

Oral Surgery

Effects of TEGDMA and HEMA on differentiation capability of dental pulp stem cells

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Aim: Resin-based materials utilized in dentistry are complex mixed materials consisting of an organic polymerizable matrix and an inorganic reinforcing filler coupled through a silanic agent. Resinous matrix is frequently composed of bisphenol A glycerolate dimethacrylate (Bis-GMA) with the addition of other methacrylic monomers like triethylene glycol dimethacrylate (TEGDMA) and 2-hydroxyethyl methacrylate (HEMA). After performing dental restorations small amounts of uncured monomers are released into the oral cavity and—through dentinal diffusion—in dental pulp cells (DPCs), where monomers like HEMA and TEGDMA may reach millimolar concentrations, high enough to cause several adverse biological effects. Because DPCs have stemness and differentiation potential, the aim of this study was to evaluate if the contact between sub-cytotoxic concentration of HEMA and TEGDMA could cause an alteration of DPCs differentiation capability. This aspect is very interesting for a possible future application of these cells in regenerative medicine.

Methods: Isolation and culture of HPCs. HPCs from healthy patient (obtained with informed consent) were used in this study. HPCs were plated in tissue culture flasks with complete DMEM, at 37°C, 5% CO₂ atmosphere and used before the fifth passage. Preparation of Methacrylates Solutions. Stock dimethyl sulfoxide (DMSO) solutions of TEGDMA

(from 0.1 mol/L to 3.0 mol/L), were prepared immediately before use. A final concentration of DMSO (0.1% v/v) was utilized in all. DMEM containing the monomer was then added to the exponentially growing HPCs at the following final concentrations: TEGDMA (3.0, 1.5, 0.7, 0.4, 0.2 and 0.1 mmol/L), DMSO was absent only in cells treated with HEMA because this monomer is hydrophilic and—therefore—it can be added purely to the medium to reach a final concentration ranging from 1.0 mmol/L to 8.0 mmol/L. Cytotoxic Assay: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) test was used to determine the subcytotoxic concentrations of HEMA and TEGDMA. Cells differentiation: HPCs were treated with sub-cytotoxic concentration of either HEMA or TEGDMA for 24h. Then the medium was removed and replaced with DMEM supplemented with 10 mmol/L β-glycerol phosphate, 0.05 mg/mL ascorbic acid and dexamethasone 10⁻⁵ mol/L (osteogenic medium). Control cells were cultured in DMEM. Medium was changed every 3 days. HPCs cultures (both control and treated cells) were analyzed for cell proliferation and the osteogenic phenotype was assessed on the basis of changes in alkaline phosphatase (ALP) activity and in Ca⁺⁺-content evidenced by Alizarin red assay with different incubation periods (days 10 and 21). Statistical Analysis: Data were expressed as mean ± Standard Deviation. Analysis was performed by ANOVA, p<0.05 was considered significant.

Results: The sub-cytotoxic concentrations obtained by MTT were: TEGDMA 0.1 mmol/L and HEMA 1 mmol/L. In our experimental conditions, the HPCs differentiation was weakly affected by monomers treatment.

Conclusions: Our results show that exposure to sub-cytotoxic concentrations of TEGDMA and HEMA for a limited period does not determine the total loss of differentiation capability of these cells. However, additional studies are needed to fully elucidate if HPCs derived from monomers treated pulp could, in

the future, be used in regenerative medicine.

Changes in temperature during the preparation of the implant sites using sonic and ultrasonic instruments: a comparative study

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Aim: Bone tissue is extremely vulnerable to temperature increase. Thus, during the preparation of the implant sites, it is crucial to avoid bone damage by limiting the heat development. While ultrasonic instruments are widely used to prepare implant sites as they have proved to be associated with an high survival rate, sonic instruments have been only newly introduced to this end. Yet, there is lack of information concerning the temperature developed using these instruments in this particular clinical situation. The aim of this study is to analyse the development of the temperature throughout the preparation of the implant sites by means of sonic instruments in comparison to ultrasonic ones.

Methods: Twenty-eight osteotomies were performed in *ex-vivo* set up by using two bisected heads of domestic pigs. Fourteen implant sites were prepared by using 4 tips (SFS 99.014, SFS 99.021, SFS 99.027, SFS 99.033, Komet Italia S.r.l., Milano, Italy) mounted on a sonic handpiece (Sonosurgery, Tekne Dental, Calenzano, Italy) and fourteen implant sites where executed by means of 4 tips (IM1S; IM2P; IP2-3; IM3P) fitted to a piezoelectric device (Piezosurgery 4, Mectron S.p.A. Carasco, Italy). All the osteotomies were suitable to host an implant 8x3mm in size. Using a digital thermometer and a K thermocouple probe conveniently fixed to the bone samples, the maximum temperature increase was recorded for each tip used. The force applied ranges between 0,01 N and 0,5 N and 50 ml/min saline solution at room temperature (20-22 C°) was provided.

Results: The maximum temperature increase (+31,0 C°) has occurred when ultrasonic device was used, whereas sonic instruments showed a maximum increase of +10,8 C°. In both cases the first tip was associated with the maximum heat development.

However, using the sonic instruments, temperature raises progressively, whereas, if ultrasonic instruments are employed, sudden peaks of temperature happened especially when the tip IM1S is used.

Conclusion: Sonic instruments seem to cause a little amount of temperature increase and unexpected peaks of temperature were not occurred. In light of these considerations, sonic instruments can be considered as safe as piezoelectric ones in terms of heat developed throughout the preparation of the implant sites. Nevertheless, further clinical studies need to be carried out to assess the survival rate of implants whose sites are prepared by means of sonic instruments

Transmigration of mandibular canine: surgical approach and etiological considerations

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Aim: An impacted tooth occasionally migrates away from the site in which it develops but usually remains within the same side of the arch. When migration of an impacted tooth crosses the midline, the phenomenon is called transmigration. Transmigration typically affects the mandibular canines. These teeth usually remain impacted and asymptomatic but in some cases can cause neurologic symptoms and pressure resorption of the adjacent teeth roots. The aetiology and pathogenesis of this pathological dental inclusion remain unknown but the intervention of various molecules and the up or downregulation of certain genes seems to play a key role in the pathogenesis of this rare phenomenon. The therapeutic option for this rare phenomenon is mainly surgical, but an early radiographic detection is crucial to have the possibility of orthodontic element recovery.

Methods: In this work we report a case solved with surgical approach. The patient was a 25-yr-old man (caucasian) with an impacted mandibular canine in ectopic position across the midline below the roots of contralateral canine. The patient underwent oral surgery with exposure of the transmigrated element through osteotomy and solved with surgical excision, using odontotomy.

Results: The case was solved successfully and without postoperative sequelae.

Conclusion: The etiology remains unknown although some Authors continue to formulate new etiological

theories. In some studies it has been found that the downregulation of matrix metalloproteinases (MMP) and upregulation of several genes of collagens in non-syndromic hyperplastic dental follicle resulting in abnormal connective tissue remodeling with defective tooth eruption. In the process of tooth eruption an exogenous factor could alter the action of the MMP and the alveolar bone resorption in the coronal area of the follicle of dental bud. Maybe, this alteration may not be the same on all sides of this area with inhibition or stimulation of MMP on only one part; a greater activity of MMP only on one side of dental follicle would lead to its rotation with its contents. Continuing the eruptive process, dental bud moves towards ectopic position. The surgical approach is almost always possible and has a predictable result, only in cases which there is no symptomatology is possible to not intervene. The orthodontic approach is possible only in a small range of cases, as there are some variables to be taken into account (distance, angulation and contact with other structures). That is why early detection, with Rx opt or Rx cbct, is important for a valuation of migration process and there are good chances of having favorable conditions for orthodontic recovery.

Lateral sinus augmentation: implants survival and success rate in mid-long term follow-up retrospective study

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Aim: The main aim of the study was to assess the influence of patient, biomaterials, and implant related variables on complications of sinus surgery and on survival rate of the implant placed in grafted sinus. Secondary aims were to analyze apical and marginal bone remodelling around implants and the patients' satisfaction.

