

Implant rehabilitation in patients irradiated for head and neck cancer: role of Intensity-Modulated Radiotherapy (IMRT) in planning the insertion site

Fabrizio Carini, MD, DMD¹
 Valeria Pisapia, BDS²
 Dario Monai, MDS³
 Lorena Barbano, BDS²
 Gianluca Porcaro, MDS³

¹ Research Professor, University of Milan-Bicocca, Monza (MB), Italy

² Postgraduate student, School of Oral Surgery, University of Milan-Bicocca, Monza (MB), Italy

³ Oral Surgery specialist, School of Oral Surgery, University of Milan-Bicocca, Monza (MB), Italy

Corresponding author:

Gianluca Porcaro
 Oral Surgery specialist, School of Oral Surgery,
 University of Milan-Bicocca
 Monza (MB), Italy
 Phone and Fax: +39 (0) 2333482
 E-mail: porcarogianluca@libero.it

Summary

Purpose: currently, head and neck irradiation is not considered an absolute contraindication for implant placement (1), especially due to the transition from conventional to conformal radiotherapy. However, there is a difference in the success rate of implant placement between irradiated and non-irradiated bones (5). Successful osseointegration is mainly affected by the total dose of radiation (6). The main purpose of this study was to minimize problems related to radiation dose by evaluating in advance the most suitable site for implant insertion on the basis of the mean absorbed dose. Additional aims were: to estimate the appropriate timing for implant insertion in irradiated bones, to analyze the difference in stability between maxilla and mandible, and to evaluate the success of implants with wrinkled microgeometry and increased layer of TiO₂.

Materials and methods: five patients who had been irradiated for head and neck cancer using intensity-modulated radiotherapy (IMRT) were recruited for our study. Surgical procedures were performed following a pre-surgical evaluation of the correct insertion position of implant fixtures. The latter was based on a scrutiny of dose-volume histograms (DVH) developed by a team of experts in medical physics and radiotherapists after dentists had contoured the volumes of interest. Student's *t* test and Pearson's correlation test were used for comparison and correlation between the variables considered.

Results: the percentage of osseointegration was 100%, which supports the usefulness of the adopted technique. A statistically significant difference in stability and crestal bone resorption emerged in the comparison between maxilla and mandible, but not between times of insertion. Moreover, there was a significant correlation between radiation dose and ISQ values: an increase in radiation dose corresponded to a decrease in primary stability. However, the correlation between ISQ values and implant length was not significant as well as that between primary stability and implant diameter.

Conclusions: implantology guided by assessment of absorbed irradiation dose in the site to be rehabilitated can lead both to an increase in implant survival into irradiated tissue bone, and to a reduction in the incidence of ORN. However, both a larger sample size and the development of long-term prospective studies are necessary to validate the described method.

Key words: implants rehabilitation, contouring, IMRT.

Introduction

Radiotherapy side effects, sometimes combined with post-surgical consequences, affect patient's social life by causing a considerable psychological discomfort and cause important complications in both oral rehabilitation and restoration of dental occlusion (1).

While the inability of many patients to tolerate conventional removable prostheses has been widely documented, the use of dental implants often increases both patient's satisfaction and quality of life by allowing a reconstruction of tumor defects, a proper retention of removable prostheses and a reduction of the overload of vulnerable soft tissues (2,3).

Prior to 1986 (4), patients who had received head and neck radiation were usually excluded from implant reconstruction because of previous reports of hard and soft tissue damage (reduced vascularity, altered cellularity and tissue hypoxia), which would have theoretically interfered with successful osseointegration of titanium endosseous implants.

Today, head and neck irradiation is not considered anymore an absolute contraindication for implant placement (1), although a difference in success rate of implant placement between irradiated and non-irradiated bones can still be observed (5).

Successful osseointegration is mainly affected by total dose of radiation (6): while doses lower than 45 Gy are not associated with implant failure, doses in the 50-60 Gy range are usually not a contraindication for implantology

(7), and doses higher than 60-66 Gy are related to a higher failure rate.

Visch et al. (8) reported a 71% survival rate for implants in tissues irradiated with doses higher than 50 Gy, compared with 84% in tissues that received less than 50 Gy. Although radiation dose itself is not a strong predictor for the onset of osteoradionecrosis, several studies showed statistically significant correlations between high radiation doses (>66 Gy) and development of osteoradionecrosis (9,10).

Besides "total administered dose" and "volume of irradiated bones", another factor increasing the overall risk of ORN is "surgical trauma following irradiation" (11): this was indeed the primary reason why implant therapy could not be applied in patients undergoing radiotherapy in the past years (12).

A decreased risk of ORN, and consequently of implant failure, could be achieved due to the development of radiation techniques, i.e. with the transition from conventional to conformal radiotherapy.

3D imaging, acquired by contouring on CT, is the most important component of modern radiation therapy, as it allows the assessment of the volumes of interest, i.e. GVT (gross tumor volume), CTV (clinical target volume) and OAR (organs at risk).

"If you can't see it, you can't hit it and if you can't hit it, you can't cure it", meaning that if we can see a tumor, then we can aim radiations at it accurately, and so we could cure it (13).

Intensity-modulated radiotherapy (IMRT) is a highly advanced type of conformal radiotherapy that uses modifications in the intensity of the photon-beam from a linear accelerator across the irradiated fields, in order to enhance dose conformation in three dimensions. It allows different radiation dosages at different target organs simultaneously: it can escalate the radiation dosage to the primary disease (local control of disease), at the same time decreasing the dose to the surrounding tissues (incidence of radio induced toxicity) (14).

Is based on an "inverse planning" computer software to optimize treatment planning (15), and it can produce a concave curve for the same dose, conforming the dose distribution to very irregular targets even if these are concave and adjacent to healthy organs, as in the case of head and neck districts.

The dose distribution across the irradiated tissues, i.e. the dose received by the different structures, is graphically illustrated by means of dose-volume histograms (DVH). In addition to radiation dosage, with the consequent risk for ORN, several other factors must be taken into account in order to predict long-term survival of implants placed in irradiated tissues. As regards the timing of insertion, studies carried out by Marx and Johnson (16), suggest that the risk for surgical complications is higher during the period between 1 and 6 months after the end of radiotherapy, whereas according to Visch et al. (8), tissue reactions to radiotherapy already decline 6 months after the end of treatment. However, Meraw and Reeve (17) suggest that it is convenient to proceed with implant placement between 12 and 18 months after completion of radiation therapy. Moreover, the quality and type of bone can affect the predictability of implant survival (18).

Mandibular implants were significantly less likely to fail than maxillary implants (19).

There is no evidence in the scientific literature that any specific type of implant would be more successful than others in irradiated bones, although there are some data concerning the suitability of the length of implants for this kind of tissue. Actually, several studies have shown that a higher proportion of short implants were lost if compared to long fixtures (20).

These results are partly explained by an increased marginal bone loss that has been reported for irradiated patients: Watzinger et al. (21) reported 2-9 mm bone loss during a 3-years follow-up period.

Taking into account these variables, our study has the following aims:

- a) To evaluate implant success in irradiated bed using as a guide for fixture insertion the information provided by dose-volume histograms (DVH) about the amount of radiation absorbed in correspondence of the alveolar area to be treated;
- b) To estimate how much time should elapse from the end of radiotherapy treatment to implant surgery in order to achieve effective osseointegration, and to observe the discrepancy between maxilla and mandible in terms of stability;
- c) To analyze long-term survival in irradiated bones of a specific type of implant, i.e. Phibo® TSA® Advance.

