

Abstracts from the 7th Joint International Lymphoedema Framework and Italian Lymphoedema Framework Conference

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This meeting was held in the beautiful city of Siracusa, Italy; a world heritage site. Of particular relevance to this meeting is the rich and deep history and involvement of Italian scientists, anatomists and clinicians in the creation of our knowledge about the lymphatic system, its structure and function, and of the impact of its failure on the patient. At this meeting, we shared many stimulating ideas, new research and looked towards innovative solutions to the many issues faced by healthcare practitioners who treat people with lymphatic dysfunction and issues faced by those who receive treatment for their conditions. We looked across the lifespan from children to the elderly and at the way international research and findings can contribute to improved patient outcomes. Below we have selected a range of abstracts to reflect these new solutions, directions and solutions. We hope they lead you along a pathway to improved knowledge and outcomes for you and your patients.

Physical treatment in lower limb oedema and cardiac implications: pro-bnp vs e.f.

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Introduction: Oedema of the lower limbs is frequently found in heart failure, especially in elderly subjects as bilateral and symmetrical oedema of the lower limbs. The physical treatment, in these conditions, can trigger acute crisis of 'heart failure' if the intensity of the same is not 'calibrated' on the heart compliance. Until recently, in this sense, an important predictive significance was attributed to cardiac ejection fraction (EF); actually, the real indicative factor of the cardiac compliance is the Pro-Brain natriuretic peptide (PRO-BNP), the value of which is indicative both from the functional point of view of the heart and for the directions of physical treatment.

Materials and Methods: EF and PRO-BNP was tested in a group of 110 patients with bilateral oedema of the lower limbs, of mixed genesis (65 females and 45 males, aged between 13 and 79 years, mean age 67 years).

Results: We found abnormalities in EF values in 15.5% of subjects. The PRO-BNP values, on the contrary, appeared altered in 86.1% of the subjects examined.

During the physical treatment of EF, values remained essentially unchanged while the PRO-BNP rose up during the first sessions of about 45% (25–115%) to return to normal values at the end of treatment in 79% of subjects with baseline alterations.

Conclusions: PRO-BNP is an important value in diagnostic and in monitoring the physical treatment in patients with bilateral lower-extremity oedema due to central and peripheral vascular problems.

Investigating the effects of lymphatic drainage therapies using near-infrared imaging

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Background: Lymphoedema is a chronic peripheral swelling caused by a dysfunction of the lymphatic system, leading to discomfort and loss of limb movement. Therapies to treat or manage lymphoedema have limited evidence, partly due to a paucity in objective measures.

Aim: To determine whether physical therapy and compression garments affect lymphatic behaviour using near-infrared imaging.

Methods: Nine healthy volunteers (age 22–58 years) underwent near-infrared fluoroscopy using a micro-dose (50µL, 0.05%w/v) of indocyanine green to quantify lymphatic behaviour before and after a 15-minute period of manual lymph drainage followed by compression garment (Juzo®, UK) application. Images were taken at the forearm and elbow after each intervention. Lymphatic function was defined by the number, size, displacement and speed of lymph packets. There was successful delineation of dermal lymphatic vessels shown in the imaging.

Conclusion: Lymphatic activity increased following manual lymphatic drainage and compression garment therapies. NIR fluoroscopy has the potential to provide an insight into lymphatic behaviour and an objective means to test the efficacy of interventions.

Pocket ultrasound device versus standard ultrasound device for imaging of subcutaneous tissue in lower lymphoedema patients

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Introduction and aim: Pocket Ultrasound Device (PUD) is an innovative method to assess subcutaneous tissue (ST) that could be used instead of Standard Ultrasound Device (SUD), which is also useful, but has its limitations. We compared the image quality of SUD with PUD for ST in lower lymphoedema patients (LLE).

