

# Facial Ultrasonography in acquired facial lipoatrophy

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**Abstract:** Facial lipoatrophy refers to the loss of adipose tissue and is manifested by flattening or indentation of the convex contours of the face while lipodystrophy is a wider term associated with abnormalities of fat tissue distribution and its metabolism, leading to excessive loss and/or accumulation of adipocytes.

Although the management of facial lipoatrophy is very important for a patient's social life and mental health, no treatment framework has been developed due to the unknown nature of the disease manifestation. Early recognition and treatment of the active stage of connective tissue diseases is of essential significance in prevention of subsequent scarring and atrophic lesions. Diagnostic techniques such as computed tomography (CT), magnetic resonance imaging (MRI) and ultrasonography (USG), are used to measure the severity of the lipoatrophy.

The present study was designed to provide sequential imaging to visualize the disease progression.

**Keywords:** face lipoatrophy, facial ultrasonography, connective tissue diseases, lupus erythematosus profundus, morphea, scleroderma.

## I. INTRODUCTION

Ultrasonography generates sound waves at frequencies beyond the limit of human hearing abilities through electrical stimulation of the customized crystal or chip mounted on the tip of the oscillatory probe. These sound waves propagate through tissues and endure partial reflection back to their starting point when the wave passes through layers of various resistance. When the wavefront returns to the transducer located in the ultrasound probe, it generates electrical energy where it is amplified and converted to a positive sine wave which is displayed as an image. (1)

Time gain compensation (TGC) is a setting applied in diagnostic ultrasound imaging to account for tissue attenuation. By increasing the received signal intensity with depth, the artifacts in the uniformity of a B-mode image intensity are reduced. The purpose of TGC is to normalize the signal amplitude with time, compensating for depth. (1)

Lipodystrophy broadly refers to a disturbance in the production, utilization, and storage of fat. These changes are subdivided into lipoatrophy and hyper adiposity. Facial lipoatrophy can be a feature of the normal ageing process. It may also be a manifestation of chronic disorders, frequently affecting HIV-infected individuals treated with highly active

antiretroviral therapy (HAART) and may occur as a complication of connective tissue diseases like lupus erythematosus profundus and scleroderma. Lupus erythematosus is a systemic disease that causes inflammatory loss of subcutaneous adipose tissue, known as panniculitis. Localized scleroderma also involves panniculitis, although it is initially characterized by an erythematous patch.

Progressive facial hemi atrophy, which is known as Parry-Romberg syndrome, is a neurocutaneous syndrome involving the progressive loss of the subcutaneous adipose tissue in the facial region innervated by the fifth cranial nerve.

Iatrogenic causes of lipoatrophy include complications of injected medications like insulin, corticosteroids, antibiotics (Penicillin G), iron, heparin, and vaccines. HIV-positive patients on anti-retroviral therapy, especially, nucleoside reverse transcriptase inhibitors (NRTs) and protease inhibitors (PI) manifest lipoatrophy as an adverse drug effect.

The lipoatrophy most frequently affects the subcutaneous fat layer causing abnormal indentation and asymmetry of the face. According to the anatomical localization, it can be classified as generalized, partial or localized. (2)

Acquired lipoatrophy is an uncommon disease that may affect people in all age groups as a result of repeated trauma, pressure, drug injections including cosmetic fillers or as a consequence of some chronic diseases. Physiological facial lipoatrophy is associated with a normal course of ageing. People with facial lipoatrophy may experience low self-esteem, depression, and social isolation. (2)

## II. DISCUSSION

Imaging studies are commonly used to determine the specific location of the disease within anatomic structures involved, degree of inflammation, the shape of infiltrated tissues, and involvement of sinuses, nasal passages, and intracranial structures. Radiographic examination of the orbit usually involves computerized tomography scan (CT) and magnetic resonance imaging (MRI) with intravenous contrast and is incredibly useful in narrowing the differential diagnoses and assessing the location and extent of the disease process. Facial ultrasonography (USG) also has a wide range of clinical indications.

