Quantitative diagnosis of salivary gland tumors with contrast-enhanced ultrasound. A systematic review.

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Abstract
Salivary gland tumors pose diagnostic challenges, with fine-needle aspiration cytology showing limitations in accuracy. Contrast-enhanced ultrasound (CEUS) has emerged as a promising alternative for preoperative differentiation. This systematic review aims to evaluate the diagnostic value of CEUS in distinguishing between benign and malignant salivary gland tumors. Electronic databases (PubMed, Embase, Scopus, Web of Science, Lilacs) were searched up to October 2024. Inclusion criteria comprised original studies (2020–2024) evaluating CEUS for salivary gland lesions. Exclusion criteria included non-English articles, reviews, and irrelevant studies. The STROBE checklist was used for quality assessment. Data were synthesized narratively. Eight studies were included. CEUS demonstrated high diagnostic value, with features such as blurring enhancement margins and increased lesion size aiding malignancy risk assessment. It effectively differentiated pleomorphic adenomas from Warthin tumors and benign from malignant lesions. CEUS is a valuable, non-invasive tool for the quantitative diagnosis of salivary gland tumors, enhancing preoperative planning and differential diagnosis.

INTRODUCTION:

Salivary gland tumors represent a clinically significant subset of head and neck neoplasms, accounting for approximately 2–6% of malignancies in this region [1]. Approximately 80% of these tumors originate in the parotid gland, with a majority being benign [2]. However, the clinical management and prognosis for benign and malignant salivary gland tumors are markedly different, necessitating precise preoperative differentiation to guide appropriate surgical planning and prognostic evaluation [3]. Conventional imaging modalities, including high-resolution ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI), are routinely employed for the initial assessment of salivary gland lesions [4]. While B-mode US provides valuable information on lesion location, size, margin, and echogenicity, its ability to reliably distinguish between benign and malignant histotypes remains limited due to overlapping imaging characteristics [5]. Fine-needle aspiration cytology (FNAC), a standard preoperative diagnostic tool, is also constrained by variable accuracy and a significant rate of false positives or inconclusive results, particularly in differentiating between specific malignant subtypes [6].

In this context, contrast-enhanced ultrasound (CEUS) has emerged as a significant advancement in diagnostic imaging. CEUS utilizes intravascular microbubble contrast

agents to provide real-time, dynamic visualization of tissue microvascularization without ionizing radiation or nephrotoxic risk [7, 8]. This technology enhances the characterization of vascular patterns within lesions, offering both qualitative and quantitative data on perfusion kinetics. Its utility has been well-established in the evaluation of focal lesions in organs such as the liver and thyroid [9, 10]. The application of CEUS to salivary gland pathology presents a promising avenue for improving diagnostic specificity by revealing unique enhancement patterns associated with different tumor types, such as the differences between pleomorphic adenoma and Warthin tumor [11].

Given the diagnostic challenges posed by conventional methods and the evolving evidence supporting CEUS, a synthesis of the current literature is warranted to clarify the diagnostic value of CEUS.

Objective

Therefore, this systematic review aims to evaluate the existing evidence on the role of CEUS, particularly its quantitative parameters, in the differential diagnosis of benign and malignant salivary gland tumors.

Materials and Methods

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [12] to evaluate the evidence on the quantitative diagnostic utility of contrast-enhanced ultrasound (CEUS) for salivary gland tumors.

Eligibility Criteria

The review focused on studies meeting the following criteria:

- Inclusion Criteria: Original research articles (including observational cohort and case-control studies) published in English between January 2020 and October 2024. Studies were required to investigate the use of CEUS in human subjects with salivary gland tumors and report quantitative or semi-quantitative diagnostic outcomes related to differentiating benign from malignant lesions or specific tumor types.
- Exclusion Criteria: Review articles, meta-analyses, case reports, conference abstracts, editorials, non-English publications, animal studies, and studies where CEUS was not the primary imaging modality of investigation or did not focus on salivary gland pathology.

