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Lymphedema treatment by means of an electro-medical device based on bioresonance and vacuum technology: clinical and lymphoscintigraphic assessment

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Aim. **The aim of the study was to assess efficacy and safety of a new medical device, based on electric microcurrents and vacuum mechanism, on lymphedema of the lower limbs.**

Methods. **This was an observational clinical and instrumental study was performed on eight patients (2 males and 6 females, mean age 40.5 years), affected by secondary (3) or primary (5) lymphedema of the lower limbs. Ten daily sessions with an electro-sound wave and vacuum medical device were performed. Patients did not discontinue antecedently worn compression stockings. Lymphoscintigraphy of the lower limbs was performed before and after the treatment and an independent observer scored the images. Circumference tape measurement and relative volumetry were calculated before and after the treatment.**

Result. **Total limb mean volumetry decreased from 9145 cc (±3439 SD) to 8714 (±3307) after 10 sessions (5% improvement); reduction in the lower leg volumetry was 8%. Ankle and mid calf mean circumference (in cm) decreased from 27.7 to 27.2 and from 36.2 to 35.2. Popliteal and inguinal lymph node visualisation at lymphoscintigraphy improved of 72%, 41%, 95% and 192% and of 0%, 33%, 110% and 245% respectively, 5', 45',120' and 180' after the injection. Radiotracer ascension along the leg and the thigh increased respectively of 48% and 33%, 39% and 64%, 50% and 62% and finally of 55% and 78% at the same intervals. Dermal back flow did not significantly vary till 45', whereas it improved of 25% both 120' and 180' after injection. No side effects were highlighted during the treatment.**

Conclusion. **In this observational study the application of a medical device, based on bioresonance and vacuum mechanisms, on limbs with lymphedema proved to be both safe and effective in terms of limb volume reduction and of lymphoscintigraphy parameters.**

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Key words: **Lymphedema - Lower extremity - Lymphatic system.**

Lymphedema (LYM) is an abnormal accumulation of extracellular (tissue) fluids caused by an organic and/or a functional deficit of the lymphatic system and it mostly affects upper or lower limbs. LYM generally implies both a locoregional increased protein content in the interstice and a natural tendency towards fibrosis and fat deposition in the diseased areas. Primary LYM may be characterised by morphologic or functional abnormalities in lymph nodes and/or in lymphatic vessels; secondary LYM is mostly caused by induced alterations of the lymphatic drainage which may be consequence of lymphadenectomy, lymph node and/or lymph vessel lesion in oncologic surgery, in other kinds of surgery (*e.g.*, saphenectomy for cardiac bypass), or which may be caused by infections, burnings, radiation injury, etc.

Notwithstanding its estimated wide diffusion worldwide,[1] LYM diagnostic and therapeutic approach is still based on procedures and modalities which have been proposed several years ago, and the outcomes of LYM therapy may be suboptimal and not long-lasting in a certain proportion of patients, especially when non-compliant.[2]

Lymphoscintigraphy (LSG) has been recognised as the cornerstone method to detect any significant lymph flow impairments. While LSG may clearly depict any functional derangement of the lymphatic drainage, LSG imaging of morphology of the lymphatic structures is still approximate with the actual instruments. Duplex ultrasound investigation proved to be of help in the diagnostic approach for LYM and more in general in any case of swollen limb.[3]

In the past years tape measurement and water displacement have been validated for edema investigation and limb volume assessment.[4] More

recently a major reappraisal of limb volumetry and of edema assessment was highlighted thanks to new methods, such as optoelectronic devices, laser-based instruments and especially multi-frequency bioimpedance spectroscopy.[5, 6] Concerning treatment of LYM, a multifaceted holistic approach is currently used in the vast majority of the cases, including manual lymphatic drainage, compression therapy, proper exercises, skin care and drugs.[1, 2, 7, 8] A few electro-medical devices (such as sequential intermittent pneumatic compression, magnetic fields coupled with hyperthermia and vibration,[9] laser [10] have been introduced since the eighties, with some contrasting evidence about their efficacy. In the latest years a medical device has been proposed in LYM treatment,[11-13] on the basis of the proprieties of the electric microcurrents which generate bioresonance sound waves and of the vacuum effect on connective tissues. The electro-sound waves interact with tissue moleculae in different and partially known manners.[14-16] Basically currents characterized by low intensity and low frequency have been shown to generate resonance in biological tissues.[12, 14] Bioresonance theory was popularised by two German doctors, R. Voll in the 1950s and subsequently F. Morell in the 1970s.[17] Basically it was discovered that all biological structures may resonate at certain frequencies, and this phenomenon is able to induce biochemical reactions and interactions among cells. The electromagnetic oscillations and signals which are at the basis of this biological activity have been used to configure the bioresonance therapy, with the aim to modulate positively the electromagnetic fields of the targeted biological structures.[17] Through the emission of microcurrents, it has been postulated a subsequent induction of resonance (hence the name of "electro-sound" waves) of the encountered bio-structures.

