

01. Lymphology: Basic Sciences & Applied Technologies

Lymphangioplasty with Surgical Threads and with a Nanofibrillar Collagen Matrix – First Experiences.

Mathias Witt⁽¹⁾ - Niklas Dellmann⁽¹⁾ - Rosmaria Thomas⁽¹⁾ - Andrej Ring⁽¹⁾

St. Rochus-Hospital Castrop-Rauxel, Plastic Surgery, Castrop-Rauxel, Germany⁽¹⁾

Traditionally, secondary lymph edemas are (micro)surgically treated by lymphovenous anastomosis and vascularized lymphatic node transfer. A novel surgical option is the implantation of a fibrillar collagene matrix (BioBridge™; Fibralign Corporation, Union City, CA). Due to its specific nanostructure, it induces directional lymphangiogenesis, an effect that has been confirmed in animal trials and clinical pilot studies.

In the present paper, the first experiences of our clinic with BioBridge™ will be presented. BioBridge™ was implanted in a patient cohort in conjunction with conventional microsurgical therapy options. Therapy planning, intraoperative procedure and the course of therapy are to be presented, evaluated on the basis of patient satisfaction and objectified by volumetric measurements as well as indocyanine green fluorescence lymphangiography (ICG-FLAG).

01. Lymphology: Basic Sciences & Applied Technologies

Lymphedema Index: Body-physique Corrected Lymphedematous Volume Evaluation

Toko Miyazaki ⁽¹⁾ - **Hayahito Sakai** ⁽¹⁾ - **Reiko Tsukuura** ⁽¹⁾ - **Nana Yamamoto** ⁽¹⁾ - **Takumi Yamamoto** ⁽¹⁾

National Center for Global Health and Medicine, Department of Plastic and Reconstructive Surgery, Tokyo, Japan ⁽¹⁾

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Toko Miyazaki, Hayahito Sakai, Reiko Tsukuura, Nana Yamamoto, Takumi Yamamoto

Department of Plastic and Reconstructive Surgery, National Center for Global Health and Medicine, Tokyo, Japan

Objective: Volume evaluation is the most commonly applied method for extremity lymphedema evaluation. However, volume comparison between different patients with different body-physique is difficult to be appropriately interpreted, because body-physique difference significantly affects extremity volume rather than lymphedematous conditions. This study aimed to evaluate feasibility of lymphedema indices, body-physique corrected volume, compared to conventional volumetry.

Methods: Extremities of participants who had no history of edema or cancer were included in this study. Extremity volumes were calculated based on a summed truncated cone model using tape measurement, and lymphedema indices were calculated using circumferences and body mass indices (BMIs). Examinees' BMI was classified into 3 groups; low-BMI (BMI < 20), middle-BMI (BMI, 20-25), and high-BMI (BMI > 25). Extremity volume and lymphedema indices were compared according to BMI groups.

Results: Ninety eight extremities were included. Extremity volume significantly increased with increase of BMI; volume was lowest in low-BMI group, and highest in high-BMI group ($P < 0.001$). On the other hand, there was no statistically significant difference in lymphedema indices between the 3 BMI groups ($P > 0.05$).

Conclusions: Extremity volume increases with increase of BMI, indicating inappropriateness of the use of volumetry for comparison of different patients with different body-physique. Lymphedema indices allows body-physique corrected lymphedematous volume evaluation, and should be routinely used for lymphedema management as a basic volume evaluation.

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Clinicodemographic Profiles and Outcomes of Complex Lymphatic Therapy among Patients with Lymphedema: A Single-Centre, Descriptive-Analytic Study

Queenette Blaise Mateo ⁽¹⁾ - Diana Jean Roxas ⁽¹⁾ - Jonathan James Bernardo ⁽¹⁾ - Roi Joseph Mendoza ⁽¹⁾ - Jason Francis Roxas ⁽¹⁾

St. Luke's Medical Center-Bonifacio Global City, Heart Institute, Taguig City, Philippines ⁽¹⁾

Introduction: Lymphedema is a chronic, progressive vascular disease entailing lifelong management that should consider a patient's physical, psychological, social, and economical perspectives. A multidisciplinary lymphedema management and care is essential, and the first step is recognizing and early diagnosing this neglected condition. Awareness of the clinicodemographic characteristics of patients with lymphedema is imperative in optimizing conservative, first-line management through complex lymphatic therapy (CLT).