Materials and methods

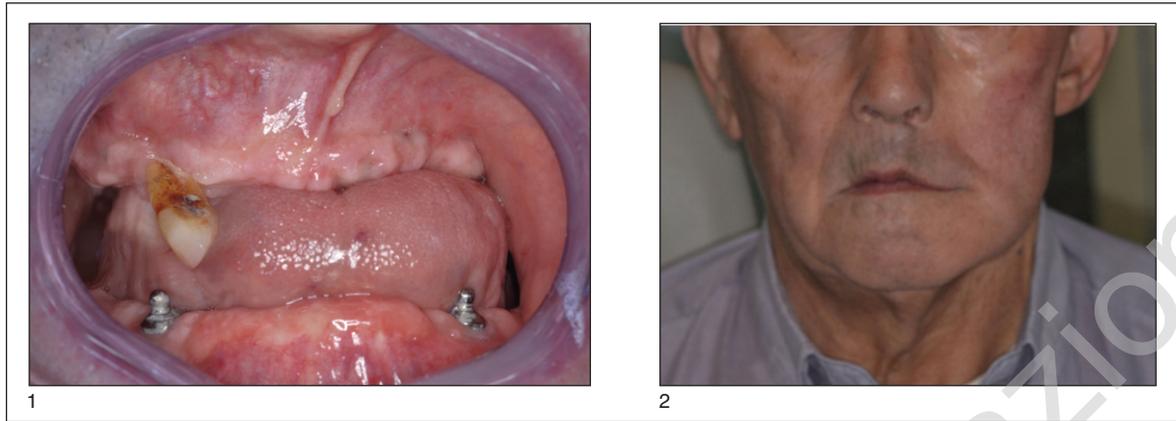
During the period between February 2011 and April 2012, 89 patients, who had been irradiated for head and neck cancer, were examined at the Oral Oncological Center of Milano-Bicocca University in order to assess their eligibility for inclusion within the protocol of implant rehabilitation.

The selection of subjects suitable for implant treatment was carried out by evaluation of resignation letters (provided by the Radiotherapy Department of San Gerardo Hospital), intra/extraoral analysis, and scrutiny of the outcome of radiographic examinations (orthopantomography and CT Dentascan) of the observed patients (Figs. 1-4).

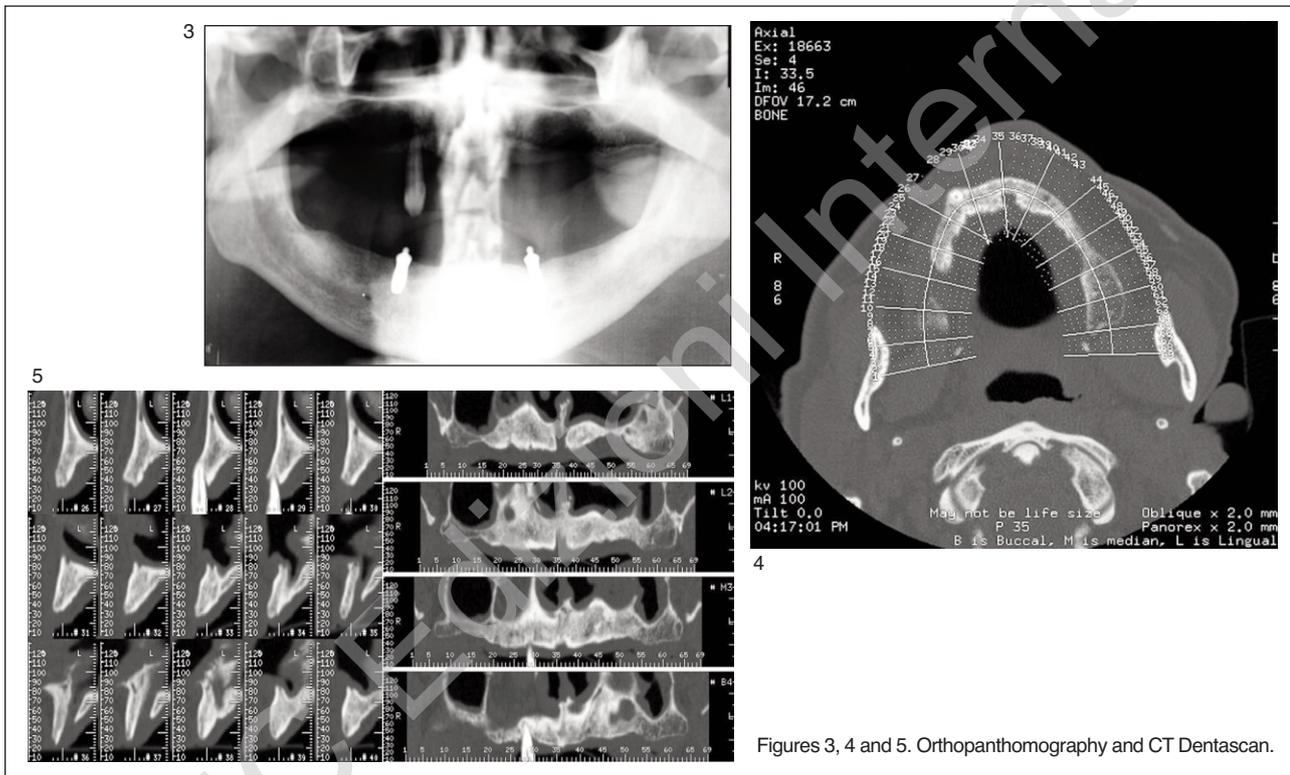
The target population consisted of subjects with partial or total edentulism with an age above 18 years who underwent head and neck irradiation as a part of the cancer treatment (Tab. 1).

For this study we recruited 5 of the 89 patients observed. The patients were three women and two men with a mean age of 64.6 years (range 54-72 years). Among the excluded patients, 9 showed evidence of osteoradionecrosis while the remaining were declared ineligible on the basis of the following parameters (Graph. 1):

- Less than 12 months elapsed after radiation treatment;
- Unfavourable cancer prognosis;
- Presence of full dentition;
- Inadequate bone support.



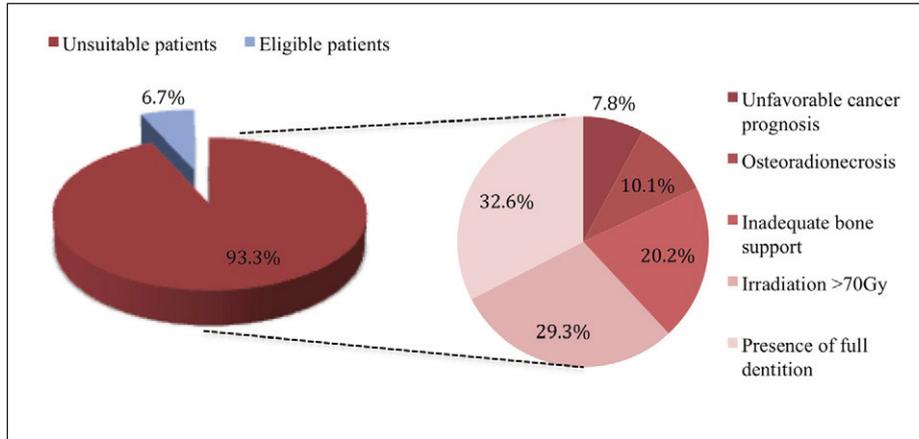
Figures 1 and 2. Intra/extraoral analysis.



Figures 3, 4 and 5. Orthopantomography and CT Dentascan.

Table 1. Inclusion criteria adopted in the trial.

INCLUSION CRITERIA
Patients with a history of head and neck cancer undergoing radiotherapy for at least 12 months
Inclusion of jaw bones in the field of radiation
Radiation dose on T≤70Gy
Favorable cancer prognosis: it's imperative that cancer is in remission
Good oral hygiene
Adequate compliance and achievable expectations
Available bone of appropriate quality and quantity, surmounted by healthy soft tissues and acceptable inter-ach distance
Absence of general medical complications and it's recommended smoking cessation and alcohol abstinence



Graphic 1. Selected patients.

