Usability of Advanced Pneumatic Compression for the Treatment of Cancer-Related Head and Neck Lymphedema

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Abstract

Background

Head and neck lymphedema (HNL) is a frequent late complication in patients treated for head and neck cancer (HNC) affecting up to 90%[1,2] of survivors. Effects of surgery and/or radiation either obstruct or destroy lymphatic vessels and damage surrounding soft tissue.[3,4] The lymphatic disruption and tissue damage leads to fluid accumulation in interstitial spaces in affected areas. This high-protein fluid activates chronic inflammatory responses and skin and subcutaneous tissue fibrosis further impairing lymphatic function.[5] Although HNL is associated with substantial chronic symptom burden, functional deterioration, disfigurement and poor quality of life in HNC survivors,[6] it remains under-recognized and undertreated.[3,4,6] Based on demonstrated clinical benefits of advanced pneumatic compression to treat lymphedema in other body areas,[7–11] a device incorporating similar principles and mechanism of action was developed for use on the head and neck. The goal of the present study was to evaluate its utility in treating HNL.

Methods

This study was a single arm, prospective, functional usability study that included 44 subjects with secondary HNL who had previously been treated for HNC. Lymphedema stage, based on tissue characteristics, was assessed using the MD Anderson Cancer Center Head and Neck Lymphedema rating scale.[12] All subjects received a single 30–35 minute treatment with the head and neck garment-based pneumatic compression device. The device is intended to treat HNL by stimulating axillary lymphatic tributary regions and directing fluid from affected areas to healthy, functioning regions. Patient-reported garment and treatment comfort were assessed using a five category survey. Patients also reported how they felt post-treatment and the likelihood of continuing home use. Pre-to-post treatment edema changes were evaluated via tape measurement which included the sum of seven standardized face metrics (FACE Composite) and the sum of three neck circumference measurements (NECK Composite). Statistical significance of these changes were assessed with a paired T-test and subjective changes assessed via chi square analyses.

Results

A single treatment produced statistically significant reductions (mean ± SD) in both FACE Composite (82.5 ± 4.3 cm vs. 80.9 ± 4.1 cm, p<0.0001) and NECK Composite (120.4 ± 12.2 cm vs. 119.2 ±12.1 cm, p<0.0001). Beyond these quantitative reductions, no adverse events were reported and no patient found the treatment to be uncomfortable with 36/44 (82%) reporting treatment to be either very or somewhat comfortable. Most patients (27/44, 61%) reported feeling much or somewhat better after treatment. Nearly all patients (41/44, 93%) reported they would be likely to use this therapy at home.

Conclusion

These pilot data suggest advanced pneumatic compression treatment for head and neck lymphedema is promising. Results found the treatment to be safe, easy to use and well tolerated while demonstrating edema reduction at initial treatment. Advanced pneumatic device treatment has the potential to reduce symptom burden in this population.

Introduction

Reported head and neck lymphedema (HNL) rates associated with head and neck cancer (HNC) treatment range from 48%[13] to 90%.[1] Combined cancer treatment methods involving tumor resection, lymph node dissection, and radiotherapy result in the most severe cases of lymphedema. HNL may involve external structures (skin and soft tissues) or internal structures (mucosa, larynx and pharynx) and both external and internal tissues are often affected and cumulatively contribute to functional impairments.[1,4] The most common areas of external swelling are the submental region and the neck.[2,12] HNL of internal tissue can impact critical physical functions (e.g., respiration, mastication, swallowing, and speaking).

HNL is generally managed by using modified techniques of a multi-modal treatment approach known as Complete Decongestive Therapy (CDT). This approach includes manual lymphatic drainage (MLD), compression, therapeutic exercise and skin care. CDT is initiated in a clinic setting with treatment performed by specially trained clinicians and is transitioned to ongoing self-management at home. Many patients experience difficulty performing this treatment at home and/or find the treatment insufficient in effectively managing symptoms long-term. To help patients meet the substantial challenge of treating HNL, an advanced pneumatic compression device (PCD) for at-home use has been developed.

Methods

Study Design and Subjects

This single arm, functional usability study included patients with HNC-related HNL. Approval for the study was obtained from the IRB at Mercy Hospital (St. Louis, MO). Patients who had previously been treated for HNC and were receiving or had completed in-clinic CDT were eligible for the study. Patients had to be cancer-free at study entry and at least 4 weeks post cancer treatment to qualify for participation.