Purpose: To determine the clinicodemographic profiles and outcomes of CLT among patients with lymphedema from a tertiary referral hospital

Methods: Utilizing a retrospective-cohort design, 153 records of purposively-sampled adult in- and out-patients with lymphedema and received CLT from the Lymphedema Clinic of a tertiary referral hospital were examined. Alongside demographic and clinical data, baseline and post-CLT limb measurements were extracted and recorded. Limb volumes and circumferences and post-CLT lymphedema status were analyzed using Wilcoxon Signed-Rank test and polynomial logistic regression.

Results: Most patients had secondary lymphedema (96.73 %) attributed to cancer treatment (47.97%), and the upper extremities were commonly affected (67.30%; RUE=46.73%, LUE=49.53%, BUE=3.74%). Majority had Stage I lymphedema (58.82%), had lymphedema for less than 12 months (62.09%), and had undergone surgery (92.81%), chemotherapy (61.44%), and radiotherapy (55.56%). With a median of five CLT sessions, baseline limb volumes (UE: MD=2,550.43mL; LE: MD=998.98mL) and circumferences (UE: MD=0.71cm; LE: MD=1.85cm) significantly decreased ($p=0.001$), and 78.57% had improved lymphedema. The

percentage change in upper and lower limb volumes were -7.01% and -1.19% , respectively, while percentage change in upper and lower limb circumferences were -2.88% and -4.15% . Moreover, higher completed CLT sessions increased the likelihood of improved lymphedema by 35% (OR=1.35, $p=0.044$).

Conclusion: Complex lymphatic therapy is effective against lymphedema, with substantial reduction in limb volumes and circumferences. Cognizant of its benefits, clinicians should encourage patients to adhere with CLT schedule to increase completed sessions and reduce lymphedema.

01. Lymphology: Basic Sciences & Applied Technologies

The quantitative metabolomic composition of human plasma and interstitial fluid of patients with breast cancer related lymphedema (pilot study).

Vadim Nimaev⁽¹⁾ - Lyudmila Yanshole⁽²⁾ - Yuri Tsentalovich⁽²⁾ - Rustam Khapaev⁽¹⁾ - Vadim Yanshole⁽²⁾

Research Institute of Clinical and Experimental Lymphology – Branch of the Institute of Cytology and Genetics SB RAS, Laboratory of Surgical Lymphology and Lymphdetoxication, Novosibirsk, Russian Federation⁽¹⁾ - International tomography center SB RAS, Laboratory of proteomics and metabolomics, Novosibirsk, Russian Federation⁽²⁾

Background. The subclinical stage of breast cancer related lymphedema (BCRL) usually requires the invasive methods of diagnostics such as radionuclide lymphoscintigraphy or fluoroscopic lymphography. The early detection of lymph flow disturbance among patients after breast cancer treatment allows for beginning the treatment or paying attention to prevention measures.

The search of biomarkers - molecules whose concentration changes significantly in the case of a disease is one of the most effective approaches to the early diagnosis of diseases. Therefore, the current research objectives are: to identify metabolomic markers - precursors of BCRL in the blood plasma of patients at the early stages of the disease, which is especially important for patients after complex treatment of breast cancer. The second task is to identify changes in metabolic cycles in various human biological fluids during the development of lymphedema, followed by the development of individualized approaches to the prevention and treatment of the disease. The metabolomic profile of biological tissues is the most dynamic and susceptible to external factors compared to such conservative components of a living organism as the genome, transcriptome, or proteome. Thus, the development of pathological processes can lead to significant changes in the metabolic cycles of both the affected tissue itself and in the metabolome of important human biological fluids – blood and interstitial (intercellular) fluid. In this regard, the study of the composition of low-molecular compounds in these biological fluids is a primary scientific task.

Methods. Human blood and interstitial fluid were obtained in the morning time at the Research Institute of Clinical and Experimental Lymphology – Branch of Institute of Cytology and Genetics SB RAS (NIIKEL-a branch of the ICG SB RAS) from patients with BCRL stage II (8 patients) and stage

III (1 patient) in age 70 [65;71] years without progress of cancer. Time after surgery (radical mastectomy and radical resection with axillar lymphadenectomy) was 8 [5; 12] years. Control blood samples were obtained from patients of the similar age, but without BCRL or breast cancer and other cancer in anamnesis, age 69 [67,8; 70,3] years. The study was approved by the local ethics committee of Research Institute of Clinical and Experimental Lymphology – Branch of the Institute of Cytology and Genetics SB RAS.

The quantitative metabolomic profiling of samples has been performed with the combined use of high frequency proton nuclear magnetic resonance spectroscopy (^1H NMR) and high performance liquid chromatography with high resolution mass-spectrometric detection (HPLC-MS).