Patients included in the study had a history of head and neck cancers (stage between II and IV), located in sites such as infratemporal fossa, rhino-hypo- and oropharynx (Tab. 2).

diotherapy (IMRT). All patients were subjected to irradiation aimed at both neoplastic mass (T) and the lymph nodes of the neck (N) (Graph. 3).

The treatment of the lymph nodes of the neck had cura-

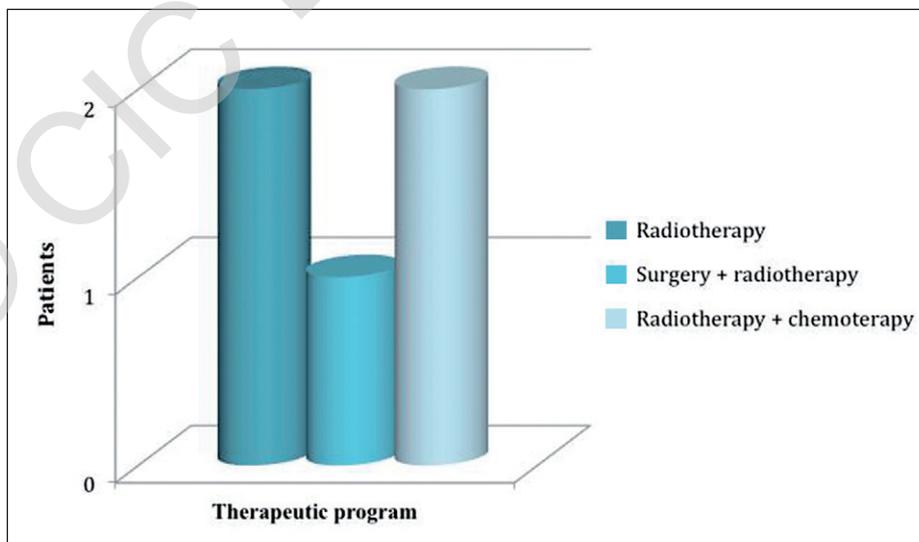
Table 2. Location and staging of tumors of recruited patients.

	CANCER LOCATION	STAGE
1	infratemporal fossa	T4 N0 M0 (stage IVA)
2	Right infratemporale region	T2 N1 M0 (stage III)
3	Hypopharynx	T2 N0 M0 (stage II)
4	Rhinopharynx	T2 N2 M0 (stage IVA)
5	Oropharynx	T4 N0 M0 (stage IVA)

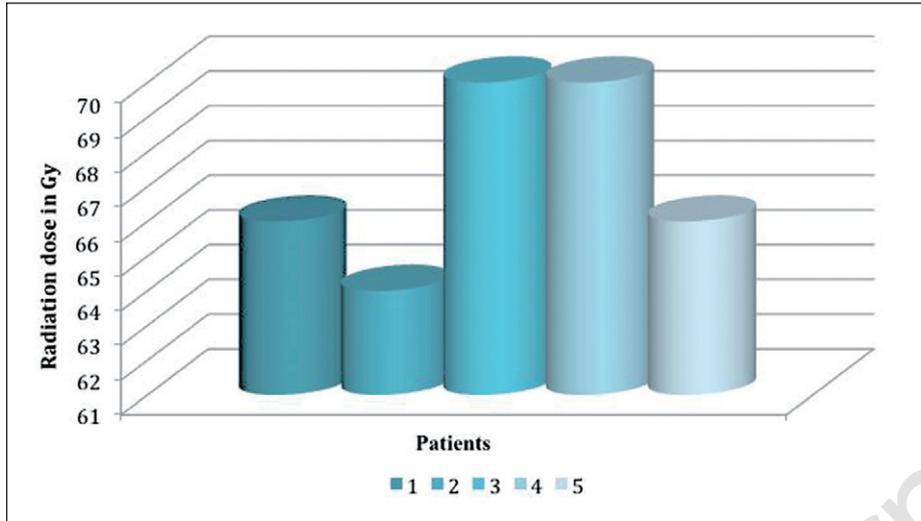
The therapeutic program proposed for the treatment of these diseases had curative purposes and consisted of an unimodal treatment (radiotherapy only) for 2 patients, and a combined treatment for the remaining (specifically, radiotherapy combined with chemotherapy for 2 subjects, and surgery combined with radiotherapy for 1 patient) (Graph. 2). All patients included in this rehabilitation protocol underwent external irradiation using intensity-modulated ra-

tive purposes for those with N>0, and prophylactic purposes for individuals with N=0.

In order to properly select the patients, it was essential to calculate the time elapsed between the ends of radiotherapy and implant surgery. Specifically, we decided that a minimum elapsed time of 12 months was a prerequisite for patients' inclusions in our study. The time elapsed between completion of radiation therapy and implant place-



Graphic 2. Cancer treatment planned for each patient.



Graphic 3.
Radiation dose aimed at T, planned for each patient.

ment was in the range of 12-18 months for two patients, and of 18-24 months for the others (Graph. 4). The rehabilitated areas concerned the maxilla in two cases and the mandible in the remaining three, for a total of 14 fixtures inserted with average length and diameter respectively equal to $(11.07 \pm 1.89, \text{mm})$ and $(3.91 \pm 0.42, \text{mm})$.

Pre-operative phase

Fixtures insertion was preceded by a pre-surgical phase for patients declared suitable for implant rehabilitation. This step was essential to define the following aspects:

- Interview with the patient in order to illustrate the treatment method and to explain both the advantages and the disadvantages concerning implant restoration and any associated hazard;
- Evaluation of the correct insertion position of implant fixtures in collaboration with the prosthetist and using data provided by DVH (Fig. 5);
- Administration of prophylactic antibiotics in order to

minimize the risk of superinfection (Amoxicillin in association with Clavulanic Acid).

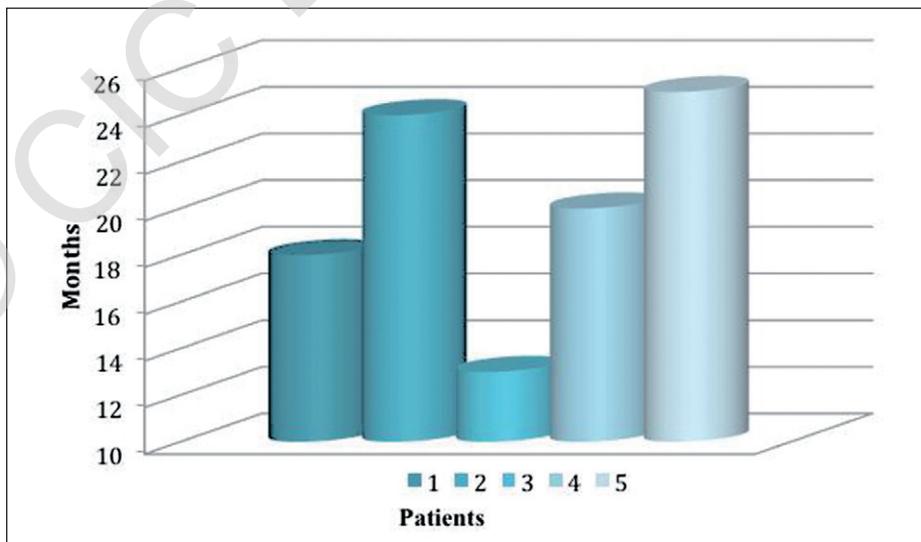
Intra-operative phase

Surgical procedures were performed after rinsing with pure chlorhexidine 0.2% for 60 seconds, and under local anesthesia with mepivacaine 2% (without epinephrine). The insertion of implant fixtures took place after a crestal incision and subsequent preparation of a mucoperiosteal flap that was used to expose the alveolar bone.

The subsequent preparation of implant sites was conducted in the least traumatic manner by means of an induction micromotor equipped with a display. The latter allowed a constant assessment of bone density thanks to a localized mechanical scanning.

