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Original Article / Оригинални рад

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SUMMARY

Introduction/Objective The incidence of radiation-induced side effects in patients with head and neck cancer (H&N) depends on technique of planning and the irradiation dose as well as primary tumor location within the H&N region.

The aim of our research is to establish the incidence of side effects in patients with head and neck cancer treated with conformal radiotherapy planning with computed tomography (CT) or computed tomography fusion with magnetic resonance imaging (CT-MRI fusion).

Methods

Prospective analysis was performed on 40 patients with oropharynx carcinoma and on 40 patients with larynx carcinoma prospectively followed after radiotherapy. 40 patients with H&N cancer were irradiated by using 3D conformal radiotherapy planning with CT, while other 40 patients were treated using 3D conformal radiotherapy planning with CT-MRI fusion. In all cases standard fractionation was used at 2 Gy per day /5 days a week.

Results

Of the total number (n=80) of treated patients, 52 patients (52/80; 65%) reported a side effect and the incidence of complications was higher in patients irradiated with 3D technique planning with CT (31/52; 60% for 3D CT vs 21/52; 40% for 3D CT-MRI; p=0.02). There were more complications in chemoradiotherapy group of the patients than observed when only radiotherapy was used 35/52 RT+HT vs 17/52 RT (67%: 33% and p=0.004).

Conclusion

3D radiotherapy technique planned solely on the basis of CT is related to high incidence of toxicity which significantly affects the quality of life of irradiated patients. 3D conformal radiotherapy planned with CT-MRI fusion reduces the incidence of oral complications. Planning technique with fusion technique using MR imaging is more suitable for delivering higher doses to the tumor with fewer side effects.

Keyword: radiotherapy; head and neck; oral complications; CT-MRI fusion in planning radiotherapy

САЖЕТАК

Увод/Циљ Учесталост нежељених ефеката зрачења код пацијената са карциномом главе и врата зависи од технике планирања, спровођења радиотерапије и примарне локализације тумора.

Циљ нашег истраживања је да се утврди учесталост нежељених ефеката зрачне терапије код болесника са тумором главе и врата лечених 3Д конформалном радиотерапијом планираној само на основу КТ и 3Д конформалном терапијом планираној на основу фузије КТ са МР (КТ-МР).

Методе Проспективно је анализирано 40 болесника са карциномом орофаринкса и 40 болесника са карциномом ларинкса код којих је спроведена зрачна терапија. 20 болесника са карциномом орофаринкса и 20 болесника са карциномом ларинкса је зрачено 3Д конформалом техником на основу КТ, а још по 20 са карциномом орофаринкса и ларинкса фузијом КТ-МР. Код свих је примењена стандардна фракционација са 2 Gy дневно, пет дана седмично.

Резултати Од укупно 80 болесника лечених зрачењем, код 52 (52/80; 65%) су забележени нежељени ефекти зрачне терапије а учесталост компликација је већа код примене 3Д КТ технике зрачења (31/52; 60% код 3Д КТ насупрот 21/52; 40% код 3Д КТ-МР; p=0.02). Било је више компликација у групи болесника код којих је примењена хемоирадијација него код болесника лечених само радиотерапијом 35/52 РТ+ХТ а 17/52 РТ (67% : 33% ; p=0.004).

Закључак 3Д техника радиотерапије планирана само на основу КТ је повезана са високом стопом токсичности које знатно утичу на квалитет живота зрачених пацијената. 3Д конформална техника радиотерапије планирана фузијом КТ-МР смањује појаву оралних компликација. За примену виших туморских доза уз мању учесталост компликација је погоднија техника планирања са фузионисаном техником помоћу МР.

Кључне речи: радиотерапија, тумори главе и врата, оралне компликације, ЦТ-МР фузија у планирању радиотерапије

INTRODUCTION

The treatment of tumors in head and neck (H&N) region most commonly combines the use of surgery, radiotherapy and chemotherapy with radiotherapy being applied in more than 50% of cases [1].

According to the data of Cancer Registry of the Institute of Oncology of Vojvodina in Sremska Kamenica, in 2010, in the province of Vojvodina in Serbia, a total of 500 people suffered from H&N cancer, which makes around 4 to 5% of all malignant tumors registered that year [2].
This data fits well with the data of the International Agency for Research on Cancer (IARC), where the H&N cancers make 5% of all malignant tumors [3].

The frequency of oral complications during radiotherapy is high and the studies show the frequency to be up to 40% [3].