Methods: Twenty legs in 10 women with LLE were examined. Their median age was 59 years old (range 41–81) and they were all secondary, ISL late II. A physician of lymphoedema got ultrasound images on the thigh and leg, then, a researcher analysed these images qualitatively. The images of dermal layer and deep fascia to define ST were classified as poor, fair, or good. Subcutaneous echogenicity, echogenic line and echo-free space (EFS) were assessed. All protocols were approved by the ethics committee at Kanazawa University (No. 587).

Results: We investigated 120 ultrasound images from 10 participants. The percentage of “good” by PUD was higher than SUD (PUD: 68.9%, SUD: 53.4%) in dermal layer, on the other hand, PUD was lower in deep fascia (PUD: 77.5%, SUD: 81.0%). Echogenicity showed that the 11.7% in PUD was “low”, while all images showed “increased” in SUD. In echogenic line, 73.3% in PUD showed “clearly”, compared to 50.0% in SUD. In EFS, 5% in PUD showed “free-space”, while 13.3% free-space in SUD.

Conclusions: PUD will be able to define ST and able to measure thickness of ST. However, it has a limitation in assessing the contents of ST to clarify the pathological condition in LLE.

Deep infrared imaging to identify venous impairment after breast cancer surgery

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Introduction: Breast cancer-related lymphoedema

(BCRL) is commonly attributed to axillary lymph node dissection (ALND) and reduction of lymph flow. Impairment of the axillary vein seems to contribute also to BCRL, leading to a deep pitting oedema of hand and forearm. When a patient with axillary vein impairment stands up, hand skin looks rapidly hyperaemic, due to a vasodilation of the capillaries. This vascular situation may result from removal of the fatty tissue containing lymph nodes, and disruption of the good emptying of the axillary vein. The orthostatic intermittent venous stenosis induces collateralisations, which are derivative evidence of the axillary vein impairment. We highlight them using an original and easy procedure, based on a deep infrared imaging (DIRI) device.

Materials and Methods: A total of 100 women were recruited, 50 BCRL patients and 50 healthy women as a control group. In all subjects, we performed visible light and DIRI pictures of the thorax, including neck, shoulders and upper arms. Images were mixed and screened by three blind operators. The operators screened for differences in thermograms, such as asymmetric and collateral pathways.

Results: The DIRI coupled with our reading grid seems to be specific and sensitive enough to identify BCRL patients with asymmetric collateralisation of the axillary vein.

Conclusion: DIRI and its reading grid seems to be a useful tool in daily clinical practice to evaluate the haemodynamic changes of the axillary vein in BCRL patients. This evaluation gives us more insight in the (future) development and eventual treatment of BCRL.

Results: At the end of treatment it was observed reduction in limb circumferences, proportional to the clinical stage, average reduction of 17% of the VAS value, average reduction of suprafascial thickness of 27%.

Perceptions and attitudes of people undergoing lymphatic venous anastomosis

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Introduction: In September 2015, a 3-year national programme for people with mild/moderate lymphoedema to access Lymphatic Venous Anastomosis (LVA) commenced in Wales. A maximum of 42 people can access this innovative

surgery on the NHS per annum. Each of the seven Health Board Lymphoedema Clinical Leads, are the gatekeepers in referring eligible patients for LVA screening. Limited in-depth qualitative data exists in establishing the impact of LVA on quality of life. This clinical research study was funded by a Tenovus Cancer Care Grant.

Aim: The aim of this study was to qualitatively explore the impact of LVA on people with lymphoedema health and wellbeing.

Methods: Following ethical approval, 16 participants eligible for LVA surgery were recruited via purposive sampling. To explore impact on health and wellbeing, in-depth digitally recorded interviews were completed pre- and 6-months post-LVA surgery. Constant comparison analysis (Green and Britten, 1998) was used to investigate the data.

Results: Key findings before LVA surgery included: ‘impact of living with lymphoedema’, ‘being different’ and ‘fear of the future’. Post LVA, the identified themes were: ‘feeling lucky’ and ‘returning to former self’.

