THE EUROPEAN JOURNAL
OF
lymphology
and related problems
VOLUME 21 • No. 61 • 2010
INDEXED IN EXCERPTA MEDICA

LYMPHOEDEMA: WHAT CAN BE MEASURED AND HOW… OVERVIEW

BELGRADO J.P., BRACALE P.*, BATES J.*, RÖH N.**, ROSIELLO R.**, CANGIANO A.***, MORAINE J.J.**

* FSM - Université Libre de Bruxelles - Belgium
** European Medical Center - Bruxelles - Belgium
*** Centro Serapide - Napoli - Italy

Corresponding author: JP Belgrado, PT Dhrs
Université Libre de Bruxelles
Faculté des Sciences de la Motricité
CP 640 Campus Erasme
808, route de Lennik
1070 Bruxelles
Belgium

e-mail belgrado@ulb.ac.be

1. INTRODUCTION

The evolution of lymphoedema during physical treatment appears quite easy to measure, especially if we limit ourselves to considering the decrease in its volume, and furthermore if we limit the volume's measurement to the geometry of the arms, forearms, legs and thighs to a cylinder (lymphoedema reside mostly in these anatomical segments). On the other hand if we want to observe more complex anatomical areas such as the breast or scrotum, and especially when we take into account other parameters that are equally as interesting, such as the quality of the skin, it's water density, the thickness of the dermis etc., the task of remaining precise becomes much more complex.
With regard to the measurement of the shape of the oedema, a series of pictures taken in standardized conditions (which are explained in detail below), can suffice for the analysis of the treatment's results and the control of its efficiency. But how can we deal with more complicated geometries like the root of the limb, hands, feet, the face, breasts, external genitalia…and again other parameters that are less visible to the naked eye such as the thickness of the dermis, the variation of the subcutaneous tissue, the skin's temperature, the quality of the skin, the tonicity of the oedema, the joint's function, the quality of life, etc. All of them are measurable and important in the evaluation of the treatment's efficacy. Regular measuring in the daily practice represents an important part in the assessment of the oedema's evolution, and the more parameters the therapist can avail of, the better equipped they will be to adapt the treatment to each patient's specificities.
Another interesting application of the knowledge that can be obtained from measuring the affected area is the predictive factor or early indicator: detecting slight changes that are invisible to the naked eye, and thus availing of this information to commence treatment before the possible onset of a clinically significant lymphoedema.
Our aim is to discuss the most common parameters that are available for measurement, and the methods used to measure them, and to weigh their advantages and disadvantages to facilitate the comparison of different treatments and methods both on a theoretical level and in a practical setting.

2. MEASURE OF VOLUME AND PERIMETERS

The first impression you get when you observe a part of the body affected by lymphoedema, is the deformation of that area, either in comparison with the other side, or compared to what can be considered as "normal".
Thus it seems logical to try to measure the variation in volume of the oedema, firstly in order to monitor the treatment and secondly to motivate the patient by providing quantifiable evidence of improvement throughout its evolution.
There are two different approaches for measuring volume: a direct and an indirect technique.

1.1. The direct technique consists of a derivation of the Archimedes's Principle: a body immersed wholly or partially in fluid (liquid or gas) displaces a quantity of liquid equal to its immersed volume. Consequently the oedematous segment will be immersed into a recipient filled with water and the water's displacement will be gauged. If you examine more closely the quality of this method, you notice that there is a non negligible potential

of errors[1]. The main reasons rely on the superficial tension, the adsorption phenomenon, the reproducibility of reference points on the wrist, the microscopic structure of the skin's surface, the temperature of the water, the texture of the recipient's inner surface, the proportion between the size of the immersed object and the water volume and finally the error on the lecture of the values.