Although imaging can help narrow the range of diagnoses to consider, images are only useful in that they reveal patterns and locations of tissue involvement which may statistically be more common in certain disease entities. Imaging is often not

specific enough to verify exact disease entities or obviate a biopsy.

The most common locations of adipose tissue loss in the course of facial lipoatrophy are cheeks, temples and the preauricular, orbital or perioral regions. (Figure 1) With the progress of the disease both bone structures and muscles may be excessively visible, especially the zygomatic arch, orbit, anatomical details of mandible and jaw, zygomaticus major and minor muscles, risorius muscle, levator muscle of the upper lip, orbicularis oculi muscles, masticator muscles and temporal muscles. A 5-degree scale can be applied in clinical practice to establish the degree of lipoatrophy severity. (Table 1) (2)

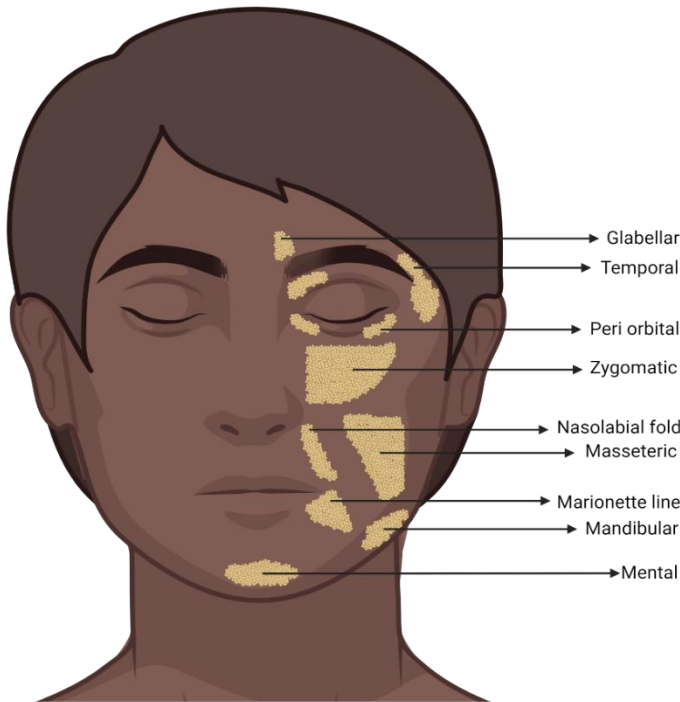
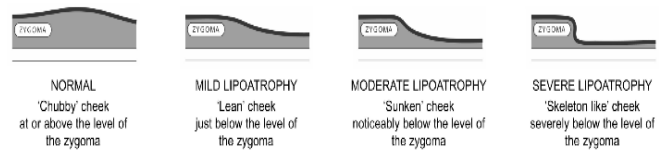


Figure 1. Schematic diagram of facial fat distribution (created with [biorender.com](https://biorender.com))

Table 1: The facial lipoatrophy can be graded as follows:

- Grade 0 — No facial lipoatrophy.
- Grade 1 — Mild flattening or shadowing on one or more facial regions; No prominent bony landmarks and no visibility of the underlying musculature.
- Grade 2 — Intermediate point between Grade 1 and Grade 3.
- Grade 3 — Moderate concavity of one or more facial regions, prominence of bony landmarks, and possible visibility of the underlying musculature.
- Grade 4 — Intermediate point between Grade 3 and Grade 5.
- Grade 5 — Severe depression of one or more facial regions, severe prominence of bony landmarks, and clear visibility of the underlying musculature.



