

STUDER GABRIELA<sup>1</sup>  
GLANZMANN CHRISTOPH<sup>1</sup>  
STUDER STEPHAN P<sup>2</sup>  
GRÄTZ KLAUS W<sup>2</sup>  
BREDELL MARIUS<sup>2</sup>  
LOCHER MICHAEL<sup>3</sup>  
LÜTOLF URS M<sup>1</sup>  
ZWAHLEN ROGER A<sup>2</sup>

# Risk-adapted dental care prior to intensity-modulated radiotherapy (IMRT)

## Results

Key words: dental care before radiotherapy, osteoradionecrosis

<sup>1</sup> Clinic for Radiation Oncology, University Hospital, Zurich  
<sup>2</sup> Clinic for Oral and Maxillofacial Surgery, University Hospital, Zurich  
<sup>3</sup> Clinic of Dentistry, Oral Medicine and Gnathic Surgery, Clinic for Oral Surgery, Center of Dental and Oral Medicine, University of Zurich

### Corresponding author

PD Dr. med. Gabriela Studer, LA  
RadioOnkologie AN 16  
UniversitätsSpital Zürich  
Rämistrasse 100  
8091 Zürich  
E-mail: gabriela.studer@usz.ch  
Tel. 044 255 29 31  
Fax 044 255 45 47  
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**Summary** *Background:* At the Clinic for Radiation Oncology at the Zurich University Hospital (UniversitätsSpital Zürich [USZ]), head-and-neck tumor (HNT) patients have been treated with intensity-modulated radiotherapy (IMRT) since 01/2002 (n > 800). This method causes less damage to normal tissues adjacent to the tumor, and thus it was possible in the head/neck region to markedly reduce the rate of osteoradionecrosis (ORN), in addition to reducing the rate of severe xerostomia. Based on these results, risk-adapted dental care (RaDC) was adopted by our clinic as the standard mode of pre-IMRT dental treatment. The guidelines as formulated by Grötz et al. were respected. ORN prophylaxis is one of the most important goals of pre-radiotherapy dental care, and the ORN rate is a measurable parameter for the efficacy of dental care, given a certain radiation technique. The *aim* of the present study was therefore to evaluate the efficacy of RaDC as reflected by the ORN rate of our IMRT patients.

*Materials and Methods:* In August 2006, RaDC was clinically implemented and has been used for all HNT patients prior to IMRT since then. Before that (01/2002–07/2006), dental restorations were performed according to the usual procedure.

*Results:* The rate of grade-2 ORN was similar in the conventionally treated and RaDC groups (2% and 1%, resp.); grade-3 ORN had not occurred by the time the analysis was conducted. As expected, fewer extractions were performed in the RaDC cohort (no extractions in 47% of the RaDC/IMRT cohort vs. 27% in the IMRT cohort receiving conventional dental care).

*Conclusion:* After considerably less invasive dental treatment, no higher-grade ORN occurred and no ORN-related jaw resections were required. Based on the present data, risk-adapted minimally invasive dental care is recommended before IMRT.

## Introduction

In keeping with international guidelines (GRÖTZ 2003; SHAW ET AL. 2000), all head-and-neck tumor (HNT) patients at our clinic since more than two decades have undergone standardized focal evaluation and dental treatment prior to all radiation therapy.

Since 01/2002, our HNT patients have been treated with intensity-modulated radiotherapy (IMRT) (n > 800, status: March,

2010). The greatest clinical advantage of this relatively new technique is that it causes substantially less damage to normal tissues while providing equally good or improved tumor control rates (LEE ET AL. 2002; EISBRUCH ET AL. 2003; EISBRUCH ET AL. 2004; CHAO ET AL. 2004; DE ARRUDA ET AL. 2006; PURI ET AL. 2005; STUDER ET AL. 2006a–c, STUDER ET AL. 2007c/d).

Details of the IMRT technique were explained in an earlier publication (STUDER ET AL. 2007a, Tab. I and Fig. 1). Even in the first years after implementation of IMRT a diminishment

Tab.1 (corresponds to Fig. 1) Schematic overview of dental treatment for patients with head-and-neck tumors before/during/after IMRT at the University Hospital Zurich (USZ)