Results. The concentrations of 50 metabolites in human serum and interstitial fluid have been measured. The most pronounced difference in serum vs. fluid was observed for ketoleucine, acetoacetate, inosine and acetone. Concentration of these compounds at least 1.8 times higher ($p < 0.05$) than in interstitial fluid, obtained from upper limbs of patients with BCRL.

Accumulation of protein rich liquid in the interstitial space have an impact to metabolic process in patients with BCRL. This preliminary report gives hope for finding of new perspective and less invasive methods of early diagnosis of BCRL.

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01. Lymphology: Basic Sciences & Applied Technologies

Polymorphism of the matrix metalloproteinases genes MMP2, MMP3, MMP9 are associated with the development of secondary lymphedema.

Alla Shevchenko⁽¹⁾ - *Victor Prokofyev*⁽¹⁾ - *Vladimir Konenkov*⁽¹⁾ - *Rustam Khapaev*⁽²⁾ - *Vadim Nimaev*⁽²⁾

Research Institute of Clinical and Experimental Lymphology – Branch of the Institute of Cytology and Genetics SB RAS, Laboratory of Clinical Immunogenetics, Novosibirsk, Russian Federation⁽¹⁾ - *Research Institute of Clinical and Experimental Lymphology – Branch of the Institute of Cytology and Genetics SB RAS, Laboratory of Surgical Lymphology and Lymphdetoxication, Novosibirsk, Russian Federation*⁽²⁾

The lymphatic system is an important part of the vascular system of the body, exercising immune control, participating in homeostasis and lipid absorption. Any acquired or congenital defect in the architecture or function of the lymphatic system can contribute to lymphatic dysfunction and the development of lymphedema [1]. Matrix metalloproteinases (MMP), acting on collagen and proteoglycan matrix, regulate vascular tissue remodeling and participate in lymphangiogenesis [2]. The genetic predisposition can be one of the risk factors of the breast –cancer related lymphedema as the most frequent form of the secondary lymphedema [3]. Since the regulatory regions of the MMP genes are polymorphic, it is possible that a different level of their expression may be associated with the development of edema characteristic of lymphedema. **Aim:** The analysis of the promoter polymorphism of the matrix metalloproteinases genes *MMP 2*, *MMP3*, *MMP9* and their combinations in patients with secondary lymphedema.

Materials and methods: The study included 101 patients with a diagnosis of secondary lymphedema, 97 women and 4 men, median age 58 [51;65] years. Concomitant diseases in the secondary lymphedema group are hypertension 47 (46%), type 2 diabetes mellitus 19 (18.6%), hypofunction of the thyroid gland 16 (15.7%) osteochondrosis of the lumbar spine 14 (13.7%). The majority of patients with secondary lymphedema of the upper extremities underwent complex treatment of breast cancer (66 patients - 97.1%). All patients included in the study had no progression or recurrence of the malignant tumor. Informed consent for participation in the study and for molecular genetic blood testing was signed by each participant of the study. The protocol of the clinical trial was approved by the NIIKEL Local Ethics Committee (Protocol No. 127). The healthy group consisted of 339 people without signs of lymphedema of a similar age. The polymorphism of the genes *MMP 2* rs2438650, *MMP3* rs3025058, *MMP9* rs3918242 was analyzed using Real-Time PCR commercial test systems by the TaqMan probe method (Syntol, Russia). Statistical processing was carried out using a specialized application software package IBM SPSS Statistics 23 (USA) and a software package for volumetric processing of bioinformation,

including multidimensional genetic analysis. **Results.** The frequency of *MMP3-11715A5A* and *MMP 9-1562 CT* genotypes was significantly increased in the group of patients relatively healthy (OR=2.06 P=0.0353 and OR=1.71 P=0.0252, respectively) The frequency of complex genotypes *MMP3-11715A5A:MMR9-1562CC* is also increased in this group (OR=2.59 P=0.0314). On the contrary, the frequency of the complex genotype *MMP2-1306 TC:MMP3-11715A6A:MMP9-1562CC* was reduced relative to the control group (OR=0.36 P=0.0401) and are protective. **Conclusion:** Thus, the data obtained may indicate a certain significance of polymorphism of matrix metalloproteinases in the pathogenesis of secondary lymphedema of the extremities.