Conclusions: All but one participant reported that LVA has had a positive impact on health and wellbeing; even those still wearing compression garments. The daily use of compression garments on people’s lives must not be underestimated. It is vital that healthcare professionals ascertain the effect garments will have on work, hobbies and relationships. Many of the participants recognised their need for psychological support.

New surgical options for the treatment of advanced stages of peripheral lymphedema

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Background: Development of microsurgical techniques has significantly advanced the field of lymphology and the treatment of lymphoedema.

Methods: Our “single-site” microsurgical technique identifies, by Patent Blue Dye/Fluorescent Microlymphography (PDE Test), the lymphatics in the axillary or groin and completes derivative multiple lymphatic-venous anastomoses (MLVA). In cases of advanced lymphoedema, we use a recently developed Fibro-Lipo-Lymph-Aspiration technique with a Lymph Vessel Sparing Procedure (FLLA-LVSP) where microlymphography techniques highlights the lymphatic pathways and the excess adipose tissue is carefully aspirated.

Results: With “single-site” MLVA, 4,000 patients obtained significant reductions in excess limb volume of over 85%, with an average follow-up of 15 years plus. Over 87% of patients with earlier stages of disease progressively stopped using conservative therapies and 42% of patients with later stages decreased the frequency of physical therapies. For 250 advanced cases involving the upper limb, there was an average pre-surgery excess volume of 20.19%, which reduced to 2.68% after the FLLA-LVSP (Z-score = -6.90, $P < 0.001$). Similarly, for the lower limb, there was an average pre-surgery excess limb volume of 21.24% and a reduction to 2.64% postoperatively (Z-score = -3.57, $P < 0.01$).

Conclusion: MLVA techniques when performed at a single-site produce excellent outcomes in the treatment of lymphoedema, giving the possibility of complete restoration of lymphatic flow in the early stages of when tissue changes are minimal. In cases of advanced lymphoedema, the FLLA-LVSP is efficient with immediate cosmetic results. More importantly, the removal of excess tissue is completed without further damage to lymphatic vessels.

Long term results of circumferential suction-assisted lipectomy in the treatment of primary and secondary end-stage lymphoedema of the leg in 88 consecutive patients

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Background: The treatment of end-stage lymphoedema of the leg is challenging, especially when conservative treatment fails. Circumferential suction-assisted lipectomy (CSAL) is a treatment option for end-stage lymphoedema of the leg.

Aims of study: To evaluate the results of CSAL treatment in end-stage primary and secondary lymphoedema of the leg, with a 2-year follow-up.

Methods: This was a descriptive study of patients treated with CSAL for unilateral chronic irreversible lymphoedema of the leg. Compression therapy was resumed after surgery. Leg volumes were measured before surgery, and at 1, 6, 12 and 24 months after the procedure.

Results: A total of 47 patients with primary lymphoedema had a median preoperative volume difference between affected and unaffected legs of 3,686 (IQR 2,851–5,121) ml. Two years after surgery, this volume difference

was reduced to 761 ml, a 79% reduction. In the 41 patients treated for secondary lymphoedema, the median preoperative volume difference was 3,320 (IQR 2,533–4,783), decreasing after 2 years to -38 ml (a 101% reduction). A larger preoperative volume difference and the male sex of the patient significantly negatively influenced the final outcome after 2 years. The outcome was not related to BMI or any other patient characteristics.

Conclusion: CSAL is safe, effective and the method of choice for treating both primary and secondary lymphoedema of the leg with excellent long-term follow-up results. Male patients had a noticeable larger volume difference after 2 years versus their female counterparts, emphasising the need for a more proactive follow-up schedule.

