Evidence Summary: Managing lymphoedema: Low level laser therapy

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QUESTION
What is the best available evidence on the effectiveness of laser therapy in managing lymphoedema?

SUMMARY
Low level laser therapy (LLLT) is a biophysical modality in which low powered laser light is applied to the tissues to reduce the signs and symptoms of lymphoedema. Early evidence failed to demonstrate effectiveness of this therapy1 (Level 1a evidence) but more recent trials2,3 (Level 1c evidence) and an observational study4 (Level 3e evidence) suggest that patients with breast cancer treatment-related lymphoedema may achieve limb volume reduction and relief of pain that contributes to improved quality of life. In general, LLLT is used as part of a multi-component regimen.

BACKGROUND
Lymphoedema is a form of chronic, progressive oedema in which there is significant, persistent swelling of a limb or other body region related to excess and abnormal accumulation of protein-rich fluid in body tissues. This fluid contains a range of inflammatory mediators and adipogenic factors5-9. The lymphatic system is unable to manage the volume of accumulated fluid8.

Lymphoedema occurs due to primary, secondary or mixed causes. Primary causes are described as congenital (e.g. an inherited disorder such as Milroy’s disease), praecox (onset at puberty, e.g. Meige’s disease) or tarda (sudden onset no apparent cause)10-12. Secondary causes arise from direct damage or trauma to the lymphatic system such as injury, surgery or radiotherapy (usually related to treatment of breast cancer), or parasitic invasion11-13. Lymphatic filariasis (also called elephantitis) is a cause of secondary lymphoedema in endemic areas primarily in Africa and Asia. Lymphatic filariasis a parasitic (roundworm) infection that is spread by mosquitoes and causes damage to the lymphatic system that may result in lymphoedema. Infection generally occurs in childhood. Management focuses on large-scale treatment programs to reduce disease spread8-14. Mixed lymphoedema describes lymphoedema arising from decompensation or failure of the lymphatic system associated with other disease or conditions, including, but not limited to obesity, immobility, venous disease or lipoedema11,12,15.

Without management, lymphoedema may lead to:6,16

• superficial tissue changes — increasing adiposity and fibrosis;
• physical and functional limitations;
• increased risk of chronic infection;
• lymphorrhoea (leaking of lymph fluid);
• pain and discomfort; and
• reduced ability to undertake activities of daily living (ADLs).

Low level laser therapy (LLLT) is a therapeutic modality that involves the application to the body of near-infrared or red-beam light at wavelengths up to approximately 1,000mW. The light particles are absorbed into the tissue without production of heat. The wavelength (measured in nanometres [nm]) determines the depth the light penetrates into the tissue. The way in which LLLT provides a therapeutic benefit in managing lymphoedema is poorly understood, but it is thought to increase lymph flow through the lymph system, and reduce excess protein and fluid in tissues4,8. The therapy is generally performed by physiotherapists with specific training.

CLINICAL BOTTOM LINE
Effectiveness in reducing oedema

• A systematic review of randomised controlled trials (RCTs) published in 2009 identified two trials at high risk of bias that investigated LLLT for the treatment of lymphoedema. Neither trial presented a comparison on the reduction of lymphoedema between participants treated with LLLT versus other or no treatments. No evidence was found to support the treatment modality1 (Level 1a evidence).

• A meta-analysis of six studies with mixed methodologies found LLLT was associated with a moderate reduction in limb volume for women with upper extremity breast cancer-related lymphoedema. Using a fixed effect model, the pooled effect size (ES) for within group comparison was statistically significant (pooled ES –0.52, 95% confidence interval [CI] –0.78 to –0.25) equating to a reduction in arm volume of 75.7ml. The between group comparison that included four studies reporting a treatment regimen including LLLT versus a treatment regimen without LLLT showed a pooled ES of –0.62 (95% CI –0.97 to –0.28). Although this was not statistically significant, the clinical impact was equivalent to 90.9ml reduction in arm volume.
Comparative treatment regimens included intermittent compression therapy (bandage, garment or pneumatic), manual lymphatic drainage or exercise regimen with education\(^7\) (Level 1b evidence).

- Regimens of LLLT that showed effect for reducing limb volume either alone or concurrently with other management strategies reported in studies in the above meta-analysis included:\(^1\) (Level 1b evidence).
  - Direct contact, 904 nm, applied to 17 places in the axilla each 2 cm apart, 1 minute at each place per session for 18 sessions.
  - Direct contact, 904 nm, applied to 3 places in the antecubital fossa and 7 places in the axilla, 2 minutes at each place per session for 36 sessions.
  - Direct contact, 904 nm, applied to 3 places in the antecubital fossa and 7 places in the axilla, 20 minutes per session for 12 sessions.
  - Non-contact scanned 50 cm above the skin, 808 nm (increased to 905 nm for 2 sessions) applied to entire axilla, 20 minutes per session for 12 sessions.
  - Non-contact scanned, 904 nm, applied to axilla, forearm and arm, 10 minutes per area (30 minutes total) for 16 sessions.

