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Pre-irradiation dental care: Ready-to-use templates for oropharyngeal cancers

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ABSTRACT

Aim: To develop a tool in order to guide pre-irradiation dental care (PIDC) for patients with oropharyngeal cancers.
Background: Osteoradionecrosis of the jaws is a potential complication of radiotherapy (RT) for head and neck cancers. To prevent this complication, PIDC can involve multiple dental extractions as a preventative measure to avoid post-RT complications. However, there is no standardized tool to guide PIDC.
Materials and methods: From January 2005 to October 2015, 120 head and neck cancer patients were prospectively included in a study investigating dysgeusia after RT. From this cohort, patients were enrolled according to the following inclusion criteria: histopathological confirmation of oropharyngeal squamous cell carcinoma; stage T1-4 N1-3 M0; ≤10 missing teeth. Individual teeth were retrospectively delineated on planning computed tomography and doses to dentition were assessed to generate templates.
Results: Thirty-three patients were included. Molars received highest doses with a mean dose of 50 Gy (range; 19–75 Gy). Ipsi-lateral and contralateral wisdom teeth received RT dose superior to 50 Gy in 92% and 56% of cases, respectively. Patients with advanced disease (T4 or N2c-3) received higher mean doses on inferior and ipsi-lateral dental arches compared to other patients (T1-3 N0-2b): 42 Gy *vs.* 39 Gy and 44 Gy *vs.* 39 Gy ($p < 0.05$), respectively.
Conclusion: Pre-RT dose distribution templates are an objective way to prepare PIDC. Further studies with a larger cohort are needed to validate these templates.

1. Background

In Europe, head and neck cancer (HNC) accounts for approximately 140,000 cases corresponding to 4% of newly diagnosed cancers.[1] In recent years, advances in treatment have been associated with an increasing number of long term cancer survivors, stressing the need for decreasing long-term complications from treatments and improving patient's quality of life. Radiotherapy (RT), alone or associated with chemother-

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apy, is a cornerstone of care for HNC, requiring 30–35 days of treatment over 6–7 weeks.[2]

Irradiation of the oral cavity, mandible and salivary glands leads to various oral complications, including mucositis,[3] xerostomia,[4] radiation-induced caries,[5,6] trismus[7] or osteoradionecrosis.[8] Osteoradionecrosis is a serious complication that can be associated with significant morbidity that can sometimes lead to radical mandibulectomy.[9] To prevent this complication, pre-irradiation dental care (PIDC) in HNC patients undergoing RT is crucial.[10] PIDC involves elimination of oral disease such as caries, abscess and periodontal disease.[11] PIDC can lead to multiple dental extractions knowing the dose on dental arches as a preventive measure to avoid post-radiotherapy complications.[12] To guide oral health professionals during PIDC, an individualized dental map is typically requested from radiation oncologists based on an estimation of expected dose distribution to dental arches.

In the last decade, intensity modulated radiotherapy (IMRT) has become the standard of care for HNC RT treatment. IMRT has been associated with significant difference in dose distribution compared with older tri-dimensional techniques.[13] However, there is currently no standardized tool to guide PIDC for locally advanced HNC.

2. Aim

The aim of this study was to develop predictive dose distribution templates, ready-to-use by oral health professionals, to guide PIDC for locally advanced oropharyngeal cancers treated with IMRT.

3. Materials and methods

3.1. *Patients characteristics*

From January 2005 to October 2015, 120 HNC patients from our institution were prospectively included in a study investigating dysgeusia after RT of the oral cavity, nasopharynx, larynx/hypopharynx, and oropharynx. From this cohort, patients with locally advanced oropharyngeal squamous cell carcinoma were included. Patients with more than 10 missing teeth were excluded from this study. All patients received IMRT with a bilateral irradiation of the neck. This study was approved by our institutional review board and ethics committee.

3.2. *Treatment characteristics*

All patients had a 1.5 mm slice thickness planning computed tomography (CT) scan in a supine position from the vertex to the carina with and without intravenous contrast injection. Immobilization was achieved with a thermoplastic mask of the head and shoulder fixed to the treatment table. When available, positron tomography (PET)-CT scan and magnetic resonance imaging for tumor imaging were fused with the planning CT.

