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Impact of Compliance on Dysphagia Rehabilitation in Head and Neck Cancer Patients – Results from a Multi-center Clinical Trial

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Abstract

Purpose—A 5yr, 16 site, randomized controlled trial enrolled 170 HNC survivors into active (estim + swallow exercise) or control (sham estim + swallowing exercise) arms. Primary analyses showed that estim did not enhance swallowing exercises. This secondary analysis determined if/how patient compliance impacted outcomes.

Methods—A home program, performed 2×/day, 6d/wk, for 12wks included stretches and 60 swallows paired with real or sham estim. Regular clinic visits ensured proper exercise execution and detailed therapy checklists tracked patient compliance which was defined by mean number of sessions performed per week (0-12 times) over the 12wk intervention period. “Compliant” was defined as performing 10-12 sessions/wk. Outcomes were change in PAS, HNCI, PSS, OPSE, and hyoid excursion. ANCOVA analyses determined if outcomes differed between real/sham and compliant/noncompliant groups after 12wks of therapy.

Results—Of the 170 patients enrolled, 153 patients had compliance data. The mean number of sessions performed was 8.57/wk (median=10.25). Fifty four percent of patients (n=83) were considered “compliant”. After 12wks of therapy, compliant patients in the sham estim group realized significantly better PAS scores than compliant patients in the active estim group (p=0.0074). When pooling all patients together, there were no significant differences in outcomes between compliant and non-compliant patients.

Conclusions—The addition of estim to swallowing exercises resulted in worse swallowing outcomes than exercises alone, which was more pronounced in compliant patients. Since neither compliant nor non-compliant patients benefitted from swallowing exercises, the proper dose and/or efficacy of swallowing exercises must also be questioned in this patient population.

Introduction

Radiation Therapy (RT) is a standard therapeutic modality in the multidisciplinary management of head and neck cancer (HNC). With advances in RT delivery, patients have experienced lower mortality rates[1] and improved locoregional control, but may be left with devastating sequelae of their cancer therapy. As many as two thirds of HNC patients are left with permanent swallowing problems, and dysphagia symptoms can deteriorate for several years post treatment[2-4]. The dysphagia impacts nutrition, hydration, and pulmonary health, and can leave patients with significantly diminished quality of life. The long term morbidity associated with RT is of increasing importance as patients develop Human Papilloma Virus (HPV) associated oral and pharyngeal cancers at younger ages than their HPV negative counterparts[5, 6]. These patients may have many years of productive life after their cancer treatment, so adequate data supporting the efficacy of dysphagia therapies is critical in the context of both pre-treatment counseling and survivorship programs.

Speech language pathologists prescribe various swallow and non-swallow exercises and interventions in an attempt to rehabilitate the dysphagia caused by the HNC treatment. Three

common swallow exercises include the Effortful swallow[7, 8], Mendelsohn maneuver[9], and the Super-supraglottic swallow[10-12]. They are often prescribed to “strengthen” the muscles involved in swallowing so that they can overcome the resistance of fibrotic tissue and to reverse any atrophy that may have occurred during radiation therapy. Despite common prescription of such exercises, little is known about their efficacy. Another more contested but highly sought after treatment for dysphagia is electrical stimulation (e-stim) [13]. Despite an aggressive marketing campaign for this product, it has no good efficacy data in the head and neck cancer population[14, 15]. Accordingly, the authors embarked on a multi-center clinical trial aimed at determining the efficacy of e-stim, and secondarily the aforementioned swallow exercises[16]. In this original clinical trial, 170 patients (Table 1) were randomized into active and sham e-stim groups in a 2:1 ratio respectively. All patients received an aggressive swallowing therapy home program that entailed 5 minutes of stretches followed by 60 swallows performed in synchrony with real or sham e-stim. This program was performed twice per day, 6 days per week, for 12 weeks. The e-stim device used was the BMR NeuroTech 2000 (Galway, Republic of Ireland) because of its highly customizable settings.