Radiation-induced changes can be divided into two groups, based on the usual time of their occurrence: early or acute side effects that are noted during or immediately after treatment and late or chronic side effects develop months or years after the end of radiation therapy [4].

Xerostomia is the most frequent complication of irradiation in patients treated with conformal (3D) radiotherapy. About 64% of patients developed permanent xerostomia of a moderate to severe degree. The most pronounced changes are found in patients with laryngeal and oropharyngeal carcinoma due to its close proximity to major salivary glands. Irradiation changes the composition of saliva, leads to difficulties in maintaining oral hygiene and affects intake of cariogenic food and drinks [5, 6].

Beside those, mucosal atrophy and fibrotic changes, radiation-related caries and bone necrosis are occurring as side effects of the treatment but they are less frequent [7, 8].

With conventionally fractionated radical doses of radiotherapy, the first signs of mucositis usually appear already during the second week of the treatment and they advance towards the end of the treatment from the enanthems to confluent forms of pseudomembranous mucositis [9]. The recovery starts within 2.5 to 3 weeks after the end of radiotherapy, and within one month mucosa is healed in about 90 to 95% of patients [10].

In addition, xerostomia predisposes infections and development of dental caries and it affects the speaking and swallowing [11].

Because of the lack of saliva the probability for development of radiotherapy-related complications is increased. In the first two weeks following the beginning of radiotherapy and received cumulative radiation tumor dose even at 20 Gy, around 80% of salivary function is changed [12].

The increase in acidogenic and cariogenic bacteria in the mouth (Streptococcus mutans, Lactobacillus and Candida species) together with the decrease in non-cariogenic microorganisms (such as Streptococcus sanguis, Neisseria and fusobacterium) increase the risk of development of oral complications [12].

Significant weight loss and deterioration of the patient's nutrition status tends to aggravate because of the pain while chewing and swallowing. Radiotherapy also incurs loss of appetite, nausea and physical discomfort. Loss of taste occurs and progressively increases at the received radiation tumor dose of about 30 Gy [13].

The characteristic of the modern radiotherapy planning are increasingly used fusion techniques such as PET-CT and MRI fusion. The adequate soft-tissue contrast of magnetic resonance imaging (MRI) allows the technique to have an increasing role in contouring the gross tumor volume (GTV), organs at risk (OAR) which leads to the decreasing incidence of treatment complications [14].

Frequency of the complications of radiotherapy in patients with head and neck cancer is about 35% [15, 16].

The aim of this research is to perceive the possibilities of lowering the radiotherapy-induced toxicity in patients with H&N carcinoma in a setting of a developing country. This aim can be reached by using the transition between 3D conformal radiotherapy planning with computed tomography (3D CT) and 3D conformal radiotherapy planning with CT fusion magnetic resonance imaging (3D CT-MRI). Acute side effects that are analysed were xerostomia, mucositis and dermatitis. On the other hand dental caries was observed as chronical complication of radiotherapy. Those side effects (acute and chronical) were monitored three times during the radiotherapy:

1) in the fifth week of radiotherapy, after the completion of the 25th fraction;
2) 30 days following the completion of radiotherapy and
3) 90 days following the completion of radiotherapy. Minimum two weeks prior to radiotherapy, initial (baseline) dental treatment (IDT) was performed, while medical examinations (ME) with documentation of complications and dental evaluation were done at every check-up. Radiotherapy complications were not monitored after 90 days of the completion of radiotherapy.

METHODS

This investigation was carried out at the Institute of Oncology Vojvodina in Sremska Kamenica, Province of Vojvodina, Serbia in the period between January 2013 and October 2014. The study included patients with diagnosed H&N cancer treated with radiotherapy. 80 prospective patients participated in the study, 40 of whom were diagnosed with laryngeal carcinoma and 40 with oropharynx carcinoma. The main aim of the study was to compare the two most commonly applied methods of planning radiotherapy, three-dimensional (3D) with CT and three-dimensional (3D) conformal with fusion CT-MRI, in relation to the incidence of complications appearance.

The study included patients over the age of 18 for whose treatment radiotherapy was indicated by the Oncology consultants' team. All the patients had good general status, ECOG Scale of Performance Status 0 or 1.

Patients who for any reason failed to complete the prescribed radiotherapy, as well as those whose general status was poor, such as ECOG 2 or more, were excluded from consideration.