Therefore many authors proposed or experimented various types of measuring systems in the field of volumetry by immersion. Some proposed to fix a pressure transducer in the bottom of a container, others measure the rate of the water displacement and still others recuperate the quantity of displaced water in a graduated beaker in order to weigh or measure it. Ph. Lefèvre[2] suggested a very sensitive method in which he set up a volumetric device which allows the measurement of the hand with an accuracy of 1%, for volumes between 250 and 300ml. In this method a metallic needle is placed on top of the water surface in order to measure the variation of the electric resistance due to changes in the height of the water.
The majority of the apparatus available today, even in the best of conditions result in a 3% error, it is for this reason that we cannot refer to the immersion technique as the golden standard, as it has sometimes been considered by other authors. *"Measurements of volume can be misleading, particularly when the swelling of an obviously oedematous limb is restricted by tissue resection or contraction from fibrosis. Furthermore, volume measurements are prone to error because all oedema varies widely according to the time of day, the stage of the menstrual cycle and physical activity"*[3].

Literature overview of this topic shows us that the immersion method is an inappropriate method in the majority of situations, except due to their complex geometry, when dealing with the particular case of an oedema of the hand or foot. In practice when dealing with the limbs, this procedure requires a whole collection of different containers and apparatus that renders it unpractical, messy and time consuming. Furthermore with regards to hygiene, since people with lymphoedema often have concomitant skin alterations, the appropriateness of this procedure is questionable and it is also not suitable for patients in the immediate postoperative period.

Another weakness of the water displacement method is that the root of the segment is not immersible. Knowing the variation within this area is important to understand the displacement of the oedema as it plays a key role in determining whether the oedema is leaving the limb. Finally the water displacement gives only a global view of the reduction in the oedema, and not a precise segmental analysis which is required for monitoring appropriately multi layer bandaging.

1.2. The indirect technique comprises the acquisition of the perimeters' values that are then integrated into geometrical formula. There are two possibilities, the simplest method is to consider the lymphoedema as the addition of little cylinders that are 4cm long. In this case we can apply the simplified formula:

$$V_{limb} \approx \frac{\Sigma Z^2}{\Pi}$$

In which Z is equal to the circumference and where it is of utmost importance to take the measures every 4cm precisely.
This simplified method induces a substantial error because of the fact that a lymphoedema is unlike a tube in that it is not uniform and produces skin folds.

The other calculating method, using the truncated cone's volume tries to reduce this error by taking into account two successive circumferences. In this case the distance between two circumferences is non defined but the closer the measurements of the circumferences the more accurate the resulting volume.

$$V_{limb} = \frac{\Sigma x^2 + y^2 + xy}{3\Pi}$$

In this equation x equals one circumference and y the other.

Authors have tested the reliability between these two methods and the water displacement volumetry and they have concluded that the circumferential measurement has a better reliability. Due to the fact that interrater reliability is quite low, but that the intrarater reliability is higher, ideally a patient should always be evaluated by the same therapist[4]. These measurements will vary according to the reproducibility of the reference marks, the moment of the day or the activity before the measurement. In a bilateral lymphooedema, the comparison between the two limbs remains interesting to evaluate if one limb reacts better than the contralateral limb after the same treatment.
The tape measurement technique has the strength that it allows the analysis of segments individually and this, up until the root of the limb.

In the situation where hands or feet cannot be immersed in water there exists another technique in which the measuring tape is wrapped around the hand forming an '8', authors[5] have shown that this technique is an ICC of 0.9 compared to the immersion technique.

1.2.1. Other technology allows us to obtain values for the circumference of the limb, such as optoelectronic systems based on infrared diodes or LASER.

- Optoelectronic volometer (Fischbach & Goltners - 1986) is a system based on infrared diodes which record the shadow of the limb. This system has a good accuracy if the geometry of the limb is regular, however if this is not

the case it can generate an inherent error of 10-15% when dealing with the complex geometry [6] of an arm affected by lymphoedema with a lot of skinfolds. Furthermore these systems require a large abduction to permit the machine to access the isolated limb especially at the root and due to the configuration of the machine the extremity and the root of the limb end up being neglected. For example in the case of the leg, the foot is held in place by a saddle that blocks the light and hence the measurement. These systems are very expensive for a private practice and therefore are realistically attainable only in much bigger organisations.