The primary outcomes in the clinical trial included the Penetration Aspiration Scale (PAS) [17], Oropharyngeal Swallow Efficiency (OPSE)[18], Hyoid Excursion, Head and Neck Cancer Inventory (HNCI)[19], and Performance Status Scale for Head and Neck Cancer (PSS)[20]. These were measured at baseline, middle of therapy and at completion of the 12 week home therapy program. The primary analysis showed that the group that received active e-stim did not realize any better swallowing, quality of life, or diet outcomes as compared to the group that received sham e-stim. In fact, the sham group realized statistically significantly better PAS scores than did the active e-stim arm, with a difference of 0.52 (95%[CI]=0.06–0.98; $p=0.027$), although this difference was not clinically significant. Both groups reported significantly better diet and quality of life at the end of the clinical trial. The complete methods and results of this clinical trial are presented in the main paper by Langmore et al 2015[16].

Given the absence of published research about how compliance affects efficacy of dysphagia therapy in the head and neck cancer patient population, the authors were interested in determining if patient compliance in this clinical trial affected the primary analyses. As with other clinical arenas that deal with rehabilitation, compliance is a very important and multifaceted issue that should be addressed in behavioral therapy programs. It is generally accepted that patients are motivated to comply with rehabilitation programs if their condition is acute and appreciably affects activities of daily living. For example, an injury that disrupts habitually tangible functions like walking may motivate a patient to comply with their rehabilitation program[21]. Conversely, less tangible conditions, like cardiac rehabilitation, may make a patient less likely to comply since their dysfunction does not appreciably inhibit their social lives[[22]. Adherence to therapy may also depend on perceived efficacy of the exercise, intentions to follow the regimen, and goals that are set by the patient (and not necessarily the treating clinician)[23]. Positive attitudes among HNC patients have also been shown to influence exercise-based rehabilitation[24].

These factors are very relevant to HNC patients who participate in dysphagia rehabilitation programs. The concept of “swallowing therapy” is an abstract one, and because eating and drinking may deteriorate slowly and progressively in HNC survivors, their dysfunction can lack the acuity that dramatically alters their daily routines. Combined with a lack of therapeutic efficacy, these factors may reduce motivation and compliance with their dysphagia therapy programs. In an attempt to determine how or if compliance affected the primary results of the clinical trial, a secondary analysis of the study data was performed.

In this secondary analysis, we determined if compliance influenced the negative results of this trial; whether patients who were more compliant realized better swallow outcomes as a result of either e-stim and/or swallowing exercises as compared to their less compliant counterparts. To do this, three main questions were analyzed. The first question was whether or not there was a difference in compliance between active and sham groups. The second question was whether non-compliance in one or both groups kept that group(s) from realizing the full therapeutic potential of the therapy program. In other words, had everyone been compliant, would the results be different when comparing real versus sham groups? The third question was whether compliant patients realized better swallowing outcomes after the 12 week swallow exercise therapy program as compared to their non-compliant counterparts, irrespective of whether they received the active or sham e-stim.

Methods

In the clinical trial, fidelity was maximized with 3 initial training visits after randomization in which study clinicians taught patients how to use the e-stim device and how to perform the swallowing exercises and stretches. The study clinicians were SLPs who regularly treated head and neck cancer patients at their institution. Prior to enrolling any subjects, these SLPs were trained on the study specific clinical and regulatory protocols by the core research team. These treating SLPs ensured that all patients were competent in performing the home program independently before the start of the home program. Every 3 weeks, a follow up clinic visit entailed reviewing the protocol to confirm continued competence and to ensure the device was in working order. Weekly calls from the treating clinician served to encourage both compliance and fidelity, answer any questions, and trouble shoot any problems between follow up clinic visits. Patients recorded their performance of the home program by completing a detailed checklist during each home program session (see figure 1). The definition of “compliant” to the prescribed home program was retrospectively determined as a mean of 0-9.9 sessions per week for “non-compliant” and a mean of 10.0-12.0 session per week for “compliant”.

