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Effects of radioiodine treatment on salivary gland function in patients with differentiated thyroid carcinoma: a prospective study

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Short title: ^{131}I effects on salivary function in DTC

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ABSTRACT

Introduction

Complaints of a dry mouth (xerostomia) and sialoadenitis are frequent side effects of radioiodine treatment in differentiated thyroid cancer (DTC) patients. However, detailed prospective data on alterations in salivary gland functioning after radioiodine treatment (^{131}I) are scarce. Therefore, the primary aim of this study was to prospectively assess the effect of high-activity radioiodine treatment on stimulated whole saliva flow rate. Secondary aims were to study unstimulated whole and stimulated glandular (i.e., parotid and submandibular) saliva flow rate and composition alterations, development of xerostomia, characteristics of patients at risk for salivary gland dysfunction, and whether radioiodine uptake in salivary glands on diagnostic scans correlates to flow rate alterations.

Methods

In a multicenter prospective study, whole and glandular saliva were collected both before and five months after radioiodine treatment. Furthermore, patients completed the validated xerostomia inventory (XI). Alterations in salivary flow rate, composition and XI score were analyzed. Salivary gland radioiodine uptake on diagnostic scans was correlated with saliva flow rate changes after radioiodine treatment.

Results

Sixty-seven patients (mean age 48±17 years, 63% female, 84% underwent ablation therapy) completed both study visits. Stimulated whole saliva flow rate decreased after

ablation therapy (from 0.92 [IQR 0.74-1.25] to 0.80 [0.58-1.18] ml/min, p=.003), as well as unstimulated whole- and stimulated glandular flow rates (p<.05). The concentration of salivary electrolytes was similar at both study visits, whereas the output of proteins, especially amylase (p<.05), was decreased. The subjective feeling of dry mouth increased (p=0.001). Alterations in saliva flow rate were not associated with (semi)-quantitatively assessed radioiodine uptake in salivary glands on diagnostic scans. For the small cohort of patients undergoing repeat radioiodine therapy, we could not demonstrate alterations in salivary parameters.

Conclusion

We prospectively showed that salivary gland function is affected after high-activity radioiodine ablation therapy in patients with DTC. Therefore, more emphasis should be placed on salivary gland dysfunction during follow-up for DTC patients receiving high-activity radioiodine treatment.

Keywords:

- Differentiated thyroid cancer
- Radioiodine (^{131}I) treatment
- Salivary gland damage

INTRODUCTION

Thyroid cancer is a common endocrine malignancy with 62,450 expected cases in the United States for 2015, and is currently estimated to be the fifth most common cancer in women*(1)*. Differentiated thyroid carcinoma (DTC), covering the papillary and follicular subtypes, is the most common malignancy of the thyroid. Patients with DTC have a favorable survival, which is presumably due to the relative indolent nature of the disease combined with an effective treatment consisting of a (near)-total thyroidectomy, radioiodine (^{131}I) treatment and thyroid hormone suppression therapy. Adverse effects of treatment are increasingly being recognized, amongst them radioiodine-induced salivary gland damage*(2)*.

The adverse effect of radioiodine on salivary glands is presumed to be related to the ability of salivary glands to concentrate (radio)iodine. This ability is probably facilitated by the sodium-iodide symporter, which is especially expressed in the striated ducts of the gland*(3)*. Primary saliva is produced in the acini of the salivary glands and subsequently drains into the intercalated, striated and excretory ducts. During the transport in the ductal system, the composition of saliva is actively changed, e.g., sodium and chloride are reabsorbed, and potassium is excreted into the saliva. As radioiodine is mainly concentrated in the ductal system, the beta radiation may generate luminal debris which may cause ducts to narrow*(4)*. These processes can lead to obstruction of the ductal system, causing an inflammatory response in the secretory tissue (sialoadenitis), and glandular degeneration*(5)*. Moreover, salivary gland stem cells, that have been proposed to mainly reside in the excretory ducts*(6)*, may be

affected due to the exposure to beta radiation resulting in a reduced regenerative potential*(2)*.

Sialoadenitis can cause complaints of pain and swelling, and result in an altered saliva composition. Ongoing sialoadenitis can lead to atrophy of the secretory parenchyma and salivary gland fibrosis, which may result in decreased saliva flow rates (hyposalivation), sensation of a dry mouth (xerostomia) and an increased risk of oral infections and dental caries*(7)*. A further loss of salivary gland function due to stem cell damage may become clinically manifest after 60-120 days, as this time is specific for salivary cell turnover*(8)*.