Once the preparation was carried out, by means of cylindrical cutters with increasing diameter, the fixtures were placed.

All implant fixtures that were used in our protocol were characterized by a self-tapping profile that was



Graphic 4.
Time elapsed between radiotherapy and implant surgery.

helpful in order to simplify implant insertion, minimize the increase in temperature of bones and search for the maximum implant stability upon insertion. Their surface was obtained by a double chemical attack allowing to achieve an increased implant surface and higher thickness of the oxide layer. Both features facilitated the biological response. The primary stability was measured by resonance frequency analysis (Osstell).

Subsequently, the mucoperiosteal flap was closely repositioned around the implant neck and was sutured (3/0 suture) in order to obtain healing by first intention (Fig. 6).

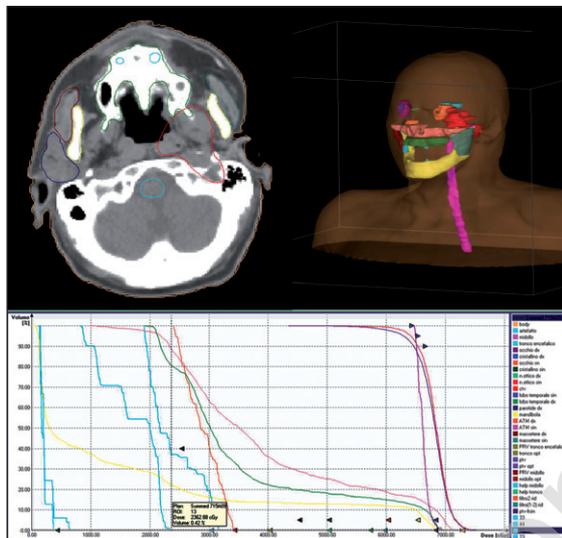


Figure 6. Contouring of the volumes of interest on CT sections; 3-D reconstruction and Dose-volume histogram (DVH).

Post-operative phase and follow-up

After verifying the achievement of hemostasis, patients were given post-operative instructions in order to obtain the best possible healing and to minimize post-surgical discomfort. The indications were as follows:

- Continuation of the antibiotic therapy;

- Assumption of analgesic drugs;
- Topical application of chlorhexidine 1% in the wound to ensure good disinfection.

Patients were encouraged to return to the Oral Clinic after one week to remove sutures and to check for the first time the status of the healing tissues.

During the periodic subsequent inspections (Fig. 6), proper healing and implant osseointegration were evaluated by referring to the first three criteria defined by Albreksson (1986), namely:

- Absence of mobility and presence of primary and secondary stability;
- Absence of peri-implant radiolucency (Figs. 7, 8);
- Absence of pain, infection, paresthesia, neuropathies.

Implant-prosthetic rehabilitation

Patients underwent a second surgical step after 4-6 months for the mandible and after 6-8 months for the maxilla.

This step was followed by prosthetic rehabilitation with metal-ceramic crowns. Providing bar overdentures performed the rehabilitation of the maxillary/mandibular edentulous bone.

Statistical analysis

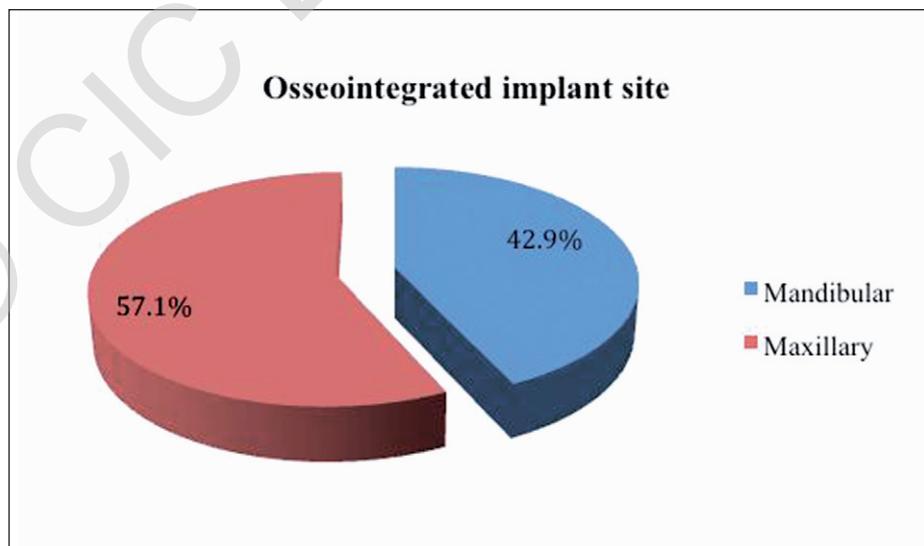
Data are presented as means \pm standard deviation. The comparison between average values was performed using the Student's *t* test (confidence interval was 95%, significance level was 0.05).

Pearson's correlation test was used to verify the presence of a linear relationship between the variables analyzed.

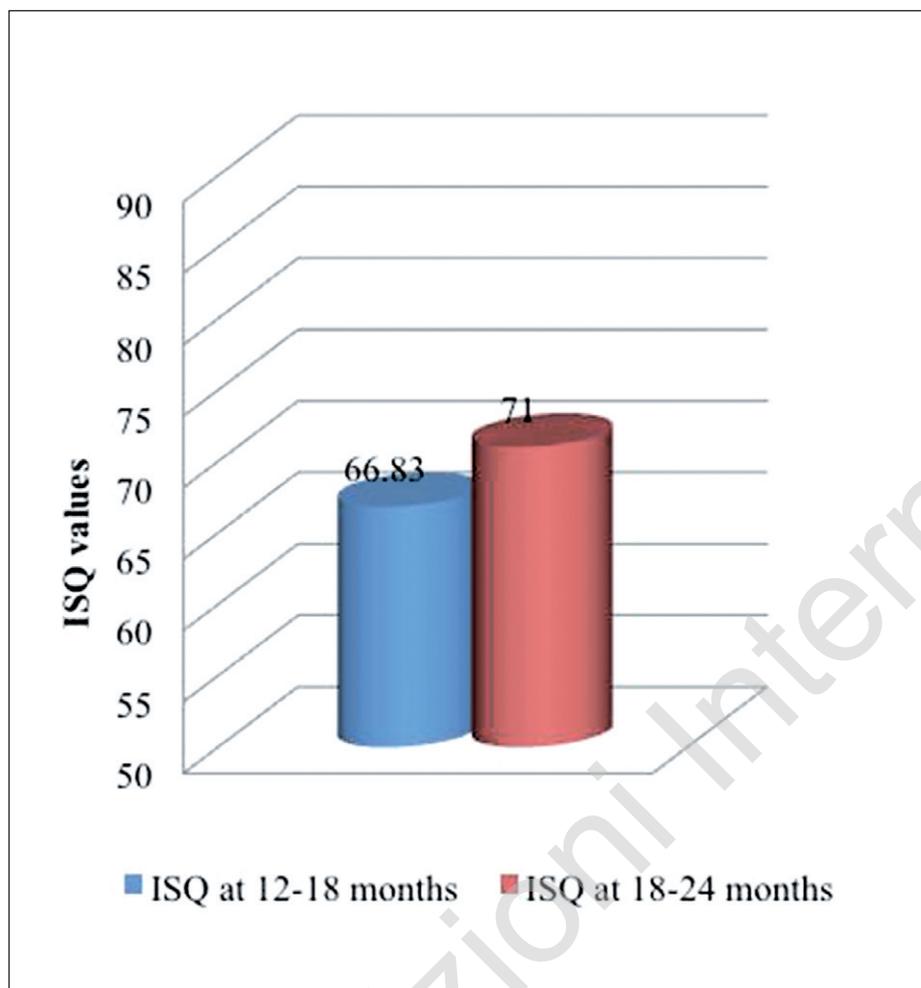
Results

The intervention was well tolerated by all patients rehabilitated in this study.