In LYM patients bioresonance therapy has been applied in recent years and an augmentation of protein/lymph fluid recovery and transport within the lymph system has been proved by a few authors.[12, 13]

The present, investigated medical device conjugates the bioresonance sound waves with the vacuum-suction principle. The latter method is based on negative atmospheric pressure and it has been proposed more than 40 years ago mostly for draining wounds and postsurgery drainages. More recently vacuum assisted closure of skin ulcers has been popularized in medical literature; also the vacuum suction method has been applied to the skin and subcutaneous layers, resulting in an improvement of connective tissue elasticity [18] and lymph vessel profileration.[19]

The authors aimed at assessing efficacy and safety of this electro-medical device (EMD), which is based on electro-sound wave and vacuum mechanisms, in LYM treatment of the lower limbs through a clinical and instrumental evaluation. An observational study has been performed to detect limb volume changes, and furthermore to detect any qualitative/quantitative changes in the lymphoscintigraphic examination after a short-term protocol with this specific EMD.

Materials and methods

— This clinical series included eight patients (two males and six females, mean age 40.5 years, SD ± 17 years) affected by secondary (three patients) or primary (five patients) lymphedema stage III (ISL classification) of the lower limbs (6 cases in the left limb and 2 cases in the righty one). Prior to the start of the protocol patients had a one month wash-out period, where no lymphatic treatment was allowed. Conversely compression stockings were worn by all patients at least one month before the beginning of the treatment and also throughout all the observational study period. The volumetric controls showed no significant changes caused by the compression treatment in the last 30 days prior to the start of the therapeutic protocol.

— The inclusion criteria were represented by primary or secondary LYM of the lower limbs stage III as to ISL classification,[1] while the exclusion criteria included: 1) pregnancy; 2) active neoplasms under treatment; 3) patients with implanted metal device/s (*e.g.*, pace-maker); 4) severe heart/liver/kidney disease; 5) acute deep or superficial vein thrombosis; 6) acute dermatolymphangioadenitis (*e.g.* erysipelas, lymphangitis).

— All patients were measured as to their body mass index (BMI) and they were instructed on the necessity to maintain their typical life style

(*e.g.*, diet, ambulation, work activities etc.) during the treatment interval, in order to minimise any bias deriving from possible factors which may alter lymphatic drainage.

— After the wash-out period, at T0, all patients underwent a complete and standardised LSG examination of the lower limbs. 1-7 days after the first LSG (T1) each patient underwent volumetry of the treated limb by means of tape measurement and through the following truncated cone formula:

— Volume of each segment of truncated cone

$$\frac{h\,(C1 \times C\,1 + C\,1 \times C2 + C2 \times C2)}{12\,\pi}$$

Where C1 is the most distal circumference (*i.e.*, at the malleolar level), C2 is the circumference immediately above C1 and Π is 3,14. The sum of the single truncated cone volumes results in the total volume of the limb.

Immediately after the limb volume calculation, each patient started the treatment protocol with the EMD during the twelve days period.

The investigated EMD (Flowave 2) generates low-frequency low-intensity microcurrents (of amplitude between -12 V and + 12 V), which produce mechanical sound waves of low frequency (like infrasound). From the physics point of view, sound waves are able to generate resonance of different biological structures (bioresonance), including the lymph proteins. Microcurrents are delivered with a carrier frequency which ranges from 0.31 to 6.16 Hz and present a modulation between 400 and 2120 Hz. In each session the two physiotherapists used two maniples and eight electrodes to deliver the electro-sound waves and to generate the vacuum action over the affected areas.

