Swallowing, nutrition and patient-rated functional outcomes at 6 months following two non-surgical treatments for T1-T3 oropharyngeal cancer

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ABSTRACT

Purpose: Altered fractionation radiotherapy with concomitant boost (AFRT-CB) may be considered an alternative treatment for patients not appropriate for chemoradiation (CRT). As functional outcomes following AFRT-CB have been minimally reported, this exploratory paper describes the outcomes of patients managed with AFRT-CB or CRT at 6 months post treatment.

Methods: Using a cross-sectional analysis design, functional outcomes of 14 AFRT-CB and 17 CRT patients with T1-T3 oropharyngeal cancers were explored at 6 months post-treatment. Clinical and instrumental swallow assessments, weight and nutritional status, and the functional impact of treatment were examined.

Results: Inferior outcomes were observed for the CRT patients on the RBHOMS ($p = 0.03$) which was reflected in diet and fluid restrictions with 18% of the CRT group requiring modified fluids and diets. Although a trend ($p = 0.07$) was noted for increased lingual deficits and aspiration risk for fluids in the CRT group, no other significant differences were observed. Both groups experienced an average of 10kg weight loss and reported reduced general and swallowing related function.

Conclusions: This preliminary data suggests functional outcomes following AFRT-CB and CRT were largely comparable at 6 months post treatment. Treatment intensification in any form may contribute to impaired function which requires multidimensional intervention. Larger cohort investigations with systematic methodology are needed to further examine these initial findings.

Keywords: swallowing, nutrition, oropharyngeal cancer, chemoradiation, altered fractionation radiotherapy

This paper aims to inform research by providing further evidence for functional outcomes following non-surgical treatment for head and neck cancer.

INTRODUCTION

The past two decades have revealed a trend for individuals with oropharyngeal cancer to receive non-surgical organ preservation treatment such as altered fractionation radiotherapy (AFRT) or chemoradiation (CRT). While evidence to date has pointed to increased acute toxicity following these more intense treatment regimens when compared with conventional radiotherapy [1-4], exactly how the outcomes for swallowing, nutrition and patient-perceived deficits vary between such intensive treatment modes is still being elucidated [5, 6]. In particular, the majority of research to date has examined outcomes following CRT, with limited detail on AFRT and how the two treatment modalities compare.

AFRT techniques have been found to improve locoregional control and survival in locally advanced head and neck squamous cell carcinoma (LAHNSCC) patients, but can result in more intense acute toxicity, which may last longer when compared with conventionally fractionated radiotherapy [2, 7], result in consequential late reactions [8, 9] and possible long-term functional injury [2]. Altered fractionation with concomitant boost (AFRT-CB) has been found to lead to significantly increased late effects (grade 3 or worse on the RTOG radiation morbidity scoring criteria) when compared with standard fractionation, hyperfractionation or accelerated fractionation with a split, although no difference was found by 6 months post-treatment [2]. In support of these findings, a retrospective study using a crude measure of dysphagia found AFRT and its acute toxicity affected swallowing function with resolution by 12 months post-treatment for most patients [6]. In addition the current evidence base for nutritional outcomes and patient-rated function following AFRT is also limited.

In comparison, documentation of swallowing and nutrition outcomes following CRT regimens is more prevalent. Although improving locoregional control and overall survival in [10], toxicity related to concurrent CRT regimens has been found to be significantly higher when compared to standard radiotherapy [1, 11], and severe late swallowing complications have been found in 30-50% of patients treated with aggressive CRT regimens [4, 11]. Reported dysphagia symptoms in HNC patients who received chemoradiotherapy regimens are diverse and have affected the oral phase [12-14], pharyngeal and upper esophageal phases of swallowing [12, 13, 15, 16]. The impact on nutritional outcomes has been reported [5, 12, 15, 17-19], with several studies finding weight loss and nutritional compromise during and following radiotherapy and CRT protocols [20, 21]. Both deleterious swallowing and nutritional outcomes following CRT have also been associated with poor patient-rated function [12, 15, 17, 18].

Despite minimal reported data proving no difference in outcomes following AFRT-CB and CRT [22], clinical perception is that the side effects and impact on function associated with the addition of chemotherapy to radiation protocols are worse than for treatment with radiotherapy alone. Subsequently, resources for the management of patients receiving treatment for oropharyngeal cancer in many clinical settings are biased toward those receiving CRT. Until this time, an exploration of patients treated with the intent to cure, with specific tumor size and location has not been undertaken to prove or disprove this clinical perception. Therefore, the current preliminary study aims to explore the functional outcomes (swallowing and nutrition), and patient-rated functional impact of curative intent AFRT-CB and CRT at 6 months post-treatment in concurrently recruited cohorts of patients with T1-T3 oropharyngeal SCC.

