

The value of contrast-enhanced ultrasound in percutaneous biopsy of retroperitoneal masses

Der Stellenwert des kontrastverstärkten Ultraschalls bei der perkutanen Biopsie retroperitonealer Raumforderungen



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ABSTRACT

Purpose To evaluate the diagnostic yield of contrast-enhanced ultrasound (CEUS)-guided biopsy of retroperitoneal masses (RMs).

Materials and Methods Between 2006 and 2023, 87 patients presented at our US center for biopsy of an RM. In all biopsies, CEUS was performed prior to the intervention. The technical success rate of biopsy, the presence of diagnostic tissue in solid tumor biopsy samples, the accuracy of the biopsy and the occurrence of post-interventional complications were evaluated.

Results A US-guided biopsy could be conducted in 84/87 cases (96.6%). In 3/87 cases (3.4%), US-guided biopsy was impossible because the planned needle path was obstructed by vital structures. Of 84 lesions, 80 (95.2%) were solid lesions, and 4 (4.8%) were lesions containing fluid. In all solid tumors, 80/80 (100%), diagnostic vital tissue was successfully obtained. CEUS-guided biopsy showed a sensitivity of 93.2%, a specificity of 100%, a positive predictive value of 100%, a negative predictive value of 72.2%, and a diagnostic accuracy of 94.2% for the differentiation between malignant and benign RMs. In one of

the 84 cases (1.2%), there was a complication of postinterventional abdominal pain.

Conclusion Percutaneous CEUS-guided biopsy is a safe procedure with a high diagnostic yield and a low complication rate.

ZUSAMMENFASSUNG

Ziel Evaluierung des diagnostischen Stellenwerts der CEUS-geführten Biopsie (CEUS: kontrastverstärkter Ultraschall) von retroperitonealen Massen (RMs).

Material und Methoden Zwischen 2006 und 2023 stellten sich 87 Patienten in unserem Ultraschallzentrum zur Biopsie einer RM vor. Bei allen Biopsien wurde vor dem Eingriff eine CEUS durchgeführt. Die technische Erfolgsrate der Biopsie, das Vorhandensein diagnostisch vitalen Gewebes in den Biopsieproben bei soliden Tumoren, die Treffsicherheit der Biopsie und das Auftreten von Komplikationen nach der Intervention wurden evaluiert.

Ergebnisse Eine ultraschallgeführte Biopsie konnte in 84 von 87 Fällen (96,6%) durchgeführt werden. In 3 von 87 Fällen (3,4%) war eine ultraschallgeführte Biopsie aufgrund von vorgelagerten lebenswichtigen Strukturen auf dem geplanten Punktionsweg nicht möglich. Von 84 Läsionen waren 80 (95,2%) solide Läsionen und 4 (4,8%) flüssigkeitsgefüllte Läsionen. Bei allen soliden Tumoren (80/80; 100%) wurde erfolgreich diagnostisch vitales Gewebe gewonnen. Die CEUS-geführte Biopsie zeigte eine Sensitivität von 93,2%, eine Spezifität von 100%, einen positiven prädiktiven Wert von 100%, einen negativen prädiktiven Wert von 72,2% und eine diagnostische Treffsicherheit von 94,2% für die Unterscheidung zwischen malignen und benignen RMs. In einem Fall (1,2%) kam es zu einer Komplikation in Form von postinterventionellen abdominalen Schmerzen.

Schlussfolgerung Die perkutane CEUS-geführte Biopsie stellt ein sicheres Verfahren dar – mit hoher diagnostischer Treffsicherheit und geringer Komplikationsrate.

Introduction

Retroperitoneal masses (RMs) encompass a varied spectrum of primary and secondary pathologies, ranging from benign to malignant mesenchymal neoplasms, lymphomas, metastasized carcinomas, germinal neoplasia, and inflammatory processes [1, 2, 3]. Imaging of retroperitoneal masses obtained using ultrasound (B-US), computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography computed tomography (PET-CT) often present with non-specific features, making it imperative to perform histological confirmation for a definitive diagnosis [4]. RMs can be biopsied using surgical approaches or less invasive percutaneous biopsy techniques such as CT or B-US guided biopsies [5]. In biopsies guided by ultrasound, the use of contrast medium can be beneficial. It has been reported that CEUS-guided biopsy can improve the rate of diagnostic accuracy by as much as 10% [6]. This improvement in diagnostic accuracy is achieved through enhanced visualization of the lesion, detection of avital tumor tissues, and avoidance of biopsy in these areas [6]. However, there is a lack of data about the diagnostic yield of ultrasound-guided biopsies of RMs when using CEUS prior to the biopsy procedure.