	Before IMRT	During IMRT	After IMRT
<b>HR</b>	<ul style="list-style-type: none"> <li>Dental treatment as with conventional radiotherapy (RT)</li> <li>Dental hygiene</li> <li>Treatment of periodontal pockets</li> <li>Tooth extraction:               <ul style="list-style-type: none"> <li>10 days prior to RT (SHAW et al. 2000)</li> </ul> </li> <li>nonvital teeth, apical pathology (BORNSTEIN et al. 2001)</li> <li>advanced periodontal disease, deep caries</li> <li>smoothing of bone edges and sharp points</li> <li>primary wound closure</li> <li>Tooth-conserving measures</li> <li>Treatment of oral lesions (e.g. candidiasis, ...)</li> <li>Construction of a fluoridation splint</li> <li>New interim support using permanent soft materials</li> </ul>	<ul style="list-style-type: none"> <li>Weekly recall (BORNSTEIN et al. 2001)</li> <li>Dental hygiene, motivation, monitoring</li> <li>Tooth extraction:               <ul style="list-style-type: none"> <li>after consultation with radiotherapist</li> <li>antibiotics until wound healing (SHAW et al. 2000)</li> </ul> </li> <li>Mucositis prophylaxis (Bepanthen® solution)</li> <li>Candidiasis prophylaxis (Ampho-Moronal®)</li> <li>Mouth-opening exercises (trismus prophylaxis)</li> <li>Maintenance of oral cavity moisture with chamomile/sage rinses (Ø Glandosan® for the dentate [NICHOLLS et al. 1998])</li> <li>Application of fluoridation splint 2–3 ×/d for 5 minutes</li> <li>Temporary discontinuation of prosthesis wear; not with obturators (SHAW et al. 2000)</li> </ul>	<ul style="list-style-type: none"> <li>Continue recall for the first year (every 6–8 weeks [BORNSTEIN et al. 2001])</li> <li>Dental hygiene, motivation, monitoring</li> <li>Dental surgery and periodontal pockets               <ul style="list-style-type: none"> <li>antibiotics until wound healing (SHAW et al. 2000)</li> <li>atraumatic tooth extraction</li> <li>grinding down sharp bone edges</li> <li>primary mucous membrane coverage</li> <li>Candidiasis prophylaxis (Ampho-Moronal®)</li> </ul> </li> <li>Maintenance of oral cavity moisture with chamomile/sage rinses (Ø Glandosan® for the dentate [NICHOLLS et al. 1998])</li> <li>Application of fluoridation splint 1 ×/d for 5 minutes</li> <li>tooth-conservation measures</li> <li>Discontinuation of prosthesis wear at night (SHAW et al. 2000)</li> <li>Restoration of masticatory function               <ul style="list-style-type: none"> <li>implantation ca. 1 year after RT (own data, unpublished)</li> </ul> </li> </ul>
<b>IR/LR</b>	<ul style="list-style-type: none"> <li>Dental hygiene</li> <li>Treatment of periodontal pockets</li> <li>No extraction of teeth if:               <ul style="list-style-type: none"> <li>the teeth are otherwise worth conserving</li> <li>in NR cases, endodontic treatment is possible instead of extraction</li> </ul> </li> <li>Selective tooth extractions:               <ul style="list-style-type: none"> <li>10 days before RT (SHAW et al. 2000)</li> <li>smoothing of bone edges and sharp points</li> <li>primary wound closure</li> </ul> </li> <li>Conservative dentistry</li> <li>Treatment of oral lesions (e.g. candidiasis, ...)</li> <li>Construction of a fluoridation splint</li> <li>New interim support using permanent soft materials</li> </ul>	<ul style="list-style-type: none"> <li>Weekly recall (BORNSTEIN et al. 2001)</li> <li>Dental hygiene, motivation, monitoring</li> <li>Mucositis prophylaxis (Bepanthen® solution)</li> <li>Candidiasis prophylaxis (topische Antimykotika)</li> <li>Mouth-opening exercises (trismus prophylaxis)</li> <li>Maintenance of oral cavity moisture</li> <li>Application of fluoridation splints 2–3 ×/d for 5 minutes</li> <li>Discontinuation of prosthesis wear at night (SHAW et al. 2000)</li> </ul>	<ul style="list-style-type: none"> <li>Continue recall (every 6–8 weeks [BORNSTEIN et al. 2001] for the first year)</li> <li>Dental hygiene, motivation, monitoring</li> <li>Restoration of masticatory function               <ul style="list-style-type: none"> <li>implantation ca. 1 year after RT (own data, unpublished)</li> </ul> </li> <li>Dental surgery and treatment of periodontal pockets               <ul style="list-style-type: none"> <li>preoperative antibiotic prophylaxis (1h preoperatively)</li> <li>atraumatic tooth extraction</li> <li>grinding down sharp bone edges</li> <li>primary mucous membrane coverage</li> </ul> </li> <li>Tooth-conservation measures</li> <li>Discontinuation of prosthesis wear at night (SHAW et al. 2000)</li> <li>Maintenance of oral cavity moisture with chamomile/sage rinses or substitution with artificial saliva</li> </ul>
<b>NR</b>	<ul style="list-style-type: none"> <li>No restrictions placed on dental treatment</li> <li>Dental hygiene</li> <li>Treatment of periodontal pockets</li> <li>Tooth extraction:               <ul style="list-style-type: none"> <li>of teeth not worth conserving</li> <li>10 days before RT (SHAW et al. 2000)</li> </ul> </li> <li>Manufacture of a fluoridation splint</li> </ul>	<ul style="list-style-type: none"> <li>No restrictions placed on dental treatment</li> <li>Dental hygiene, motivation, monitoring</li> <li>Tooth extraction:               <ul style="list-style-type: none"> <li>of teeth not worth conserving</li> </ul> </li> <li>Application of fluoridation splint for 5 minutes</li> </ul>	<ul style="list-style-type: none"> <li>No restrictions placed on dental treatment</li> <li>Treatment of periodontal diseases</li> <li>Dental hygiene, motivation, monitoring</li> <li>Extraction of teeth not worth conserving</li> <li>Application of fluoridation splint for 5 minutes</li> </ul>