Prior to the radiotherapy, the participants had IDT performed. IDT was performed at least two weeks prior to the radiotherapy and all the tooth lesions were identified and repaired. Teeth that could not be repaired had to be extracted. Clinical examination (CE) and dental evaluation (DE) was

performed five weeks into the radiotherapy (i.e. after the completion of the 25th fraction). The second examination was performed 30 days and the third 90 days following the completion of radiotherapy.

Radiation treatment

The patients were irradiated using two techniques: 3D conformal radiotherapy with CT and 3D conformal radiotherapy with fusion CT-MRI. The participants in the study were irradiated with a daily dose of 2 Gy, five days a week, with a curative radiotherapy tumor dose from 60 Gy to 70 Gy. Each patient was provided with a thermoplastic mask in order to immobilize the treated region and to deliver the radiation tumor dose more precisely.

3D conformal radiotherapy technique for oropharyngeal cancer includes tumor/tumor bed with a margins of 2 cm and lymph node: N0 include levels II-IV and retropharyngeal lymph nodes (RPN), N1 include levels Ib-IV and RPN, N2-3 include Ib-V and RPN [17]. Radiation dose for adjuvant 3D radiotherapy for oropharyngeal cancer is 60 Gy (60 Gy to the preoperative tumor bed and 50 Gy to the lymph nodes with 2 Gy per day/5 days a week).

For inoperable oropharyngeal cancer tumor radiation dose was 70 Gy (70 Gy on the tumor and involves lymph nodes and 50 Gy on elective lymph nodes with 2 Gy per day/5 days a week) [18].

Curative 3D conformal radiotherapy technique for laryngeal cancer included primary tumor and any involved lymph nodes. Irradiation depended on laryngeal localization of the primary tumor. The levels that are included are II-IV, level VI with subglottic tumors, and level V if >1 node involved in that side of the neck.

Curative dose for oropharyngeal and laryngeal cancer was 60 Gy. For locally advanced tumor the radiation dose was escalated up to 70 Gy.

Indication for chemoradiotherapy included advanced stage of the disease (T3, T4) and positive surgical margin and extranodal capsular extension.

Every day the patients themselves made notes of subjective difficulties with skin, oral pain and the sense of (insufficient) saliva. During the radiotherapy course analgesic therapy was optionally included as well as corticosteroid therapy when stronger pain appeared, and was left at the discretion of involved radiation oncologist.

A modified scale recommended from the Radiation Therapy Oncology Group was used for monitoring acute complications (xerostomia, mucositis and dermatitis), actually the part which relates to monitoring the complications of head and neck region (RTOG-Acute radiation morbidity scoring criteria). In this classification, the acute complications are divided into a four-point scale [19]:

0 – no change

1 – mild changes which demand no therapy

2 – changes which demand symptomatic therapy and necessary analgesics

3 – sufferings which demand opioid analgesics and

4 – changes which demand the termination of radiotherapy [19]

RESULTS

Results were statistically analyzed using Chi-Square and Fischer exact probability tests. There were 80 participants in the study, 59 men and 21 women. The ratio 3:1 in favor of men fits into the general trend of the incidence of this disease, p=0.61. Age ranged 18-65 years, with the median age at presentation of 54.7 years in 3D CT and 52.9 in 3D CT+MR radiotherapy. All patients had ECOG 0-1, p=0.82 (Table 1).

Table 1. Patient and tumor characteristics.

Characteristics	3D-CT radiotherapy (n=40)	3D CT-MR radiotherapy (n=40)	*p*
Age range (median)	54.7	52.9	
Gender (M:F)	31:9	28:12	0.61
ECOG (0:1)	26:14	24:16	0.82
Oropharynx	20	20	1
Supraglotic larynx	10	12	0.81
Glottic larynx	6	7	0.99
Subglottic larynx	4	1	0.36
T stage 1/2/3/4	3/8/17/12	8/12/15/5	0.11
N stage 0/1/2/3	7/13/16/4	12/20/7/1	**0.04**
Radiotherapy (RT)	11	20	0.07
Concurrent RT+HT	29	20	0.07
Early stage T1-T2	3+8=11	8+12=20	0.07
Advanced stage T3-T4	17+12=29	15+5=20	0.07
TD 60 Gy	24	21	0.49
TD 70 Gy	16	19	0.49

The study involved 40 patients diagnosed with primary laryngeal carcinoma (22 patients with supraglottic localization tumor, 13 glottic and 5 subglottic) and 40 with oropharynx carcinoma. The number of patients irradiated with 60 Gy and 70 Gy in both groups was nearly same, p=0.49 (Table 1). According to the p>0.05, we concluded that the groups were homogeneous concerning age, gender, ECOG performance and tumor dose.