Treatment volumes were as follows: the gross tumor volume (GTV) was defined as the macroscopic primary tumor and involved lymph nodes based on planning CT as well as multimodality imaging when available; the clinical tumor volume (CTV1) was defined as the GTV volume with an additional margin for microscopic spread (2–5 mm); the high-risk CTV (CTV2) was defined as the CTV1 with an additional 1 cm margin and inclusion of nearby high risk anatomic areas, as well as the adjacent lymph node levels; the low-risk CTV (CTV3) included the contralateral uninvolved lymph node level. An additional 2–5 mm margin was added to each CTV for planning target volume (PTV). Patients were planned to receive a dose of 59.4 in 33 fractions Gy to PTV2, with a simultaneous integrated boost to 69.96 Gy in 33 fractions to PTV1. Low risk PTV (PTV3) was treated with 50.4 Gy in 28 fractions. Patients were treated using 6-MV photons, and treatment was given in 5 daily fractions per week. Treatment plans were normalized so that the prescription dose (100%) covered at least 95% of the PTV volume. Treatment techniques included Helical Tomotherapy and volumetric modulated arc therapy (VMAT).

3.3. *Teeth delineation*

Because dose to individual teeth was not routinely evaluated, each tooth was retrospectively delineated on all planning CTs. Teeth delineation was done under a window level and width of 650 and 2000 Hounsfield unit. Teeth delineation was reviewed with an expert oral and maxillofacial surgeon and included the crown as well as the entire root and adjacent bony structure. In the case of a missing tooth, the corresponding dental alveoli, including tooth socket and adjacent bony structure, were contoured. The international teeth numbering system was used for numerical identification of individual teeth[14] (Fig. 1).

3.4. *Statistics*

Statistical analysis was performed by SPSS software (SPSS Inc., Chicago, IL, USA). Teeth structures were used to evaluate the maximum point dose (Dmax) received by each tooth and the mean dose to dental arches (superior, inferior, ipsi-lateral and contralateral). All dosimetric parameters were extracted from dose-volume histogram analysis. Teeth receiving >60 Gy, 50–60 Gy and 40–50 Gy were considered as high risk, intermediate risk and low risk, respectively.[15,16] Doses to dental arches were then compared using Student's T-test. p values less than 0.05 were considered statistically significant.

4. Results

4.1. *Patients and lesions characteristics*

Among the 120 patients from the dysgeusia database, 33 were eligible for analysis. Patient and lesion characteristics are summarized in Table 1. Regarding RT technique, 27 (82%) patients were treated with Helical Tomotherapy while 6 (18%) patients were treated using VMAT.

4.2. *Dental arches*

Superior dental arches received lower RT dose than inferior dental arches: 36 Gy *vs.* 40 Gy ($p < 0.05$); and ipsi-lateral hemi-arches received higher RT dose than contralateral: 41 Gy *vs.*

Superior (Maxillary)

Right	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28	Left
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38	

Inferior (Mandibular)

Fig. 1 – Dental arches according to the international teeth numbering system.

Table 1 – Sample and lesion characteristics.

Sample ($N = 33$)	
Male	25 (76%)
Female	8 (24 %)
$\text{Age}_{\text{median (range)}}$	60 (44–76)
Tobacco exposure	5 (15%)
$\text{Missing teeth}_{\text{median (range)}}$	5 (1–10)
Location	
Base of tongue	13 (39%)
Tonsil	18 (55%)
Soft palate	2 (6%)
Right/left	17 (52%)/16 (48%)
T stage	
T1	5 (15%)
T2	16 (49%)
T3	7 (21%)
T4	5 (15%)
N stage	
N0	4 (12%)
N1	4 (12%)
N2a, N2b, N2c	5 (15%), 11 (34%), 5 (15%)
N3	4 (12%)

35 Gy ($p < 0.05$). Patients who had advanced disease (T4 or N2c-N3) received a higher RT dose to the inferior dental arch and ipsi-lateral hemi-arches than other patients (T1-3 N0-2b): 42 Gy (superior dental arch) *vs.* 39 Gy (inferior dental arch) and 44 Gy (ipsi-lateral hemi-arch) *vs.* 39 Gy (contralateral hemi-arch) ($p < 0.05$).