**HR:** High-risk areas; **IR/LR:** intermediate- and low-risk areas; **NR:** no radiation-specific risk

of the greatly feared osteoradionecrosis (ORN) was observed (GLANZMANN & GRÄTZ, 1995; STUDER ET AL. 2004; STUDER ET AL. 2006d; STUDER ET AL. 2007a; BEN-DAVID ET AL. 2007). In contrast to conventional radiation techniques, as applied to a tonsil carcinoma for instance, in which the jawbone is at risk bilaterally due to laterally opposing radiation beams, IMRT can much more selectively deliver the required dose to the tumor region. During IMRT of tonsil carcinoma the contralateral jawbone is no longer endangered and the ipsilateral much less so. Hence, adapting Grötz's (Tab. II) guidelines for focused dental care seemed expedient (Tab. I). This adapted method, termed "risk-adapted dental care" (RaDC), has been employed on our IMRT patients since mid-2006 (STUDER ET AL. 2007b). It requires that ORN risk areas, i. e. IMRT high-dose areas on the jawbone, be topographically defined by the radiation oncologist prior to dental treatment. Areas with low and intermediate ORN risk are also defined for the dentist, so that dental restorations can be performed conventionally in high-risk areas, but less invasively in the regions that will receive lower doses

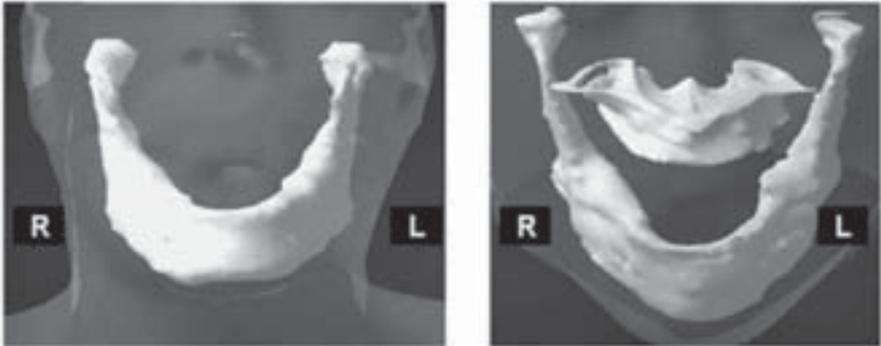
of radiation. The hypothesis tested was that a constantly low ORN rate would be found in IMRT patients after RaDC compared to IMRT patients who received conventional dental treatment.

## Materials and Methods

### Patient cohorts

In the present study, two patient groups were compared (Tab. III): in group 1, from January 2002 to July 2006, 143 HNT patients were given conventional dental care with standard restorations prior to IMRT: 100 patients with oropharyngeal carcinoma and 43 with a carcinoma of the oral cavity. The mean/median observation period of this group was 40/33 months (5–86).

In group 2, between August 2006 and December 2008, 161 patients received IMRT: 106 with oropharyngeal carcinoma and 55 with oral cavity carcinoma. With all patients risk-adapted dental care (RaDC) was performed prior to IMRT. The mean/median observation period of this group was 19/13 months (6–44).

<div style="border: 1px solid black; padding: 5px; margin-bottom: 10px;">                 Radiation oncologist: .....                  Pager             </div> <p><b>Diagnosis/TNM stage:</b> .....</p>	<div style="border: 1px solid black; padding: 10px; text-align: center;"> <b>Patient ID label</b> </div>
<div style="border: 1px solid black; padding: 10px; margin-bottom: 10px;">                 Dental Care prior to IMRT risk definition                  (to be marked by the responsible radiation oncologist)             </div> <p style="text-align: center;"> <b>High Risk area:</b> HR (in red)  <b>Intermediate/Low Risk area:</b> MNR (in green)  <b>No Risk:</b> NR (in yellow)             </p>	
<div style="display: flex; justify-content: space-around;">  </div>	
Universitätsspital Zürich  Dept. Medizinische Radiologie Klinik für Radio-Onkologie Zürich	

**Fig. 1** (corresponds to Tab. I): Zurich University Hospital's internal form for marking (IMRT dosage-dependent) individual risk areas for dental treatment before intensity-modulated radiation therapy (IMRT). The risk areas (high, intermediate/low, no risk of jaw osteonecrosis) for each patient are marked by the radiation oncologist as the basis for the dental treatment planned (see Tab. I).

