The Journal of Laryngology & Otology

cambridge.org/jlo

Improved swallow outcomes with early intervention using combined swallow therapy in advanced oropharyngeal carcinoma

D I Kwon[1,2], B C Villegas[1], L M Ouyoung[2] and U K Sinha[1,2]

[1]Department of Otolaryngology – Head and Neck Surgery, Keck School of Medicine, University of Southern California, Los Angeles, USA and [2]Keck Medical Center of University of Southern California, Los Angeles, USA

Abstract

Objective. To evaluate the impact of early intervention using combined swallow therapy, consisting of traditional swallow exercises and transcutaneous neuromuscular electrical stimulation, on patients with advanced oropharyngeal squamous cell carcinoma.

Methods. A cohort study of 60 prospectively enrolled patients was performed. Thirty patients with advanced oropharyngeal squamous cell carcinoma starting combined swallow therapy two weeks after surgery that continued throughout chemoradiotherapy were compared with a matched cohort of 30 patients starting combined swallow therapy after cancer treatment completion. Gastrostomy tube status, modified barium swallow, and Functional Oral Intake Scale scores were assessed before and after therapy.

Results. Both cohorts demonstrated a statistically significant improvement in Functional Oral Intake Scale scores. All patients in the early intervention cohort discontinued gastrostomy tube use, compared with one-third in the control cohort, with greater improvements in Functional Oral Intake Scale scores. The tongue base was the site of greatest improvement in the early intervention group.

Conclusion. Early initiation of combined swallow therapy may optimise swallow outcomes in patients with advanced oropharyngeal squamous cell carcinoma.

Introduction

Oropharyngeal squamous cell carcinoma is diagnosed in approximately 130 000 patients each year globally.[1] The ability to maintain normal eating habits with avoidance of a gastrostomy tube is commonly considered one of the most important quality of life outcomes, and is a perpetual focus for clinicians treating oropharyngeal squamous cell carcinoma. The oropharynx has a crucial role in the mechanics and physiology of swallow function and is adversely affected by the disease process, as well as by surgical and non-surgical treatment, in patients with oropharyngeal squamous cell carcinoma. Rates of long-term gastrostomy tube dependence have historically been reported to be as high as 30–60 per cent in patients with advanced oropharyngeal squamous cell carcinoma receiving chemoradiotherapy; although, with advances in the field, including increased use of intensity modulated radiotherapy and improved swallow therapy protocols, these rates have improved.[2,3]

Many predictive factors of swallowing function have been identified and may be categorised. Treatment-related factors include extent of surgery, radiation dosimetry and treatment fields, and use of chemotherapy. Patient-related factors include baseline dysphagia, odynophagia, mucositis, xerostomia, and general health and performance status. Tumour-related factors include clinical stage and tumour site. Chemoradiotherapy has been shown to have the most pervasive impact, with multiple tissue effects ultimately leading to disordered inflammatory pathways, neuromuscular atrophy and fibrosis.[3–8] Several studies have demonstrated a benefit of muscle activation and swallow therapy to combat the onset of atrophy and fibrosis.[9–11] Molecular pathways leading to radiation-induced fibrosis have been described, such as the transforming growth factor β1 pathway and its repression of MyoD (myoblast determination protein 1) expression. Prior research in this area has shown the potential for transcutaneous neuromuscular electrical stimulation to prevent the molecular and histological effect of radiation on muscles involved in swallowing.[11,12]

On this basis, we have instituted an approach to provide aggressive intervention during chemoradiotherapy for the rehabilitation of swallowing and the maintenance of molecular homeostasis of cervical and pharyngeal muscles. Several years ago, we introduced a novel protocol at our institution that combines traditional swallow exercises and transcutaneous neuromuscular electrical stimulation, known as 'combined swallow therapy'. The current study aimed to evaluate the impact of combined swallow therapy on swallow function in patients with advanced oropharyngeal squamous cell carcinoma, and to determine the effect of early intervention by initiating this protocol prior to starting chemoradiotherapy.