Information Sources

A comprehensive literature search was performed across five major electronic databases: PubMed (including MEDLINE), Embase, Scopus, Web of Science, and Lilacs (Latin American and Caribbean Health Sciences Literature). The final search for all databases was conducted on October 31, 2024. No date filters were applied within the search interface to ensure all relevant articles from the target period were captured; subsequent manual filtering was performed.

Search Strategy

A systematic search strategy was developed using Boolean operators (AND, OR) and Medical Subject Headings (MeSH) terms where applicable. The core concepts were "contrast-enhanced ultrasound," "salivary gland," and "diagnosis." The full search strategy for PubMed is presented below and was adapted for syntax in the other databases:

- ("Contrast-enhanced ultrasound" OR CEUS OR "ultrasonography, contrast-enhanced" [MeSH]) AND
- ("Salivary Glands" [MeSH] OR "salivary gland" OR parotid OR "salivary tumor" OR "salivary neoplasm") AND
- (diagnosis OR differentiation OR "sensitivity and specificity" OR "predictive value of tests" OR quantitative)

Selection Process

The selection process involved two stages. Initially, two reviewers (K.S. and E.C.D.) independently screened the titles and abstracts of all retrieved records against the eligibility criteria. In the second stage, the full texts of potentially relevant articles were obtained and assessed independently by the same reviewers. Any disagreements regarding inclusion or exclusion at either stage were resolved through discussion and consensus with the third reviewer (D.G.D.). The selection process was documented using a PRISMA flow diagram.

Risk of Bias Assessment

The methodological quality and risk of bias of the included observational studies were critically appraised using the STROBE (Strengthening the Reporting of Observational

Studies in Epidemiology) checklist [13]. This 22-item checklist evaluates the reporting of key elements in observational research, including the title, abstract, introduction, methods, results, and discussion sections. Each study was assessed, and its overall reporting quality was noted to inform the interpretation of findings.

Synthesis of Results

Due to heterogeneity in study designs, CEUS parameters measured and outcome measures reported across the included studies, a quantitative meta-analysis was deemed inappropriate. Instead, a narrative synthesis approach was employed. A data extraction table was created to summarize key information from each included study, including: first author, publication year, country of origin, study design, sample size, patient/tumor characteristics, specific CEUS parameters analyzed (e.g., enhancement patterns, time-intensity curve parameters) and the primary diagnostic outcomes (e.g., sensitivity, specificity, accuracy in differentiating tumor types). Findings were thematically synthesized to describe the evidence on the diagnostic performance of CEUS for salivary gland lesions.

RESULTS
Study Selection:

The search yielded 78 records. After screening, eight studies met the inclusion criteria (Figure 1). Excluded studies were irrelevant or did not meet the date/language criteria.

Results of Individual Studies:

All included studies reported CEUS as a useful tool for differentiating benign from malignant salivary gland lesions. Key features included enhancement patterns, margin characteristics, and quantitative perfusion parameters. Detailed findings are summarized in Table 1.
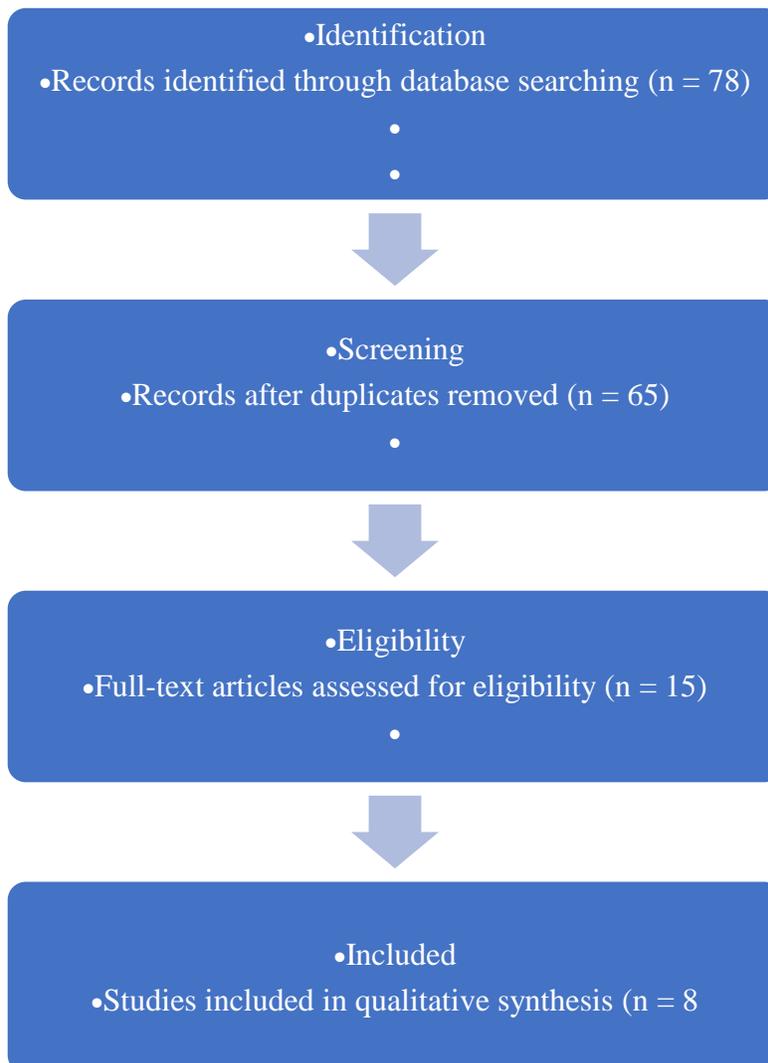
Table 1 — An overview

Author	Title	Journal	Outcome
Karolina Krupa, Patryk Wieczorek, Olga Scrinscaia, Anna Puzio, Zbigniew Kozłowski, Wioletta Pietruszewska and Ludomir Stefańczyk	Correlations between Contrast-Enhanced Ultrasound Imaging and Histopathological Results in Salivary Gland Lesions	Krupa K, Wieczorek P, Scrinscaia O, Puzio A, Kozłowski Z, Pietruszewska W, Stefańczyk L. Correlations between contrast-enhanced ultrasound imaging and histopathological results in salivary gland lesions. Diagnostics. 2022 Oct 31;12(11):2636. doi: 10.3390/diagnostics1211 2636.	Contrast-enhanced ultrasonography is a promising tool for preoperative diagnostics.
Yanqing Wang, Fang Nie, Peihua Wang	Clinical Diagnostic Application of Contrast-Enhanced Ultrasound in Focal Lesions of the Salivary Glands	Wang Y, Nie F, Wang P. Clinical Diagnostic Application of Contrast-Enhanced Ultrasound in Focal Lesions of the Salivary Glands. Journal of Ultrasound in Medicine. 2022 Oct;41(10):2535-46. doi: 10.1002/jum.15943.	CEUS has important clinical value in distinguishing benign and malignant salivary glands
Liuhong Shi, Dingting Wu, Xu Yang, Caoxin Yan, Pintong Huang	Contrast-Enhanced Ultrasound and Strain Elastography for Differentiating Benign	Shi L, Wu D, Yang X, Yan C, Huang P. Contrast-Enhanced ultrasound and strain elastography for differentiating benign and malignant Parotid	CEUS is valuable for distinguishing MPT from BPT