Assessment of Face and Neck Lymphedema

Lymphedema stage, based on tissue characteristics, was assessed using the MD Anderson Cancer Center Head and Neck Lymphedema (MDACC HNL) rating scale.[12] To determine acute changes in edema pre-and post-device use, measurements of the neck and face were performed as illustrated in Figure 1. Use of this method has been reported in previous research.[12]

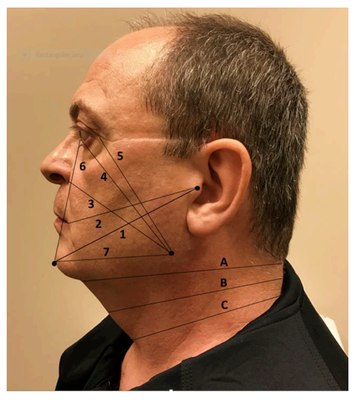
Three circumferential neck measurements were summed to provide a single Total Neck Composite score. Seven facial measurements were performed on both sides of the face. The sum of the hemi-facial composite scores is termed the Total Facial Composite and was the parameter used to assess facial edema change. Pre- and post-treatment face and neck composite values were compared using paired t-tests with a p-value less than 0.05 considered a statistically significant change.

Figure 1.
Face and Neck Measurements to Determine Face and Neck Composite Metrics

Measurement start and endpoints for facial metrics as follows: Line 1=tragus to chin; Line 2= tragus to mouth corner; Line 3 = mandible to nasal wing; Line 4 = mandible to medial canthus; Line 5 = mandible to exocanthus; Line 6 = chin to medial canthus; Line 7 = mandible to chin.

Measurements for the neck perimeter as follows: A = superior neck, B = middle neck and C = inferior neck.

*Facial metrics on both face sides are summed to yield a single **Total Face Composite** value. Neck A, B and C perimeters are summed to yield a single **Total Neck Composite** value.*

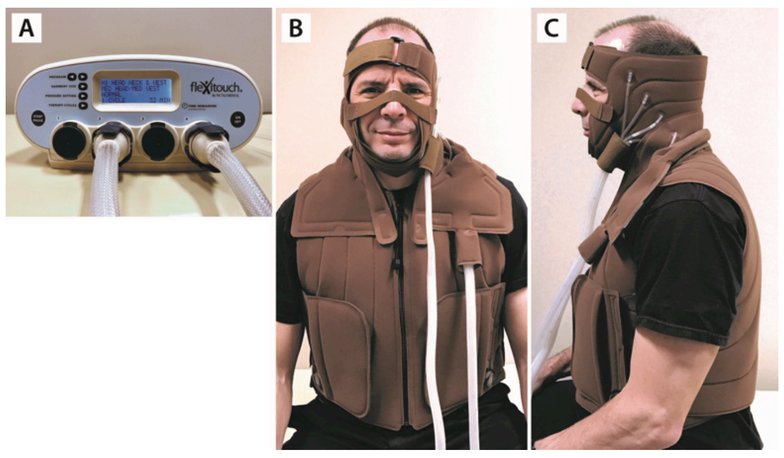


Treatment Device and Procedures

The advanced PCD (Flexitouch® System, Tactile Medical,™ Minneapolis, MN) achieved FDA 510(k) clearance in September of 2016 with an indication for the treatment of HNL. The nylon garments have a total of 14 pneumatic chambers covering part of the head, neck and chest as illustrated in Figure 2. The device applies brief applications of dynamic pressure in a wave-like manner to the treatment area. The system is designed to treat HNL by stimulating the adjacent axillary lymphatic tributary regions prior to directing fluid from the affected area to functioning regions. Each subject received a brief training session on device application followed by one 32-minute treatment session with the device. Safety outcomes were captured on adverse event forms.

Subject reported outcomes were obtained via a series of questions to assess garment application, fit and comfort. The following major categories were queried: (1) Garment Comfort, (2) Treatment Comfort, (3) Feeling Post-treatment and (4) Likeliness to use at home. The possible responses to these four queries are summarized in Table 3.

Figure 2. *Flexitouch System for Head and Neck. A) Controller; B) Front view; C) Side view*



Results

A total of 44 subjects participated; 34 males with ages of 61.0 ± 9.7 (mean ± SD) years (range 42–81) and 10 females with ages of 60.0 ± 5.4 years (range 51–67). Subject demographics and HNC treatment characteristics are provided in Table 1. Table 2 summarizes lymphedema stage by number and percentage of subjects within each stage. Within two attempts, the majority of patients demonstrated the ability to apply (70%) and remove (95%) the garments independently.