Main Article

Dr U K Sinha takes responsibility for the integrity of the content of the paper

Cite this article: Kwon DI, Villegas BC, Ouyoung LM, Sinha UK. Improved swallow outcomes with early intervention using combined swallow therapy in advanced oropharyngeal carcinoma. *J Laryngol Otol* 2022;**136**:433–438. https://doi.org/10.1017/S0022215121003212

Accepted: 5 May 2021
First published online: 27 October 2021

Key words:
Oropharyngeal Neoplasms;
Deglutition Disorders;
Squamous Cell Carcinoma Of Head And Neck;
Neuromuscular Diseases; Radiotherapy;
Gastrostomy

Author for correspondence:
Dr Uttam K Sinha, Department of Otolaryngology – Head and Neck Surgery, Keck School of Medicine, University of Southern California, Suite 204M, 1540 Alcazar St, Los Angeles, CA 90033, USA
E-mail: uttam.sinha@med.usc.edu

Materials and methods

Participants

The study included 60 patients with advanced oropharyngeal squamous cell carcinoma who were treated and underwent swallowing rehabilitation in the Department of Otolaryngology – Head and Neck Surgery of Keck School of Medicine at the University of Southern California.

Study design

Approval for this prospectively enrolled cohort study was obtained from the local institutional review board. The inclusion criteria were: patients with advanced oropharyngeal squamous cell carcinoma (American Joint Committee on Cancer (7th edition) stage III or IV)[13] with primary tumours of the tongue base, or lateral pharyngeal wall or tonsil, who were treated with surgery followed by chemoradiotherapy, and who underwent swallow rehabilitation in our multidisciplinary head and neck cancer clinic. Additional inclusion criteria included compliance with a twice-weekly swallow therapy protocol for the duration of the treatment plan, and follow up in the head and neck cancer clinic for at least one year.

Thirty consecutive patients were enrolled into an early intervention cohort, who started combined therapy two weeks after surgery (prior to chemoradiotherapy) and continued this combined therapy throughout chemoradiotherapy.

A control cohort of 30 patients were matched with the study group based on tumour and patient characteristics. These patients initiated combined therapy after chemoradiotherapy completion, representing a more traditional treatment timeline. The control cohort were otherwise subject to the same twice-weekly combined therapy protocol.

Compliance for both arms of the study was defined as greater than 90 per cent attendance at out-patient therapy sessions with completion of the home exercise log. In addition to non-compliance with swallow treatment protocol, other exclusion criteria included any behavioural disorder that interfered with the administration of treatment, patients with cardiac pacemakers and/or arrhythmias, and patients with any implanted electrodes, including but not limited to automatic implantable cardioverter defibrillators, cochlear implants, and so on.

All patients had a gastrostomy tube, placed prior to the start of chemoradiotherapy. At the completion of combined therapy, all patients continued to undergo routine head and neck surveillance follow up in the head and neck cancer clinic for at least 12 months. A retrospective chart review was performed to collect data at the conclusion of the study.

Swallow evaluation

All study participants were evaluated by an experienced speech-language pathologist specialising in working with patients who have head and neck cancer.

All study patients were evaluated with modified barium swallow studies. The variables evaluated in the modified barium swallow study were: bolus manipulation, initiation of the pharyngeal swallow, base of tongue retraction, laryngeal elevation, epiglottic position, penetration, aspiration, cough reflex, and residue. Modified barium swallow was used to assign a swallow function score based on the Functional Oral Intake Scale (Table 1). The Functional Oral Intake Scale is a commonly used scale that has been shown to closely approximate true everyday swallow function based on an ordinal scale ranging from '1', representing nil by mouth status, to '7', representing a normal diet.[14] Modified barium swallow findings and Functional Oral Intake Scale scores were obtained at the start of treatment and at four months following completion of swallow therapy.