The aim of this retrospective study is to investigate the diagnostic yield and complication rate of US-guided biopsies after the use of CEUS.

Patients and methods

Between 2006 and 2023, 87 patients presented to the Interdisciplinary Center of Ultrasound Diagnostics (a tertiary healthcare facility at a university hospital) for B-US, CEUS, and biopsy of an RM. The patients were referred by their treating physicians. All patients were examined by a single technician qualified as a German Society for Ultrasound in Medicine (DEGUM) Level III examiner, with more than 40 years of experience in the field of abdominal

sonography (C.G.) [7, 8]. The interventions, including biopsies, were conducted by either the DEGUM Level III qualified examiner or, under his supervision, by a physician with more than five years of experience in the field of abdominal sonography.

This retrospective study was approved by the local ethics committee and conducted in accordance with the amended Declaration of Helsinki. Informed consent was obtained from each patient.

The inclusion criteria were: 1) location of the mass in the retroperitoneal cavity; 2) standardized documentation of B-US and CEUS examinations; and 3) confirmation of the diagnosis of RM, with a follow-up of at least 12 months in the case of a benign histological finding.

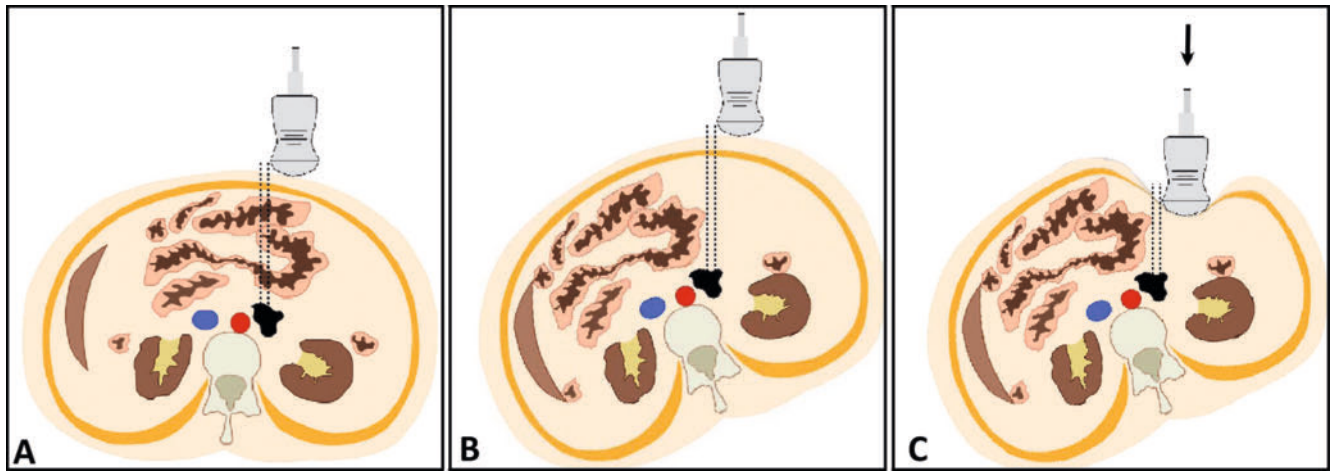
Ultrasound examination

The B-US examinations were performed with an Acuson Sequoia 512 GI US machine (Siemens, Germany) and a 4C1 curved-array transducer with a frequency of 4 MHz.

The CEUS investigations were conducted with the same transducer in contrast-specific mode (1.5 MHz) and in accordance with the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines [7]. A bolus injection of 2.4 ml of the contrast medium SonoVue (Bracco Imaging S.p.A., Milan, Italy) was performed via peripheral venous access. This was followed by 10 ml of NaCl 0.9%. For the first 30 seconds, the perfusion patterns of the lesions were continuously examined and recorded in a video clip. Subsequently, several short examinations were performed at one-minute intervals for up to three minutes. In the CEUS examination, the non-perfused area was considered avital tissue throughout the examination and attempts were made to avoid this area during biopsy.