4.3. *Tooth-by-tooth results*

Ipsi-lateral as well as contralateral incisors never receive more than 40 Gy and thus do not seem to be at risk of osteoradionecrosis (range: 21–38). The canine teeth also receive low RT dose with less than 10% receiving 40–50 Gy (low risk). Values are more heterogeneous for pre-molars and molars. Among molars, wisdom teeth are the most irradiated teeth receiving more than 50 Gy in 92% of cases for ipsi-lateral teeth (middle to very high risk) *vs.* 56 % for contralateral wisdom teeth. Tooth-by-tooth risk distribution is summarized in Table 2. To picture the tooth-by-tooth dose distribution and help oral health professionals with PICD, 4 predictive dosimetric templates were created (Fig. 2). Two situations were considered: (1) T1-3/N0-2b and (2) T4 and/or N2c-N3. For each situation, 2 scenarios were considered: The average maximum RT dose (mean case scenario) for each tooth and the worst case of our studied patients. As an example, the RT plans of two patients that fitted to the mean case scenario templates are presented in Fig. 3.

5. Discussion

Pre-radiotherapy dental dose estimation is difficult for radiation oncologists and can lead to a misestimation of the dose received by each tooth. However, the risk-level evaluation in PIDC is mostly based on this estimation. Misestimating can lead to extensive dental extractions that can be painful, unaesthetic or lead to non-functional denture. Multiple exodontias can also delay oncologic treatment since the healing time can be longer. Furthermore, there is a dose-volume correlation between the dose to the mandible and the risk of osteoradionecrosis.[17] This is why pre-radiotherapy templates seem to be the best objective way to prepare PIDC.

It is well known that HNC patients have often poor oral health[18] due to co-factors exposure: tobacco[19] and alcohol. This is why HNC patients often have dental extractions during PIDC. In our cohort; only 33 patients were eligible because of the wide number of edentate patients in the dysgeusia database. In addition, none of the patients included in our study was fully dentate, which can be explained, on one hand, by the high rate of unerupted/missing wisdom teeth in the general population[20] and, on the other hand, by a frequent occurrence of dental extractions before RT. Surprisingly, the smoking rate is low in our cohort considering HNC patients (15%); this is likely due to the selection of highly dentate patients who are in a better oral health than standard HNC patients.

The dose evaluation shows us a clear difference in terms of dose distribution between dental arches. Unsurprisingly, ipsi-lateral arches are significantly more irradiated than contralateral arches. We also show that mandibular teeth receive significantly higher dose than maxillary teeth. Considering tooth-by-tooth evaluation, molars receive higher doses than the rest of the teeth, due to their proximity to the oropharyngeal cavity. Among molars, wisdom teeth are the most irradiated teeth receiving above 50 Gy in 92% of cases for ipsi-lateral teeth. This data supports the practice of systematically extracting unerupted wisdom teeth in PIDC for oropharyngeal cancer.[21]

The main challenge in PIDC is to provide the most accurate dose estimation before the treatment and, consequently, without the RT plan. Although there is no clear dose cut-off, empiric dose-risk levels do exist: 40–50 Gy, 50–60 Gy and >60 Gy.[15,16,22] In this study, we present dose distribution templates for patients receiving bilateral irradiation of the neck with both small and large tumors. We also propose a worst-case scenario for both situations. This allows the dental team to choose the template that fits the patient best without underestimating the dose for locally advanced HNC patients, when considering dental extraction.

Table 2 – Tooth-by-tooth risk distribution.

		Low risk		Intermediate risk		High risk	
		Ipsi.	Contr.	Ipsi.	Contr.	Ipsi.	Contr.
Incisors (1–2)	Sup.	0%	0%	0%	0%	0%	0%
	Inf.	0%	0%	0%	0%	0%	0%
Canines (3)	Sup.	3%	0%	0%	0%	0%	0%
	Inf.	6%	0%	0%	0%	0%	0%
Pre-molars (4–5)	Sup.	21%	6%	3%	0%	0%	0%
	Inf.	33%	18%	15%	3%	3%	0%
Molars (6–7)	Sup.	27%	48%	42%	18%	21%	0%
	Inf.	10%	55%	45%	24%	45%	6%
Wisdom teeth (8)	Sup.	15%	45%	33%	33%	48%	2%
	Inf.	0%	24%	18%	64%	82%	9%

A similar approach has been proposed by Thariat et al.[23] in the post-RT setting. In fact, they proposed an automatic atlas-based segmentation framework of the dental structures in the context of IMRT. They concluded that the dose estimation using this framework was more accurate than visual dose estimation and could be helpful to prevent post-RT osteoradionecrosis or implant failure.[24] However, the necessity for rapid treatment start does not allow for PIDC after RT plan generation. This is why in our approach dental templates are provided before RT setting. The solution of pre-RT templates are, therefore, likely to be more accurate than a hand drawn dose-estimation, the latter also being associated with high inter-observer variability.