Tab. II Dental care of patients receiving radiotherapy for head-and-neck tumors (Grötz K A, Strahlenther Onkol 2003; 179 [4]: 275–278)

	Before radiotherapy	During radiotherapy	After radiotherapy
<b>Conventional radiation therapy</b>	<b>Dental treatment</b> <ul style="list-style-type: none"> <li>– Removal of hard and soft plaque</li> <li>– Extraction of nonvital, periodontally diseased, carious, partially retained teeth</li> <li>– Conservative treatment of remaining dentition</li> <li>– Surgical treatment of                             <ul style="list-style-type: none"> <li>– mucosal lesions</li> <li>– removal of sharp bone ridges (mylohyoid line)</li> </ul> </li> </ul> <b>Extent of extractions</b> depends on inclusion of salivary glands in the irradiated field; four groups: <ul style="list-style-type: none"> <li>– Edentulous patients without mucosal lesions = no pre-irradiation therapy</li> <li>– If conservative treatment is impossible = total extraction, clearing</li> <li>– Conservative caries treatment possible = elective extraction</li> <li>– No active caries, good oral hygiene = no tooth extractions</li> </ul>	<b>Tissue-conserving treatment</b> <ul style="list-style-type: none"> <li>– Mucosa retractors (reduction of surface dose to adjacent mucosa via secondary irradiation)</li> <li>– Fluoridation splint and continuous fluoride rinsing</li> <li>– Temporary discontinuation of prosthesis wearing due to sore spots or denture ulcers</li> <li>– Mucositis prophylaxis especially due to xerostomia (Candida colonization)                             <ul style="list-style-type: none"> <li>– Bepanthen®</li> <li>– topical antimycotics (Nystatin = Moronal®)</li> <li>– mouth rinses (chamomile, sage, chloramine tea); Sucralfat suspension</li> </ul> </li> <li>– Diflucan® (local &amp; systemic yeast infections)                             <ul style="list-style-type: none"> <li>– alcohol, nicotine</li> <li>– no hot, spicy, or acidic drinks</li> </ul> </li> <li>– Dermatitis prophylaxis</li> <li>– Mouth-opening exercises, if masticatory muscles and TMJ lie in irradiated field</li> <li>– Xerostomia treatment</li> <li>– Ethylol (Amifostin®) or Cumarin/Troxerutin (Venalot-Depot®)</li> </ul>	<b>Tissue-conserving treatment</b> <ul style="list-style-type: none"> <li>– Continuation of fluoride application</li> <li>– Discontinuation of prosthesis wearing for 3–6 months after irradiation</li> <li>– Tooth- or implant-borne prostheses or maxillary prostheses can be re-inserted earlier, after mucositis has subsided</li> <li>– Restoration of masticatory function is often impossible due to xerostomia or jaw lesions</li> <li>– Special guidelines for dental surgery after radiotherapy to avoid osteoradionecrosis:                             <ul style="list-style-type: none"> <li>– Perioperative, systemic antibiotic prophylaxis (e.g., Amoxicillin), at the latest 24 h pre-operatively</li> <li>– Atraumatic tooth extraction without osteotomy, if possible</li> </ul> </li> <li>– Removal of sharp bone ridges</li> <li>– Primary plastic mucosal closure</li> <li>– Xerostomia treatment</li> <li>– Artificial saliva (warning: Glandosan® = mineral loss; mucine-containing Saliva-medac® and lysozyme-containing BioXtra® products)</li> <li>– Salivary gland stimulants Sialor®</li> <li>– Mouth-opening exercises against trismus</li> </ul>

Tab. III Overview comparing the two subgroups of patients. RT: radiotherapy; FU: follow-up; RaDC: risk-adapted dental care

Parameter	Group 1 n = 143	Group 2 n = 161
<b>Dental treatment</b>	standard	RaDC
<b>RT technique</b>	IMRT	IMRT
<b>Timespan of treatment</b>	1/2002–7/2006	8/2006–12/2008
<b>Diagnosis</b>		
Oropharynx (n = 206)	100	106
Oral cavity (n = 98)	43	55
<b>Average/median FU time</b> in months	40/33	19/33

Only patients at risk of developing ORN – that is, patients with a tumor of the oropharynx (n total = 206) and the oral cavity (n total = 98) – were evaluated.

### Methods

The ORN incidence in the clinic's IMRT cohort since RaDC was introduced (08/2006–12/2008, group 2) was compared with the incidence after conventional dental treatment (01/2002–07/2006, group 1). We expected to find an unchanged, low incidence of ORN in group 2 vs. group 1, since ORN occurs in areas exposed to high doses (usually at doses >66 Gy), in which lesion extirpation was performed according to the usual standard.

Based on the various known tolerance thresholds of different normal tissues for a given radiation dose, it was possible to define the risk level for patients scheduled for oral cavity radiation treatment (see below, a–d). Because the radiation oncologist can identify and mark topographic IMRT high-dose

areas, i.e. high ORN-risk areas, prior to treatment, the dentist can use this information to know regions requiring risk-adapted dental care in each individual patient (see STUDER ET AL. 2007b). The patient form used for marking risk areas for RaDC is shown in Figure 1 and Table I.