Ultrasound-guided biopsies

Before the biopsy, the patient's clinical and laboratory data, the indication for biopsy, and the availability of written, informed



► **Fig. 1** Graphical illustration of patient positioning for the biopsy of a retroperitoneal mass. A para-aortic and retroperitoneal mass that was initially obstructed by overlapping bowel loops (A) becomes accessible by positioning the patient to the right (B), and compression sonography reduces the distance and needle path to the lesion (C).

consent from the patient were reviewed. The lesion was identified using B-US, and CEUS was used to avoid obtaining biopsy samples from necrotic areas or causing damage to large vessels. The depth of the lesion was gauged to guide the progression of the biopsy tool. Targeted biopsy procedures were carried out in real time, aided by a needle guidance system attached to the US transducer. Everything was kept sterile, and a local anesthetic (10 mL of 1% Ultracain; Sanofi, Paris, France) was used. Before conducting the full core biopsy using an 18-gauge needle (BioPince, Argon Medical, Texas, USA), the throw length of the instrument was set. This could range from 13 mm (resulting in a 9-mm sample size), to 23 mm (producing a 19-mm sample size), to 33 mm (capturing a 29-mm sample size). When visualization of the lesions was hindered by other organs, patients were turned on their side, either to the right or left, and compression sonography was subsequently performed to get close to the RM (► **Fig. 1**).

This adjustment improved visualization of the lesion, reduced the risk of damage to vital structures, and helped to determine the most suitable acoustic setting and biopsy method.

Each sample was kept in a tube with 1% formaldehyde and submitted to the local department of Pathology. The procedure took approximately 10–15 minutes. Afterward, a small sandbag was placed on the biopsy spot for two hours to prevent bleeding, and the patient's condition was monitored.

The following histologic and clinical data were evaluated retrospectively.

1. Technical success rate, defined as the feasibility of performing a US-guided biopsy via an appropriate access route.
2. Presence of vital tissue in solid tumors
3. Accuracy of the percutaneous needle biopsy. Biopsies were deemed non-diagnostic when the samples were either too small or could not provide a clear diagnosis and a different finding was obtained in the subsequent clinical course.

A specific malignant histopathological finding, consistent with the patient's clinical context, was established as the definitive diagnosis. In the case of a benign result on histopathological examination, a clinical reevaluation was performed, and the

final diagnosis was confirmed by repeat biopsy, surgery, complete regression under therapy, or stable findings in a follow-up of at least one year.

4. Presence of a post-interventional complication.

Statistical analysis

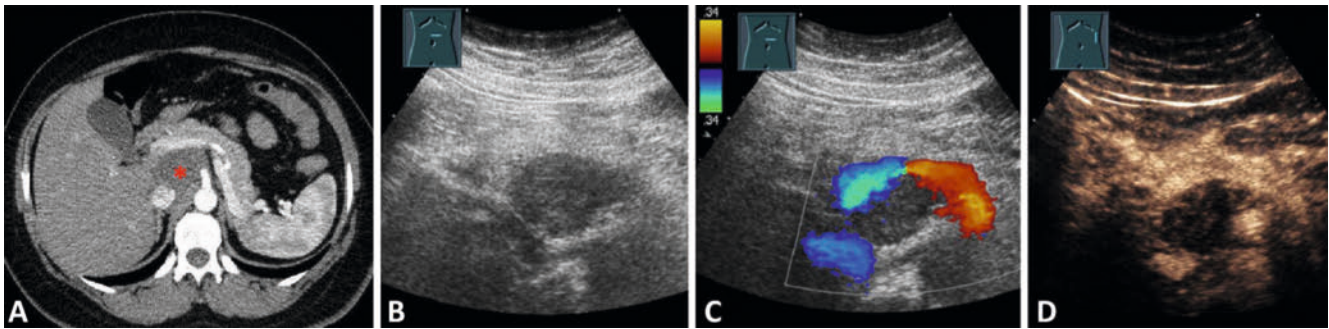
Diagnostic yield for malignancy was established based on sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy.