Following the main lymphatic pathways of the lower limbs (*e.g.*, along the great saphenous vein territory and at the groin) (Figure 1), the treatment was performed once a day for ten standardised sessions of about one hour, on an outpatient basis within a 12-day period. Immediately after the end of the last (10th) session (T2) all patients repeated the limb volumetry by tape measurements.

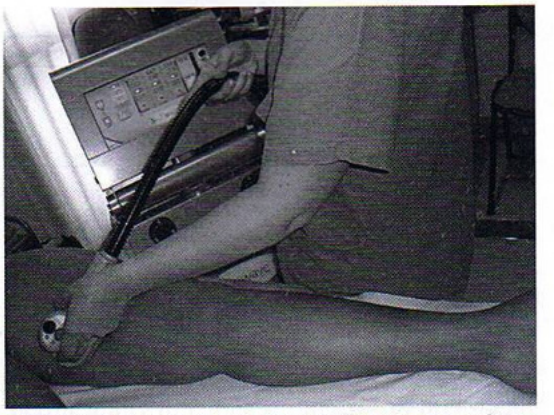

Figure 1.—Electro-medical device application on a lower limb.

Within seven days after the completion of the treatment (T3) all patients repeated a detailed LSG of the lower limbs. LSG was always performed by the same operator employing 74 MBq of 99Tc-nanocoll, and images were taken by means of a Gamma Camera Basicam-Siemens in plane mode.

LSG qualitative images and quantitative results were reviewed and scored by an independent observer (E.C.) on the basis of a visual analogue score (VAS) system with 1 (worst) to 10 (best) mark.

More in detail the following parameters were scored: 1) radioisotope progression in the leg and in the thigh; 2) proximal (inguinal and popliteal) lymph nodes visualisation; 3) dermal back flow (lymph stagnation). The assessment of radioisotope progression was based on the progressive visualization (and subsequent scoring) of the lymphatic pathways 5', 45', 120' and 180' after the injection. The 1-10 scores (Table I) of the three parameters as to above (1, 2, 3), were included in an excel (R) software file. Subsequently a mean value for each parameter at the differ-

TABLE I.—*Visual Analogue Scoring system for lymphoscintigraphic findings.*

SCORE	Lymph node Visualisation	Radioisotope Progression	Dermal back flow
1	Non visible	Absent	Present and diffused
5	Visible but not as normal	Visible but not as normal	Present in a low extent
10	Visible	Normal	Normal

TABLE II.—*Circumferences/volumes.*

	Pretreatment (values in cc ±SD)	Post-treatment (values in cc ± SD)
Volumetry	9145.52±3439.34	8714.48±3307.88
Ankle circumference	27.72±4.49	27.23±4.48
20 cm from ankle circumference	36.18±12.20	35.17±12.05
60 cm from ankle circumference	52.67±9.81	51.80±9.31

ent time intervals and for each segment of the limbs was entered, both for pre-treatment and for post-treatment figures. Finally the resulting changes of the mean values were transformed in percentages and the statistical analysis was applied to the entered data through excel (R) software.

Patients were asked to report any side effect or adverse event occurring during the treatment period and about their overall acceptance of the therapeutic sessions.

Results

All patients completed the scheduled protocol and no significant change in their BMI was highlighted at the end of the study.

A significant decrease of the total lower limb volumetry has been recorded and more in detail mean volume of the affected limb was 9145 cc (±3439 SD) before the treatment and 8714 (±3307) after completion of the treatment, which corresponds to 431 cc (-5%) difference. As to the localization of pre-post-therapy edema, the lower leg area showed a more pronounced reduction (8%) than the total volume of the limb (5%). Table II details the figures related to circumference/volume changes.

After the scheduled treatment, lymphoscintigraphic investigation showed an overall significant improvement of the various parameters which were investigated, concerning both the inguinal/popliteal node stations, and the radiotracer progression along the limb at various time intervals (Figure 2). Dermal back flow was scored as basically stable in the early part of the post-therapy investigation, while later time intervals showed a moderate improvement.

