liver metastasis [7,8,9]. In these first reports the procedures were performed after the injection of Levovist (Schering AG, Germany), a first generation contrast agent using pulse inversion harmonic imaging and stimulated acoustic emission [10].

The potential added value of CEUS in tumoral diagnosis by means of percutaneous biopsy may be related to several factors:

a) targeting of the needle in the vascular, viable areas of several tumors;

b) avoiding avascular areas (truly necrosis) in larger tumors (retroperitoneal, renal, adrenal) [8] or in those with frequent necrosis (kidney, liver metastases, especially the larger ones – i.e. those arising from colon or renal cancer)

c) avoiding hypovascular areas in certain tumors. The hypovascularity may be explained by the presence of marked fibrosis in pancreatic adenocarcinoma (and in liver metastasis from those tumors), fat areas in hepatocellular carcinomas (HCCs) and desmoplastic tissue in sarcomas or pancreatic tumors.

c) directing the needle in the tumor-affected areas of an organ (ganglion, prostate) in the case of patchy involvement.

d) targeting of otherwise invisible lesions or those hardly visible (small nodules of HCC on cirrhosis, adenocarcinoma's areas in the prostate, lung tumors in an atelectatic consolidation) [9,11].

Technique

CEUS guided biopsy is performed using an ultrasound system capable to scan at low MI (0.06-0.1) and a convex 2-5 MHz transducer for abdominal applications. An attached needle guide is not mandatory but should be used especially for biopsies performed in arterial phase.

For prostate biopsy an endocavitary transducer 5-10MHz with a needle guide is used.

When using hexafluoride microbubbles (SonoVue, Bracoo, Milan, Italy) a two-step algorithm may be used. Prior to the biopsy procedure the ultrasound contrast agent is prepared according to the manufacturer's recommendations (4.8 ml total) and a vial is divided into two doses of 2.4 mL each. Typically, the first dose is injected intravenously for the *preprocedural planning CEUS* and the second dose was used for the CEUS-guided biopsy. Each dose was immediately followed by a 10 mL normal saline flush [12,13].

Using the 2–5 MHz transducer, imaging was performed in a split-screen mode, which displays the CEUS image on the right side and the background B-mode US image on the left side, simultaneously, on a single moni-

tor. The mechanical index is usually set to 0.06-0.1. Focus is positioned at the bottom of the screen to minimize microbubble destruction. Field of view and gain are optimized to provide the clearest depiction of the lesion.

Preprocedural planning CEUS

The first dose is aimed to characterize the target lesion in arterial phase (10-30 seconds after injection) regarding the presence of hypervascular, hypovascular or avascular areas and to select a zone for biopsy. For liver tumors, scanning in portal (30-120 second after injection) and parenchymal phase (120-600 seconds after injection) is important to detect invisible or poorly visible lesions, to characterize them and to select a proper one for a subsequent CEUS biopsy. Moreover, it is important to locate the target lesion with reference to surrounding intrahepatic anatomical landmarks, to measure the diameter and depth of the lesion, plan a safe needle trajectory, and rehearse the biopsy procedure, including the instruction to the patient to suspend respiration [12,13].

CEUS guided biopsy procedure

After the skin is sterilized the predicted needle path is anesthetized with 2% lidocaine. Prior to the i.v. injection of the second dose of SonoVue, the needle is inserted into the biopsy guide and the skin entry. When the lesion begins to clearly appear following the contrast agent injection, the needle is advanced, via either an intercostal, abdominal or transrectal approach.

In cases where large unenhanced areas were found on the planning CEUS, the needle is directed in the arterial phase into the enhanced, perfused areas. For poorly visible tumoral lesions in B mode ultrasound the biopsy is performed in the parenchymal phase when the lesions wash out and the tissue to lesion contrast ratio is maximal.

The biopsy needles are visible clearly under CEUS conditions due to the fact that the needle causes tissue motion in the vicinity of the needle which generates harmonic signals, detected by the transducer. For automatic TruCut needle (i.e.Bard type) the presence of air in the side notch is easily visible after the automatic tissue retrieval [12]. Sometimes the bright contrast enhancement in the surrounding parenchyma masks the echogenic biopsy needle in CEUS image [13].

One technical difficulty is related to the short period of arterial enhancement available for puncture. If the tip of the needle is lost it may take some time to find it and to perform the biopsy without losing the arterial enhancement. This limitation may be overcome by the use of needle guides and an appropriate selection of the needle path in the planning CEUS.

Applications and results of CEUS guided biopsy in tumoral diagnosis

Liver tumors

In liver tumors the indications to perform CEUS guided biopsy are depicted in Table I.

Table I. Indications for CEUS guided biopsy in liver tumors

1. Large hepatic tumors with necrotic areas (large metastasis, cholangiocarcinomas, large HCC)
2. Tumors invisible or poorly visible on B mode ultrasound
3. Cystic tumors with solid component

Large hepatic tumors, especially large metastasis arising from colon or renal tumors have frequently areas of necrosis. This technique allows the targeting of a viable, enhanced area and sampling of a non-necrotic specimen (fig.1). Less defined or invisible lesions in conventional ultrasound become well demarcated in portal and parenchimal phases and can be easily punctured (fig.2).

