Results of Quality of Life for Phase II NRG Oncology RTOG 0244 Study Using Submandibular Salivary Gland Transfer Procedure for Prevention of Radiation-Induced Xerostomia in Head and Neck Cancer Patients

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Key words: Salivary gland transfer procedure, xerostomia, radiation, quality of life, prevention, head and neck cancer

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Abstract

Background: We report quality of life results of phase II NRG Oncology RTOG 0244 study which used submandibular salivary gland transfer (SGT) procedure for prevention of radiation (XRT) induced xerostomia.

Methods: Patients had surgery for primary, neck dissection, SGT and XRT where transferred gland was shielded. Intensity modulated RT (IMRT), amifostine, and pilocarpine were not allowed. Modified version of University of Washington Quality of Life questionnaire (UW-QOL) was used. Results of all patients and those treated "per protocol" are reported.

Results: At baseline, all 44 patients completed UW-QOL. Compliance at 3, 6 and 12 months was 85.7%, 67.9% & 64.3% respectively. Sixteen were not treated "per protocol". For all 44 patients, 51.7% and for 28 patients treated "per protocol", 66.6% had either normal amount or mild loss of saliva at three months. Median follow up is 2.68 years.

Conclusions: Submandibular salivary gland transfer procedure is useful in prevention of radiation induced xerostomia.

Background

Over 40,000 individuals are diagnosed as having head and neck cancer every year in the United States.[1] Radiation treatment is a primary or secondary therapeutic modality in most cases resulting in xerostomia and adversely affecting patient's quality of life.[2-5] Xerostomia impairs mastication, deglutition, gustation, causes nutritional compromise, sleep disruptions and change in oral microbial flora leading to caries.[4,5] Several strategies such as amifostine,[6-8] intensity modulated radiation therapy (IMRT),[9-16] pilocarpine[17-22] and acupuncture[23-25] have been tried over the years in an attempt to reduce xerostomia.

The submandibular gland transfer (SGT) procedure, whereby the contralateral submandibular salivary gland is translocated to the submental space prior to the initiation of radiation treatment and then shielded during treatment, was first described by Seikaly and Jha et al.[26-28] They conducted a phase III randomized multi center prospective trial comparing SGT with Pilocarpine and demonstrated excellent results of the SGT procedure for the prevention of XRT induced xerostomia.[29] Similar positive results of preservation of saliva using SGT procedure were reported and confirmed by other investigators in different institutions and countries.[30-33]

A phase II multicenter trial NRG Oncology RTOG 0244 confirmed the reproducibility of surgical technique of SGT in a multi institution setting.[34] We now report the quality of life (QOL) outcomes from this trial.

Methods

A phase II multi-center NRG Oncology RTOG 0244 study was conducted from 2003 to 2007 and its detailed methodology and results have been published elsewhere.[34] Prior to patient enrollment, each participating institution provided institutional review board approval and each patient provided written informed consent. IMRT, prophylactic use of amifostine and/or pilocarpine were not allowed. All patients were required to fill out a quality of life questionnaire. A modified version of the self-administered, validated instrument University of Washington Quality of Life questionnaire (UW-QOL) was used. The UW-QOL was selected because of its inclusion of symptom specific effects that may result from the intervention of salivary gland transfer (i.e., related to saliva, eating, taste, swallowing, pain). The UW-QOL – RTOG modification contains all questions in UW-QOL Version 3 except for shoulder disability[35], the employment question from Version 1[36], as well as four additional questions assessing mouth pain, throat pain, mucous amount, and mucous consistency. The QOL assessments included a baseline assessment, then at three, six, and 12 months from start of XRT. Acute radiotherapy toxicities (≤ 90 days from start of XRT) and systemic effects at any time were scored using the Common Toxicity Criteria (CTC) version 2.0. Late RT toxicities were scored by the RTOG/EORTC criteria. Of all 44 analyzable patients, 28 were treated “as per protocol”.

