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ORIGINAL ARTICLE

Impact of parotid gland dose and patient-related factors on radiation damage to dental hard tissues

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Abstract *Background/purpose:* To evaluate whether radiation damage to dental hard tissues depends on patient-related factors in addition to irradiation dose on the spared parotid gland.
Materials and methods: Seventy curatively irradiated patients with head and neck cancer underwent dental treatment prior to, during, and after radiotherapy. During a follow-up period of 24 months, damages to dental hard tissues were classified. Mean doses (D_{mean}) during spared parotid gland radiotherapy, patients' oral hygiene practice, and socioeconomic status were determined.
Results: No carious lesions were observed in 30 patients (Group A), while sporadic and general carious lesions were noticed in 18 patients (Group B) and 22 patients (Group C), respectively. The D_{mean} of Group A (21.2 $\pm$ 11.00 Gy) was significantly lower than that of Group C (33.9 $\pm$ 9.9 Gy; $P < 0.001$). Patients with an intermediate level of schooling qualification showed a higher risk for radiation caries than patients with higher education entrance qualification ($P = 0.018$).

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Conclusion: Radiation damage to dental hard tissues correlates with increased mean irradiation doses and a lower educational level.

Introduction

A common chronic side effect of head and neck cancer radiotherapy (RT) is radiation damage to the dental hard tissues (so called radiation caries). Because of its rapid onset and progression, a previously healthy dentition can be completely lost within a year. Therefore, its prevention is an important aspect in dental treatment related to RT.[1,2]

In a previous study, we demonstrated that parotid gland sparing in RT for head and neck cancer preserves the salivary flow rate (SFR), thereby reducing the extent of radiation damage to dental hard tissue after RT.[3] Our results showed that, particularly 6 months after RT, patients without alterations in dental hard tissues showed a comparatively higher SFR than patients with general carious lesions. Deeper analysis, however, revealed that patients in this group who were given a high irradiation dose on the parotid glands had a completely dry mouth. Conversely, in the group of patients with general carious lesions, a few who had received a low irradiation dose on the parotid glands showed normal SFR. Both situations might appear exceptional in the two groups. However, they indicate that radiation caries are multifactorial in origin and do not necessarily appear in the absence of saliva.

In general, the most important aspect for caries prevention is an adequate oral hygiene practice (OHP). There is unanimous evidence in the literature that a good OHP in combination with daily application of fluoride gel considerably reduces the risk of damage to the dental hard tissues.[4–6] *In-vivo* studies have demonstrated the positive effect of an intensive OHP on irradiated teeth and the ineffectiveness of weekly fluoride application without good oral hygiene.[5,7] Therefore, many investigators provide intensive oral hygiene instructions before RT and a frequent follow-up program in the course of RT.[1,8,9]

However, according to Jham et al,[9] up to 81% of patients do not correctly follow the recommendations of the dentist. They showed retrospectively that patients with a lower socioeconomic status (SES) frequently have poor oral hygiene and lower compliance to oral hygiene instructions than those with a higher SES.[9] SES comprises different aspects characterizing the living conditions of the patients and is usually based on their profession, income, and educational level.[10–12] Recent investigations have confirmed the correlation between a low SES and an increased oral cancer risk, finding longer survival associated with a higher SES.[11,13,14] The combination of poor oral hygiene and low SES has resulted in the frequent practice of extracting teeth liberally prior to RT in order to avoid later complications.[13,15] However, the cohort of patients with head and neck cancer is very inhomogeneous and variable with respect to their SES. Moreover, not every dentulous patient with a low SES and poor oral hygiene develops radiation caries after RT.[13] Therefore, the widely followed recommendation of extensive tooth extraction in head and neck cancer patients undergoing RT, especially in those with a low SES and poor oral hygiene, has to be scrutinized critically.

Compounding the problem of adequate caries prevention is the fact that susceptibility to general caries seems to increase with age and male sex.[16–18]

Hence, recent restoration programs and recommendations do not consider the above-mentioned factors and instead completely focus on dental aspects.

The objective of this study was to evaluate a possible association between patients' age, sex, profession, educational level, OHP, and the development of radiation caries while accounting for the irradiation dose in the spared parotid gland.

Patients and methods

Patient selection

This study included 70 patients with head and neck cancer who were treated between June 2003 and September 2008 at Martin-Luther-University Halle-Wittenberg, Halle, Germany. They were part of a prospective nonrandomized clinical study evaluating the recovery potential of the parotid glands after RT.[19,20] The Institutional Review Board at our institution approved this study and informed consent was obtained from each patient.