	and Malignant Parotid Tumors	tumors. Ultraschall in der Medizin-European Journal of Ultrasound. 2023 Aug;44(04):419-27. doi: 10.1055/a-1866-4633	
Marta Rogalska, Lukasz Antkowiak, Anna Kasperczuk, Wojciech Scierski	Contrast-Enhanced Ultrasound in the Differentiation between the Most Common Benign Parotid Gland Tumors: A Systematic Review and Meta-Analysis	Rogalska M, Antkowiak L, Kasperczuk A, Scierski W. Contrast-enhanced ultrasound in the differentiation between the most common benign parotid gland tumors: a systematic review and meta-analysis. Journal of Clinical Medicine. 2022 Dec 12;11(24):7360. doi: 10.3390/jcm11247360	CEUS measurements have a greater potential to distinguish PAs from WTs
Salahaden R Sultan, Mohammed AlKharaiji, Shahad H Rajab	Diagnosis of parotid gland tumours with Contrast-Enhanced Ultrasound: a systematic review and meta-analysis	Sultan SR, AlKharaiji M, Rajab SH. Diagnosis of parotid gland tumours with Contrast-Enhanced Ultrasound: a systematic review and meta-analysis. Medical Ultrasonography. 2022 May 25;24(2):211-8. Doi: 10.11152/mu-3119.	CEUS is promising in differentiating benign parotid tumours from malignancies.
M.T. Fontanilla Echevestea, T. Ripollés González, E. Aguirre Pascual	Contrast-enhanced ultrasound fundamentals: the pharmacodynamics and pharmacokinetics of contrast. Basics of contrast-enhanced ultrasound imaging	Echeveste MF, González TR, Pascual EA. Contrast-enhanced ultrasound fundamentals: the pharmacodynamics and pharmacokinetics of contrast. Basics of contrast-enhanced ultrasound imaging. Radiología (English Edition). 2024 Oct 1;66:S36-50. doi: 10.1016/j.rxeng.2024. 10.003.	contrast-enhanced ultrasound, the different ways to optimise the image
Daisuke Saito, Kiyoto Shiga, Katsunori Katagiri, Shin-ichi Oikawa, Aya Ikeda, Kodai Tsuchida, Jun Miyaguchi, Takahiro Kusaka, Hidekatsu Kuroda, Fumiaki Takahashi	Contrast-enhanced ultrasonography for the differential diagnosis of pleomorphic adenomas and Warthin tumors in salivary glands	Saito D, Shiga K, Katagiri K, Oikawa SI, Ikeda A, Tsuchida K, Miyaguchi J, Kusaka T, Kuroda H, Takahashi F. Contrast-enhanced ultrasonography for the differential diagnosis of pleomorphic adenomas and Warthin tumors in salivary glands. Laryngoscope investigative otolaryngology. 2021 Jun;6(3):425-31. doi: 10.1002/lio2.565	CEUS is helpful for the differential diagnosis of pleomorphic adenomas and Warthin tumors.

Hong Chen, Xinyu Bao, Long Wan	Application of Contrast-Enhanced Ultrasound Combined with Elastic Imaging Technology in Differential Diagnosis of Salivary Gland Tumors	Chen H, Bao X, Wan L. [Retracted] Application of Contrast-Enhanced Ultrasound Combined with Elastic Imaging Technology in Differential Diagnosis of Salivary Gland Tumors. Journal of Healthcare Engineering. 2022;2022(1):4600751. doi: 10.1155/2022/4600751	Contrast-enhanced ultrasound has advantages in differentiating benign and malignant enlarged lymph nodes.

- Identification
- Records identified through database searching (n = 78)
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  -

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- Screening
- Records after duplicates removed (n = 65)
  -

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- Eligibility
- Full-text articles assessed for eligibility (n = 15)
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↓

- Included
- Studies included in qualitative synthesis (n = 8

DISCUSSION

Salivary gland tumors account for approximately 3% of head and neck tumors.[1] About 80% of salivary gland tumors are in the parotid gland and less frequently in the submandibular, sublingual, and minor salivary glands.[2]

Benign tumors account for more than 80% of these tumors, with pleomorphic adenomas (PAs) being the most common. The common malignant tumors are mucoepidermoid carcinoma and adenoid cystic carcinoma.[3]

Currently, surgery is often used to treat salivary gland tumors, but the surgical approach often varies between different types of tumors.[4]

The preoperative differential diagnosis of benign and malignant salivary gland lesions is of great importance in selecting the surgical approach and improving the quality of life of patients after surgery.[5]

Imaging is often used for the preoperative diagnostic evaluation of salivary gland tumors. Common imaging methods include ultrasound, computed tomography, magnetic resonance imaging (MRI), nuclide imaging, and positron emission tomography-computed tomography.[6]

