https://www.scirp.org/journal/jbise
J. Biomedical Science and Engineering, 2025, Vol. 18, (No. 10), pp: 401-407

# The Hyperechoic Nodules in Lipedema Are Not All the Same: Description of Criteria and Their Qualitative Patterns

**Thais Oliveira Foureaux, Deise Vargas, Rute Facchini Lellis, Lucas Campos Chagas, Isabela Werneck da Cunha, Paulo Yukio Saiki, Eduardo Augusto Sousa Soares, Gabriela Nogueira Monteiro Bizareli, Alexandre Sacchetti Bezerra, Alexandre Campos Moraes Amato, Anderson Nadiak Bueno**

Ultrasound Department of Rede D'Or Radiology, São Paulo, Brazil

**Correspondence to:** Anderson Nadiak Bueno, andersonnb@hotmail.com
**Keywords:** Lipedema, Ultrasound, Nodules, Classification, Hemorrhage
**Received:** September 15, 2025 **Accepted:** October 26, 2025 **Published:** October 29, 2025



## ABSTRACT

**Lipedema is characterized by symmetrical accumulation of subcutaneous fat in the lower and upper limbs, sparing the trunk, feet and hands. Although diagnosis is primarily clinical, ultrasound has proven to be a valuable, non-invasive, reproducible, and cost-effective tool for the assessment of lipedema. Ultrasound (US) facilitates diagnosis through quantitative evaluation of subcutaneous tissue thickness and enables qualitative Lipedema Dermal and Hypodermal Classification (LDHC), with morphological changes. The presence of hyperechoic nodules in patients with lipedema has been previously described and classified as LDHC 3; recently, a case report analyzing the microscopic features of such nodules demonstrated hemorrhagic areas and steatonecrosis, resulting from disorganized hypodermal expansion leading to increased pressure within the subcutaneous compartment—causing hypoxia and stimulating immature neovascularization (fragile wall, predisposing to hemorrhage). However, these nodules are not uniform and exhibit different morphologies, enabling subclassification. The first type presents with poorly defined margins; the second is well-defined margins; the third has an anechoic area, and the fourth shows a faint posterior shadow. These different nodule presentations in lipedema may be correlated with evolutionary stages or previously described clinical presentations, requiring future correlation with pathological anatomy or other diagnostic methods.**

## 1. INTRODUCTION

Lipedema is a progressive disorder characterized by the accumulation of adipose tissue in the subcutaneous

of the lower and upper limbs, bilaterally and symmetrically, sparing the trunk, hands, and feet; affecting approximately 12.3% of women in Brazil [1, 2]. Its etiology remains uncertain but is primarily associated with genetic factors and hormonal exposure to estrogen [3]. The diagnosis is clinical, based on leg heaviness, pain or tenderness upon palpation, negative Godet's sign for edema, spontaneous hematomas, and difficulty with weight loss despite diet [2, 4, 5].

The two main clinical classifications currently in use are: the first based on the distribution of fat accumulation, and the second on skin and adipose tissue morphology (**Table 1**) [2, 5]. Although clinical classification is widely used, some details revealed through ultrasound (US) make it possible to visualize the pathophysiological and evolutionary mechanisms of the disease.

**Table 1. Progressive functional classification of lipedema based on skin, subcutaneous tissue, and lymphatic involvement.**

| Stage | Skin | Subcutaneous tissue | Lymphatic Involvement |
|---|---|---|---|
| 1 | Smooth | Increased, Nodules | Absent |
| 2 | Irregular | Increased, Nodules | Absent |
| 3 | Skin folds | Increased, Nodules, Fibrosis | Absent |
| 4 | Skin folds | Increased, Nodules, Fibrosis | Present |

Source: Adapted from Herbst, 2012 [5].

The US is increasingly used as an auxiliary tool in diagnosing lipedema, with quantitative measurements of subcutaneous tissue at specific points and cutoff values (**Table 2**) [6]. More recently, a qualitative assessment of dermal and hypodermic alterations called Lipedema Dermal and Hypodermal Classification (LDHC) has been proposed, which may correlate with an inflammatory or fibrotic environment, thus potentially guiding therapy and indicating response to treatments.