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01. Lymphology: Basic Sciences & Applied Technologies

The perforator-based monitoring skin island - a human model for secondary lymphedema

Martin Zimmermann ⁽¹⁾ - ***Katja Kilian*** ⁽²⁾ - ***Christoph Hirche*** ⁽³⁾

University of Heidelberg, Medical Faculty, Heidelberg, Germany ⁽¹⁾ - *BG Trauma Centre, Plastic and reconstructive surgery, Ludwigshafen, Germany* ⁽²⁾ - *BG Trauma Centre, Plastic and reconstructive surgery, Frankfurt a. Main, Germany* ⁽³⁾

The perforator-based monitoring skin island – a human model for secondary lymphedema

Secondary lymphedema results from pathological accumulation of interstitial fluid due to inadequate drainage of lymphatic fluid. The pathophysiology, underlying pathomechanisms and signaling pathways of secondary lymphedema are not well understood. Since current knowledge has been largely based on studies in animal models and to advance comprehensive basic research, the establishment of a human lymphedema model is essential.

The perforator-based monitoring skin island (PBM) in vascularized free muscle flaps is used in plastic reconstructive surgery to monitor blood flow of transferred muscle flaps. The PBM receives arterial and venous blood supply but is disconnected from the lymphatic system. We postulate that the PBM is suitable as a human model of secondary lymphedema.

In our study, tissue samples were obtained from a total of 15 patients that received tissue transfer with free muscle flaps at the BG Trauma Centre in Ludwigshafen, Germany. Excess skin tissue was collected intraoperatively and compared with the PBM from the same patient between 7 and 14 days after surgery.

Histologically, the PBM tissue showed swelling of the epidermis and dermis, smoothing of the dermis with leukocyte infiltration and loosening of subcutaneous tissue correspond to the microscopic features of lymphedema.

In the analysis of gene expressions, we were able to demonstrate on a molecular level that the PBM exhibits specific lymphedema gene clusters. The lymphangiogenic marker (PROX-1, FLT4, LYVE-1), inflammation-associated (IL-6, IL-1, IL-10, TNF-alpha, TGF-beta, IFN-gamma), typical extracellular matrix (MMP-9, CCN2, ACTA2, COL1A1) and adipogenic marker (adiponectin) genes showed alterations consistent with lymphedematous molecular changes. Further examinations at the protein level and immunofluorescence staining are planned to ensure a comprehensive analysis regarding the suitability of the model.

Our previous investigations on the PBM show similarities with the characteristics of the acute and subacute phases of secondary lymphedema. These findings support the assumption that the PBM is a suitable human model of lymphedema. The establishment of such a model will enable us, for the first time in the future, to investigate the molecular foundations of lymphedema, especially in its onset phase, using human samples. This forms the basis for a holistic understanding of the pathophysiology of human secondary lymphedema and the development of causal therapeutic concepts to alleviate the suffering of patients with chronic lymphedema.

02. Anatomy and Pathology of the Lymphatic Circulation for Clinical Practice

MILTIADES PAPAMILTIADES; A GREAT ANATOMIST AND LYMPHOLOGIST (1907-1987)

ALEXANDRE PISSAS⁽¹⁾ - MURIEL SCARATO⁽²⁾ - FRANCOISE GALLON⁽¹⁾ - OLIVIER GRAS⁽¹⁾

GENERAL HOSPITAL, 30, BAGNOLS SUR CEZE AND PONT SAINT ESPRIT, France⁽¹⁾ - GENERAL HOSPITAL, 30, TRESQUES, France⁽²⁾

MILTIADES PAPAMILTIADES ; A GREAT ANATOMIST ,A GREAT LYMPHOLOGIST (1907-1987)

A.PISSAS,M.SCARATO, F.GALLON, O.GRAS

General hospital of Bagnols sur Cèze and of Pont Saint Esprit

Faculty of medicine of Montpellier FRANCE

The authors report the history of M.PAPAMILTIADES born in 1907 and died in 1987.

He started his medical studies in Athens in 1925 was graduated MD and Phd in 1935 with the mention « excellent ».He was appointed assistant in the laboratory of anatomy of Athens till 1939.After the war , he obtained a bourse , a scholarship from the french government and came in Paris .He worked as assistant of professors ROUVIERE ,CORDIER ,OLIVIER and DELMAS was appointed as

associated professor .He came back in Greece in 1962 , director of the laboratory of anatomy of Athens .In 1968 , after the pusch of colonels he was obligated to go in Switzerland and worked till 1974 He came back after democratie was restored and was director of the laboratory of anatomy .He retired in 1977 .His fundamental research concerned cytology , as a pupil of PAPANICOLAOU with peculiar coloration .As pupil of Henri ROUVIERE his research concerned the lymphatics of lung of ovary

But the principal paper in our opinion was in 1961 in Stain technology : « injection of lymphatics with colored cedar oil , with plastic » : a solution associating 25% cedar oil,25% oil paint , 50% toluen ; just before use add 10% of ether .After the publications and work of GEROTA in the end of XIX e century , this solution represented a very great progress in anatomy ol the lymphatic system .

