Interventions for Upper Quadrant Lymphedema: CPG from the Academy of Oncologic Physical Therapy - Preliminary Results

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Disclosure

- **Laura Gilchrist, PT, PhD**
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No relevant financial relationship exists

Session Learning Objectives

- Describe the systematic review process for communication with other health care providers, clients, and their caregivers.
- Discuss the evidence regarding interventions for upper quadrant cancer-related lymphedema.
- Review the preliminary guideline statements and discuss changes needed.
- Consider the implications of the preliminary guideline statements.

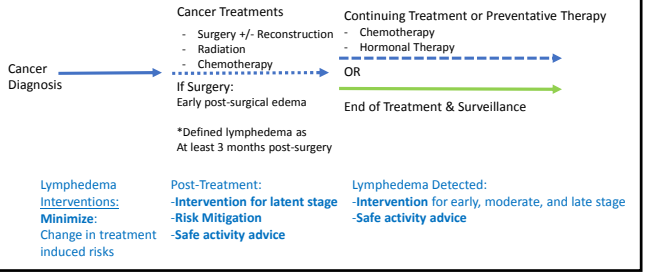
Background

- 15.5 million cancer survivors in the US (American Cancer Society, 2016)
- Various side effects of cancer and its treatment (NCI, 2016, https://www.cancer.gov/about-cancer/coping)
- Breast cancer related lymphedema can occur within days and up to 30 years after diagnosis/treatment (Brennan and Weitz 1992, Petrek et al 2001)
- Other cancers such as melanoma and head and neck tumors can cause upper quadrant lymphedema

Background

- Eighty percent of BCRL occur within 3 years of surgery; the remainder develop edema at a rate of 1% per year (Brennan and Weitz 1992, Petrek et al 2001)
- Quality of life is lower for patients diagnosed with lymphedema or arm symptoms than those not diagnosed (Ahmed 2008)
- Interventions are needed at many different points in the cancer trajectory
  - Minimize Lymphatic Interruption – medical interventions
  - Risk Mitigation
  - Interventions for multiple stages

Timeline for Onset and Intervention



Classifications	ISL Stage - Description of Stages
Latent stage lymphedema	0 - Subclinical state where the peripheral swelling is not visible, but lymphatic transport is impaired. Symptoms and subtle tissue changes may be noted.
Early-stage lymphedema	I - Early onset of swelling that is visible and subsides with elevation. Pitting may be present.
Moderate/established lymphedema	II - Consistent volume change with pitting present. Elevation rarely reduces the swelling, and progressive tissue fibrosis occurs.
Late-stage lymphedema	III - Skin changes such as thickening, hyperpigmentation, increased skinfolds, fat deposits, and warty overgrowths occur. Tissue is very fibrotic, and pitting is absent.

How should I be treated?

- Patient being treated for Breast Cancer with some risks of lymphedema including: 10 axillary nodes dissected, and overweight prior to surgery. Just completed surgery 2 weeks prior and has no appreciable arm or hand swelling. Chemotherapy, axillary and chest wall radiation planned.

How should I be treated?

- Patient who is 1.5 years post treatment for breast cancer with intermittent symptoms of swelling of the upper extremity and breast tissue. Volume differential of 245 ml between extremities and L-Dex score of 11.5 (> diagnostic threshold).

How should I be treated?

- Patient is 4 years post-treatment for Melanoma of chest with a 2 year history of arm and hand swelling. Fibrosis noted along with some skin thickness increase. Volume differential of 350 ml between extremities and BIA is increased but not above diagnostic threshold.

How should I be advised?

- Patient with stable stage II lymphedema post-breast cancer diagnosis for 1 year who wants to begin training for a triathalon. Normal echocardiogram post-cancer treatment that included left chest wall radiation.

Many different clinical questions

- What can the medical community do differently to minimize lymphatic damage during treatment?
- Given that cancer treatments often interrupt the lymphatic system, what can we do to mitigate other risk factors and minimize or delay progression beyond the latent stage?
- How do we intervene with those patients who present to us with early, moderate, or late-stage lymphedema?
- How do we advise those with any stage lymphedema (exercise, air travel…)?

Construction of the CPG – Systematic Review

- Literature searched from Jan 2000 – Dec 2017
  - PubMed
  - CINAHL Plus with Full Text
  - Cochrane
  - AHRQ
  - National Guideline Clearinghouse
  - Scopus
  - SPORTDiscus with Full Text
  - PEDRo Physiotherapy Evidence Database
  - OTseeker Occupational Therapy Systematic Evaluation of Evidence
- Terms: *Lymphedema, Elephantiasis,* and truncated text words *lymphedema*, lymphoedema*, elephantiasis*
- Excluded: *filariasis, parasites*, *congenital*, *hereditary,* as well as *editorial*, *letter*, and *comment*

Literature Review

- Title and Abstract review for inclusion criteria
  - Cancer-related upper quadrant lymphedema and intervention
- Pull included articles and review
  - Confirm inclusion/exclusion
  - Study design
  - Appropriate outcome measure
  - Data can be extracted
- Quality Review
  - APTA's CAT-EI review tool

Army of Reviewers! Thank you!!!