Combined swallow therapy protocol

Patients received a combination of traditional swallow exercises and transcutaneous neuromuscular electrical stimulation therapy twice a week with an experienced speech-language pathologist specialising in working with patients who have head and neck cancer. Each swallow therapy session lasted 1 hour. Each session incorporated the use of both traditional swallow exercises and transcutaneous neuromuscular electrical stimulation into the swallow therapy.

Traditional swallow exercises included tongue-hold, pretending to gargle, tongue retraction or tongue pull-back with resistance, range of motion, effortful swallow, and the Mendelsohn manoeuvre, based on previous studies.[15,16] Patients were instructed to perform these same exercises using 10 repetitions for each, 3 times daily, at home. Patients maintained an exercise log, which was reviewed with the speech pathologist during each in-person session for compliance.

Transcutaneous neuromuscular electrical stimulation therapy was always administered by a certified transcutaneous neuromuscular electrical stimulation speech-language pathologist trained in this modality. The objective of transcutaneous neuromuscular electrical stimulation in dysphagia therapy is to stimulate tongue, pharyngeal and laryngeal musculature through intact peripheral nerves, using electrical stimulation.[17,18]

Two horizontal electrodes were placed on the skin at the submental area to enhance contraction of the base of tongue area and laryngeal elevation. Each treatment session comprised a gradual increase in intensity (in milliamperes) to maximal tolerated intensity, with optimal stimulation being confirmed by visual identification of muscle contraction. Subjects were taught to swallow with visual cues from the device in concert with the electric current, and to rest between cycles. Trials of food and liquid in varying consistencies and amounts were performed with these exercises based upon the severity of swallow dysfunction.

The device used was the BMR NeuroTech neuromuscular electrical stimulator, model NT2000 (Galway, Republic of Ireland). The unit generates a fixed pulse rate of 80 Hz, to maximise the benefit of stimulation of the fast twitch muscle fibres (dominant in swallowing musculature), with a fixed pulse duration of 700 μs to ensure stimulation of both fast twitch and slow twitch muscle fibres.

Swallow therapy duration

The swallow therapy course was completed when the patient achieved normal swallow function, or when the patient demonstrated a clinical plateau in therapy, as determined by the experienced head and neck cancer speech-language pathologists (who are authors of this manuscript). The modified barium swallow was used as an objective measure during therapy as needed, to re-assess swallowing function.

Outcome measures

All patients had a previously placed gastrostomy tube. Thus, the status of gastrostomy tube dependence and the incidence

https://doi.org/10.1017/S0022215121003212 Published online by Cambridge University Press

Table 1. Functional Oral Intake Scale scoring

Score	Description
1	Severe impairment & dysfunction; nil by mouth
2	Moderate–severe dysfunction; gastrostomy tube dependent, with limited oral intake
3	Moderate impairment; gastrostomy tube dependent, with consistent oral intake
4	Mild–moderate impairment; oral diet possible with single consistency
5	Mild impairment; oral diet with modifications
6	Within functional limits; oral diet with some impairments
7	Normal oral diet with no impairment

Table 2. Characteristics of study participants by group

Characteristic	Early intervention group	Control group
Total patients (*n*)	30	30
Primary tumour site (*n*)		
– Base of tongue	15	15
– Lateral pharyngeal wall	15	15
Mean age (years)	56	58
Tumour stage (*n*)		
– III	15	15
– IV	15	15

of aspiration pneumonia were primary outcome measures. A modified barium swallow study was conducted at the beginning of treatment and at four months following the completion of combined therapy, in order to assign a pre- and post-therapy Functional Oral Intake Scale score. Changes in Functional Oral Intake Scale scores were recorded as a secondary outcome measure.

Statistical analysis

Pearson chi-square and Fisher exact tests were used to analyse patient characteristics. Ordinal logistic regression was performed to analyse the Functional Oral Intake Scale score measurements. We assessed the significance of the Functional Oral Intake Scale scores by computing the *t*-value of its coefficient and approximating the sampling distribution of the *t*-value as the standard normal distribution to obtain a *p*-value. In order to adjust for confounding by the tumour site (base of tongue or lateral pharyngeal wall), secondary analyses were performed after stratifying by tumour site. All statistical analyses were performed using the SAS statistical package (version 9.1; SAS Institute, Cary, North Carolina, USA). Statistical significance was set at $p < 0.05$.

