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Advances in Ophthalmic Ultrasonography and Emerging Multimodal Imaging Technologies in the Lacrimal Gland

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ABSTRACT

Conventional ophthalmic ultrasonography is a cornerstone in ocular diagnostics, providing essential structural and functional insights into the eye and orbit. Traditional techniques such as brightness mode (B-mode) and amplitude mode (A-mode) imaging have enabled clinicians to evaluate ocular and orbital morphology and characterize diverse pathological entities. However, the inherently two-dimensional (2D) nature of these techniques limits spatial comprehension in a fundamentally three-dimensional (3D) anatomic environment. This limitation often results in partial data interpretation and potential diagnostic inaccuracies. Recent advancements—including 3D ultrasound reconstruction, photoacoustic tomography, contrast-enhanced ultrasonography, and thermo-imaging—have revolutionized the visualization of ocular structures. These innovations promise enhanced spatial resolution, quantitative vascular assessment, and improved detection of subtle pathological changes, thereby defining a new era in ophthalmic and orbital imaging.

INTRODUCTION

Ultrasonography remains one of the most accessible, safe, and versatile tools in ophthalmic diagnostics. The technique relies on high-frequency sound waves to generate real-time images of the ocular and orbital structures, facilitating the evaluation of lesions, hemorrhages, retinal detachment, and neoplasms. Despite the increasing adoption of MRI and CT in complex cases, ultrasound continues to be the primary modality for dynamic and bedside ocular assessment.

B-mode imaging provides topographic details of ocular and orbital lesions by displaying cross-sectional structural information, while A-mode imaging measures variations in echo amplitude to determine tissue interfaces and lesion density. Furthermore, color Doppler ultrasonography extends this diagnostic armamentarium by assessing ocular hemodynamics, offering real-time visualization of blood flow within the retinal, choroidal, and orbital vasculature.

Limitations of Conventional 2D Ultrasonography

Ophthalmic and orbital anatomy are inherently three-dimensional; however, conventional ultrasound presents data in 2D planes—axial, transverse, or longitudinal. Interpreting this data requires the clinician to mentally reconstruct 3D spatial relationships, which can be both cognitively demanding and prone to interpretive error. Even highly trained examiners may lose diagnostic details when correlating multiple 2D slices.

Challenges become particularly significant in the following scenarios:

- Scans acquired by technicians with limited ocular specialization.
- Static review of selected 2D images without dynamic sweep data.

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- Lesions with diffuse or poorly demarcated borders that blend with surrounding tissue.
- Difficulty reproducing the same imaging plane during follow-up assessments.

Consequently, some clinically relevant out-of-plane features remain undocumented or misinterpreted, leading to variability in diagnosis and treatment planning.

Transition to 3D and Advanced Ultrasound Modalities

The evolution from 2D to 3D ophthalmic ultrasound has addressed many of these diagnostic challenges. Volumetric acquisition allows the reconstruction of complete orbital datasets, enabling multiplanar reformatting and 3D visualization of complex pathologies. This approach enhances the reproducibility of measurements and facilitates longitudinal comparisons.

Other emerging modifications include:

- Speckle reduction and beamforming optimization, improving contrast resolution.
- Elastography, which assesses tissue stiffness to differentiate between benign and malignant masses.
- Contrast-enhanced ultrasonography, using microbubbles to map microvascular perfusion in orbital tumors or inflammatory lesions.

These techniques combine structural and functional information, supporting more precise diagnostic stratification and monitoring of therapeutic responses.

Photoacoustic Tomography and Thermo-Imaging

Photoacoustic tomography (PAT) and thermographic imaging represent transformative innovations in non-invasive ocular imaging. PAT integrates optical excitation with ultrasonic detection, generating images based on the differential absorption of pulsed laser light by endogenous chromophores such as hemoglobin and melanin. This hybrid method provides high-resolution vascular and biochemical information without the need for exogenous contrast agents. PAT has shown particular promise in:

- Mapping retinal and choroidal microvasculature.
- Characterizing intraocular tumors based on optical absorption spectra.
- Monitoring oxygen saturation dynamics in diabetic retinopathy and retinal ischemia.