- Kathy Bartley
- Chris Beuthin
- Linda Boyle
- Jennifer Brooks
- Barbara Feltman
- Amy Flinn
- Brandi Johnson
- Meagan Kaley
- Jean Kastner
- Kiersten Kilczewski
- Linda Koehler
- Vince Lepak
- Anne Lehman
- Vicki Naugler
- Lisa O'Block
- Nancy Potter
- Kristin Ryan
- Christina Wright

Criteria

Inclusion criteria
- English publications
- 2000 to 2017
- Upper quadrant cancer related lymphedema
- Lymphedema intervention primary study objective
- Exacerbation or onset of lymphedema
- Quality of evidence score of high or acceptable

Exclusion criteria
- Non-English publications
- Not within the eligible time period
- Lower extremity or non-cancer related lymphedema
- Lymphedema intervention not primary or secondary study objective
- Abstract only
- Duplicates
- Quality of evidence score of low or unacceptable

CAT-EI Review Tool

- Developed by APTA – to review quality of intervention trials
- Includes ratings of:
  - Population
  - Blinding
  - Control groups
  - Outcome measure reliability and validity
  - Sample size
  - Rated for each outcome measured
- **High quality**: Appropriate patient population; Randomized, *Controlled Trial*; *Tester Blinded*; Sufficient follow-up; Valid and Reliable Outcome Measure; Adequate Sample Size; Appropriate Statistical Analysis
- **Acceptable Quality**: Appropriate patient population; Randomized; *Lesser* follow-up; Valid and Reliable Outcome Measure; Adequate Sample Size; Appropriate Statistical Analysis

Library Search Yielded — 11,716

→ Excluded: Not cancer related, animal studies, lower extremity

Title and Abstract indicate Interventions — 1,539

→ Excluded: Reviews, mixed populations, protocols, Medical interventions (surgeries, medications…)

Articles Included and Rated for Quality — 163

6 High
27 Acceptable
108 Low
22 Unacceptable

Review of Evidence and Statements

- Data Extracted
- Evidence from high and acceptable articles synthesized
- Effect sizes calculated where able
  - Quantitative measure of magnitude
  - Takes into account variability in the population
  - Can compare across measurement types (volume change vs. BIA change)
  - Cohen's d: mean group 1 – mean group 2 / pooled SD
  - Medium = 0.5, Large = 0.8, Very Large = 1.3

Preliminary statements constructed

- Based on the quality of evidence (APTA CPG Manual)
  - **Grade A**: High quality studies (Level I) with moderate to substantial benefit/harm – "Must/Should" or "Must not/Should not"
  - **Grade B**: High Level studies (Level I) with slight to moderate benefit/harm OR Moderate level evidence (Level II) for moderate level benefit/harm -"Should" or "Should not"
  - **Grade C**: Moderate level evidence (Level II) for slight level benefit or harm OR Weak level evidence (level III) for substantial benefit/harm – "May" or "May not"
  - **Grade P**: Best Practice – based on current clinical norms or expert opinion

*All Statements in this handout are preliminary drafts and are likely to undergo revision prior to finalization and publication

*Revisions may have occurred between handout construction and today's presentation

- Further Review and Revisions
  - Upon public presentation to APTA members at CSM
  - Review by external PTs, OTs, and MDs
  - Review by other experts and professional groups
  - Public comment period on Academy website

Exercise

Exercise Review of the Literature

Exercise	High/ Acceptable # Articles	Risk Mitigation & Latent Stage	Intervention- Reduction Stage I-III	Intervention- No Exacerbation Stage I-III	Low/ Unacceptable # Articles
Early Intervention	3	2			4
Aquatic	1		1		4
Resistance	5	2		4	13
Aerobic/Nordic walking/pole walking	2		1	1	4
Group	1		1		0
Telehealth/Homebased	1	1			6
Pilates					1
Yoga					5
PNF					3
Arm Exercise/Arm Ergometer					6
Holistic/Tai Chi					3

Definition of Safe

- Did not cause short- or long-term exacerbation in patients with BCRL
- Did not result in lymphedema in patient at risk for BCRL
- Determined during the study's follow up time period
  - 24 hours to 2 years
  - 3 months post surgery to determine diagnosis of BCRL

Risk Mitigation Interventions

- In the acute phase (1-2 weeks):
  - Therapists should not restrict activity and should gradually progress resistance exercises. (Level I)
- It is safe for patients with latent stage BCRL to perform weightlifting activities. (Level I)

Early Resistance Training vs. No Advice Post Hospitalization: Risk Mitigation

Author, Year	Interventions	Results
Kilbreath, 2012 (High) **Population:** 4 weeks post BC sx either SLNB or ALND **No BCRL** **Dx Criteria:** 10% interlimb difference Level I	**Post op care in hospital same for both groups**: Active assistive sagittal and frontal plane ROM, no heavy lifting or prolonged activities; avoid precautionary behaviors. **Resistance training** (free weights) (n=81) shoulder mm, passive stretching in supine of shoulder flex/abd, pect major, pect minor, with adaptive strategies applied if not able to achieve 90°. HEP consisting of theraband and passive stretching vs. **No ex or advice after hospitalization** (n=79), fitted for compression garment if BCRL identified	Both groups reported few impairments including BCRL 6 months post intervention (p=0.35) Ex group did gain slightly greater ROM in flex, abduction and strength in abduction following intervention