#### a) High-risk regions:

≥ 60 Gy to the mandibular bone and/or >50 Gy to gingival areas.

#### b) Intermediate-risk regions:

>45 Gy to the gingiva, mandibular bone <60 Gy, or: mandibular bone <60 Gy, and relevant reduction of salivation caused by irradiating mucous membranes and salivary glands (no ORN risk, but increased caries risk – for instance after certain types of cervical irradiation in Hodgkins lymphoma).

#### c) Low-risk regions:

Mandible < 60 Gy or only ascending ramus in the RT field, and gingiva <45 Gy and at least a parotid volume equivalent with an intermediate dose of ≤ 26 Gy.

#### d) No radiotherapy-specific risk:

Mandibular bone <50 Gy, gingiva <40 Gy, and both parotids outside the RT field (<10 Gy intermediate dose).

Examination for ORN (Tab. IV) was conducted as part of the routine oncological follow-up examinations (by the clinics for Oral and Maxillofacial Surgery, ENT, and Radiation Oncology, University Hospital, Zurich) that were performed regularly 4–6 weeks after completion of treatment, then every 2 to 3 months during the first 2 years. In suspected or positively identified cases of ORN patients are referred to the Clinic for Maxillofacial Surgery for further evaluation and treatment.

Only three patients in this study group failed to participate in the routine progress check-ups, and therefore could not be evaluated.

## Results

### Tumor control

In 90% of the patients, chemotherapy (Cisplatin or Cetuximab) was also performed simultaneously. At the last performed follow-up examination ("last time seen"), 74% of the patients were living tumor-free, 12% were living with cancer, 12% had died of cancer, and 3% had died of other causes. The 2-year local control rate of the entire patient group was 85% among patients with oropharyngeal cancer, and 65% among patients with cancer of the oral cavity.

### ORN incidence

ORN incidence is shown in Table V. The rates of grade-2 ORN (sequester formation) were identical in groups 1 and 2; all

Tab. IV Grades of osteoradionecrosis (GLANZMANN & GRÄTZ 1995)

#### Classification of osteoradionecrosis (ORN) by grade

Grade	Event
1	Exposed bone without signs of infection for at least 3 months
2	Exposed bone with signs of infection or sequester, but not grades 3–5
3	Osteonecrosis, treated with mandibular resection, with satisfactory result
4	Osteonecrosis with persistent problems despite mandibular resection
5	Death due to osteoradionecrosis

Tab. V Occurrence of osteoradionecrosis (ORN) after conventional or risk-adapted dental care (RaDC)

	conventional 1/2002–7/2006 n = 143	risk-adapted 8/2006–12/2008 n = 161	Total n = 304
Grade-1 ORN	0	0	0
Grade-2 ORN	3	2	5 (1.6%)
Grade-3 ORN	0	0	0

Tab. VI Details on the 5 patients with grade-2 ORN: comparable grade-2 ORN rates in oropharyngeal and oral-cavity cancer patients with 2% (4/206) vs 1% (1/98), resp.

	Diagnosis	Stage	ORN location	ORN therapy	outcome	Occurrence after IMRT	Duration (months)
1	Oropharynx	cT4cN2c	Boost region	O	Healed	12	20
2	Oropharynx	cT3cN2b	Boost region	Partial decortication	Regenerated	4	5
3	Oropharynx	cTcN2b	Boost region	O	Healed	22	30
4	Floor of mouth	pT2pN0	Boost region	Partial decortication	Regenerated	0	6
5	Oropharynx	cT3cN2b	Boost region	O	Healed	6	20

Patients 4 and 5 received risk-adapted dental care (RaDC) before IMRT  
 In terms of local radiation dose, nothing remarkable was found compared to other patients without ORN.  
 The 5 events were located in region 37/retromolar left/31–32/37/47.  
 pTpN: postoperative stage  
 cTcN: definitive IMRT without prior surgery

5 cases observed also correspond to the NCI and EORTC classification of a grade-2 ORN. Table VI presents details on the 5 sequester patients. All ORN events were found in the high-dose region. Other, unexpected reactions of the mucosa or teeth outside the high-dose areas were not observed; the less invasive tooth restorations outside the high-dose areas in RaDC group 2 did not demonstrate any clinically apparent, unfavorable results.

### Tooth extractions

Table VII lists the number of teeth extracted in each group. As expected/by definition, fewer teeth were extracted in the RaDC cohort. In this context, the clinically relevant (but not quantified) fact must be mentioned that almost no radiation planning computed tomography ("planning CT") had to be delayed due to pronounced facial soft-tissue swelling after multiple extractions performed as part of the prior dental care. This was, however, frequently the case in the period of conventional dental treatment (group 1), with an ensuing delay of 1 to 2 weeks until the swelling had gone down; thus, the start of radiotherapy was also delayed.