**Table 2. Reference values for ultrasonographic diagnosis of lipedema of the lower limbs.**

| Topography | Thickness (mm) |
|---|---|
| Pre-tibial (mid-region) | Greater than 11.7 |
| Anterior thigh (mid-distal) | Greater than 17.9 |
| Lateral leg (mid-proximal) | Greater than 8.4 |
| Medial leg (supramalleolar region) | Greater than 7.0 |

Source: Adapted from Amato *et al.*, 2021 [6].

**Table 3. US Lipedema Dermal and Hypodermal Classification (LDHC).**

| LDHC | Architecture | Hypodermal septa | Echogenic nodules | Dermal-hypodermal junction |
|---|---|---|---|---|
| 1 | Preserved | Linear and thin Less than 50% rupture | Absent | Preserved |
| 2 | Bulging | Irregular and curved ≅50% rupture | Absent | Preserved |
| 3 | Bulging deep Disorganized superficial | Irregular Disruption superficial | Present | Irregular |
| 4 | "Marbled" | Irregular Branching and verticalization | Absent | Irregular ("serrated") |

Source: Adapted from Vargas *et al.*, 2021 [7].

A recent case report selected a female patient with lipedema (ultrasonographic LDHC 3) and painful nodules in the thigh and arm (LDHC 3), who then underwent biopsy and histopathological analysis (**Table 3**). It was demonstrated that the nodule represented a hemorrhagic focus with hemosiderin deposition. Fibrous proliferation, steatonecrosis, newly formed capillaries, granular eosinophilic content, and histiocytic reaction were also demonstrated [8]. This is the first microscopic analysis to confirm hypoxic-ischemic changes, all others had observed only inflammatory and fibrotic reactions [9-11]. In addition to microscopic findings, the Resistance Index (RI) was assessed through Doppler evaluation of subcutaneous arteries, showing increased RI in the lipedema patient compared to the control patient (without lipedema) [8].

The LDHC 3 classification already highlights the echogenic nodule as the ultrasonographic marker of advanced lipedema; however, this finding presents distinct patterns such as margin alterations, different echogenicities, the presence of anechoic areas, and a faint posterior acoustic shadow. These data support the elaboration of a subdivision of the LDHC 3 classification, believing that we may be facing evolutionary phases of the same echographic finding.

## 2. MATERIALS AND METHODS

The study selected 20 patients who were ultrasonographically classified as LDHC 3, characterized by the presence of echogenic nodules and their morphological variations. The mean age of the participants was 41.95 ± 8.39 years. The recruitment took place between January and September 2025. The study was approved by the institutional research ethics committee, and all patients signed the informed consent form.

US images were obtained and classified according to protocol and described by Vargas *et al.* [7], using high-frequency linear transducers (10 to 15 MHz) on Samsung V6 (Samsung Medison Co. Ltd., Republic of Korea, 2024) and LOGIQ e (GE Medical Systems Co. Ltd., China, 2024) in order to assess the reproducibility of the findings across different platforms. The examinations were performed by two radiologists with at least 10 years of experience in musculoskeletal and dermatological ultrasonography. Patients with a diagnosis of lipedema who also presented concomitant obesity were excluded from this analysis.

Our sample included patients with an average BMI of 26.65 ± 1.45, with a focus on a primary diagnosis of lipedema to concentrate on its pathological features and variants. It is important to emphasize that typical dermal and hypodermic structural changes of lipedema can be found in obese individuals, however, obese individuals without lipedema only demonstrate an increase in the subcutaneous layer and do not present the typical findings described by the LDHC classification. Ultrasound showed a relevant role in distinguishing between isolated obesity and lipedema or the coexistence of both conditions.

## 3. RESULTS: FINDINGS AND PROPOSED CLASSIFICATION

A total of 62 nodules were identified by US in subcutaneous tissue, analyzed, and classified according to their characteristics, as shown in **Table 4**. This analysis can enlarge the original proposal of LDHC, which described stage 3 as containing the characteristic echogenic nodules. Subsequently, upon identifying four distinct variants (LDHC 3a, 3b, 3c, and 3d), this detailed subclassification fits within the scope of LDHC 3, allowing for a more refined characterization of the echogenic nodules and providing additional information on potential evolutionary patterns of the disease.