Statistical Methods

For the analysis, exploratory factor analysis results were used. Four items, disfigurement, employment, chewing and speech, were removed from the total score and each of these items is provided along with the mucus, pain, activities and eating factor scores as well as the total score. The four factors derived from the 11 remaining items are:

Factor 1: Mucus (amount of mucus or phlegm, consistency of mucus or phlegm)

Factor 2: Eating (swallowing, amount of saliva, consistency of saliva, taste)

Factor 3: Pain (general pain, mouth pain, throat pain)

Factor 4: Activities (activity, recreation/entertainment).

The total score uses the 11 items that were retained by the factor analysis. All items were scored from 0 to 100 and the mean was used to calculate the total and factor scores. In addition to missing data, a concern is missing items on a single assessment. The scoring procedure of the validated tool on how to handle missing items was then followed. For the total score, at most two missing items were allowed (communication with Dr. Bevan Yueh). For subscale scores, all items must be answered. Due to the limited sample size, no modeling was conducted on this data.

Fisher's exact test for categorical variables and two-sided Wilcoxon signed rank test with normal approximation for continuous variables were used for statistical testing. A subgroup analysis of patients who received both RT and surgery as per protocol or with acceptable variation was also performed.

Results

Eight institutions enrolled 49 patients between August 2003 and August 2007. 44 patients were analyzable (Figure 1). Median follow up is 2.68 years. There was not a separate QOL consent, therefore all patients were included in the analysis. At baseline, all 44 analyzable patients completed the UW-QOL – RTOG modification as well as 28, who completed treatment as "per protocol".

Pretreatment characteristics are shown in Table 1. Pretreatment characteristics based on compliance at three, six, and 12 months were compared to determine if patients who did not complete the assessment differed from those who did complete the assessment (results not shown). The only difference observed between the patients who completed the assessment at three months and those who did not was the primary site (p=0.047); patients who completed the assessment were more likely to have oropharyngeal primary site than those who did not (71% vs. 46.2%).

Due to the smaller number of patients who completed the UW-QOL – RTOG modification questionnaire at six and 12 months, only scores at three months are presented (six and 12 months results are provided in the Appendix). Distributions of each UW-QOL item as categorical variables are presented in Table 2. Change scores are provided in Table 3 for the four removed items, the overall score, and the factor scores. Change scores are calculated by subtracting the follow-up assessment from baseline. Since a low score indicates better function, a positive change score indicates improvement. The total score and factor scores showed improvement in function from baseline to three months while the remaining four items showed either improvement in function or no change in function.

The main utility of SGT procedure relates to the prevention of XRT induced xerostomia. The “amount of saliva” scores as reported by the participants on UW-QOL – RTOG modification questionnaire are therefore of interest. At three months, 51.7% of all analyzable patients had either mild or no loss of saliva. For the 28 patients treated as “per protocol”, 66.6% had mild or no loss of saliva. In regards to consistency of saliva, at three months 46.7% of all 44 analyzable patients had normal or slightly thicker saliva and for the 28 patients treated as “per protocol”, 56.5% reported normal or slightly thicker saliva.

The recurrence pattern was not altered by the salivary gland transfer procedure and there was no submental space recurrence noted as of the latest follow up.

Discussion

Humans produce approximately 600 ml of saliva per day.[37] Parotid secretions are primarily serous and predominate when stimulated during eating, whereas submandibular salivary gland secretions are relatively more mucinous, and represent the majority of basal, unstimulated saliva. Parotids contribute only about 20% of the total volume of unstimulated saliva, while the submandibular salivary gland contributes 65% and the sublingual 7-8%.[38] At high flow rates, the parotid contribute about 50% of the whole saliva. Unstimulated saliva (resting state) is more important in the subjective feeling of xerostomia. Stimulated saliva is produced during eating, which lasts for approximately 54 minutes per day.[38] Submandibular salivary glands contribution is the most important in perception of xerostomia.