The authors will bring their own experience from 1974 till now .

02. Anatomy and Pathology of the Lymphatic Circulation for Clinical Practice

Combined treatment of lower limbs of patients affected by elephantiasis as results of multiple bariatric surgery

Arianna Demoro ⁽¹⁾ - **Roberto Risso** ⁽²⁾ - **Mirko Ponsini** ⁽²⁾ - **Elena Parodi** ⁽³⁾ - **Corrado Campisi** ⁽⁴⁾

Campisi e Partners, Podiatrist, Genoa, Italy ⁽¹⁾ - *Campisi e Partners, Physiotherapy, Genoa, Italy* ⁽²⁾ - *Campisi e Partners, Physiotherapy, Genova, Italy* ⁽³⁾ - *Campisi e Partners, Medical, Genova, Italy* ⁽⁴⁾

Combined treatment of lower limbs of patients affected by elephantiasis as results of multiple bariatric surgery:

The study that we are presenting deals with a clinical case of primary lymph. in the lower left limb and of lipofibromatosis in the lower right limb, involving both superficial and deep structures.

The patient had multiple bariatric surgeries with weight loss, opposed by worsening lymphatic disease: reaching the 3rd stage of elephantiasis, ulceration, movement difficulties, worsening the general conditions. When the patient first arrived we measured with the perometer a volume of 16753mL for the left leg and 20176 for the right leg. After multiple medications on several ulcerations and functional multilayered bandages to reduce the edema, the patient began to perform the CPT. After one month the clinical status of the patient has improved enough for a MLVA to the left leg. The results were astonishing, showing weight loss, decrease of edema, improved physical abilities. Volumes have decreased, with the right leg measuring 9153mL and the left leg 8670mL. The patient will have more MLVA and FLLA surgeries in order to reach a standard quality of life.

Author: Demoro A. Risso R. Parodi E. Ponsini M. Campisi C.

23. Translational Lymphology: From Basic Sciences to Clinical Implications and Therapeutic Procedures

Seromas and punctures after axillary lymph node dissection for breast cancer: the impact of per-operative and pre-operative ICG administration

Mirela Roman ⁽¹⁾ - **jean marie nogaret** ⁽¹⁾ - **pauline delrue** ⁽¹⁾ - **clarence karler** ⁽²⁾ - **veronique del marmol** ⁽³⁾ - **pierre bourgeois** ⁽⁴⁾

Institute Jules Bordet, Surgery, Brussels, Belgium ⁽¹⁾ - *HIS-IZZ Hospitals, Anesthesiology, Brussels, Belgium* ⁽²⁾ - *hospital Erasme, Dermatology, brussels, Belgium* ⁽³⁾ - *hospital Erasme and HIS)IZZ hospitals and Inst J Bo'rdet, Dermatology and nuclear medicine and vascular surgery, brussels, Belgium* ⁽⁴⁾

Background: Near Infra-red fluorescence imaging (NIRFI) with Indocyanine Green (ICG) has been shown to detect lymph leakages in patients with complete axillary lymph node dissection (CALND) for breast cancer. The current study investigates the impact of the pre-operative (Pre) and per-operative (Per) administration of ICG on the volumes (V) of liquids collected in the drains (Vd) and/or in the punctures (Vp).

Methods: Fifty-five women had one subcutaneous injection of ICG in the ipsilateral hand either the day before (n = 26) or the same day as the op (n = 29). The volumes of liquids (Vd, Vp and Vd+Vp) were compared in pre- and per-operative injections of ICG and in the function of the presence or absence of fluorescence in the axillary drains, in the axillary lymph nodes (LN) and of the per-op detection of fluorescence on the compress put in the axilla.

Results: Pre and Per groups of patients did not differ statistically. Vd in pre and per groups did not differ significantly while Vd and Vd+Vp trended to be lower in the pre-op group than in the per-op one. When fluorescence was observed in the drains, in LN, and on the compress put in the axilla, no differences between the pre and per-op ICG injected groups were observed. On the opposite, when no fluorescence was detected, Vd and Vd+Vp were significantly lower in the group with ICG injected pre-operatively.

Conclusion: ICG NIRFI enables us to detect lymph leakages and ICG injected pre-operatively seems to reduce collected volumes when no fluorescence is observed in the axilla.