Results

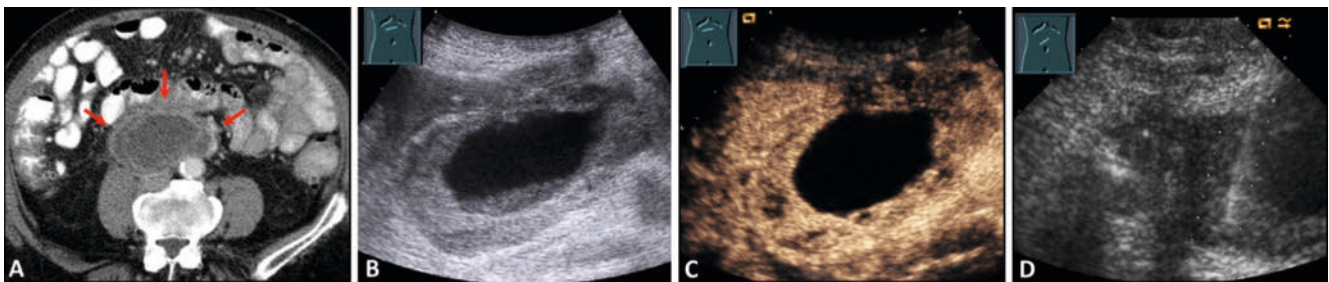
Demographic and clinical data

Of the 87 patients, 49 were men and 38 were women. The mean age was 63.8 years, with a range of 24–88 years. The final diagnosis was malignant RM (mRM) in 68/87 cases (78.2%) and benign RM (bRM) in 19/87 cases (21.8%).

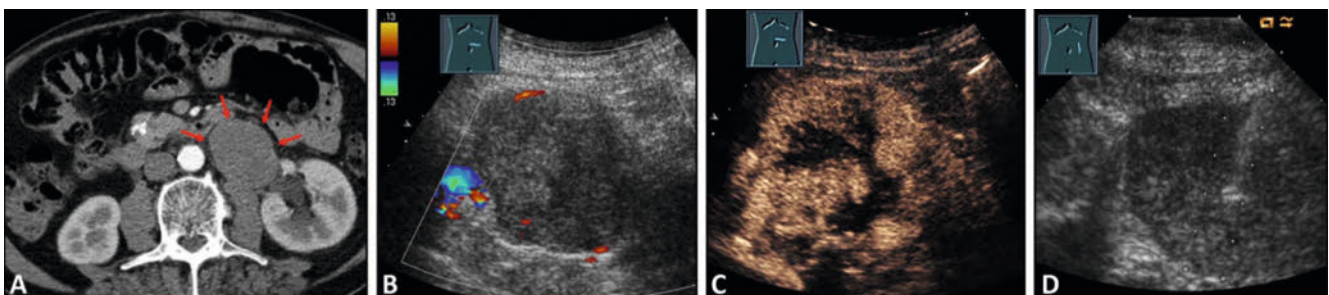
Among the malignant lesions, lymphomas were found in 32/68 cases (47.1%), comprising non-Hodgkin's lymphoma in 30/68 cases (44.1%) and Hodgkin's lymphoma in 2/68 cases (2.9%). Mesenchymal tumors were identified in 14/68 cases (20.6%), including liposarcoma in 4/68 cases (5.9%), gastrointestinal stroma tumor in 3/68 cases (4.4%), leiomyosarcoma in 2/68 cases (2.9%), angiosarcoma in 1/68 cases (1.5%), desmoplastic small round cell tumors in 1/68 cases (1.5%), malignant solitary fibrous tumor in 1/68 cases (1.5%), myxofibrosarcoma in 1/68 cases (1.5%), and chloroma in 1/68 cases (1.5%). Carcinoma metastases were present in 22/68 cases (32.4%), with colorectal carcinoma in 5/68 cases (7.4%), seminoma in 4/68 cases (5.9%), gastric carcinoma in 2/68 cases (2.9%), prostate carcinoma in 2/68 cases (2.9%), neuroendocrine tumor in 1/68 cases (1.5%), breast carcinoma in 1/68 cases (1.5%), lung carcinoma in 1/68 cases (1.5%), carcinoma of unknown primary in 1/68 cases (1.5%), and teratocarcinoma in 1/68 cases (1.5%).



► **Fig. 2** (A) A 36-year-old female patient with a retroperitoneal mass. On computed tomography, the lesion (*) extensively contacts the inferior vena cava, superior mesenteric artery, and portal vein, while also encircling the celiac trunk. A CT-guided biopsy was not possible due to the high risk of injury to the abdominal vessels. Visualization of the lesion on (B) B-mode ultrasound, (C) color Doppler sonography, and (D) contrast-enhanced-ultrasound. An ultrasound-guided biopsy was not possible due to the high risk of injury to the abdominal vessels. The diagnosis of a ganglioneuroma was confirmed by an endosonographic-guided biopsy. Source of the CT images: Prof. Dr Andreas H. Mahnken, MD.



