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LETTER TO THE EDITOR

Orthodontic appliances in patients allergic to nickel

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To the Editor,

In recent years there has been an increase in the incidence of allergies, contact dermatitis and sensibilization to nickel and resin (PMMA) in patients wearing orthodontic appliances (1). The use of orthodontic resins and stainless steel devices requires a long permanence in the oral cavity, direct contact with tissues and therefore requires their proper adaptation to the biological environment (2-4). Nickel is a metal contained in stainless steel while resins are polymers obtained by the addition or condensation of substances ad high molecular weight; both are used for the realization of the most orthodontic appliances (3).

The biocompatibility of materials in orthodontics represents an emerging problem, especially for the spread in the population of fashion piercing that can cause an increase in sensitization to nickel. The most used metals for the production of orthodontic appliances are the 18/8 stainless steels, containing 18% of chromium and 8% of nickel, and the super-elastic alloy NiTi, containing 50% of nickel. Both nickel and chromium can cause hypersensitivity that usually occurs with widespread itching, eczema, vesicles, hives and flaking. In severe cases, respiratory symptoms may be detected, such as asthma and gastrointestinal disorders. Nickel is an ubiquitous substance that can be found in ornamental metal objects, especially in jewelry, kitchen utensils, cosmetic products, detergents, and hair dyes, as well as in numerous foods.

The incidence of allergies to metals is found in 1% of men and in 10% of women. Piercing, on the ears or on other areas of the body, is considered one of the major trigger factors of this sensitization. It has been shown that once hypersensitivity occurs, all surfaces of the oral mucosa may be involved. The diagnosis of allergy is made with a skin test (patch test) which consists of placing on the skin a patch containing calibrated slowly-released quantities of the material to be tested for sensitivity. The test is positive if, on the removal of the patch, there are red areas with itchy vesicles.

These issues have led to the search for alternative materials for the realization of orthodontic appliances. The purpose of this work is to show the use of titanium orthopedic devices in patients with allergy to resin and nickel. Furthermore, the aim is to underline the resolution of problems, such as stomatitis and perilabial dermatitis, that can occur with the use of traditional acrylic resin and steel tools.

MATERIALS AND METHODS

Sixty patients from the Department of Orthodontics of the IRCCS of Milan, who needed a first orthognatodontic

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visit and orthopedic therapy (such as rapid palatal expander and morfocorrector), were recruited. Informed consent was given by all patients or, if minors, by their parents or legal representatives, before being recruited in this work. Each patient had undergone a dental, dermatological anamnesis and a two patch test to check hypersensitivity to materials. The first test was performed before the treatment phase while the second one year later.

The first test carried out highlighted the nickel sensitivity in 8 patients, 2 males and 6 females, showing sexual dimorphism. The second patch test confirmed the results of the previous test, highlighting 37 positivity, again emphasizing the sexual dimorphism with a prevalence of nickel sensitization much higher in women (25) than in men. The familiarity of the patients who presented positivity at the first test was assessed: 7 out of 8 patients presented a familiar anamnesis positivity. Of the 37 patients who were positive at the second test, 34 presented positive familiarity. A significant correlation between familiarity atopy and nickel sensitization was therefore identified. In patients with this problem, two devices were tested: the morphocorrector and the rapid palate expander, both constructed entirely in titanium.

The construction phases of the device were:

• taking silicone impressions with double impression technique and model development;

• duplication of models in refractory for titanium;

• waxing for the carrying out of mergers;

• coating;

• construction of the merger;

• printing and polishing of the structure;

• laser welding, titanium mergering.

The master model, obtained from the development of impressions, was duplicated and poured using the specific Ultra type coating with "spiniello", that avoids the formation of Alfacase (impurities present in the fusions). The smelter with the Rematitan Dentaurum system was used to obtain mechanically valid structures with full biocompatibility features. On the model, an extention of 1 mm was constructed in the anterior and lateral vestibular fornix, depending on the prescription of the morphocorrector (I, II, III Class).