- LASER technology is a promising technique that can also be used in measuring the evolution of lymphoedema. These techniques have been used for a long time when dealing with lumbar problems, casts and corset fabrication. When applied to lymphoedematous limbs it will allow a fast, precise and reproducible perimetry. It has passed its phase of development, but remains expensive and is in hand of industry.

3. MEASUREMENT OF THE SKIN FOLDS

The components of a lymphatic oedema, depending on the conditions and different elements considered, can leave the affected area by three different evacuation routes; venous, lymphatic and interstitial. Intermittent compression therapy and multilayered bandaging applied to the limb cover the whole oedema up until the root of the limb, at this level part of the oedema is therefore pushed closer to the root of the limb and to the chest or hip area directly in relation with the limb. The trained hands of a physiotherapist can aid these fluids in rejoining lymphatic substitution pathways that drain into the contra-lateral lymphnodes, or simply attaining sub cutanous region where physiological drainage continues to run well. These sub cutanous routes are filled with interstitial fluid, and for this reason skin folds in this region are much thicker. The measurement and comparison of these skin folds with a caliper, compared to the contra-lateral side, enable us to establish a clear picture of which regions are receiving the liquid coming from the affected limb. This tool is therefore very useful for the management and treatment of lymphoedema.
Another advantage of this utensil is its use when we have to deal with “flatter” areas of the body like the chest, hips or breasts. A caliper is much better adapted to these forms, and presents the ideal solution for evaluating lymphoedema through the measure of skin folds in this area with an acceptable reliability and accuracy.

4. IMAGERY BY PHOTOGRAPHY

An easy, quick, and cheap method in the assessment of the evolution of a lymphoedema through out treatment remains photography. Taking pictures helps patients on the one hand to visualize the reduction of their swelling, and can act as a form of psychological support especially when the treatment is heavy and the oedema persistent, on the other hand it’s a precious piece of evidence for communication with other therapists. In both cases, they only have to throw a glance at the pictures to acknowledge the relevance of the treatment.
The relative simplicity of photography also represents its weakness: small modifications of the volume are not visible, the picture is only two-dimensional, the control of luminosity and the difficulty of placing patients in the same conditions for every picture pose a problem.
Thus, the use of photography helps the therapist to demonstrate with ease the treatment’s benefit in the case of a big lymphoedema, where the volume reduces quickly, but for smaller oedema or slower evolutions, because of the difficulty of taking measures from the pictures, it is not exhaustive. Accordingly, photography constitutes thus first and foremost a qualitative and not a quantitative tool.

In order to obtain a reproducible photograph where we can assure that the patient is in the exact same position, we propose a simple method based on the grid function that is available on all modern cameras.
This grid is made up of 9 rectangles, each composed of a ratio between their width and length. This ratio is based on the Golden Ratio and Fibonacci Numbers [7].
Our idea is to magnify these rectangles and draw then on the wall, or background, in front of which the photograph can be taken every time. We therefore enable a referential that can be reproduced with ease, and that is reliable, so when taking the photograph the lines can be aligned and thus the exact same frame is used.

5. IMAGERY BY DEEP INFRA-RED THERMOGRAM

The backflow of lymph into the superficial tissues, also called « dermal backflow », is a pathognomic sign of lymphatic insufficiency. The backflow is due to the incapacity of lymphatic collectors of one area to drain the lymph properly. The lymph recedes into the initial lymphatic network inside the dermis, where liquids and macromolecules cannot be reabsorbed. Because of local pressure, they have to find their way through the dermis to another area of the body, for example up to the root of the limb until they find areas where the physiological drainage is efficient. The dermal area that is not sufficiently drained firstly increases in pressure, and then becomes more voluminous. This lymphatic stasis increases the pressure on local tissues causing among other things a compression of the arteriovenous capillaries.
From a clinical point of view, in the first stage this physiopathological state occasions a paleness and coldness of the skin. This cold area can be identified and measured precisely with a deep infra red camera, that therefore pin points the areas that are affected by dermal backflow, directing the clinician to this site that demands specific attention in the global treatment of lymphoedema.
Despite the fact that lymphoscintigraphy represents the golden standard examination for the diagnosis of the dermal backflow, because it requires an injection of radiocolloids, it is not conceivable in a regular follow-up of a treatment. This leaves a greater place for thermograms in treating lymphoedema.

