LTU-904H Laser Therapy. for Treating Post-Mastectomy Lymphoedema.

Results of a randomised, double blind, placebo controlled, clinical trial.

Randomised, Double Blinded, Placebo Controlled, Crossover Trial Determining the Effect of Treating Post-Mastectomy Lymphoedema with LTU-904H Laser Therapy.

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INTRODUCTION

Upper limb Lymphoedema is a common and distressing complication of breast cancer surgery[1]. Reported incidence after surgery is around 5%, increasing to 30% with administration of adjunctive radiotherapy[1,2].

Untreated the condition often gradually worsens and a hardening of the superficial fascia (brawny oedema) often occurs. Patient discomfort is common with symptoms of limb heaviness and weakness, pain, restricted shoulder mobility, burning pains and elevated skin temperature, obvious swollen limb disfigurement, social isolation and psychological morbidity[3].

Traditional treatments for this condition have included compression bandaging, manual lymphatic drainage and extended limb elevation[4]. Due to the nature of these treatments none have been validated with placebo controlled trials. Also a number of issues exist – these treatments are expensive, time consuming and labour intensive.

Low level laser therapy (LLLT) has been trialed for the treatment of fibrous scar tissue[6] and has been shown to affect fibroblasts[7]. These effects are important both in treating surgical scars associated with post-mastectomy lymphoedema and in treating the brawny oedema that often develops in lymphoedematous limbs. As well as this there is some evidence that LLLT encourages lymphogenesis and stimulates lymphatic motoricity[8,9]. Finally LLLT is seen to affect macrophage cells[10] and to stimulate the immune system. All of these actions indicate that LLLT would be an appropriate treatment for post-mastectomy lymphoedema.

This trial has been approved by the Flinders Medical Centre Ethics Committee.

SAFETY

The LTU-904 is a class 1 laser and therefore no additional safety procedures are required (ASNZ 4672).

METHODS

This was a prospective, double blinded, placebo controlled, randomised, crossover trial investigating the effectiveness of **LTU-904H Therapy** as a treatment for Post-Mastectomy Lymphoedema. All patients currently attending, or newly presenting to, the Flinders Medical Centre Lymphoedema Assessment Clinic were considered for entry into the trial. A standard procedure was used to screen patients for inclusion. The following criteria had to be met before a patient was entered into the trial.

INCLUSION CRITERIA

Age – at least 18 years. *Sex* – female only. *Diagnosis* – clinically manifest Post-Mastectomy Lymphoedema (>200ml difference between arms or ≥ 2cm difference in arm circumference at ≥ 3 positions). *Administrative* - the patient understood the trial and was able to provide informed consent.

EXCLUSION CRITERIA

Presence of certain comorbidities – current metastases, history of severe trauma / disruptive surgery to the arm. *Instability of condition* – significant changes to the arm in the past 3 months including, change in treatment regime or occurrence of cellulitis. *Clinical* – inability to abduct arm sufficient for measuring purposes. *Diagnosis* – presence of primary Lymphoedema in the lower limbs.

TREATMENT REGIME

Treatment was delivered in blocks where 1 treatment block of consists of therapy (active or placebo) 3 times per week for 3 weeks. Each treatment session took 17 minutes and is described below.

A grid designed to sit in the axilla with treatment points marked at 2cm intervals guided application. Each treatment point was treated for 1 minute and there were a total of 17 points. The laser was held in contact with, and at right angles to, the skin. The average output of the **LTU-904H** is 5 mW, thus the total energy applied was 5.1 Joules at a dosage of 1.53 Joules per square centimetre. Treatment head size 0.2cm^2.

Participants were randomly allocated into either the active or placebo group. Those participants entering the active group received 2 blocks of **LTU-904H** therapy, separated by an 8 week break. The placebo group received 1 block of sham therapy, followed by an 8 week break, then 1 block of **LTU-904H** therapy. Thus those in the active group received a total of 6 weeks of active therapy while those in the placebo group received 3 weeks of active therapy.