The models were mounted in an articulator with average values and we proceeded with the waxing phase on the vestibular fornix, which were made of titanium, similarly to the traditional processing for a resin and steel morphocorrector. The 1.5-mm thick preformed cylindrical wax was modeled for the construction of the palatal bar; 1.2mm-thick preformed wax was used for the the occlusal stops on the molars, for the upper vestibular arch and the activation loops in the canine area, for the inferior vestibular arch, for the connectors, for the activation loops between the lower anterior vestibular shields and the lateral vestibular shields. Finally, the anterior vestibular "pelotes" were modeled. Once the modeling process was completed, the wax structures were removed and with the preparation phase for the fusion was started.

The coating was carried out by applying a plastic support cone to the primary modeling. The casting cylinder was placed and fixed on the appropriate support where the coating mass was cast (Ultra type). After 2 hours from the setting and hardening, the cylinder was put in the preheating furnace.

The electronically programmed Rematitan smelter machine was used for titanium processing. The pure titanium ingot was put in a copper crucible. The oxygen was completely aspirated and replaced with type C Argon gas. The melting point of the titanium was reached through a voltaic arc at approximately 1700°C. The casting by pressure drop occurs in hundredths of a second with a remarkable temperature changing. A first radiographical check was made of the fused structure for any porosity that could weak the different parts, failing or fracturing during the orthodontic treatment. Subsequently, the printing, polishing, cleaning and finishing of titanium structures was initiated. A second radiographic control of the melted structure was then carried out.

The morphocorrector was used in patients with skeletal class II and III open bite disorder. Construction of the circuit breaker was made with a screw made entirely of titanium (Dentaurum), the Rematitan fusion system and the laser welding technology (Dentaurum Desktop) to match the screw in titanium with the titanium arms (5, 6). The use of laser welding is essential to obtain a monometallic structure that avoids electro-galvanic effects and gives adequate mechanical characteristics.

The critical area for unloading orthopedic forces, applied on the upper maxilla, is the joining area between the titanium arms and the titanium screw. Currently, titanium bands are not available on the market (5), and for this reason, crowns in melted titanium were used to anchor the expander to the dental elements. For the production

phases of rapid palatal expander, the model was obtained from the impression made of silicone materials. Then the model was duplicated and poured with the material used as a refractory for titanium castings. On this model a wax-up of all structures was made. After placing a spacer paint on the molars, we modeled on them the caps and, with the use of waxes for casting channels, we modeled the joint arms to the screw and the extension arms in the canine area. Finally we positioned the screw adapting waxes in the areas where subsequently we made the

At the end of this process, the preparation of the fusion was carried out, channeling all the waxes with the main casting channel. The model was inserted in refractory with all the waxes in the casting box. The dryer phase was made and, subsequently, the fusion. The structures obtained were roughed down. The surfaces were uniformed and satinized to complete the polishing of the structure. The arms and the screw of junction in titanium were welded onto the model obtained. The rapid palatal expander was cemented in the oral cavity using an orthodontic glass-ionomeric cement and the caps and the extension arms have been fixed with a light-curing composite. Activations were carried out two times a day for 2 weeks to obtain an orthopedic action on the maxilla with the restoration of the nasal respiratory function (6, 7). At the end of these 2 weeks, the central screw was locked with a titanium welding wire. The contention phase lasted for 6 months.

RESULTS

The structure of both the morphocorrector and the rapid palatal expander showed high resistance, in particular in moments of maximum mechanical stress, i.e., during the activations. No breakages or cracks occurred in the castings. There was no allergic reaction in the patients treated, confirming the hypoallergenic properties of titanium. In the sensitized patients there was the total regression of the symptomatology, and in subjects with a history of nickel allergy there was no allergic reaction.

DISCUSSION

It is already known that the phenomenon of corrosion inside the oral cavity is the basis of allergies. This event determines the release of ions which are the allergens that could activate the cell-mediated reaction mechanisms responsible for allergic manifestations. The biocompatibility of the materials is directly dependent on the corrosive phenomenon (2, 3). The opinion of the Authors is that if an alloy or a metal does not allow the release of ions, it will not have an action of damage or destruction on the cellular DNA. The oxidation state is very important for the reactivity of the ions, which can also confer a carcinogenic action. Nickel and PMMA are among the most common allergens in orthodontics, which are the main components of orthodontic appliances (8).