Thermo-imaging, or thermal infrared imaging, complements ultrasound and PAT by capturing minute temperature differentials across ocular tissues. Pathologic processes such as inflammation, neovascularization, and tumor metabolism often produce localized hyperthermic zones, which can serve as early diagnostic markers when fused with ultrasound datasets.

Integration of Multimodal Imaging and AI

Integration of AI and multimodal analytics into ophthalmic ultrasonography represents the next frontier. Machine learning algorithms can automate segmentation of orbital structures, identify subtle pathologic signatures, and perform predictive modeling based on combined echogenic, photoacoustic, and thermographic data. Deep learning models trained on large image repositories may enable real-time lesion characterization and facilitate point-of-care diagnostic decision-making.

Such systems could ultimately transform ophthalmic imaging into a quantitative, data-driven discipline capable of continuous learning and adaptive performance in clinical workflows.

Keywords: Orbital 3D ultrasonography; Lacrimal gland; Thyroid-associated ophthalmopathy.

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INTRODUCTION

The lacrimal glands (LGs) are paired, almond-shaped structures located at the upper-outer portions of orbits, adjacent to the lateral and superior rectus muscles [1]. The LG is a target tissue, especially in autoimmune and granulomatous diseases. Changes in LG size may be helpful in the diagnosis of these atypical and difficultly identified pathologies [2,3]. Imaging may enable early diagnosis and treatment of the mentioned pathologies [4]. Previous studies stated that LG dimensions and volumes may change with age, gender, and race [5]. Bukhari et al. calculated LG volumes in both CT and MRI of 36 patients and reported no significant difference in the two modalities [5].

Previous studies in the literature reported different LG sizes between different ethnicities. Tamboli et al. published the first study establishing non-diseased LG dimensions with CT [6]. They calculated LG dimensions in Caucasian patients with normal LGs. Significant difference was observed only in the mean coronal length between the right and left orbits; other dimensions were similar between the two sides. The second study describing non-diseased LG dimensions with CT was published by Lee et al., in a Korean population with normal LGs [11]. They suggested that the axial and coronal widths were slightly larger in the left orbits.

In another study, the axial length, coronal length, and coronal width were similar in both right and left sides, and no statistically significant difference was observed. Statistically significant difference was found only in axial width between right and left orbits ($p=0.03$). The axial length in both orbits in our study was larger than in the previous studies. The other dimensions were variable. The coronal length was longer, and axial and coronal widths were shorter than those observed by Tamboli et al., in a Caucasian population [6]. According to the study of a Korean population, the axial width was equal in the right orbits but smaller in the left [11]. Coronal width was larger and coronal length was shorter on both sides when compared to the study reported by Lee et al [11]. The results of the current study might imply the importance of the national difference in normal values of LG dimensions.

In a previous study, Avetisov et al. calculated LG volume with ultrasound in healthy subjects [12]. The LG volume was reported in a range of 0.66 to 1.0cm3. In the first study to report the LG volume in CT imaging, Bingham et al. calculated the normal LG volumes in a Caucasian population [13]. The LG volume measurement with MRI was also recently published. LG volumes were studied in different ethnicities and found that volume changes significantly according to the ethnical origin. Bingham et al. did not report a significant difference between males and females, similar to the present study results [13]. But Bukhari et al. reported higher gland volume in women [5].

The laterality had no effect in volumetric measurements of LGs in Bingham et al. [13]. However, Bukhari et al. had found right gland volumes to be larger than the left [5].

METHODS:

LG dimensions were calculated with the method described by Tamboli et al., in magnified images [6]. Lacrimal gland length was calculated from the most anterior tip to the most posterior tip of the gland. The width was calculated from the medial to lateral edge at the widest location perpendicular to the length in the same image. In the selected coronal image, the length was calculated from the most-superior tip to the most-inferior tip. The width was calculated perpendicular to the length at the widest location from the medial edge to the lateral edge. The volume of the LG was measured from axial images. The gland was outlined with a free-hand technique by the pencil tool in all consecutive images, including the LG. The volume of the selected area was calculated by the software (Aquariousi Ntuition edition, version 4.6; TeraRecon, San Mateo, CA, USA).