In addition, a tendency of more frequently possible dental rehabilitation was observed (no statistical analysis of these retrospective data).

## Discussion

In addition to severe xerostomia, ORN is the most important criterion for radiation tolerance in oral cavity and oropharyngeal carcinoma patients, and is the main justification for consistently performing dental treatment prior to the start of radiotherapy. Comprehensive dental and/or oral surgery treatment prior to radiotherapy in the orofacial region is of fundamental importance in the prevention of osteonecrosis of the irradiated jaw.

ORN has been variously classified according to different definitions in earlier publications. In our clinics, the classification by Glanzmann and Grätz is used (GLANZMANN & GRÄTZ 1995, Tab. IV). The advantage of this classification vs. that of EORTC (LENT/SOMA) or NCI (JERECZEK-FOSSA ET AL. 2002) is its connection to therapeutic and clinical consequences; nevertheless, grade-2 events mutually correspond in all of the named classification systems.

With the radiotherapeutic technology of the past the required tumor dosage was chiefly delivered via laterally opposed fields, which also simultaneously irradiated most of the oral

Tab. VII Retrospective overview of the number of teeth extracted during dental treatment prior to radiotherapy and during dental care after IMRT (dental implants, removable partial or complete dentures)

Parameter	Conventional dental care (IMRT group 1)	RaDC (IMRT group 2)
<b>Edentulous patients</b>	17%	15%
<b>Dentate patients</b>		
– no extractions	27%	47%
– 1–3 teeth extracted	36%	29%
– 4–15 teeth extracted	37%	24%
<b>Dental rehabilitation</b>	23%	36%

cavity and/or jawbone. This resulted in a greater radiation impact on the jawbone, associated with a higher ORN rate, than seen today in the IMRT era; accordingly, the entire dentate jaw usually had to be considered a “region at risk” and correspondingly dentally treated. IMRT is a method which makes it possible to restrict the high-risk region to the volume of jawbone adjacent to the tumor. IMRT enabled the ORN rate to be reduced from ca. 5–10% to  $\leq 1\%$  (GLANZMANN & GRAETZ, 1995; STUDER ET AL. 2004; STUDER ET AL. 2006d; STUDER ET AL. 2007a; BEN-DAVID ET AL. 2007), a success of considerable relevance in the attempt to reduce late complications of radiation treatment. The “focussed” high-dose exposure and the pronounced drop in the ORN rate after IMRT shown in our patients in 2006 indicated the logic of also keeping dental treatment “focussed”, which our center has therefore done since mid-2006. Table I shows the steps of dental treatment in RaDC: adaptation of methods to the local risk for jawbones and soft tissues before/during/after IMRT; Table II summarizes the standard procedures which have existed up to now. As already mentioned, the main difference lies in the focussed approach of RaDC.

After an observational period of over 3 years since introducing the guidelines for pre-IMRT RaDC, no detrimental effects have yet been found in patients of group 2, most importantly, no increase in ORN incidence compared to the IMRT group 1, which in the previous years had undergone focal treatment according to the conventional standard. Although the duration of observation differed in the two groups, the results are considered reliable because both groups are IMRT cohorts, i. e., it was possible to very conservatively treat jawbones in both groups and include only relatively low volumes of bone in the high-dosage area. Thus, due to the use of the IMRT technique, an increase in ORN was not expected. As already mentioned, dental treatment in the high-risk regions in the RaDC groups was also performed in accordance with the general standard. Less invasively treated intermediate or low-risk areas by definition receive intermediate or very low radiation doses, so that, theoretically, only limited side-effects are expected in these tissue areas in RaDC group 2. In fact, 3 years of RaDC experience confirmed this. However, due to the paucity of data in literature, comparisons cannot be made.

Thanks to RaDC, it was possible to reduce the number of or even totally avoid tooth extractions in the majority of patients (50% more patients with no extractions, Tab. VII), since IMRT creates more low- and intermediate-risk areas (that would previously have been high-dose areas), allowing less invasive dental treatment to be performed.

In this context, the rarity of facial swelling after RaDC is also clinically relevant. This is yet another advantage of RaDC, since time is no longer lost waiting for swelling to abate: the planning CT serves as the basis for computer-assisted 3-dimensional calculation of radiation dose delivery to the tissues/tu-

mor, and is performed as soon as possible after dental treatment. This CT is conducted with a custom-modelled fixation facial mask made of plastic (for the purpose of reproducibly positioning the patient over the weeks of treatment, every radiotherapy session is carried out using this mask). If the mask is made on a swollen face, it will be loose after the swelling has subsided; both the fixation mask and the millimeter-exact radiation plan are thus rendered worthless.

Experience has shown that careful manipulations/interventions on the jawbone and its mucous membrane covering are well tolerated after radiation doses of up to  $\sim 50$  Gy, but at doses over  $>50$  Gy, invasive interventions are accompanied by an increased risk of ORN and lower tissue tolerance. If the status of the remaining dentition and surrounding tissues is better, this greatly improves the outlook for any subsequent dental care, which in turn positively influences the tumor patient's quality of life (ZWAHLEN ET AL 2008). The retrospective data on dental treatment seems to confirm this (Tab. VII).