The limitations of our study include its retrospective nature, the small number of patients and the fact that it was limited to tumors of the oropharyngeal cavity. Further studies are warranted to evaluate dental RT dose distribution in other locations. Additionally, these dental templates fit for patients treated with rotational IMRT techniques (Helical Tomotherapy or VMAT) using similar dose schedules as those used in this study. Consequently, the relevance of these templates should be discussed according to RT technique and patient disease. However, it is the first study that proposes dental templates in the pre-radiotherapy setting. This study confirms that unrestorable teeth or teeth with advanced periodontal involvement need to be extracted before RT due to the significant RT dose received by teeth and the potential for post-RT complications. Despite these limitations, these dental templates are highly relevant in routine practice, considering the limitations associated with currently used hand drawn dose-estimation.

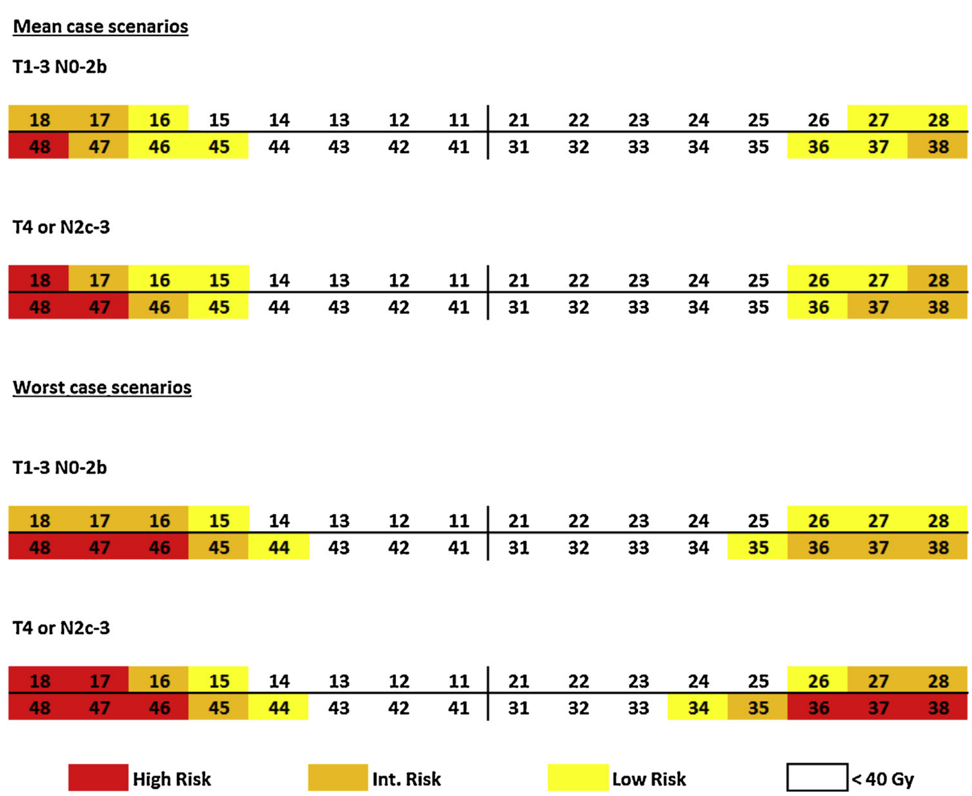

Fig. 2 – Dental dosimetric templates.