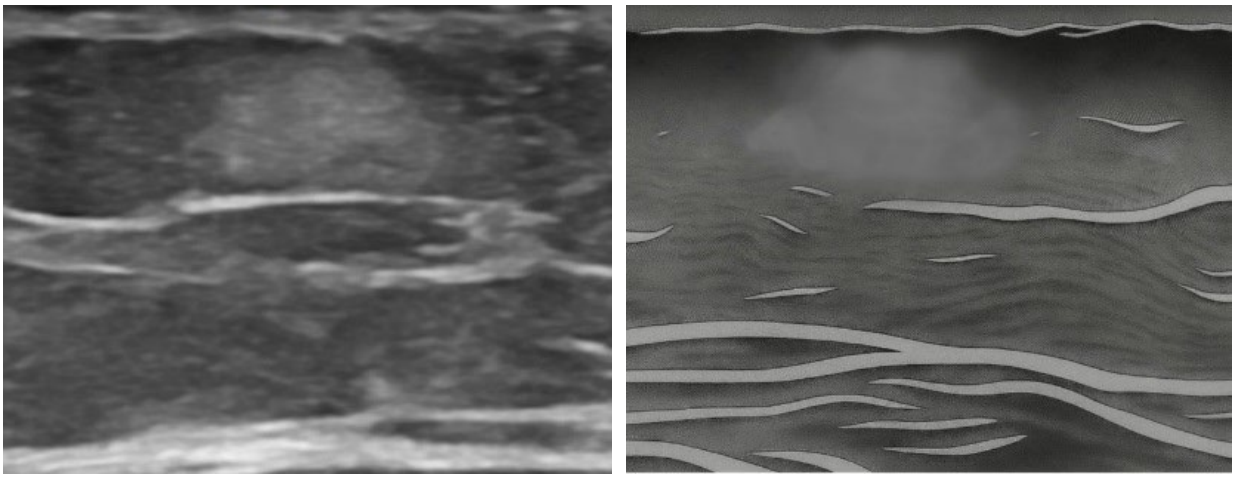
The subcutaneous echogenic nodules identified varied in distribution, predominantly in the posterior and lateral thigh. Regarding clinical correlation, 13 patients (65%) were classified as grade 2, while 7 patients (35%) were classified as grade 3. Despite efforts to correlate the higher number of nodules or their subtype with clinical factors such as BMI, age, or duration since the diagnosis of lipedema, the factor that demonstrated the most significant association with the distribution of more nodules was the site identified as the most painful point reported by the patient.

The nodules were categorized into four distinct types based on their ultrasonographic characteristics: **Figure 1(a)** represents an US image of the LDHC 3a nodule and **Figure 1(b)** an illustrative image of the same nodule. **Figure 2(a)** and **Figure 2(b)** show the LDHC 3b nodule in US and in an illustrative image, respectively. **Figure 3(a)** and **Figure 3(b)** demonstrate the characteristics of the LDHC 3c nodule in US and

illustration, respectively. Figure 4(a) and Figure 4(b) illustrate the LDHC 3d nodule in US and illustration, respectively. The quantity of each type of nodule identified is shown in Table 5.

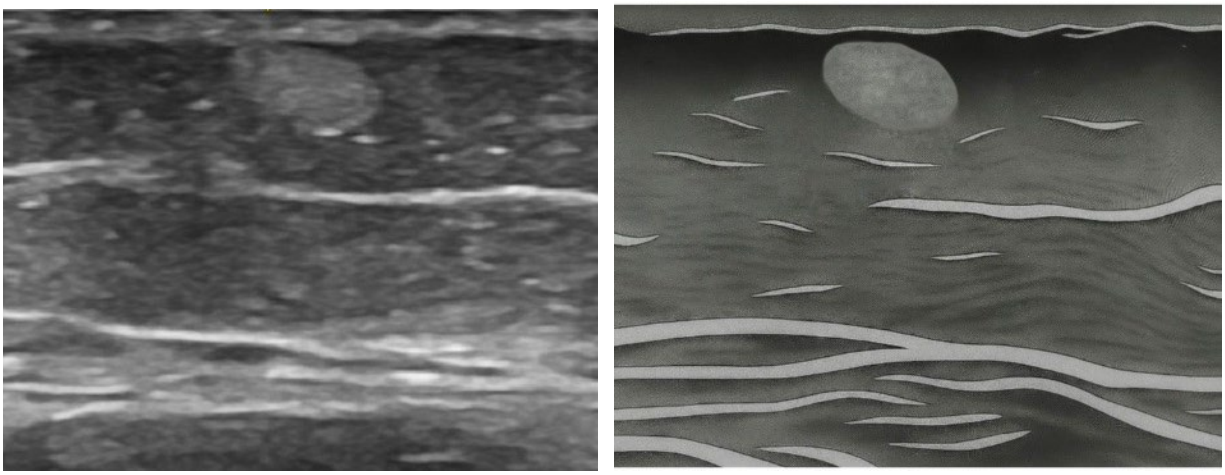
**Table 4. Proposed qualitative ultrasonographic classification for hyperechoic nodules in lipedema.**