Results

The patient characteristics of the two cohorts are summarised in Table 2. As the control patients were included in the study based on similarities between the two groups in terms of cancer and treatment, there were no significant differences in baseline characteristics. All patients tolerated combined therapy with no known complications directly related to therapy.

All patients in the early intervention group were able to discontinue gastrostomy tube use, irrespective of primary tumour site. In contrast, 23 per cent of patients (7 out of 30) in the control group still had a gastrostomy tube at four months, with 50 per cent of patients continuing gastrostomy tube use when the primary tumour was at the base of the tongue. No patients in either group had a documented aspiration pneumonia from the initiation of swallow therapy to the 12-month follow-up appointment.

Comparison of Functional Oral Intake Scale scores before and after the completion of combined therapy, for both cohorts, is presented in Table 3. The initial Functional Oral Intake Scale scores of the early intervention treatment cohort versus controls were 3.8 and 3.4, respectively. There were no statistically significant differences in initial Functional Oral Intake Scale scores. Both the study group and the control group demonstrated a statistically significant improvement in the Functional Oral Intake Scale scores at the end of the combined therapy, with the early intervention group achieving a statistically greater score improvement. The early intervention group achieved an average final Functional Oral Intake Scale score of 6.8 (normal diet), requiring an average of 12 combined therapy sessions. In contrast, the controls achieved an average final Functional Oral Intake Scale score of 5.5 (mild impairment), requiring an average of 18 combined therapy sessions. There was a statistically significant difference in the improvement of (pre- *vs* post-therapy) swallow scores achieved by the early intervention group (difference of 3) compared with the control group (difference of 2.1).

On analysis of tumour site, patients with base of tongue tumours had more severe impairment of swallowing compared to those with lateral pharyngeal wall tumours (Table 4). The control group with a primary tumour in the tongue base had the most severe swallowing impairment, with a Functional Oral Intake Scale score of 2.95 (moderate impairment) at the start of swallow therapy, eventually improving to 4.75. This was the most limited improvement in Functional Oral Intake Scale scores of any subset. The patients in the early intervention cohort were able to return to normal or near-normal swallow function regardless of whether the primary tumour was at the tongue base or the lateral pharyngeal wall, with average Functional Oral Intake Scale scores of 7 and 6.5, respectively, with the most marked improvement being observed in the base of tongue subset.

Discussion

Advanced oropharyngeal squamous cell carcinoma is a difficult diagnosis, often requiring multimodality cancer treatment including ablative and reconstructive surgery, chemotherapy, and radiation. The adverse effects of chemoradiotherapy on tissues can occur long after treatment; these effects include dysregulated inflammation, capillary occlusion, soft tissue and muscle fibrosis, atrophy, and collagen replacement.[5–8] Pharyngeal fibrosis, xerostomia, and structural disruption from oncological surgery are believed to result in dysphagia in patients with oropharyngeal squamous cell carcinoma.[4] Dysphagia highly correlates with quality of life measures, as well as contributing to aspiration pneumonia, which is potentially life-threatening.

The improvement of functional swallowing and prevention of major sequelae in oropharyngeal squamous cell carcinoma treatment has been a major focus of cancer care over the past few decades. Preventative measures including dose

https://doi.org/10.1017/S0022215121003212 Published online by Cambridge University Press

