AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
2019, Vol. 160(4) 622–626

DOI: 10.1177/0194599818823180
http://otojournal.org
SAGE

Head and Neck Lymphedema: Treatment Response to Single and Multiple Sessions of Advanced Pneumatic Compression Therapy

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract

Ten head and neck cancer survivors diagnosed with head and neck lymphedema (HNL) were imaged using near-infrared fluorescence lymphatic imaging (NIRFLI) prior to and immediately after an initial advance pneumatic compression device treatment and again after 2 weeks of daily at-home use. Images assessed the impact of pneumatic compression therapy on lymphatic drainage. Facial composite measurement scores assessed reduction/increase in external swelling, and survey results were obtained. After a single pneumatic compression treatment, NIRFLI showed enhanced lymphatic uptake and drainage in all subjects. After 2 weeks of daily treatment, areas of dermal backflow disappeared or were reduced in 6 of 8 subjects presenting with backflow. In general, reductions in facial composite measurement scores tracked with reductions in backflow and subject-reported improvements; however, studies are needed to determine whether longer treatment durations can be impactful and whether advanced pneumatic compression can be used to ameliorate backflow characteristic of HNL.

Keywords

lymphedema, near-infrared fluorescence imaging, pneumatic compression therapy, lymphatics, head and neck cancer survivorship

Received August 24, 2018; revised November 8, 2018; accepted December 14, 2018.

Head and neck lymphedema (HNL) with its associated functional losses[1-4] affects as many as 75% of head and neck cancer (HNC) survivors 3 months or more after HNC treatment.[5] Using near-infrared fluorescence lymphatic imaging (NIRFLI), we previously observed persistent lymphatic "dermal backflow" (retrograde lymphatic drainage to initial lymphatics) over the cancer treatment course in patients with HNC,[6] similar to patients with breast cancer–related lymphedema (BCRL).[7,8] Lymphedema treatment consists of skin care and complete decongestive therapy (CDT),[9] but unfortunately, HNL is often undiagnosed, and when it is, treatment is often inaccessible. Herein, NIRFLI and anatomic facial and neck measurements[10] were made on 10 HNC survivors to assess the impact of single treatments and 2 weeks of daily treatments using advanced pneumatic compression devices.[11]

Study approval was obtained from the Institutional Review Board of the University of Texas Health Science Center at Houston under IND 102,765 for NIRFLI. Subjects ≥18 years of age, diagnosed with HNL, and ≥4 weeks post-radiation were recruited and provided written informed consent. After measurements to obtain composite facial and neck scores,[9] intradermal indocyanine green injections (25 μg/0.1 cc saline) were administered fore and aft each ear and bilaterally along the jawline as previously reported.[6] NIRFLI was conducted before and after an initial 32-minute pneumatic compression treatment. Subjects were then provided a pneumatic compression device for home use and asked to complete and document treatments. Cases 1 to 5 completed 1 treatment daily while cases 6 to 10 completed 2 treatments, typically 1 each morning and evening. After 2 weeks, NIRFLI was again conducted before and after treatment. In all cases, composite scores were acquired before and, in cases 5 to 10, after treatment at each imaging

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Table 1. Percent Change[a] in the Area of Dermal Backflow and the Facial and Neck Composite Scores as Measured by Tape Measure.