Methods: A retrospective study was performed on consecutive patients treated at the oral surgery department of University of Florence (Florence, Italy). Patients that had computer tomography before sinus surgery (T0), orthopantomography after implant surgery (T1) and at the follow-up (T2) were included. Variables for sample description, type of biomaterials, implant characteristics were registered. All survived implants were analyzed with clinical and radiographic evaluation (OPT) at the follow-up. The radiographic analysis measured the height of the residual bone (HRB), apical (aGH, IP) and marginal (MBL, VBH) bone remodelling around the fixture and it was performed at three different time points: T0 (CT before sinus surgery), T1 (OPT after implant surgery), T2 (OPT at the

follow-up).

Results: Forty-three lateral sinus lifts were performed in 32 patients and 83 implants were inserted. In 18 sinuses augmentation were recorded premature complications leading 3 graft failures. A total of 19 implants failed. Mean follow-up was $6 \pm 1,8$ years. Patient and sinus related factors not influenced premature rate of complications. Height of residual bone (HRB) resulted to have a significant influence on mid-long term implant failure, with odds ratio (OR) of 3.8 (p-value 0.0034) for each millimeter less of residual bone before the surgery. A significant implant failure difference was registered between smoking and non-smoking group, with OR of 8.3 (p-value 0.0173). Number of cigarettes/day had negative effects on implants survival, with OR of 1.14. No statistically significant difference was registered for implant failure among the biomaterials used for sinus lift, nor among various implants surfaces. A significant reabsorption was recorded for apical (aGH -0.8 mm) and marginal (VBH -1.4 mm) bone around dental implants between T1 and T2, but no difference were recorded between different materials and implant characteristics. General therapy satisfaction measured in a visual analogue scale (VAS) was 8.4 ± 1.4 .

Conclusions: Lower height of residual bone prior to the surgery and smoking habits had negative prognostic effect on dental implants in grafted sinuses.

Effects of culture system on long-term expansion and differentiation of mesenchymal stem cells derived from periodontal ligament

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Aim: Periodontal ligament (PDL) has been reported to be a source of mesenchymal stem cells (MSCs). In this study, we characterized human periodontal ligament stem cells (PDLSCs) maintained in different culture media to establish the most suitable medium formulation for dental tissue engineering and regenerative applications. We evaluated the effects of the culture medium and conditions (normoxia and hypoxia) on cell proliferation, mesenchymal phenotype and osteoblast potential of PDLSCs. This study was the first report to compare the proliferation and differentiation potential of PDLSCs from the same person in three different culture media.

Methods: PDLSCs were harvested from healthy third molars (single patient) after tooth extraction. PDL tissue was mechanically removed by a Gracey curette, and a

single-cells suspension was obtained enzymatically by digesting with 2mg/ml collagenase. PDLSCs were cultured in the most widely used culture media (a-MEM and DMEM) and compared to a new culture medium formulation (Enriched Ham's F12 Medium, EHF_M). Isolated cells were seeded in a 6-well culture dish. When cells became 80-90% confluent, they were subcultured ($4 \times 10^3/\text{cm}^2$ in a 6-well dish) until passage 6. The characterization of PDLSCs includes flow cytometry analysis, immunofluorescence analysis and cell proliferation assay in both normoxic and hypoxic (1%) conditions. The osteogenic differentiation of PDLSCs was performed by culturing cells in a specialized culture medium containing -glycerophosphate, dexamethasone, and L-ascorbic acid for 3 weeks. The osteogenic differentiation was assessed by alkaline phosphatase (ALP) activity, mineralization (alizarin red staining) and gene expression of osteogenic markers. Osteoblastic differentiation was also evaluated under hypoxic conditions.

Results: PDLSCs isolated from three third molars of the same patient (in duplicate) were grown in a-MEM, DMEM, and EHF_M. PDLSCs cultured in EHF_M showed an increased proliferation rate. Flow cytometry analysis of PDLSCs revealed that more than 99% were positive for mesenchymal markers CD73, CD90 and CD105 in all culture media, and negative for CD14, CD34 and CD45. However, the expression levels of CD73 in PDLSCs grown in EHF_M appeared much higher than that maintained in the other culture systems. In general, no significant differences were reported among cells grown in normoxic and hypoxic conditions. PDLSCs grown in a-MEM and DMEM showed the production of mineralized tissue and ALP activity in vitro, although the levels were dependent on the culture medium; conversely, no mineralization was observed in cells grown in EHF_M. Also in this case, no significant differences were reported among cells grown in normoxic and hypoxic conditions.

Conclusion: On the basis of these preliminary results, we propose a two stages protocol for the osteogenic induction/differentiation of PDLSCs, in which the early expansion stage could be performed in EHF_M without loss of cell stemness. Furthermore, the comparable results obtained in the different culture conditions (normoxia and hypoxia) seem to encourage us to study, more thoroughly, the microenvironment of the oral cavity wounds.

Proposal of a research protocol for a new piezoelectric tool for the extraction of mandibular impacted third molars

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Aim: As already demonstrated in literature, the piezoelectric technology, in the extraction of impacted third molars, according to its less invasiveness, is a valuable aid in the reduction of intra and postoperative complications. The study is focusing on a new piezoelectric tool, Surgybone of Silfradent factory, to assess whether the results are valid with this piezoelectric instrument compared to the extraction of third molars with traditional rotating method, and then, if these results with this tool will be proved valid as much as another one piezoelectric instrument of a different factory.

Methods: 50 patients will be selected for a randomized prospective study according to the inclusion and exclusion criteria. They will be randomized into two groups: 25 patients will undergo third molar extraction with rotating and 25 with piezoelectric instrument, using for all of them the same clinical protocol. The protocol provides, according to the Italian Ministerial Guidelines of 2014, the use of antibiotic (amoxicillin), nerve block anesthesia (articaine), ice pack immediately after surgery and then during the following 24 hours the alternation every 20 minutes of the use and the removal of ice packs, the use of ibuprofen 600 mg immediately after completion of extraction and 600 mg when needed by the patient during the following days. The patient then will be instructed on how to fill the form for the research and on the precautions to follow such as abstention from smoking in the pre and postoperative, assumption of a soft or liquid diet for the first 24-48 hours and the use of oral antiseptics in the postoperative for the first 3 days. The form, to be filled at home by the patient, wants to evaluate the amount of pain through a visual analogue scale, the amount of analgesics consumption within 5 days and the ability to perform daily activities immediately after the extraction. Then, by clinical and photographic investigations, the study will evaluate trismus and swelling after 5 days when the patient will come for the suture removal. The operator who collects data will be completely blind of the type of intervention carried out by the surgeon and he will simply collect and evaluate data by statistical analysis.

Results: According to results of scientific research already published, it is expected, from a preliminary investigation, a postoperative course more favorable for patients that will undergo extractions with the piezoelectric tool over conventional rotating burs, then, from these results, using data present in literature, it will evaluate the actual effectiveness of the Surgybone tool based on these parameters in relation to another standard piezoelectric instrument.

Conclusion: According to the expectations, the

piezoelectric tool will demonstrate a lower rate of intra and postoperative complications, a better postoperative course for the patient and the quickly recovery of daily life activities. As advertised by the factory, in addition, according to its less invasiveness, it will be evaluated if the Silfradent tool will show results even more favorable compared to a standard piezoelectric instrument.

Dental implant rehabilitation at the dental clinic, department of dentistry, San Raffaele Hospital, Milan: a report of 2015/2016

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Aim: The aim of our study was to evaluate the whole number of dental implant rehabilitations in patients referred to the Dental Clinic of San Raffaele Hospital, Milan in the academic year 2015/2016. This unit is aimed to allow vulnerable social classes to equally and easily access to dental care, ensuring quality and excellence. A key-role in this context is held by a synergic relation between students and the renowned tutors of the Department.