MATERIALS AND METHODS

Eligibility

This cross-sectional study recruited eligible participants from consecutive presentations to a Multidisciplinary Head and Neck Cancer Clinic at a large tertiary hospital in Brisbane, Australia, over a 33 month accrual period (between November 2006 and August 2009). Patients with T1, T2, or T3 SCC of the oropharynx (tonsil, base of tongue [BOT]), pharyngeal wall, or supraglottis [within 1cm of the oropharynx]) who were recommended for treatment with CRT or AFRT-CB were targeted for recruitment. Decisions regarding the preferred treatment for each patient were reached by consensus and were the responsibility of senior physicians and surgeons. Ineligible patients included those with a previous diagnosis of oropharyngeal LAHNSCC, neurological or neurodegenerative condition which may have impacted on swallowing function. All patients received their treatment at the Metro South Radiation Oncology Service in Brisbane, Australia. This research was approved by the Human Research and Ethics Committees at the Princess Alexandra Hospital, Australia and the University of Queensland, and all participants consented to involvement in the study.

AFRT-CB was the recommended treatment for 17 patients, all of whom were eligible for recruitment. Two patients declined to participate, leaving a cohort of 15 participants who consented to involvement. Of these participants, 14 completed all aspects of the study with one participant's data set incomplete as a result of death unrelated to cancer. A second group of 23 patients who received CRT were matched for tumor size and location, and were approached 6 months post-treatment for recruitment into the CRT group. Twenty participants consented to involvement in the study. Of these participants, 17 completed all aspects of the study, with three participants' data set incomplete due to errors in recording of modified barium swallow assessments or incomplete data. Analysis was conducted on the 31 participants with complete data sets.

Participants in both groups were predominantly male (AFRT-CB: 12 male, 2 female; CRT: 15 male, 2 female), with the CRT group significantly younger than the AFRT-CB group (Table 1). Although not statistically different, a large proportion of AFRT-CB patients had stage I and II disease, a group which was not represented in the CRT group. This is likely due to the incidence and severity of nodal disease in CRT patients, and often a reason for prescribing CRT as the treatment of choice. For all other demographic variables (sex, tumor site or size, nodal disease, or alcohol and smoking history, dysphagia for solids/liquids at presentation), both the AFRT-CB and CRT groups were similar.

(insert table 1 near here)

Planned Treatment

All patients were treated with 3D conformal RT. Patients were treated with either AFRT-CB or conventionally fractionated radiotherapy with or without systemic therapy. Patients with lower volume disease (eg. T1-2, N1) were generally considered for single modality radiotherapy. Elective sites were treated to 50Gy in 2Gy/day over 5 weeks. Known sites of disease received either a concomitant boost schedule to a total of 66Gy over 5 weeks with an afternoon boost dose (minimum of 6 hours apart) of 1.6Gy/day in weeks 4 and 5 or 2Gy/fraction to a total of 70Gy over 7 weeks. Planned concurrent systemic therapy consisted of either high-dose cisplatin (100mg/m^2) in weeks 1, 4 and 7 or fractionated weekly cisplatin (40mg/m^2). Patients with contraindications to cisplatin, such as renal/hearing impairment or pre-existing neuropathy, received either carboplatin/5-fluorouracil or cetuximab. Selection of systemic therapy was at the discretion of the treating physician.

Outcome Measures

As the aim of this study was to outline functional outcomes at 6 months post-treatment, baseline data was not routinely collected. Pre-treatment diet and fluid tolerance and weight recordings were collected retrospectively from speech pathology and dietitian medical chart entries at the initial Multidisciplinary Head and Neck Cancer Clinic appointment.

At 6 months post-treatment, all participants underwent a range of assessments relating to swallowing, nutrition and the functional impact of treatment which have been described in detail elsewhere [23]. Swallowing was assessed both clinically and objectively. Clinical assessment included trials of diet (full, soft, minced, pureed) and fluid (extremely thick, moderately thick, mildly thick, or thin) consistencies in line with Australian national standards [24], with function scored with the Royal Brisbane Hospital Outcome Measure for Swallowing (RBHOMS, [25]). Objectively, swallowing was assessed with videofluoroscopy (VFS) and analysed with Subscale One (oral, oropharyngeal transit, pharyngeal and crico-esophageal parameters) of the New Zealand Index for Multidisciplinary Evaluation of Swallowing NZIMES [26]. Penetration and aspiration events were rated using the validated Penetration-Aspiration Scale [27]. Both scales were rated by a speech pathologist blinded to group, with greater than 5 years clinical experience in head and neck oncology.

Nutritional status at 6 months post-treatment was assessed by a dietitian using the Patient-Generated Subjective Global Assessment (PG-SGA, [28]). Weight was recorded pretreatment and at 6 months post-treatment. Requirements for alternative or supplemental feeding were also noted. Patient-rated functional impact was assessed using the M.D. Anderson Dysphagia Inventory (MDADI, [29]) and the Functional Assessment of Cancer Therapy Additional Concerns for Head and Neck version 4 (FACT-H&N, [30]).