Conventional ultrasound, considered to be the imaging modality of choice for the evaluation of salivary gland tumors, is a safe, non-invasive, economical, and convenient method.[7]

However, it is difficult to determine the benignity or malignancy of the lesion and the histotype of the lesion by the conventional ultrasound indices alone, and the conventional ultrasound signs often overlap and have limited discriminatory ability.[8]

In recent years, contrast-enhanced ultrasound (CEUS), an important ultrasound modality, has played an important role in the differential diagnosis of focal lesions in the liver, thyroid, breast, and other organs [9]

Contrast-enhanced ultrasound (CEUS) is a technique with numerous applications for the study of different disorders, which is both accepted and recommended in clinical and radiological guidelines.[10]

Intravenous ultrasound contrast, solely with intravascular distribution, provides information about blood vessels and enables vascular studies to be performed and the vascularisation of different organs and lesions to be dynamically assessed, improving the sensitivity and specificity of basic ultrasound (B-mode and Doppler) and adding complementary information to other contrast imaging techniques.[11]

Being a portable, real-time, repeatable, and highly enhancement-sensitive examination, CEUS provides reliable diagnoses made quickly, in any location, without having to move patients (ICU, intraoperative ultrasound).[12]

Ultrasound contrast agents - First-generation

First-generation ultrasound contrast agents contained microbubbles of air dissolved in blood when exposed to acoustic pressure in the ultrasound field. First-generation contrast agents were therefore present in the bloodstream for a limited time. Examples include: Levovist (Bayer AG). .[13]

Second-generation - Second-generation contrast agents include microbubbles of perfluorocarbon, nitrogen gas, or sulfur hexafluoride stabilized in a phospholipid membrane.[14]

The bubbles oscillate when exposed to the ultrasound beam (they are being compressed by the effect of positive pressure created by the ultrasound waves, and they expand in the negative pressure phase).[15]

The compression of the gas is greater than the expansion, which creates a non-linear response (echo). This greatly affects ultrasound backscatter and increases vascular contrast similarly to intravenous contrast media used in CT and MRI.[16]

Examples of ultrasound contrast agents (brand names) available commercially:[17]

- Definity/Luminity (Lantheus Medical Imaging)
- Optison (GE Healthcare)
- Sonazoid (GE Healthcare)
- Lumason/SonoVue (Bracco)

SonoVue is a purely intravascular (blood pool) contrast agent; therefore, it allows assessment of the vascularity and non-specific contrast agent retention of lesions. Due to its widespread approval, it is by far the most utilized ultrasound contrast agent. [18]

The ultrasound contrast used in Spain for non-cardiological purposes is sulphur hexafluoride (SF6), marketed under the name SonoVue. It is an inert gas, slightly soluble in blood and water in the form of microbubbles and surrounded by a lipid membrane.[19]

Each SonoVue package contains a 25 mg vial of freeze-dried powder containing the active ingredient and the other components of the molecule, and 5 ml of sterile 0.9% saline solution pre-filled in a syringe for injection into the vial.[20]

The contrast is reconstituted by mixing the saline solution with the powder and shaking vigorously for 20 seconds to

obtain a milky-looking microbubble suspension. Once reconstituted, it is chemically and physically stable for six hours, but must be shaken for 20 seconds before each administration.[21]

Intravenous is the most common application. The reconstituted and pre-shaken contrast is administered as a bolus through a peripheral line with a ≤20 Gauge lumen or through a central line, pushed by a 5 - 10 ml bolus of normal saline solution.[22]

Intracavitary route - The contrast can be administered in physiological or nonphysiological cavities, mixing it with normal saline or water.[23]

The dose of contrast and the amount of saline or water to be administered depend on the volume of the cavity to be examined. As the volume of any cavity is less than the volume of the entire blood flow, the dose to be administered is lower than for intravascular use [24]

Contrast-enhanced ultrasound imaging is based on the microbubbles being subjected to a sound field and oscillating through their elastic membrane.[25]