Methods: A retrospective analysis of the total number of dental implants placed in different categories of patients was performed. We considered different and heterogeneous types of oral rehabilitations: from single implant to full-arch rehabilitation of maxillary and mandibular jaws, both in healthy and compromised conditions. Patients were affected by different diseases like viral hepatitis, diabetes, acquired immunodeficiency syndrome (AIDS), myocardial or renal insufficiency, and also patients who have had or have a neoplasia. Follow-up controls were performed at 3 (T1), 6 (T2), 9 (T3) and 12 (T4) months after implant insertion and included both radiographic assessments of bone level around the implants and clinical parameters evaluation (plaque accumulation and bleeding index). The radiographic evaluation was based on the analysis of bone levels on the mesial and distal ridges around the fixtures, as shown by intraoral radiographs taken with Rinn's film holders.

Results: Single implants were placed in 32 patients (71 implants), while the overall number of complete-arch immediately loaded prostheses was 15 (60 implants). Low incidence of complications and long-term survival rates were recorded after twelve months of follow-up. Implant failure occurred in 4 patients (5 fixtures out of 131), one healthy and four with pathological systemic conditions. The implant survival rate was 96,2%, while prosthetic provisional failure occurred

in only 2 patients. The most common complication was mucositis around implants, while the most negative prognostic factor was found to be plaque accumulation around implants.

Conclusion: In harmony with the current literature, our analysis confirms the high predictability of the modern protocols in implant dentistry, even in healthy compromised patients where implant rehabilitation can have a higher risk of failure. A huge percentage of patients showed confidence in complying on the service we offer.

Human dental pulp stem cells vs stem cells from human exfoliated deciduous teeth: isolation protocol and comparative *in vitro* study of two populations of stem cells from tooth-related tissues

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Aim: Adult mesenchymal stem cells have recently been isolated and characterized from tooth-related tissues. Dental pulp stem cells (DPSCs), extracted from normal impacted third molars' pulp are the first identified and isolated, as well as the most studied. They are reported to be clonogenic and highly proliferative, being able to form *in vitro* calcified sporadic nodules and possessing multipotent differentiating capabilities.

Stem cells from human exfoliated deciduous teeth (SHEDs) represent a distinctive population of multipotent stem cells from the remnant pulp of exfoliated deciduous teeth which derive from a readily accessible tissue source. The aim of this *in vitro* study compare SHED to DPSCs according to their isolation protocol, proliferating and differentiating capability.

Methods: Thirty patients in good state of systemic and oral health, candidates to tooth extractions for clinical needs, were selected for the current study and divided into two groups. Patients in the first group (n = 15), aged between 20 and 35 years, underwent to wisdom teeth extraction without performing tooth section. Patients in the second group (n = 15) underwent to exfoliated deciduous teeth extraction. All patients underwent to oral hygiene 7 days before extractions. Teeth with previous trauma or clear clinical and radiographic signs of pulp necrosis were excluded from the study. The extracted third molars are put in a chlorhexidine damp subsequently sectioned with manual instruments; the pulp tissue is then extracted by a curette or an endodontic file and placed in test tube containing saline or culture medium. The entire procedure is performed in a sterile field. The cell extraction from deciduous teeth is similar, but does

not require the placement in chlorhexidine since this would be in contact with the pulp already exposed in exfoliated teeth. At the laboratory, samples are placed under the hood; thereafter they are placed in the digestion solution, and then stirred at 37°C for 60 minutes (DPSCs) and 45 minutes (SHED). Afterwards they are filtered at 70µm and then PBS is added to the culture medium to neutralize the digestion. A centrifugation at 1300 rpm is performed for 7 min, and then the cells are put in 6-well flask and placed in an incubator at 37°C, 5% CO₂ microclimate. The culture times were at 7 and 15 days, and the change of the culture medium was performed at least 2 times a week. Cells were studied with SEM, flow cytometric analysis, PCR, Western blot.

Results: SHED can be isolated in vivo and demonstrate capacity for expansion in vitro, and their proliferation rate resulted to be higher than DPSCs. SHED collected from dental elements with advanced state of root resorption have a greater chance of setting and proliferating. Our observations showed that it was possible to obtain a significant osteogenic differentiation, with production of an appreciable amount of bone specific proteins, from SHED.

Conclusion: Our study shows encouraging results concerning SHED, which appear as a possible tool for regenerative dentistry. Since that human deciduous teeth that are expendable and routinely exfoliated in childhood with little or no morbidity to the patient, SHED also appear to be a readily available material. However further studies are necessary to determine if these cells can effectively be used in the future as therapeutic tool in clinical practice.

Pharmacokinetic of articaine in third molar extraction

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Aim: The aim of this study is to investigate the articaine pharmacokinetics measuring drug concentration in tissue, in the local blood and in the peripheral blood.

Methods: A protocol was designed and approval of ethical committee (Area Vasta Centro) was obtained. Patients that need third molar extraction were selected. Data about condition of local tissue were collected before surgery. A peripheral intravenous catheter (PIC) line was inserted in the patient's brachial vein. A maximum quantity of 1,8ml of Articaine 4% with epinephrine 1: 100,000 was injected locally. Following samples were collected: tissue from the flap, local blood using a calibrated

pipette (250 µl) and 2cc peripheral blood from PIC. Samples were collected after local anaesthesia at 3 minutes, 10 minutes and 17 minutes. At the end of the intervention the samples were labelled. The evaluation of the anaesthetic concentration of the sample material was carried out by High-performance liquid chromatography (HPLC).

Results: Ten patients were selected for a total of 30 samples of local tissue, 30 samples of local blood and 30 samples of peripheral blood. It was not possible to perform the analysis in one sample of peripheral blood. The values of the concentration of the drug in the local blood were always significantly greater than those detected in the peripheral blood. The average concentration of articaine in local blood in the three intervals of time varied from a minimum of 492.3 mg/ml to a maximum of 651.65 mg/ml, while in the peripheral blood varied from 2167.85 ng/ml to 4783 ng/ml. Measures of drug concentrations at local level (blood and tissue) and in the peripheral blood showed interesting differences between patients with moderate levels of local inflammation in which it was not necessary to resort to more anaesthesia to maintain the analgesic effect and patients with markedly higher levels of local inflammation in which it was appropriate to proceed with further infiltrations. In particular, patient with moderate levels of local inflammation shows a gradual increase of articaine concentration in the peripheral blood, differently we observe initial peak of anaesthetic concentration in patients with higher levels of local inflammation. At local level, the analysis of blood samples shows a gradual increase of articaine concentration in patient with moderate inflammation while in those with marked inflammation, it reveals an initial decrease of concentration and a successive increase caused by the further anaesthetic infiltration.

Conclusion: In the study we have found the average values of articaine concentration in local blood samples greater than those detected in peripheral blood samples. This result is probably due to the articaine efficacy of tissue protein binding and to the peculiar metabolism of this amide anaesthetic. However drawing conclusions based on such a limited number of cases is not possible and further study are necessary.

Removal of mandibular third molar and periodontal healing of adjacent mandibular second molar: a systematic review

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Aim: The purpose of this study was to conduct a systematic review and network meta-analysis of RCTs with the following specific aims: (1) to systematically review best available evidence on effect of M3M surgical removal interventions on periodontal health of M2M; (2) to establish a ranking in efficacy of the treatment options; and (3) to identify the best approach, in terms of clinical attachment gain (CALg) and probing pocket depth reduction (PPDr) at the distal surface of the M2M.

Methods: Medline, Cochrane and Embase databases were interrogated to identify randomized controlled trials (RCTs) up to 22 December 2014. Patients with M3Ms fully developed, unilaterally or bilaterally impacted, were considered. Outcomes were clinical attachment level gain (CALg) and probing pocket depth reduction (PPDr) with a follow-up \geq 6 months. Patient-subjective outcomes as pain, discomfort and complications, financial aspects and chair-time were also explored. A Bayesian network meta-analysis (NMA) model was used in order to estimate direct and indirect effects and to establish a ranking of treatments.