Following this first stage of coldness if the stasis is important and makes the tissues suffer, the skin becomes warmer, because of the beginning of the inflammation process. Deep infra red thermograms enable us to make an early detection, because of the sensitivity of the camera and are a valuable tool in this situation. The use of infra red thermal cameras enables us to obtain surface thermograms of high precision and excellent resolution for the diagnosis and evaluation of the treatment's efficiency with lymphoedema accompanied by dermal backflow. Thanks to their easy mode of operation and quick manipulation, these cameras can be used in a daily routine. We have completed preliminary studies with promising results, but further investigation is needed on this topic.

6. TONOMETRY

Tissue tonometry is the measurement of mechanical change due to external pressure that displaces interstitial fluid to leave a depression or pit in an oedema. Tonometry registers the depth of tissue compression by a known mass over a fixed time interval. It can be an important tool to mesure the success of a lymphoedema treatment and management program, although rarely used. The measurement of the depth of pitting in lymphoedema has been described using a tonometer by various authors [8].

The Tissue Tonometer appears to be an easy-to-use, fast and non-invasive method available to assess the characteristics of the swollen limb. Its accuracy and reproducibility in assessing pitting oedema in oedematous and lymphoedematous tissues were confirmed by a number of authors [9]. The Tonometer can be set at different weight levels of 70, 140 and 210 [10] grams that gently push a plunger onto the skin.
The reliability between tonometry and water displacement or circumference measurements seems not to be effective [11].
The interpretation of results obtained through tonometry need to be closely scrutinized. Firstly they should be analyzed with relation to time, secondly it is very important to correlate the results with histological evidence. Often we are too quick to conclude that a non pitting oedema is fibrotic and therefore non reversible. Through clinical experience we know that these oedemas are more resistant to the pitting test as observed with the tonometer, but also we know that with intensive physical treatment and adapted technique we can obtain substantial improvements. Authors consider that the more an oedema is "tonic" the more fibrotic it is, they asses "fibrotic indurations" by tonometry [12]. We are not convinced by these conclusions, because there exist non pitting oedemas, that are resistant to a tonometer, but that react very well and quickly under intensive treatment. We agree that all fibrotic oedema are resistant to tonometers, but consider that not all resistant oedemas are fibrotic. A tough oedema could be because water is imprisoned in the very small and tight extracellular compartments that generate a very strong pressure. Other authors [13] sustained that *"A harder swelling is dominated by adipose tissue and can be treated with liposuction, while the softer one is treated conservatively"*.