Jha, Seikaly et al performed a prospective, phase II study investigating prevention of xerostomia by surgical transfer of the submandibular salivary gland (SMG) to the submental space prior to starting postoperative XRT.[27 - 28] 81% patients had no or minimal xerostomia and 19% had moderate to severe xerostomia at the end of XRT. Long-term results of patients two years after XRT were also published showing preservation of saliva in 83% of patients, and normal or slightly thicker saliva consistency in 72%. These results have been duplicated by other investigators.[28] Table 4 summarizes the results of prevention of XRT induced xerostomia using SGT procedure by various investigators. Zhang et al, using SGT in 32 patients and the University of Washington QOL questionnaire reported 81.3%% of patients with none or minimal xerostomia at one year and 84.6% at five years.[33] These results are similar to what is reported here. Xue – Kui Liu et al using SGT procedure and Wijer's xerostomia questionnaire in patients with nasopharyngeal carcinoma, reported none or minimal xerostomia in 86% of patients in the gland transfer group after three months and in 87% at five years after treatment.[31-32] In a prospective phase III multicenter randomized study comparing SGT procedure to pilocarpine for the management of xerostomia, superiority of submandibular salivary gland transfer over Pilocarpine was convincingly shown.[29]

Sood Day et al published a systematic review and meta-analysis of 177 patients treated with SGT procedure, with a mean follow up of 22.7 months. At three months, 85.3% patients had none or minimal loss of saliva and at 18 – 24 months, it was 88.8%.[39]

It has been universally observed that the incidence of xerostomia decreases with time, and this is presumably due to the hypertrophy of the transferred submandibular salivary gland over time.

For NRG Oncology RTOG 0244, IMRT, 3D-CRT, or any form of image guided radiation treatment was not allowed. Currently, however, most centers use IMRT, often in conjunction with image guided radiation techniques. With the use of such advanced modern techniques, it is possible to protect and decrease the dose to the contralateral salivary gland even without gland transfer. However, the mean doses delivered to the spared submandibular gland frequently exceeded ≥40Gy, which are significantly higher than doses achieved when the gland is shielded in the submental space after SGT. In a phase II prospective study, combining the salivary gland transfer procedure with postoperative IMRT to protect both the parotid and the "transferred submandibular salivary gland" for the prevention of XRT-induced xerostomia yielded superior functional outcomes with 100% of patients with no or minimal xerostomia two years after treatment (Table 4).[40]

IMRT strategies initially had focused primarily on sparing one or both of the parotid glands.[9-12] Investigators are now however focusing their attention on the importance of submandibular gland salivary contributions.[41-45] Saarilahti et al. demonstrated the importance of sparing the contralateral submandibular salivary gland using IMRT.[46] In a selected subset of patients (n=18), the mean unstimulated saliva flow was 60% of the baseline vs. 25% (p=0.006) among patients with one submandibular salivary gland spared. Patients in whom both the submandibular and the parotid salivary glands were spared, reported less grade 2 or 3 xerostomia (p= 0.018).[46] However, they were able to protect the contralateral submandibular salivary glands in only 50% of selected patients in order not to compromise the target volume coverage.

Therefore, for further prevention of xerostomia, future studies must focus on better sparing of the submandibular salivary gland in addition to the parotid glands.

This paper has several limitations. While it presents patient reported outcomes pertaining to quality of life after the SGT procedure, the completion rate of the questionnaires dropped off over time. As such, only the three month data is robust. As a sizable number of patients were not treated per protocol, this created two distinct groups for which the QOL could differ. Unfortunately, due to the small numbers overall, formal statistical analysis could not be performed to directly compare salivary outcomes in those patients treated per protocol and those that were not. Nevertheless, the nominal difference in no to mild xerostomia between the groups suggests a clinically meaningful improvement in xerostomia for those patients treated per protocol. The overall values presented also are given in isolation as this was a single arm study. While most patients had oropharyngeal cancer, the sample size does not allow more granular analysis of the association of symptoms with tumor site, stage, use of surgical reconstruction and the like. Finally, the patient reported outcome presented here differ somewhat from the objective toxicity measures presented in our initial publication of this trial. However, differences between objective and subjective measures of toxicity, especially after head and neck radiation, are well known and ultimately, the value of this paper is to present the patient side of the equation and characterize how they experience their toxicity.