Statistical Analysis

Sample size accrual was targeted to 30 participants in each of the AFRT-CB and CRT groups, but could not be achieved after a collection period of 33 months. The authors acknowledge that due to the small participant numbers, statistical analyses are underpowered, limiting the ability to make definitive statements. However in recognition of the small group numbers, nonparametric statistics (Chi square, Mann-Whitney U) were used for all comparisons and significance was set at $p < 0.05$, with values falling between > 0.05 and <0.08 considered as trends. All statistical analysis was conducted using STATA version 10 for Mac.

RESULTS

Functional swallowing outcomes were found to be inferior for the CRT group, with significant differences noted in the RBHOMS score (AFRT-CB M = 7.57, $SD = 0.85$; CRT M = 6.89, $SD = 1.02$, $Z = -2.14$, $p = 0.03$). This finding was also reflected in the diet and fluid consistencies tolerated at this time point (Table 2). While the majority of participants from both groups were managing thin fluids and a full or soft diet, there were a small number of CRT participants requiring thickened fluids and a texture-modified diet.

(insert table 2 near here)

Measures of physiological swallow impairment, as scored by the NZIMES, revealed no significant differences between the AFRT-CB and CRT groups in the small sample studied (Table 3). A trend ($p = 0.07$) was observed for more severe lingual impairment in the CRT group. Penetration and aspiration events, scored using the Penetration-Aspiration Scale, did not differ significantly between AFRT-CB and CRT groups (Table 3), although a trend for more severe penetration/aspiration on fluids in the CRT group ($p = 0.07$) was observed.

(insert table 3 near here)

To further explore the data and aid descriptive interpretation of the patterns of physiological impairment in the two groups, the NZIMES ratings were compressed into a binary scale of “impairment” (score of >0) versus “no impairment” (score of 0) to reveal the frequency of specific impairments (Table 4). Impairment in mastication, pharyngeal contraction/bolus propulsion, laryngeal excursion, bolus propulsion through the UES and clearance of pyriform sinus residue was found in 50% or more of all participants irrespective of treatment received. Additional impairments in palatal closure and position of the bolus at the onset of the swallow were evident in more than 30% of all participants. Similarly, for descriptive analysis the PAS ratings were reclassified into three broad categories of “nil penetration or aspiration”, “penetration”, and “aspiration” (Table 5). Almost 90% of the AFRT-CB did not have any penetration or aspiration or fluids compared with 53% of CRT patients. Patterns revealed a three-fold increase in penetration and aspiration frequency on fluids in the CRT group (47%) when compared with AFRT-CB patients (14%), although more than 40% of the AFRT-CB group also had penetration/aspiration of solids.

(insert table 4 and 5 near here)

Nutrition outcomes for weight (AFRT-CB M = 71.42kg, *SD* = 17.61; CRT M = 71.71kg, *SD* = 19.19; $Z = 0.04$, $p = 0.97$) did not reveal any significant differences between the AFRT-CB and CRT groups at 6 months post-treatment. Both groups experienced an average 10kg weight loss to 6 months post-treatment compared with pretreatment weight. No significant difference was found for the PG-SGA global rating (AFRT-CB A = 79%, B = 21%; CRT A = 82%, B = 18%; $\chi^2 = 0.07$, $p = 0.79$) or the PG-SGA numerical score (AFRT-CB M = 4.79, *SD* = 3.79; CRT M = 5.26, *SD* = 5.37; $Z = 0.12$, $p = 0.9$). At 6 months post-treatment, supplemental tube feeding was required for 12% of the CRT group (2 gastrostomy tubes), while none of the AFRT group continued to need supplemental tube feeding.

Analysis of patient-rated functional impact as scored by the FACT-H&N and MDADI revealed no significant differences between patients receiving AFRT-CB and CRT at 6 months post-treatment (Table 6). The overall FACT-H&N score revealed a pattern of greater patient-rated dysfunction for CRT, similar to the patient-rated global, emotional, functional and physical swallowing scores on the MDADI, although this sis not reach significance.

(insert table 6 near here)

DISCUSSION

This exploratory analysis suggests that treatment intensification with the addition of chemotherapy to conventional radiotherapy for patients with T1-T3 oropharyngeal SCC resulted in significant negative outcomes for functional swallowing at 6 months post-treatment compared with patients treated with AFRT-CB. Although preliminary in nature, these results affirm clinical perceptions that swallowing is worse for those who receive CRT. Despite this finding, all other parameters were not significantly different between the groups, with physiological swallow impairment, nutritional status and patient-rated functional impact found to be largely comparable between the AFRT-CB and CRT patients. The study results have been limited by small sample size however it may be hypothesized that patients who receive AFRT experience long term negative swallowing and nutritional outcomes, and that the nature and severity of the impairments are not dissimilar to those experienced by patients undergoing CRT.