The questions presented in the introduction were answered in the following manner. To answer the first question, a chi-squared statistic was used. To answer the second question, the primary analysis was repeated, but only with the compliant patients in each group. As in the primary analysis, an ANCOVA was used to measure differences in all primary outcomes (PAS, HNCI, PSS, OPSE, Anterior Hyoid Excursion and Superior Hyoid Excursion). To answer the third question an ANCOVA was again used to measure differences in the aforementioned primary outcomes. The ANCOVA analyses controlled for between group

differences in baseline measures of swallow performance, diet, quality of life, and any demographic covariates at the $p < 0.1$ level.

For our outcomes of interest, the total, or composite PAS score, was the average of 14 PAS scores (one for each bolus swallowed minus the swallow in the AP projection). OPSE scores and hyoid excursion were calculated similarly. Total PSS scores were calculated as a mean of the three domain scores (diet, public, and speech). Total HNCI scores were also calculated as the mean of each domain scores (speech, eating, aesthetics, and social disruption).

Results

Of the 170 patients enrolled in this clinical trial, 153 patients had compliance data (Figure 2). The 17 patients who did not have compliance data withdrew before starting the program or were lost to follow-up before any outcome measures could be assessed. The mean number of sessions performed per week (max 12) over the course of the 12-week program was 8.57 sessions per week. The median number of sessions was 10.25 per week. Over half of patients (54%, $n=83$) were deemed “compliant” (performing 80-100% of possible sessions), whereas 46% ($n=70$) were characterized as non-compliant (performing less than 80% of possible sessions). Of note, with very few exceptions, if a patient started a therapy session they would complete the entire 60 swallow treatment session, so there was no need to account for partially completed sessions. The mean and median weekly compliance rates for enrolled subjects were remarkably stable for each of the 12 weeks of treatment for actively enrolled subjects (Table 2). Patient demographics between compliant and non-compliant patients demonstrated no significant differences between groups (Table 3).

With regard to whether or not there was a difference in compliance between the study arms, there was no significant difference in compliance rates between active (57% compliant) and sham (48% compliant) e-stim groups ($p=0.2958$). For question 2, when re-analyzing the primary outcomes but only with compliant patients, there was a statistically significant difference in PAS scores after 12 weeks of therapy between active and sham groups ($p=0.0074$). However, like in the primary analysis, it was the sham e-stim group that realized better PAS scores than the active e-stim group. In terms of raw PAS scores, the active NMES arm experienced a mean increase of 0.23 points where the sham NMES arm experienced a mean decrease of 0.71 points on the PAS scale (Table 4). The adjusted difference in PAS score was significant (0.86 points; $p=0.0074$). None of the other adjusted outcomes were significantly different between groups ($p=0.12-0.86$) (Table 5).

For question 3, when pooling all patients and re-grouping them into compliant versus non-compliant groups to test if the swallowing exercises were of benefit irrespective of the e-stim therapy, the ANCOVA revealed no significant differences between compliant versus non-compliant groups on any of the outcome measures of interest after 12 weeks of therapy ($p=0.09-0.92$) (Table 5).

Discussion

To date, the dysphagia rehabilitation literature lacks any consistency in therapy type, dose, or duration, and has inconsistently reported compliance definition and/or rates. Not all studies comprehensively delineate their interventions, and often do not report (or only partially report) compliance, which limits the interpretability of their data[25-29]. Among the studies that completely or partially report compliance, the dose and type of interventions vary widely making comparisons on efficacy or dose effect difficult or impossible[30-33]. Coupled with the fact that no dysphagia rehabilitation intervention has been proven efficacious in this patient population, no “acceptable” or “target” dose or frequency of dysphagia rehabilitation therapy exists. This, in turn, makes “high” or “low” compliance rates largely meaningless since they do not correspond to any differences in clinical outcome.