With reference to the detailed data of LSG, popliteal lymph node visualisation improved of 72%, 41%, 95% and 192% at 5', 45',120' and 180' interval time after the injection; similarly the inguinal lymph nodes were imaged after the treat-

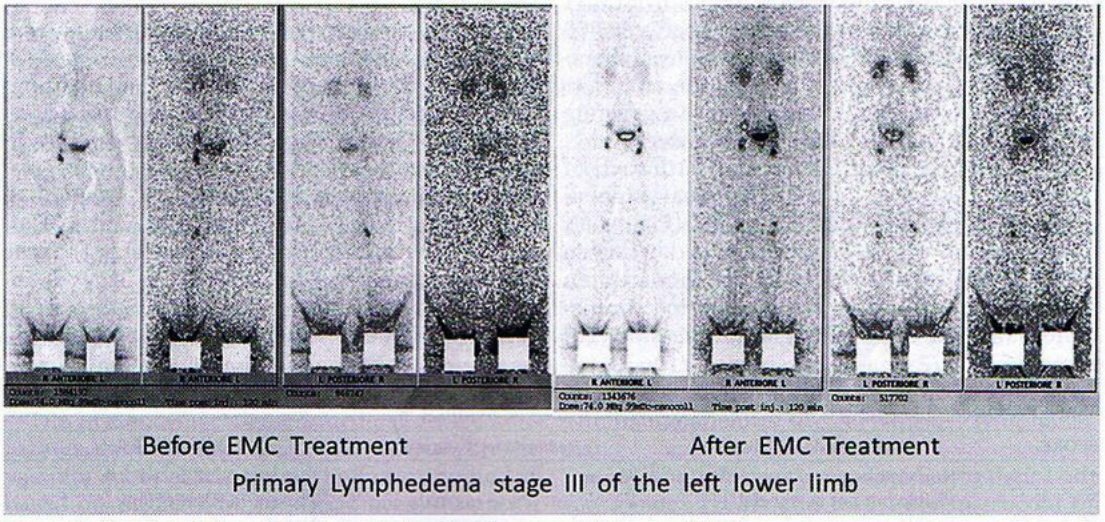

Figure 2.—Lymphoscintigraphy before and after the 10 sessions of Flowave 2(TM).

TABLE III.—*Lymphoscintigraphy findings.*

	After 5'	After 45'	After 120'	After 180'
Inguinal Lymph node Visualisation	0%	33%	110%	245%
Popliteal Lymph node Visualisation	72%	41%	95%	192%
Radioisotope Progression in the thigh	33%	64%	62%	78%
Radioisotope Progression in the leg	48%	39%	50%	55%
Dermal back flow	-13%	5%	25%	25%

ment with an improvement of 0%, 33%, 110% and 245% at the same time intervals respectively. Radiotracer ascension along the leg and the thigh increased of 48% and 33% respectively after 5', of 39% and 64% after 45', of 50% and 62% after 120' and finally of 55% and 78% after 180'. Dermal back flow at pre-post-treatment LSG investigation did not significantly vary till 45', where imaging improved of 25% at 120' and of 25% after 180'.

No complications or side effects were reported by the patients throughout the treatment period and all eight patients showed a good compliance to the application of the medical device.

Discussion

LYM therapy is usually based on multiple therapeutic modalities, in an integrated and complex decongestive treatment (CDT). Physiotherapy (manual lymphatic drainage and compression in primis) is complemented with drugs and electromedical devices, as well as hygiene rules, skin care and some exercises should be part of the CDT. Notwithstanding the multi-modality treatment, LYM of the lower limbs generally shows a natural trend to recur or deteriorate over time. Among the possible electro-medical devices which are applicable in LYM therapy, since 2001 [11] our team had the opportunity to apply with success an electro-sound wave based medical device within LYM holistic integrated treatment. Furthermore two observational studies [12, 13] and a cross-over single-blind randomised clinical trial proved that this innovative modality may be of some efficacy in lymphedematous patients. The present study focuses on the second generation medical device (Flowave 2 (TM)) which is based on bioresonance principles as well, plus an additional vacuum mechanism included in the machine technology.