With respect to the food and fluid diets managed by patients at 6 months, inferior functional swallowing was observed in the CRT patient group compared with those who received AFRT-CB. In the CRT group a small proportion still required modified fluids at 6 months, however over 80% had not returned to managing a normal diet, with most managing soft foods. Two CRT patients still had a gastrostomy tube insitu although were managing some oral intake. In comparison the AFRT-CB group were all managing thin fluids at the time of assessment and just under half had returned to a normal diet. These results are similar to those previously reported where the majority of patients resumed soft diets, although reported ongoing diet restrictions at 12 months post-treatment [12, 15-17]. A number of reports describe “swallowing solids” [31] or “more or less normal oral feeding” [32] as positive outcomes for the CRT population without quantifying their function in more detail. Less information is known about the AFRT population diet tolerance post-treatment with initial data suggesting mild difficulty swallowing solids post-treatment [6].

Despite the statistical difference in diet consistency managed, group comparisons found no significant difference between the physiological impairments observed in both participant groups. Irrespective of treatment received, more than half the participants developed mild or mild-moderate physiological impairment in swallowing function, specifically in mastication, pharyngeal contraction/bolus propulsion, laryngeal excursion, bolus propulsion through the UES and clearance of pyriform sinus residue at 6 months post-treatment. This may suggest a comparable physiological outcome, or may be due to small numbers studied. The fact that both cohorts presented with similar physiological swallow impairments could potentially be attributed similar physiological structures included in the treatment field required for curative intent radiotherapy for oropharyngeal SCC, regardless of the treatment intensification modality (AFRT-CB or CRT) used [5, 16].

The reasoning behind why the two groups presented with significantly different diet restrictions and yet were not different on physiological assessment may be attributable to the large variance associated with small participant numbers. However, restrictions in oral intake have been previously associated with videofluoroscopic measures of reduced laryngeal excursion, reduced cricopharyngeal opening, and evidence of aspiration and/or residue [33]. In the current study, descriptive analysis revealed that the pharyngeal and crico-esophageal phases were impaired with slightly higher frequency in the CRT group, which may have resulted in greater texture restriction, perceived need for supplemental feeding and overall inferior functional swallowing. However, it is also possible that the lack of agreement between the clinical and physiological swallowing findings may be due to other factors such as ongoing xerostomia, pain or fatigue further limiting oral intake for the CRT participants. In the absence of any systematic investigation of these aspects in the current study, further research is needed to determine the influence of such factors on texture limitations in a large cohort.

Although statistical comparison between the two groups failed to identify any significant differences in physiological swallowing characteristics, descriptive analysis did reveal some patterns which were more distinctive in each group. In the CRT group there were statistical trends observed for more deficits in lingual control and increased aspiration risk on thin fluids, possibly due to the potential sequelae of the addition of chemotherapy to conventional radiotherapy. Late effects of CRT treatment have been reported to include chronic fibrosis resulting in stiffening of the tongue and hyolaryngeal complex [14], reduced glottic closure and oesophageal stenosis [34], that leads to significant oropharyngeal residue and aspiration. Indeed, a systematic review by van der Molen [35] found that chemoradiation regimens were associated with an increased aspiration rate, and this may result from the toxic effect on the neuromuscular junctions causing generalised weakness, fatigue, and sensory changes [36].

Specific to AFRT-CB, physiological assessment revealed that aspects of oral and oropharyngeal dysfunction were slightly more severe and frequent, although mild in nature, compared to the CRT group. This may be subsequent to the severe acute injury associated with altered fractionation protocols [8, 9], including delayed healing of mucosa, early onset of late tissue injury (soft tissue or bone necrosis), and chronic oedema [3]. These effects may result in ongoing oral ulceration and pain, trismus, and xerostomia that may affect the oral and oropharyngeal transit parameters of swallowing including palatal closure, mastication, and relative timing of the onset of swallow, as found in the current study.

With respect to patient perceptions, functional impact at 6 months post-treatment was found to be similarly impaired between the two treatment groups, with both experiencing less than optimal function in the head and neck specific concerns and overall function assessed by the FACT-H&N, and in all domains of the MDADI. Comparisons with studies of CRT populations at 6 months revealed that the current data is similar, with ongoing patient-reported deficits in xerostomia, mastication, swallowing, taste and pain noted to have improved. This may indicate adjustment to ongoing impairment [17, 31]. While there are limited reports of patient-rated function following AFRT, the FACT-H&N scores reported by the current groups of participants are comparable to those reported by Ringash, et al. [37] for a cohort of 171 heterogenous patients treated with accelerated AFRT at 6 months.

Considering that only 43% of the AFRT-CB group and 18% of the CRT group could manage a normal diet, it is not surprising that most patients perceived they had less than optimal self-rated swallowing function. Although it may be argued that a soft diet is “near-normal” and is a good outcome, it is important to note that the majority of participants in the current cohort, independent of treatment, were consuming soft diets and reported reduced functioning across the global, emotional, functional and physical domains on the MDADI. This supports that even when able to resume "near-normal" oral intake consistencies, patients continue to regard their function as far less than normal. This relationship between slight texture modification and reduced patient perception of function has been noted previously by other researchers [38, 39], and highlights that even small limitations to oral intake variety may translate as negative outcomes for patients. Clinicians need to be sensitive to this as they support patients through recovery and rehabilitation.