7. THE MULTI-FREQUENCY BIO-IMPEDANCE

Multi-Frequency Bio-impedance Analysis (MFBIA) is a physical application of a derivation of Ohm's law. It allows us to measure the total water content of the body, both intra and extra cellularly. MFBIA can be applied to the quantification of unilateral lymphoedema. MFBIA involves passing an extremely small AC current at frequencies from 4 kHz to 1MHz, through the body and measuring the opposition to the flow of this current (defined as impedance). At low frequencies, current passes through the extracellular fluid (ECF) space and does not penetrate the cell membrane, characterized by the theoretical resistance at zero frequency (R0). At high frequencies, however, the current passes through both the intracellular fluid (ICF) and ECF.
Based on this concept, together with the fact that the impedance of a geometrical system is related to conductor length, cross sectional area and signal frequency, a value of impedance can be calculated from a current passed through the body. The measured impedance is inversely proportional to the amount of fluid. By appropriate choice of signal frequency, this can be made specific for ECF or for total fluid determination.
MFBIA analysis of a limb requires that the electrodes be placed at the extremities and the root of the limb. There are various methods for doing this, either at predetermined anatomical sites like the wrist and shoulder [14], or as some authors have proposed at a determined length (40cm apart) [15].
These machines were created for whole body measurements with electrodes placed at the hands and feet. When dealing with lymphoedema because the electrodes are placed specifically to measure a limb, the majority of results for the different volumes indicated on the screen of the machine cannot be interpreted. The impedance is the only data that can be exploited, since the other values are calculated by an algorithm, which takes into account the BMI, statistic data of fluid volume determined by isotope dilution for the whole body, and anthropometric parameters from peer-reviewed published journal articles.
The liquid content of a normal limb and more specifically an oedematous limb varies depending on different variables: temperature, relative humidity, physical activity, diet, variations in the adipose tissue, alternation of decline and orthostatic position, tight clothing, the dominant arm, elastic sleeves, metabolism, and hormonal cycles to name only a few. Because of the changes in liquid content, impedance also varies from one measure to the next. We need to considerate these aspects in the methodology of studies, despite the fact that the results obtained may be erroneous or at least disputable.
When dealing with lymphedema, the use of MFBIA can be considered when taking into account the flaws described above. Then, we concentrate on the impedance ratio between two limbs, the presumed affected and non affected limb, at a precise moment in time.
Even though MFBIA is less time consuming than water immersion methods, it provides us with a global overview that doesn't indicate towards which anatomical area the interstitial part of the oedema is being displaced.
MFBIA is more sensitive than circumferential measurements at low levels of oedema and so it can be used to discriminate between affected and non affected limbs. This method of

measurement can be useful for detecting the beginning of oedemas, enabling the rapid installation of focused treatments in order to reduce consequences of lately diagnosed, and therefore treated, oedema. Further prospective and multicentric studies are necessary to validate and expand the use of this preventative methodology.

8. QUALITY OF LIFE SCALE

Lymphoedema decreases the quality of life of affected patients and up until recently has been neglected. Consequently little data on this subject is available. Generally studies use the SF-36, a generic quality of life instrument [16], more recently specific questionnaires relating to quality of life with lymphoedema are being or have been validated such as the FACT-B questionnaire and LYMQOL[28].
R. Launoix et al. suggested an original ladder : l'ULL-27 test [17] defined by 27 items and 3 dimensions. Physical (14 questions), Psychological (7 questions) and social (6 questions). Its validity is debated in the principal articles which specify its construction and utilization's method.

9. VEINOUS ECHOCOLOR DOPPLER SCAN

Lymphoedema are always associated with a more or less important venous insufficiency, for this reason echocolor Doppler needs to be integrated in the assessment of lymphoedema. The echography is an undisputable examination for investigating lymphnodes. Some authors have demonstrated that is also possible to visualize large lymphvessels by means of echography using linear probes of 15 MHz [18].

10. THE SUB-CUTANEOUS TISSUES ECHOGRAPHY

This inexpensive and non invasive examination allows us to appreciate the fibrosis and the local thickness of the oedema and overall the thickness of the dermis involve in the dermal backflow. High-resolution cutaneous ultrasonography makes it possible to differentiate lymphoedema from lipoedema [19].
This imaging tools can be useful in the case of functional limitation without notable volumetric deterioration. Actually, volumetry does not show the underlying muscular waste when it is masked by an oedema. By means echography authors has describe that it seems that there exists a preclinical "pathological" state, where the thickness of the dermis increases and the fat tissue is modified without visible increases in the volume of the limb [20].
These results raise hope that a prevention approach of lymphoedema is possible using echography, but further prospective studies still have to be achieved.