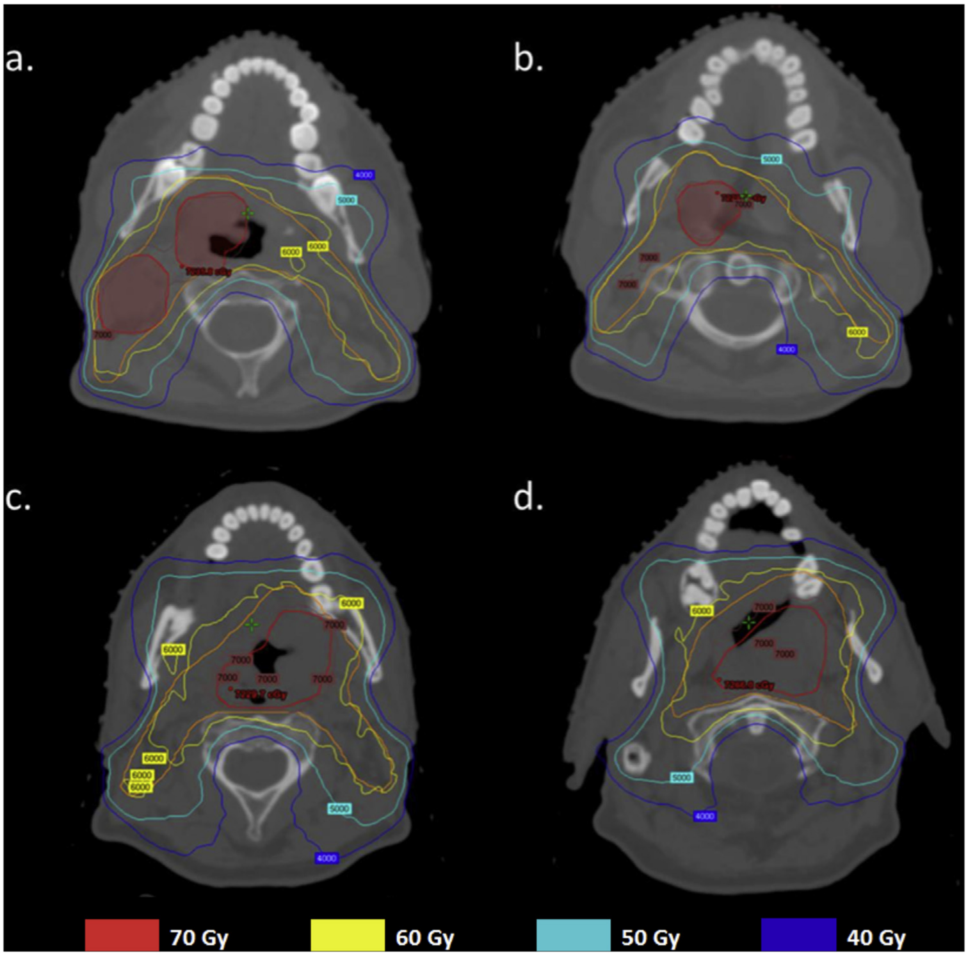

Fig. 3 – Patients fitting dental templates in mean case scenario. T1-3 N0-2b: inferior and superior dental arches at the level of GTV (a, b). T4 and/or N2c3: inferior and superior dental arches (c, d).

6. Conclusion

Based on our series, we propose two scenarios (mean and worst case) for early and advanced cases that can help oral health professionals in their pre-RT evaluation. Further studies with a larger cohort are needed to validate these templates.

Conflict of interest

None declared.

Financial disclosure

None declared.

REFERENCES

[1]. Gatta G, Botta L, Sánchez MJ, et al. Prognoses and improvement for head and neck cancers diagnosed in Europe in early 2000s: the EUROCARE-5 population-based study. *Eur J Cancer* 2015;**51**(October (15)):2130–43.

[2]. Nguyen-Tan PF, Zhang Q, Ang KK, et al. Randomized phase III trial to test accelerated versus standard fractionation in combination with concurrent cisplatin for head and neck carcinomas in the radiation therapy oncology group 0129 trial: long-term report of efficacy and toxicity. *J Clin Oncol* 2014;**32**(January (34)):3858–67.

[3]. Elting LS, Cooksley CD, Chambers MS, Garden AS. Risk, outcomes, and costs of radiation-induced oral mucositis among patients with head-and-neck malignancies. *Int J Radiat Oncol Biol Phys* 2007;**68**(July (4)):1110–20.

[4]. Hey J, Setz J, Gerlach R, et al. Parotid gland-recovery after radiotherapy in the head and neck region – 36 months follow-up of a prospective clinical study. *Radiat Oncol* 2011;**6**:125.