With a clear lack of consensus regarding optimal dose of swallow therapy and therefore acceptable compliance rates, the authors arbitrarily defined “compliant” in our cohort as having performed 80% or more of our prescribed home therapy program. Since over half (54%) of our patients were considered “compliant”, it also allowed for sample dichotomization, especially since there was almost a threefold difference in mean number of therapy sessions performed per week between non-compliant and compliant patients (4.3 vs. 11.1 respectively). It was assumed that such a difference could reasonably yield clinically and statistically relevant differences in outcome if the tested therapies were indeed efficacious.

It was important to determine if compliance differed significantly between active and sham e-stim groups. By demonstrating that there was no difference in compliance rates between groups, non-compliance in the active e-stim arm could not have been the reason why the patients in the sham e-stim arm performed equal or better than the patients in the active e-stim arm. To test the theory of compliance rates affecting outcome further, we eliminated all non-compliant patients in a re-analysis of the primary statistical analyses. This was done to probe into whether or not similar non-compliance rates could affect one arm (active or sham) more than another, thereby skewing the primary analysis data. This repeated ANCOVA using only compliant patients revealed results that paralleled those in the initial primary analysis[16]. However, it also unexpectedly showed that the active e-stim arm realized even worse outcomes on PAS than had been revealed in the primary analysis that included all compliant and non-compliant patients. This tentatively suggests that the more compliant a patient is with active e-stim, the worse their swallowing could become as compared to a patient who is not using e-stim, but is receiving the same traditional swallow exercises. One theory may be that e-stim actually interferes with a person's ability to execute proper normal and exercise swallows, and thereby somehow weakens the swallow (or prevents strengthening) over time as compared to a patient performing the same exercise swallows with no e-stim. Further, while the primary analyses in the main paper revealed that the difference was likely not clinically significant (PAS difference of 0.52), this current analysis using only compliant patients revealed an adjusted difference in PAS scores of 0.86. This is almost a full point on the PAS scale which some people may argue is closer to a clinically meaningful difference (perhaps the difference between penetration and aspiration,

or the difference between a normal swallow and a swallow that demonstrates penetration). Additionally, the raw data demonstrated that mean PAS scores for patients using active NMES increased from baseline while mean PAS scores for patients using sham NMES decreased from baseline. Collectively, these findings combined with the findings from the primary analyses suggest that e-stim should not be used with HNC patients who are greater than 3 months post radiation therapy and who are suffering from moderate-severe dysphagia.

With the understanding that e-stim does not help, and may even hinder a patient's swallowing ability, it was hoped that by regrouping all patients into compliant vs. non-compliant arms, the data would show some positive effects of compliance with the traditional swallowing exercises. This regrouping was possible since all patients received the same swallow exercises as part of the therapy program. Unfortunately there were no significant differences in any of the swallow, diet and quality of life outcomes between these compliant and non-compliant patients. This is disappointing as it suggests that adhering to an aggressive swallow exercise rehabilitation program may not be of much benefit to HNC patients with moderate to severe long-term dysphagia. Unfortunately it is also somewhat unsurprising since such dysphagia is caused by a fibrotic process that is thought to progressively entrap muscles [34-36], and swallowing exercises likely have no effect on stopping or reversing this aberrant biomolecular process. We cannot, however, rule out the possibility that swallowing exercises slow the progression of swallowing dysfunction in this specific patient population. Nor can we rule out the possibility that some patients may be outliers that do realize significant benefits from such exercises. In the absence of post-RT dysphagia therapies with proven efficacy, dysphagic patients should still be encouraged to perform swallowing exercises, although they should be properly informed of both the rationale behind their use as well as their potential limitations. Doing so will prevent false hope or a sense of failure if a patient does not realize any benefit despite their ardent adherence to a prescribed dysphagia rehabilitation protocol.

It is important to acknowledge the limitations of this secondary analysis. First, the original clinical trial was not powered a priori to specifically address outcome differences between compliant and non-compliant patients. The re-analysis of the primary outcomes with only compliant patients also had a sample size that was a little more than half of the original sample. Accordingly, for all of these secondary analyses, it is possible that a lack of statistical significance may have been attributed to an underpowered analysis. However, these outcomes are derived from the largest and most rigorously collected prospective clinical trial testing the efficacy of dysphagia therapy in the HNC population, so it likely represents our best evidence to date. Future clinical trials designed specifically to measure the impact of dysphagia treatment dose and compliance are warranted.