Nutritional outcomes following both AFRT-CB and CRT did not differ significantly at 6 months post-treatment, with both groups losing close to 10kg. However, there was an indication for poorer outcomes in the CRT group with ongoing requirements for supplemental tube feeding in a small number of participants. The current study found 12% of CRT patients required gastrostomy tube feeding at 6 months post-treatment, a similar rate to that found previously [16], but less than the 38-64% requiring supplemental PEG feeding at 5-6 months post-treatment in other studies [12, 15]. These reports of higher alternative feeding rates were related to higher rates of aspiration (64-78%) and therefore greater recommendations to utilise alternative feeding. Participants who received AFRT-CB in the current study did not require alternative feeding at 6 months which is in agreement with previous studies [6].

While this is the first study to elucidate whether functional outcomes (swallowing, nutrition and patient-rated functional impact) following non-surgical treatment for oropharyngeal cancer differ between CRT and AFRT, the limitations of this study are recognized. Small accrual has not allowed for detailed inferential analysis, and therefore the results discussed here cannot be generalized across this population. Further limitations include the absence of objective baseline and longitudinal data, and treatment selection causing age differences in groups. Increasing age has been associated with dysphagia in normal elderly populations [40], and may have contributed negatively to functional outcomes in the AFRT-CB population. However, age has been found to be an important factor in determining tolerance of treatment in the HNC population, with lower compliance and higher toxicity rates in older patients receiving CRT [10]. In this way, the feasibility of comparing age-matched groups across these two treatment types may continue to prove difficult. Treatment selection also caused staging variability across groups (although not statistically different), another factor which may have confounded results.

CONCLUSIONS

The current preliminary study found inferior outcomes in functional swallowing for CRT patients compared with AFRT-CB patients and was reflected by increased food/fluid restriction, and greater requirements for supplemental feeding at 6 months post-treatment. Differences in functional swallowing did not translate into significant differences in swallowing physiology, nutrition or patient-rated functional impact. This lack of significant findings may have resulted from small participant numbers, or may suggest that patients who receive AFRT are largely comparable to those who receive CRT, experience similar mild-moderate physiological swallowing impairment that impacts on nutrition and patient-rated function in an equivalent manner. Although further research is required to elucidate these findings, there may be some suggestion that equal service provision should be provided to both populations rather than resources being biased toward CRT groups. Future investigations require a multicentred approach to ensure a large cohort of participants. It is hoped that the current study may inform the development of appropriately powered studies to prospectively examine the functional outcomes following intensified non-surgical treatment modalities in patients with oropharyngeal cancer.

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CONFLICT OF INTEREST

No source of funding was involved in study design, data collection, data analysis or interpretation, manuscript writing or the decision to submit the manuscript for publication. The author has had full control of the primary data which is available for review if requested.

REFERENCES

[1] Adelstein D, Li Y, Adams G, Wagner Jr H, Kish J, Ensley J, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. J Clin Oncol. 2003;21(1):92-8.

[2] Fu KK, Pajak TF, Trotti A, Jones CU, Spencer SA, Phillips TL, et al. A radiation therapy oncology group (RTOG) phase III randomized study to compare hyperfractionation and two variants of accelerated fractionation to standard fractionation radiotherapy for head and neck squamous cell carcinomas: First report of RTOG 9003. Int J Radiat Oncol Biol Phys. 2000;48(1):7-16.

[3] Jackson S, Weir L, Hay J, Tsang V, Durham J. A randomised trial of accelerated versus conventional radiotherapy in head and neck cancer. Radiother Oncol. 1997;43(1):39-46.

[4] Caudell JJ, Schaner PE, Meredith RF, Locher JL, Nabell LM, Carroll WR, et al. Factors associated with long-term dysphagia after definitive radiotherapy for locally advanced head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2009;73(2):410-5.

[5] Logemann JA, Rademaker AW, Pauloski BR, Lazarus CL, Mittal BB, Brockstein B, et al. Site of disease and treatment protocol as correlates of swallowing function in patients with head and neck cancer treated with chemoradiation. Head Neck. 2006;28(1):64-73.

[6] Yu K, Chua M, Vlantis A, Kam M, Lee W, Tsang R, et al. Swallowing function after altered fractionation radiotherapy for head and neck carcinoma. Journal Hong Kong College of Radiologists 2005;8(4):207-13.

[7] Ang KK, Peters LJ, Weber RS, Maor MH, Morrison WH, Wendt CD, et al. Concomitant boost radiotherapy schedules in the treatment of carcinoma of the oropharynx and nasopharynx. Int J Radiat Oncol Biol Phys. 1990;19(6):1339-45.

[8] Denham JW, Peters LJ, Johansen J, Poulsen M, Lamb DS, Hindley A, et al. Do acute mucosal reactions lead to consequential late reactions in patients with head and neck cancer? Radiother Oncol. 1999;52(2):157-64.

[9] Dörr W, Hendry JH. Consequential late effects in normal tissues. Radiother Oncol. 2001;61(3):223-31.