[5]. Gupta N, Pal M, Rawat S, et al. Radiation-induced dental caries, prevention and treatment – a systematic review. *Natl J Maxillofac Surg* 2015;**6**(December (2)):160–6.

[6]. Michelet M. Caries and periodontal disease in cancer survivors. *Evid Based Dent* 2012;**13**(September (3)): 70.

[7]. Wu VWC, Lam Y-N. Radiation-induced temporo-mandibular joint disorder in post-radiotherapy nasopharyngeal carcinoma patients: assessment and treatment. *J Med Radiat Sci* 2016;**63**(June (2)):124–32.

[8]. Ray-Chaudhuri A, Shah K, Porter RJ. The oral management of patients who have received radiotherapy to the head and neck region. *Br Dent J* 2013;**214**(April (8)):387.

[9]. Dhanda J, Pasquier D, Newman L, Shaw R. Current concepts in osteoradionecrosis after head and neck radiotherapy. *Clin Oncol* 2016;**28**(July (7)):459–66.

[10]. Jawad H, Hodson NA, Nixon PJ. A review of dental treatment of head and neck cancer patients, before, during and after radiotherapy: part 1. *Br Dent J* 2015;**218**(January (2)):65–8.

[11]. Thariat J, Ramus L, Darcourt V, et al. Compliance with fluoride custom trays in irradiated head and neck cancer patients. *Support Care Cancer* 2012;**20**(August (8)):1811–4.

[12]. Jansma J, Vissink A, Spijkervet FKL, et al. Protocol for the prevention and treatment of oral sequelae resulting from head and neck radiation therapy. *Cancer* 1992;**70**(October (8)):2171–80.

[13]. Lohia S, Rajapurkar M, Nguyen SA, Sharma AK, Gillespie MB, Day TA. A comparison of outcomes using intensity-modulated radiation therapy and 3-dimensional conformal radiation therapy in treatment of oropharyngeal cancer. *JAMA Otolaryngol Head Neck Surg* 2014;**140**(April (4)):331–7.

[14]. Ahlberg J. We must get the numbers right. *FDI Newslett* 1987;**158**:8–9.

[15]. Wahl MJ. Osteoradionecrosis prevention myths. *Int J Radiat Oncol* 2006;**64**(March (3)):661–9.

[16]. Tsai CJ, Hofstede TM, Sturgis EM, et al. Osteoradionecrosis and radiation dose to the mandible in patients with oropharyngeal cancer. *Int J Radiat Oncol* 2013;**85**(February (2)):415–20.

[17]. Studer G, Studer SP, Zwahlen RA, et al. Osteoradionecrosis of the mandible. *Strahlenther Onkol* 2006;**182**(5):283–8.

[18]. Critchlow SB, Morgan C, Leung T. The oral health status of pre-treatment head and neck cancer patients. *Br Dent J* 2014;**216**(January (1)):E1.

[19]. Petersen PE. Tobacco and oral health – the role of the world health organization. *Oral Health Prev Dent* 2003;**1**(4):309–15.

[20]. Doğan N, Orhan K, Günaydin Y, Köymen R, Okçu K, Uçok O. Unerupted mandibular third molars: symptoms, associated pathologies, and indications for removal in a Turkish population. *Quintessence Int* 2007;**38**(September (8)):e497–505.

[21]. Oh H-K, Chambers MS, Garden AS, Wong P-F, Martin JW. Risk of osteoradionecrosis after extraction of impacted third molars in irradiated head and neck cancer patients. *J Oral Maxillofac Surg* 2004;**62**(February (2)):139–44.

[22]. Gourmet R, Chaux-Bodard A-G. [Tooth extraction in irradiated areas]. *Bull Cancer (Paris)* 2002;**89**(April (4)):365–8.

[23]. Thariat J, Ramus L, Maingon P, et al. Dentalmaps: automatic dental delineation for radiotherapy planning in head-and-neck cancer. *Int J Radiat Oncol Biol Phys* 2012;**82**(April (5)):1858–65.

[24]. Pompa G, Saccucci M, Di Carlo G, et al. Survival of dental implants in patients with oral cancer treated by surgery and radiotherapy: a retrospective study. *BMC Oral Health* 2015;**15**(January (5)).