Conclusion

This secondary analysis reinforced the conclusions made in the primary analyses which demonstrated that electrical stimulation did not add any benefit to traditional swallowing exercises in HNC patients who suffer from long-term post-radiation dysphagia. In fact, the patients who were most compliant in the active e-stim group performed even worse than the most compliant sham e-stim patients, raising the question whether e-stim has a potential

negative effect in this patient population. Further, patients who were compliant with the swallowing exercises did not realize significantly better outcomes than non-compliant patients, suggesting that traditional swallow exercises may not be effective in this patient population either. Based on these results, e-stim should not be recommended in this patient population, clinical trials formally testing the efficacy of swallowing exercises should be undertaken, and efforts should be made to develop truly novel dysphagia therapy interventions that address the unique pathophysiology in HNC patients.

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Patient Daily Log Sheet

Subject ID:

DAY 2																														
Session	Super-Supraglottic					Regular					Mendelsohn					Regular					Effortful					Regular				
1	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
	6	7	8	9	10	6	7	8	9	10	6	7	8	9	10	6	7	8	9	10	6	7	8	9	10	6	7	8	9	10
	E-stim minutes: _____ Amplitude: _____																													
2	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
	6	7	8	9	10	6	7	8	9	10	6	7	8	9	10	6	7	8	9	10	6	7	8	9	10	6	7	8	9	10
	E-stim minutes: _____ Amplitude: _____																													

Fig. 1.

Detailed therapy checklist used to track home program compliance. Patient performed 10 normal “regular” swallows in between sets of 10 “exercise” swallows, all in synchrony with e-stim.

Fig. 2.

Compliance with Prescribed Therapy (n=153) ^a, ^aThe x-axis represents the mean number of sessions performed per week over the course of the 12 week therapy program. Compliant was defined as performing 10-12 sessions per week (orange bars).

Table 1
Baseline patient demographics presented in the main study paper by Langmore, et al. (2016)

Characteristic	Overall (N=168)	NMES (N=116)	Sham (N=52)	p-value
Gender				0.814
Male	144 (85.7%)	100 (86.2%)	44 (84.6%)	
Female	24 (14.3%)	16 (13.8%)	8 (15.4%)	
Age				0.722
Mean $\pm$ SD	61.9 $\pm$ 9.6	62.1 $\pm$ 9.2	61.5 $\pm$ 10.6	
Median and Range	62 (33-87)	62 (33-83)	62 (33-87)	
Ethnicity				0.756
Hispanic or Latino	13 (7.9%)	10 (8.8%)	3 (5.9%)	
Not Hispanic or Latino	152 (92.1%)	104 (91.2%)	48 (94.1%)	
Race				0.911
White	121 (72%)	82 (70.7%)	39 (75%)	
Black	19 (11.3%)	14 (12.1%)	5 (9.6%)	
Hispanic	13 (7.7%)	10 (8.6%)	3 (5.8%)	
Asian	14 (8.3%)	9 (7.8%)	5 (9.6%)	
Multiple	1 (0.6%)	1 (0.9%)	0 (0.0%)	
Cancer Stage				0.082
1	7 (5%)	7 (7.4%)	0 (0.0%)	
2	14 (9.9%)	7 (7.4%)	7 (15.2%)	
3	26 (18.4%)	20 (21.1%)	6 (13%)	
4	94 (66.7%)	61 (64.2%)	33 (71.7%)	
Cancer Site				
Oral	14 (8.4%)	11 (9.5%)	3 (5.9%)	0.555
Nasopharynx	17 (10.2%)	10 (8.6%)	7 (13.7%)	0.404
Oropharynx	78 (46.7%)	55 (47.4%)	23 (45.1%)	0.867
Hypopharynx	23 (13.8%)	14 (12.1%)	9 (17.6%)	0.339
Larynx	22 (13.2%)	13 (11.2%)	9 (17.6%)	0.320
Other	18 (10.8%)	14 (12.1%)	4 (7.8%)	0.589
Time since completion of radiation therapy				0.395
Mean $\pm$ SD	53.7 $\pm$ 60.9	56.5 $\pm$ 65.1	47.4 $\pm$ 50	
Median and Range	24.5 (3-267)	29 (3-267)	23 (3-186)	
Treatments				
Prior Radiation Therapy	8 (4.9%)	5 (4.5%)	3 (5.9%)	0.706
Chemotherapy	121 (75.6%)	83 (74.1%)	38 (79.2%)	0.552
Surgery	82 (49.4%)	58 (50%)	24 (48%)	0.866
RT Modality				0.423
IMRT	84 (50.3%)	55 (47.4%)	29 (56.9%)	