All fixtures inserted were osseointegrated and there was no evidence of ORN (Graph. 5).



Graphic 5. Implant insertion site.



Graphic 6.
ISQ values for implants
at t_1 and at t_2 .

The percentage of implant success was evaluated both clinically and radiographically. Clinical evidences of implant success were the presence of good soft tissue conditioning and the absence of pain, inflammation, paresthesia and mobility. The absence of peri-implant radiolucency was considered as radiographic evidence of implant success. The mean value and standard deviation for primary stability, calculated during the immediate post-operative phase, was 69.2 ± 6.7 (range = 59-84).

The mean value and standard deviation for ISQ of implants inserted in the period between 12-18 months (t_1) after the end of radiotherapy was not significantly different from that of implants placed in the period between 18-24 months (t_2) after the completion of irradiation (66.83 ± 5.42 vs 71 ± 7.28 $P = 0.26$; significance level was 0.05) (Graph. 6).

A difference that was not due to chance ($t = 4.15$, $P = 0.0013$) was observed between the ISQ values for implants placed in the maxilla (64.93 ± 3.76) and those placed in the mandible (74.91 ± 5.28). Therefore, there was a probability less than 0.1% that the higher ISQ values observed for the mandible implants were due to chance (Graph. 7).

We continued the analysis of ISQ values by applying Pearson's correlation test. This is useful to assess whether there is a linear relationship between two vari-

ables. In other words, it evaluates the tendency of two variables to co-vary.

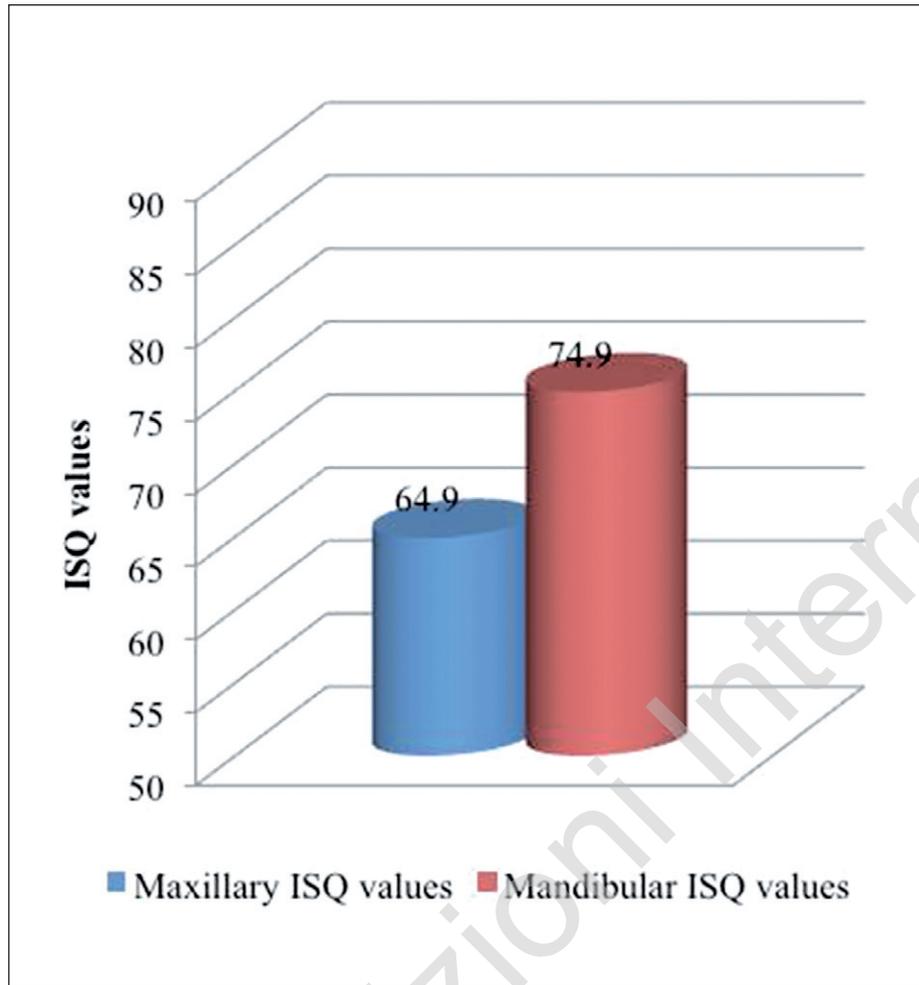
Specifically, we tested the correlation between ISQ values and the radiation doses absorbed in correspondence of the treated areas (Tab. 3, Graph. 8).

The Pearson correlation coefficient is calculated as the ratio between the covariance of the two variables and the product of their standard deviation. It allowed to evaluate whether an increase in radiation dose corresponded to a reduction in primary stability, or whether these two variables were not linearly related.

The Pearson correlation coefficient was $\rho = -0.69$. Then, we tested the significance of the obtained Pearson's coefficient, the null hypothesis (H_0) being that variables were not linearly related, or that the reduction in primary stability with an increasing radiation dose was due to chance.

The observed value of ρ , converted to $t = 4.92$, was then compared with the Student's t random variable (with $n-2$ degrees of freedom) to test the hypothesis that ρ was significantly different from zero.

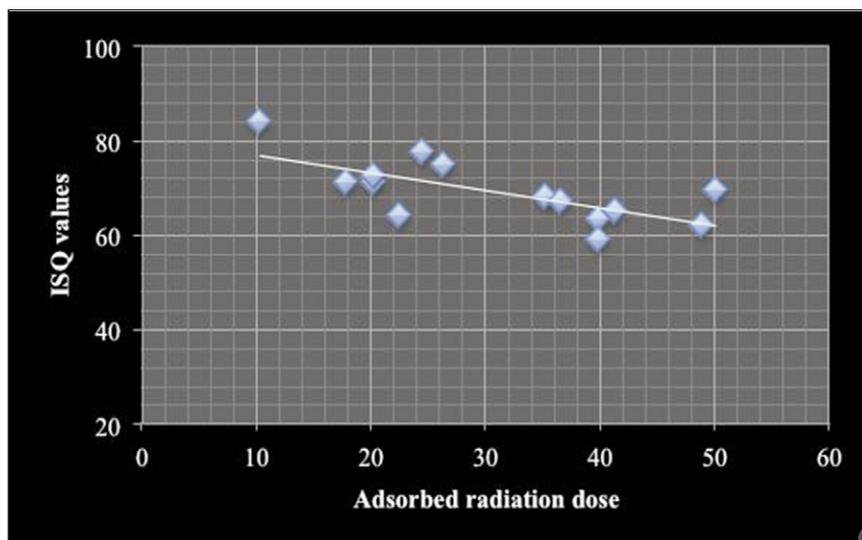
Specifically, the comparison of the obtained t value with the critical value ($t = 2.06$) allowed to reject the null hypothesis H_0 , and to accept the alternative hypothesis H_1 that the two variables were significantly correlated.



Graphic 7.
Maxillary and mandibular ISQ values.

Table 3. Data for Pearson's correlation (ISQ and radiation dose).

RADIATION DOSE	ISQ	$\chi_i - \mu_x$	$\gamma_i - \mu_y$	$(\chi_i - \mu_x)(\gamma_i - \mu_y)$	$(\chi_i - \mu_x)^2$	$(\gamma_i - \mu_y)^2$
39.76	63.5	8.38	-5,7	-47.76	70.22	32.49
17.69	71	-13.62	1,8	-24.51	185.5	3.24
39.76	59	8.38	-10,2	-85.47	70.22	104.04
22.44	64	-8.94	-5,2	-46.48	79.92	27.04
48.83	62	17.83	-7,2	-128.37	317.9	51.84
41.22	65	9.84	-4,2	-41.32	96.82	17.64
35.21	68	3.83	-1,2	-4.59	14.66	1.44
36.44	67	5.06	-2,2	-11.13	25.60	4.84
20.18	71	-11.2	1,8	-20.16	125.44	3.24
20.18	72.5	-11.2	3,3	-39.96	125.44	10.89
50.03	69.5	18.65	0,3	5.59	347.82	0.09
26.21	75	-4.69	5,8	-27.20	21.9	33.64
24.45	77.5	-6.93	8,3	-57.51	48.02	68.89
10.21	84	-20.8	14,8	-307.84	432.6	219.04



Graphic 8. Correlation between ISQ values and radiation dose.