► **Fig. 3** (A) A 79-year-old male patient with a 6 × 4 cm retroperitoneal mass located on the right paraaortic region on CT and (B) on B-mode ultrasound. (C) Contrast-enhanced ultrasound (CEUS) revealed extensive non-perfused areas indicative of avital tissue (necrosis). (D) Prior utilization of CEUS facilitated the avoidance of avital tissue. Histological analysis confirmed the diagnosis of a gastrointestinal stromal tumor (GIST). Source of the CT images: Prof. Dr Andreas H. Mahnken, MD.



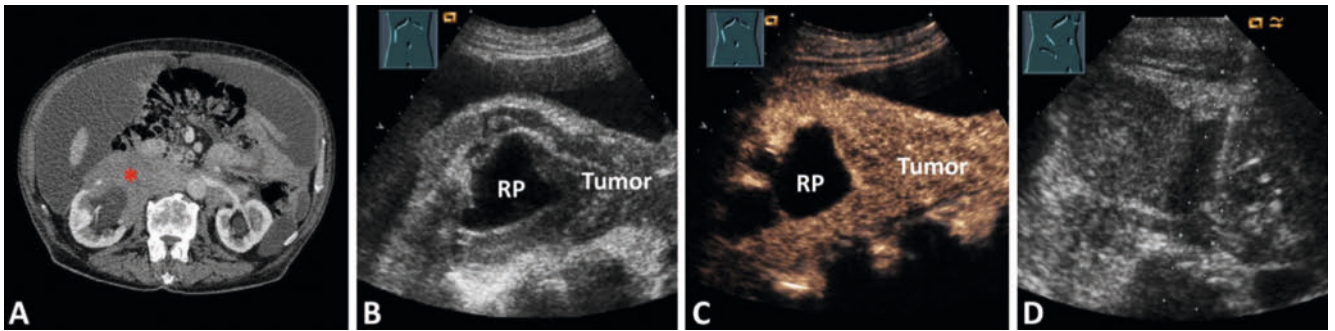
► **Fig. 4** (A) A 66-year-old male patient with a history of colorectal cancer and with a left-sided retroperitoneal mass on computed tomography (arrows). Visualization of the lesion on (B) B-mode color Doppler ultrasound and (C) on contrast-enhanced ultrasound with inhomogeneous enhancement and central non-perfused areas due to necrosis. (D) The biopsy was performed within perfused areas without complications, and the diagnosis of metastasis from a colorectal carcinoma was made. Source of the CT images: Prof. Dr Andreas H. Mahnken, MD.

In the benign category, neurogenic tumors totaled 5/19 cases (26.3%), with schwannoma in 3/19 cases (15.8%) and ganglioneuroma in 2/19 cases (10.5%). Ormond's disease was diagnosed in 4/19 cases (21.1%). Inflammatory conditions, including abscess in 2/19 cases (10.5%) and inflammatory pseudotumor in 1/19 cases (5.3%) accounted for 3/19 cases (15.8%). Other benign conditions included extramedullary hematopoiesis in 2/19 cases (10.5%), echinococcosis in 1/19 cases (5.3%), lymphocèle in 1/19 cases (5.3%), leiomyoma in 1/19 cases (5.3%), lymph

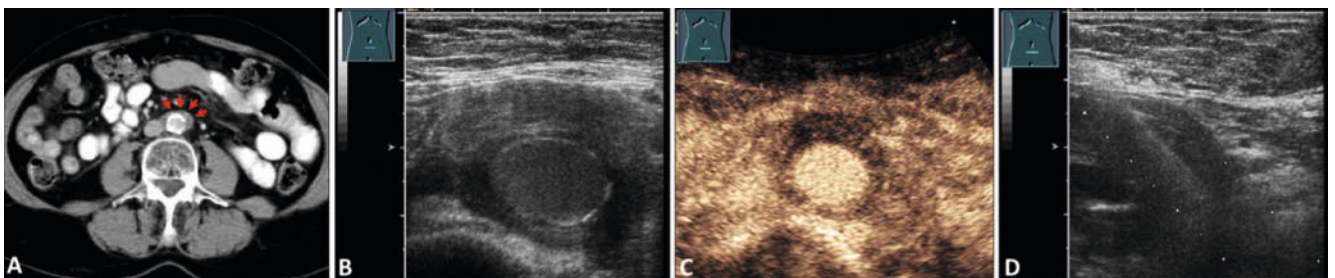
node tissue in 1/19 cases (5.3%) and lymphangioliomyomatosis in 1/19 cases (5.3%).