Previous studies focused on oral complaints that occur in roughly 30% of patients*(9-11)*, and assessment of salivary gland function by technetium-99m salivary scintigraphy*(12,13)*. Detailed, prospective data on salivary gland function by measurement of whole and/or glandular saliva flow rates (sialometry) including analysis of saliva composition (sialochemistry) are scarce for DTC patients*(14)*. When such data are available, these may provide us with detailed knowledge on the effects of radioiodine treatment on salivary gland function.

The primary aim of this study was to assess the effect of high-activity radioiodine treatment on stimulated whole saliva flow rate when the acute effect has passed. Secondary aims were to study unstimulated whole- and stimulated glandular saliva flow rate and composition, as well as xerostomia alterations after radioiodine treatment. Furthermore, we aimed to identify characteristics of patients at risk for salivary gland dysfunction, and study whether radioiodine uptake in salivary glands as assessed on

diagnostic scintigraphic and SPECT/CT scans correlates with post-therapy salivary gland dysfunction in radioiodine-treated DTC patients.

PATIENTS AND METHODS

Design and study population

We performed a multicenter prospective study in the three centers in the north of The Netherlands where patients with DTC are treated with radioiodine; the University Medical Center Groningen, Isala Clinics Zwolle and the Medical Center Leeuwarden. The study was approved by the institutional ethics committee (METc 2013.039), and was registered at The Netherlands National Trial Register (NTR4354). All patients provided written informed consent.

All consecutive patients of at least 18 years old with DTC who were scheduled for radioiodine ablation (i.e. treatment targeting remnant normal thyroid tissue post-thyroidectomy) or repeat high-activity radioiodine treatment, were asked to participate in this study. Exclusion criteria were a history of Sjögren's syndrome or another salivary gland disease affecting baseline salivary gland function, oral ulceration, and radioiodine treatment preparation with recombinant human thyroid-stimulating hormone (rhTSH). Preparation with rhTSH was chosen as an exclusion criterion to ensure a homogeneous patient population, and, moreover, the side effects of endogenous TSH stimulation are probably more profound. Included patients were scheduled for two study visits: the first at least one week before radioiodine treatment, and the second approximately five months after treatment. The latter was chosen because after five months the acute phase has passed, but patients are not yet scheduled for another radioiodine therapy, if

necessary. At both study visits, whole and glandular saliva were collected, and patients completed a validated xerostomia inventory (XI) containing 11 multiple-choice questions related to xerostomia*(15)*. In addition, data were collected on patient characteristics, see supplemental data.

Treatment and follow-up

Patients were treated according to the Dutch thyroid carcinoma guideline*(16)*, see supplemental data. In general, treatment included a (near)-total thyroidectomy with a central or lateral neck lymph node dissection if indicated. Four to six weeks after surgery, radioiodine ablation therapy was applied, usually with an activity of 3.7–5.5 GBq, depending on the risk stratification. All radioiodine therapies were performed under endogenous TSH stimulation, and patients were prescribed an iodine restricted diet one week prior to the radioiodine treatment. Patients were advised to drink plenty of water, and regularly use chewing gum or sour candies after administration of radioiodine therapy. No further recommendations about the time point of initiation, frequency, and duration of salivary gland stimulation were made, and no other salivary gland protection measured were applied.

Saliva collection

During the two study visits, whole and glandular saliva were collected using standardized methods (see supplemental data). Unstimulated whole saliva was collected during five minutes by regularly spitting in a container. Thereafter, paraffin-stimulated whole saliva was collected in a similar fashion during five minutes. During the

glandular saliva collection, saliva of the left and right parotid, and the submandibular/sublingual glands (later referred to as submandibular saliva) were separately collected for ten minutes. The salivary glands were stimulated by applying a cottonwool swab with 2% citric acid solution on both the lateral surfaces of the tongue every 30 seconds.

Sialochemistry

Sodium and potassium were quantified using atomic emission spectrometry (Thermo Fisher Scientific, Inc). Chloride, amylase, and total protein were measured using a Roche Modular analyzer (Roche, Mannheim, Germany), see supplemental data.