Table 3. Swallow outcome data

Parameter	Early intervention group*	Control group*	Mean difference in swallow scores (treatment *vs* control group)	Statistical *p*-value for treatment *vs* control group scores
Functional Oral Intake Scale (mean (SD))				
– Initial score	3.8 (0.42)	3.4 (1.62)	0.4 (1.23)	0.4
– Final score	6.8 (0.42)	5.5 (1.43)	1.3 (1.10)	0.02
– Mean difference (pre- *vs* post-therapy scores)	3 (0.66)	2.1 (1.71)		
Statistical *p*-value for pre- *vs* post-therapy scores	<0.001	0.008		
Mean number of therapy sessions	12	18		
Presence of gastrostomy tube (*n*)				
– Prior to therapy	30	30		
– At 4 months post-therapy	0	7		

*$n = 30$. SD = standard deviation

modulation (intensity modulated radiotherapy), and treatment measures such as aggressive swallow rehabilitation, have been used to improve outcomes.

The role and sophistication of swallow therapy have greatly expanded in recent years, and the therapy has been a major determinant in good functional outcomes in oropharyngeal squamous cell carcinoma. While swallow therapy outcomes for the head and neck cancer population are quite variable, broadly, more rigorous rehabilitation therapy in a multidisciplinary setting has been shown to be more successful in ameliorating dysphagia.[19–21] Unfortunately, swallow rehabilitation is often relegated to the role of an adjunctive treatment in many centres, often starting many months following the completion of cancer therapy.

The present study demonstrated significant improvements in swallow function in all our advanced oropharyngeal squamous cell carcinoma patients utilising combined therapy. In particular, we demonstrated greater improvements in swallow function in those undergoing early intervention, with most achieving normal Functional Oral Intake Scale scores, compared with patients for whom swallow therapy was initiated after completion of chemoradiotherapy. Pre-therapy swallow scores in the treatment and control groups indicate that patients in both groups were at similar levels of swallow function.

Understanding the pathophysiological processes leading to dysphagia is critical. We believe that the significant improvement in the swallow scores after early intervention when compared with the control indicates that, in addition to helping restore swallow function after surgery, early initiation of swallow treatment may help prevent disuse atrophy and subsequent fibrosis, which may already be present in traditionally timed therapy.

Our most striking result was the dramatic improvement in swallow function in patients with a base of tongue primary who received early combined therapy. As this tumour site was associated with worse pre-treatment dysfunction, this indicates that this group may benefit more from an early aggressive rehabilitation strategy. This is supported by other studies that have shown the tongue to respond well to strengthening exercises in both normal and cancer populations.[9,19] The results of our study are in agreement with previous smaller studies that also examined the value of early traditional swallow exercises.[20–23]

The usage of transcutaneous neuromuscular electrical stimulation has been well described for dysphagia, with favourable results.[18,24,25] However, its efficacy in head and neck cancer patients, especially those who have undergone radiation treatment, is less promising.[26] Nevertheless, previous study populations have been heterogeneous, with a variety of cancer sites and primary treatments (chemoradiotherapy *vs* surgical). Our study population was focused on oropharynx cancers, and had a more rigorous therapy schedule than has been described in other studies. Perhaps, most importantly, previous studies utilised transcutaneous neuromuscular electrical stimulation late after the completion of chemoradiotherapy, as opposed to early intervention.

As suggested by our findings, transcutaneous neuromuscular electrical stimulation may have preventative benefits; in select patients, it may prevent or ameliorate the effects of atrophy and fibrosis. A potential concern regarding electrical stimulation is whether the use of this modality enhances tumour growth. Although some epidemiological studies have suggested that long-term exposure to electromagnetic fields could increase the incidence of several cancers,[27–29] there is no evidence that short-term exposure to electromagnetic fields increases the risk of tumourigenesis. In addition, increased recurrence of disease has not been seen in our practice, which utilises transcutaneous neuromuscular electrical stimulation in swallow therapy for a variety of head and neck cancers.