No Activity Restrictions vs. Activity Restrictions: Risk Mitigation

Author, Year Population	Interventions	Results
Sagen, 2009 (High) **Population:** BC surgery (mastectomy or breast conserving) with ALND (levels I and II), +/-radiation, +/- chemotherapy, +/- antihormone treatment; **no BCRL** **Dx Criteria:** Voldiff arm volume, interlimb difference Level I	**No activity restrictions** (n=104) Supervised, individualized PT program: Moderate progressive resistance ex program (45 min) 2-3 times/wk; first two weeks low resistance and then gradually increasing to enhance mm strength and endurance but keeping to 15 reps through 6 months of tx **vs.** **Activity restriction** (n=100) And usual care OP PT: Passive manual techniques emphasizing light massage and flexibility to shoulder arm and scar. Once/wk for 6 months	No difference between groups BCRL increased significantly in both groups over the 2-year study period but higher in control group. Effect size: -0.18 (Moderate)

Early Shoulder Exercise vs Delayed Shoulder Exercise: Risk Mitigation

Author, Year Population	Intervention	Results
Bendz, 2002 (Acceptable) **Population**: BC: Surgery with +/- radiation; **no BCRL** **Dx Criteria:** >10% interlimb diff Level II	**Early Shoulder Exercise** (n=101) Starting Day 1 and 2 after sx gradual increase to UE flex/abd starting with: intermittent hand contractions elbow flex/ext; forearm pron/supination, in supine with arm on wedge pillow; Day 3 UE flex and abd to 90° with elbow flex in sitting; Day 8 arm flex and abd to 90° w/ straight elbows in IR Day 14 OP clinic. 5 times in every set and repeat 3 x/day vs. **Delayed Exercise** (n=104) Shoulder exercises starting Day 14 OP Clinic	Mobility in intervention group recovered earlier but shoulder flexion and abduction remained decreased at **2 yrs** (follow up) in both groups Early ex safe with no increase risk of lymphedema onset (p=<0.001)

Early Aerobic and Resistance Exercise Face to Face or via Phone : Risk Mitigation

Author, Year Population	Interventions	Results
Hayes, 2013 (Acceptable) **Population: No BCRL**, 6 wks post BC sx Dx Criteria: BIS, L-Dex score ≥10 Level II	**Aerobic and Resistance training** individualized sessions in person (n=67) or via phone(n=67) starting weekly and tapering to monthly for 8 months with an overall goal of 4 days/wk for 45 minutes vs. **Usual care** (n=60)with no advice regarding exercise	QOL (p=0.030), aerobic fitness (p=0.016) improved, and fatigue declined (p=0.032) in the ex group not the UC group Trends similar between phone and face to face intervention groups No statistical or clinical difference between groups in L-Dex measurement with 12-month f/u

Weight Lifting vs No Exercise: Risk Mitigation in Stage 0

Author, Year	Intervention	Results
Schmitz, 2010 (High) **Population:** BC survivors between 1-5 years at risk but **no BCRL** with at least 2 lymph nodes removed. **Dx Criteria:** WD >5% increase Level I	**Weight lifting** (n=77) 1-year fitness membership; First 13 weeks 2x/wk 90-minute group instruction on safe ex performance. vs. **No change in activity** (n=77)	Slow progressive weight lifting did not increase incidence of lymphedema w/ 1 yr f/u All participants: Cumulative incidence ratio (95% CI): 0.64 (0.28-1.45) p=0.003 >5 LN removal: cumulative incidence ratio (95% CI): 0.30 (0.09-1.00) p=0.001

Exercise for Patients with BCRL

- For those who have BCRL (stage 0 – III), weightlifting and high load and low load resistance exercise appears to be safe and may included(Level II)
- Supervised aerobic and resistance exercise should not exacerbate BCRL (Level I)
- Best practice is to use compression garments with exercise

Weight Lifting vs Baseline Physical Activity: No Exacerbation

Author, Year	Intervention	Results
Zhang, 2017 (Acceptable) **Population:** BC survivor 1-5 yrs, >1 lymph node removed with **BCRL (Stage 0-III)** **Dx Criteria:** >10% interlimb difference Level II	**Weight lifting** Supervised safe, slow progressive instruction for 13 weeks then unsupervised weight lifting for 39 weeks vs. **Baseline physical activity** **Compression worn during exercise**	After 12 months of weight-lifting, composition of the affected arm improved in lean mass (p=0.01), bone mineral density (p=0.02) and decreased arm fat % (p=0.003) No changes in arm volume (p=0.60) Increases in lean mass associated with less severe BCRL symptoms

High Load vs Low Load Resistive Exercise: No Exacerbation

Author, Year Population	Intervention	Results
Cormie, 2013 (Acceptable) **Population:** at least 1 yr with BC dx, ALND, +/- chemo, radiation, or antihormone therapy and clinical dx of **BCRL (avg 5.4 yrs)** **Dx criteria:** BIS Level II	**High load upper body resistance** exercises (n=17) (chest press, lateral pull downs, biceps curl, triceps extension, lateral raise), 2 sets/ 6-8 RM vs. **Low load upper body resistance** exercises (n=17) (chest press, lateral pull downs, biceps curl, triceps extension, lateral raise), 2 sets/15-20 RM **Compression wear determined by participant**	Same participants in each group with 10-12 day wash out period between sessions No differences in the acute response (arm volume) in high or low load resistant exercise from pre to any of the timepoints post exercise (up to 72 hours)