Imaging protocol

Planar whole body imaging was performed 24 hours after administration of 40 MBq radioiodine (^{131}I) before ablation planning, or 72 hours after administration of 74 MBq radioiodine (^{131}I) for planning of repeat treatment. Post-therapy whole body scans (WBS) were acquired 7 days after high-activity radioiodine (^{131}I) administration. SPECT/CT imaging of the head and neck was performed immediately after the post-therapy WBS, see supplemental data.

Iodine uptake measurement on diagnostic scans

Iodine uptake in both parotid and submandibular glands was scored semi-quantitatively on the planar pre- and post-therapy WBS. Furthermore, radioiodine uptake in the salivary glands was quantified on the post-therapy SPECT/CT scan. The

radioiodine activity concentrated in each gland was expressed in Bq and Bq/ml, see supplemental data.

Statistical analyses

Data are presented as numbers (percentages), medians with inter quartile ranges (IQR), or means with standard deviation, as appropriate. Data were analyzed separately for patients who underwent ablation and repeat radioiodine treatment. Paired salivary flow rates (i.e., when both pre-and post-treatment measurements were available of a particular gland in the same individual) were compared using the Wilcoxon signed rank test. In case gland dysfunction was observed at baseline, or when oral anatomy did not allow parotid saliva collection (of which a note was taken during measurement), the patient was excluded from the analysis with regard to the corresponding flow-rate, see supplemental data. Alterations in saliva composition and XI scores were tested using the Wilcoxon signed rank-test for paired data.

We analyzed differences between patients (age, sex, TNM stage, tumor histology, and cumulative radioiodine activity) who did, or did not have a decrease of at least 50% in stimulated whole saliva flow rate using the chi-squared test, t-test and non-parametric tests, as appropriate, see supplemental data.

Correlations between XI scores and the primary outcome parameter, and between radioiodine uptake in parotid and submandibular glands and sialometry measures were tested using Spearman's rho.

All tests were two-sided, and a p-value <0.05 was considered statistically significant. A Bonferroni corrected alpha for multiple testing was used for analysis of

individual XI questions. IBM SPSS for Windows (version 22.0) was used for all analyses.

RESULTS

Patients

Ninety-five patients were approached for study participation, of whom 75 patients consented and were included in the study (Fig. 1). Eight patients were excluded, due to cancellation of treatment (n=7) or a change in radioiodine therapy preparation, from endogenous TSH stimulation to rhTSH (n=1). The remaining 67 patients (of whom 56 underwent ablation, and 11 repeat radioiodine therapy) completed both study visits. Mean age of these patients was 47.7±17.1 years. Forty-two (63%) patients were female (Table 1). An overview of the numbers of paired saliva measurements available for analysis is provided in Supplemental Fig. 1.

The majority of patients (88%) was treated with an activity of 5.55 GBq; cumulative radioiodine activities are shown in Supplemental Fig. 2. The second study visit took place 5.3±0.6 months after radioiodine treatment.

Sialometry

In patients undergoing ablation therapy (n=56), stimulated whole saliva flow rate decreased from 0.92 [0.74–1.25] to 0.80 [0.58–1.18] ml/min (p=.003). Unstimulated whole-, and stimulated left and right parotid and submandibular flow rates decreased significantly as well (Table 2). In patients undergoing repeat radioiodine treatment (n=11), stimulated whole saliva was 0.96 [0.45–1.31] before, and 0.53 [0.39–1.54]

ml/min after treatment (p=.328). Unstimulated whole- and stimulated glandular flow rates did not significantly change either. Please refer to Supplemental Table 1 for an overview of sialometry reference ranges.

There was a wide dispersion in baseline saliva flow-rates, and flow rate alterations post-treatment (Fig. 2 and Supplemental Fig. 3). Of the total study population, 23 patients (34%) experienced a decrease of at least 25% in stimulated whole saliva flow rate, of which seven had a decrease of more than 50% (Fig. 2), A higher cumulative radioiodine activity, but not age, gender, tumor histology and TNM stage, was associated with a reduction in stimulated whole saliva flow rate of at least 50% (p=.026).

Sialochemistry

Overall, clinically relevant differences were not observed in the pre- and post-radioiodine treatment salivary concentrations of sodium, potassium and chloride, while the output of total protein and amylase was reduced after ablation therapy (Table 3).