In a recent study published in 2006 it was shown that using harmonic ultrasound with contrast agent (CEUS) the diagnostic accuracy of percutaneous biopsy in the diagnosis of liver tumors (both benign and malignant ones) increased from 87% (obtained by classical guided technique) to 95.3%. The excess of accuracy was even greater in lesions less than 2 cm, 97.1% versus 78.8% [11]. Another consequence of using CEUS in that study was the decrease of number of passages. This study was, however, conducted on different patient groups.

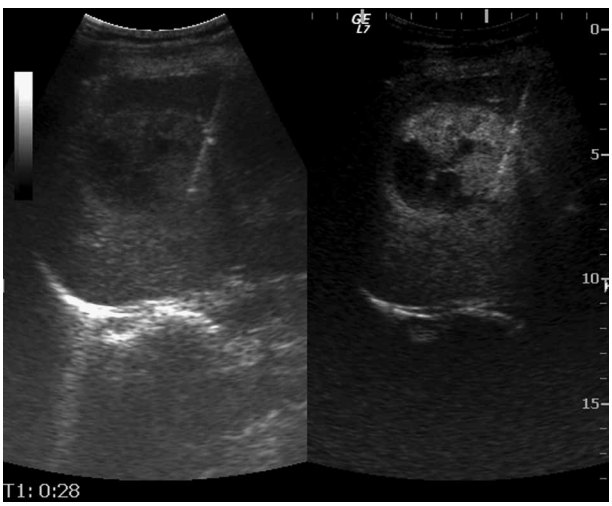


Fig 1. Large hepatic tumor with unenhanced central areas sugestive of necrosis. CEUS guided liver biopsy. The needle is seen within one enhanced area. Histology: metastatic adenocarcinoma

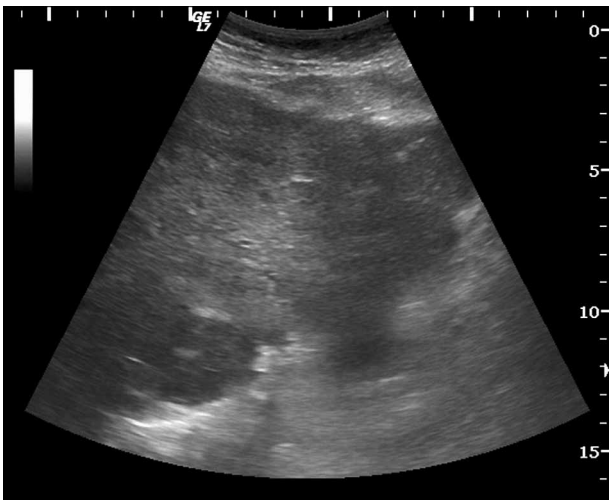


Fig 2a. Small, ill defined hepatic metastasis in case of gastric carcinoma.

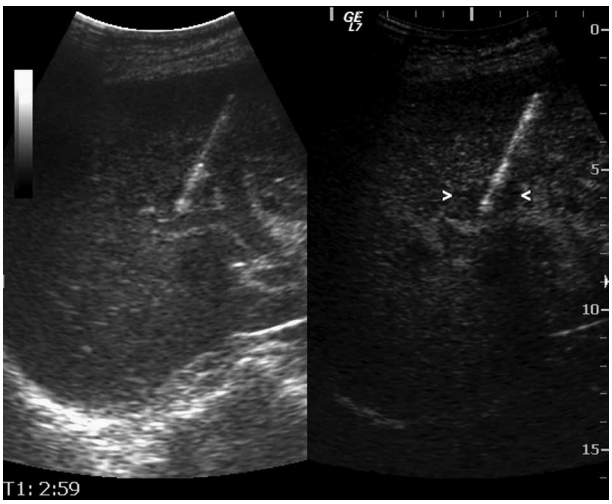


Fig 2b. In portal phase the lesions are well deliniated (> <) and punctured

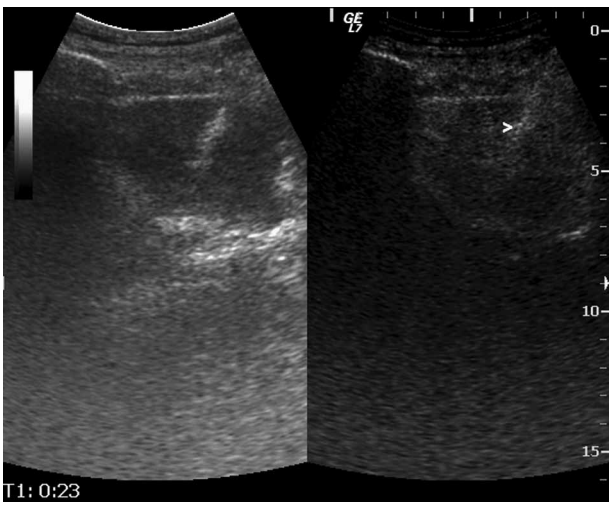


Fig 3. Subpleural lung tumor, arterial phase. The needle (>) is guided into an enhanced area. Histology: epidermoid cancer