Conclusions

In conclusion, the results of NRG Oncology RTOG 0244 demonstrated that the technique of SGT procedure is reproducible in a multicenter setting and is a useful approach to prevent of radiation induced xerostomia.

Availability of data and materials

The dataset(s) supporting the conclusions of this article will be available according to the NCI's data sharing policy.

Ethics approval

Prior to patient enrollment, each participating institution provided institutional review board approval and each patient provided written informed consent.

Abbreviations

CTC: Common Toxicity Criteria; Gy: Gray; IMRT: intensity modulated RT; QOL: quality of life; Q1: first quartile; Q3: third quartile; RT: Radiation therapy; RTOG: Radiation Therapy Oncology Group; SGT: salivary gland transfer; SMG: submandibular salivary gland; UW-QOL: University of Washington Quality of Life questionnaire; XRT: external radiation therapy; 3D-CRT: three-dimensional conformal radiation therapy

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Figure legend

Figure 1: CONSORT Diagram

Figure1. CONSORT Diagram

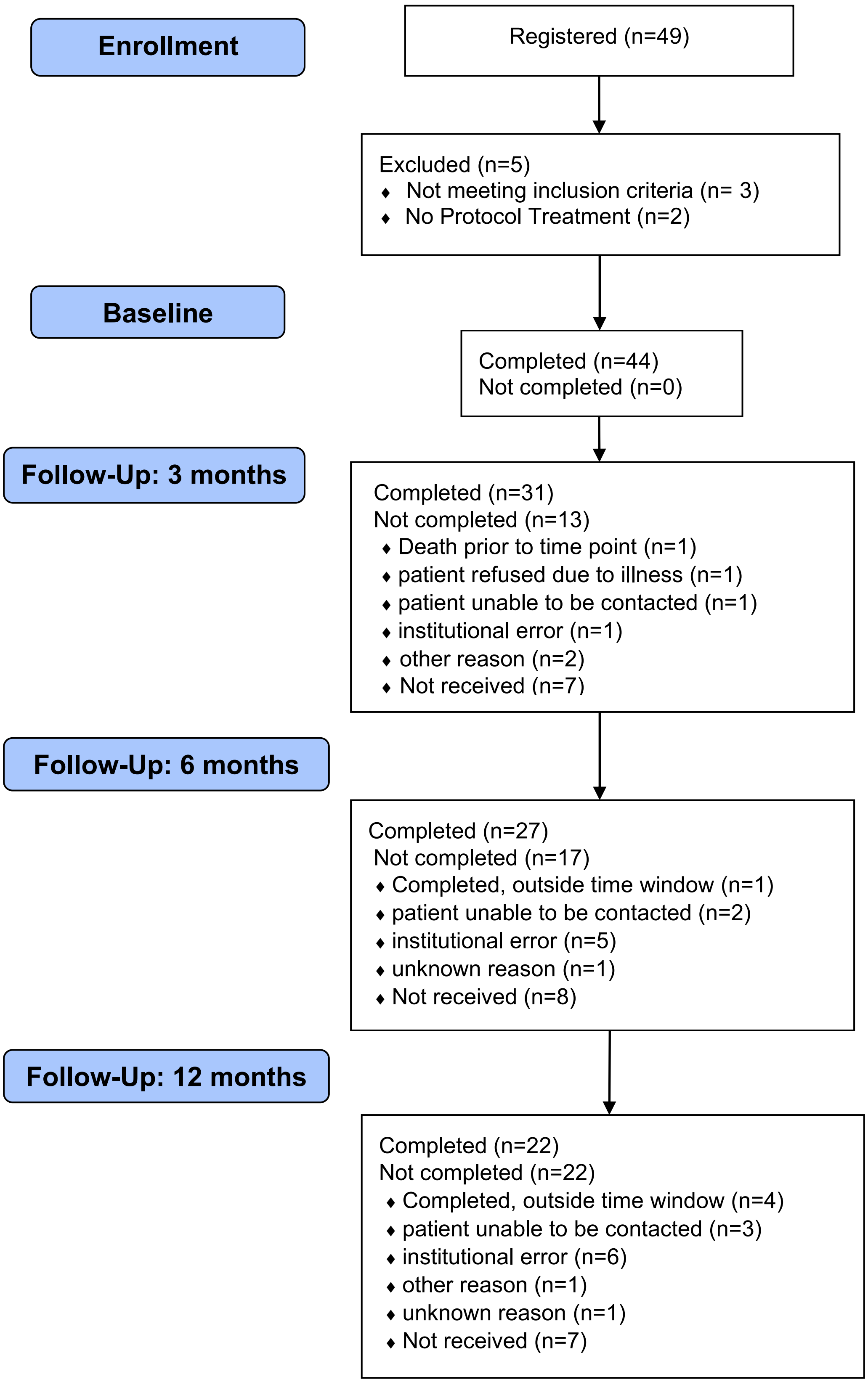