Aerobic and Resistance Exercise vs Habitual Activities: No Exacerbation

Author, Year Population	Intervention	Results
Hayes, 2009 (High) **Population:** Completed BC tx 6 months to >5 yrs with unilateral BCRL **Dx Criteria:** Perometry >10% difference; BIS Level I	**Supervised, group, aerobic and resistance ex** (n=16) 20 sessions over 12 wks at mod intensity vs. **Habitual activities** (n=16)	No significant differences in lymphedema status at baseline or between phases. Exercise does not exacerbate lymphedema (3 month follow up)

Resistance vs Aerobic Exercise: No Exacerbation

Author, Year Population	Intervention	Results
Buchan, 2016 (Acceptable) **Population:** Completed BC tx +/- radiation chemo, -antihormone; BCRL Stage 1 or II, completed all intensive lymphedema therapy **Dx Criteria:** BIS, Calculated Vol >5%, self report Level II	**Resistance Exercise** (n=21) 150 minutes of supervised and unsupervised each wk at a MET level of 3-3.5 and RPE of 11-13 (wks 1-6) to a level 5 and RPE 12-14 (wks 7-12) vs. **Aerobic exercise** (n=20) 150 minutes of supervised and unsupervised each wk at a MET level of 3-3.5 (wks 1-6) to level 5 in wks 7-12. Walking, jogging, cycling, or swimming (personal preference) Both groups: Normal lymphedema management & **compression wear determined by participant**	No differences between groups or over time in BCRL (BIS: p=0.91; Interlimb vol diff: p=0.48) or BCRL related symptoms (p=0.56) Aerobic exercise showed clinically meaningful decline in number of lymphedema related symptoms from baseline to 12wks (-1.5, 95% CI=-2.6 to -0.4)

Resistive Exercise w/without Compression: No Exacerbation

Author, Year Population	Intervention Cross-over Design	Results
Singh, 2015 (Acceptable) **Population:** Dx of BC, +/- chemo, radiation, but no antihormone therapy BCRL (mean 8 yrs) with no stage reported **Dx Criteria:** Calculated Arm volume >10% vol diff; BIS L-Dex Scores pre/post Level II	Completed 4 familiarization sessions over 2 weeks, performed learned **resistive exercises with and without a compression garment**, separated by 14-day median wash-out period (n=25)	Statistically significant (p=<0.01) decrease in lymphedema when using **BIS** following mod load resistance ex w/ compression but transient Effect size: -0.15 (-0.073 to 0.43) No exacerbation in arm volume (calculated) (p=0.89) before or after exercise (24 hr f/u) or between compression and non-compression sessions with moderate load resistant exercises Effect size: -0.18 (-0.74 to 0.39)

Intervention Short Term Reduction

- Upper extremity exercise, initiating with the proximal muscles, may result in a short-term but not long-term volume reduction (Level II)
  - May recommend for self-care
- Pole walking and aquatic therapy may be included in intervention plan (Level II)

Group Arm Exercise Proximal vs Distal: Short Term Reduction but No Long-Term Reduction

Author, Year Population	Self Controlled Multiple Intervention	Results
Bracha, 2012 (Acceptable) **Population:** Unilateral BCRL for at least 6 months, and completed BC txs, stage not described **Dx Criteria:** 10% arm volume difference Level II	**Group sessions** (n=7) held 1x/wk for 3 wks: Proximal group exercise sessions first, distal for second session and third session combination of prox and distal vs. **Group sessions** (n=9) held 1x/wk for 3 wks: Distal exercise first, proximal for second session and third session combination of prox and distal **Compression worn**	• Prox arm exercise and combination of prox and distal mm ex caused significant immediate decrease in arm volume compared to distal exercise alone (p=<0.01) • Did not reach minimal detectable change values • There was no carry over from session to session

Pole Walking vs Normal Activity: Short Term Reduction but No Long-Term Reduction

Author, Year Population	Intervention	Results
Jonsson, 2014 (Acceptable) **Population:** Unilateral BCRL (duration avg 53.6 months, Stage not specified) **Dx Criteria:** >3% Lymphedema Relative Volume Level II	**Control period** of 2 weeks w/ normal activity prior to the intervention vs **Pole walking** (sport – walking with ski poles) for 30-60 minutes (70-80% max HR) 3-5 times a week for 8 weeks **Compression worn by subjects**	After intervention, a significant reduction in total arm volume, lymphedema absolute vol and lymphedema relative vol compared to the before the intervention (**F/u period within 3 days of completing intervention**) Improve fitness without exacerbation