Usage of modified barium swallow studies and the Functional Oral Intake Scale has been well described in other studies as an effective tool for measuring global swallow function, and has been used in studies with head and neck cancer.[14,30,31] In this study, modified barium swallow evaluations and Functional Oral Intake Scale scores were obtained by head and neck cancer trained speech-language pathologists to prevent subjective bias. Additionally, we were aware that 'learned non-use', wherein patients become dependent on use of the gastrostomy tube as a compensatory behaviour pattern and are reluctant to have it removed, could be one of the confounding factors in the study.[32] During each therapy session, the speech-language pathologist spent time with the patient discussing the importance of trying to achieve normal swallowing function. We chose to have the post-operative endpoint evaluation at four months following combined therapy. Studies have shown that swallowing function continues to

https://doi.org/10.1017/S0022215121003212 Published online by Cambridge University Press

Table 4. Swallow outcome data by tumour site

	Base of tongue ($n = 30$)		Lateral pharyngeal wall ($n = 30$)	
Parameter	Early intervention group*	Control group*	Early intervention group*	Control group*
Functional Oral Intake Scale (mean (SD))				
– Initial score	3.67 (0.52)	2.95 (1)	4 (0)	3.88 (1.73)
– Final score	7 (0)	4.75 (1.71)	6.5 (0.58)	6.13 (1.12)
– Mean difference (pre- *vs* post-therapy scores)	3.33 (0.52)	1.8 (1.89)	2.5 (0.58)	2.25 (1.75)
Statistical *p*-value for pre- *vs* post-therapy scores	<0.0001	0.09	0.0032	0.0084
Mean number of therapy sessions	12	18	12	17
Presence of gastrostomy tube (*n*)				
– Prior to therapy	15	15	15	15
– At 4 months post-therapy	0	7	0	0

*$n = 15$. SD = standard deviation

deteriorate many months after chemoradiotherapy is completed.[22] However, all patients included in the study received follow up beyond 12 months, and no significant changes in swallowing function were noted on surveillance evaluation.

- Swallow function and gastrostomy tube status is the most important functional outcome in advanced oropharyngeal carcinoma
- Radiation-induced fibrosis is primarily an aetiology of long-term dysphagia
- Understanding muscle atrophy and fibrosis pathophysiology is key to determining strategies to prevent or reverse dysphagia
- Combined therapy, comprising traditional swallowing exercises and transcutaneous neuromuscular electrical stimulation, is effective in treating dysphagia in advanced oropharyngeal carcinoma patients
- Early therapeutic intervention, prior to chemoradiotherapy, may prevent and further improve swallowing function

Some study-specific limitations include the relatively small number of patients who could be included, and the selection bias inherent in prescribing treatment plans. We believed that, to determine the efficacy of our treatment approach, adherence to our rigorous treatment plan was crucial to our functional outcomes, and therefore some patients were not able to be included. Similarly, while patients in both cohorts were matched based on basic demographic and tumour characteristics, enrolment in the early intervention group was likely to correlate with other determinants of outcomes. Patients enrolled in the early intervention group were generally those who: did not experience post-operative healing delays, were often treated within our Norris National Cancer Institute designated Comprehensive Cancer Center, and had adequate support and psychosocial resources to adhere to our protocol. We must acknowledge that head and neck cancer patients often have multiple social, geographic and economic barriers to obtaining high-quality care. Not all patients have access to head and neck cancer centres with specialty therapists experienced in transcutaneous neuromuscular electrical stimulation. Nevertheless, we believe our findings support the principle of early intervention and prevention of fibrosis, as shown in other studies that employed traditional swallow exercises alone. Best practice trends for head and neck cancers clearly support multidisciplinary care at high-volume centres. In the future, multi-centred studies may allow larger, controlled trials.

Finally, we did not include or address the impact of human papilloma virus positivity or the rapidly evolving staging and treatment guidelines for our oropharyngeal cancer patients.[1] Enrolment in this study was carried out prior to these changes or the implementation of any treatment reduction protocols. As this study focuses on advanced oropharyngeal cancers, we feel our findings are relevant for this population, who still require multimodality therapy.