Xerostomia inventory

The score for ‘My mouth feels dry’ significantly increased after ablation (p=.001), albeit there was no significant increase in the total XI score (p=0.064) (Supplemental Table 2). Two patients (4%) had xerostomia always or frequently before ablation treatment, as compared to 11 patients (20%) after therapy (Table 4). The pre- and post-therapy XI scores of patients receiving repeat therapy were similar. The post-therapy XI

score was related to post-therapy stimulated whole saliva flow rate (Supplemental Fig. 4).

Salivary gland radioiodine uptake on diagnostic scans

In Fig. 3 a case is presented with clear accumulation of radioiodine in the salivary glands on the SPECT/CT scan, which was performed 7 days after ablation therapy. Semi-quantitatively assessed radioiodine uptake in the parotid and submandibular glands on the pre- and post-therapy WBS did not correlate with saliva flow rate alterations after radioiodine treatment (Supplemental Table 1). Quantitatively assessed uptake of radioiodine in the salivary glands (expressed in Bq and Bq/ml), did not correlate with alterations in saliva flow rates either (Supplemental Table 2).

DISCUSSION

In the current prospective study we found a decreased salivary gland function in DTC patients five months after high-activity radioiodine ablation therapy with endogenous TSH stimulation, as compared to pre-ablation. Salivary flow rates decreased, the lowered output of amylase indicated acinar dysfunction, and patients had an increased subjective feeling of a dry mouth after ablation therapy. Overall xerostomia related morbidity was limited though, and salivary gland dysfunction was not a universal problem as there was a wide dispersion in flow rate alterations after radioiodine treatment. We did not find evidence for sialoadenitis five months post-treatment, as the concentration of salivary electrolytes was not altered. Uptake of radioiodine in the salivary glands on diagnostic scans did not correlate to flow rate

alterations post-treatment, and in the small group of patients who underwent repeat treatments no alterations in salivary parameters were found.

Previous studies on sialometry analyses in DTC patients are scarce. In one prospective study, parotid saliva composition alterations that correspond to an acute sialoadenitis were found one week after radioiodine treatment*(14)*, whereas two cross-sectional studies on long-term effects of radioiodine treatment on whole saliva flow rates in DTC patients showed contradictory results*(17,18)*. Studies using salivary gland scintigraphy, which assesses both the uptake and the excretion ability of the gland, are more abundant*(12,13,19)*. In most studies an affected gland function was found after radioiodine therapy*(12,19)*, although in a recent paper this was found only after activities higher than 5.55 GBq*(13)*.

It is hard to precisely indicate the percentage of DTC patients who suffer from salivary gland damage after radioiodine treatment, as a uniform definition of this condition is lacking. A decrease of more than 50% in saliva flow rate is generally regarded as the critical value for initiation of oral complaints*(20)*. Ten percent of patients had such a decrease in stimulated whole saliva flow rate after radioiodine treatment. Approximately one third of patients had a decrease of at least 25%, which could already be relevant to this population since baseline saliva flow rates were rather low*(20)*. The latter can possibly be explained by the gradually increasing hypothyroid state following endogenous TSH stimulation, which has been associated with reduced saliva secretion*(21)*. Although study visits took place at least one week prior to radioiodine therapy to limit the effect of hypothyroidism, it may still have affected baseline saliva flow rates. Other factors like medication use*(22)*, or increased emotional stress after

DTC diagnosis,*(23)* may also have contributed to rather low baseline saliva secretion rates. Despite this, we were still able to find a decrease in flow rates at the second study visit when patients were in a euthyroid or (subclinical) hyperthyroid state due to thyroid hormone substitution, which emphasizes the adverse effects of radioiodine on saliva secretion.

The subjective feeling of a dry mouth increased after ablation therapy, although xerostomia-related morbidity was still limited. This may be explained by the finding that only seven patients experienced a decrease in stimulated whole saliva flow rate of more than 50% that generally results in xerostomia*(20)*. However, a decrease in stimulated saliva flow rate between 25-50% was common. This may progress and cause more pronounced oral complaints in case of further radioiodine treatment for high-risk patients. On the other hand, reversibility of salivary gland dysfunction is not precluded as a regenerative capacity for the parotid glands has been suggested based on data from patients treated with external radiotherapy for head and neck cancer*(6)*.