Aquatic Therapy vs Usual Care: Short Term but No Long-Term Reduction

Author, Year Population	Intervention	Results
Tidhar, 2010 (Acceptable) **Population:** Unilateral lymphedema (12.8% RLV, mild) in the self management phase of CDT **Dx Criteria:** WD Level II	**Aquatic therapy** (n=16) 45 min sessions, 1x/wk for 3 months; 1.2 m pool 32-33°C Sequence: 1st healthy lymphotomes activated through breathing ex; prox movements of chest, shoulder and vertical position of the arm in the water performing self-massage and distal ex involving the elbows, wrists and fingers vs. **Usual care** (n=32) Self-Care (exercise and self-massage instruction booklets) **Compression worn**	Statistical and clinical effect on limb volume immediately (p=0.02) but no long-term effect (12 wk f/u) (p=0.51) No adverse events of infection or aggravation in limb volume during study period. Positive correlation with severity and ex adherence r=0.51 p=<0.05

Take Home Points for Exercise

- Exercise is SAFE and should be incorporated as an intervention in patients/clients with/without BCRL
  - Aerobic
  - Resistance/Strength training
- Aquatic exercise may be incorporated as an intervention in patients with BCRL
- Interventions should be individualized and gradually increased
  - Face to face vs Phone vs Group
- More research is needed
  - Yoga
  - Pilates
  - Longer follow up times in the early intervention groups
- EXERCISE HAS MANY OTHER BENEFITS

CDT – Complete Decongestive Therapy

Definition of Complex Decongestive Therapy

- A.k.a Complex decongestive physiotherapy (CDP)
- Historical description
  - 2 phase intervention:
    - Intensive phase
    - Maintenance phase

    Includes: skin/nail care, manual lymphatic drainage techniques, compression bandages exercise typically remedial/ ROM, compression garment.
- International Society of Lymphology 2013 Consensus report
  - Modified interventions based on stage and severity of lymphedema
  - MLD used alone usually has limited benefit
- Future research is still needed to determine which of the components are necessary for each stage of lymphedema

CDT Review of the Literature

CDT	High/ Acceptable # Articles	Risk Mitigation & Latent Stage	Intervention Reduction Stage I-III	Intervention Exacerbation	Low/ Unaccept # Articles
CDT	4	1	3		32
Compression; bandaging / garments	0				13
MLD only	1		1		8

CDT – Prevent Progression from Stage 0

- Early modified CDT (MLD, AROM exs, Skin and Nail care, and Education – w/o compression) may be used to reduce the risk of progression of secondary lymphedema in the upper extremity in individuals who have undergone ALND. (Level II, 1 study)

CDT for Risk Reduction Prevention:

Author, Year Population	Intervention	Results
Lacomba, 2010 (Acceptable) Breast surgery with ALND Dx Criteria:>2 cm at 2 points Level II	**Complete Decongestive Therapy** (n=59) **MLD** early –post operative Modified strokes for post-operative edema and progressive scar massage **Compression;** none provided **Exercises;** AAROM and AROM shoulder **Skin and nail care;** education on risk of infection **Education**; general- use of arm, identification of triggers 3 times per week for 3 weeks Vs. **Educational strategy** (n= 57)	Volume ratio was higher in control to intervention group initially. At 1-year early CDT reduces risk of secondary lymphedema in post-op surgery for breast cancer with axillary lymph node dissection ES = 0.52 (0.16 – 0.88)

CDT for Volume Reduction in Secondary Lymphedema (Stage I-III)

- CDT may be used as an intervention to reduce arm volume in those diagnosed with secondary lymphedema (Level I no significant difference, Level II – mixed results)
  - Stages I – III
  - Components of CDT: MLD, Bandaging, Exercise, and Skin Care
  - Various components tested:
    - CDT vs compression garments
    - CDT with and without MLD
  - Current best practice?

CDT for Volume Reduction in Secondary Lymphedema

	Intervention	Results
Dayes, 2013 (High) BC with LE (Stages 1-3 ISL) Dx Criteria:10% increase in arm vol Level I	**Complete Decongestive Therapy (n= 56)** **MLD;** Vodder or Foeldi one-hour daily **Compression;** short stretch bandage 23 hours per day and self bandaging at weekends After 4 weeks sleeve and glove provided **Exercise;** advice **Skin care;** advice **Treatment** - 5 times per week for 4 weeks Vs. **Compression garment (n= 39)** 30 – 40 mmHg and glove, fitted 12 hours per day	After intervention: CDT: 29% excess volume reduction +/- 38 Compression: 24% excess volume reduction +/- 12 One year follow up - No significant difference between groups in the percentage of reduction of lymphedema. ES = 0.23 (=-0.18 - 0.64)

CDT for Volume Reduction in Secondary Lymphedema

Author, Year	Intervention	Results
Badger, 2000 (Acceptable) BC with LE, 12 months post- tx Dx Criteria: 20% excess volume Level II	**Complete Decongestive Therapy (n= 34)** **MLD**; Self-Massage based on principals of manual lymph drainage **Compression**; Multi-layer bandaging for 18 days Sleeve fitted on day 18 **Exercises**; to promote lymph drainage **Skin care**; daily **Treatment** -18 days Vs. **Arm sleeves alone** (n= 49) *Replaced every 3-4 months; compression class determined base on each pt's needs*	At 6 months multilayer bandaging reduces limb volume more than just an arm sleeve alone and maintains it. ES = 1.25 (0.77 – 1.72)