The first degree indicates discrete flattening or indentation of one or more facial regions (cheeks, temple, preauricular, orbital and perioral area), lack of protrusion of bones and invisible facial muscles, whereas the fifth scale degree is linked with excessive indentation of one or more regions of the face with strongly protruding facial bone structures and muscles. (3)

There is no universal or precise proven reason for lipoatrophy; however, literature suggests impairment of adipocyte differentiation, adipocyte apoptosis and mitochondrial dysfunction the heterogeneous pathogenesis, reflecting the different subtypes. (4)

Because the image quality and interpretation usually depend upon the echographer, diagnostic sensitivities conferred within the literature for specific conditions and diagnoses vary considerably. Diagnostic sensitivity is especially high in large trials performed in educational centers or ocular oncology practices that hire trained ultra-sonographers. Recently, researchers have used imaging to spot lesion-based risk factors for prognosis and survival.

Challenges to using imaging are generally associated with the clinician's familiarity with the technique and competence level with image interpretation. Whereas highly-trained, highly-skilled echographers are true specialists with the art of acquiring and decoding pictures, an understanding of the fundamental technique of performing the scan and deciphering its results are still quite helpful in clinical practice.

Subcutaneous fat provides volume and mobility, and is supported by fibrous reticular cutis, which connects the dermis to the muscle aponeurotic system. The subcutaneous layer is critical, because, wasting of subcutaneous fat results in atrophy, whereas its increased thickness leads to lengthening of the reticular fibers and therefore, weakness and distention. Paucity or complete absence of fat in the confined subdermal layer, with lack of inflammatory signs, is known as idiopathic localized involutinal lipoatrophy (ILIL). (5)

According to previous research, significant and rapid fat loss may cause increased tightness, with the skin positioned directly on the facial bone. An individual may feel discomfort due to this abnormal tension of the skin. The parotid gland on the affected side may show inflammatory and atrophic changes as its volume decreases. These inflammatory changes of the duct and gland may be due to stenosis of the main duct caused by facial skin tension. On CT images, the Stensen's duct is thickened and contrast-enhanced which is a sign of sialodochitis and the hilar region appears contrast-enhanced. (6) Lipoatrophy in the extremities presenting with muscle pain

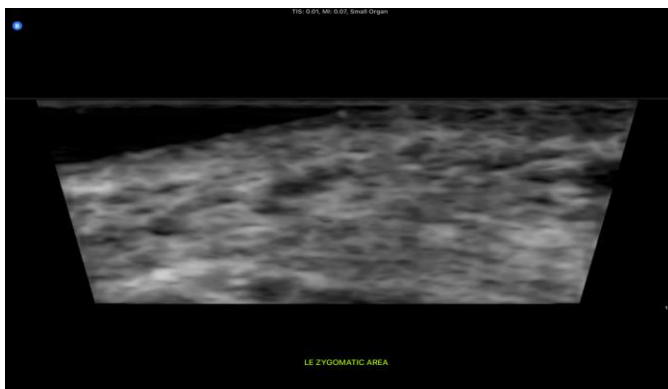
has been reported, but those cases were confirmed to be myositis on MR images. (7) However, the electromyogram and MR images of the patient with facial lipoatrophy may show no specific pathologic findings associated with facial and masticatory muscles.

At 7.5 to 10MHz ultrasound probe, the dermis appears as a thin regular stratum that is more echogenic than subcutaneous fat. The epidermis, even at its thickest, cannot be resolved, and skin ap-ependages, such as hair follicles, cannot be visualized. The inter-face between the echogenic skin and the hypoechoic hypodermis is clearly visible, allowing measurement of dermis thickness. The thickness of the skin measured with 10MHz probe has been reported to range between 1.4 mm at the dorsal aspect of the hand and 4.8 mm at the heel of the foot. Ultrasound assessment of subcutaneous malar and brachial fat inpatients with HIV-associated lipodystrophy has been found to be both sensitive and specific to the diagnosis of abnormal fat distribution.