The clinical implications of improving swallow function in oropharyngeal squamous cell carcinoma patients with dysphagia are enormous. These include the reduced risk of aspiration pneumonia, and the avoidance of special diets including typical diet modifications. An important psychosocial implication of improved swallowing function is the participation in social activities associated with eating without the presence of a feeding tube, which is a constant reminder of the disease despite the completion of therapy or eradication of the cancer.

Conclusion

Combined therapy, consisting of traditional swallow exercise and transcutaneous neuromuscular electrical stimulation that started two weeks after surgery and continued during chemoradiotherapy, was effective in restoring swallowing in our patients with advanced squamous cell carcinoma of the oropharynx. This was a significant improvement when compared with patients who received the same combined therapy after the completion of chemoradiotherapy, who had higher gastrostomy tube retention rates as well as worse functional oral intake scores. Early intervention with combined therapy may be an effective tool to prevent long-term dysphagia in patients undergoing treatment for advanced oropharyngeal cancer.

Competing interests. None declared

References

1 Warnakulasuriya S, Greenspan JS. Epidemiology of oral and oropharyngeal cancers. In: Warnakulasuriya S, Greenspan JS, eds. *Textbook of Oral Cancer*. Cham: Springer, 2020;5–21
2 Neumann S, Bartolome G, Buchholz D, Prosiegel M. Swallowing therapy of neurologic patients: correlation of outcome with pretreatment variables and therapeutic methods. *Dysphagia* 1995;**10**:1–5
3 Shiley SG, Hargunani CA, Skoner JM, Holland JM, Wax MK. Swallowing function after chemoradiation for advanced stage oropharyngeal cancer. *Otolaryngol Head Neck Surg* 2006;**134**:455–9
4 Varma VR, Eskander A, Kang SY, Kumar B, Brown NV, Zhao S *et al.* Predictors of gastrostomy tube dependence in surgically managed oropharyngeal squamous cell carcinoma. *Laryngoscope* 2019;**29**:415–21
5 Ben-Yosef R, Kapp DS. Persistent and/or late complications of combined radiation therapy and hyperthermia. *Int J Hyperthermia* 1992;**8**:733–45

https://doi.org/10.1017/S0022215121003212 Published online by Cambridge University Press

6 Bentzen SM, Thames HD, Overgaard M. Latent-time estimation for late cutaneous and subcutaneous radiation reactions in a single-follow-up clinical study. *Radiother Oncol* 1989;**15**:267–74

7 Law MP. Radiation-induced vascular injury and its relation to late effects in normal tissues. In: Lett J, Adler H, eds. *Advances in Radiation Biology*, Vol 9. New York: Academic Press, 1981;37–73

8 Peters LJ, Harrison ML, Dimery IW, Fields R, Goepfert H, Oswald MJ. Acute and late toxicity associated with sequential bleomycin-containing chemotherapy regimens and radiation therapy in the treatment of carcinoma of the nasopharynx. *Int J Radiat Oncol Biol Phys* 1988;**14**:623–33

9 Sullivan P, Hind JA, Robbins JA. Lingual exercise protocol for head and neck cancer: a case study. *Dysphagia* 2001;**16**:154

10 Stenson KM, MacCracken E, List M, Haraf DJ, Brockstein B, Weichselbaum R *et al.* Swallowing function in patients with head and neck cancer prior to treatment. *Arch Otolaryngol Head Neck Surg* 2000;**126**:371–7

11 Peng G, Masood K, Gantz O, Sinha U. Neuromuscular electrical stimulation improves radiation-induced fibrosis through Tgf-B1/MyoD homeostasis in head and neck cancer. *J Surg Oncol* 2016;**114**:27–31

12 Leask A, Abraham DJ. TGF-beta signaling and the fibrotic response. *FASEB J* 2004;**18**:816–27

13 Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, eds. *AJCC Cancer Staging Manual*, 7th edn. New York: Springer, 2010

14 Crary MA, Mann GD, Groher ME. Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. *Arch Phys Med Rehabil* 2005;**86**:1516–20

15 Logemann JA. Protocol for swallowing management in patients treated for head and neck cancer. *Perspectives on Swallowing and Swallowing Disorders* 2006;**15**:22–6