Table 1. Pretreatment Characteristics

	All patients (n=44)	Per protocol patients (n=28)
Age (years)		
Median	56.5	55
Min - Max	42 - 74	42 - 73
Q1 - Q3	50.5 - 61.5	48.5 - 60
Gender		
Male	36 (81.8%)	24 (85.7%)
Female	8 (18.2%)	4 (14.3%)
Race		
American Indian or Alaskan native	1 (2.3%)	1 (3.6%)
Black or African-American	4 (9.1%)	2 (7.1%)
White	38 (86.4%)	24 (85.7%)
Unknown	1 (2.3%)	1 (3.6%)
Ethnicity		
Hispanic or Latino	1 (2.3%)	1 (3.6%)
Not Hispanic or Latino	41 (93.2%)	26 (92.9%)
Unknown	2 (4.5%)	1 (3.6%)
Zubrod Performance Status		
0	35 (79.5%)	25 (89.3%)
1	9 (20.5%)	3 (10.7%)
Primary Site		
Oropharynx	28 (63.6%)	19 (67.9%)
Hypopharynx	3 (6.8%)	1 (3.6%)
Larynx	3 (6.8%)	3 (10.7%)
Unknown	10 (22.7%)	5 (17.9%)
T Stage		
T0	1 (2.3%)	1 (3.6%)
T1	12 (27.3%)	10 (35.7%)
T2	16 (36.4%)	12 (42.9%)
T3	4 (9.1%)	1 (3.6%)
T4	2 (4.5%)	1 (3.6%)
Tis	1 (2.3%)	0 (0.0%)
Tx	8 (18.2%)	3 (10.7%)

N Stage		
N0	5 (11.4%)	2 (7.1%)
N1	14 (31.8%)	10 (35.7%)
N2a	12 (27.3%)	7 (25.0%)
N2b	13 (29.5%)	9 (32.1%)
AJCC Stage		
II	3 (6.8%)	2 (7.1%)
III	12 (27.3%)	8 (28.6%)
IV	27 (61.4%)	17 (60.7%)
Unknown	2 (4.5%)	1 (3.6%)