11. THE LYMPHOSCINTIGRAPHY

This technique of imagery makes it possible to appreciate the performance of a lymphatic network and to reveal its topographical anatomy. It permits us to locate and to appreciate the function of the collateral lymphatic pathways, the dermal backflow, the lymphatic clearance of a certain spot, and the lymphnodes activity… It constitutes an invaluable help for the diagnosis [21], and the golden standard examination for the evaluation of lymphoedema. The examinations' result must be interpreted by a nuclear physcian specialized in the lymphatic field.
The method of injection (sub-cutaneous or intradermal) [22] is important and should be closely regulated as they influence the results greatly. Typically, the traditional protocols include injecting directly into the first inter digital space. A supplementary injection at the root of the limb, followed by a manual drainage on the potential drainage pathways enables us to visualize the functional pathways being used by the body to drain the lymphoedematous limb.
This information provides the therapist with clinical evidence so that they can adapt and base their treatment on facts.
According to the invasive aspect and the cost of a lymphoscintigraphy it doesn't appear judicious to propose it in first intention when a lympho-veinous oedema appears.
On the other hand, after a cycle of a dozen physical treatments, if the results are disappointing [5] it's useful to carry out a lymphoscintigraphy to clarify the problem by identifying the presence or not of lymphnodes and the routes of evacuation.

12. CT SCAN

The CT scan is not routinely proposed for the development and the evaluation of the lymphoedema because the cost / profit ratio is very unfavorable. The analysis of the cross sectional area allows us however to differentiate between the volume of the muscular mass compared to the oedema, and therefore to identify eventual muscular wasting [23].

13. MRI

MRI whitout contrast furnish an iconography in honey combs of the oedema. Examinations with contrast products by injection of Gd- DTPA only allow the visualization of large lymphatic vessels. More recently authors consider that MR Lymphangiography at 3.0 T provides very high spatial resolution and anatomical detail of normal and abnormal peripheral lymph vessels [24]. MRL may thus become a valuable tool for microsurgical treatment planning and monitoring.
This technique enables us to appreciate the relative composition of the oedemas as well as the eventual muscular wasting. TSE T1 and TSE T2 magnetic resonance images, provide a higher resolution imaging to distinguish the components of the oedema. MR spectroscopy permits us to calculate the relative proportions of water and fat, and this is interesting to evaluate the evolution of the composition of the oedema [25].

14. MEDICAL ELASTOGRAPHY

Is an emerging diagnostic tool for the assessment and real-time colour display of tissue elasticity. This technique based on the elastic answer of a tissue subjected to ultrasonic waves, provides a cartography of the elasticity of an anatomical area with a

millimetre-length resolution in 3D. This innovating non invasive method might be able to contribute to the study and evaluation of fibrosis of lymphoedema, therefore complementing studies with tonometry.
Results of preliminary study on lymphoedema arm and leg subcutis [26] demonstrate that at least *"in some cases it is feasible to generate poroelastograms from different lymphoedematous tissues in vivo. They also suggest that lymphoedematous tissues exhibit a temporal poroelastographic behavior that is significantly different from the behavior that characterizes normal tissues. Thus, poroelastographic techniques may be of use in the diagnosis and evaluation of lymphoedema".*

CONCLUSION

Our overview is certainly not an exhaustive paper, but aims to investigate briefly the most frequently available techniques to assess lymphoedema.
The challenge that the clinician faces nowadays in treating lymphoedema is finding the adequate tools to evaluate the situation and to make the right decisions regarding the treatment, not only in function of the volume, but taking into count other parameters as well.

The most accessible techniques beside the obvious cost benefits do have their advantages. In the case of segmental lymphoedema (referring to the segment of a limb), the measuring tape method remains the easiest and comparatively most sensitive method; it is sensitive to the perimeter, graphically reproducible, and gives clear evidence of the displacement of the oedema.
Concerning the hands and feet, the immersion technique is the most adequate, while for flat surfaces, the caliper provides the easiest information concerning the thickness of the skin.

More sophisticated techniques require training, and can be less accessible on a routine basis. Never the less these techniques can reveal much more information than the naked eye. The most available of these techniques is the echography: with this we can visualize the thickness of the dermis, and of the sub cutaneous space where the oedema is situated. Because lymphatic diseases are often connected with venous insufficiency the echocolor Doppler is an indisputable tool in the diagnostic of phlebo-lymphoedema insufficiency.
MRI and CT-scan remain reserved for scientific research or particular complex clinical case. Other than in particular cases this approach cannot be used in a routine basis, because of their high cost and limited availability.

The whole body laser scanner is a promising new perometer, but quite expensive and still requires more research to evaluate its interest in the field of lymphology.