23. Translational Lymphology: From Basic Sciences to Clinical Implications and Therapeutic Procedures

Volumetric flow rate of fluid delivery into interstitium during lymphotropic therapy depends on the flow rate of syringe pump, injection site, age, vibroacoustic therapy and massage

***Fahed Alzawahreh*⁽¹⁾ - *Tatyana Tsvetkova*⁽²⁾**

People Friendship University of Russia, Moscow, Russian Federation, Medical Institute, Moscow, Russian Federation⁽¹⁾ - *People Friendship University of Russia, Medical Institute, Moscow, Russian Federation*⁽²⁾

Purpose was to study the volumetric flow rate changes of fluid delivery into the interstitium by means of syringe pump during lymphotropic therapy under various conditions.

The volumetric flow rate during fluid delivery in the hip joint region and interspinous ligaments at the level of C₆₋₇ were calculated.

Objectives and methods. 6.0 and 9.6 ml/hour volumetric flow rates of syringe pump (vfrSP) were used in 3 patients aged 20, 45 and 46 years, without and with vibroacoustic therapy and massage. The patients with osteochondrosis of the cervical spine and hip joint disorders were kept for observation in polyclinic. Chondrolone liophylisate for injection (50 µg) was administered to patients lymphotropically (subcutaneously) after dissolving in 10.0 ml of normal saline. The volumetric rate was calculated as volume fluid travelled through the infusion system for every 5 minutes.

Results. Only one peak volumetric rate of administered fluid in hip joint region, from 0.12 ml/min at the procedure beginning to 0.24 ml/min by 65 minute was observed in 46-year-old patient when the vfrSP was 9.6 ml/hour. After the peak there was a gradual decrease of the index to 0.16 ml/min. Time period from 20 to 60 minutes showed a plateau with 0.16 ml/min.

At lower vfrSP, 6 ml/h, two peaks in the 15th and 75th minutes were found (0.12 ml/min and 0.17 ml/min, respectively). 20th minute performs a significant decrease of index till 0.08 ml/min. Within 30 minutes before the second peak, a plateau formed with 0.12 ml/min. All 5 minute-points of volumetric rate corresponding to 6 ml/hour vfrSP were less than those at 9.6 ml/hour.

Analysis of the volumetric rate in hip joint region at 6 ml/hour vfrSP in 20-year-old patient revealed an earlier time second peak and it 1.5 times exceeds (40 minutes and 0.24 ml/min, respectively) the same index in 46-year-old patient. The peak volumetric rate was almost 3 times higher than the initial volumetric rate, 0.07 ml/min. The plateau before the second peak was short and amounted to 10 min, the time distance between two peaks was about 30 minutes.

Thus, similar 46-year-old patient qualitative regularities were observed in 20-year-old patient in hip joint with vfrSP. However, the volumetric rate of the second peak at 6 ml/h vfrSP exceeded 1.5 times the same time point corresponding to higher vfrSP (9.6 ml/h) (0.24 and 0.19 ml/min, respectively).

We studied the influence of various physical factors, massage and vibroacoustic therapy, on the volumetric rate of fluid injected into interspinous ligaments at the C₆₋₇ level at 6 ml/hour vfrSP in 45-year-old patient. Without physical factor influence, two peak volumetric rates were also revealed (0.15 ml/min and 0.16 ml/min, correspondingly), but with a short time interval between them, at 55th and 65th minutes. Further, the volumetric rate levelled off at 0.10 ml/min.

After manual massage of the collar zone lymphotropically injected fluid performed only single peak, by 35th minute of the procedure. It reached 0.18 ml/min, which was 1.2 times higher than that of without massage. Further, the volumetric rate didn't exceed 0.12 ml/min.

The most pronounced changes were observed after vibroacoustic exposure. There were two peaks, in the 35th and 70th minutes. The volumetric rate showed 0.22 ml/min and 0.15 ml/min, respectively. Further, the volumetric flow rate was 0.12 ml/min.

Conclusion. The administration of additional fluid volume into the interstitium by means of lymphotropic therapy leads to an increase in the functional activity of the lymphatic system, which is expressed in the volumetric rate increase, which is more pronounced in hip joint region and in younger patient. Massage or vibroacoustic exposure contribute to further increase in the reserve capacity of the lymphatic system.

23. Translational Lymphology: From Basic Sciences to Clinical Implications and Therapeutic Procedures

Predictive risk factors of lymphedema occurrence in breast cancer patients

Shahpar Haghighat⁽¹⁾ - Anaram Yaghoobi Notash⁽²⁾ - Aidin Yaghoobi Notash⁽³⁾ - Zahra Omidi⁽¹⁾

Breast Cancer Research Center, ACECR, Cancer Quality of Life, Tehran, Iran (islamic Republic Of)⁽¹⁾ - Rasht Branch, Islamic Azad University, The computer engineering department, Rasht, Iran (islamic Republic Of)⁽²⁾ - Tehran University of Medical Science (TUMS), Shariati Hospital, Tehran, Iran (islamic Republic Of)⁽³⁾

Abstract:

Background: One of the prevalent breast cancer treatment side effects is lymphedema which affect patient's quality of life negatively. This study aimed to select an appropriate model to predict the risk factors of lymphedema occurrence in breast cancer patients.