Only dentulous patients were chosen and subjected to strict dental care management and alterations in the dental hard tissue were documented.[3]

Radiotherapy

Patients received three-dimensional conformal radiation therapy (3D-CRT, 2003—2006) or intensity modulated radiation therapy (IMRT, 2006—2008). No randomization was done. The planning target volumes and the organs at risk, such as the spinal cord, both parotid glands, and the mandible, were outlined on the transversal slices of the planning computed tomography scans. The goal was to minimize the mean dose in the contralateral parotid while maintaining a homogeneous dose distribution in the target volumes. No effort was made to spare the submandibular or minor salivary glands.

The 3D-CRT was performed by standardized six- or seven-portal arrangements as described in a previous study.[21] Patients receiving 3D-CRT were treated with 6 MV and 10 MV photons of a linear accelerator (Primus [Siemens

Medical Solutions, Erlangen], Germany). Intensity modulated radiation therapy was based on the step-and-shoot approach with seven or nine equidistant 6 MV beams (Oncor, Siemens Medical Solutions). The treatment technique was similar to that described by Georg et al.[22] The planning strategy was to cover 95% of the planning target volumes with 95% of the prescribed dose. The volume concepts were based on the International Commission on Radiation Units and Measurements report No. 50.[23]

Oral treatment

Prior to RT, all patients underwent dental restoration according to the guidelines and recommendations of the German Dental Association.[24,25] Teeth with poor prognosis due to periodontal factors, carious lesions, endodontic aspects and large fillings, fractures, or significant occlusal wear were removed prior to RT. Furthermore, teeth that were thought to be severely affected due to compromised mouth hygiene were also extracted. To achieve a patient-perceived acceptable function, the dental arch was shortened[26]; the canines were preserved for later prosthodontic treatment. All patients received oral hygiene instructions and professional tooth cleaning before RT. Moreover, the patients received custom-made fluoride carriers and were instructed to use the carriers without fluoride gel during the course of radiation and to apply the gel on their carriers for 10 minutes, at least once a day after brushing teeth.

During the treatment course of RT, the oral cavity was inspected weekly by a radiation oncologist and oral hygiene instructions were reinforced.

After RT, all patients were advised to participate in a special quarterly dental follow-up treatment, during which they were offered free professional tooth cleaning. If necessary, teeth were treated.[1,3,25]

Classification of radiation damage to dental hard tissue

Radiation damages to dental hard tissues after RT were classified according to the guidelines of the Radiation Therapy Oncology Group and European Organization for Research and Treatment of Cancer.[24] To simplify, classification Grades 1 and 2 along with classification Grades 3 and 4 were pooled and patients were divided into three groups: Group A, no effects on dental hard tissue; Group B, sporadic carious lesions; and Group C, general carious lesions.

Determination of the parotid gland doses

The mean dose and partial volumes receiving specified doses were determined for each parotid gland from a dose-volume histogram. The histograms were transformed based on an algorithm initially proposed by Lyman and Wolburst.[27]

Determination of OHP and SES

A standardized interview was created to determine OHP and SES. Overall, the interview contained six items: four items concerning OHP and two items concerning SES. The interview was constructed and proven by the Psychology Department of the Martin-Luther-University Halle-Wittenberg.

Regarding OHP, the frequency and duration of tooth cleaning prior to RT were inquired. Patients received points between 0 and 4 for their answers. Large values represented a high duration or frequency of OHP. For statistical analysis, values of *duration* and *frequency* were added, thereby generating a sum between 0 and 8. Values of 0–3, 4–5, and 6–8 represented poor, good, and very good OHP, respectively.

The SES was determined based on the Hollingshead two-factor index referring to the patients' educational level and profession.[28] The items for the determination of the SES were based on the study by Leplow and Friege.[28]

The interviews took place during the follow-up examinations in a quiet room. The patients answered the questions without any time limit imposed and had, in case of questions, instant access to a study supervisor.

Statistical analysis

Statistical analysis was done using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA) for Windows. Chi-square tests were performed in order to evaluate a possible association between OHP and SES (divided into educational level and profession) and the three groups of radiation caries. Additionally, an ordinal logistic regression was done. The regression model included the covariates *age*, *sex*, *mean irradiation dose in the spared parotid gland*, *OHP*, and *educational level and profession*. Odds ratios (ORs) were analyzed in order to determine the degree of influence of the different factors on the development of radiation caries.

Results

Patient characteristics

Data from 70 patients were analyzed. The observation period ranged from 24 months to 54 months with a mean of 34 months. The dental status recorded at 24 months was used for statistical analysis. The patients and tumor characteristics are shown in Table 1.

Eight patients refused to participate in the questionnaire; therefore, data from only 62 patients could be used for the evaluation of OHP and SES.