Table 2. Treatment-related toxicity.

Toxicity	3D-CT radiotherapy (total 40)	3D CT-MR radiotherapy (total 40)	*p*
Total complications	31	21	0.02
Acute complications 1, 2 & 3	31	21	0.02
Acute complications RT vs. RT+HT	RT=10 RT+HT=21	RT=7 Total=17 RT+HT=14 Total=35	0.004
1. Xerostomia	27	13	0.002
Xerostomia (oroph/larynx)	16/11	8/5	
2. Mucositis	24	12	0.006
Mucositis (oroph/larynx)	17/7	8/4	
3. Dermatitis	10	14	0.46
Dermatitis (oroph/larynx)	4/6	7/7	
Grade 0-2 RTOG scoring criteria	17	15	0.64
Grade 3-4 RTOG scoring criteria	14	6	0.03
Chr. complications (dental caries)	15	7	0.04
DC (larynx)	4	1	0.16
DC (oropharynx)	11	6	0.14
TD 60 Gy	17	15	0.64
TD 70 Gy	14	7	0.07
Corticosteroid therapy	35	17	0.004

Fewer patients had early stages of the disease (n= 31) while advanced stage disease was present in 49 patients. In advanced stages of the disease (T3 and T4), as well as with postoperative high risk (positive surgical margins and extranodal extension) concomitant radiotherapy and chemotherapy was used with 5 fluorouracil plus cisplatin (5FU/CDDP). 49 patients with advanced stage of the disease were treated with chemoradiotherapy.

20 patients with laryngeal or oropharynx carcinoma were irradiated with 3D CT, the other group of 20 patients of both tumor localization were treated with 3D CT-MRI conformal radiotherapy (2 Gy per fraction, 5 fractions a week, from 60 Gy to 70 Gy), p>0.05 (Table 1).

Of the total number of 80 irradiated patients, 52 of them (65%) reported a side effect of radiation therapy. 31 patients were irradiated by using 3D CT, while 21 patients were irradiated by using 3D CT-MRI, p=0.02 (Table 2). In this study p was < 0.05 which suggested that incidence of side effects in those groups was statistically significantly different.

Oropharyngeal mucositis developed in 36 out of 52 patients, being observed in 24 and 12 patients for the 3D CT and 3D CT-MRI technique, respectively (p=0.006). Xerostomia was present in 40/52 in irradiated patients, in oropharyngeal cancer 3D CT vs. 3D CT+MRI=16:8, in laryngeal cancer 11/5 (p=0.002). According to the p, which was p<0.05 the incidence of complications was statistically higher in the group where radiotherapy was planned without fusion with MRI.

Skin changes on face and neck during the radiotherapy in the form of radiation dermatitis has manifested in 24 patients, being observed in 10 and 14 patients for the 3D CT and 3D CT-MRI technique, respectively p=0.46 (Table 2). Based on the results of the p there was no statistical difference in incidence of the radiation dermatitis (3D vs. 3D+MRI). The reason could be the number of the radiation fields which in conformal technique were 4-10 [20].

Dental caries (DC) was identified in 22 out of 80 patients who were irradiated (Figure 1). Dental caries was identified in three patients during the radiotherapy, in eight patients 30 days following the completion of radiotherapy and in eleven patients 90 days after the radiotherapy (Figure 2).

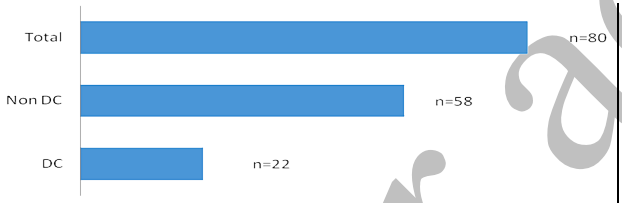

Figure 1. Distribution of Dental caries (DC) in irradiated patients.

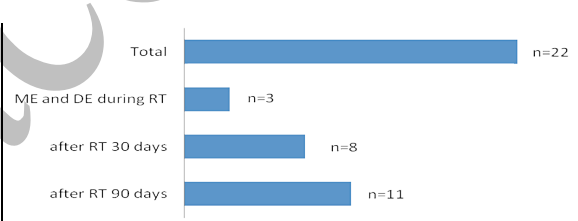

Figure 2. Distribution of dental caries at the first, second and third patient medical examination (ME) and dental evaluation (DE).