[10] Pignon J, Maître A, Maillard E, Bourhis J. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients. Radiother Oncol. 2009;92:4-14.

[11] Machtay M, Moughan J, Trotti A, Garden AS, Weber RS, Cooper JS, et al. Factors associated with severe late toxicity after concurrent chemoradiation for locally advanced head and neck cancer: An RTOG analysis. J Clin Oncol. 2008;26(21):3582-9.

[12] Graner D, Foote R, Kasperbauer J, Stoeckel R, Okuno S, Olsen K, et al. Swallow function in patients before and after intra-arterial chemoradiation. The Laryngoscope. 2003;113(3):573-9.

[13] Kotz T, Costello R, Li Y, Posner M. Swallowing dysfunction after chemoradiation for advanced squamous cell carcinoma of the head and neck. Head Neck. 2004;26(4):365-72.

[14] Lazarus C, Logemann JA, Pauloski BR, Rademaker AW, Helenowski IB, Vonesh EF, et al. Effects of radiotherapy with or without chemotherapy on tongue strength and swallowing in patients with oral cancer. Head Neck. 2007;29(7):632-7.

[15] Goguen L, Posner M, Norris C, Tishler R, Wirth L, Annino D, et al. Dysphagia after sequential chemoradiation therapy for advanced head and neck cancer. Otolaryngology-Head and Neck Surgery. 2006;134(6):916-22.

[16] Logemann JA, Pauloski BR, Rademaker AW, Lazarus CL, Gaziano J, Stachowiak L, et al. Swallowing disorders in the first year after radiation and chemoradiation. Head Neck. 2008;30(2):148-58.

[17] List MA, Siston A, Haraf D, Schumm P, Kies M, Stenson K, et al. Quality of life and performance in advanced head and neck cancer patients on concomitant chemoradiotherapy: A prospective examination. J Clin Oncol. 1999;17(3):1020-8.

[18] Oates J, Clark J, Read J, Reeves N, Gao K, Jackson M, et al. Prospective evaluation of quality of life and nutrition before and after treatment for nasopharyngeal carcinoma. Archives of Otolaryngology- Head and Neck Surgery. 2007;133(6):533.

[19] Lee H, Havrila C, Bravo V, Shantz K, Diaz K, Larner J, et al. Effect of oral nutritional supplementation on weight loss and percutaneous endoscopic gastrostomy tube rates in patients treated with radiotherapy for oropharyngeal carcinoma. Support Care Cancer. 2008;16(3):285-9.

[20] Hammerlid E, Wirblad B, Sandin C, Mercke C, Edstrom S, Kaasa S, et al. Malnutrition and food intake in relation to quality of life in head and neck cancer patients. Head Neck. 1998;20(6):540-8.

[21] van den Berg M, Rasmussen-Conrad E, Gwasara G, Krabbe P, Naber A, Merkx M. A prospective study on weight loss and energy intake in patients with head and neck cancer, during diagnosis, treatment and revalidation. Clin Nutr. 2006;25(5):765-72.

[22] Schueller P, Schaefer U, Micke O, Willich N. Results of simultaneous radiochemotherapy vs concomitant boost radiation in patients with inoperable cancer of the head and neck. Eur J Cancer. 1999;35(Supplement 4):S174-S.

[23] Cartmill B, Cornwell P, Ward EC, Davidson W, Porceddu SV. A prospective investigation of swallowing, nutrition, and patient-rated functional impact following altered fractionation radiotherapy with concomitant boost for oropharyngeal cancer. Dysphagia. in press.

[24] Limited DAoAaSPAoA. Texture-modified foods and thickened fluids as used for individuals with dysphagia: Australian standardised labels and definitions. *Nutr Diet* 2007:S53-S63.

[25] Ward EC, Conroy A-L. Validity, reliability, and responsivity of the Royal Brisbane Hospital Outcome Measure for Swallowing. Asia Pacific Journal of Speech Language and Hearing. 1999;4:109-29.

[26] Huckabee M-L. New Zealand Index for Multidisciplinary Evaluation of Swallowing (NZIMES). n.d.

[27] Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. Dysphagia. 1996;11(2):93-8.

[28] Ottery F. Patient-Generated Subjective Global Assessment. In: McCallum P, Polisena C, eds. *The Clinical Guide to Oncology Nutrition*. Chicago: The American Dietetic Association 2000:11-23.

[29] Chen AY, Frankowshi R, Bishop-Leone J, Hebert T, Leyk S, Lewin J, et al. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: The M. D. Anderson Dysphagia Inventory. Archives of Otolaryngology - Head and Neck Surgery. 2001;127(7):870-6.

[30] Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The functional assessment of cancer therapy scale: Development and validation of the general measure. J Clin Oncol. 1993;11(3):570-9.

[31] Abdel-Wahab MMDP, Abitbol AMD, Lewin AMD, Troner MMD, Hamilton KP, Markoe AMDS. Quality-of-life assessment after hyperfractionated radiation therapy and 5-fluorouracil, cisplatin, and paclitaxel (Taxol) in inoperable and/or unresectable head and neck squamous cell carcinoma. Am J Clin Oncol. 2005;28(4):359-66.