Bio impedance analysis appears interesting but procedures need to be validated to evaluate the intrinsic qualities of measurements, like the sensitivity and the resolution in order to use this system to detect lymphoedema before its visible onset.

Thermography was abandoned twenty years ago but nowadays with new advances in technology it has become an affordable and easy to use piece of equipment to evaluate the skin thermogram throughout the evolution of the oedema.
Lymphoscintigraphy remains the golden standard to visualize the physiology and physiopathology of the lymphatic system. It is now being used in synchronization with a scanner that enables a 3D visualization. By means of additional injection at the root of the limb, it is possible to visualize the pathways used and therefore direct the hands of the physiotherapist to work in accordance with evidence.

Another aspect that is often put in second place is the quality of life and also the functional impact of lymphooedema27. For example, we have only found one study that investigates gait analysis in lower limb lymphoedema, and validated questionnaires about quality of life remain rare.
Finally it is becoming more and more apparent that a myriad of techniques are available to evaluate lymphoedema, so we are hopeful for the future, knowing that possible combinations of these techniques will enable us to progress in the diagnosis, treatment and research of lymphoedema.

REFERENCES

1. Lefèvre Ph., Lewillie L., Rooze M., Sporcq J.: *Methodological approach of the measurement of the hand volume with an ordinary device.* Cahiers d'Anthropologie et Biométrie Humaine, Paris, 1996, XIV, n. 3-4, p. 427-438.
2. Lefèvre Ph., Leduc B., Carlens D., Mannaert G., Rooze M.: *Adjustment of a volumetric device. Application to the hand volume.* Biom. Hum. Et Antropol., 18, 1-2, p. 101-107, 2000.
3. Browse N., Burnand K., Mortimer P.: *Diseases of the lymphatics.* Arnold 2003.
4. Deltombe T., Jamart J., Recloux S., Legrand C., Vanderbroeck N., Theys S., Hanson P.: *Reliability and limits of agreement of circumferential water displacement, and optoelectronic volumetry in the measurement of upper limb lymphoedema.* Lyphology, 40 (2007); 26-34.
5. Leard J., Breglio L., Fraga L. et al.: *Reliability and concurrent validity of the figure-of-eight method of measuring hand size in patients with hand pathology.* J. Orthop. Sports Phys. Ther., 2004; 24: 335-340.
6. Leduc O., Klein P., Rasquin C., Demaret P.P.: *Reliability of a volume measuring device (volometer) for human limb.* Progress in Lymphology, XIII, 617-620.
7. Richard A. Dunlap: *The Golden Ratio and Fibonacci Numbers.* World Scientific Publishing, 1997.
8. Bates D.O., Levick J.R., Mortimer P.S.: *Quantification of rate and depth of pitting in human oedema using an electronic tonometer.* Lymphology, 1994; 27: 159-72.
9. Stanton A.W., Badger C., Sitzia J.: *Non-invasive assessment of the lymphoedematous limb.* Lymphology, 2000 Sep; 33(3): 122-35.
10. Kar S.K., Kar P.K., Mania J.: *Tissue tonometry: a useful tool for assessing filarial lymphoedema.* Lymphology. 1992 Jun; 25(2): 55-61.
11. Chen Y.W., Tsai H.J., Hung H.C., Tsauo J.Y.: *Reliability study of measurements for lymphoedema in breast cancer patients.* Am. J. Phys. Med. Rehabil., 2008 Jan; 87(1): 33-8.

12. Harris R., Piller N.: *Three cases studies indicating the effectiveness of manual lymph drainage on patients with primary and secondary lymphoedema using objective measuring tools.* Journal of bodywork and movement therapies. October 2003: 213-221.

13. Bagheri S., Ohlin K., Olsson G., Brorson H.: *Tissue tonometry before and after liposuction of arm lymphoedema following breast cancer.* Lymphat. Res. Biol., 2005 Summer; 3(2): 66-80.

14. Scheltinga M.: *Bioelectrical impedance analysis: a bedside method for fluid measurement.* Ph.D. Thesis, VU University Press 1992, Amsterdam.