16 Veis S, Logemann JA, Colangelo L. Effects of three techniques on maximum posterior movement of the tongue base. *Dysphagia* 2000;**15**:142–5

17 Lazzara DG, Lazarus C, Logemann JA. Impact of thermal stimulation on the triggering of the swallowing reflex. *Dysphagia* 1986;**1**:73–7

18 Gary Y, Shaw M, Kristina K. VitalStim curative therapy for severe dysphagia: myth or reality. *Laryngology* 2007;**116**:36–44

19 Greco E, Simic T, Ringash J, Tomlinson G, Inamoto Y, Martino R. Dysphagia treatment for patients with head and neck cancer undergoing radiation therapy: a meta-analysis review. *Int J Radiat Oncol Biol Phys* 2018;**101**:421–44

20 Kulbersh BD, Rosenthal EL, McGrew BM, Duncan RD, McColloch NL, Carroll WR *et al.* Pretreatment, preoperative swallowing exercises may improve dysphagia quality of life. *Laryngoscope* 2006;**116**:883–6

21 Carroll WR, Locher JL, Canon CL, Bohannon IA, McColloch NL, Magnuson JS. Pretreatment swallowing exercises improve swallow function after chemoradiation. *Laryngoscope* 2008;**118**:39–43

22 Kotz T, Federman AD, Kao J, Milman L, Packer S, Lopez-Prieto C *et al.* Prophylactic swallowing exercises in patients with head and neck cancer undergoing chemoradiation: a randomized trial. *Arch Otolaryngol Head Neck Surg* 2012;**138**:376–82

23 Mortensen HR, Jensen K, Aksglæde K, Lambertsen K, Eriksen E, Grau C. Prophylactic swallowing exercises in head and neck cancer radiotherapy. *Dysphagia* 2015;**30**:304–14

24 Carnaby-Mann GD, Crary MA. Adjunctive neuromuscular electrical stimulation for treatment-refractory dysphagia. *Ann Otol Rhinol Laryngol* 2008;**117**:279–87

25 Ryu JS, Kang JY, Park JY, Nam SY, Choi SH, Roh JL *et al.* The effect of electrical stimulation therapy on dysphagia following treatment for head and neck cancer. *Oral Oncol* 2009;**45**:665–8

26 Langmore SE, McCulloch TM, Krisciunas GP, Lazarus CL, Van Daele DJ, Pauloski BR *et al.* Efficacy of electrical stimulation and exercise for dysphagia in patients with head and neck cancer: a randomized clinical trial. *Head Neck* 2016;**38**:E1221–31

27 Loomis A, Kromhout H, Kleckner RC, Savitz DA. Effects of the analytical treatment of exposure data on associations of cancer and occupational magnetic field exposure. *Am J Ind Med* 1998;**34**:49–56

28 Bianchi N, Crosignani P, Rovelli A, Tittarelli A, Carnelli CA, Rossitto F *et al.* Overhead electricity power lines and childhood leukemia: a registry-based, case-control study. *Tumori* 2000;**86**:195–8

29 Caplan LS, Schoenfeld ER, O'Leary ES, Leske MC. Breast cancer and electromagnetic fields—a review. *Ann Epidemiol* 2000;**10**:31–44

30 Lee S, Kim BH, Park YH. Analysis of dysphagia patterns using a modified barium swallowing test following treatment of head and neck cancer. *Yonsei Med J* 2015;**56**:1221–6

31 Bleier BS, Levine M, Marc S, Mick R, Rubesin SE, Sack SZ *et al.* Dysphagia after chemoradiation: analysis by modified barium swallow. *Ann Otol Rhinol Laryngol* 2007;**116**:837–41

32 Taub E, Uswatte G, Elbert T. New treatments in neurorehabiliation founded on basic research. *Nat Rev Neurosci* 2002;**3**:228–36

https://doi.org/10.1017/S0022215121003212 Published online by Cambridge University Press