Table 4. Data for Pearson's correlation (ISQ and implant length).

IMPLANT LENGHT	ISQ	$\chi_i - \mu_x$	$\gamma_i - \mu_y$	$(\chi_i - \mu_x)(\gamma_i - \mu_y)$	$(\chi_i - \mu_x)^2$	$(\gamma_i - \mu_y)^2$
11.5	63.5	0.43	-5.7	-2.45	0.184	32.49
11.5	71	0.43	1.8	0.77	0.184	3.24
10	59	-1.07	-10.2	10.91	1.14	104.04
10	64	-1.07	-5.2	5.56	1.14	27.04
10	62	-1.07	-7.2	7.7	1.14	51.84
10	65	-1.07	-4.2	4.49	1.14	17.64
13	68	1.93	-1.2	-2.32	3.72	1.44
13	67	1.93	-2.2	-4.24	3.72	4.84
10	71	-1.07	1.8	-1.92	1.14	3.24
10	72.5	-1.07	3.3	-3.53	1.14	10.89
11.5	69.5	0.43	0.3	0.12	0.184	0.09
11.5	75	0.43	5.8	2.49	0.184	33.64
11.5	77.5	0.43	8.3	3.56	0.184	68.89
11.5	84	0.43	14.8	6.36	0.184	219.04

The Pearson's correlation coefficient was also applied to test the relation between ISQ values and two other parameters of interest, i.e. length and diameter of implant fixtures.

In the first case, Pearson's index was 0.29, indicating a low correlation between ISQ and length of implant fixtures (Tab. 4, Graph. 9).

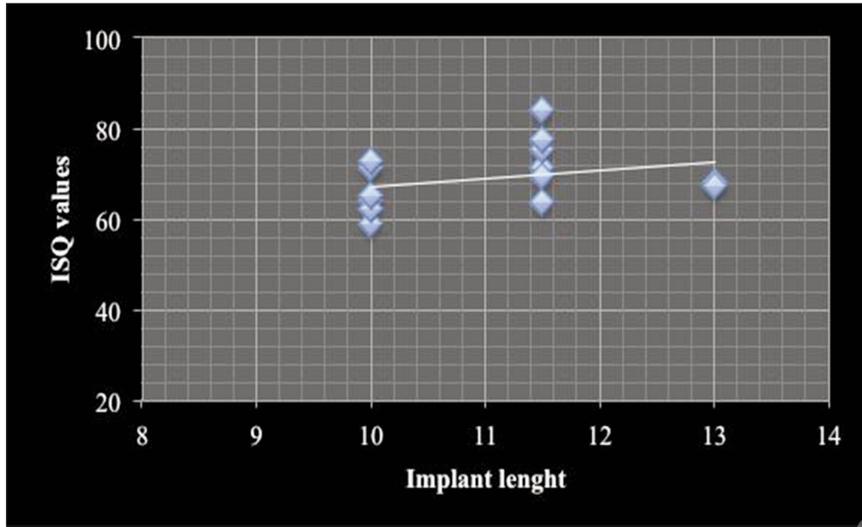
As previously, we tested the significance of the Pearson's coefficient to verify that it was actually different from zero. The obtained *t* value (1.81) did not exceed the critical value (2.06), leading us to accept the null hypothesis *H*₀, i.e. that the two variables were not significantly correlated.

In the second case Pearson's coefficient was 0.23, indi-

cating the existence of a low correlation between ISQ and the diameter of implant fixtures (Tab. 5, Graph. 10).

Again, we found that the obtained *t* value (1.77) did not exceed the critical value (2.06), meaning that even this correlation was not significant.

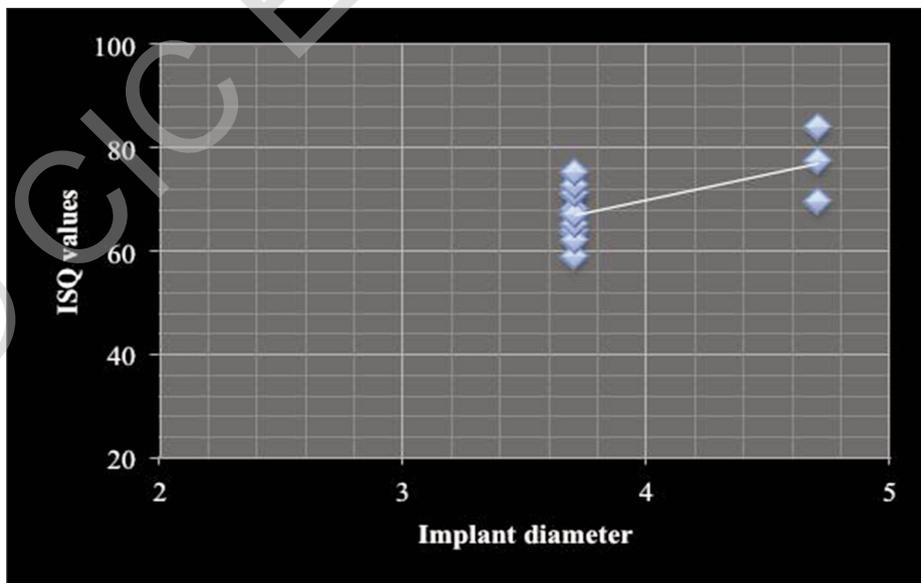
Mean value ± standard deviation for crestal bone resorption, calculated for the whole implant, was 0.23 ± 0.11 mm. Crestal bone resorption was significantly higher (*t* = 2.28, *P* = 0.03) in maxillary implants (0.275 ± 0.100, mm) than in mandibular ones (0.183 ± 0.100, mm). Nevertheless, there was no significant difference between crestal bone resorption at *t*₁ and crestal bone resorption at *t*₂ (0.208 ± 0.100, mm Vs 0.25 ± 0.12, mm; *t* = 0.94, *P* = 0.35) (Graphs. 11,12).



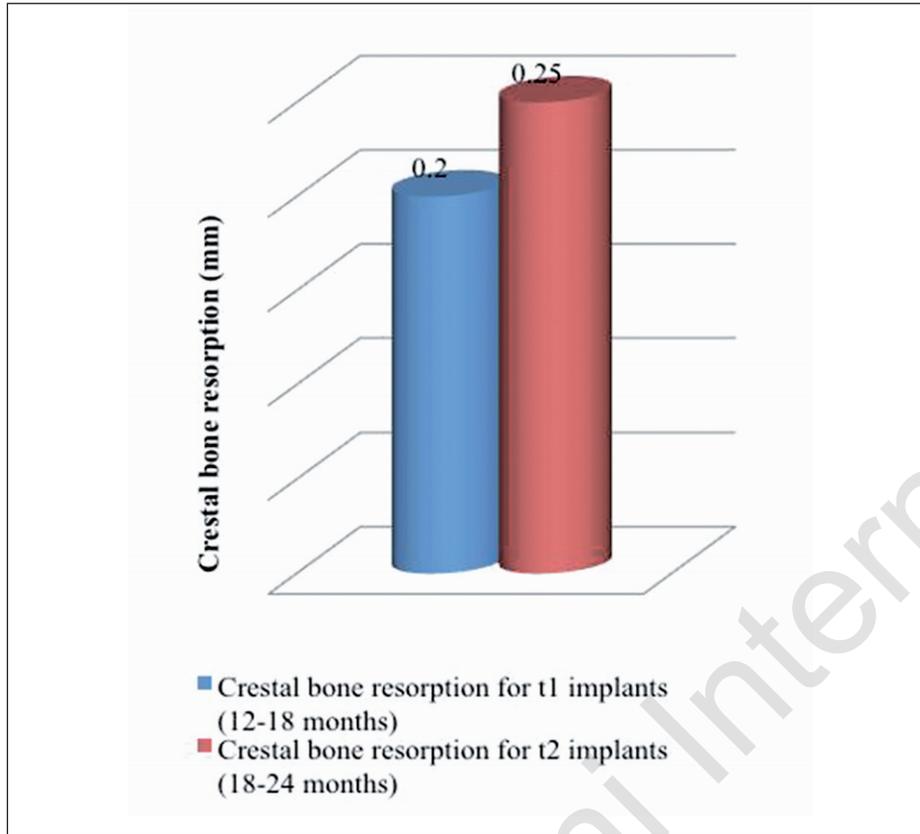
Graphic 9. Correlation between ISQ values and implant length.