Titanium is a light noble metal with a low thermal conductivity. The stability of this metal to corrosion (biocompatibility) is linked to the ability to form oxides on its surface, reacting with oxygen. This process creates a film that gives chemical inertia to the material, self-limiting the oxidation process (passivation). Sensitization to nickel occurs in about 30% of the population. Often this phenomenon goes unnoticed because there is a certain tolerance threshold in a large number of patients, who often do not show any apparent symptoms. However, the inflammatory phenomena are actually due to cell-mediated reactions and therefore to phenomena of sensitization to nickel (9-12). This could be due to the fact that the amount of nickel needed to determine a hypersensitive reaction is different for each subject, furthermore, there can be a protective action by salivary secretions and crevicular fluids. Titanium allows to create appliances with good mechanical strength, light and totally hypoallergenic.

Resins are polymers obtained by addition or condensation of high molecular weight substances. Among the acrylic resins, the most used is methyl-methacrylate. Finished products rarely cause allergies that can arise through contact with not completely polymerized resins, which are able to release monomers derived from the incomplete processing of the product. The substance that could be responsible for the allergenic power seems to be the excess of methacrylate residual monomer that remains on the surface because of an incomplete polymerization of the autopolimerizing acrylic resins or because of incorrect procedures in thermopolymerizing resins.

In the present study, light-curing resins were used but, in sensitized subjects, there was no improvement or disappearance of allergic reactions. Allergic reactions appear 24-48 hours after the exposure to the allergen factor and they can be located in the contact areas (primary lesions) or extend into nearby areas or appear at long-distance (secondary lesions). The titanium devices used gave excellent results, thanks to their property of forming superficial oxides, blocking the oxidation phenomena and, therefore, the corrosion phenomena.

Today, the difficulties of processing titanium-cast structures have been solved by new laboratory techniques, such as the Rematitan Dentaurum system, that allows to obtain mechanically valid structures with biocompatibility characteristics. The results of this study allow us to confirm the anallergic property of titanium and propose it as an alternative material in subjects with a history of allergy to metals and resins.

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Extraction socket healing in leukemic patients: a preliminary radiographic evaluation

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To the Editor,

Hematopoietic stem cell transplantation (HSCT) is an essential treatment for patients with malignant hematological diseases such as acute and chronic leukemias (1-3). Three chemotherapy cycles are routinely used to prepare for the treatment. Autologous or allogeneic bone marrow transplantation is recommended to consolidate remission, and transplantation has to be performed within a few months (1). An infection during chemotherapy for hematologic malignancy can be life-threatening, therefore the elimination of odontogenic foci is recommended before initiation of chemotherapy (1), however complete elimination is sometimes impossible because of time limitations and a problematic lack of criteria for deciding appropriate dental management before myelosuppressive chemotherapy (2, 4).

Tooth extraction is recommended for severe dental diseases or when conservative treatments are not completely predictive. Such pre-HSCT dental treatments are anticipated to decrease the risk of local and systemic odontogenic infections during patient immunosuppression. Some studies have established dental intervention protocols and analyzed sequelae and complications for patients with hematologic malignancy, including indications and contraindications for dental extraction (1, 3, 5). No information, however, is currently available on the alveolar healing process after tooth extraction in acute myelogenous leukemia (AML)-patients. Only the healing of the surgical wound (socket healing, in this case) is a guarantee of avoiding side effects and complications.

The aim of this preliminary study is to evaluate, by means of subtractive radiology, the alveolar healing of extraction sockets in AML patients. The study is aimed to establish whether, in leukemic patients who are candidates to HSTC, bone tissue healing is compromised after tooth extraction in comparison with healthy individuals and to define the ideal timing of surgical intervention in relation to leukemic therapy.

MATERIALS AND METHODS

Screening

This study was performed at the Unit of Dentistry and Oral-Maxillofacial Surgery of Modena University Hospital from January 2006 to December 2008. All the

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selected patients signed the informed consent detailing all procedures of the treatment, as requested by Helsinki protocols.