Case ID	Measurement Comparisons[b]	% Change, Area of Dermal Backflow	% Change, Facial Composite Score	% Change, Neck Composite Score	Subject Reported Impact on Lymphedema Symptoms
Case 1	At visit 1	38.7	—	—	Visits 1 and 2, felt somewhat better
	At visit 2	ND	—	—	
	Between visits	−100.0	−1.2	−1.3	
Case 2	Between visits	ND	−3.8	0.2	Visit 1, felt somewhat better; improved swallow
Case 3	At visit 1	116.8	—	—	Visit 1, felt somewhat better; visit 2, felt the same; improved swallow
	At visit 2	49.3	—	—	
	Between visits	18.1	1.0	1.6	
Case 4	At visit 1	87.2	—	—	Visit 1, felt somewhat better; visit 2, felt the same; reduced tightness in throat
	At visit 2	264.9	—	—	
	Between visits	−39.3	−1.9	−0.9	
Case 5	At visit 1	22.5	2.0	−2.6	Visit 1, felt the same; visit 2, felt somewhat better
	At visit 2	85.9	−2.0	−0.2	
	Between visits	−26.0	1.2	−1.3	
Case 6	At visit 1	1319.4	−0.7	−6.4	Visit 1, felt the same; visit 2, felt somewhat better; reduced swelling and "thickness" and "hardness" of tissues
	At visit 2	1802.0	2.5	4.2	
	Between visits	−23.9	3.1	−3.6	
Case 7	At visit 1	84.5	−2.2	1.8	Visit 1, felt much better; visit 2 felt somewhat better; reduced tightness
	At visit 2	116.0	−1.8	−2.4	
	Between visits	−27.7	0.1	−0.2	
Case 8	At visit 1	23.3	−0.8	−1.7	Visit 1, felt much better; visit 2, felt somewhat better
	At visit 2	86.3	−0.1	2.8	
	Between visits	−29.1	−0.5	−5.2	
Case 9	At visit 1	ND	−0.6	1.2	Visits 1 and 2, felt somewhat better; improved swallow
	At visit 2	ND	1.5	−1.9	
	Between visits	ND	−3.0	7.0	
Case 10	At visit 1	154.7	−0.5	−0.4	Visits 1 and 2, felt somewhat better; improved swallow, reduced swelling
	At visit 2	28.8	−0.1	−3.5	
	Between visits	15.5	1.3	−1.6	

Abbreviations: ND, no dermal backflow; —, no data.
[a]Positive changes reflect an increase in the measurements and negative (–) changes reflect a reduction in the measurements.
[b]At visit X—compares the pre- and posttreatment measurements at visit X; between visits—compares the pretreatment measurements from visits 1 and 2.

session. Subjects completed surveys assessing fit and comfort of the device and treatment. Areas of dermal backflow, observed by NIRFLI, were computed and profilometry measurements acquired as described in the online supplemental material (available in the online version of the article).

Subject demographics, cancer-related history, and study compliance are available in Supplemental Table S1 (in the online version of the article). **Table 1** presents percent changes in the area of backflow and composite scores after treatment at each visit and the pretreatment (baseline) measurements from both imaging sessions. No apparent differences were observed between daily and bidaily treatment groups. No adverse events were observed.

Impact of Single Treatment

In all subjects, we observed enhanced lymphatic uptake after *single* treatments as indicated by more functional lymphatic vessels, drainage to lymph nodes, and/or acute increases in backflow (**Figure 1A-D**), indicating treatment promotes movement of lymph toward functional lymphatics as observed in patients with BCRL[12] and venous stasis ulcers.[13]

Impact of 2 Weeks of Treatment

Because differences in pretreatment images allow assessment of longitudinal treatments without the acute treatment impact, we compared pretreatment areas of backflow across visits. Taking a 20% difference as the threshold of reportable change, we found longitudinal treatment reduced backflow in 6 subjects and 4 had no change in backflow, with 2 of those subjects never initially presenting with backflow. Backflow did not increase across 2 weeks of treatment in any study subject.

Of the 6 of 8 subjects who presented with backflow and experienced backflow reduction after 2 weeks of treatment,