| LDHC | Margins | Echogenicity | Anechoic area | Posterior acoustic shadow |
|---|---|---|---|---|
| 3a | Ill-defined | Slightly echogenic | Absent | Absent |
| 3b | Well-defined | Echogenic | Absent | Absent |
| 3c | Variable | Echogenic | Present | Absent |
| 3d | Well-defined | Echogenic | Absent | Present (faint) |



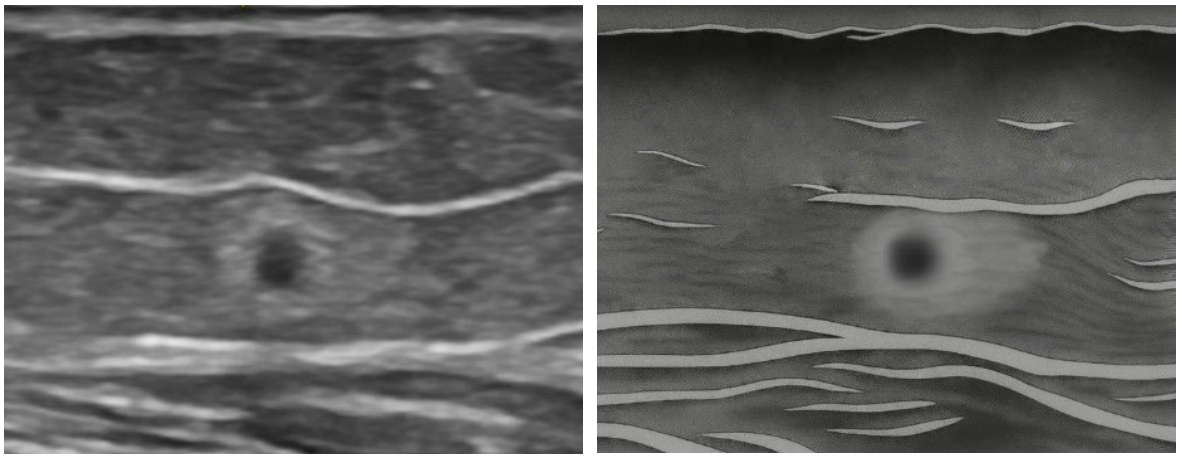
(a) (b)

**Figure 1. US image (a) and schematic (b) of LDHC 3a classification. Nodule with ill-defined margin, slightly echogenic, without anechoic area and without posterior acoustic shadow.**



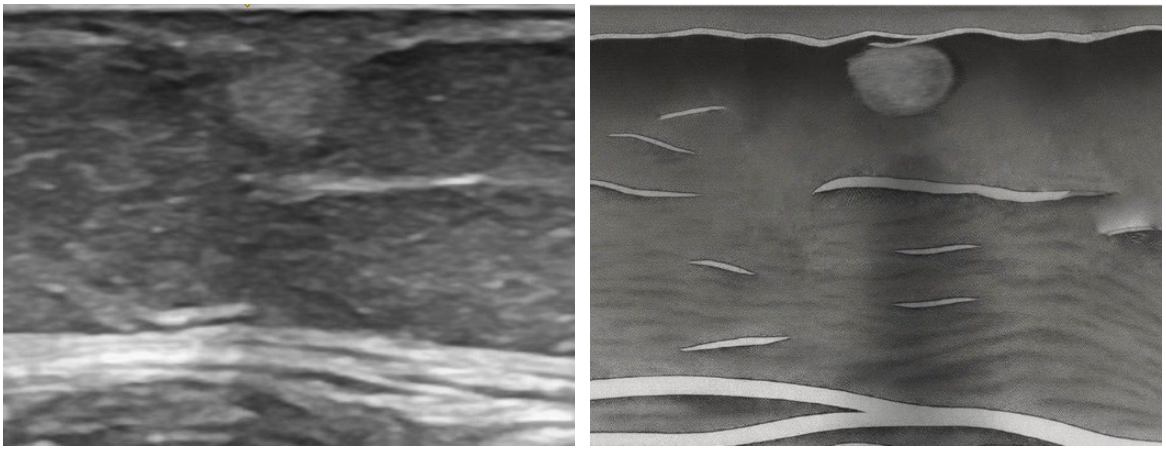
(a) (b)