Table 1. *Subject Demographics and Cancer Treatment History*

Age	Mean (SD)	61 (8.9)
Gender	Male	34/44 (77%)
	Female	10/44 (23%)
Ethnicity	Not Hispanic or Latino	42/44 (95%)
	Hispanic or Latino	2/44 (5%)
Race	White	41/44 (94%)
	Black or African American	1/44 (2%)
	American Indian or Alaska Native	1/44 (2%)
	Asian	1/44 (2%)
HNC Treatment	Surgery and Radiation and Chemotherapy	17/44 (39%)
	Surgery and Radiation	11/44 (25%)
	Radiation and Chemotherapy	15/44 (34%)
	Radiation	1/44 (2%)
Surgery Type	Combined (resection of primary tumor and lymph nodes)	26/44 (59%)
	No Surgery	16/44 (37%)
	Resection of primary tumor	1/44 (2%)
	Resection of regional lymph nodes	1/44 (2%)
Surgical Procedure (not mutually exclusive)	Glossectomy	10
	Neck Dissection †	7
	Pharyngectomy	2
	Tonsillectomy	2
	Submandibular gland resection	2
	Mandibulectomy	1
	Laryngectomy	1
	Other ‡	2
Feeding Tube	Yes	8/44 (18%)
Tracheotomy	Yes	2/44 (5%)

† (1) Radical; (3) Modified; (1) Selective; (2) Unspecified ‡ (1) Lip Reconstruction; (1) Thyroidectomy

Table 2. *Stage of Lymphedema using the MDACC HNL Rating Scale*

Stage	Description	Number (%)
0	No visible edema but patient reports heaviness	0 (0%)
1a	Soft visible edema; no pitting, reversible	1 (2.3%)
1b	Soft pitting edema; reversible	15 (34%)
2	Firm pitting edema; not reversible; no tissue changes	24 (54.5%)
3	Irreversible; tissue changes	4 (9.1%)

Subjective Patient Assessments

Table 3 shows the response count for each of the analyzed response parameters. For purposes of the present analysis responses 1 or 2 were considered as positive responses and responses 3, 4, 5 or 6 were considered non-positive responses. This places category 3 (the indifferent category) in the non-positive response as a conservative estimate. To determine if the number of positive responses differed significantly from the non-positive responses a 1 x 2 contingency table was used for a chi square analysis with an exact Fisher test for significance. Results of these analyses are shown in Table 4.

Results show statistically significant differences between positive and non-positive responses with respect to the questions of treatment comfort, how the subject feels post-treatment and the likeliness of the patient using the treatment device at home. For all three of these response parameters positive responses were statistically greater than non-positive responses.

Table 3. *Range of possible patient responses and response count for each of the analyzed patient response parameters.*

	Patient Response Count			
Possible Patient Responses	Garment Comfort	Treatment Comfort	Feeling post Treatment	Likeliness of Home Use
1	Very Comfortable 9	Very Comfortable 21	Much Better 7	Very likely 36
2	Somewhat Comfortable 16	Somewhat Comfortable 15	Somewhat Better 20	Somewhat likely 5
3	Neutral 15	Neutral 8	About the same 12	Unsure 2
4	Somewhat Uncomfortable 4	Somewhat Uncomfortable 0	Somewhat worse 0	Somewhat Unlikely 0
5	Very Uncomfortable 0	Very Uncomfortable 0	Much worse 0	Very Unlikely 1
6	n/a	n/a	Too brief to tell a difference 1	n/a

Table 4. *Patient Subjective Positive vs. non-Positive Responses*

	Garment Comfort	Treatment Comfort	Feeling Post-Treatment	Likeliness of Home Use
χ^2	0.818	17.818	7.364	32.818
df	1	1	1	1
Exact Significance	0.451	0.000*	0.01*	0.000*

**statistically significant*

Changes in Facial and Neck Measurements

A single treatment session was associated with an overall small but highly statistically significant reduction (p-value < 0.0001) in both the neck and the face composite metrics as summarized in Table 5. Further analysis of individual responses showed that 20% of patients demonstrated a neck composite reduction of at least 2%, and 43% of patients demonstrated a face composite reduction of at least 2%. A 2% change in face or neck composite values is relevant as it has been defined in previous literature as the threshold for clinically important reduction in HNL.[10] No adverse events in this study were reported.