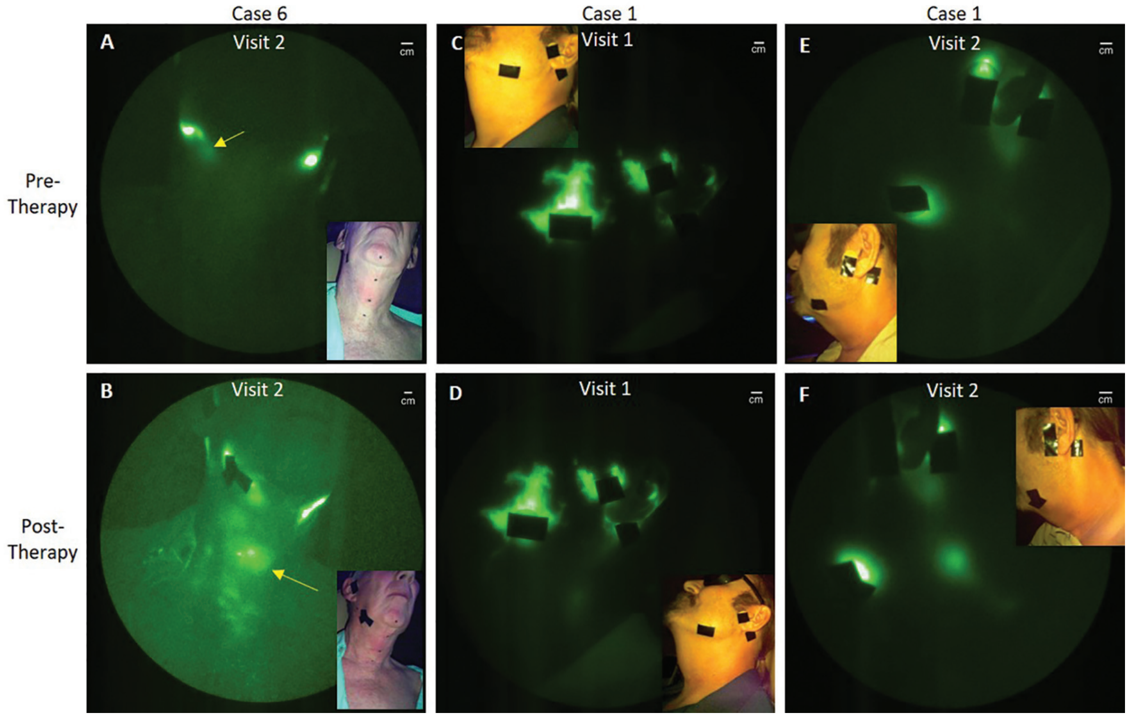

Figure 1. Near-infrared fluorescence lymphatic imaging illustrating (A, B) increased dermal backflow (case 6, visit 2) and (C-F) drainage to lymph nodes (case 1, visits 1-2) after single treatment sessions and (C, E) backflow (case 1) ameliorated by 2 weeks of treatment.

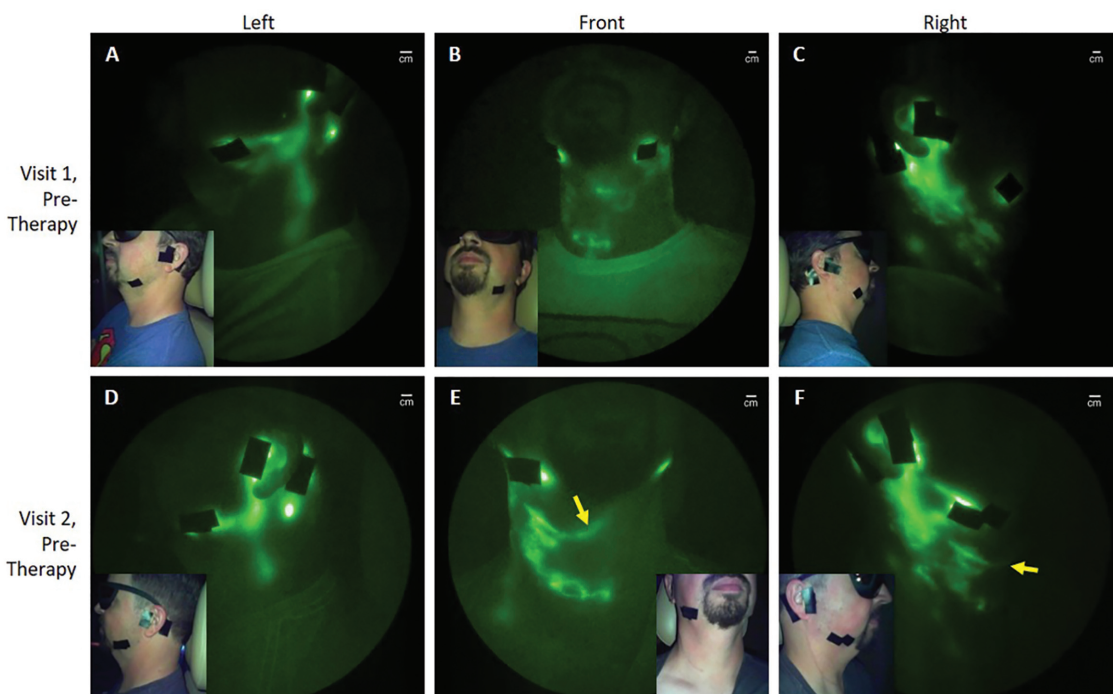

Figure 2. Near-infrared fluorescence lymphatic imaging illustrating case 5's pretreatment lymphatics at visits 1 (A-C) and 2 (D-F). Better-formed lymphatics are observed (D) along the jawline and (E, F) pumping lymph (arrows) right to left toward healthier vessels.