Q1 = first quartile; Q3 = third quartile

Table 2. UW-QOL 3 Month Distributions

	All patients (n=31)	Per protocol patients (n=24)
General Pain	(n=30)	(n=24)
I have no pain	11 (36.7%)	10 (41.7%)
There is mild pain not needing medication	10 (33.3%)	7 (29.2%)
I have moderate pain - requires regular medication	7 (23.3%)	5 (20.8%)
I have severe pain controlled only narcotics	1 (3.3%)	1 (4.2%)
I have severe pain not controlled by narcotics	1 (3.3%)	1 (4.2%)
Mouth Pain	(n=31)	(n=24)
I have no pain	13 (41.9%)	11 (45.8%)
I have mild pain but it is not affecting my eating	5 (16.1%)	4 (16.7%)
I have moderate pain that is affecting my eating	10 (32.3%)	8 (33.3%)
I have severe pain and need medication in order to eat	2 (6.5%)	1 (4.2%)
I have severe pain and cannot eat even with medication	1 (3.2%)	0 (0.0%)
Throat Pain	(n=30)	(n=24)
I have no pain	7 (23.3%)	7 (29.2%)
I have mild pain but it is not affecting my eating	10 (33.3%)	7 (29.2%)
I have moderate pain that is affecting my eating	12 (40.0%)	9 (37.5%)
I have severe pain and cannot eat even with medication	1 (3.3%)	1 (4.2%)
Disfigurement	(n=31)	(n=24)
There is no change in my appearance	3 (9.7%)	2 (8.3%)
The change in my appearance is minor	24 (77.4%)	19 (79.2%)
My appearance bothers me but I remain active	4 (12.9%)	3 (12.5%)
Activity	(n=31)	(n=24)
I am as active as I have ever been	2 (6.5%)	1 (4.2%)
There are times when I can't keep up with my old pace but not often	8 (25.8%)	6 (25.0%)
I am often tired and I have slowed down my activities although I still get out	16 (51.6%)	14 (58.3%)
I don't go out because I don't have the strength	2 (6.5%)	1 (4.2%)
I am usually in a bed or chair and don't leave home	3 (9.7%)	2 (8.3%)
Recreation/Entertainment	(n=31)	(n=24)
There are no limitations to recreation at home and away from home	5 (16.1%)	2 (8.3%)

There are few things I can't do but I still get out and enjoy life	12 (38.7%)	12 (50.0%)
There are many times when I wish I could get out more but I'm not up to it	8 (25.8%)	6 (25.0%)
There are severe limitations to what I can do	6 (19.4%)	4 (16.7%)
Employment	(n=27)	(n=22)
I work full time	9 (33.3%)	6 (27.3%)
I have a part time but permanent job	4 (14.8%)	4 (18.2%)
I am unemployed	7 (25.9%)	6 (27.3%)
I am retired	7 (25.9%)	6 (27.3%)
Chewing	(n=30)	(n=23)
I can chew as well as ever	5 (16.7%)	3 (13.0%)
I have slight difficulty chewing solid foods	13 (43.3%)	10 (43.5%)
I have moderate difficulty chewing solid foods	6 (20.0%)	4 (17.4%)
I can only chew soft foods	5 (16.7%)	5 (21.7%)
I cannot chew soft foods	1 (3.3%)	1 (4.3%)
Swallowing	(n=31)	(n=24)
I swallow normally	5 (16.1%)	3 (12.5%)
I cannot swallow certain solid foods	16 (51.6%)	14 (58.3%)
I can only swallow soft foods	6 (19.4%)	3 (12.5%)
I can only swallow liquid foods	1 (3.2%)	1 (4.2%)
I cannot swallow	3 (9.7%)	3 (12.5%)
Amount of Saliva	(n=31)	(n=24)
I have a normal amount of saliva	2 (6.5%)	2 (8.3%)
I have a mild loss of saliva	14 (45.2%)	14 (58.3%)
I have a moderate loss of saliva	12 (38.7%)	6 (25.0%)
I have a severe loss of saliva	3 (9.7%)	2 (8.3%)
Consistency of Saliva	(n=30)	(n=23)
My saliva has normal consistency	2 (6.7%)	2 (8.7%)
My saliva is slightly thicker	12 (40.0%)	11 (47.8%)
My salvia is moderately thicker	12 (40.0%)	8 (34.8%)
My saliva is extremely thicker	4 (13.3%)	2 (8.7%)
Taste	(n=30)	(n=23)
I can taste food normally	2 (6.7%)	2 (8.7%)
I can taste most foods normally	3 (10.0%)	3 (13.0%)
I can taste some foods normally	12 (40.0%)	8 (34.8%)
I can taste few foods normally	10 (33.3%)	7 (30.4%)