Table 5. *Change in face and neck composite values pre to post-treatment.*

Total Neck Composite			Total Face Composite		
Pre	Post	p-value	Pre	Post	p-value
120.4 ± 12.2	119.2 ± 12.1	< 0.0001	82.5 ± 4.3	80.9 ± 4.1	< 0.0001
Overall % Reduction	1.00 ± 1.18		Overall % Reduction	1.18 ± 1.23	
Patients with Reduction >=2%	**9 (20%)**		Patients with Reduction >=2%	**19 (43%)**	

Data entries are overall mean ± SD in units of cm for absolute values. Overall percent reduction (% Reduction) is calculated as 100 (post – pre)/pre for each patient and then averaged overall.*

Discussion

The functional deficits associated with HNL are particularly distressing for patients. To date, the self-management of HNL has been challenging. MLD provided by a skilled clinician has proven effective in a clinic setting, but self-administered MLD can be arduous for a patient to perform independently. The proper technique is difficult to master, especially if functional impairments in upper extremity and/or cervical range of motion are present. The difficulty in performing self-treatment often results in poor treatment adherence, which further limits effective self-management.

The favorable results shown in this pilot study suggest a variety of possible long-term clinical outcomes. In this sample, 67% of subjects experienced a clinically significant reduction in either neck or facial composite measurements after just one treatment. Almost 70% reported feeling better after the treatment. In addition, a high majority (93%) reported likelihood of at-home use of this device. These impressive results suggests that consistent use of the device at home may elicit cumulative long term edema reduction, or at minimum, maintenance of reduction achieved during in-clinic therapy.

Conclusion

Results found the PCD treatment to be safe, easy to use and well tolerated while demonstrating edema reduction at initial treatment. This treatment has the potential to reduce symptom burden in this population. Future research is needed to assess the long-term effectiveness of device treatment on symptom burden and quality of life in HNL patients. Further investigations should consider use of instrumentation to visualize and measure the internal lymphedema-affected areas to assess whether treatment benefits can be documented at these critical sites.

References

1. Ridner, S.H., et al., *A Prospective Study of the Lymphedema and Fibrosis Continuum in Patients with Head and Neck Cancer.* Lymphat Res Biol, 2016. 14(4): p. 198-205.
2. Deng, J., et al., *Prevalence of secondary lymphedema in patients with head and neck cancer.* J Pain Symptom Manage, 2012. 43(2): p. 244-52.
3. Smith, B.G. and J.S. Lewin, *Lymphedema management in head and neck cancer.* Curr Opin Otolaryngol Head Neck Surg, 2010. 18(3): p. 153-8.
4. Deng, J., et al., *Factors associated with external and internal lymphedema in patients with head-and-neck cancer.* Int J Radiat Oncol Biol Phys, 2012. 84(3): p. e319-28.
5. Avraham, T., et al., *Radiation therapy causes loss of dermal lymphatic vessels and interferes with lymphatic function by TGF-beta1-mediated tissue fibrosis.* Am J Physiol Cell Physiol, 2010. 299(3): p. C589-605.
6. Deng, J., et al., *Impact of secondary lymphedema after head and neck cancer treatment on symptoms, functional status, and quality of life.* Head Neck, 2013. 35(7): p. 1026-35.
7. Karaca-Mandic, P., et al., *The cutaneous, net clinical, and health economic benefits of advanced pneumatic compression devices in patients with lymphedema.* JAMA Dermatology, 2015: p. 1-7.
8. Brayton, K.M., et al., *Lymphedema Prevalence and Treatment Benefits in Cancer: Impact of a Therapeutic Intervention on Health Outcomes and Costs.* PLoS ONE, 2014. 9(12): p. e114597.
9. Blumberg, S.N., et al., *Pneumatic Compression Improves Quality of Life in Patients with Lower-Extremity Lymphedema.* Ann Vasc Surg, 2016. 30: p. 40-4.
10. Adams, K.E., et al., *Direct evidence of lymphatic function improvement after advanced pneumatic compression device treatment of lymphedema.* Biomed Opt Express, 2010. 1(1): p. 114-125.
11. Muluk, S.C., A.T. Hirsch, and E.C. Taffe, *Pneumatic compression device treatment of lower extremity lymphedema elicits improved limb volume and patient-reported outcomes.* Eur J Vasc Endovasc Surg, 2013. 46(4): p. 480-7.
12. Smith, B.G., et al., *Lymphedema Outcomes in Patients with Head and Neck Cancer.* Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery, 2015. 152(2): p. 284-291.
13. Buntzel, J., et al., *Influence of amifostine on late radiation-toxicity in head and neck cancer--a follow-up study.* Anticancer Res, 2007. 27(4a): p. 1953-6.