It was observed that radiation-related caries appeared in 17 patients treated for primary oropharynx carcinoma, and in only 5 patients treated for primary laryngeal carcinoma (Table 2). According to the DVH (dose volume histogram) the coverage of the PTV (planning volume) was homogeneous with 95% tumor dose.

Caries was identified in 15 patients treated with conventional 3D CT radiotherapy and in 7 patients treated with 3D CT-MRI conformal radiotherapy, p=0.04 (Table 2). Results in our study showed that incidence of dental caries was statistically more frequent if radiotherapy has been planned only according to CT.

Regardless of the used treatment technique, acute complications were more common in chemoradiotherapy regimen (35/52 pts.) than in the application of radiotherapy alone (17/52 pts.), (p=0.004). This implies that in chemioirradiation the incidence of side effects was statistically significantly higher than in the radiotherapy without concomitant chemotherapy.

52 patients out of the total number of 80 examined and irradiated patients received some form of corticosteroid therapy during the period of radiation 35 (67%) for 3D CT vs 17 (33%) for 3D CT-MRI, p=0.004 (Table 2). The use of corticosteroid therapy in 3D conformal radiotherapy has been correlated with increased incidence of side effects.

Corticosteroid therapy was included as a symptomatic therapy with irradiated patients when non-steroidal analgesics could not eliminate the pain. Dexamethasone was usually used in the form of tablets with total daily dose 1.5-3 mg per 24 hours or parenteral 4-12mg per 24 hours.

Complications of radiation treatment grade 0, 1, 2 which do not require interruption of radiotherapy or analgesics have the same incidence in both techniques, p=0.64. Grade 3 and 4 have been statistically more frequent in patients treated with 3D CT technique, p=0.03. There was no difference in incidence of side effects in both techniques when tumor dose was 60 Gy, while we noticed increase in 3D CT technique when the dose was 70 Gy, p=0,07.

DISCUSSION

Our study involved 80 patients of both genders. According to the results of the study the incidence of head and neck cancer is higher in men than women (59 M:21 W). The approximate ratio of 3:1 in favor of men corresponds to the general trend of incidence of this disease as shown in medical literature [21].

Complications of radiotherapy were observed in 65% of patients (52/80). In the literature, this percentage goes around 40%, and in our study it is higher, which can be explained by infrequent usage of planning radiotherapy based on computerized tomography with MRI fusion as well as fusion methods with PET-CT and IMRT technic [22].

Complications in the mucous membrane of oral cavity in the form of radiation-related mucositis was registered in 36 out of 80 participants in the study, and approximately one half of the patients reported some kind of a problem. Although this complication was the most common, the manifestation of mucositis was mild (Grade 0-2: 32/52) and did not cause the interruption of radiotherapy [23]. Acceding our results we can make a conclusion that there is statistically significant difference in the incidence of side effects if radiotherapy is planned using CT rather than using MRI fusion. This especially applies to the delivery of higher tumor dose of 70 Gy (3D CT:3D CT+MR=14:7; P=0.07).

Xerostomia appeared in 40 patients and that is one half of the irradiated patients. Xerostomia is one of the most common symptom in cancer patients [24]. Based on the results we concluded that for delivery of higher tumor dose with fewer side effects the optimal radiation technique is planning with fusion MRI.

These patients often suffered from skin changes and complications. These changes were seen in 24 patients and are mainly manifested in the form of Grade 0-1 with the presence of skin erythema. Dermatitis more often occurred in 3D CT-MRI technique because there was a larger number of fields

(3D CT : 3D CT-MRI=10:14) (Table 2). The level of manifestation of acute radiation complications (Acute Radiation Morbidity Scoring Criteria) in the form of radiation-related dermatitis was classified into four categories [19].

All 49 patients with negative prognostic factors (RT: RT+HT=31:49) received radiotherapy concomitant with chemotherapy. Side effects were reported by 35 patients (35/49; p=0.004). According to this, the frequency of complications increase when chemotherapy is applied concomitant with radiotherapy.

In 22 out of a total of 80 patients dental caries was identified. As expected, radiation-related caries had higher incidence in patients treated for oropharyngeal then in those treated for laryngeal carcinoma (17:5=O:L, p=0.14). Participation of supraglottic localization was the most frequent of all laryngeal carcinoma in our study (22/40; 55%). The likely reason for this could be the size of irradiated area and localization which encompasses large salivary glands. It was also found that 15 patients irradiated with 3D CT technique developed radiation-related caries. Such high incidence (15/40; 37.5%) of dental caries can be linked to the use of 3D CT planning and execution technique, which is in many centres already proven as inferior and, hence, outdated. Different studies explain the impact of irradiation on the composition of teeth in a different way. Some claim that the immediate effect of irradiation is demineralization and damage of prismatic structure of tooth, while others argue that the exposure to radiotherapy does not change tooth structure and composition [25, 26].