CDT for Volume Reduction in Secondary Lymphedema

Author, Year	Intervention	Results
Ochalek, 2014 (Acceptable) BC with LE (Stages 1-3 ISL) DX Criteria: ISL stages Level II	**Modified Complete Decongestive Therapy** (n= 40) **MLD - none** **Compression**; initially short stretch bandage followed by a compression sleeve and glove **Exercises**; individual program **Skin care**; preventative and hygienic instructions **Treatment** - Intensive phase 5 times per week for 2 weeks (10 days) Vs. **Compression garment only** (n=20)	No significantly reduced volume over time **Follow up** – 6 months No effect size *MLD is an important component

CDT for Volume Reduction in Stage 2

Author, Year	Intervention	Results
Gradalski, 2015 (Acceptable) BC with LE >Stage 2 ISL Dx Criteria: ISL with a decrease of 200ml minimal limb difference to be clinical meaningful Level II	**Complete Decongestive Therapy** (n= 12) **MLD** Vodder II for 30 minutes first 2 weeks then self MLD **Compression** 3 layers short stretched bandage 20-30 mmHg Garment; custom flat knit **Exercises;** light aerobic ex 10-15 mins, AROM and self assisted ex's proximal to distal 15 mins/day, diaphragmatic breathing **Skin and nail care;** education on risk of infection **Treatment** - daily for 2 weeks then 6 months maintenance phase Vs. **Modified CPT (no MLD)** **No MLD** (n= 13) **Compression** 3 layers short stretched bandage 20-30 mmHg Garment; custom flat knit **Exercises;** light aerobic ex 10-15 mins, AROM and self assisted ex's proximal to distal 15 mins/day, diaphragmatic breathing **Skin and nail care;** education on risk of infection	Not significant after intensive phase as both groups had approx. 47% reduction in limb volume Not significant at 6 months (the end of maintenance phase) both groups demonstrated comparable volume losses ES = -0.42 (-1.2 - 0.39)

CDT - Take Home

- Need to define CDT
- Early CDT (MLD, AROM exs, Education skin and nail and general) may be used to reduce the risk of secondary lymphedema in the upper extremity
- CDT may be used as an intervention to reduce arm volume in those already diagnosed with secondary lymphedema
- Further high-quality research is needed:
  - at different intervention time points
  - determine which components of the intervention are needed based on characteristics of the lymphedema

Manual Therapy

Manual Therapy Review of the Literature

Manual Therapy	High/ Acceptable # Articles	Risk Mitigation & Latent Stage	Low/Unaccept # articles
MFT	1	1	
Hand held massager			1

Manual Therapy Recommendation

- The addition of MFT to standard physical therapy appears to be safe in patients greater than 3 months post-radiation. (Level II)

Myofascial therapy (MFT) for upper limb dysfunction

Author, Year	Intervention (2 groups)	Results
DeGroef 2017 (acceptable) Females treated for primary breast cancer; average time since surgery 3.4 years Point Prevalence ≥5.0% increase from pre-surgical baseline Level II	**Standard physical therapy with MFT** (n=23): 2x/week fading out to 1x/week for 12 weeks x 30 min • Passive mobilizations, stretching, A/PROM, scar tissue massage, exercise to improve flexibility, strength and endurance. Myofascial therapy 1x/week x 12 weeks for 30 min each • MFT to active trigger points in the upper limb region; adhesions in the pectoral, axillary and cervical regions, diaphragm, and scars. Vs. **Standard physical therapy with placebo MFT** (n=25): 6 and 12 month follow up.	No significant increase in volume in either group. • There was a decrease in point prevalence in the intervention group at 3 months, but not significant. Significant long term function achieved in both groups. The effect of MFT in shoulder dysfunction did not differ between the two groups. ES = -1.8 (-5.4 – 1.4)

Intermittent Pneumatic Compression Pumps (IPC)

IPC Pump Review of the Literature

IPC (all BCRL except 1 for H&N)	High/ Acceptable # Articles	Intervention-Reduction Stage I-III	Intervention-No Exacerbation Stage I-III	Low/Unaccept # articles
IPC only				5
IPC and CDT	1	1		6
IPC and MLD				2
IPC and exercise				1

IPC

- IPC may not enhance the volume reduction gained by complete decongestive therapy when applied *following MLD* in patients with established lymphedema of the upper extremity. (Level II)
- IPC does not have evidence at this time to support its use as a stand alone treatment for upper quadrant lymphedema.

IPC vs. CDT

Author, Year Population	Interventions (2 groups)	Results
Uzkeser 2015 (acceptable) BCRL stage I & II duration of 8-14 months Dx Criteria: >2 cm at 3 points or a 10% volume difference between limbs Level II	**Group 1: CDT** (n=15) MLD, CB, skin care, exercise, garments vs. **Group 2: CDT and IPC** (n=16) CDT with addition of IPC x 45 min @ 40 mmHg following MLD All subjects received treatment 5x/week x 3 weeks with a 7 week follow up	Significant difference in volume reduction for both groups. Both groups demonstrated comparable volume losses. Results of this study showed that the addition of IPC with CDT did not have any additional effect in reducing BCRL.