For example, in a study by Martinez et.al , patients with and with-out HIV-related lipodystrophy, values of malar fat 4 mm were 74% sensitive and 87% specific to the clinical diagnosis of HIV-associated LA. Ultrasonography using 7–10 MHz frequency linear probe revealed a normal superficial skin layer bilaterally in a case report of unilateral facial lipoatrophy. (8)

We have reported a similar case with right sided facial lipoatrophy after injection of Hydroxyapatite cosmetic filler in zygomatic area. Apparently, patient had developed an inflammatory reaction to the filler two days after injection and developed unilateral facial lipoatrophy after local inflammation subsided. The thickness of the subcutaneous plane was 0.18 cm on the right side and 0.28 cm on the left side. Altered echogenicity was noted on the right zygomatic and master muscles. On the affected side, the muscle thickness was 0.63 cm, whereas on the normal side it was 1.18 cm. (Figure 2)

The extra-cranial part of the facial nerve was scanned bilaterally along its longitudinal axis inside the parotid gland using a chip embedded 10 MHz linear array transducer probe (Butterfly IQ+).



(Figure 3)

Figure 2: Ultrasound image reveals normal facial anatomy on the left side and altered echogenicity (Necrotic area) on the right cheek at the subcutaneous and muscular layer.

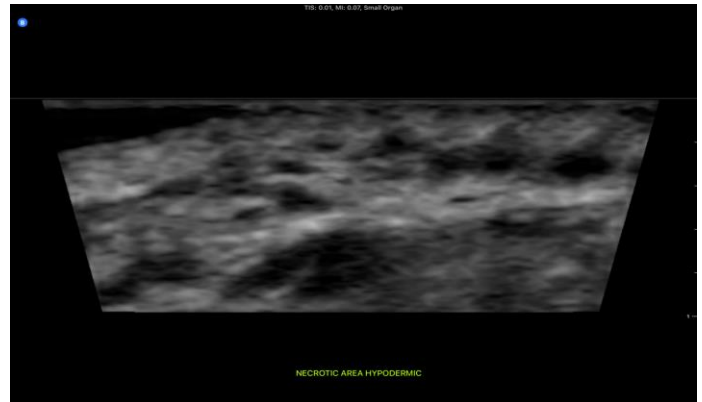


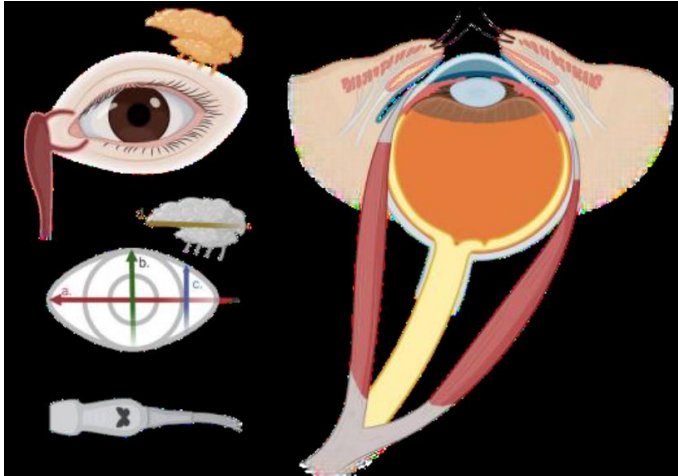
Figure 3: The facial nerve diameter is measured at the thickest part of the nerve immediately inside its hyperechoic border. Measurement calipers are extended to span between the inner borders of the hyperechoic edges of the facial nerve.