We did not find convincing associations between radioiodine uptake in salivary glands on diagnostic planar and SPECT/CT scans and alterations in flow-rate of the particular glands, despite detailed evaluations of radioiodine uptake in salivary glands on several scans. Possibly, an explanation for this may be the non-dynamic nature of the scans*(24)*, or a patient-specific regeneration capacity of the salivary glands. Altogether, these date indicate that it is hard to predict salivary gland dysfunction post-radioiodine treatment using scans that are routinely performed. #

A limitation of this study is that patients were assessed during different degrees of hypo- to hyperthyroidism at the two study visits, which may have influenced salivary

gland function. Furthermore, we intended to evaluate the effects of repeat radioiodine therapy on salivary gland function as well, but within the inclusion period an insufficient number of patients underwent repeat therapy with endogenous TSH stimulation to gain sufficient statistical power. Unfortunately, extension of the inclusion period with several more years was not feasible. Additionally, we did not routinely record in all patients whether they had experienced clinical signs of acute and chronic sialoadenitis, and our secondary outcomes are less robust than our primary outcome, due to exclusion of several patients for especially glandular saliva flow rate analyses (which may have led to a selection of patients with normal baseline flow rates), and incomplete nuclear scan data.

In conclusion, salivary gland function is affected after radioiodine ablation therapy. Although overall morbidity was limited, and salivary gland dysfunction after a single high-activity of radioiodine treatment does not seem to be a universal problem, approximately 10% of patients experience a steep decline in stimulated whole saliva flow rate. Therefore, more emphasis should be placed on salivary gland dysfunction during DTC follow-up, and early referral to a dentist or oral medicine specialist should be considered when patients suffer from xerostomia-related complaints. This is especially important for patients at high risk for residual, recurrent or metastatic DTC who are expected to receive high-activity radioiodine therapy repeatedly with endogenous TSH stimulation, and those with a pre-existent decreased salivary function, to maintain quality of life after radioiodine treatment.