From an economic point of view, avoiding a grade-3 or -4 ORN amounts to a savings of about € 30,000 (based on Swiss conditions); the improved possibilities for dental treatment and the advantages of more remaining teeth are more difficult to express in terms of costs. Nevertheless, the health advantages and improved quality of life for the patients are indisputable. It is interesting to note that the incidence of bisphosphonate-associated osteonecrosis currently considerably exceeds that of ORN after IMRT (18.6%, WALTER ET AL. 2008; DANNEMANN ET AL. 2008).

## Conclusion

Following much less invasive dental treatment, no higher-grade ORN or ORN-related jaw resections occurred in our IMRT patient cohort, as before. The more invasive standard guidelines for dental treatment prior to radiotherapy which have been valid up to now no longer appear justifiable for IMRT patients. Based on the data presented here, a risk-adapted, less invasive approach to pre-IMRT dental care is recommended.

## Résumé

Introduction: L'IMRT est implémentée au Département de radio-oncologie de l'Hôpital de Zurich depuis 2002. Outre une diminution de la xérostomie, son avantage principal dans les régions de la tête et du cou réside dans une réduction substantielle du RON (de  $\sim 5$ –10% à  $\sim <1\%$ ).

Les procédures standards lors des soins dentaires préradiothérapeutiques ont été ajustées afin d'être moins invasives pour les patients soumis à l'IMRT depuis août 2006.

Patients et méthode: Cet article présente les résultats d'une période d'un suivi de 3 ans pour des patients qui ont reçu des

soins dentaires adaptés aux risques avant l'IMRT pour des cancers de la tête et du cou (n=161). Des patients traités avec des soins dentaires standards (n=143) avant l'IMRT de 01/2002 à 07/2006 ont servi de contrôle.

Résultats: Les analyses du RON ont révélé des taux d'incidence égaux pour les deux périodes (1,5% degré 2, pas d'oc-

currence de degré 3, et pas de résection de la mandibule), et moins d'extractions dentaires grâce au traitement dentaire adapté aux risques.

Conclusion: Sur la base des données présentées ici, le traitement dentaire adapté aux risques est fortement recommandé pour les patients soumis à l'IMRT.