Table 5. Data for Pearson's correlation (ISQ and implant diameter).

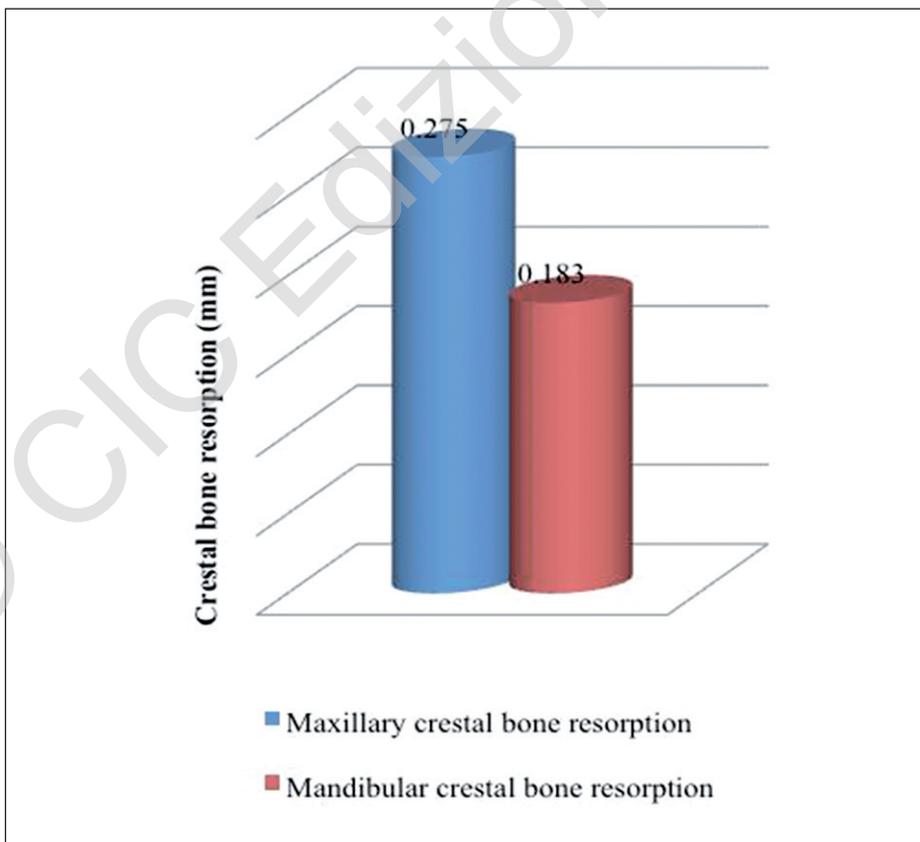
IMPLANT DIAMETER	ISQ	$\chi_i - \mu_x$	$\gamma_i - \mu_y$	$(\chi_i - \mu_x)(\gamma_i - \mu_y)$	$(\chi_i - \mu_x)^2$	$(\gamma_i - \mu_y)^2$
3.7	63.5	-0.21	-5.7	1.19	13.69	32.49
3.7	71	-0.21	1.8	-0.37	13.69	3.24
3.7	59	-0.21	-10.2	2.14	13.69	104.04
3.7	64	-0.21	-5.2	1.09	13.69	27.04
3.7	62	-0.21	-7.2	1.51	13.69	51.84
3.7	65	-0.21	-4.2	0.88	13.69	17.64
3.7	68	-0.21	-1.2	0.25	13.69	1.44
3.7	67	-0.21	-2.2	0.46	13.69	4.84
3.7	71	-0.21	1.8	-0.37	13.69	3.24
3.7	72.5	-0.21	3.3	-0.69	13.69	10.89
4.7	69.5	0.79	0.3	0.23	22.09	0.09
3.7	75	-0.21	5.8	-1.21	13.69	33.64
4.7	77.5	0.79	8.3	6.55	22.09	68.89
4.7	84	0.79	14.8	11.69	22.09	219.04



Graphic 10. Correlation between ISQ values and implant diameter.



Graphic 11. Crestal bone resorption for implants at t_1 and at t_2 .



Graphic 12. Maxillary and mandibular crestal bone resorption.

Discussion

Radiation causes a reduction in the number of osteogenic cells, alterations of cytokine capacity (TGF- β 1), delays and damages in the process of bone remodeling (22).

Cortical and trabecular bone remodeling are thus altered, although the extent to which this process is irreversible varies greatly at the individual level and depends also on qualitative and quantitative cellular changes.

Osseointegration is often possible, although failure rate is higher in irradiated bones than in non-irradiated ones.

Some authors suggest that the risk for implant loss in irradiated bones is two or three times greater than in non-irradiated bones (23). Data found in the literature (23,24) regarding the success rate of endosseous implants in irradiated patients suggest that it ranges from 75% to 100%, and this variability is due to several factors, including radiation dose.

The main purpose of this study was to minimize the impact of radiation dose by evaluating in advance the most suitable site for implant insertion on the basis of the mean absorbed radiation dose.

The assessment of the most suitable sites for implant insertion was based on inspection of DVH. The latter were developed by a team of experts in medical physics and radiotherapists, following contouring of the volumes of interest that was carried out by dentists.

In the previous literature there are no indications of a clear cut-off value for absorbed radiation dose that would be linked to implant failure, or of any increasing trend in failure linked to RT dose (25).

Therefore, our choice fell on the areas that were subjected to irradiation lower than 55-60 Gy, i.e. a value associated with a greater tendency for implant fibrous-encapsulation (5,8).

In the present study, the percentage of osseointegration was 100%, which confirms the usefulness of the adopted technique.

Implant success was not affected by variables such as timing of placement, insertion site and adsorbed dose.

It was not possible to state the same with respect to the recorded values for primary stability (69.2 ± 6.7). In light of our achievements in terms of osseointegration, these values could be considered as a positive prognostic factor for implant success. The difference in ISQ between implants inserted at t_1 (12-18 months) and at t_2 (18-24 months) after the completion of irradiation was not statistically significant. This reflected the fact that timing of insertion did not hinder the achievement of primary stability for implants placed in our study.

However, the difference between primary stability of implants placed in the maxilla and of implants placed in the mandible was statistically significant and hardly attributable to chance (probability estimated at 0.1%).

Therefore, it can be concluded that both quality and type of bone have an influence on the initial bone-fixture contact. In particular, implants inserted in the maxilla show higher primary stability than implants placed in the mandible.