DISCLOSURES

The authors have nothing to disclose

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Figure legends

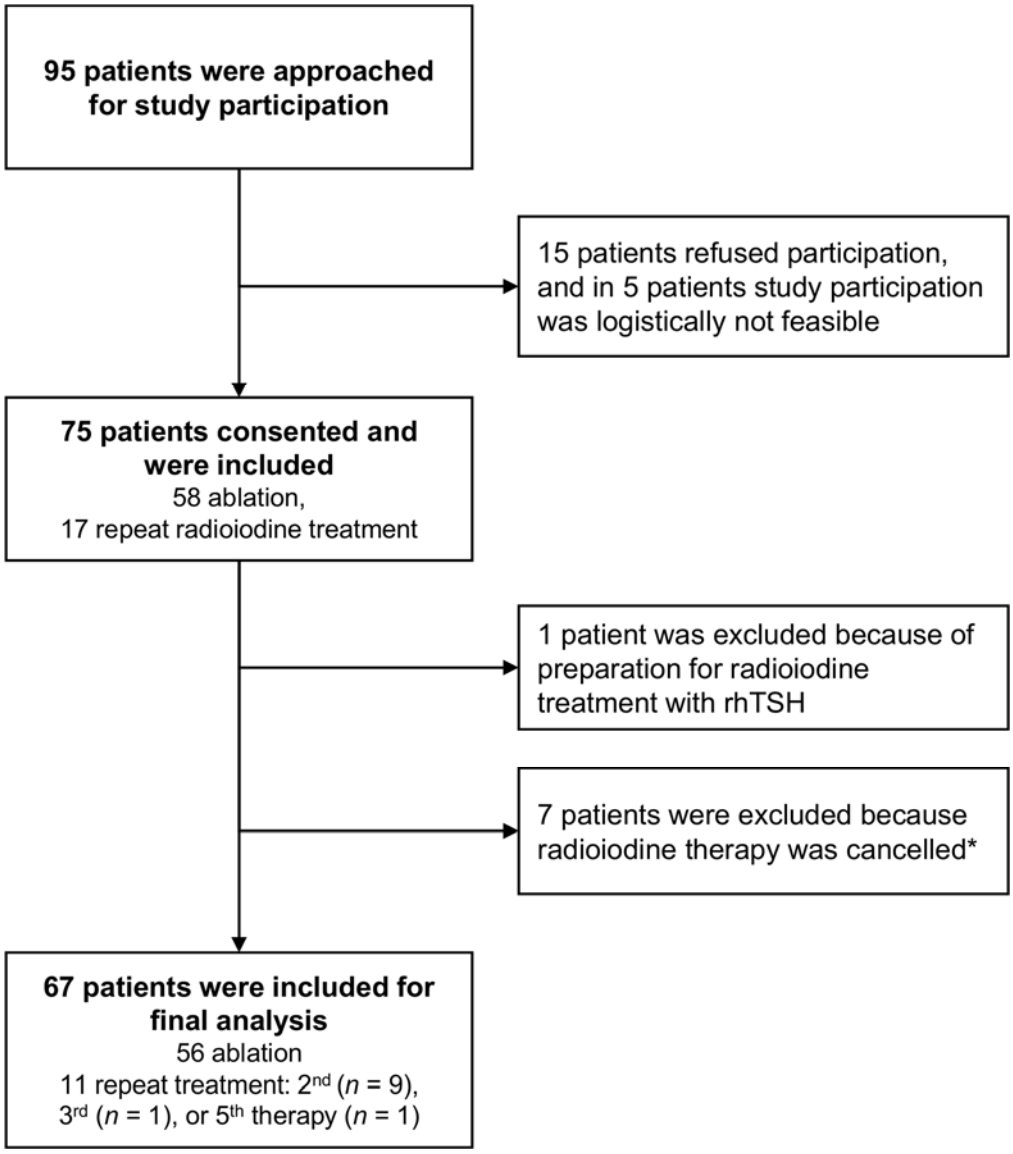

Figure 1. Flowchart

* In one patient radioiodine ablation treatment was cancelled when a malignancy other than DTC was found after revision of the pathology report. In the remaining six patients repeat radioiodine therapy was cancelled following a negative diagnostic WBS and thyroglobulin value <1.0 ng/ml in the absence of thyroglobulin antibodies.