Characteristic	Overall (N=168)	NMES (N=116)	Sham (N=52)	p-value
Brachytherapy	1 (0.6%)	1 (0.9%)	0 (0.0%)	
Conventional	68 (40.7%)	50 (43.1%)	18 (35.3%)	
Stereotactic	1 (0.6%)	0 (0.0%)	1 (2%)	
Multiple Modalities	13 (7.8%)	10 (8.6%)	3 (5.9%)	

Abbreviations: RT, radiotherapy; CRT, chemoradiotherapy; IMRT, intensity-modulated radiotherapy.

Table 2
Mean and Median Sessions Completed by Patients during Weeks 1-12 of Treatment

Week	N	Mean Session Completed $\pm$ SD	Median Sessions Completed and IQR
week 1	153	7.7 $\pm$ 5.0	11.0 (2.0-12.0)
week 2	148	8.5 $\pm$ 4.8	11.0 (6.0-12.0)
week 3	148	7.8 $\pm$ 5.1	11.0 (0.0-12.0)
week 4	143	9.1 $\pm$ 4.5	12.0 (9.0-12.0)
week 5	142	9.3 $\pm$ 4.5	12.0 (10.0-12.0)
week 6	141	9.2 $\pm$ 4.4	12.0 (9.0-12.0)
week 7	132	9.4 $\pm$ 4.3	12.0 (9.5-12.0)
week 8	130	9.6 $\pm$ 4.1	12.0 (10.0-12.0)
week 9	128	9.2 $\pm$ 4.2	12.0 (8.0-12.0)
week 10	117	9.0 $\pm$ 4.6	12.0 (8.0-12.0)
week 11	111	9.3 $\pm$ 4.3	12.0 (8.0-12.0)
week 12	103	8.8 $\pm$ 4.6	12.0 (6.0-12.0)

Table 3
Demographics of compliant vs. non-compliant patients

Characteristic	Non-Compliant (N=70)	Compliant (N=83)	p-value
Gender			0.488
Male	62 (88.6%)	70 (84.3%)	
Female	8 (11.4%)	13 (15.7%)	
Age			0.699
Mean $\pm$ SD	59.6 $\pm$ 9.9	62.4 $\pm$ 10	
Median and Range	62 (33-75)	63 (33-87)	
Ethnicity			0.570
Hispanic or Latino	7 (10.3%)	6 (7.3%)	
Not Hispanic or Latino	61 (89.7%)	76 (92.7%)	
Race			0.708
White	47 (67.1%)	63 (75.9%)	
Black	8 (11.4%)	7 (8.4%)	
Hispanic	7 (10%)	6 (7.2%)	
Asian	7 (10%)	7 (8.4%)	
Multiple	1 (1.4%)	0 (0.0%)	
Cancer Stage			0.952
1	2 (3.4%)	4 (5.8%)	
2	6 (10.3%)	7 (10.1%)	
3	11 (19%)	14 (20.3%)	
4	39 (67.2%)	44 (63.8%)	
Cancer Site			
Oral	5 (7.1%)	9 (10.8%)	0.576
Nasopharynx	7 (10%)	8 (9.6%)	1
Oropharynx	35 (50%)	36 (43.4%)	0.422
Hypopharynx	5 (7.1%)	15 (18.1%)	0.055
Larynx	10 (14.3%)	10 (12%)	0.811
Other	8 (11.4%)	9 (10.8%)	1
Time since completion of radiation therapy			
Mean $\pm$ SD	57.5 $\pm$ 59.3	56.1 $\pm$ 61.7	
Median and Range	24 (4-170)	36 (3-260)	
Treatments			
Prior Radiation Therapy	4 (5.8%)	4 (5%)	1
Chemotherapy	49 (73.1%)	65 (81.3%)	0.321
Surgery	37 (52.9%)	38 (46.3%)	0.515
RT Modality			0.142
IMRT	29 (41.4%)	47 (56.6%)	
Brachytherapy	0 (0.0%)	1 (1.2%)	