Effectiveness in reducing pain
- A meta-analysis of three RCTs found LLLT was associated with a statistically significant reduction in pain for women with upper extremity breast cancer-related lymphoedema. Using a fixed effect model, the pooled ES for within group comparison was −0.62, (95% CI −1.06 to −0.25) equating to a reduction in pain of 13.5mm on a 100mm visual analogue scale (VAS). Pooled results from the two studies that measured pain immediately post-intervention had non-significant results\(^1\) (Level 1a evidence).

Effectiveness in improving function
- In an RCT, LLLT (20 minutes at 2800Hz, 1.5J/cm\(^2\) three times weekly for four weeks) was effective in significantly improving grip strength measured using a hand dynamometer in women with breast cancer treatment-related lymphoedema (n=23) immediately following treatment and at three, six- and 12-month follow-up (p=0.05 or p<0.01 for all). There was no significant difference in effect compared with a group (n=24) receiving pneumatic compression therapy\(^2\) (Level 1c evidence).
- Low level laser therapy (two courses of nine sessions each over three weeks each) was associated in improved shoulder range of movement in women with breast cancer treatment-related lymphoedema (n=17), improvements were reported for 76.4% of the women\(^3\) (Level 3e evidence).

**CHARACTERISTICS OF THE EVIDENCE**
This evidence summary is based on a structured literature and database search combining search terms that describe lymphoedema and laser therapy. The evidence in this summary comes from:

- Systematic review, meta-analysis of RCTs\(^1,17\) (Level 1a evidence).
- Systematic reviews of studies of various design\(^6,17\) (Level 1b evidence).
- Randomised controlled trials\(^2,3\) (Level 1c evidence).
- Observational studies with no control group\(^4,13\) (Level 3e evidence).
- Case series report\(^15\) (Level 4c evidence).
- Expert consensus\(^9,11\) (Level 5b evidence).
- Expert opinion\(^5,7,8,10,12,14,16\) (Level 5c evidence).

**BEST PRACTICE RECOMMENDATIONS**
- There is some evidence that low level laser therapy is associated with reduction in limb volume, improved function and reduced pain in women with breast cancer treatment-related lymphoedema. (Grade B)
- There is insufficient evidence to make recommendations on the most appropriate LLLT regimen. Greater benefit from treatment is expected to be achieved when combined with compression therapy or manual lymphatic drainage.

**REFERENCES**
Evidence Summary: Managing lymphoedema: Complex lymphoedema therapy

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QUESTION
What is the best available evidence on the effectiveness of complex lymphoedema therapy/complete decongestive therapy in managing lymphoedema?

BACKGROUND
Complex lymphoedema therapy (CLT), also known as complete decongestive therapy (CDT) or complex physical therapy (CPT), is a holistic, multi-component management strategy for reducing the signs and symptoms of lymphoedema. There is evidence from a systematic review of clinical trials¹ (Level 1.b evidence), additional trials and consensus guidelines that CLT is an effective strategy for reducing limb oedema¹, improving quality of life (QOL) and reducing recurrent cellulitis² (Level 3.d evidence) in patients with both upper and lower limb lymphoedema.

Lymphoedema is a form of chronic, progressive oedema in which there is significant, persistent swelling of a limb or other body region due to excess and abnormal accumulation of protein-rich fluid in body tissues. This fluid contains a range of inflammatory mediators and adipogenic factors³⁷. The lymphatic system is unable to manage the volume of accumulated fluid².

Lymphoedema occurs due to primary, secondary or mixed causes. Primary causes are described as congenital (e.g. an inherited disorder such as Milroy’s disease), praecox (onset at puberty, e.g. Meigs’ disease) or tarda (sudden onset no apparent cause)⁴⁶. Secondary causes arise from direct damage or trauma to the lymphatic system such as injury, surgery or radiotherapy (usually related to treatment of breast cancer), or parasitic invasion⁵⁷. Lymphatic filariasis (also called elephantitis) is a cause of secondary lymphoedema in endemic areas primarily in Africa and Asia. Lymphatic filariasis is a parasitic (roundworm) infection that is spread by mosquitoes and causes damage to the lymphatic system that may result in lymphoedema. Infection generally occurs in childhood. Management focuses on large-scale treatment programs to reduce disease spread⁸⁹. Mixed lymphoedema describes lymphoedema arising from decompensation or failure of the lymphatic system associated with other disease or conditions, including but not limited to obesity, immobility, venous disease or lipoedema⁵⁶,¹⁰.

Without management, lymphoedema may lead to:³¹
• progressive swelling;
• superficial tissue changes — increasing adiposity and fibrosis;
• physical and functional limitations;
• increased risk of chronic infection;
• lymphorrhoea (leaking of lymph fluid);
• pain and discomfort; and
• reduced ability to undertake activities of daily living (ADLs).

Complex lymphoedema therapy/complete decongestive therapy is an holistic management strategy for lymphoedema. This multi-component management strategy includes:
• patient education;
• skin care;
• manual lymph drainage (MLD);