The oscillation, which is not linear, causes emission of harmonic signals, which are used to obtain the CEUS image.[26]

To obtain the image, specific programs are used that allow resonance of the bubble without breaking it: they are preset to a low mechanical index (MI) for the incident sound beam, a parameter that is related to the acoustic power.[27]

The scan is performed in real time, and the dynamics of the enhancement are seen throughout the duration of the microbubbles (3−5 min). This allows CEUS to detect enhancements in the early arterial phase, which may go unnoticed on CT or MRI.[28]

Ultrasound imaging has also started to benefit from the use of contrast agents that take the form of microbubbles. Microbubbles are bubbles of gas that are smaller than red blood cells.[29]

Microbubbles are changing the perception and utilization of ultrasound today. They enable a greater range of diagnostic applications as well as extend the use of ultrasound to therapeutics [30]

The unique acoustic properties of the microbubbles enable them to produce high-frequency echoes (harmonics) that can be used to enhance the ultrasound images and aid in therapeutic endeavors [31]

They observed during an echocardiographic examination that agitated saline injection into the ≤left ventricle of the heart produced strong echoes in the aorta.[32]

The agitated saline solution had air bubbles that changed the ultrasound image being produced. However, the natural solubility (instability) and size of the gas bubbles limited their use as a contrast agent for the heart.[33]

Since then, other types of microbubbles have been found with desirable properties for ultrasonography. Microbubbles have been improved to increase the time they last in the blood.[34]

The two major enhancements made to microbubbles are: (i) encapsulating the bubbles in a thin film to prevent the gas or air from dissolving in the blood, and (ii) using gases other than air that take longer to escape the protective film.[35]

In 1984, the first stable encapsulated microbubble was produced from human serum albumin insonation. It had the benefit that it could cross the pulmonary capillary network, as its size was comparable to that of red blood cells (RBC). .[36]

These microbubbles (2-6mm in diameter) are dense, hydrophobic gases encapsulated by a shell composed of galactose, albumin, lipid, or polymers.[37]

A higher density of gases like perfluorocarbons and sulfur hexafluoride makes them last longer in circulation because of their slow diffusion across the capsule membrane and less solubility in the blood, thus increasing microbubble stability over a longer period.[38]

The choice of size for clinical microbubbles is determined by the diameter of the pulmonary capillaries.[39]

In practice, this means that they must be smaller than 7 mm in diameter. Both the gas they contain and the stabilising shell are critical to their effectiveness as contrast agents [40]

The first widely used agent, Albunex, had an albumen shell and contained air; it was mainly used in cardiology. Levovis, the first agent for general use, is made of galactose microcrystals whose surfaces provide nidation sites on which air bubbles form when they are suspended in water.[41]

A family of perfluoro gas-containing agents, such as SonoVue and perflutren, that use phospholipids as the membrane is the most important in clinical practice.[42]

The change in density at the surface of a bubble in plasma represents a major impedance mismatch, and the echogenicity this produces is exploited in the uses of microbubbles to improve Doppler studies, so-called "Doppler rescue". .[43]

The increase in the signals from blood is obvious and useful for Doppler, but is not visible on conventional grey-scale imaging because the microbubble concentration is too low.[44]

They vibrate most readily at a particular frequency, their resonance frequency. For microbubbles less than 7 μm in

diameter, this corresponds to the frequencies used in diagnostic ultrasound (2–10 MHz). .[45]

With low acoustic powers, symmetrical oscillations occur, and the frequency of the scattered signals is the same as the transmitted pulse.[46]

This response is said to be "non-linear," and the returning signals contain multiples of the insonating frequency [47]

At still higher powers, the microbubbles are disrupted and dissolved. Harmonics may be used to image US contrast agents by passing the signals through a low-pass filter that removes the fundamental signals.[48]

However, tissues also produce harmonics, especially when higher acoustic powers are used, and distinguishing between them is challenging [49]