The study was a two-branch design: the control cohort (CC) considered healthy patients, particularly ruling out bone disease (6, 7), whilst the test cohort (TC) considered ALM-affected patients. Moreover, they had to satisfy the following inclusion criteria: over 18 years of age, non-pregnant or lactating, non-smokers, not undergoing antibiotic or anti-inflammatory therapy and no recent suffering from relevant affective symptoms (e.g. anxiety, depression) or personality disorders in lifetime medical history (8). In particular, the study concerned only mandibular monoradicular teeth. Sites needing two or more adjacent extractions were excluded. The full-mouth plaque score (FMPS) and the full-mouth bleeding score (FMBS), had to be maintained ≤20% (measured at 4 aspects per tooth) in all the patients.

For the CC, healthy patients were chosen from a list of patients who underwent at least one tooth extraction that matched the criteria of selection. CC patients having at least one periodontal hopeless tooth were grouped as CC1, while patients needing at least one dental root extraction were grouped as CC2. The TC comprised patients suffering from AML diagnosed at the Division of Haematology and Hemopoietic Stem Cell Transplant Program and assigned to the Section of Dentistry and Maxillofacial Surgery, University of Modena and Reggio Emilia, for the evaluation of dental status of all patients. The screening consisted of clinical examination of the hard and soft oral tissues and radiographic survey, including periapical films for symptomatic teeth. The extraction of teeth that could represent a source of septic complication where any other less aggressive treatment would not be predictable, was performed (1, 3, 5).

Operative protocol

The same team carried out all clinical evaluations during the pre-surgical, surgical and post-surgical phases. Descriptive criteria were used to classify the initial appearance of tissue changes during the therapy and final healing results (9).

Haematologists generally referred TC patients to the dental and oral- maxillofacial unit for pre-therapeutic assessment of their dental condition and provided information about diagnosis, regimen and schedule of chemotherapy, myelosuppression grade of chemotherapy, and other details (1-3, 5). Alveolar sites were clinically and radiographically (orthopantomography and periapical radiographs) examined.

A complete radiographic study was performed before surgical interventions by the surgical protocol. In particular, periapical radiographs were taken with standardized projection geometry using a Rinn individual film holder by a single clinical examiner. An acrylic stent was prepared for each patient from chalk models and, after tooth extraction, in correspondence to the teeth that would be extracted a radiopaque rod of well-known length was inserted in the stent. The rod represented as a benchmark index to evaluate the baseline alveolar width and depth dimension and then regenerative activity. The film holder was particularized by an adaptation. The biteblock of the Rinn film holder was embedded in a double bite impression consisting of a silicon bite. This device always permitted to cog in the same manner the film holder, allowing reproducible, comparable and reliable evaluations of periapical radiographs. Immediately after the extraction, a baseline periapical radiograph was taken, scanned and digitalized using a Polaroid SprintScan 35-mm slide scanner connected to a PC. A line joining the highest bone crest, mesial and distal to the socket (taken from the sagittal projection of each periapical radiograph), was plotted for each periapical post-extractive radiograph after the digitalization. As a result, the plotted line had a particular length, slope and, primarily, a fixed spatial relation with the rod (and the stent) that permitted to replace it in exactly the same position in the following periapical radiographs. The measure between the more coronal radiolucent part of the socket and the plotted line following the axial plane of the socket (Fig, 1) was recorded on each post-surgical radiograph. The data were considered both numerically and as a percentage ratio of the alveolar whole depth and surface (100% immediately after surgery). In particular, percentage ratios were used to perform a comparison among the cohorts at following times from immediate post-surgical phase.

Immediately after tooth or residual root extraction (T0-baseline), 15 days after (T1), 30 days after (T2) and 45 days after (T3), a periapical radiograph was taken using the acrylic stent and film holder individually prepared for each patient. The results from periapical radiographs following the post-surgical phase were obtained in the same way as previously described. The landmark was

represented by the rod and, consequently, by the plotted line (the line joining the highest bone crest, mesial and distal to the socket) and the more coronal radiolucent part of the socket on the way to recovery, always following the socket axial plane.