I cannot taste any foods normally	3 (10.0%)	3 (13.0%)
Speech	(n=30)	(n=23)
My speech is the same as always	13 (43.3%)	11 (47.8%)
I have difficulty with saying some words but can be understood over the phone	16 (53.3%)	12 (52.2%)
I have moderate difficulty saying some words and cannot use the phone	1 (3.3%)	0 (0.0%)
Amount of Mucus or Phlegm	(n=30)	(n=23)
I have a normal amount of mucus	3 (10.0%)	3 (13.0%)
I have a mild amount of mucus	10 (33.3%)	8 (34.8%)
I have a moderate amount of mucus	12 (40.0%)	9 (39.1%)
I have a severe amount of mucus	5 (16.7%)	3 (13.0%)
Consistency of Mucus or Phlegm	(n=31)	(n=24)
My mucus has normal consistency	2 (6.5%)	2 (8.3%)
My mucus is slightly thicker	12 (38.7%)	10 (41.7%)
My mucus is moderately thicker	13 (41.9%)	8 (33.3%)
My mucus is extremely thicker	3 (9.7%)	3 (12.5%)
I have no mucus	1 (3.2%)	1 (4.2%)

Table 3. UW-QOL 3 Month Change Score Distributions

	All patients (n=31)	Per protocol patients (n=23)
Total Score	(n=30)	(n=23)
Median	22. 7	21.8
Min - Max	-7. 3 - 41.8	-7.3 – 40
Q1 - Q3	16. 4 - 31.1	12. 7 - 29.1
Factor scores		
Mucus	(n=29)	(n=22)
Median	20	20
Min - Max	-10 - 50	-10 – 50
Q1 - Q3	10 - 40	10 – 40
Eating	(n=26)	(n=19)
Median	30	30
Min - Max	0 - 55	0 – 55
Q1 - Q3	25 - 40	20 – 40
Pain	(n=30)	(n=24)
Median	6. 7	6. 7
Min - Max	-13.3 - 46.7	-13.3 – 40
Q1 - Q3	0 - 26. 7	0 - 23.3
Activities	(n=31)	(n=24)
Median	30	30
Min - Max	-10 - 70	-10 - 70
Q1 - Q3	0 - 30	0 - 30
Removed item scores		
Disfigurement	(n=30)	(n=23)
Median	20	20
Min - Max	0 - 40	0 - 40
Q1 - Q3	0 - 20	0 - 20
Employment	(n=27)	(n=22)
Median	0	0
Min - Max	-20 - 80	-20 - 80
Q1 - Q3	0 - 20	0 - 20
Chewing	(n=28)	(n=22)
Median	20	20

Min - Max	0 - 80	0 - 80
Q1 - Q3	0 - 40	0 - 40
Speech	(n=30)	(n=23)
Median	10	0
Min - Max	0 - 40	0 - 20
Q1 - Q3	0 - 20	0 - 20

Q1 = first quartile; Q3 = third quartile.