**Figure 2. US image (a) and schematic (b) of LDHC 3b classification. Nodule with well-defined margin, echogenic, without anechoic area and without posterior acoustic shadow.**



(a) (b)

**Figure 3.** US image (a) and schematic (b) of LDHC 3c classification. Nodule with variable margin (in this case ill-defined), echogenic with anechoic area, and without posterior acoustic shadow.



(a) (b)

**Figure 4.** US image (a) and schematic (b) of LDHC 3d classification. Nodule with well-defined margin, echogenic, without anechoic area, and with faint posterior acoustic shadow.

**Table 5.** Quantity of nodules classified according to the qualitative US evaluation.

| LDHC | Number of nodules |
|---|---|
| 3a | 35 |
| 3b | 12 |
| 3c | 8 |
| 3d | 7 |

## 4. DISCUSSION

According to the systematic review that proposed to compare different methods for non-clinical diagnosis of lipedema it is necessary to establish an imaging method that unveils the pathogenesis of the disease and a tool capable of distinguishing lipedema from obesity, both requirements found in ultrasound [12].

Ultrasound is a widely accessible imaging modality that can be performed without radiation exposure or contrast agent administration, and it can be applied in overweight individuals without the limitations encountered in MRI and CT, where gantry diameter and table load capacity often represent the main constraints for patient size. Moreover, within the same examination, ultrasound can diagnose lipedema and differentiate it from obesity, lymphedema or venous insufficiency.

Ultrasonographic dermal and hypodermic alterations associated with hyperechoic nodules in patients with lipedema were already known; however, their microscopic analysis in a case report, demonstrated that they represent hemorrhage, as well as providing new insights into the presence of ischemia in these tissues. The different patterns of nodules suggest the need for subclassifications that consider these variables, which appear to encompass the evolutionary phases from ischemia to fibrosis and could propose distinct therapies for each one [8].

Identifying a subcutaneous nodule on US in a patient with lipedema is a marker of hemorrhagic focus, resulting from immature neoangiogenesis secondary to ischemia and increased pressure in the subcutaneous compartment (suggested by the increased RI). Other factors were also revealed by microscopy, including inflammation and fibrosis [8].

Nodules classified as LDHC 3a and 3b were more frequent, given the absence of anechoic areas and faint posterior acoustic shadow, which may indicate an evolutionary correlation or time since their formation, indicating the degree of degradation or resorption of hemorrhagic tissue. There may also be a correlation with the degree of ischemia or even the volume of local hemorrhage.

LDHC 3c classification was the least frequent, with the same proportion as LDHC 3d. The reason for the finding of an anechoic area is uncertain, but it can match a focal resorption of hemorrhage, possibly corresponding to hemosiderin deposition. It could represent an area of central necrosis, which microscopically could correspond to steatonecrosis. Another possibility is that it represents a new recent hemorrhagic area within an older one.

In LDHC 3d, the posterior acoustic shadow could correspond to an area with increased tissue density, either due to expansion of the hemorrhagic area or even transformation into fibrosis, as part of the evolution toward chronicity of these nodules.

It is important to note that the different types of nodules are not correlated with clinical findings of skin bruises or palpable irregularities of the skin. Instead, they may be clinically related to a painful point that possibly presents sonographically as hemorrhage in different evolutionary patterns, which could be categorized and monitored by ultrasound.

It is emphasized that, in clinical practice, physicians should systematically apply this subclassification to more accurately monitor disease progression and evaluate therapeutic response, ensuring uniformity in describing findings and facilitating comparability between different centers.

## 5. CONCLUSION

Ultrasound (US) is an essential tool in the diagnosis of lipedema; providing objective, qualitative and highly reliable data. The LDHC classification complements the quantitative diagnostic evaluation by describing structural changes in the dermis and hypodermis. Nodules identified in the subcutaneous tissue of patients with lipedema (LDHC 3) can be further subdivided into four distinct US patterns, suggesting different stages of evolution of the same nodule or different consequences of the same cause. Further studies with histological analysis, elastography or Doppler are needed to better assess the composition of each of these nodules. This could help with more precise staging and therapeutic monitoring. A high inter-observer agreement was observed applying the new subclassification of the nodules, demonstrating the consistency of the method regardless of the equipment used. The integration of imaging with histopathology promises to enhance diagnostic accuracy and guide personalized management strategies.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this paper.