Lipofilling of the axilla to reduce secondary lymphedema after axillary lymph node dissection

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Introduction: Upper-limb lymphoedema remains a frequent complication (3–60%) of axillary lymph node dissection (ALND) for breast cancer. Part of these lymphoedema present also venous impairment. During surgery, adipose tissue surrounding the axillary vein is removed and the axillary sheath can also be damaged. This anatomical disruption could reduce the local hemodynamic condition, and increase microvascular filtration at the distal part of the affected limb. Patients with a venous impairment after ALND present clinical signs that allows us to identify them. In order to reduce their oedema, we propose an original and simple surgical approach that could partially restore the axillary hemodynamic impairment.

Materials and Methods: BCRL patients with positive clinical signs for axillary hemodynamic changes underwent lipofilling under the axillary vein. Patients remain without any treatment nor sleeves during 10 days after surgery. Precise volumetry was performed the day before, the day after and 10 days after surgery. Subjective symptoms were also evaluated.

Results: 49 BCRL patients underwent lipofilling surgery. Oedema volume reduced significantly in the majority of patients. Subjective symptoms like heavy arm, numbness, and functional impairment of the upper limb in daily activities started to decrease directly after the operation. After 36 months of follow up, no complications were recorded.

Conclusion: In selected BCRL patients, lipofilling under the axillary vein improves local hemodynamic, reduces distal hyperfiltration and consecutively reduces part of the oedema. Results of this pilot study need to be empowered by multicentre studies.

“Lymphaletics”: overcoming barriers for children with lymphoedema

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Aims: Primary lymphoedema in children is relatively rare and poorly recognised, often resulting in long delays in referral to appropriate treatment centres. This inevitably leads to detrimental effects on the physical and psychosocial wellbeing of such children and their families (Todd et al, 2010). To try and re-dress this, The Children’s Lymphoedema Special Interest Group (CLSIG) has developed dedicated events (Lymphaletics) for children with lymphoedema to encourage physical activity and social interaction, and to provide a source of parent-to-parent support.

Description: The events have been designed to provide children with lymphoedema (and their families) to meet each other with a similar condition. In a supportive/safe environment, the days provide a mixture of fun-filled exercise-based activities including team games, water and sensual therapies, alongside educational seminars, an arena to meet the manufacturers and a network for everyone to maintain contact after the day is over.

Outcome: Three events (held biannually) have enabled lymphoedema specialists to address some of the problems facing children with lymphoedema. Quantitative data of the days is gathered, but positive qualitative data is also captured through an online survey tool to demonstrate how beneficial the days have proved to be for the children, siblings and parents alike.

Evaluation of impact: Provision of the ‘Lymphaletics’ days has been extremely well received. Mixing with other children with similar problems has increased confidence to try new exercise/activities so helpful in managing lymphoedema and has generated a network of parent contacts enabling them to keep in touch and share experiences.

Keloid/hypertrophic scarring: do they impact on the lymphatic system and lymphoedema risk?

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Background: Descriptions of the mechanisms involved in the pathogenesis of lymphoedema vary widely. A major cohort affected by lymphoedema are those who undergo breast cancer treatment with adjunct therapies. There is an estimated pooled incidence of almost 17% of unilateral arm lymphoedema in this cohort, with peak incidences occurring ~24 months' post-treatment/diagnosis. This could be attributed to an increase in mechanical occlusions or pulsatility restrictions of existing lymphatic vessels, due to aberrant fibrotic changes within, or extending from the wound.

Results: Specific mechanisms for keloid scarring development are yet to be determined. However, pathogenetic features suggest that the immune system plays a pivotal role in keloid development and, perhaps, lymphatic transport. Currently, treatment for keloid scarring is limited. However, a 2015 study of 32 patients by Kawamura et al noted that 24% of Asian patients receiving intra-operative radiotherapy for breast cancer developed hypertrophic scarring within a 5-year follow-up period, although no clinical lymphoedema was reported. They were unable to develop reliable predictors for scar development, but noted that tension was pivotal.