Methods: This study was conducted on data of 970 breast cancer patients with lymphedema referred to a lymphedema clinic, Tehran, Iran. This study was designed in two phases: The first phase included data preprocessing, optimizing feature selection for each base learner by the Genetic algorithm, optimizing the combined ensemble learning method, and estimating fitness function for evaluating an appropriate model for predicting the risk of lymphedema. In the second phase, the influential variables were assessed and introduced based on the average number of variables in the output of the proposed algorithm.

Results: The Support Vector Machine algorithm with RBF kernel had the best medical and clinical data results regarding sensitivity (92%) and accuracy (89%). While in ensemble learning method, the sensitivity and accuracy were increased to 94% and 91%. The significant lymphedema risk factors in the proposed model consisted of the number of involved to excised lymph nodes ratio (68%), feeling of heaviness (67%), decreased range of motion (65%), the number of the excised lymph nodes (64%), radiotherapy (63%), misalignment of the dominant and the involved limb (62%), having fibrotic tissue (62%), type of surgery (62%), paresthesia (62%),

involved lymph nodes number (61%), BMI (61%), the number of chemotherapy sessions (60%), age (58%), limb injury (53%), chemotherapy regimen (53%), and occupation (50%).

Conclusion: Achieved risk factors through the confirmed model in this study can predict the likelihood of developing lymphedema with a high accuracy. Designing applications considering these risk factors can be helpful in estimating the lymphedema risk and introducing the feasible and effective preventive or therapeutic methods.

Keywords: Breast cancer, Lymphedema, Risk factors, Ensemble learning

23. Translational Lymphology: From Basic Sciences to Clinical Implications and Therapeutic Procedures

Racial and Ethnic Representation in Lymphedema Clinical Trials: A Systematic Review

Marie José Escobar ⁽¹⁾ - Valeria P. Bustos ⁽¹⁾ - Dominick Falcon ⁽¹⁾ - Erin Kim ⁽¹⁾ - Jose Foppiani ⁽¹⁾ - James Fanning ⁽¹⁾ - Samuel J. Lin ⁽¹⁾ - Dhruv Singhal ⁽¹⁾ - Bernard T. Lee ⁽¹⁾

Beth Israel Deaconess Medical Center, Division of Plastic and Reconstructive Surgery, Boston, United States Of America ⁽¹⁾

Racial and Ethnic Representation in Lymphedema Clinical Trials: A Systematic Review

Maria José Escobar, MD; Valeria P. Bustos, MD, MSc; Dominick Falcon, BS; Erin Kim, BA; Jose Foppiani, MD; James E. Fanning, BS; Samuel J. Lin, MD, MBA; Dhruv Singhal, MD; Bernard T. Lee, MD, MBA, MPH

Background: Clinical trials (CTs) are held in high regard within the medical community, as they provide the most robust evidence by minimizing the risk of systematic errors. Lymphedema has a profound health burden, reducing patients' quality of life. The generalizability of findings from CTs assessing diverse lymphedema treatment modalities hinges on the accurate representation of the target population. Thus, this systematic review aims to evaluate race and ethnicity representation in lymphedema CTs and to evaluate the breadth of diversity in the current literature.

Methods: A comprehensive systematic literature search was conducted on April 19, 2023 using the MEDLINE database, following the PRISMA protocol. All CTs published from 2018 to 2023 were included. A two-stage screening process was conducted to identify eligible articles.

Results: A total of 805 studies were initially identified. Of these, 65 articles met our eligibility criteria and were included in this review. A total of 5,023 participants were included in the analysis: 587(11.7%) males and 4,436(88.3%) females. Geographically, 24(36%) of the CTs were conducted in Asia, followed by Europe 17(26%) and North America 10(15%). Sixty-one(93%) articles addressed secondary lymphedema, of which 53(82%) were related to breast cancer. Only 9(14%) of CTs reported race or ethnicity. Of these, only 4(44%) reported race and 2(22%) reported ethnicity according to FDA guidelines. The highest represented race was White(79%; CI: 65-93%), followed by Asians(7.6%; CI: <1 – 22%) and Black(6.8%; CI: <1 – 22%). Similarly, from the studies reporting ethnicity, there was a predominance of Non-Hispanic representation(82.9%; CI: 61 – 100%).