## References

- DE ARRUDA F F, PURI D R, ZHUNG J, NARAYANA A, WOLDEN S, HUNT M, STAMBUK H, PFISTER D, KRAUS D, SHAHA A, SHAH J, LEE N Y: Intensity-modulated radiation therapy for the treatment of oropharyngeal carcinoma: the Memorial Sloan-Kettering Cancer Center experience. *Int J Radiat Oncol Biol Phys* 2006; 64 (2): 363–373
- BEN-DAVID M A, DIAMANTE M, RADAWSKI J D, VINEBERG K A, STROUP C, MURDOCH-KINCH C A, ZWETCKENBAUM S R, EISBRUCH A: Lack of osteoradionecrosis of the mandible after intensity-modulated radiotherapy for head and neck cancer: likely contributions of both dental care and improved dose distributions. *Int J Radiat Oncol Biol Phys* 2007; 68 (2): 396–402
- BORNSTEIN M, BUSER D, FILIPPI A: Concepts of prevention and therapy of radiation-induced side effects. *Schweiz Monatsschr Zahnmed* 2001; 111 (8): 962–977
- CHAO K S, OZYIGIT G, BLANCO A I, THORSTAD W L, DEASY J O, HAUGHEY B H, SPECTOR G J, SESSIONS D G: Intensity-modulated radiation therapy for oropharyngeal carcinoma: impact of tumor volume. *Int J Radiat Oncol Biol Phys* 2004; 59 (1): 43–50
- DANNEMANN C, GRÄTZ K W, ZWAHLEN R A: Bisphosphonate-induced osteonecrosis of the jaws – a guide to diagnosis, therapy and prevention of BON in dental practice. *Schweiz Monatsschr Zahnmed* 2008; 118 (2): 113–123
- EISBRUCH A, MARSH L H, DAWSON L A, BRADFORD C R, TEKNOS T N, CHEPEHA D B, WORDEN F P, URBA S, LIN A, SCHIPPER M J, WOLF G T: Recurrences near base of skull after IMRT for head-and-neck cancer: implications for target delineation in high neck and for parotid gland sparing. *Int J Radiat Oncol Biol Phys* 2004; 59 (1): 28–42
- EISBRUCH A, SHIP J A, DAWSON L A, KIM H M, BRADFORD C R, TERELL J E, CHEPEHA D B, TEKNOS T N, HOGIKYAN N D, ANZAI Y, MARSH L H, TEN HAKEN R K, WOLF G T: Salivary gland sparing and improved target irradiation by conformal and intensity modulated irradiation of head and neck cancer. *World J Surg* 2003; 27 (7): 832–837
- GLANZMANN C, GRÄTZ K W: Radionecrosis of the mandibula: a retrospective analysis of the incidence and risk factors. *Radiother Oncol* 1995; 36 (2): 94–100
- GRÖTZ K A: Zahnärztliche Betreuung von Patienten mit tumortherapeutischer Kopf-Hals-Bestrahlung. Gemeinsame Stellungnahme der Deutschen Gesellschaft für Zahn-, Mund- und Kieferheilkunde, Deutschen Gesellschaft für Radioonkologie MPuS, Abstimmung mit dem Vorstand der Deutschen Gesellschaft für Zahnheilkunde. (Dental care for patients with anti-neoplastic radiotherapy of the head and neck.) *Strahlenther Onkol* 2003; 179 (4): 275–278
- JERECZEK-FOSSA B A, ORECCHIA R: Radiotherapy-induced mandibular bone complications. *Cancer Treat Rev* 2002; 28: 65–74
- LEE N, XIA P, QUIVEY J M, SULTANEM K, POON I, AKAZAWA C, AKAZAWA P, WEINBERG V, FU K K: Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: an update of the UCSF experience. *Int J Radiat Oncol Biol Phys* 2002; 53 (1): 12–22
- PURI D R, CHOU W, LEE N: Intensity-modulated radiation therapy in head and neck cancers: dosimetric advantages and update of clinical results. *Am Journal of Clinical Oncology* 2005; 28 (4): 415–423
- SHAW M J, KUMAR N D, DUGGAL M, FISKE J, LEWIS D A, KINSELLA T, NISBET T: Oral management of patients following oncology treatment: literature review. *Br J Oral Maxillofac Surg* 2000; 38 (5): 519–524
- STUDER G, GRÄTZ K W, GLANZMANN C: Osteoradionecrosis of the mandibula in patients treated with different fractionations. *Strahlenther Onkol* 2004; 180 (4): 233–240
- a) STUDER G, LÜTOLF U M, DAVIS J B, GLANZMANN C: IMRT in Hypopharyngeal Tumors. *Strahlenther Onkol* 2006; 182 (6): 331–335
- b) STUDER G, HUGUENIN P, DAVIS J, KUNZ G, LUTOLF U, GLANZMANN C: IMRT using simultaneously integrated boost (SIB) in head and neck cancer patients. *Radiat Oncol* 2006; 1 (1): 7
- c) STUDER G, FURRER K, DAVIS J, STÖCKLI S, ZWAHLEN R A, LÜTOLF U, GLANZMANN C: Postoperative IMRT in head and neck cancer. *Radiat Oncol* 2006; 1 (1): 40
- d) STUDER G, STUDER S P, ZWAHLEN R A, HUGUENIN P, GRÄTZ K W, LÜTOLF U M, GLANZMANN C: Osteoradionecrosis of the mandible: minimized risk profile following intensity-modulated radiation therapy (IMRT). *Strahlenther Onkol* 2006; 182 (5): 283–288
- a) STUDER G, GRÄTZ K W, GLANZMANN C: In response to Dr. Merav A. Ben-David et al. ("Lack of osteoradionecrosis of the mandible after IMRT", *Int J Radiat Oncol Biol Phys* 2007). *Int J Radiat Oncol Biol Phys* 2007; 68 (5): 1583–1584
- b) STUDER G, GLANZMANN C, STUDER S P, GRÄTZ K W, LÜTOLF U M, ZWAHLEN R A: Recommendations for dental care prior to intensity-modulated radiotherapy (IMRT). Adaptation of the University Hospital Zurich (USZ) guidelines. *Schweiz Monatsschr Zahnmed* 2007; 117 (6): 637–647
- c) STUDER G, ZWAHLEN R A, GRÄTZ K W, DAVIS B J, GLANZMANN C: IMRT in oral cavity cancer. *Radiat Oncol* 2007; 2: 16
- d) STUDER G, LÜTOLF U M, GLANZMANN C: Loco-regional failure analysis in head-and-neck cancer patients treated with IMRT. *Strahlenther Onkol* 2007; 183 (8): 417–423; discussion 424–425
- WALTER C, AL-NAWAS B, GRÖTZ K A, THOMAS C, THÜROFF J W, ZINSER V, GAMM H, BECK J, WAGNER W: Prevalence and risk factors of bisphosphonate-associated osteonecrosis of the jaw in prostate cancer patients with advanced disease treated with zoledronate. *Europ Urol* 2008; 54:1066–1072
- ZWAHLEN R A, DANNEMANN C, GRÄTZ K W, STUDER G, ZWAHLEN D, MOERGELI H, DRABE N, BÜCHI S, JENEWEIN J: Quality of life and psychiatric morbidity in patients successfully treated for oral cavity squamous cell cancer and their wives. *J Oral Maxillofac Surg* 2008; 66 (6): 1125–1132