1 (case 1) had complete resolution of dermal backflow (**Figure 1C**,**E**) with facial and neck composite score reductions. Interestingly, active lymphatic propulsion was observed before and after treatment at visit 2 but not visit 1, possibly indicating improved lymphatic function. In case 5, backflow reduced by 26% and active propulsion in a new vessel was observed draining from right to left with another observed pumping cranially toward functional lymphatics (**Figure 2** and Supplemental Video S1, available in the online version of the article). This subject's first treatment

resulted in an increase in facial composite score, while the last treatment resulted in a decrease. Why some composite scores increase immediately after treatment remains unknown, although in this case, it may be attributed to stimulation of the vessel actively pumping fluid upward toward other functional lymphatics.

Case 3 and 10 had no reportable changes in backflow, but both reported improved swallow and/or speech. While these self-reported improvements may be influenced by treatment bias, case 10 reported that, after 3 days of treatment, he regained the ability to swallow liquids without forced nasal drainage, an improvement he directly attributed to the treatment and, which we hypothesize, indicates a reduction in internal swelling not readily assessed by measurements or NIRFLI. The lack of response in case 3 may be a function of the 1.6-year delay between radiation and lymphedema treatment as lymphedema patients with early intervention typically have better outcomes.[14] We hypothesize that continued treatment may result in measurable improvements in both cases.

Two subjects, who did not present with backflow before or after treatment, nonetheless experienced a reduction in the pretreatment composite scores and reported improved swallow function.

Subjective patient reports included being more relaxed, neck softer, voice better, and less swollen, with less fluid in the face and less tightness in throat (**Table 1**). It may be noteworthy that case 10 reported that the left side of his face felt more swollen after treatment but that he experienced similar feelings after manual lymphatic drainage; however, his facial composite score decreased after treatment.

In conclusion, 2 weeks of advanced pneumatic compression treatment improved self-reported outcomes, stimulated lymphatic function, reduced the area of backflow in 6 of 8 subjects with backflow, and, in 1 case, ameliorated backflow. This latter result may be striking as previous HNL studies demonstrated persistent backflow during months of observation.[6] Future studies evaluating lymphatic response to longer durations of treatment and its durability could definitively determine whether advanced pneumatic compression treatment can ameliorate all backflow and potentially mitigate or prevent HNL.

Author Contributions

Carolina Gutierrez, acquisition and interpretation of data, critical revising, approved final work, agrees to accountability of work; **Ron J. Karni**, conception or design of the work, critical revising, approved final work, agrees to accountability of work; **Syed Naqvi**, acquisition of data, critical revising approved final work, agrees to accountability of work; **Melissa B. Aldrich**, acquisition/analysis/interpretation of the data, critical revising, approved final work, agrees to accountability of work; **Banghe Zhu**, acquisition/analysis/interpretation of the data, critical revising, approved final work, agrees to accountability of work; **J. Rodney Morrow**, acquisition of the data, critical revising, approved final work, agrees to accountability of work; **Eva M. Sevick-Muraca**, conception or design of the work and interpretation of data for the work, drafting and critical revising, approved final work, agrees to accountability of work; **John C. Rasmussen**, acquisition/analysis/interpretation of the data, drafting and revision of work, approved final work, agrees to accountability of work.

Disclosures

Competing interests: Ron J. Karni is on the Scientific Advisory Board and Speaker's Bureau for Tactile Medical, who sponsored in part this study. Eva M. Sevick-Muraca is on the Speakers Bureau for Tactile Medical, is listed as an inventor on patents related to near-infrared fluorescence lymphatic imaging, and may receive future financial benefit from commercialization of imaging technology. John C. Rasmussen received research funding from Tactile Medical for the study, is listed as an inventor on patents related to near-infrared fluorescence lymphatic imaging, and may receive future financial benefit from commercialization of imaging technology.

Sponsorships: Tactile Medical provided funding for the study and access to the pneumatic compression devices used in this study, as well as approved the manuscript.

Funding source: National Institutes of Health, Cancer Prevention and Research Institute of Texas provided in part the funds to develop and translate the near-infrared fluorescence imaging technology used in this study.

Supplemental Material

Additional supporting information is available in the online version of the article.

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