DISCUSSION:

Lacrimal gland lesions generally present as palpable masses in the superolateral aspects of the orbits. Approximately 50% of lacrimal gland masses are inflammatory lesions, 25% are lymphoid lesions or lymphoma, and the other 25% are salivary gland-type tumors. Chronic inflammatory dacryoadenitis may develop in a variety of other entities, including tuberculosis, amyloidosis, thyroid ophthalmopathy, and anti-neutrophil cytoplasmic

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antibody–associated granulomatous vasculitis (formerly known as Wegener granulomatosis). Involvement in these conditions may be unilateral or bilateral, and treatment is targeted to the underlying disease. (15)

Although there are overlaps and exceptions, features such as laterality, portion of gland involvement, presence or absence of bony findings, enhancement pattern, and clinical presentation are valuable in differentiating among lacrimal gland lesions (Table 1).

Both magnetic resonance imaging (MRI) and CT can be used effectively for the detection of LG pathologies [3,8-10]. It is important to reveal the anatomic characteristics of LGs because many pathologies, such as sarcoidosis, Sjögren disease, thyroid ophthalmopathy, benign and malignant tumors, manifest with changes in LG sizes [3,9,10]. Apart from the evaluation of the gland, particularly, knowing the gland size and imaging characteristics is also important since LG might fall into the head and neck radiologic examination.

Obata showed that lacrimal gland atrophy and fibrosis correlated with increasing age [14]. Studies both performed with MRI and CT reported a decrease in the lacrimal gland sizes with increasing age [5,6,13]. Also, there was a negative correlation between age and gland dimensions and volume. A decrease in LG volume was correlated with all axial and coronal dimensions.

In another study, the mean volume of the lacrimal gland in TAO patients was 0.816 cm^3 in the right orbit (standard deviation [SD], 0.048) and 0.811 cm^3 in the left orbit (SD, 0.051), with no significant difference between right and left ($p = 0.192$). However, significant differences were observed between TAO patients and healthy individuals ($p < 0.001$). There was no significant difference between mean lacrimal gland volumes of males (0.812 cm^3; SD, 0.037) and females (0.816 cm^3; SD, 0.029) ($p = 0.513$). There was a negative correlation between gland volume and age in TAO patients (Pearson r = -0.479, $p = 0.00$).[16]

In a similar study, the mean volume of the lacrimal gland in patients with TED was 0.890 cm in right orbits (standard deviation [SD] 0.348), 0.851 cm in left orbits (SD 0.350), with no significant difference between right and left (p = 0.311). The mean volume was 0.811 cm in right male orbits (SD 0.386) and 0.911 cm in right female orbits (SD 0.335), with no significant difference between men and women (p = 0.774). These findings were confirmed in an analysis of left orbits. The volume of right and left orbits correlated well (r = 0.777, p < 0.0001). The lacrimal gland volume in patients with TED was greater compared with the normal population using a 2-sample t-test (p < 0.0001). Exophthalmometry (right: r = 0.225, p = 0.0115; left: r = 0.267, p = 0.0026) and subjective tearing (right: r = 0.226, p = 0.0138; left: r = 0.197, p = 0.0322) correlated with lacrimal gland volume.[17]

TABLE 1: Common Patterns of Lacrimal Gland Masses

Cell Type	Lesion	Laterality	Lobe Involved	Bone	Pain
Epithelial	Pleomorphic adenoma	Unilateral	Orbital	Scalloping	No
	Adenoid cystic carcinoma	Unilateral	Orbital	Destruction	Yes, with or without paresthesia
	Mucoepidermoid carcinoma	Unilateral	Orbital	Scalloping, destruction	Yes
Lymphoid	Lymphoid hyperplasia	Bilateral	Orbital and palpebral	None, with or without occasional remodeling	No
	Lymphoma	Variable	Orbital and palpebral	None, with or without occasional remodeling	No
Leukemic	Chloroma	Variable	Orbital and palpebral	Variable	Yes
Metastasis	Metastases	Variable	Variable	Variable	Variable
Inflammatory	Infectious dacryoadenitis	Unilateral	Orbital and palpebral	None	Yes
	Sarcoidosis	Bilateral	Orbital and palpebral	None	Yes
	Pseudotumor (inflammatory dacryoadenitis)	Variable, unilateral more than bilateral	Orbital and palpebral	None	Variable
	Sjögren syndrome	Bilateral	Orbital and palpebral	None	Yes (dryness)
Others	Sickle cell disease	Variable	Orbital and palpebral	None	Yes