Data regarding this topic is scarce in literature. The phase III study which compared side-effects of radiotherapy techniques 2D, 3D and IMRT, did not give any detail on dental management and complications [27]. Using newer radiation techniques, 3D CT-MRI fusion and IMRT, protection of critical organs became possible and decreased the incidence of early and late complications of the irradiated areas of head and neck.

In their study, Walker's et all. have proven that doses above 60 Gy caused irreversible changes in the structure of the teeth and induced dental caries development. Dose between 30–60 Gy likely exists and it is related to salivary gland damage. Critical threshold seems to be at the ≥ 60Gy level, and these findings suggest that 3D treatment planning process should be carefully done respecting this dose level. All patients in the present study had received radiation doses of 60 Gy or 70 Gy which depends on the type of radiotherapy-adjuvant vs. primary treatment in locally advanced head and neck cancer.

With patients receiving parotid-sparing radiotherapy, where salivary output has been largely maintained, caries risk was reduced [17].

Late radiotherapy-related complications, such as post irradiation caries that were analyzed 90 days after radiation treatment occurred in about 27.5% of cases as it was mentioned earlier (22/80; 27.5%). Studies have shown higher incidence of radiation-related caries, around 35%, mostly in patients which were irradiated for nasopharyngeal carcinoma [16]. The favourable results of this study

can be explained by a small number of patients and localization of irradiated areas as well as by avoidance of radiation of big salivary glands. It is obvious that, direct effect of irradiation may not be solely responsible for the occurrence of dental caries, and that other factors such as hyposalivation, xerostomia, mucositis, loss of taste and diet may be present. This clearly confirms multifactorial genesis of radiation-related caries [28].

New radiotherapy techniques make possible for the radiation dose to be localized to a smaller volume of mandible, which will certainly result in lower incidence of oral complications and radiation-related caries [29]. However, despite the expectations of lower incidence of oral complications, some authors claim that there is no great benefit to this. Ben David MA et al. claim that the daily intake of fluoride supplements up to 18 months following the completion of radiotherapy, has a greater effect on reduction of oral complications [30].

Around 65% (52/80) of our patients received some form of corticosteroid therapy during radiation (table 2). The combination of radiation-related complications with simultaneous application of corticosteroid therapy is very high in our patients and it is about 75%. Application of corticosteroid therapy during radiation and its impact on the increase of incidence of complication is not well understood in the literature [31]. Unreasonably frequent application of corticosteroid therapy is present and it can certainly affect the patient's immunity and the composition of saliva. It can also be related to a higher rate of oral complications during radiotherapy.

The pain is certainly not an absolute indication for the use of these medications, and the therapy should be directed to analgesic therapy and cancer pain therapy in the form of non-opioid and opioid analgesics as well as coanalgesics. Further recommendations for research would certainly include the effect of corticosteroid systematic therapy on the development of radiation-related complications.

Finally, it is worth saying that direct effect of radiation is not the sole factor in occurrence of oral complications and radiation-related caries. The complications that have been researched have a multifactorial genesis and depend on composition and quantity of saliva, bacterial colonization, age, dental hygiene and fluoride intake [32]. Minimizing the use of corticosteroid therapy has also been associated with the decrease in incidence of oral complications. Studies involving patients which were not irradiated also document the occurrence of secondary caries, which supports the finding that direct effect of radiotherapy is not the only causal factor in the occurrence of dental caries [21]. Use of IMRT can certainly reduce the incidence of radiotherapy complications at head and neck cancer [32, 33].

CONCLUSION

3D radiotherapy technics planning with computed tomography was associated with a high rate of toxicities which affect patients' quality of life. In our study, 3D CT-MRI radiotherapy reduced incidence of radiation-related oral complications. The experience of institutions of developed countries, based on the fusion - techniques in radiotherapy planning, shows successful decrease of side effects incidence. This benefit should be included in the clinical practice of radiotherapy planning

in institutions of developing countries. Curative radiotherapy treatment methods should be planned with best available imaging techniques in the form of conformal techniques based on computerized tomography fusion with MRI alone or, whenever possible using fusion with PET CT and/or IMRT.

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