Alignment of the post-surgical baseline (T0) and the following (T1, T2 and T3) images was made using the aforesaid references. Following selection of the socket area for all the patients in the 3 groups (CC1, CC2 and TC) on the images, the T1-image was subtracted from the corresponding T0 image, the T2 from T1 and T0, and the T3 image from T2, T1 and T0 using an image analysis software (ImageJ-NIH). Changes between images were depicted as a lightened area for an increase in alveolar bone mass. The resulting lightened areas were measured (using ImageJ) and reported as numerical data and calculated the percentage value with respect to that of the entire socket (at T0). Statistical comparisons were performed on linear and area recorded data.

In T0 images, the residual socket depth (RSD) and the residual socket area (RSA), measured between the plotted line and more coronal radiolucent part of the socket, but not as a percentage (it would have been 100% in all events) were considered. The regeneration percentage was considered at T1, T2 and T3 comparison analyses. If 100% is represented by the entire depth and area of the residual socket measured at T0, the depth regeneration percentage (DRP) is the decrease per cent of the residual socket depth. The area regeneration percentage (ARP) is the decrease per cent of the residual socket area measured at T1, T2 or T3 (Fig. 1). It represents the reciprocal of the direct measurements because it considers the regenerated part and not the share to be regenerated and standardizes the defects to 100% which are different from each other as absolute metrical value. The regeneration percentage was used for cross-comparisons between the 3 cohorts of patients, while, in the same cohort, only metric values were considered in the longitudinal comparisons between the different phases (T0-T1-T2-T3), to avoid 0% at T0.

Surgical procedure

The attending dental hygienist provided oral hygiene instruction to maintain a plaque index lower than 20%. According to the authors' established dental intervention protocol for patients, teeth with marginal periodontitis and probing depth greater than 8 mm, severe mobility or with dental caries involving the endodontic canal (hopeless teeth or roots) were removed. All dental extractions were performed under local anaesthesia with prophylactic antibiotic administration. The extractions were performed by flapless operation following the same alveolar bone conservative criteria scheduled in post-extractive implantology. In particular, any injury or removal of the healthy alveolar ridge was accurately avoided and supra-crestal soft tissue was preserved. Absorbable suture by means of a copolymer of lactic and glycolic acid (Vicryl® -Ethicon) was carried out to increase gingival stabilization and haemostasis.

Periapical radiographic projections (X-Safe 70, Castellini, Bologna, Italy) were taken immediately after surgery (T0 – baseline) and repeated after 15 (T1), 30 (T2) and 45 (T3) days. A 0.12% chlorexidine mouthwash, 10 ml 3 times per day was prescribed for 45 days post-surgery. Antibiotic therapy (Bassado® - doxycycline – 100 mg twice daily – Pharmacia Upjhon, Nerviano, Italy) for 4 consecutive days, starting from the day before the surgery was carried out.

Statistical analysis

Statistical analysis was performed using the non-parametric Kruskal–Wallis test for the comparison of the 3 cohorts of patients (CC1, CC2 and TC) at each phase (T0, T1, T2 and T3), and the Friedman test for repeated measures on the same cohort along the 4 phases. The χ^2 test (nominal data) was applied to compare the gender distribution between the three treated cohorts (10). Both the Kruskal–Wallis and Friedman test were followed by Student-Newman-Keuls multiple comparison test if the former tests resulted significant (10). For all measured variables, the null hypothesis (H_0) of no difference among groups was rejected for a critical significance level of $p < 0.05$.

RESULTS

Fifteen patients, (5 females and 10 males), ranging in age from 20 to 55 years (mean ± standard deviation: 35.8±10.11) were selected and completed the 45-day follow-up period. Ten healthy individuals formed the control cohort (CC), five of whom, aged between 32 and 50 years (39.4±3.311), requiring extractions of periodontally hopeless teeth, formed the CC1. The other 5 patients, aged between 29 and 55

years (43.6±10.43) needing residual root extractions, formed CC2. Both the control cohorts were formed by three males and two females, so the control cohort (CC) was formed by 6 males and 4 females). The test cohort (TC), contained three males and two females, aged 25–51 years (40.2±9.471. Five patients had acute myeloid leukaemia (AML, subtypes M2-M4).

A total of 15 sockets was considered for analyses. The patients considered showed a normal blood count. The surgical procedure was successful without serious complications in almost all patients. No infection, alveolitis, dehiscence or neurovascular injuries were observed. A satisfactory post-surgical course was achieved in all the patients. No statistically significant differences were found among groups for age (p=0.7) and gender (p=1).