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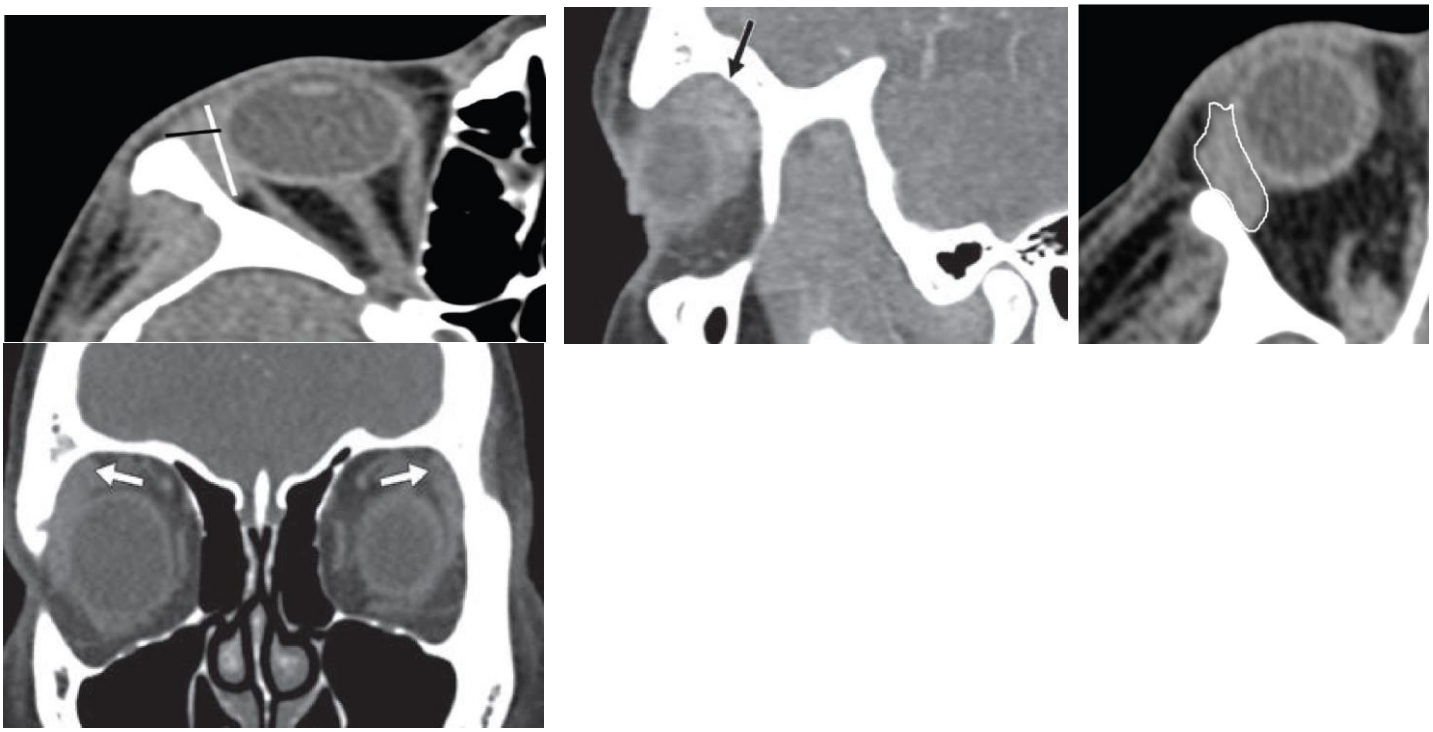
CONCLUSIONS

This study is the first to report the characteristics of the lacrimal gland on ultrasound 3D for patients with TED. The 3D ultrasound has been used to define lacrimal gland shape, size, density, structural features, and the pattern of blood supply, as well as the anatomic and topographic position in the orbit. The study was conducted in the

B-mode and 3D modes of ultrasonography with color and energy Doppler mapping on both sides. The lacrimal gland is larger in patients with TED and correlates with subjective clinical activity of the disease.

Figure 1: The White line represents the axial length, and the black line represents the axial width in the axial CT image. The lacrimal gland was outlined with the pencil tool in the axial image.



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