Kinesiotape (KT)

KT for reduction of BCRL lymphedema

Theory

- Appropriate application causes a stretch of the skin which increases the space between the dermis and fascia (Tarada et al).
  - The increased space promotes lymph drainage.
  - Creates tissue deformation (convoluted application)
- Lack of scientific evidence for the clinical effects in the treatment of lymphedema.

Kinesiotape Review of the Literature

High/ Acceptable # Articles	Risk Mitigation & Latent Stage	Intervention	Low/ Unaccept # Articles
2		2	4

KT may not replace short stretch bandaging in CDT when trying to reduce volume in stage II and III lymphedema. (Level II)

KT for reducing BCRL – Stage II and III

Author, Year	Intervention (2 groups)	Results
Tsai 2009 (Acceptable) BCRL for at least 3 months "moderate to severe" in nature Dx Criteria: >2cm difference between affected and unaffected limbs. Level II	**KT*** (n=21) • 5x/week x 4 weeks • 3 month follow up to assess for retention **Vs.** **Short stretch compression bandage***: (n=21) *all groups received routine treatment of skin care, 1 hour of compression pump (40mmhg), 30 min of MLD, 20 min of exercise in addition to either KT or short stretch bandages	Although both groups showed a reduction in edema, the compression bandage group showed a significant reduction whereas reduction for the KT group was not significant.

KT for reducing BCRL – Stage II and III

Author, Year	Intervention	Results
Smykla 2013 (Acceptable) BCRL stage II and III **Dx criteria:** limb volume >20% compared to uninvolved limb Level II	**KT (n-20):** anchored at the hand with the tails of the tape applied to the anterior, medial, and posterior aspects of the forearm and arm and anterior chest (anastomoses). 5-15% tension **Quasi KT (n=22):** Applied same as group 1 without tension applied. **Multilayered compression therapy (MCT) n= 23):** 4 layers using short stretch bandages and finger wraps. **3x/week x 1 month** *all groups received routine treatment of skin care, 45 min compression pump, 1 hour of MLD in addition to either KT, quasi KT, or short stretch bandages.	Most significant decrease in volume was in the MCT group. % volume reduction affected limb compared to unaffected. **% volume reduction between groups:** KT vs MCT 24.45% vs 53.21% p=0.02 Quasi KT vs MCT 24.78% vs 53.21% p=0.02 KT vs. Quadi KT 24.45 % vs 24.78% p=0.455

KT for reducing BCRL – Stage I

Author, Year	Intervention (2 groups)	Results
Malicka 2014 (Low) Grade I BCRL (n=28) Level III	**KT (n=14)** • 1x/week x 4 weeks (4 applications total) • (N=7)Applied in a fan like distribution along the lower and upper arm and along anastomoses • (n-=7) Applied in fan like distribution to the upper and lower arm only. • 15% tension for both applications Vs. **No treatment** (n=14)	Both subgroups that received KT had a significant reduction from Initial to final evaluation which suggests that either application method may be successfully used.

KT Summary/Take Home

- KT may be safe but must consider the risk for wounds when removing the tape. (Level II)
- Higher quality studies are needed to assess the effectiveness of KT for volume reduction in the early stages of upper quadrant lymphedema.
- Further high quality evidence needed that elucidates the physiologic effects, and controversies connected with methodology, application technique, and pressure values in the treatment of lymphedema.

Modalities

Overview of Evidence

Modalities	High/Accept # Articles	Risk Mitigation & Latent Stage	Intervention-Reduction Stage I-III	Intervention Exacerbation	Low/ Unaccept # Articles
Laser	4		4		4
Far-Infrared					1
Extracorporeal Shockwave therapy					1
Electrotherapy					1
Cooling					1
Hyperbaric Oxygen					1

Laser Treatment and Other Modalities

- Laser may be considered either alone or in combination with decongestive therapy in patients with established lymphedema of the upper extremity. (Level II evidence)
- Electrotherapy, and extracorporeal shockwave therapy, and hyperbaric oxygen treatment do not have sufficient evidence to support their use at this time. (Level III evidence)

Laser Therapy vs. Compression Pump

Author, Year Population	Interventions	Results
Kozanglu, 2009 (acceptable) BC with LE > 3 mo Dx Criteria: >2 cm at 3 points Level II	**Low Level Laser** (n=25) 20 minutes 3x per week, 4 weeks Ga-As 904 nm laser at 3 points antecubital and 7 points axilla vs. **Pneumatic Compression** (n=25) 2 hours per day for 4 weeks *All patients performed daily exercises and skin care	Reduction in circumferential measure: Low level laser and Pneumatic Compression result **similar reductions** post-treatment (-4.9 vs. -5.1 cm) ES = -0.05 At 1 year Low level laser retained reduction better (-5.3 vs. -1.3 cm) (p=0.03) ES= 0.64 (CI)