Table 4. "None or minimal loss of amount of saliva" at various time intervals for patients who had salivary gland transfer procedure

STUDY	Patients #	3 Mths	6 Mths	12 Mths	24 Mths	60 Mths	QOL Instrument
Jha – Seikaly (2000)	7	100%					University of Washington QOL
Jha – Seikaly (2003)	43	65%	71%				University of Washington QOL
Seikaly – Jha (2004)	26				83%		University of Washington QOL
Khalid Al – Khatani (2006)	8	87.5%					University of Washington QOL
Jha (2009)	120	41%	50%				University of Washington QOL
Xue – Kui Liu (2010) (Nasopharynx)	36	86.1%				87.1%	Wijers Xerostomia questionnaire
Ye Zhang (2011)	26			79%	92.3%		Wang Zhong – he Xerostomia score
Scrimger (2012)	43	83%	93%	95%	100%		RTOG Salivary Gland Toxicity
Amit Sood (2014) Meta analysis	177				85.3%		University of Washington QOL
Zhang (2014)	32	62.6%	71.9%	81.3%			University of Washington QOL
Jha (2014) NRG Oncology RTOG 0244	All analyzable 44 28 (per protocol)	51.7% 66.6%					University of Washington QOL

Appendix Table 1 UW-QOL 6 Month Change Score Distributions

	All patients (n=27)	Per protocol patients (n=23)
Total Score		
Median	16. 4	14.5
Min - Max	-1. 8 - 50.9	-1.8 - 50.9
Q1 - Q3	10. 9 - 25.5	10.9 - 25.5
Factor scores		
Mucus		
Median	20	20
Min - Max	10 - 50	10 – 50
Q1 - Q3	20 - 40	20 – 35
Eating		
Median	30	25
Min - Max	10 - 65	10 – 65
Q1 - Q3	20 - 40	20 – 40
Pain		
Median	0	0
Min - Max	-26. 7 - 40	-26. 7 – 40
Q1 - Q3	0 - 20	0 – 20
Activities		
Median	10	10
Min - Max	-10 - 40	-10 – 40
Q1 - Q3	0 - 20	0 – 30
Removed item scores		
Disfigurement		
Median	20	20
Min - Max	-20 - 40	0 - 40
Q1 - Q3	0 - 20	0 - 20
Employment		
Median	0	0
Min - Max	-60 - 80	-60 - 80
Q1 - Q3	0 - 20	0 - 0
Chewing		

Median	20	20
Min - Max	0 - 60	0 - 60
Q1 - Q3	0 - 40	0 - 40
Speech		
Median	0	0
Min - Max	0 - 20	0 - 20
Q1 - Q3	0 - 20	0 - 20

Q1 = first quartile; Q3 = third quartile.

Appendix Table 2 UW-QOL 12 Month Change Score Distributions

	All patients (n=22)	Per protocol patients (n=23)
Total Score		
Median	13. 6	13.6
Min - Max	-3.6 - 29.1	-3.6- 29.1
Q1 - Q3	7. 7 - 16.5	7. 7 - 16.4
Factor scores		
Mucus		
Median	20	20
Min - Max	-20 - 40	-20 – 40
Q1 - Q3	10 - 30	20 – 30
Eating		
Median	20	20
Min - Max	0 - 45	0 – 45
Q1 - Q3	15 - 35	10 – 35
Pain		
Median	26. 7	0
Min - Max	20 - 60	-33. 3 – 20
Q1 - Q3	20 - 33.3	-13.3 - 6.7
Activities		
Median	30	10
Min - Max	20 - 80	-10 – 30
Q1 - Q3	20 - 40	0 – 10
Removed item scores		
Disfigurement		
Median	10	20
Min - Max	-20 - 40	0 - 40
Q1 - Q3	0 - 20	0 - 20
Employment		
Median	0	0
Min - Max	-40 - 80	-40 - 80
Q1 - Q3	0 - 20	0 - 20
Chewing		
Median	0	10

Submandibular salivary gland transfer

Min - Max	-20 - 40	-20 - 40
Q1 - Q3	0 - 40	0 - 40
Speech		
Median	0	0
Min - Max	0 - 20	0 - 20
Q1 - Q3	0 - 0	0 - 0

Q1 = first quartile; Q3 = third quartile.