Modified colour Doppler software has been developed to optimise the display with an emphasis on improving spatial resolution. Known as stimulated acoustic emission (SAE), it is particularly successful in the late phase using contrast agents that selectively accumulate in the liver and spleen [50]

The phase inversion mode (PIM) was a key development in that it uses wide-band pulses and thus retains the spatial resolution of conventional imaging. The returning echoes are summed, thus cancelling the linear echoes because they are out of phase, leaving only the non-linear signals to form the image.[51]

CEUS examination - Perform a standard detailed examination of the target structure of interest and surrounding anatomy using conventional ultrasound imaging tools (B-mode, colour/power Doppler, spectral Doppler, 3D). .[52]

Identify the most favourable acoustic window considering anatomical and acoustic features, including target depth, characteristics of overlying tissues, and the presence of artifacts [53]

The advantage of ultrasound over CT and MRI is the ability to continuously observe the contrast behaviour rather than recording snapshots at specific time intervals that may not accurately represent the physiology of the patient.[54]

It is recommended that the CEUS examination be observed in real-time without the interruption and distraction of freezing, labelling, measuring, and recording still images. Representative video clips, still images, and measurements can be post-processed and stored after the examination [55]

POTENTIAL USE

Sentinel lymph node (SLN) detection - Lymphosonography, or CEUS-guided SLN detection, as a technique for demonstrating lymphatic drainage, has been introduced in some experimental studies [56]

In this procedure, transcutaneous injection of a UCA is performed, and CEUS is used to identify draining lymphatic channels and SLNs. This use of CEUS is technically feasible, as was demonstrated by various studies.[57]

Drug or gene delivery - The microbubble contrast agent interacts with the acoustic wave in the acoustic field. The contrast agent itself will serve as a cavitation nucleus and lower the threshold level for cavitation [58]

Molecular imaging - Techniques for non-invasive imaging of specific disease-related molecular changes are being developed to enhance diagnosis and therapeutic decision-making. [59]

Molecular imaging with CEUS relies on the detection of the acoustic signal produced by microbubble or nanoparticle agents that are targeted to the sites of disease.[60]

The potential use of CEUS-based molecular imaging in atherosclerosis, post-ischemic inflammation, angiogenesis, transplant rejection, and thrombus formation has been investigated and is undoubtedly an important development trend [61]

TABLE 2: Advantages of CEUS [62]

Safety: ✓ No ionising radiation, ✓ Not nephrotoxic ✓ Can be performed in a patient with compromised renal function ✓ Extremely low contrast allergy risk ✓ No need to check liver or renal function tests before imaging	Diagnostic confidence: ✓ Characterises pathologies indeterminate on conventional US ✓ Identifies pathologies undetectable on conventional US ✓ Characterises pathologies indeterminate on CT and MRI ✓ Unlimited opportunity to follow up
Real-time: ✓ Real-time, dynamic, continuous observation ✓ Avoids discontinuous jumping from phase to phase, unlike CT and MRI ✓ Patient movement does not affect imaging ✓ Allows instant cavitation of microspheres and repeated observation	Cost effectiveness: ✓ Significantly cheaper than CT or MRI ✓ Cheaper than repeating a conventional ultrasound Superior Resolution: ✓ Higher spatial resolution than CT or MRI ✓ Allows characterisation of lesions that are too small for CT or MRI
Patient Friendly: ✓ Suitable for a variety of patients: ✓ Renal impairment ✓ Past CT contrast allergy ✓ Claustrophobia ✓ Unable to lie still (Parkinsonian, neurological problems) ✓ Unable to lie flat ✓ On ventilator	Excellent Guidance Modality: ✓ Guides interventional procedures such as biopsy, radiofrequency, microwave, or chemical ablation ✓ Identifies lesions that are isoechoic on B-mode ✓ Can be combined with fusion imaging

About parotid tumors, pleomorphic adenoma (PA) and Warthin tumor (WT) comprise the vast majority (83–93%) of all benign tumors. Malignant lesions are relatively rare and have a variety of histopathological subtypes.[63]