Characteristic	Non-Compliant (N=70)	Compliant (N=83)	p-value
Conventional	34 (48.6%)	28 (33.7%)	
Stereotactic	1 (1.4%)	0 (0.0%)	
Multiple modalities	6 (8.6%)	7 (8.4%)	
Baseline Dysphagia Outcomes			
PAS Total	5.33±1.85	5.13±1.82	0.56
PSS Total	63.20±22.13	58.67±21.03	0.25
HNCI Total	31.87±21.55	28.52±19.81	0.38
OPSE Total	41.30±22.51	39.08±19.86	0.59
Hyoid Anterior	7.59±3.64	6.39±4.01	0.12
Hyoid Posterior	18.35±9.07	15.73±8.55	0.14

Abbreviations: RT, radiotherapy; CRT, chemoradiotherapy; IMRT, intensity-modulated radiotherapy.

Table 4
Change in mean raw outcome scores for compliant active NMES vs. compliant sham NMES groups

Characteristic	Baseline	Week 13	Change
PAS Total			
NMES	5.00±1.85	5.23±1.80	0.23±0.99
Sham	5.47±1.73	4.75±2.25	-0.71±1.84
PSS Total			
NMES	58.48±22.58	64.39±20.84	5.91±13.96
Sham	59.17±16.53	64.33±20.94	5.17±14.40
HNCI Eating			
NMES	30.85±20.83	41.09±25.96	10.24±18.24
Sham	21.77±15.02	27.46±18.42	5.69±13.64
OPSE Total			
NMES	41.33±19.75	40.57±19.61	-0.76±11.58
Sham	32.98±19.45	40.08±22.57	7.11±19.73
Hyoid Anterior Total			
NMES	6.39±4.26	6.10±4.71	-0.29±3.29
Sham	6.40±3.38	5.94±3.17	-0.46±2.16
Hyoid Superior Total			
NMES	15.33±8.24	15.19±8.70	-0.15±5.25
Sham	16.74±9.45	16.67±10.05	-0.07±5.93

Table 5
Adjusted differences between compliant subjects in Real vs. Sham arms and adjusted differences between Compliant vs. Non-compliant subjects

NMES vs. Sham	Estimate	Confidence Interval	p-value
PAS Total	0.8566	0.2298 – 1.4833	0.0074
PSS Total	0.5818	-6.0651 – 7.2288	0.8638
HNCI Eating	5.5959	-3.6065 – 14.7982	0.2333
OPSE Total	-6.0270	-13.5525 – 1.4985	0.1165
Hyoid Anterior Total	0.1633	-1.3963 – 1.7230	0.8374
Hyoid Superior Total	-0.2759	-3.1326 – 2.5808	0.8499
Compliant vs. Non-compliant	Estimate	Confidence Interval	p-value
PAS Total	0.2729	-0.1618 – 0.7075	0.2186
PSS Total	-1.0086	-5.9763 – 3.9590	0.6907
HNCI Eating	5.1729	-0.8062 – 11.1519	0.0899
OPSE Total	-1.4962	-6.8518 – 3.8593	0.5840
Hyoid Anterior Total	0.3804	-0.8135 – 1.5743	0.5323
Hyoid Superior Total	0.1196	-2.1265 – 2.3658	0.9169