At T0 (baseline) phase, the RSD and RSA were respectively 18.8±3.6 mm and 124.7±25.8 mm^2 in CC1, 21.4±2.4 mm and 140.3±15.5 mm^2 in CC2, and 18.8±5.1 mm and 123.7±23.5 mm^2 in TC. No statistically significant differences were found among groups for RSD (p=0.4) and RSA (p= 0.5).

At T1 phase, in CC1, RSD and RSA were respectively 17±3.8 mm and 115.2±27.3 mm^2, while DRP and ARP were respectively 10.1±3.9% and 8±3.1%. In CC2, RSD and RSA were respectively 17.8±1.9 mm and 121.5±12.7 mm^2, while DRP and ARP were 16.7±3% and 13.3±2.4%. In TC, RSD and RSA were respectively 16.8±4.4 mm and 112.8±29.7 mm^2, while DRP and ARP were respectively 10.2±7.5% and 8.5±5.3%. No statistically significant differences were found among groups for RSD (p=0.8), RSA (p= 0.7), DRP (p=0.09) and ARP (p=0.09).

At T2 phase, in CC1, RSD and RSA were respectively 11.8±2.6 mm and 88.7±20.8 mm^2, while DRP and ARP were 37±7.9% and 29.2±6.2%. In CC2, RSD and RSA were respectively 12.4±1.8 mm and 93.7±12.6 mm^2, while DRP and ARP were respectively 42.2±2.5% and 33.3±2.9%. In TC, RSD and RSA were respectively 15±4.2 mm and 102.9±27.9 mm^2, while DRP and ARP were 19.9±11.9% and 16.7±7.3%. No statistically significant differences were found among groups for RSD (p=0.4) and RSA (p= 0.6). DRP and ARP resulted significant at Kruskal-Wallis test (p=0.007)

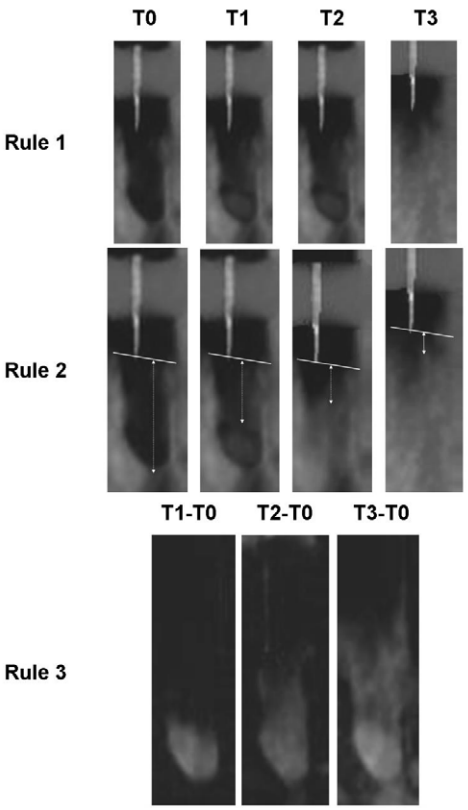

Fig. 1. *Periapical X-ray - Schematic figure showing the measurements performed by the radiopaque rod inserted in the acrylic stent (Rule 1 – raw periapical x-ray), the rod (of well-known length and embedded in an acrylic stent) was positioned in parallel with to the long axis of the tooth allowing reproducible, comparable and reliable radiologic periapical evaluations performed by a biteblock of Rinn film holder embedded in a silicon double bite (Rule 1). Immediately after the extraction at baseline (T0) and at each phase (T1, T2 & T3) periapical radiograph was taken, scanned and digitalized. A line joining the highest bone crest, mesial and distal to the socket (taken from the sagittal projection of each periapical radiograph), was plotted for each periapical post-extractive radiograph after the digitalization (white line - Rule 2 - Linear and Area measurement). The axial lineal measurement was taken from the more coronal radiopaque area of the residual socket to the plotted line on the axial plane (white double arrow). The area measurement regarded the socket area defined coronally by the white plotted line and then the area bordered the socket perimeter and deeply edged the newly formed bone (Rules 2 and 3). The reciprocal of direct linear and area measurements represented the regenerated part and gave its origin to the subtractive radiology (Rule 3). The regeneration percentage was used for cross-comparisons between the 3 patient cohorts while only metric values in the longitudinal comparisons between the different phases (T0-T1-T2-T3) within the same cohort were considered.*

so Student-Newman-Keuls multiple comparison test was performed showing a lower regeneration percentage in TC for both DRP and ARP.