Results: 16 RCTs were included and categorized into 4 groups investigating: regenerative/grafting procedures (10 RCTs); flap design (3 RCTs); type of suturing (1 RCT); periodontal care of M2M (2 RCTs). Guided tissue regeneration (GTR) with resorbable (GTRr) and non-resorbable (GTRnr) membrane, and GTRr with anorganic xenograft (GTRr+AX) showed the highest mean ranking for CALg (2.99, 90%CrI: [1; 5]; 2.80, 90%CrI: [1; 6]; and 2.29, 90%CrI: [1; 6], respectively) and PPDr (2.83, 90%CrI: [1; 5]; 2.52, 90%CrI: [1; 5]; and 2.77, 90%CrI: [1; 6], respectively). GTRr+AX showed the highest probability of being the best treatment for CALg (Pr=45%) and PPDr (Pr=32%). Direct and Network quality of evidence rated from very low to moderate.

Conclusions: 1) GTR therapies with non-resorbable and resorbable membranes and their grafting-combined therapies achieved some additional clinical benefit compared to standard non-regenerative/-non-grafting procedures in terms of CALg and PPDr. However, the overall low quality of evidence suggests low degree of confidence and certainty in treatment effects. 2) The body of evidence for therapies consisting on alternative access flap design, type of suturing, periodontal care for M2Ms indicates that none of these aspects of is decisive on M2M periodontal healing. 3) In view of the importance of M3M extraction as a common dental surgical intervention, more well-designed and well-conducted RCTs are necessary in order to suggest robust evidence-based guidelines.

Influence of pretreatment with PRF (platelet rich fibrin) on wettability of implant surface

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Aim: The objectives of this study were three: 1) obtaining electronic microscopy images before and after a PRF pretreatment from three different implant surfaces, 2) evaluating the angle contact obtained wetting, with a blood drop, three different implant surfaces and 3) evaluating if the PRF pretreatment of the same implant surfaces, modifies their wettability.

Methods: Six implant surface's samples were selected: two machined, two blasted and two with laser treatment. Four images for implant surface were acquired by SEM (Scanning Electron Microscope) before and after a PRF pretreatment, respectively with 200x, 500x, 1000x and 2000x magnification. Afterwards the angle contact formed between three different implant surfaces and 10 μ l blood drop was calculated by optical microscope with 10x magnification. With other three samples, that were pretreated with PRF, the angle contact formed between the different implant surfaces and 10 μ l blood drop was evaluated by the same microscope. The pretreatment of the implant surfaces was made soaking the samples in the PRF and after drying them with sterile gauze. The entire procedure was performed five times in five different days to obtain five measurements for implant surface with and without the PRF pretreatment. The human blood, for the drops and for the PRF production, was drawn from the same volunteer for all the time.

Results: The results obtained with SEM were poorly relevant. It was possible to observe only a few fibrin deposits on implant surfaces with PRF pretreatment. The results obtained with optical microscopy, evaluating different surfaces between them, were relevant: by using "non parametric" tests with software SPSS for Mac OS X (SPSS inc. Chicago, IL, USA) a significant wettability difference from different implant surfaces was observed. The average angle contact of the different surfaces were: for the machined surface 56.58 ± 12.83 , for the sandblasted surface 76.45 ± 6.93 and for laser treated surface 51.02 ± 3.49 . The results obtained, calculating the angle contact after PRF pretreatment of implant surfaces, were very interesting and satisfying. It was possible to observe an important wettability improvement of implant surfaces: machined surface had 33.67 ± 3.06 , sandblasted surface had 38.84 ± 8.49 and laser treated surface had 32.88 ± 1.59 . The statistical analysis highlighted a significant wettability difference from the same implant surface before and after PRF pretreatment but there was not significant angle contact difference between the different surfaces after PRF pretreatment; in fact the angle contact values were very similar

Conclusions: Compelling evidence from our study lead us to suggest, according to scientific literature, that the machined surfaces have more wettability than sandblasted surfaces and a similar one compare to the laser treated surfaces. The PRF pretreatment have a positive effect on wettability of implant surfaces. This effect is independent from the kind of surface, probably because the wettability improvement is directly related to PRF proprieties and not to the characteristics of the implant surface even if the results with SEM were not significant; perhaps due to chemical changes on implant surfaces (not visible by microscopy) thanks to PRF pretreatment. So the PRF could be used as a helper to make the osseointegration process faster by using a rough surface, which stimulates the cell differentiation, with an optimal wettability, which allows to improve the cell adhesion.

Keratocystic odontogenic tumor before and after marsupialization: a histological evaluation

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Aim: A keratocystic odontogenic tumor (KOT) is a benign neoplasm of the jaws that originates either from the dental lamina or from the primordial odontogenic epithelium. KOTs are more commonly found in the mandible than in the maxilla, usually in the posterior maxillary region. The treatment of KOTs includes enucleation and marsupialization. Moreover, resection and adjuvant therapy such as cryotherapy, peripheral ostectomy and Carnoy solution are applied to reduce recurrences. Several authors report that marsupialization reduces the dimensions of extensive KOTs allowing a second, less complex procedure to remove the neoplasm with low morbidity. After marsupialization, the fibrous capsule becomes thicker and less friable, facilitating the surgical procedure of enucleation and reducing the recurrence rate. The aim of the present study was the histological evaluation of the epithelial lining and fibrous capsule in histological specimens of keratocystic odontogenic tumors (KOTs) before and after marsupialization.

Methods: Ten patients were recruited at the oral surgery department of Careggi hospital of Florence. Participants signed an informed consent form. Patients who underwent marsupialization (incisional biopsy) and decompression followed by a second surgery to remove the neoplasm were included in this study. After marsupialization, the reduction in the size of their KOTs was examined quarterly through clinical and radiographs. The enucleation was performed

when a dimensional reduction of the tumor could not be radiographically identified within a 3-month period. Keratocysts were kept in communication with the intraoral environment from a gauze impregnated with gentamicin ointment. Change of the gauze was performed once a week until the second surgery. Tissue samples were fixed in 10% buffered formalin and processed for hematoxylin-eosin staining. The thickness of the epithelial lining and fibrous capsule at the time of marsupialization and after enucleation was measured using Olympus dp-soft analysis software. The images of the specimens were viewed under a microscope and photographed using a Canon Power Shot A-640 digital camera. The morphology of the epithelial lining and fibrous capsule was observed and recorded both before and after the marsupialization.

Results: In all cases, it was clinically obvious upon enucleation that the appearance of the tumor had changed from the time of marsupialization, with a considerable thickening of the tumor's fibrous capsule. The thickness measurements of the epithelium during marsupialization ranged from 54,12 to 167,71 μm (median of 101,74 μm), whereas the thickness in the KOT specimens after enucleation ranged from 180,20 to 370,77 μm (median of 255,22 μm). This thickness difference was statistically significant ($p < 0,05$ Wilcoxon test). The fibrous capsules from the incisional biopsy (marsupialization, 1552,55 μm) were not as thick as the capsules obtained from the final enucleation (2804,51, $p = 0,0015$, Wilcoxon test).

CONCLUSION: In the present study, a morphometric evaluation demonstrated that the epithelium and fibrous capsule in the specimens from enucleation were statistically significantly thicker than in the specimens from the incisional biopsy. These modifications facilitate full surgical treatment and may well be related to a low KOT recurrence rate.

Genetic investigation in patients with non-syndromic supernumerary teeth and similarities with overproduction of dental tissues (as odontomas)

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Aim: Supernumerary teeth are odontostomatologic anomaly characterized by the existence of excessive number of teeth in relation to the normal dental formula. This condition is commonly seen with several congenital genetic disorders such as Gardner's syndrome, cleidocranial dysostosis and cleft lip and palate. However, it is uncommon to find multiple supernumeraries in individuals with no other associated disease or syndrome. Presence of multiple supernumerary teeth is thought to have genetic component. Our research began by the finding of a non-syndromic family in which the father was a carrier of supernumerary teeth and their two daughters presented each multiple supernumerary teeth. The aim of the present work is to conduct genetic investigation in patients with non-syndromic supernumerary teeth. It has been the doubt about the possibility that they were occasional pathological events or anomaly of odontogenesis that led our research. Having found recent scientific studies reporting associations between the etiology of supernumerary teeth and odontomas, highlighting similarities from topographical and pathological point of view but also some indication of common genetic and immuno-histochemical factors. We tried to analyze scientific evidences to verify whether similarities supporting a unified explanation for odontomas and supernumerary teeth exist. From a nosological point of view, odontomas and supernumerary teeth are still classified as distinct entities, although from an etio-pathogenetic and, even more, from a clinical point of view, they seem to be the expression of the same pathologic process, malformative or hamartomatous.