Previous studies have shown that sono-elastography and CEUS could provide useful and progressive information for accurate diagnosis between tumors in many organs, including the thyroid, breast, and parotid. Sonoelastography is an innovative diagnostic tool for assessing tissue elasticity and stiffness [64]

Known data on the value of sonoelastography in diagnosing malignant parotid tumors showed a wide range in sensitivity (38–100%) and specificity (26–97%). A meta-analysis revealed a low pooled sensitivity and specificity for differentiating benign and malignant parotid lesions.[65]

CEUS represents another relatively new, promising ultrasound technique for the head and neck to describe the microvascularity of lesions. Numerous studies have reported that CEUS can differentiate between benign and malignant lesions.[66]

Previous studies also revealed that heterogeneous enhancement indicated the presence of malignant lesions. This may be due to the inclusion of a relatively small number of malignant lesions and all types of malignant lesions in previous studies.[67]

In addition, overlap characteristics in benign and malignant lesions have been found in the use of SE and CEUS alone. Some studies have shown that combining sonoelastography and CEUS improved the diagnostic efficacy of malignant lesions in multiple organs.[68]

However, the diagnostic power of SE plus CEUS has not been assessed in the parotid. In the present study, SE combined with CEUS significantly increased the sensitivity of malignant lesions, and the specificity did not significantly decrease.[69]

Limitations - Contrast-enhanced ultrasound imaging has the limitations of any ultrasound: window and depth limitations (especially in the case of hepatic steatosis). .[70]

It also has a size limitation: it depends on the probe, the organ, and the conditions, but, in general, lesions smaller than 3−5 mm are not detected, and characterising lesions

smaller than 8 mm can be difficult, even if they are detected.[71]

Another limitation is the multiplicity of lesions, as it is very difficult to study all the lesions in all phases if they are not in the same plane, such that the advantage of the temporal resolution of CEUS compared to CT and MRI, being a real-time examination and seeing all phases, has the disadvantage of limited spatial resolution [72]

Authors reporting that in benign tumours parotid gland demonstrated with clear delineation, lack of cervical lymphadenopathy, homogeneous vascularity, and homogeneous distribution of the circulatory bed, whereas malignancy is demonstrated with unclear delineation of the gland, the presence of large cervical lymphadenopathy, inhomogeneous vascularization, and uneven distribution of the circulatory bed [73]

However, overlap characteristics in benign and malignant tumors have been reported in which both types demonstrated hypervascularity with homogenous and inhomogeneous contrast enhancement [74]

This suggests that values of CEUS parameters in benign tumours differ depending on their type, which affects the overall outcome of comparison between benign and malignant tumors [75]

CONCLUSION

The CEUS enhancement of the salivary gland masses revealed several unique features that could provide useful diagnostic data. However, further research and experience are required for the qualitative diagnosis of salivary gland masses. Diagnostic accuracy can be significantly increased in clinical practice when CEUS is used in conjunction with the case history and traditional ultrasound examination. CEUS is a diagnostic process that can be crucial to follow-up imaging as well as the planning, execution, and monitoring of therapies. As a result, this method has many potential clinical applications in everyday practice. The overall benefits of CEUS imaging are combined with the potential for integrated access to data from additive CT or MRI for follow-up, treatment, and detection through CEUS and image fusion.

Acknowledgments

List of Abbreviations

CEUS – Contrast-Enhanced Ultrasound
PA – Pleomorphic Adenoma
WT – Warthin Tumor
MPT – Malignant Parotid Tumor
BPT – Benign Parotid Tumor
US – Ultrasound
STROBE – Strengthening the Reporting of Observational Studies

Source of Funding

Conflict of Interest

The authors declare no conflict of interest.

Availability of Data

Data supporting this review are available within the included articles.

Author Contributions

Dr. D. G. Dharanidharan: Conceptualization, Writing – Review & Editing.
Dr. Karthik Shunmugavelu: Methodology, Formal Analysis, Writing – Original Draft.
Dr. Evangeline Cynthia Dhinakaran: Data Curation, Validation, Writing – Review & Editing.

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