At T3 phase, in CC1, RSD and RSA were respectively 9.6±11.5 mm and 66.7±14.3 mm^2, while DRP and ARP were respectively 48.3±6.5% and 46.6±6.3%. In CC2, RSD and RSA were respectively 10.2±11.6 mm and 69.4±11 mm^2, while DRP and ARP were respectively 52.6±2.7% and 50.8±2.6%. In TC, RSD and RSA were respectively 9.2±2.9 mm and 62.6±19.1 mm^2, while DRP and ARP were respectively 51.4±6.5% and 49.7±6.3%. No statistically significant differences were found among groups for RSD (p=0.8) and RSA (p= 0.9), DRP (p=0.5) and ARP (p=0.5).

The CC1 longitudinal analysis resulted significant both for RSD (p=0.002) and RSA (p=0.002) at Friedman test. An increasing regeneration share was observed step by step from T0 to T3. However, only comparing not subsequent phases (T0 *vs* T2, T1 *vs* T3, etc.) a statistically significant result (Student-Newman-Keuls multiple comparison) for both RSD and RSA was observed.

The CC2 longitudinal analysis resulted significant both for RSD (p=0.002) and RSA (p=0.002) at Friedman test. An increasing regeneration share was observed step by step from T0 to T3. As before, only comparing not subsequent phases (T0 *vs* T2, T1 *vs* T3, etc.) a statistically significant result (Student-Newman-Keuls multiple comparison) for both RSD and RSA was observed.

The TC longitudinal analysis resulted significant for both RSD (p=0.005) and RSA (p=0.002) at Friedman test. An increasing regeneration share was

Table I. *Raw data with mean and staandard deviation of the radiological measurements of the patients considered in the study.*

	T0			T1				T2				T3			
CC1	pt	RSD	RSA	RSD	RSA	DRP	ARP	RSD	RSA	DRP	ARP	RSD	RSA	DRP	ARP
	1	18	117.5	16	107.1	11.1	8.8	11	81.5	38.9	30.7	9	60.8	50	48.3
	2	13	84.8	11	74.4	15.4	12.2	9	64.2	30.8	24.3	8	53.3	38.5	37.1
	3	22	153.6	21	148.4	4.5	3.6	15	117.6	31.8	25.1	12	90.6	45.5	43.9
	4	21	137	19	126.6	9.5	7.6	14	101	33.3	26.3	10	67.7	52.4	50.6
	5	20	130.5	18	120.1	10	8	10	79	50	39.4	9	61.2	55	53.1
	M	**18.8**	**124.7**	**17.0**	**115.3**	**10.1**	**8.0**	**11.8**	**88.7**	**37.0**	**29.2**	**9.6**	**66.7**	**48.3**	**46.6**
	SD	**±3.6**	**±25.8**	**±3.8**	**±27.3**	**±3.9**	**±3.1**	**±2.6**	**±20.8**	**±7.9**	**±6.2**	**±1.5**	**±14.3**	**±6.5**	**±6.3**
CC2	pt	RSD	RSA	RSD	RSA	DRP	ARP	RSD	RSA	DRP	ARP	RSD	RSA	DRP	ARP
	1	18	120.3	15	104.4	16.7	13.3	10	78.1	44.4	35	8	55.8	55.6	53.7
	2	23	150.1	20	134.5	13	10.4	14	103.8	39.1	30.9	11	74.5	52.2	50.4
	3	20	127.6	17	112.4	15	11.9	11	82.3	45	35.5	9	59.8	55	53.1
	4	22	146.8	18	125.6	18.2	14.5	13	99.4	40.9	32.3	11	75.9	50	48.3
	5	24	156.6	19	130.7	20.8	16.6	14	105.1	41.7	32.9	12	81	50	48.3
	M	**21.4**	**140.3**	**17.8**	**121.5**	**16.7**	**13.3**	**12.4**	**93.7**	**42.2**	**33.3**	**10.2**	**69.4**	**52.6**	**50.8**
	SD	**±2.4**	**±15.5**	**±1.9**	**±12.7**	**±3.0**	**±2.4**	**±1.8**	**±12.6**	**±2.5**	**±1.9**	**±1.6**	**±11.0**	**±2.7**	**±2.6**
TC	pt	RSD	RSA	RSD	RSA	DRP	ARP	RSD	RSA	DRP	ARP	RSD	RSA	DRP	ARP
	1	20	135.5	18	18	10	8	16	114.1	20	15.8	9	63.5	55	53.1
	2	12	78.3	11	11	8.3	6.6	9	62.9	25	19.7	5	34.2	58.3	56.3
	3	17	110.9	17	17	0	2	17	105.4	0	5	10	66.8	41.2	39.8
	4	19	124	15	15	21	16.7	13	93.5	31.6	24.6	9	60.9	52.7	50.9
	5	26	169.7	23	23	11.5	9.2	20	138.8	23.1	18.2	13	87.8	50	48.3
	M	**18.8**	**123.7**	**16.8**	**16.8**	**10.2**	**8.5**	**15.0**	**102.9**	**19.9**	**16.7**	**9.2**	**62.6**	**51.4**	**49.7**
	SD	**±5.1**	**±33.5**	**±4.4**	**±4.4**	**±7.5**	**±5.3**	**±4.2**	**±27.9**	**±11.9**	**±7.3**	**±2.9**	**±19.1**	**±6.5**	**±6.3**