[32] Ackerstaff AH, Balm AJM, Rasch CRN, de Boer JP, Wiggenraad R, Rietveld DHF, et al. First-year quality of life assessment of an intra-arterial (RADPLAT) versus intravenous chemoradiation phase III trial. Head Neck. 2009;31(1):77-84.

[33] Pauloski BR, Rademaker AW, Logemann JA, Newman L, MacCracken E, Gaziano J, et al. Relationship between swallow motility disorders on videofluorography and oral intake in patients treated for head and neck cancer with radiotherapy with or without chemotherapy. Head Neck. 2006;28(12):1069.

[34] Trotti A. Toxicity in head and neck cancer: A review of trends and issues. International Journal of Radiation Oncology Biology Physics. 2000;47(1):1-12.

[35] van der Molen L, van Rossum M, Burkhead L, Smeele L, Hilgers F. Functional outcomes and rehabilitation strategies in patients treated with chemoradiotherapy for advanced head and neck cancer: a systematic review. Eur Arch Otorhinolaryngol. 2009;266(6):889-900.

[36] Mittal BB, Pauloski BR, Haraf DJ, Pelzer HJ, Argiris A, Vokes EE, et al. Swallowing dysfunction: Preventative and rehabilitation strategies in patients with head-and-neck cancers treated with surgery, radiotherapy, and chemotherapy: A critical review. International Journal of Radiation Oncology Biology Physics. 2003;57(5):1219-30.

[37] Ringash J, Lockwood G, O'Sullivan B, Warde P, Bayley A, Cummings B, et al. Hyperfractionated, accelerated radiotherapy for locally advanced head and neck cancer: Quality of life in a prospective phase I/II trial. Radiother Oncol. 2008;87(2):181-7.

[38] Gillespie M, Brodsky M, Day T, Lee F, Martin-Harris B. Swallowing-related quality of life after head and neck cancer treatment. The Laryngoscope. 2004;114(8):1362-7.

[39] Pauloski BR, Rademaker AW, Logemann JA, Lazarus CL, Newman L, Hamner A, et al. Swallow function and perception of dysphagia in patients with head and neck cancer. Head Neck. 2002;24(6):555-65.

[40] Logemann J, Pauloski B, Rademaker A, Colangelo L, Kahrilas P, Smith C. Temporal and biomechanical characteristics of oropharyngeal swallow in younger and older men. J Speech Lang Hear Res. 2000;43(5):1264.

Table 1. Demographic comparisons between AFRT-CB and CRT groups

Demographic		AFRT-CB M (SD) or n (%)	CRT M (SD) or n (%)	Statistic Z / χ^2	*p*
Age (years)		66.6 (8.7) range = 53-82	54.9 (10.9) range = 34-69	$Z = 2.81$	0.005
Weight[a] (kgs)		83 (18.9)	80 (22.7)	t = -0.34	0.36
Sex	Male	12 (86)	15 (88)	$\chi^2 = 0.18$	0.67
	Female	2 (14)	2 (12)		
Site	Tonsil	9 (64)	10 (59)	$\chi^2 = 16.72$	0.053
	BOT	1 (7)	3 (18)		
	Supraglottis	3 (21)	2 (12)		
	Pharyngeal wall	1 (7)	2 (12)		
Size	T1	4 (29)	4 (24)	$\chi^2 = 0.67$	0.96
	T2	7 (50)	7 (41)		
	T3	3 (21)	6 (35)		
Nodal	N0	9 (64)	1 (6)	$\chi^2 = 16.72$	0.34
	N1	2 (14)	3 (18)		
	N2a	2 (14)	2 (12)		
	N2b	1 (7)	6 (41)		
	N2c		1 (6)		
	N3		2 (18)		
Stage	I	2 (14)	0	$\chi^2 = 2.91$	0.41
	II	4 (29)	0		
	III	5 (36)	4 (24)		
	IV	3 (21)	13 (76)		
Smoking	Current	3 (21)	6 (35)	$\chi^2 = 6.99$	0.14
	Ex	7 (50)	9 (53)		
	Never	4 (29)	2 (12)		
Alcohol[b]	Current	12 (86)	15 (88)	$\chi^2 = 0.09$	0.76
	Ex	2 (14)	1 (6)		
	Never		1 (6)		
Dysphagia for liquids	Yes	0	0	-	-
	No	14 (100)	17 (100)		
Dysphagia for solids	Yes	3 (21)	6 (35)	$\chi^2 = 0.72$	0.4
	No	11 (79)	11 (65)		

[a] Pre-treatment weight
[b] No information re: alcohol intake available for one AFRT-CB participant

Table 2. Diet and fluid consistencies reported at 6 months post-treatment

	Consistency	AFRT-CB n (%)	CRT n (%)
Fluids	Thin	14 (100)	14 (82)
	Mildly thick	0	3 (18)
Solids	Full	6 (43)	3 (18)
	Soft	8 (57)	11 (65)
	Minced	0	2 (12)
	Pureed	0	1 (6)
Supplemental tube feeding*		0	2 (12)