Low Level Laser vs. MLD

Author, Year Population	Intervention	Result
Ridner, 2013 (acceptable) BC with LE ISL Stage I – III; primarily Stage II Dx Criteria: MD diagnosis Level II	**MLD** 40 min (n=16) Followed Foldi standards vs. **Low Level Laser** 20 min (n=15) RianCorp LTU 904, 20-30 sec per point vs. **Combined MLD** 20 min + **Low Level Laser** 20 min (n=15) *All received compression post-tx	Lymphedema measured by BIA, CM, and LSIDS-A No difference between interventions, all demonstrated improvements, no follow-up Effect Sizes: **MLD**: BIA ES= -0.54 CM ES= -0.42 **LLL**: BIA ES = -0.55 CM ES = -0.64 **MLD + LLL**: BIA ES = -0.53 CM ES = -0.64

Laser Therapy vs. Placebo with CDT

Author, Year	Intervention	Results
Khalaf, 2013 (acceptable) Lymphedema duration approx. 18-19 months No dx criteria stated Level II	Treatment 3x/week for 6 months **Helium-Neon Laser** (15 min, 17 points in axilla) + Decongestive lymphatic therapy (n=15) vs. **Placebo Laser** + Decongestive lymphatic therapy (n=15) Decongestive Lymphatic Therapy: Skin care, Manual Lymphatic Therapy, Low-stretch Bandages, Exercises	By Circumferential Measure: Laser Reduction: -284.54 +/- 88.68 Placebo Reduction: -158.13 +/- 109.71 ES = -1.27 Also improved shoulder mobility by about 10 degrees

Laser vs Placebo, no other active treatment

Author, Year	Intervention	Results
Storz, 2016 (acceptable) BC Lymphedema >3 mo No dx criteria stated Level II	**Cluster Laser** 16 diodes 980 nm, 640 mW 10 min, 2x/week 4 weeks (n=17) vs. **Placebo Laser** – inactivated unit (n=19) *Advised to continue daily limb exercises and skin care	By Circumferential Measure: No significant difference between groups **Laser**: - 8.64 (328.41) **Placebo**: -76.43 (351.97) P=0.13

Complementary and Alternative Medicine

High/ Acceptable # Articles	Risk Mitigation & Latent Stage	Intervention-Reduction Stage I-III	Intervention-Exacerbation Stage I-III	Low/ Unacceptable # Articles
0				10

Complementary and Alternative Medicine

Low or unacceptable CAM interventions included:

- Acupuncture with or without moxibustion
- Reflexology
- Aromatherapy
- Diet restriction/ calorie intake reduction

Further high quality research is needed in CAM interventions

Compiling the Recommendations: Risk Mitigation and Latent Lymphedema

- In the acute phase (1-2 weeks):
  - Therapists should not restrict activity and should gradually progress resistance exercises. (Level I)
- Early modified CDT (MLD, AROM exs, Skin and Nail care, and Education – w/o compression) may be used to reduce the risk of progression of secondary lymphedema in the upper extremity in individuals who have undergone ALND. (Level II, 1 study)
- It is safe for patients with latent stage BCRL to perform weightlifting activities. (Level I)

Interventions for Early – Late Stage Lymphedema

- CDT may be used as an intervention to reduce arm volume in those diagnosed with secondary lymphedema (Level I no significant difference, Level II – mixed results)
- Upper extremity exercise, initiating with the proximal muscles, may result in a short-term but not long-term volume reduction (Level II)
  - May recommend for self-care
- The addition of MFT to standard physical therapy appears to be safe in patients greater than 3 months post-radiation. (Level II)
- IPC may not enhance the volume reduction gained by complete decongestive therapy when applied *following MLD* in patients with established lymphedema of the upper extremity. (Level II)
- Laser may be considered either alone or in combination with decongestive therapy in patients with established lymphedema of the upper extremity. (Level II evidence)

Interventions for Early – Late Stage Lymphedema

- KT may not replace short stretch bandaging in CDT when trying to reduce volume in stage II and III lymphedema. (Level II)
- Pole walking and aquatic therapy may be included in intervention plan (Level II)
- IPC does not have evidence at this time to support its use as a stand alone treatment for upper quadrant lymphedema.
- Electrotherapy, and extracorporeal shockwave therapy, and hyperbaric oxygen treatment do not have sufficient evidence to support their use at this time. (Level III evidence)
- CAM modalities including acupuncture, reflexology, aeromatherapy, and dietary changes do not have sufficient evidence to support their use at this time. (Level III)

Interventions that could Exacerbate Early – Late Stage Lymphedema

- For those who have BCRL (stage 0 – III), weightlifting and high load and low load resistance exercise appears to be safe and may included(Level II)
- Supervised aerobic and resistance exercise should not exacerbate BCRL (Level I)

*Best practice is to use compression garments with exercise

Reminder

*All statements presented are preliminary drafts

- We want your constructive feedback to improve the statements!
  - Evidence-based
    - Other Best Practice statements?
  - Clarity

CPG Limitations

- Many of the intervention articles were pilot studies and therefore lacked sufficient follow up times
- Articles may have been published outside of review timeframe
  - On-going effort to include additional articles
- Non-published studies

Important Research Questions

- Stages of lymphedema
  - How does this impact the interventions needed?
  - Trials need to better clarify the intervention population and do sub-population analysis
- Larger scale intervention trials are needed!
  - Need to use validated measures for inclusion of subjects and outcome measures, as well as longer follow-up periods
- Interventions we may feel are best practice needs higher level research evidence

Audience Feedback and Discussion