T0: Baseline; T1: 15-days after surgery; T2: 30-days after surgery; T3: 45-days after surgery; CC1: control cohort -1 patients; CC2: control cohort-2 patients; TC: test cohort patients; pt: series of patients for each cohort; RSD: residual socket depth; RSA: residual socket area; DRP: depth regeneration percentage; ARP: area regeneration percentage; M: mean; SD: standard deviation.

observed step by step from T0 to T3. However, only comparing not subsequent phases (T0 *vs* T2, T1 *vs* T3, etc.), with the exception of the RSD comparison of T0 *vs* T2, a statistically significant result (Student-Newman-Keuls multiple comparison) for both RSD and RSA was observed. The raw data with mean and standard deviation of the radiological records are reported in Table I.

DISCUSSION

In the present study, all the TC patients had already started chemotherapy and the median time from the last chemotherapy (consolidation phase) to the following conditioning phase (severe myelosuppression and persistent immunodeficiency - that constituted the third therapeutic phase) was two months. This was the entire period of time available for dental evaluation, treatment and alveolar recovery.

The RSD and RSA trend was similar for CC1 and TC without statistical significance among groups. However, CC1 is formed by periodontally diseased patients and periodontal disease produces the hindering of periodontal and bone regeneration (6). On the contrary, at T2 phase (30 days after surgery) both DRP and ARP resulted significantly lower in TC, showing a lower regeneration percentage in TC than in CC1 and CC2. Both the DRP and ARP showed a similar regeneration trend for CC1 and CC2 which is deeply different from TC in T2 phase.

The longitudinal analyses of RSD, RSA, DRP and ARP showed an increasing regeneration share, step by step, proceeding from T0 to T3. However, statistical significance was only observed in the comparisons of phases distant at least one phase between them and, in the TC case, with the exception of T2 with T0. At T3 phase, regeneration was alike among cohorts. Due to its high accuracy, it was decided to employ digital subtraction radiography to evaluate bone tissue changes in post-extraction sockets (11, 12). No previous studies exist regarding bone healing in extraction sockets in acute leukemic patients.

In conclusion, the healing process and the regenerative potential of post-extractive sockets seems to be affected by the leukemic condition during the 30 days after the extraction. Although a longer healing time seems to be necessary for the regenerative process to occur, the final result is identical to that observed in healthy patients 45 days after surgery. Because the scanty average lapse of time from consolidation phase and conditioning phase, it is momentous to make the best use of the available time to avoid devoting only 1 month for tooth extraction and healing.

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