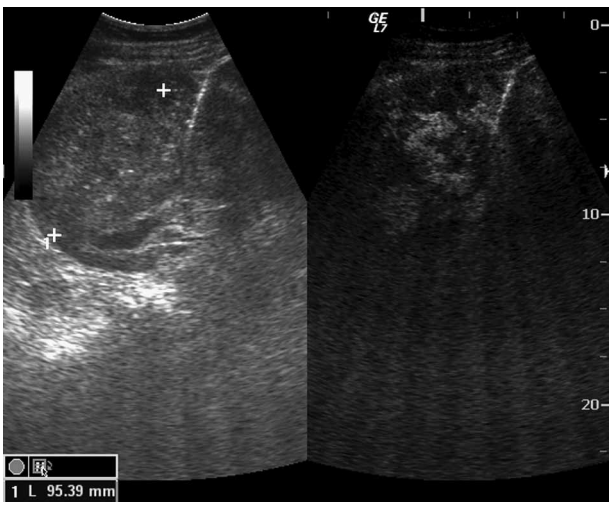


Fig 4. Large renal tumor with extensive necrotic areas. CEUS guided biopsy. Note the tip of the needle in an enhanced, peripheral area. Histology: renal carcinoma, clear cell type

Pulmonary tumors

The US-guided percutaneous biopsy in **pulmonary tumors** may lead to sampling of tissue from necrotic areas with consecutive decreased sensitivity. Although sonography can depict liquefaction necrosis inside the tumor and can guide the needle in the periphery in order to avoid necrotic tissue, inadequate specimens can be sampled in 9% to 26% of cases when the necrosis is large [14,15].

When examined with contrast enhanced ultrasound, lung cancer without atelectasis is characterized by delayed time to enhancement (15-20 seconds) and sparse tissue enhancement, suggesting bronchial arterial supply. By means of CEUS, areas of necrosis or abscess in the tumoral or atelectatic tissue can be demarcated [16].

In the clinical practice the use of CEUS guidance allows the puncture of vascularized, active tumoral areas thus avoiding the sampling of a necrotic fragment [15] (fig 3).

There are no controlled studies published comparing the CEUS guided biopsy with conventional biopsy in the diagnosis of pleural based pulmonary tumors.

Kidney and adrenal tumors. There are no studies regarding the benefits of CEUS guided biopsy in the **kidney and adrenal tumors**, though an experience regarding the use of CEUS in renal tumors is quite important . Generally these tumors may grow very large with frequent and extensive necrosis so they would be very suitable for this technique [17-19] (fig 4).

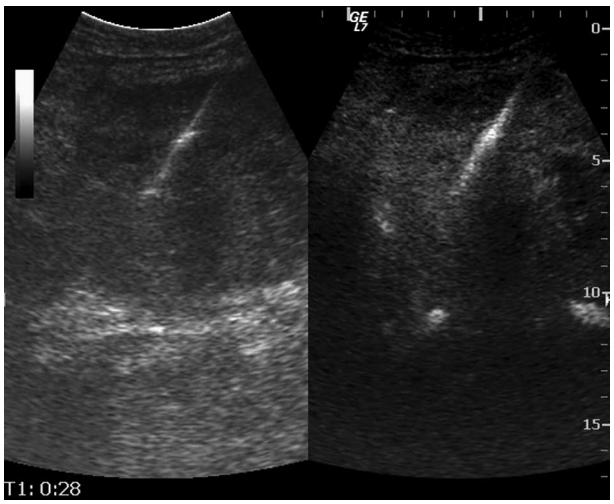


Fig 5. Massive retroperitoneal tumor. CEUS in arterial phase showed unenhanced, necrotic areas. Percutaneous biospy was performed guided by CEUS in arterial phase. Histology: fibrosarcoma

Retroperitoneal tumors may reach important sizes and are easily punctured with US guidance. Due to the presence of necrosis the sensitivity of US guided biopsy is around 80%. It is advisable to attend several passages and to sample specimens from the periphery. CEUS guidance may increase the accuracy of percutaneous biopsy by sampling tissue from vascularized, active tumoral areas [6] (fig 5).

There are several studies regarding the diagnosis of **prostate adenocarcinoma (PADK)** using CEUS guided biopsy in targeting the tumoral areas in the peripheral zone [20,21]. The optimized technique detects 15.6% of all cancers compared to 6.8% for in case systematic biopsy [22]. The advantage is more pronounced to PADK located on small glands and with lower PSA values [21].

Conclusions

CEUS guided percutaneous biopsy is a new, feasible technique that should be applied in large tumors with consistent necrosis, in hypovascular tumors or in those invisible or poorly visible to conventional ultrasound. The increased accuracy has been demonstrated in liver tumors and in prostate adenocarcinoma.

Conflict of interest: none

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