Methods: All patients were subjected to venous blood sample collected in test tubes containing EDTA, for the extraction of DNA. Molecular analysis was conducted by amplifying the two exons of the gene SOSTDC1, the thirty-eight exons of the gene LRP4 and part of the adjacent intronic regions. Subsequently, the PCR products were subjected to automated direct sequencing and the sequences obtained were compared with the wild-type.

Results: The goal of our work was to verify whether there is a pure form of hyperdontia or it is only a correlation with genetic disorders. From the results obtained, currently in our possession, the isolated genes analyzed showed negative results.

Conclusion: It can be assumed that in the future we can identify the gene abnormality through genetic engineering techniques evolving and that we can correct this anomaly and prevent the expressiveness. Today it is in progress a gene analysis as can be seen from this work.

Ultrasonographic characterization of an oral

fibroma as diagnostic and pre-surgical aid

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Aim: The oral mucosa is constantly under the influence of various internal and external stimuli, so it is interested by a range of developmental disorders, irritation, inflammation, and neoplastic conditions. Reactive lesions are tumor-like hyperplasia which show a correlation to a low-grade irritation or injury, such as chewing, food impaction, calculus. Also iatrogenic injuries can determine this type of lesions, such as broken teeth, overhanging dental restorations and extended flanges of denture. Traumatic fibroma is one of this lesions. Recent advances in the field of sonography have extended the spectrum of applications to soft tissues, adding the skin layers among the possibilities for study. Among all of the imaging modalities, sonography has several advantages for studying the skin and the mucosa, in addition to the optimal penetration/resolution balance that allows good discrimination of the different cutaneous layers. The aim of this work is to have an ultrasound characterization of a lip fibroma with a high frequency probe (8-18 MHz) as feasibility and experimental model of this non-invasive technique in the oral mucosa.

Methods: The exam was performed with a portable GE Logiq-e R7 Ultrasound Machine. The monitor was a 15" LCD, with a resolution of 1024x768. The transducer was an hockey stick transducer 8-18 MHz. The axial field of view was from 0.4 mm to 2 cm and the lateral from 0.7 mm to 2 cm. In a second time, an excisional biopsy was performed followed by an histological examination.

Results: The ultrasound image shows a lesion about 5.46 mm long and 3.14 mm deep. The lesion appears as an heterogeneously hyper-echoic nodule, with distinct margin and posterior acoustic shadowing: this detail gives informations on the fibrous nature of the lesion. On the top of the nodule is visible a layer of 0.3 mm a little more hyper-echoic than the core of the lesion, expression of the epithelial hyperkeratosis that is also clinically visible. The deeper layers seem to be separated from the epithelial tissue from an anechoic area that should represent the dermal-epidermal junction. The area below the epithelial tissue is distinctly recognizable by a lower echogenicity compared to that seen in the most superficial tissues; this could be the sub-epithelial stromal component

below. The histological image, to a 5x enlargement, shows a polypoid lesion appearance and a stromal proliferation; this sample shows hyperkeratosis; a pattern of parakeratosis, with small nuclei in stratum corneum's cells; acantosis; papillomatosis; a continue basal membrane; sub-epithelial vascular proliferation and a mild chronic inflammatory infiltrate. A correlation between the two different images was found.

Conclusion: Although the ultrasonographic exam can't replace the biopsy to get a diagnosis of a lesion, this technique presents many advantages: it is a non invasive, in vivo, real time technique that provides images conform to reality. Further investigations are necessary to determine the potential of ultrasonographic images as an aid in the diagnosis of oral lesions.

Changes of the oral biofilm following assumption of probiotics in a sample of children decay receptive

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Aim: The potential application of probiotics for oral health has recently attracted the attention of several teams of researchers. Although clinical studies have been conducted, the results to date could not safety suggest that probiotics could be useful in preventing and treating oral infections, including dental caries, periodontal disease and halitosis. Mucous membranes, the organism is in permanent contact with different antigens. The changing food habits and lifestyle has resulted in deterioration of oral health in the people of all ages. Our research to check whether the 90 days period of intake leads to a modification of the oral bacterial flora in the children who are predisposed to caries, using salivary tests which select the Lactobacilli strain and Streptococci mutans, responsible of the onset of dental caries.

Methods: We recruited 30 child, pedodontics patients that to developed caries in pediatric age. After give your instruction of preservation a good oral hygiene and after cleaning of oral cavity, we have take a sample of salive and reseed a culture medium and then incubation for 48h at the temperature of 37°C. We give to patients probiotics (Lactoflorene child plus-Montefarmaco OTC) for three months and then control if change the results. The salivary test show we the number of colonies of lactobacilli and Streptococchi mutans to assess if there occurs a modification of the oral ecosystem.

Results: The number of colonies of Lactobacilli is

maintained after the intake of lactic fements with a probiotic action, at an optimum level for the health of the oral cavity.

Conclusion: Probiotics are living microorganism, that are either the same as o similar to organisms found naturally in the human body and may be beneficial to health. Dental caries can be seen as a microbial imbalance where the oral microbiota shift toward community dominance which produces acidogenic gram positive bacteria. Similaly, the accumulation of bacteria within the biofilm, facilitated by poor hygiene, predispose to allogenic shifts in the microbial community, leading to the onset of periodontal inflammation. Probiotics bacteria belonging to the genus of Lactobacillus, Bifidobacterium and Streptococcus have been proven effective for preventing caries by reducing the number of cariogenic bacteria in saliva after a short period of consuming the probiotic. It is concluded that improving the immune response that starts in the intestines you get a very good response in other parts of the body, including the oral cavity.

Pigmented oral mucosa lesions in a 19-year-old female patient: a case report

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Aim: This case report show how to approach a pigmented lesion of the oral cavity.

Methods: In November 2015, a 19-year-old female patient was referred to our department for evaluation of two pigmented lesions in hard palate mucosa. Patient reported the following anamnestic data: congenital nevocanities and a kidney transplant from a living donor (her mother) in 2014. The Chronic Kidney Disease was the result of an acute tubular necrosis arose in 1997 after surgery for congenital giant pigmented nevus reduction. The patient was treated with immunosuppressant for life. She was followed by the Dermatological Department for the cutaneous and oral nevi mapping. The pigmented lesions in hard palate were well known to the dermatologist and they have not changed over time. The lesions were no symptomatic, with no history of pain, trauma or bleeding. Intraoral examination revealed two light-brown macule, with no irregular features, ulcerations or thickening. We decided to perform a surgical excision of the lesions, despite having no appearance of malignancy, because pigmented lesions of the oral cavity is a rare disease and have a poorly predictable trends over time. Diagnostic biopsy is required for oral pigmented

lesion to exclude melanoma. Excision facilitates histologic sampling to exclude melanoma, and presumably, may prevent malignant transformation. After surgery we planned a continuous follow-up every 6 months. We examine the patient both with the clinical inspection and with the help of VELscope. The low sensitivity of VELscope does not allow to exempt ourselves from a surgical excision, but help us in follow-up program.

Results: An excisional biopsy was performed including both lesions. Histological examination identified the lesions as intramucosal nevi of palate. Six months after the surgery the patient has a good healing and no visually apparent recurrence. Programming follow-up every six months.