Conclusions: There is a paucity of race and ethnicity reporting among lymphedema CTs, and minimal representation of minority populations. This lack of racial and ethnic diversity limits the generalizability of current lymphedema CTs. Thus, this study serves as a call for future studies to not only appropriately present the demographic profiles of participants, but also to develop strategies to enhance diversity in their sample.

23. Translational Lymphology: From Basic Sciences to Clinical Implications and Therapeutic Procedures

Synthesis and physiological remodeling of CD34 cells (telocyte) in reversal of fibrosis with Godoy method for lymphedema treatment

Jose Maria Pereira de Godoy⁽¹⁾ - Maria de Fatima Guerreiro Godoy⁽²⁾ - Henrique Jose Pereira de Godoy⁽¹⁾

Faculdade de Medicina de Sao Jose do Rio Preto-FAMERP, Vascular Surgery, Sao Jose do Rio Preto, Brazil⁽¹⁾ - International School of Lymphatic Therapy-Clinica Godoy, Vascular Surgery, Sao Jose do Rio Preto, Brazil⁽²⁾

Synthesis and physiological remodeling of CD34 cells (telocyte) in reversal of fibrosis with Godoy method for lymphedema treatment

Authors: Godoy JMP, Godoy MFG, Godoy HJP

Affiliation: Faculdade de Medicina de São Jose do Rio Preto-FAMERP-Brazil and Godoy & Godoy International School of Lymphatic Therapy-Sao Jose do Rio Preto-Brazil

Background: A novel type of cell underwent identification between 2005 and 2008 and was denominated the “telocyte” in 2010. In 2012, transmission electron microscopy revealed the presence of telocytes in the dermis. Objective: The aim of the present study is report changes in immunostained CD34 cells following the treatment of lower limb lymphedema using a technique Godoy method of lymphatic therapy. **Method:** A clinical study involving the evaluation of changes in immunostained CD34 cells in the epidermis and dermis (20 randomly selected histological fields) of a patient before and after intensive treatment for clinical stage II lymphedema was conducted using the

Godoy Method, which was adapted to the treatment of skin fibrosis. The evaluation involved the use of the Weibel multi-point morphometric method. Comparisons were performed using the t-test with a 95% significance level. **Results:** An important increase in CD34 cells was found with redistribution occurring following treatment. **Conclusion:** The treatment of primary lymphedema of the lower limbs resulted in the clinical reversal of fibrosis and an increase in the number of immunomarked CD34 cells.

Key words: Lymphedema, telocyte, fibrosis, histological.

23. Translational Lymphology: From Basic Sciences to Clinical Implications and Therapeutic Procedures

Physiological stimulus of the synthesis of proteins of the basement membrane leading to its reconstruction skin in treatment of lymphedema by Godoy Method

Jose Maria Pereira de Godoy⁽¹⁾ - Maria de Fatima Guerreiro Godoy⁽²⁾ - Henrique Jose Pereira de Godoy⁽¹⁾

Faculdade de Medicina de Sao Jose do Rio Preto-FAMERP, Vascular Surgery, Sao Jose do Rio Preto, Brazil⁽¹⁾ - Godoy & Godoy International School of Lymphatic Therapy-Clinica Godoy, Vascular Surgery, Sao Jose do Rio Preto, Brazil⁽²⁾

Physiological stimulus of the synthesis of proteins of the basement membrane leading to its reconstruction skin in treatment of lymphedema by Godoy Method

Abstract

Background: Basement membranes (BMs) are thin lamina of extracellular matrix that provide support for epithelia, muscle fibers, blood vessels and peripheral nerves.

Objective: The aim of the present study was to report the remodeling of the basement membrane through physiological stimulus during the treatment of fibrosis in a lower limb with lymphedema. **Method:** A clinical trial was conducted involving the evaluation of the basement membrane in skin biopsies before and after treatment for clinical stage II lower limb lymphedema using the Godoy Method® for the reversal of lymphedema and skin fibrosis. The samples were stained with Gomori's reticulin stain and evaluated using Weibel's multipoint morphometric method at the Clinica Godoy-Brazil in 2022. Prior to treatment for lymphedema, rupture and important discontinuity of the basement

membrane was found. After treatment, structural continuity and thickness had returned to the regions of previous rupture. **Results:** The difference was statistically significant ($p < 0.05$, paired t-test). **Conclusion:** The present study reports that physiological stimuli targeting the lymphatic system lead to the clinical reversal of fibrosis as well as stimulate the synthesis of extracellular matrix proteins and the reconstruction of the basal lamina of the skin.

Key Words: Physiological stimulus, Synthesis of proteins, Basement membrane.