15. Cornish B.H., Bunce I.H., Ward L.C., Jones L.C., Thomas B.J.: *Bioelectrical impedance for monitoring the efficacy of lymphoedema treatment programmes.* Breast Cancer Research and Treatment,1996; 38: 169-176.

16. Velanovich V.: *Quality of life of breast cancer patients with lymphoedema.* The American Journal of Surgery, Volume 177, Issue 3, Pages 184-188.

17. Launois R., Megnigbeto A.C., Pocquet K. et al.: *A specific quality of life scale in upper limb lymphoedema: the ULL-27 questionnaire.* Lymphology, 35 suppl. 2002; 181-187.

18. Matter D., Grosshans E., Muller J., Furderer C., Mathelin C., Warter S., Bellocq J.P., Maillot C.: *Sonographic imaging of lymphatic vessels compared to other methods.* Journal de radiologie, 2002; vol. 83, no. 5, pp. 599-609.

19. Naouri M., Samimi M., Atlan M., Perrodeau E., Vallin C., Zakine G., Vaillant L., Machet L.: *High resolution cutaneous ultrasonography to differentiate lipoedema from lymphooedema.* Br. J. Dermatol., 2010; Apr 16.

20. Tassenoy A., Vermeiren K., van der Veen P., Stadnik T., De Ridder F., Peeters E., Van Schuerbeek P., Lamote J., Lievens P.: *Demonstration of tissue alterations by ultrasonography, magnetic resonance imaging and spectroscopy, and histology in breast cancer patients without lymphoedema after axillary node dissection.* Lymphology, 2006 Sep; 39(3): 118-26.

21. Bourgeois P., Munck D., Belgrado J.P., Leduc O., Leduc A.: *Limb oedema and lymphoscintigraphy.* Rev. Med. Brux., 2003 Feb; 24(1): 20-8. Review.

22. Bourgeois P., Leduc O., Belgrado J-P., Leduc A.: *Scintigraphic investigations of the superficial lymphatic system: intradermic or subcutaneous injection?* The European Journal of Nuclear Medecine, 2002.

23. Cardone M., Failla A., Michelini S., Moneta G., Santambrogio F., Zinicola V.: *Muscolar and articular involvement in primary and secondary lymphoedema.* European Journal of Lymphology - Volume 19 - No. 54 – 2008.

24. Notohamiprodjo M., Baumeister R.G., Jakobs T.F., Bauner K.U., Boehm H.F., Horng A., Reiser M.F., Glaser C., Herrmann K.A.: *MR-lymphangiography at 3.0 T. A feasibility study.* Eur Radiol. 2009 Nov; 19(11): 2771-8. Epub 2009 Jun 6.

25. Fumiere E., Leduc O., Fourcade S., Becker C., Garbar C., Demeure R., Wilputte F., Leduc A., Delcour C.: *MR imaging, proton MR spectroscopy, ultrasonographic, histologic findings in patients with chronic lymphoedema.* Lymphology, 2007 Dec; 40(4): 157-62.

26. Raffaella Righetti, Brian S. Garra, Louise M. Mobbs, Christina M. Kraemer-Chant, Jonathan Ophir, Thomas A. Krouskop.: *The feasibility of using poroelastographic techniques for distinguishing between normal and lymphoedematous tissues in vivo.* Phys. Med. Biol., 52 (2007); 6525–6541 _ doi:10.1088/0031-9155/52/21/013

27. Forner-Cordero I., Forner-Cordero A., Maldonado-Garrido D., Cervera-Deval J.: *Biomechanical study of the gait in patients with Lower Limb Lymphoedema.* The European Journal of Lymphology, 2009, Vol. XX, No. 58: 1-6.

28. Vaughan Keeley, Sue Crooks, Jane Locke, Debbie Veigas, Katie Riches, Rachel Hilliam: *A quality of life measure for limb lymphooedema (LYMQOL).* Journal of Lymphoedema, 2010, Vol. 5, No. 1.