With regard to adsorbed radiation dose, although in the literature there is no positive association between radiation

dosage and rate of implant failure, this study detected a significant and negative correlation between radiation dose and ISQ values. The Pearson's correlation coefficient calculated for these two variables was -0.69, indicating a significant negative association between these variables. This result suggests that an increase in radiation dose corresponds to a decrease in primary stability. Moreover, it should also be considered as a suggestion to adopt protocols for implant placement that take into account the adsorbed radiation dose in the areas that must be treated. Based on our data, the linear relationship between ISQ and implant length and diameter were weak. Actually, the Pearson's correlation coefficients were respectively $r = 0,29$ and $r = 0,23$, indicating positive low correlations that were not statistically significant and thus forced us to reject the alternative hypothesis H_1 . As a consequence, we suggest that a good primary stability and consequently an appropriate osseointegration could be obtained irrespective of implants' length and diameter.

Another parameter investigated in our study regards the survival and predictability of a particular type of implant characterized by wrinkled microgeometry, obtained by means of double chemical attack and increased layer of TiO_2 . It is known that surface properties of dental implants, such as topography and chemistry, are relevant with respect to the osseointegration process because they influence bones interaction, protein adsorption and cellular activity at the surface. The implants with a rough surface, such as those tested in our study, usually show a higher rate of bone-to-implant contact than those with smooth surface (25). Osseointegration rate and ISQ values obtained in this study confirmed these assertions.

Finally, the results concerning the crestal bone resorption could be attributed to the neck design of implant fixtures used, characterized by microspires that favour the preservation of marginal bones during the phase of osseointegration.

Conclusions

The restoration of function after oncologic surgery and radiotherapy of the oral cavity represents one of the major challenges for head and neck oncology.

The realization of prostheses on osseointegrated implants is considered one of the best ways to restore the aesthetic and functional status of patients, thereby significantly improving their quality of life.

Guiding implantology on the basis of the absorbed irradiation dose in the site to be rehabilitated can lead both to an increase in implant survival into irradiated bone tissues and to a reduction in the incidence of ORN. Thus, we understand that a close collaboration between dentists and radiotherapists is urgently needed in the context of medical skills integration. Dentists have to assist the radiotherapists in the pre-radiation therapy phase, in order to reduce the incidence and severity of complications resulting from the administered treatment, whereas cooperation between the two specialists is also crucial in the post-radiation rehabilitation phase.

Both a larger sample size and the development of long-term prospective studies are necessary in order

to confirm our results and to validate the described method.

References

1. Cuesta-Gil M, Ochandiano Caicoya S, Riba-Garcia F, Duarte Ruiz B, Navarro Cuellar C, Navarro Vila C. Oral rehabilitation with osseointegrated implants in oncologic patients. *J Oral Maxillofac Surg*, 2009;67(11):2485-96.
2. Buddula A, Assad DA, Salinas TJ, Garces YI, Volz JE, Wealer AL. Survival of turned and roughened dental implants in irradiated head and neck cancer patients: a retrospective analysis. *J Prosthetic Dentistry*, 2011;106(5):290-6.
3. Heydecke G, Locker D, Awad MA, Lund JP, Feine JS. Oral and general health-related quality of life with conventional and implant dentures. *Community Dent Oral Epidemiol*, 2003;31(3):161-8.
4. Keller E, Tolman E, Zuck SL, Eckert SE. Mandibular endosseous implants and autogenous bone grafting in irradiated tissue: a 10-year retrospective study. *Int J Oral Maxillofac Implants* 1997;12(6):800-13.
5. Buddula A, Assad DA, Salinas TJ, Garces YI, Volz JE, Wealer AL. Survival of dental implants in irradiated head and neck cancers patients: a retrospective analysis. *Clin Implant Dent Relat Res*, 2011;22(5):644-8.
6. Parliament M, Alidrisi M, Munroe M, Wolfaardt J, Scrimger R, Thompson H et al. Implications of radiation dosimetry of the mandible in patients with carcinomas of the oral cavity and nasopharynx treated with intensity modulated radiation therapy. *Int J Oral Maxillofac Surg*, 2005;34(2):360-6.
7. Colella G, Cannavale R, Pentenero M, Gandolfo S. Oral implants in radiated patients: a systematic reviews. *Int J Oral Maxillofac Implants*, 2007;22(4):616-22.
8. Vish L.L, van Waas MA, Schmitz PI, Levendag PC. A clinical evaluation of implants in irradiated oral cancer patients. *J Dent Res*, 2002;81(12):865-59.
9. Nguyen NP, Vock J, Chi A, Ewell L, Vos P, Mills M et al. Effectiveness of intensity-modulated and image-guided radiotherapy to spare the mandible from excessive radiation. *Oral Oncol*, 2012;48(7):653-7.
10. Goldwaser BR, Chuang SK, Kaban LB, August M. Risk factor assessment for the development of osteoradionecrosis. *J Oral Maxillofac Surg*, 2007;65(11):2311-6.
11. Chopra S, Damdar D, Tulunay U, Chen G, Peshek B, Marunick M et al. Factors predictive of severity of osteoradionecrosis of the mandible. *Head Neck*, 2011;33(11):1600-5.
12. Ben David MA, Diamante M, Radawsky JD, Vineberg KA, Stroup C, Murdoch-Kinch CA et al. Lack of osteoradionecrosis of the mandible after intensity-modulated radiation therapy for head and neck cancer: likely contributions of both dental care and improved dose distribution. *Int J Radiat Oncol Biol Phys*, 2007;68(2):396-402.
13. Thompson S. Intensity-modulated radiation therapy (IMRT): a clinical reality for cancer treatment "any fool can understand this". *Br J Radiol*, 2005;78:564-572.
14. Verdonck HW, de Jong JM, Granzier ME, Nieman FH, de Baat C, Stoeltinga PJ. Intensity-modulated radiation therapy for oropharyngeal cancer: radiation dosage constraint at the anterior mandible. *Oral Oncol*, 2009;45(6):511-4.
15. Maingon P, Truc G, Peignaux K, Créhange G, Lagneau E. Radiothérapie par modulation d'intensité. *Oncologie*, 2007;9:417-21.
16. Marx RE, Johnson RP. Studies in the radiobiology of osteoradionecrosis and their clinical significance. *Oral Surg Oral Med Oral Pathol*, 1987; 64(4):379-90.
17. Meraw SJ, Reeve CM. Dental considerations and treatment of the oncology patient receiving radiation therapy. *J Am Dent Assoc*, 1998;129(2):201-5.
18. Harrison JS, Stratemann S, Redding SW. Dental implants for patients who have had radiation treatment for head and neck cancer. *Spec Care Dentist*, 2003;23(6):223-9.
19. Hide S, Kopp S, Gundlach K, Kostantinovic VS. Effects of radiation therapy on craniofacial and dental implants: a review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 2009;107(1):56-65.
20. Granström G, Bergstrom, K.; Tjell-strom, A.; Branemark, P. A detailed analysis of titanium implants lost in irradiated tissues. *Int J Oral Maxillofac Implants* 1994;9:653-662.
21. Watzinger F, Ewers R, Henninger A, Sudasch G, Babka A, Woelfl G. Endosteal implants in the irradiated lower jaw. *J Craniomaxillofac Surg*, 1996;24(4):237-44.
22. Jegoux F, Malard O, Goyenville E, Aguado E, Daculsi G. Radiation effects of bone healing and reconstruction: interpretation of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol and Endod*, 2010;109(2):173-84.
23. Moy PK, Medina D, Shetty V, Aghaloo TL. Dental implant failure rates and associated risk factors. *International J Oral Maxillofac Implants*, 2005;20(4):569-77.
24. Nelson K, Heberer S, Glatzer C. Survival analysis and clinical evaluation of implant-retained prostheses in oral cancer resection patients over a mean follow-up period of 10 years. *J Prosthet Dent*, 2007;98(5):405-10.
25. Heberer S, Kilic S, Hossamo J, Raguse JD, Nelson K. Rehabilitation of irradiated patients with modified and conventional sandblasted acid-etched implants: preliminary results of a split-mouth study. *Clin Oral Implants Res*, 2011;22(5):546-551.