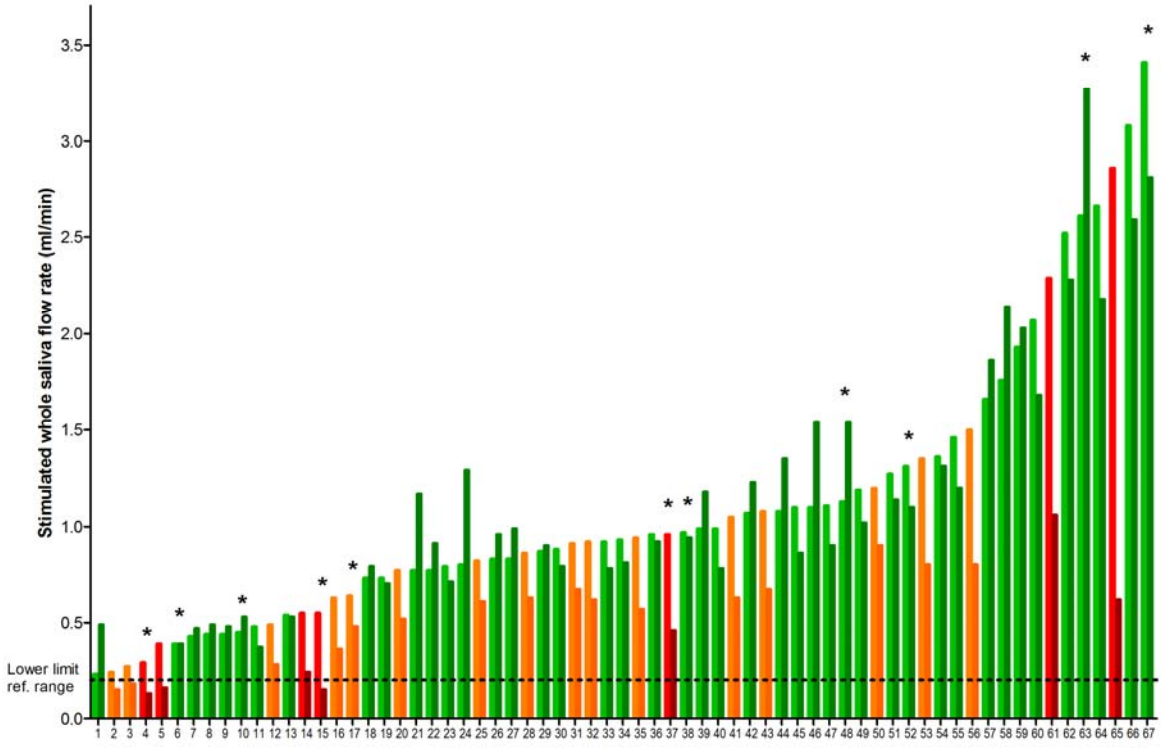

Figure 2. Displayed are changes in stimulated whole saliva flow rate for each of the 67 study subjects, ordered by basal flow rate. The lighter and paired darker bars represent flow rates before and after radioiodine treatment, respectively. The flow rate changes are color coded – green bars for subjects with less than 25% decrease, orange for 25-50% decrease, and red for > 50% decrease in stimulated whole saliva flow rate.

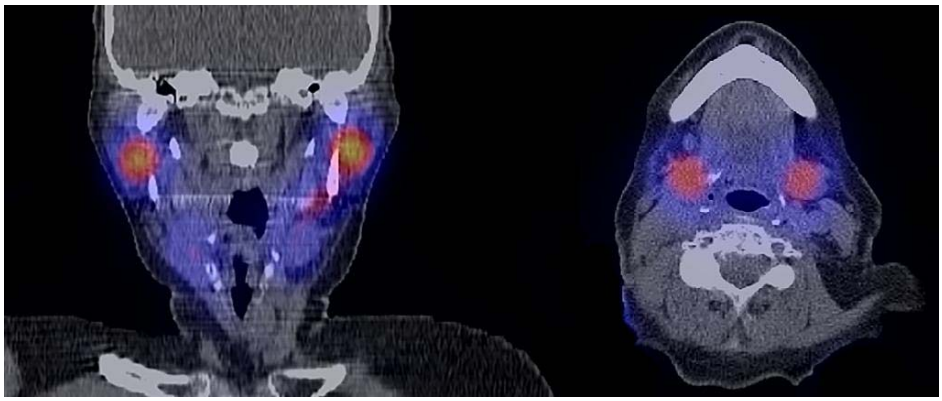

Figure 3. Uptake of radioiodine in the parotid (left panel) and submandibular (right panel) glands on the SPECT-CT scan, performed 7 days after radioiodine therapy.

Table 1. Baseline characteristics of DTC patients with paired measurements included for final analyses, and all patients initially included.

		Patients with paired measurements (n=67)	**All included patients** (n=75)
Age (years)	*mean±SD*	47.7±17.1	48.6±17.2
Female sex	*n (%)*	42 (62.7)	46 (61.3)
Histology	*n (%)*		
Papillary		54 (80.6)	58 (77.3)
Follicular		7 (10.4)	10 (13.3)
Hürthle		6 (9.0)	7 (9.3)
TNM Tumor stage	*n (%)*		
T stage			
Tx-T2		41 (61.2)	45 (60.0)
T3		21 (31.3)	25 (33.3)
T4		5 (7.5)	5 (6.7)
N stage			
Nx-N0		30 (44.8)	38 (50.7)
N1		37 (55.2)	37 (49.3)
M stage			
Mx-M0		64 (95.5)	72 (96.0)
M1		3 (4.5)	3 (4.0)
Medications used at first study visit	*n (%)*		
Oral beta blockers		7 (10.4)	7 (9.3)
Diuretics		8 (11.9)	9 (12.0)
Neuropsychiatric drugs		8 (11.9)	10 (13.3)
Any ≥ 4 medications		23 (34.3)	26 (34.7)
Co-morbidity	*n (%)*		
Diabetes mellitus*		4 (6.0)	5 (6.7)
Hypertension*		16 (23.9)	18 (24.0)
Systemic diseases **		2 (3.0)	2 (2.7)

DTC = Differentiated Thyroid Carcinoma, SD = Standard Deviation

* defined as documented treatment for these conditions, ** both patients had fibromyalgia

Table 2. Salivary flow rates before and after radioiodine therapy.