Mean irradiation dose in the spared parotid gland

The spared parotid gland of patients in Groups A–C was exposed to a mean irradiation dose (D_{mean}) of 21.2 ± 11.0 Gy, 26.5 ± 11.6 Gy, and 33.9 ± 9.9 Gy, respectively. The D_{mean} of Group A was significantly lower than the D_{mean} of Group C ($P < 0.001$, analysis of variance).[3]

OHP

No patient achieved a value > 5 (Table 2). Patients who did not clean their teeth prior to RT (sum 0) were, in four of

Table 1 Patient and tumor characteristics.

Study population	Group A	Group B	Group C
Patient number	30/70 (43%)	18/70 (26%)	22/70 (31%)
Sex (male/female)	21/9	12/6	18/4
Age (y), median (range)	57 (26–77)	59 (36–71)	58 (46–73)
Tumor sites			
Oral cavity	10	6	8
Oropharynx/nasopharynx	10	8	9
Larynx/hypopharynx	6	4	5
Unknown primary (CUP)	1		
Other (myeloma, lymphom, nasal cavity, paranasal sinus)	3		
Radiation technique			
3D-CRT/IMRT	15/15	13/5	20/2

3D-CRT = three-dimensional conformal radiation therapy; CUP = cancer of unknown primary; IMRT = intensity modulated radiation therapy.

Table 2 Oral hygiene practice (OHP) within the three caries groups.

Sum of items *duration* & *frequency*	Group A	Group B	Group C	Total
Modest OHP (sum 4, 5)	9 (35)	7 (27)	10 (38)	26
Poor OHP (sum 0–3)	18 (50)	6 (17)	12 (33)	36

Data are presented as *n* (%).

five cases, in Group C (80%). The distribution of OHP was different in Groups A–C (P = 0.257; Table 2).

SES

About one third of all patients (18/62, 29%) had a school-leaving qualification of lower than 10 years of education (intermediate level of schooling qualification or lower). The proportion of patients with higher education entrance qualification was the highest in Group A and decreased from Group A to Group C (P = 0.076; Table 3).

Twenty patients of Group C (20/22, 91%) had an employee status. Most of the patients who were highly qualified employees and those in positions of higher management were in Group A. The frequency of individuals holding these positions decreased from Group A (45%) to Group C (9%; P = 0.051; Table 4).

Ordinal logistic regression

All factors considered, ordinal logistic regression revealed no clinically relevant influence of the factors investigated (Table 5). Only the P value of the parameter *dose volume on the spared parotid gland* tended to show a clinical relevance (P = 0.052).

To emphasize the factors influencing the model the most, ordinal regression was reduced progressively by the factors of *age*, *profession*, *OHP*, and *sex*. Table 6 shows the final ordinal logistic regression including the factors *dose volume on the spared parotid gland* and *educational level*.

In this analysis, an OR of 1.075 for *dose volume on the spared parotid gland* means that for one unit increase in this variable, we expect an increase of the odds of being in a higher level (B instead of A or C instead of B) by a factor 1.075. Thus, an increasing mean irradiation dose on the spared parotid gland augmented the risk for radiation caries by 7.5% with each additionally applied Gray on the spared parotid gland. Moreover, patients with an intermediate level of schooling qualification (School 2) showed a higher risk for radiation caries than patients with a higher education entrance qualification (School 3; OR 4.958, P = 0.018). However, although a similar correlation was found between patients having a low school leaving qualification (School 1) and patients with a higher education entrance qualification (School 3), it was not significant (OR 2.770, P = 0.172).

Discussion

This study investigated the influence of different patient-specific factors on the development of radiation caries. Besides the irradiation dose on the spared parotid gland, radiation caries were influenced by educational level.

Table 3 Distribution of educational level across the three caries groups.

Group	No certificate/secondary modern school-leaving certificate (School 1)	Intermediate level of schooling qualification (School 2)	Higher education entrance qualification (School 3)	Total
A	6 (22)	9 (33)	12 (45)	27
B	5 (38)	5 (38)	3 (24)	13
C	7 (32)	13 (59)	2 (9)	22
Total	18	27	17	62

Data are presented as *n* (%).

Table 4 Distribution of profession across the three caries groups.

Group	Laborer, employee or similar (Profession 1)	Highly skilled workers, officials, or similar (Profession 2)	Management function, self-employed workers, managing director, or similar (Profession 3)	Total
A	15 (55)	8 (30)	4 (15)	27
B	9 (69)	4 (31)	0	13
C	20 (91)	1 (4.5)	1 (4.5)	22
Total	44	13	5	62

Data are presented as *n* (%).

Table 5 Initial ordinal logistic regression: odds ratio, significance, and 95% confidence interval of all factors determined.