Standard operating procedure for Facial ultrasonography(1) : (Figure 4)

- 1) Complete consent and authorization form
- 2) Clean and prepare the site of interest and ultrasound probe
- 3) Apply sterile coupling agents on ultrasound probe headpiece
- 4) Connect the probe to mobile device and launch the app
- 5) Select the appropriate preset to start scanning

- Horizontal linear scan (medial orientation) - adjust depth and  $\Delta$ TGC
- Vertical linear scan (superior orientation) - adjust depth and  $\Delta$ TGC
- Doppler scan - volumetric and  $\Delta$ TGC
- Facial Nerve scan- along its longitudinal axis inside the parotid gland



To improve esthetics, common treatment modalities with evidence of safety and efficacy are using permanent and non-permanent types of fillers. The possibility of severe infection, contour abnormalities and facial nerve and muscle damage restrict the use of permanent type of fillers like silicone oil. Non-permanent fillers, being biodegradable, can diminish over time and may necessitate a revamp, but they do not cause foreign body reactions or granulomas. Injection of a biodegradable and bioabsorbable poly-L- lactic acid (PLA) filler causing cutaneous thickening by fibrous connective tissue formation calls for multiple treatment sessions, high cost and transitory relief, limiting its use for augmentation. Autologous fat transfer (AFT) is a secure and cost-effective option, exclusively for non-HIV patients with lipoatrophy. (9)

### III. CONCLUSION AND FUTURE NEEDS

Facial Ultrasonography plays a useful role in the diagnosis of facial lipoatrophy as fat can be easily appreciated on USG. Ultrasound can demonstrate asymmetry of the face and loss of fat in focal lipoatrophy. (10)

In a time of profound technological advancement in imaging, facial ultrasonography has often been relegated to a niche/ancillary test. With the affordability of available ultrasonography systems, now is the time to take advantage of the many applications of ultrasonography to best serve our patients.

This review adhered to the ethical principles outlined in the Declaration of Helsinki as amended in 2013. (<https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/>).

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### BIBLIOGRAPHY:

- [1] Khazaei H, Khazaei D, Ashraf D, Mikkilineni S, Ng JD. Overview of Orbital Ultrasonography. *Ann Ophthalmol Vis Sci.* 2022; 5(1): 1028.
- [2] Ascher B, Coleman S, Alster T, et al. Full scope of effect of facial lipoatrophy: a framework of disease understanding. *Dermatol Surg.* 2006; 32:1058–69.
- [3] Szczerkowska-Dobosz A, Olszewska B, Lemańska M, Purzycka-Bohdan D, Nowicki R. Acquired facial lipoatrophy: pathogenesis and therapeutic options. *Postepy Dermatol Alergol.* 2015; 32:127–133.
- [4] Giralt M, Domingo P, Villarroya F. Adipose tissue biology and HIVinfection. *Best Pract Res Clin Endocrinol Metab* 2011; 25:487-99.
- [5] Yamamoto T, Yokozeki H, Nishioka K. Localized involutinal lipoatrophy: Report of six cases. *J Dermatol* 2002; 29:638-43.
- [6] Lee C, Kim JE, Yi WJ, Heo MS, Lee SS, Han SS, Choi SC, Huh KH. Acquired facial lipoatrophy: A report of 3 cases with imaging features. *Imaging Sci Dent.* 2020 Sep;50(3):255-260.
- [7] Gdynia HJ, Weydt P, Ernst A, Klein S, Sperfeld AD, Riecker A. Myositis associated with localized lipodystrophy: an unrecognized condition? *Eur J Med Res.* 2009; 14:228–230.
- [8] Anbarasi K, Sathasivasubramanian S, Krithika CL, VenkataSai PM. Focal Lipoatrophy of Face: A Rare Esthetic Complaint. <https://dx.doi.org/10.4103/2156-7514.94229>  
*Journal of Clinical Imaging Science* (<https://clinicalimaging-science.org>)
- [9] Imagawa K, Ohkuma S. A case of fat injection for treating subcutaneous atrophy caused by local administration of corticosteroid. *Tokai J Exp Clin Med* 2010; 35:66-9
- [10] Bonnet E. New and emerging agents in the management of lipodystrophy in HIV-infected patients. *HIV/AIDS* 2010; 2:167-78. 10.