Saliva flow rates of DTC patients (n=67)		**Before treatment**	**After treatment**	p-value
Ablation patients (n=56)				
Unstimulated whole saliva (n=50)	*ml/min*	0.44 [0.27–0.66]	0.33 [0.22–0.51]	.009
Paraffin-stimulated whole saliva (n=56)	*ml/min*	0.92 [0.74–1.25]	0.80 [0.58–1.18]	.003
Acid-stimulated left parotid saliva (n=33)	*ml/min*	0.10 [0.07–0.18]	0.09 [0.05–0.13]	.027
Acid-stimulated right parotid saliva (n=29)	*ml/min*	0.10 [0.07–0.16]	0.06 [0.02–0.11]	<.001
Acid-stimulated SM saliva (n=44)	*ml/min*	0.33 [0.22–0.48]	0.31 [0.19–0.45]	.044
Repeat therapy patients (n=11)				
Unstimulated whole saliva (n=10)	*ml/min*	0.32 [0.18–0.48]	0.26 [0.09–0.47]	.169
Paraffin-stimulated whole saliva (n=11)	*ml/min*	0.96 [0.45–1.31]	0.53 [0.39–1.54]	.328
Acid-stimulated left parotid saliva (n=6)	*ml/min*	0.26 [0.16–0.35]	0.14 [0.06–0.26]	.249
Acid-stimulated right parotid saliva (n=4)	*ml/min*	0.19 [0.09-0.23]	0.20 [0.03-0.29]	.715
Acid-stimulated SM saliva (n=10)	*ml/min*	0.47 [0.33–0.66]	0.25 [0.16–0.71]	.059

Numbers (n) of patients with valid paired measurements (i.e. both a pre- and post-treatment measure were available of the same patient and salivary gland) are indicated for the particular flow-rate.
SM = submandibular

Table 3. Salivary composition of patients treated with ablation and repeat radioiodine therapy.

Patients with DTC (n=67)	**Before radioiodine therapy**	**After radioiodine therapy**	p-value
Ablation patients (n=56)			
Total protein ***mg/min***			
Unstimulated whole saliva (n=44)	.18 [.11–.32]	.15 [.09–.21]	.031
Chewing-stimulated whole saliva (n=56)	.40 [.27–.61]	.32 [.20–.46]	.001
Acid-stimulated parotid saliva (n=41)	.05 [.02–.08]	.03 [.02–.06]	.101
Acid-stimulated SM (n=49)	.05 [.02–.08]	.04 [.02–.07]	.126
Amylase ***U/min***			
Unstimulated whole saliva (n=44)	55.4 [27.9–111]	37.7 [19.1–78.6]	.017
Chewing-stimulated whole saliva (n=56)	161 [101–259]	116 [48.4–192]	.006
Acid-stimulated parotid saliva (n=37)	25.5 [11.0–46.7]	16.2 [7.4–30.0]	.023
Acid-stimulated SM (n=48)	11.7 [5.4–26.2]	10.5 [4.3–20.2]	.028
Repeat treatment patients (n=11)			
Total protein ***mg/min***			
Unstimulated whole saliva (n=9)	.13 [.06–.38]	.09 [.06–.27]	.859
Chewing-stimulated saliva (n=11)	.33 [.19–.49]	.26 [.16–.60]	.424
Acid-stimulated parotid saliva (n=7)	.05 [.02–.11]	.03 [.01–.09]	.600
Acid-stimulated SM (n=11)	.06 [.04–.13]	.03 [.02–.10]	.021
Amylase ***U/min***			
Unstimulated whole saliva (n=9)	37.3 [16.0–136]	20.8 [10.2–110]	.028
Chewing-stimulated whole saliva (n=11)	131 [90.6–187]	139 [6.4–266]	.328
Acid-stimulated parotid saliva (n=7)	28.9 [9.3–57.9]	20.7 [6.9–63.1]	.463
Acid-stimulated SM (n=11)	11.6 [7.0 –48.2]	5.3 [3.6–51.6]	.248

Numbers (n) of patients with valid paired measurements are indicated, dependent upon saliva quantity.
SM = submandibular gland saliva

Table 4. Numbers of patients treated with radioiodine ablation and repeat treatment who indicated several extents of xerostomia before and after treatment

Response to the question: **My mouth feels dry**	**Radioiodine ablation treatment (n=56)**		**Repeat radioiodine treatment (n=11)**	
	Before therapy n (%)	*After therapy n (%)*	*Before therapy n (%)*	*After therapy n (%)*
Never	19 (34)	9 (16)	3 (27)	3 (27)
Hardly ever	18 (32)	20 (36)	0	2 (18)
Occasionally	17 (30)	16 (29)	5 (46)	3 (27)
Frequently	2 (4)	7 (13)	2 (18)	3 (27)
Always	0	4 (7)	1 (9)	0