Ultrasound-guided biopsies

Regarding the technical success rate, biopsy could be conducted in 84/87 cases (96.6%). In 3/87 cases (3.4%), US-guided biopsy was not possible because the planned needle path was obstructed by vital structures (► **Fig. 2**). In one case, diagnosis was achieved



► **Fig. 5** (A) A 71-year-old male patient with a retroperitoneal mass on computed tomography (*). Significant ascites and bilateral hydronephrosis were observed. Prior to the US-guided biopsy, an ascites puncture was performed to reduce the biopsy risk. Visualization of the lesion on (B) B-mode ultrasound and (C) contrast-enhanced ultrasound with dilatation of the right renal pelvis (RP). (D) To minimize the risk of complications and to prevent damage to the RP and displacement of ascites, the patient was positioned laterally to the right. The biopsy was performed without complications, and the diagnosis of metastasis from prostate carcinoma was confirmed. Source of the CT images: Prof. Dr Andreas H. Mahnken, MD.



► **Fig. 6** A 76-year-old female patient with a retroperitoneal mass on (A) computed tomography (arrows) and (B) B-mode ultrasound. (C) On contrast-enhanced ultrasound, the lesion showed arterial homogeneous hypoenhancement. (D) An ultrasound-guided 18G-core needle biopsy of the hypo-echoic paraaortic lesion was performed and the diagnosis of Ormond's disease was made. Source of the CT images: Prof. Dr Andreas H. Mahnken, MD.

by an endosonographic-guided biopsy, and, in the other two cases, it was achieved by a CT-guided biopsy.

Of 84 lesions, 80 (95.2%) were solid lesions and 4 (4.8%) were fluid-containing lesions that included abscesses, echinococcal cysts, and lymphoceles. In all solid tumors, 80/80 (100%), diagnostic tissue was successfully obtained (► Fig. 3 and ► Fig. 4).

The biopsy was successful and sufficient for diagnosis in 78/84 cases (91.7%) (► Fig. 5 and ► Fig. 6).

In 6/84 cases (7.2%), the initial diagnosis was inconclusive. In 5/6 cases (83.3%), the diagnosis was false-negative (final diagnoses: one liposarcoma metastasis, one GIST tumor metastasis, one case of Hodgkin's lymphoma, one gastric carcinoma metastasis, one prostate carcinoma metastasis), and, in one case, a specific diagnosis could not be made based on the biopsy (final diagnoses: Ormond disease). Of these six cases, the diagnosis was confirmed by a second US-guided biopsy in four lesions (66.7%). In one case (16.7%), the diagnosis was validated through surgical resection of the primary tumor, whereas, in another case (16.7%), it was confirmed by surgical resection of distant infiltration of the primary tumor.

US biopsy with prior CEUS showed a sensitivity of 93.2%, a specificity of 100%, a positive predictive value of 100%, a negative predictive value of 72.2%, and a diagnostic accuracy of 94.2% in the differentiation between malignant and benign RMs.

In one of the 84 cases (1.2%), there was a complication of postinterventional abdominal pain. No other complications were recorded.

Discussion

The evaluation of RM malignancy is a diagnostic challenge due to the nonspecific symptoms and features of these lesions on cross-sectional imaging [9]. Therefore, the definitive diagnosis is made histologically.

In this retrospective study, we investigated the diagnostic accuracy of US-guided biopsy of RMs, with prior CEUS examination. The technical success rate for the US-guided biopsies in this study was 96.6%. This is slightly lower than the technical success rate for CT-guided procedures, which is reported in the literature to be between 99.7% and 100% [5, 10, 11, 12]. This slight variation can be attributed to the additional access routes afforded by CT compared to US. Furthermore, CT-guided biopsy can also be performed in the prone position from the dorsal/paravertebral approach. This provides an additional access route that is not possible due to the limitations of ultrasound.