Conclusion: It is possible that lymphoedema may be caused by excessive deposition of fibrotic scar tissue, especially when cancer treatments include node removal and/or adjunct therapies, such as radiotherapy. It may be that fibrotic induration causes an alteration in the functional capacity of lymphatic vessels. Therefore, a focus on literature with respect to both lymphoedema and keloid/hypertrophic scarring, and the correlation between the two, is needed. Limited data/research is available at this time, details will be presented at the meeting.

Lymphedema associated with everolimus in a renal transplant recipient: the efficacy of complete decongestive therapy

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Background: Lymphoedema is an increasingly observed complication of rapamycin inhibitors, mostly due to sirolimus therapy. Herein, we report a renal recipient with everolimus-induced lymphoedema of upper extremity. A 57-year-old white female who received a living-related kidney transplant 2.5 years ago, presented with left arm lymphoedema since 5 months. Her immunosuppressive regimen consisted of high-dose everolimus (mean daily/dose: 5.25 mg) and corticosteroids. Venography and duplex ultrasound were normal. Lymphangioscintigraphy revealed delayed lymphatic drainage in the left upper limb. She also underwent mammography and breast-ultrasonography to rule out breast cancer. She had grade 2 lymphoedema with Stemmer-sign positivity on the left arm and hand. The dose of everolimus was decreased and she received CDT comprising; skin-care-education, manual-lymphatic-drainage, multilayer-bandaging and exercises for 3 weeks, as a total of 15 sessions.

Results: The difference between right and left upper limb volumes and percentage of volumes were decreased significantly at the end of CDT phase 1 (1,842 cm³(R) and 2,725 cm³(L) vs 1,818 cm³ (R) and 2,196 cm³ (L), 47.9% vs 20.8%). The DASH scores were assessed as 77.3 and 65, before and after treatments respectively. There was also significant improvement in quality-of-life(QoL) scores assessed by LymphQOL. The patient was prescribed a suitable pressure garment and continued self-massage and exercises after the discharge.

Conclusion: The early recognition of lymphoedema as a side effect of everolimus therapy is important, in order to avoid the development of severe clinical complications. CDT for a duration of 3 weeks is effective in the improvement of lymphoedema, functional status and QoL in patients suffering from this chronic condition.

Identifying the lymphatic pathways and presentation of the piezo1 mutation using nirx imaging

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Background: PIEZO1 is a newly recognised gene responsible for generalised lymphatic dysplasia (GLD) and is a rare form of primary lymphoedema. It involves four limbs often with additional pulmonary and intestinal disturbances. A patient was referred to the lymphatic mapping clinic to assist with treatment.

Aim: Lymphofluoroscopy, has advanced as a diagnostic and imaging tool in recent years. This technique provides the ability to identify lymphatic abnormality, individual lymphatic drainage pathways, functional lymphatics and map them accordingly. This case study will discuss the unique images and pathway seen following the imaging of this a patient with PIEZO1.

Case description: Following consent, patient received an intradermal injection of 0.1 ml of ICG into the first interdigital web space of the worst foot and contralateral arm. Normal protocol was followed and deviated on as drainage was not as expected.

Discussion: This first mapping of PIEZO1 showed an unusual pathway to the arm via the non-anatomical pathway draining to the palm of the hand and arriving at the axilla. The appearance of the pathway was enlarged with wider vessels. The leg, showed dermal backflow to the dorsum and planter sole and popliteal, consistent with lymphoscintigraphy. This case study will use video evidence to describe the particular pathways and possible adaptations to management to achieve better treatment outcomes. These pathways maybe unique to the patient with this gene mutation.

Obstructive lymphedema of lower limbs can be successfully controlled by silicone tube implants replacing obliterated lymphatics — six-years follow-up

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Background: Obliteration of lymphatics recognised as lymphoedema is followed by stasis of oedema fluid with dilatation of intercellular space. The question arises whether decongestion of oedematous tissue can be accomplished by implantation of artificial channels replacing function of lymphatics and support tissue fluid flow by application of external compression.