Conclusion: Solitary pigmented melanocytic intraoral lesions of the oral cavity are rare. Oral nevus is a congenital or acquired benign neoplasm. The differential diagnosis includes the malignant melanoma. Mucosal melanoma involving the oral cavity and head and neck regions is not well understood or characterized. This is due to the fact that this subtype of melanoma accounts for less than 1% of all cases. A definitive precursor lesion for mucosal melanoma has not been identified; however, atypical melanocytic hyperplasia may represent a proliferative phase before overt tumorigenesis occurs. Solitary pigmented oral lesions should be clinically evaluated and the conservative surgical excision followed by histo-pathological confirmation of the lesion is strongly recommended for diagnosis and ruling out the dysplastic changes. Follow up is advised to rule out the recurrence of oral nevi.

Activation and platelets degranulation in the PRP (platelet-rich plasma): cytofluorimetric evaluation and kinetic analysis of TGF- β 1 release through immunotest (ELISA)

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Aim: The Platelet-Rich Plasma is a blood compound with high platelets density. By using immunotest ELISA. this study evaluates the activation and degranulation of the platelets during stocking procedure of the PRP, considering the role of the TGF- β 1, a growth factor of the tissues, that is found in the α -platelet granules. Finally, to gain a better understanding of the quality and the quantity activations state these datas are compared to the ones obtained with the cytofluorimetric analysis of the activation state of the

platelets in the PRP.

Methods: This study focuses on a sample of 19 patients (21-71 years-old), with no major diseases and waiting for an invasive oral-surgery. 24h before surgery each patient was sampled for 400ml of venous blood (+sodium citrate). Subsequently, the obtained blood sack was centrifugated to divided the erythrocytes from the plasma (900RPM, 13min, at 20°C). The plasma was then centrifugated (3300RPM, 15min) to respectively obtain the P.R.P. and the P.P.P. (Platelet-Poor Plasma). Thus, P.R.P. was then shaken to prevent platelet aggregation. Instead, from the P.P.P. were took the autologous-thrombin and cryoprecipitate. Finally, P.R.P. (5ml), cryoprecipitate (2ml), calcium-gluconate (1ml) and autologous-thrombin (2ml) were mixed in 10ml syringe; after gelification the compound was placed in the chirurgic site. Through test-ELISA were calculated the pg of TGF- β 1 into P.R.P. and into compound after the gelification.

Results: The results for the TGF- β 1 obtained through test-ELISA are the following. 1) For the diluted solution SN (1:300) is has been estimated a release after 1 hour (h) of 22366.50 pgTGF β /ml, after 6h of 30527.50 pgTGF β /ml, after 24h of 19138.88 pgTGF β /ml and in post gel of 11791.63 pgTGF β /ml. 2) For the diluted solution (1:150) is has been estimated a release after 1h of 15712.33 pgTGF β /ml, after 6h of 26850.00 pgTGF β /ml, after 24h of 29450.00 pgTGF β /ml and in post gel of 15321,43 pgTGF β /ml. The TGF- β 1 percentage released has been calculated using two formulas: (SN/SN+TOT) e (SN/TOT). The results using first formula were respectively after 1h of 7.6%, after 6h of 8.6% and after 24h of 20.5%. The results using second formula were after 1h of 8.4%, after 6h of 14.8% and after 24h of 19.9%. These results have been matched with the ones obtained through cytofluorimetric analysis of the samples marked with monoclonal antibodies. They reveal the following datas: for CD 42 the percentage of exposure are after 1h of 79.1%, after 6h of 90.2% after 24h of 87.6% and in post gel of 11.9%; for CD 62p is after 1h of 29.1%, after 6h of 32.4%, after 24h of 52.7%; for CD 63 is after 1h of 64.5%, after 6h of 67.1%, after 24h of 80.3%.

Conclusion: From the cytofluorimetric analysis of the datas we state the procedure to produce P.R.P. it is satisfying since the gel has demonstrated a high platelets density. When the activation and degranulation of the platelets rise (cytofluorimetric), the release of the TGF- β 1 increases (ELISA), but only 20% of the total present in the platelets has been effectively released in the first 24h. This implies that a great quantity of growth factors remains in the paltelets and is available in the chirurgic-site. Untill the 24h it has been observed an increasing of release of the TGF- β 1, with a drop in the quantity once the gel was formed, bringing the levels close to the first hour.

Computerized tomographic and clinical signs evolution in medication-related osteonecrosis of the jaw: is regression of osteosclerosis possible?

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Aim: The objective of this study is to evaluate the evolution of the cone beam computed tomography (CBCT) radiographic signs in a group of patients affected by bisphosphonates-related osteonecrosis of the jaws (BRONJ), while also comparing them with the clinical progress of the disease.

Methods: Seven cases were selected among the patients being treated at Turin University Dental School, using the following inclusion criteria: Diagnosis of BRONJ; Zoledronate treatment for oncological disease; First CBCT performed within 6 months of the Zoledronate therapy beginning; clinical follow-up and yearly CBCTs were performed to evaluate the development of the disease, even after the sequestrectomy, for a total of at least 4 CBCTs for each patient. The CBCT scans have been performed with Newtom (QR, Verona, Italy) equipment and were analyzed by 3 radiologists with experience in the field, whose evaluated the images and the changes over time. Spongy bone osteosclerosis was qualitatively evaluated with regard both to extension and structural characteristics, the last being evaluated with a 4-point scale: Grade 1: trabecular thickening with preserved trabecular architecture; Grade 2: increase of thickening and alteration of the architecture of the trabeculae, stuffed but still recognizable; Grade 3: diffuse osteosclerosis of the spongy bone with loss of identifiability of the trabeculae. Spongy bone still distinguishable from the cortical bone; Grade 4: relevant diffuse osteosclerosis of the spongy bone. Spongy bone not distinguishable from the cortical bone.

Results: In the initial CBCT the patients showed no sign of osteosclerosis. In the CBCTs following the BRONJ diagnosis, all the patients showed signs of osteosclerosis of various degree: specifically, 3 patients showed an increase of the osteosclerosis severity over time, 2 patients a stable osteosclerosis severity over time, 2 patients a reduction of the osteosclerosis severity over time. In these last 2 patients, who presented a progressive osteosclerosis in the earlier CBCT images and had interrupted the bisphosphonates therapy 2 years before and 6 years before respectively, a reduction of the osteosclerosis was noticed, with a return to an almost normal appearance of the spongy bone. Both these patients initially presented a stage 2 BRONJ (AAOMS 2014 staging system), which healed

after therapy.

Conclusion: The originality of this study is the availability of consecutive CBCTs series, which allows an evaluation of the changes that happen in the patient's bone since the start of the bisphosphonates therapy. For the first time an osteosclerosis regression was noticed in 2 BRONJ cases, in patients who had interrupted the bisphosphonates therapy since at least 2 years. It's worth noticing how the osteosclerosis represents a variable parameter over time, even though the mechanisms that determine an increase, a stabilization or a regression over time, in different patients, are still unclear. Considering the limits of this study, mostly attributable to the small sample size, further research would be recommended. Further studies could also investigate the importance of early radiological signs as a predictive factor of the disease.

0,25 mm of switching platform reduces bone resorption: perspective evaluation on 84 consecutive cases

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Aim: This perspective study is aimed to evaluate the hard-tissue maturation around titanium implants. In detail is investigated the influence of the platform switching concept on the evolution of the interproximal bone stability.

Methods: The study includes 84 consecutively enrolled implants: 39 Non Switching (NSP) and 45 Switching (SP) with only 0,25mm of horizontal mismatch. The total follow-up time is 3 years with a planned evaluation at implant placing (baseline), temporary crown placing and 1,2,3 years. All implants were clinically and radiologically monitored at each year follow-up and data regarding facial mucosa height (the distance between the gingival zenith and the incisal edge of the prosthetic restoration) and 4 points probing depth were collected. The x-rays are performed with individualized positioning by the use of a silicon relined rx holder, in order not to change the perspectives, therefore a mean between the mesial and the distal value is measured from the shoulder of

the implant to the first bone to implant visible contact point. All data were inserted in a statistical software (SPSS 20, IBM) and processed. Afterwards delta, mean and statistical correlation results were analyzed (Pearson Two-Tailed 95% Conf. Int.).