*Supplemental tube feeding required with some oral intake

Table 3. Severity of swallowing impairment at 6 months post-treatment

	Parameter	Component	AFRT-CB N = 14 M (SD)	CRT N = 17 M (SD)	*Z*	*p*
NZIMES[a]	Oral	Labial closure	-	-	0	0
		Lingual control	0.07 (0.27)	0.35 (0.49)	1.84	0.07
		Palatal closure	0.57 (0.65)	0.35 (0.49)	-0.94	0.35
		Mastication	1.5 (0.65)	1.12 (0.6)	-1.52	0.13
	Oral Pharyngeal Transit	Position of bolus at onset of swallow	0.71 (0.91)	0.65 (0.79)	-0.09	0.93
		Relative timing of onset of swallow	0.43 (0.51)	0.24 (0.44)	-1.13	0.26
	Pharyngeal	Velopharyngeal closure	0 (0)	0.18 (0.53)	1.31	0.19
		Pharyngeal contraction + bolus propulsion	1 (0.56)	1 (0.87)	0.00	1.0
		Laryngeal excursion	0.5 (0.52)	0.88 (0.78)	1.37	0.17
	Crico-esophageal	Bolus propulsion through UES	0.57 (0.65)	0.77 (0.75)	0.7	0.49
		Clearance of pyriform sinus residue	0.57 (0.65)	0.88 (0.93)	0.86	0.39
		Upper esophageal parameters	-	-	0	0
Penetration-Aspiration Scale[b]		Fluids	2.21 (1.85)	3 (1.9)	1.8	0.07
		Solids	2.79 (1.76)	3.59 (2.81)	3.89	0.7

[a] New Zealand Index for Multidisciplinary Examination of Swallowing: severity ratings for each component from 0 (no significant impairment) to 4 (profound impairment)

[b] Penetration-Aspiration Scale: severity ratings from 1 (material does not enter the airway) to 8 (material enters the airway, passes below the vocal folds, and no effort is made to eject)

Table 4. Frequency of swallowing impairment at 6 months*

NZIMES Parameter	Component	n (%) rated with "impairment"	
		AFRT	CRT
Oral	Labial Closure	0	0
	Lingual Control	2 (7)	6 (35)
	Palatal Closure	7 (50)	6 (35)
	Mastication	14 (100)	15 (88)
Oral Pharyngeal	Position of bolus at onset of swallow	6 (43)	8 (47)
	Relative timing of onset of swallow	6 (43)	4 (24)
Pharyngeal	Velopharyngeal Closure	0	2 (12)
	Pharyngeal Contraction/Bolus Propulsion	12 (86)	11 (65)
	Larygneal Excursion	7 (50)	11 (65)
Crico-esophageal	Bolus Propulsion through UES	7 (50)	10 (59)
	Clearance of Pyriform Sinus Residual	7 (50)	10 (59)
	Upper Esophageal Parameters	0	0

*NZIMES data compressed into binary scale of "no impairment" vs "impairment"

Table 5. Frequency of penetration and aspiration events

Penetration-Aspiration Scale		6 months post-treatment n (%)	
		AFRT-CB	CRT
Nil	Fluids	12 (86)	9 (53)
	Solids	8 (57)	8 (47)
Penetration	Fluids	1 (7)	6 (35)
	Solids	4 (29)	2 (12)
Aspiration	Fluids	1 (7)	2 (12)
	Solids	2 (14)	7 (41)

Table 6. Patient-rated functional impact outcomes at 6 months post-treatment

Tool	Domain (range)	AFRT-CB N = 14 M (SD)	CRT N = 17 M (SD)	*Z*	*p*
FACT- H&N[a]	Emotional (0-24)	21 (2.5)	18.5 (4.3)	-1.59	0.11
	Functional (0-28)	19.1 (6.9)	17.9 (6.4)	-0.78	0.44
	Physical (0-28)	21.5 (6.1)	18.9 (7.0)	-1.22	0.22
	Social/Family (0-28)	21 (7.4)	19.9 (6.2)	-0.74	0.46
	Head and Neck Specific (0-44)	30.1 (6.6)	28.5 (7.7)	-0.56	0.58
	Overall (0-152)	115.6 (22.7)	103.6 (24.9)	-1.31	0.19
MDADI[b]	Global (0-100)	68.6 (21.8)	62.4 (28.2)	-0.48	0.63
	Emotional (0-100)	76.2 (17.6)	68.8 (19.7)	-1.08	0.28
	Functional (0-100)	77.4 (13.9)	68 (23.8)	-1.04	0.3
	Physical (0-100)	69.3 (12.1)	60.3 (21.6)	-1.67	0.1

[a] Functional Assessment of Cancer Therapy Additional Concerns for Head and Neck version 4

[b] M. D. Anderson Dysphagia Inventory