	Odds ratio	95% confidence interval	P
Age	1.013	0.941–1.088	0.730
Sex	0.643	0.126–1.209	0.596
Dose volume on the spared parotid gland	1.058	1.001–0.119	0.052
School 2 vs. School 3	0.404	0.028–5.743	0.503
School 1 vs. School 3	2.474	0.021–2.399	0.217
Profession 2 vs. Profession 3	0.470	0.018–12.604	0.653
Profession 1 vs. Profession 3	0.824	0.055–12.293	0.888
OHP = 0	1.680	0.072–39.173	0.747
OHP = 1[a]			
OHP = 2	0.406	0.035–4.693	0.470
OHP = 3	0.640	0.059–6.869	0.712
OHP = 4	1.231	0.122–12.429	0.860
OHP = 5[a]			

OHP = oral hygiene practice.
[a] no patient provided OHP = 1, only one patient provided OHP = 5.

Table 6 Final ordinal logistic regression: odds ratio, significance, and 95% confidence interval of the factors *dose volume on the spared parotid gland* and *educational level*.

	Odds ratio	95% confidence interval	P
Dose volume on the spared parotid gland	1.075	1.02–1.12	0.004
School 2 vs. School 3	4.958	1.31–18.77	0.018
School 1 vs. School 3	2.770	0.64–11.94	0.172

Patients' age, sex, OHP, and profession showed no effect on the development of radiation caries.

To the best of our knowledge, the present study is the first to verify the influence of SES on the development of radiation caries. Therefore, independent results are not available to qualify the results of our study.

In general, irrespective of the measures used to determine SES (income, profession, or educational level), there is abundant evidence on the association between lower SES and worse health outcome.[29] In particular, socioeconomic factors have been emphasized to be highly relevant in oral cancer risk.[11] Hence, the debate about a causal relation between low SES and worse health outcome is still controversial.

Besides poor access to medical care or deleterious behavior in patients of lower SES, Goldman and Smith[29] referred to their reduced ability to "comply with and maintain complex health regimes that are often prescribed to deal effectively with severe health problems." Oral treatment regimens require, especially after irradiation, persistent patient self-management on a daily basis. Mandatory compliance requires the patients' understanding of the medical necessity and the ability to select an appropriate regimen. Moreover, the willingness to understand the future costs of incomplete compliance is required. Because education serves as a basis for many of these personal traits, it is thought to play a key role in health outcomes for patients with chronic illnesses.[29] Confirming this assumption, Mejia et al[12] found oral health inequalities more apparent in measures of disease management than in measures of disease experience. Regarding the often painless progress of radiation caries, even patients with a high awareness of their disease symptoms and frequent dental check-ups often do not recognize the first symptoms and onset of radiation caries.

In our study, we found that lower educational level was associated with a higher risk for radiation caries. This result confirms the association already found by Vano et al[18] between the incidence of general caries and periodontal inflammation and patients' educational level. Therefore,

although patients with intermediate level of schooling qualification showed a higher risk for radiation caries than patients with higher education entrance qualification, the former did not tend to develop more radiation caries than the latter. This lack of association between the patients' profession and the development of radiation caries could be attributed to the small sample size of 66 patients.

Against our expectations, and despite the consensus on adequate OHP and the incidence of caries,[18] no correlation was found between OHP and radiation caries in this study. However, besides the reduced number of patients, another limitation of the present study is that results related to oral health attitude and behaviors relied on self-reported data. Thus the answers given might be biased due to social desirability, which might, given the low number of patients, lead to a distorted result.[12,18] However, self-reported health care utilization in large cohorts have been shown to be valid proxies for medical and dental claims as well as administrative data.[30,31]

The two last aspects analyzed in this study were the influence of patients' age and sex on the development of radiation caries. Although older patients (especially) with additional physical limitations or chronic diseases often undergo dental neglect due to difficulties or incapability in maintaining a daily oral hygiene regimen without assistance,[17] no correlation was found between age and radiation caries. This might be due to the wide age range from 26 years to 77 years across 70 patients. Regarding sex, previous studies found a significant relationship between female sex and improved OHP.[18,32] This could be attributed to the fact that women are usually more concerned about their bodies and less tolerant regarding their appearance and health, resulting in quick seeking of medical advice. We could not confirm this aspect, which might be, besides the already mentioned reduced patient numbers, due to the unequal proportion of men ($n = 51$) and women ($n = 19$). To evaluate these aspects properly, further studies comprising more patients are necessary.

In conclusion, this study evaluated the influence of different patient-specific factors on the development of radiation caries. Besides the irradiation dose on the spared parotid gland, radiation caries also seems to correlate with patients' educational level. Further large multicenter studies are required to investigate whether this aspect might be used reliably as a surrogate for a higher radiation caries risk.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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