PATIENT ASSESSMENT

Participants were assessed on a number of subjective and objective criteria.

Subjective. Participants were asked about their ability to perform specific activities of daily living, their quality of life as well as being asked to rate their symptoms on a scale of 1 – 10. The symptoms included were: pain, tightness, heaviness, pins and needles, cramps, burning feelings, limb size difference, limb temperature difference and range of movement limitation. The subjective questionnaire was administered before and after each 3 week treatment block and at each follow-up visit.

Objective. Objective measures were as follows. Bio-impedance: measures Ohmic resistance to electrical current thereby giving an extremely accurate representation of extra-cellular fluid levels within the limb. Perometry: uses infrared sensors to measure the limb circumference at every 4 mm's, giving extremely accurate volume measures. Tonometry: measures tissue resisitance to pressure thereby giving an indication of the extent of fibrotic induration in a limb. Shoulder range of movement and body mass index were also monitored. Objective measures were taken at the start of every visit.

SIDE EFFECTS

No significant side effects were reported during the trial. A few participants reported a slight increase in pain, or a feeling of tightness in the upper arm but overall there was no difference between reporting of side effects in active versus placebo groups.

RESULTS

In all, 64 participants have completed the trial, 37 of who were given active **LTU-904H** laser therapy and 27 of whom received placebo treatment.

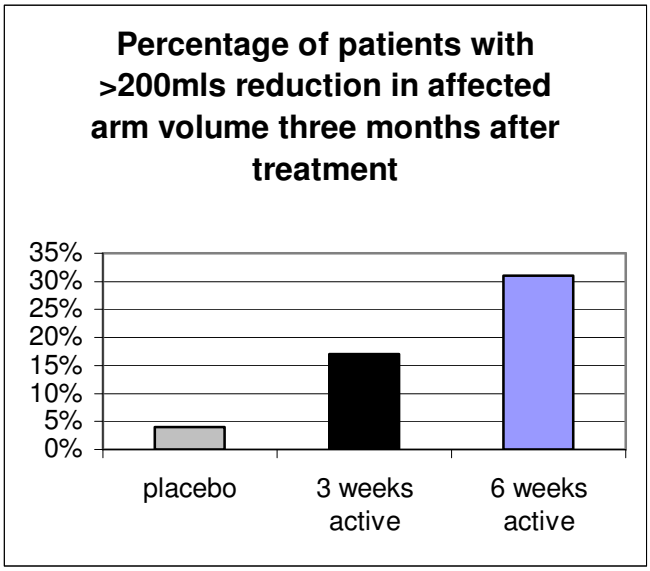
Objective results include ECF, whole arm volume and tonometry.

ECF was significantly reduced following 6 weeks of LTU-904 therapy, in the following regions

- the affected arm (immediately after the course of treatment and maintained at 1 and 3 month follow-up)
- the trunk (immediately after the course of treatment and maintained at 1 month follow-up) AND
- the unaffected arm (immediately after treatment).

52% of participants experienced a clinically significant decrease in ECF after 6 weeks of active laser. In contrast only 19% of people who had placebo treatment achieved the same reduction.

Volume of the affected arm was reduced by a minimum of 200mls in 31% of participants, 3 months after receiving 6 weeks of active **LTU-904H** therapy, as opposed to 4% of those who received placebo treatment.



Tonometry is used to measure the amount of fibrotic induration in the tissues. We found that the tonometry readings were significantly softer in the active group than the placebo group, in the posterior thorax (treated and untreated) and in the upper arm on the treated side.

Subjective results showed statistically significant decreases in:

- pain
- tightness
- heaviness
- cramps
- limb temperature difference
- size difference between the limbs
- pins and needles.

(however, not significantly different to placebo group)

CONCLUSION

The **LTU-904H**

decreases affected limb volume
decreases whole upper body fluid
improves tonometry of upper arm and posterior torso

In post mastectomy lymphoedema patients one to three months after treatment.

The results suggest a systemic effect of **LTU-904H** therapy.

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US Patent Pending