Some literature data highlight the potential diagnostic and therapeutic uses of bioresonance in medicine (children dermatitis, intestine diseases).[14-22] Similarly the delivery of specific microcurrents showed to interfere with microvascular permeability to lymph proteins.[23] In breast cancer related LYM, the additional application of low-intensity/low-frequency electrostatic fields (under the form of deep oscillations) combined with manual lymphatic drainage (MLD) resulted in an improvement of breast edema and pain over single MLD treatment.[24] Christ [18] recently confirmed the positive effect of planar acoustic waves (at 0.25 mJ/mm^2 energy level) on biologic tissues, more significantly on skin elasticity and microcirculation.

Finally effectiveness of bioresonance sound waves on inflammation and edema was demonstrated on rat muscles through a histology study.[25]

The vacuum technology has been applied to connective tissues and lesions in general,[26] to skin ulcers,[27] to cellulite in esthetic medicine.[28] Finally an anti-edema action has been proved with vacuum technology as well.[26]

The results derived from this clinical and instrumental observational study show the potentials of the applied electromedical device, which is based on bioresonance and vacuum mechanisms, in patients affected by LYM. The short duration of the treatment period on one side results in moderately improved volumetry and LSG imaging, on the other side further improvements with a more durable treatment are to be awaited. The limited number of patients who were enrolled in this cohort study has been justified by the complexity of the protocol (*e.g.*, LSG was performed in the single regional center, which is located about 100 km far from the residential town). Anyway the resulting clinical and LSG data invariably showed an uniform positive trend in all patients, hence we may tentatively

speculate that larger cohort studies could produce similar results.

For ethical reasons all patients were allowed to wear the usual medical compression stockings which they were wearing in the previous months. Volumetry assessment 30 days before the start of the study and at T1 showed no relevant changes, which can confirm somehow the neutral effect of compression stockings on the final outcomes.

The overall decrease of limb volumes after ten sessions of treatment was more significant in the lower leg (731 cc, which corresponds to 8%) than in the whole limb (431 cc, corresponding to 5%), due also to the presence of a severe blockage at the groin level in a few secondary LYM patients. Similarly the quite high standard deviation in pre-/post-therapy limb volumetry (3439 and 3307 cc, respectively) accounts for a remarkable difference among the lymphedematous limbs which were treated (two patients had a volumetry over 12500 cc due to the high BMI and to the severity of the disease).

Lymphoscintigraphy results show a significantly improved imaging of lymph node uptake, which was more pronounced at the inguinal area (110% and 245% improvement at 120' and 180' respectively) than at the popliteal area (95% and 192% respective improvement percentage at the same time intervals). Furthermore the post-therapeutic cycle improvement of the drainage of the lymph collectors was slightly higher in the thigh than in the lower leg, but again this difference was more visible in the late LSG assessments (after 120'-180'). A late (after 45') improvement in radioisotope stagnation was showed at post-treatment LSG, while early images did not show any significant improvement of dermal back flow.

These LSG findings are coherent with an overall improvement of the lymphatic drainage, but the increase of the radiotracer uptake and of the lymph transport take place especially at a later stage (*e.g.*, after 45-120' at LSG investigations). These outcomes are likely related to the activation of the lymph nodes which were previously hypofunctioning in primary LYM, or which were reduced in number and overloaded after cancer surgery. Also activation of the collateral pathways may explain the LSG better images at a late stage.

As all the enrolled patients were affected by severe LYM, *i.e.* stage III, the final outcomes are somehow influenced by this clinical condition which notoriously responds in a lower extent to any therapeutic approach.[29]

The absence of any early/late onset side effect throughout the whole protocol time is a confirmation of the good safety profile of the present electro-medical device, in agreement with other studies.[12, 13] Similarly the good compliance showed by the patients could represent a positive factor as LYM invariably deteriorates in non-compliant patients.[1]

Conclusions

Notwithstanding the small cohort of patients and the short-duration treatment, the clinical and instrumental results of this preliminary observational study proved the safety and efficacy of this electro-medical device (Flowave 2) in patients affected by primary or secondary LYM of the lower limbs. Further, larger cohort studies, possibly in a randomized controlled fashion, are awaited in order to corroborate the data emerging from this study and from the previous ones,[11-13, 20] which seem to justify the inclusion of the present EMD in the CDT of LYM.

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