Results: After three years, it is observed that the interproximal bone around SP implants is more stable than in NSP implants in every follow-up. While at the third year follow-up the zenith around conventional implants (NS) shows an average resorption of 0,080 mm, in SP conditions the average resorption is just 0,037mm. This results are statistically significant at every follow up. Provisional crown ($p = 0,002$), 1 year ($p = 0,016$), 2 years ($p = 0,011$), 3 years ($p = 0,068$). (Pearson Two-Tailed 95% Conf. Int.).

Conclusions: Whenever a correct surgery is performed, patient's domiciliar maintenance is observed and good prosthetic design is reached, platform switching implants play a cutting edge role on inter-proximal bone stability. The evidence confirms that a Platform Switching value of 0,25mm is enough to reduce interproximal bone resorption around implants, especially in the first 2 years period of maturation.

Management of post surgical pain in third molar extraction. Non pharmacological treatment with kinesiotopeing

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Aim: Although the extraction of an impacted third molar is a routine procedure, patients are often subject to postoperative morbidities such as swelling, pain, and trismus. After its introduction in the 1970s, kinesiologic tape (KT) has increasingly become popular in the treatment of sport injuries and a variety of other conditions. There are several claims to the effects of KT including supporting injured muscles and joints, relieving pain, and increasing blood and lymph flow in the injured area. The main purpose of KT method to improve the blood and lymph flow, remove congestions of lymphatic fluid or hemorrhages, and thus, its use has gained popularity in the management of lymphedema. These effects are due to the elevation of the space under skin and soft tissue, so that the space for movement can be enlarged, the circulation of blood and lymph fluid can be facilitated, and healing rate of tissue can be increased. Besides there is positive effect on opening microvalves due to dynamic pressure variation. Since periodic compression and decompression to superficial and deep lymphatics, through expansion

and contractile properties of the tape during active movement, the flow and circulation are improved, pressure in each segment can be changed. The lymph and interstitial fluid can recirculate and decrease the swelling and pain sensation. Given scientific literature has yet to completely address KT method in oromaxillofacial surgery, the aim of the present pilot study is to investigate whether the application of elastic therapeutic tape prevents or decreases postoperative complications after third molar surgery, thus improving patients' well-being.

Methods: Tape was applied directly on 5 patients after surgery (third molar removal in local anesthesia) and maintained for at least 3 days postoperatively. Pain, degree of mouth opening and facial swelling were measured. Pain scores were assessed using a 10-level visual analog scale (VAS) subdivided in 10 mm increments, where 0 indicates no pain; 5, moderate pain; and 10, severe pain. Patients were asked to place a mark along the line to specify their pain sensation. Mouth opening range was assessed by means of standard calipers. Facial swelling was quantified comparing the operated side with contralateral. In addition patients' objective feeling and satisfaction was queried: they were asked to evaluate overall satisfaction and swelling and the effect of the tape on movement and comfort.

Results: The results of this pilot study seem encouraging. The postoperative application of kinesiologic tape reduced significantly all investigated parameters: swelling, pain, and trismus. Furthermore, patients with kinesiologic tape reported a significantly lower morbidity rate.

Conclusion: Although the removal of third molars is one of the most frequent and routine operations in oral cavity, postoperative morbidity affect patients' quality of life. This pilot study shows that KT after third molar surgery is a simple, less traumatic, and economical approach for managing postsurgery swelling that is free from systemic adverse reactions, thus improving patients' well-being. Given these qualities, KT application holds promise to enhance the quality of life of a large cohort of the population.

Bleeding events after simple dental extraction among patients undergoing anticoagulation therapy: cohort prospective comparative study

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Aim: The aim of the study is to evaluate and compare the intra- and post-operative bleeding during a

simple dental extraction, among patients undergoing conventional Oral Anticoagulant Therapy (OAT) and patients assuming Direct Oral Anticoagulants (DOACs).

Methods: Patients in chronic oral anticoagulant therapy (at least 6 months) with indication of a single dental extraction were enrolled and divided between OAT e DOACs group. All the participants were evaluated at four different time-points: T0 during the first examination, T1 during surgery, T2 thirty minutes after surgery and T3 the day of suture removal (seven days after surgery). At the different time-points anagraphic, medical history, local periodontal and dental variables were collected. The surgical protocol consisted in a simple dental extraction lead by the same surgeon (FB), in the least invasive procedure. Bleeding occurrence and biological complications were registered, according to Iwabuchi classification.

Results: 15 patients (mean age $77,27 \pm 5,72$) and 18 patients (mean age $75,94 \pm 12,18$) were enrolled respectively in OAT e DOACs group. Overall 33 teeth were extracted within 20 minutes of surgical time (cut off that defined the simple extraction in our research protocol). The results of the present study showed no statistical difference between the two groups regarding the intraoperative bleeding and post-extraction bleeding complications. In detail, no intra-operative bleeding occurred, two patients for each group reported a post-operative bleeding managed with a single gauze compression during the week after the extraction, three patients of OAT group and one subject belonging to DOACs group needed more than two compressions in the week, and finally one patient for each group referred to our dental first aid. In these two cases, the urgency was managed with the local application of tranexamic acid and the complication could be attributable to high blood pressure values.

Conclusion: Within the limits of the present study, apparently, patients assuming DOACs can be treated for simple oral surgery like patients undergoing OAT with INR index in therapeutic range. No discontinuation or changes of anticoagulation treatment with novel oral anticoagulants are possibly required. The adoption of local hemostasis techniques represents the most important precaution to prevent bleeding complications and to discriminate between bleeding caused by anticoagulation therapy and surgical technique. The patient education for the post-operative care of surgical site appears also strictly necessary.

Mandibular ameloblastic fibroma: a case report

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Aim: Ameloblastic fibroma is an uncommon benign odontogenic tumor, composed of proliferating odontogenic epithelium embedded in a cellular ectomesenchymal tissue. This type of neoplasm comprises about 1.5–4.5% of all odontogenic tumors. It is located in the posterior mandible, corresponding to the second primary molar or first permanent molar region, and associated with an impacted tooth in 75% of cases. Ameloblastic fibroma is frequently diagnosed between the 1st and 2nd decades of life and it is primarily considered tumor of childhood and adolescence. Males show a slightly higher prediction than females (M : F = 1.4 : 1). This odontogenic tumor appears as well-defined unilocular or multilocular radiolucencies. Unilocular lesions are predominantly asymptomatic, while the multilocular cases are often associated with jaw swelling. Frequently, ameloblastic fibroma is encountered as an incidental finding reiterating their radiographic significance in the differential diagnosis with entities such as dentigerous cyst, ameloblastoma, odontogenic keratocyst, and ameloblastic fibrosarcoma. In this case report we describe the diagnosis and surgical therapy of mandibular ameloblastic fibroma found in a child.

Methods: A 7-year-old boy was referred to Dentistry Unit of Bambino Gesù Children's Hospital for dental treatment. During radiographic evaluation, we found the presence of an unilocular radiolucent area, with sclerotic borders, extending from the right first permanent molar to the mandibular ramus on the same side. Extraoral physical examination showed an unperceivable swelling in the mandibular angle on the right side, which caused a light facial asymmetry. Intraoral examination revealed a light swelling of the alveolar ridge in the right posteroinferior region. His medical history revealed no pathologies and the parents reported no eating difficulties. Tomographic examination through three-dimensional reconstruction indicated a neoplastic mass involving the labial and buccal cortex and extending up to mandibular ramus and its dimensions were 32x20x40 mm (DAPxDTxDL). The lesion was excised and curettage of the adjacent mandibular bone was performed under general anesthesia. The surgical specimen was then sent for histopathological analysis. Microscopically, the lesion showed proliferation of strands of ameloblastic epithelial cells within an cellular connective tissue stroma that closely simulates the dental papilla.

Results: The young patient is followed up for 2 years

and no clinical or radiographic signs of recurrence or malignant transformation were observed, demonstrating the success of treatment.