## REFERENCES


1. Amato, A.C.M., Amato, F.C.M., Amato, J.L.S. and Benitti, D.A. (2022) Lipedema Prevalence and Risk Factors in Brazil. *Jornal Vascular Brasileiro*, **21**, e20210198. https://doi.org/10.1590/1677-5449.202101982
2. Forner-Cordero, I., Szolnoky, G., Forner-Cordero, A. and Kemény, L. (2012) Lipedema: An Overview of Its Clinical Manifestations, Diagnosis and Treatment of the Disproportional Fatty Deposition Syndrome—Systematic Review. *Clinical Obesity*, **2**, 86-95. https://doi.org/10.1111/j.1758-8111.2012.00045.x
3. Allen, M., Schwartz, M. and Herbst, K.L. (2020) Interstitial Fluid in Lipedema and Control Skin. *Women's Health Reports*, **1**, 480-487. https://doi.org/10.1089/whr.2020.0086
4. Herbst, K.L., Mirkovskaya, L., Bharhagava, A., Chava, Y. and Te, C.H.T. (2015) Lipedema Fat and Signs and Symptoms of Illness, Increase with Advancing Stage. *Archives of Medicine*, **7**, 1-8. https://www.archivesofmedicine.com/abstract/lipedema-fat-and-signs-and-symptoms-of-illness-increase-with-advancing-stage-6744.html
5. Herbst, K.L. (2012) Rare Adipose Disorders (RADs) Masquerading as Obesity. *Acta Pharmacologica Sinica*, **33**, 155-172. https://doi.org/10.1038/aps.2011.153
6. Amato, A.C.M., Saucedo, D.Z., Santos, K.d.S. and Benitti, D.A. (2021) Ultrasound Criteria for Lipedema Diagnosis. *Phlebology*: *The Journal of Venous Disease*, **36**, 651-658. https://doi.org/10.1177/02683555211002340
7. Vargas, D., Santos, A.M.R., Bueno, A.N., Bezerra, A.S., Bianchi, M.d.A. and Amato, A.C.M. (2025) The Challenge of a Qualitative Ultrasonographic Classification in Lipedema. *Journal of Biomedical Science and Engineering*, **18**, 106-112. https://doi.org/10.4236/jbise.2025.184008
8. Vargas, D., Lellis, R.F., Chagas, L.C., Saiki, P.Y., Santos, A.M.R., Bianchi, M.d.A., *et al.* (2025) Case Report of Painful Nodules in Lipedema: Correlation between Qualitative Ultrasonographic Classification and Histological Findings. *Journal of Biomedical Science and Engineering*, **18**, 372-383. https://doi.org/10.4236/jbise.2025.188026
9. Poojari, A., Dev, K. and Rabiee, A. (2022) Lipedema: Insights into Morphology, Pathophysiology, and Challenges. *Biomedicines*, **10**, Article No. 3081. https://doi.org/10.3390/biomedicines10123081
10. von Atzigen, J., Burger, A., Grünherz, L., Barbon, C., Felmerer, G., Giovanoli, P., *et al.* (2023) A Comparative Analysis to Dissect the Histological and Molecular Differences among Lipedema, Lipohypertrophy and Secondary Lymphedema. *International Journal of Molecular Sciences*, **24**, Article No. 7591. https://doi.org/10.3390/ijms24087591
11. Kruppa, P., Gohlke, S., Łapiński, K., Garcia-Carrizo, F., Soultoukis, G.A., Infanger, M., *et al.* (2023) Lipedema Stage Affects Adipocyte Hypertrophy, Subcutaneous Adipose Tissue Inflammation and Interstitial Fibrosis. *Frontiers in Immunology*, **14**, Article ID: 1223264. https://doi.org/10.3389/fimmu.2023.1223264
12. van la Parra, R.F.D., Deconinck, C. and Krug, B. (2023) Diagnostic Imaging in Lipedema: A Systematic Review. *Obesity Reviews*, **25**, e13648. https://doi.org/10.1111/obr.13648