Aim: To follow effect of silicone tube implants replacing obliterated collecting lymphatics.

Material and methods: Study included 60 patients with lymphoedema of lower limbs stage III and IV. All patients developed oedema after hysterectomy and radiotherapy with inflammatory episodes, five had infectious skin incidents in the

past. Lymphoscintigraphy showed lack of flow of tracer from foot to the groin. Three medical grade hydrophobic silicone tubes o.d.3.2, i.d. 1.8mm, perforated every 2cm, were implanted subcutaneously from mid-calf to hypogastrium. Subcutis and node fragments were taken for on-plate bacteriology. Elastic stockings grade II and 2 weeks of intermittent pneumatic compression were applied postoperatively.

Results: After 3–6 years, mean decrease in circumference in mid-calf was from 1.5–5 cm (3–17%) and increase in elasticity by 7–23%. On lymphoscintigraphy tracer was seen in tubes or around them. On ultrasonography, accumulation of fluid around tubes could be shown. In four cases inflammatory episodes at calf and hypogastric end of implant were observed. Retrospective analysis of bacteriology from time of implantation revealed presence of *Proteus*, *Acinetobacter* and *Neisseria*.

Conclusion: Silicone tube implants in lymphoedematous is a low-invasive effective method for decompression of obstructive lymphoedema. Bacteriology of deep tissues at time of implantation is helpful for controlling infective inflammation episodes with specific antibiotics.

ICF core sets: a new way of status-reporting for the lymphedema patient

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Introduction: For understanding the challenges of patients with lymphoedema, it is important to describe functioning and to measure the effectiveness of treatment in changing functioning. The International Classification of Functioning, Disability and Health (ICF) offers an international framework

to classify functioning of persons in their personal environment. ICF Core Sets are lists of selected ICF categories concerning those important aspects of functioning that are most likely to be affected by a specific health problem or disease. These Core Sets make it easier and faster to describe and communicate the patient's problems and to define treatment goals. Furthermore, they are available to healthcare providers of all professions, researchers, health insurance companies and policymakers.

Description: In this presentation a new way of reporting the functional status of the lymphoedema patient will be shown. ICF Core Sets can be a guideline in the clinical reasoning to come to treatment goals and monitor the treatment process.

Implications: By means of an electronic tool (e-tool), standardised data of patients' functioning and environmental factors can be systematically collected and taken in at a glance.

Recommendations: Existing electronic patient files should be remodeled including the ICF Core Sets for lymphoedema.

Management of venous edema and lymphedema by general practitioners

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Introduction: Chronic venous insufficiency (CVI) is a common cause of secondary lymphoedema. The appropriate management of leg swelling provided by primary care is important.

Aims: To evaluate the management of edema and lymphoedema in CVI provided by general practitioners (GPs).

Methods: The 2-center cross-sectional study involved 445 patients with the presence of the oedema of the legs diagnosed and treated by GPs during a one-month period. The serious edema of the lymphoedema type was noted in 1.6% patients. Demographic and clinical data were obtained by physical examinations and standardised interviews.

Results: The GPs' management of patients with oedema and lymphoedema of the legs according to gender and age showed virtually no gender- or age-related differences. The management of patients included different types of treatment; venoactive drugs were recommended to 91.5%, lifestyle advice to 89% and compression therapy included bandages and stockings to 52.8% of patients. The other types of treatment such as physical therapy, topical therapy or exercises were prescribed to 7.4% patients. Dual and triple combination therapies were the most frequently recommended types of treatment. More than half of patients were referred to a vein specialist.

Conclusions: Despite GPs had undergone a course in phlebology before they were included in the study, patients did not receive complete management of their condition, such as compression and physical therapy, whether they had oedema or lymphoedema. Continuous training of GPs and clinical guidelines for the management of peripheral oedema may help GPs to make adequate decisions.