In this study, non-vital tissue, such as necrosis or hemorrhage, was successfully avoided in 100% of the biopsies of solid lesions. Furthermore, the accuracy of US-guided biopsy with prior CEUS to determine malignancy was 94.2%. These results suggest a higher

► **Table 1** Diagnostic performance and complication rate of US-guided biopsy and computed tomography.

Imaging modality	Cases	Year	Author	Needle diameter (gauge)	Technical success rate (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Complication rate (%)
CT	49	2008	Stattaus et al. [10]	16 and 18	100.0	95.2	100.0	95.9	2.0
CT	74	2011	Tomozawa et al. [12]	18	100.0	93.0	100.0	93.0	9.5
CT	334	2018	Shao et al. [11]*	18 and 22	99.7	91.5	100.0	92.8	11.3
CT	86	2021	Singh et al. [5]	16 and 18	100.0	Not analyzed	Not analyzed	91.9	2.3
US	96	1984	Juul et al. [13]	23	95.0	85.0	100.0	Not analyzed	0.0
US with prior CEUS	84	2023	Present study	18	96.6	93.2	100.0	94.2	1.2

CEUS: contrast-enhanced ultrasound; CT: computed tomography, US: B-mode ultrasound; * CT-guided percutaneous needle biopsy of retroperitoneal and pelvic lymphadenopathy.

sensitivity compared with a US-guided biopsy without prior CEUS. Juul et al. reported a sensitivity of 85 % and a specificity of 100 % for US-guided biopsies without CEUS of retroperitoneal masses (excluding the kidney, adrenal gland, and pancreas) [13]. Furthermore, in the study by Juul et al., there were no reported complications. However, it must be emphasized that only fine-needle biopsy was performed in this study, thus limiting the comparability [13]. The results regarding the accuracy of US-guided biopsy with prior CEUS are similar to those for CT-guided biopsies reported in the literature, which range from 91.9 % to 95.6 % [5, 10, 11, 12]. Importantly, only one minor complication (abdominal pain) was observed, and this was in just one patient. Remarkably, the complication rate in this study was lower than the complication rates described in the literature for CT-guided biopsies of RMs, which are reportedly between 2 % and 11.3 % [5, 10, 11, 12, 14]. The reasons could include the possibility of real-time imaging in US, the higher spatial resolution of US, and the strict intravascular containment of the US contrast agent, all of which contribute to the detailed visualization of minute vessels and critical structures before and during the examination. It should also be noted that comparisons with CT data are of only limited feasibility due to the use of various types of biopsy needles.

The diagnostic performance and complication rate of US-guided biopsies in the present study, compared with the findings of previously performed CT studies, are summarized in ► **Table 1**.

Although the results of this study are promising, it must be emphasized that CEUS is only a complementary method for enhancing the visualization of vascular structures, organ perfusion, and the differentiation of vital and avital tissues, which can be beneficial in biopsy. The diagnostic performance of this method depends on the experience of the examiner [6]. Furthermore, there are many additional factors, such as the patient's physique, the anatomical location, and the limitations of US, that play a significant role in each biopsy and can influence the procedure. The decision for and execution of a biopsy should consider multiple factors, such as patient preferences and therapeutic and prognostic consequences. Furthermore, a biopsy should be conducted if a diagnosis cannot be established through noninvasive methods, such as imaging and clinical information. If a decision is made for a US-guided biopsy, considering all clinical imaging data, a CEUS examination prior to the US biopsy may be helpful.

There are some limitations to this study. The study was performed only in patients who were referred to the Interdisciplinary Center of Ultrasound and a selection bias cannot be excluded. Furthermore, all examinations were conducted by experienced investigators. Therefore, the results of this study may not be generalizable to all examiners. Due to the retrospective nature of the study and the relatively small number of subjects ($N = 87$), further prospective multicentric studies are needed to validate our findings.

Conclusion

In summary, this study's findings suggest that, given adequate visualization of retroperitoneal lesions and the requisite experience of the investigators, US-guided biopsy with prior CEUS examination is equivalent to CT-guided techniques in terms of success rate, diagnostic accuracy, and low complication rates.

Acknowledgement

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Conflict of Interest

C. Görg received funding from Bracco Imaging. Bracco Imaging supported CEUS workshops at the University Hospital Marburg.

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