Conclusion: A careful treatment planning is necessary considering their recurrence rate and ability to undergo malignant transformation. During childhood or adolescence, the first choice of treatment should be a conservative surgical approach to minimize morbidity, allow mastication and continued facial and tooth development.

Evaluation of intra- and post-operative parameters in third molar extraction: conventional surgery vs laser ER:YAG and piezosurgery. A pilot study

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Aim: Third molar surgery is the most common procedure performed by oral and maxillofacial surgeons. Surgical removal of an impacted third molar often involves postoperative pain, swelling and oedema. Principal factors that contribute to post-operative discomfort originate from inflammatory process created by intra-operative trauma. Different methods and innovative instruments have been used to reduce postoperative sequelae, including the applications of low level laser therapy (LLLT), the use of corticosteroids and the use of new techniques and technologies. Er:YAG laser and piezosurgery have been extensively used in dentistry for different purposes. The aim of our study is to compare the use of Er:YAG laser and piezosurgery with rotary instruments for bone removal in third molar surgery with regard to surgery time and severity of postoperative sequelae.

Methods: We present a clinical trial in which 73 subjects were consecutively assigned into 3 groups according to the instruments used for the osteotomy. In Group A (29 patients) the Er:YAG laser was used (Fidelis Plus, Fotona - Slovenia: 300 mJ, 30 Hz, fluence di 60 J/cm²), Group B (37 patients) conventional bur (Lindemann bur-1.6 mm) and Group C (7 patients) piezosurgery (Mectron Medical Technology). All surgical procedures were standardized. Interventions were performed at the Unit of Oral Medicine and Laser Surgery of the University of Parma.

Intra-operative parameters considered have been 1) time of intervention; 2) number of stitches and 3) compliance of patients. Measurement for facial swelling, pain and mouth opening were recorded preoperatively and postoperatively (at 2 and 7 days). Data were analysed using the Statistical Package for

the Social Sciences (SPSS) IBM version 20.

Results: The time needed to complete the third molar extraction was significantly greater for the piezosurgery group (2120") than for the rotatory group (1859") and the laser group (1083"). A statistically significant differences emerged between the 3 methods ($p=0,002$). With regard to number of stitches and compliance of patients, no statistically significant differences was found into 3 groups ($p=0,93$ and $p=0,70$). During all evaluations patients treated with Er: YAG laser had significantly less pain, measured through self-report questionnaire, than those in the other groups. Post-operative swelling was present in all 3 groups. However, values of swelling were significantly higher in traditional group, at day 2 and 7 for all distances between anatomical points considered in the face. Mouth opening (inter-incisal distance) was reduced on day 2 and 7 in traditional and piezosurgery groups. Patients in laser group had significantly less trismus.

Conclusion: In our experience, the osteotomy technique with Er: YAG laser instrument has produced a significant reduction of operative time, facial swelling, trismus and pain compared than rotatory instruments and piezosurgery. Er: YAG offers several advantages in third molar extraction and it can be considered a reliable alternative to conventional bur for wisdom tooth surgery.

Vitamin D and osseointegration a systematic review

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Aim: Currently the roles of vitamin D and his efficacy on osseointegration of dental implants is not clear. The aim of this study was to do a literature sitematic review on the vitamin D influence over the osseointegration processes.

Methods: This review is done using PRISMA (Preferred reporting items for systematic reviews and meta-analyses) statement tools. For studies identification to include in our analysis, we have researched on database Pubmed, Cochrane Central Register of Controlled Trials ed Embase, with the last access 05/2/2017. We have also hand searched following journal: Clinical Oral Implant Res, J Oral Maxillofacial Res e Oral Surg Oral Med Pathol Oral Radiol. We have checked the bibliography of the studies included for additional studies. We have used different key words like: Vitamin D, Vit. D, Vitamin D3, Vit. D3, osseointegration, dental implants, 1,25 dihydroxyvitamin D3. We have included

only studies written in English language published until february 2017.

Results: With electronic and paper research we have found 229 articles. After the duplicates elimination are remained 72 articles. After titles and abstracts screening we have decided to read full-text 27 articles. At the end we have refused 15 articles and included 12 articles. For parameters and criteria heterogeneity used in the studies analyzed was not easy to compare the results and was not possible to perform a meta-analysis. We found five main topics in the included studies: 1) Effect of vitamin D deficiency on osseointegration in rat model 2) Effect of vitamin D surface implant coating on osseointegration in dog and rabbit model 3) Effect of vitamin D supplementation on osseointegration in a ovariectomized rat model 4) Effect of vitamin D genic polymorphism on osseointegration in human and rat model 6) Effect of vitamin D supplementation in diabetic rat model. Overall, these studies provide first hints that vitamin D supplementation can have a moderate therapeutic benefit on osseointegration. Certainly is sure that restore good level of vitamin D is healthy. From this studies comes out also that vitamin D efficacy is proportional to is shortage. Vitamin D lower level and osseointegration greater impairment means greater effectiveness of supplementation. However at this time of research there isn't a very efficacy protocol to subministration vitamin D.

Conclusion: However studies indicates a relationship between vitamin d and osteointegration, at the current knowledge is not possible to drawn conclusion. We need further studies.

One-year follow-up of the outcome of treatment of localized gingival recession using the connective tissue graft (CTG) combined with coronally advanced flap (CAF); a case report

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Aim: The treatment of buccal gingival recessions is a common requirement due to aesthetic concern, root sensivity or keratinized gingiva. Various techniques have been employed for increasing the width of keratinized gingiva. The connective tissue graft (CTG) effectively increased the width of keratinized gingiva. This case describes the outcome of treatment of single gingival recession using the connective tissue graft (CTG) combined with coronally advanced flap (CAF).

Methods: A 42-year-old female patient, sistematicly healthy, was apply to the our clinic with complain of

an un-aesthetic maxilae canine tooth (tooth #23) with sensitivity to hot and cold stimulus. The management involved scaling and root planning, root surface conditioning (24% EDTA), elevation of full-split-full thickness flap, harvested the CTG. Probing pocket depth (PPD) and clinical attachment level (CAL) were measured at baseline, 6 and 12 months post-surgery. Gingival thickness (GT) was recorded at baseline and 12 months post-surgery.

Results: Healing was uneventful. One-year observations and measurements showed satisfying root coverage, a gingival margin that was harmonious with the neighboring teeth. Final root coverage of 100% was achieved.

Conclusion: Within the limitations of the present case report observations, it is suggested that the connective tissue graft (CTG) combined with coronally advanced flap (CAF) may be a valuable surgical procedure for the achievement of soft tissue root coverage and gain of clinical attachment in the treatment of of localized gingival recession.

Surgical oral treatment of patients receiving new oral anticoagulation (NOAC) therapies: management of the risk of bleeding and of thromboembolic events

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Aim: Because of the relatively recent introduction of new oral anticoagulation (NOAC) therapies, there are few clinical reports in the literature concerning oral surgeries on patients receiving new oral anticoagulants. This is why we thought it worthwhile to report the outcome of the first tooth extractions and implant placements performed in our institution on a small number of such patients. Our aim was to discuss the outcome of oral surgery on NOAC patients with the need to balance hemorrhagic and thrombotic risks and to give dentists who will have to perform dental surgical procedures on this new type of patient a preliminary indication on the possibility of managing surgical and cardiac risks, specifically, the need to contain severe bleeding after surgery with the clinical advice of the EHRA and the indications of the patient's cardiologist.

Methods: This retrospective study considered 12 patients receiving therapy for non-valvular atrial fibrillation (NVAf) or thromboembolic events undergoing tooth extraction and/or implant procedures. According to the suggestions of the European Heart Rhythm Association (EHRA), each patient was attributed a pre-surgery risk factor based on her/his comorbidities and estimated filtration



glomerular rate (eGFR); additionally, for NVAF patients, each patient was given CHA2DS2-VASc and HAS-BLED scores. Patients' cardiologists prescribed the pre-surgery protocol, no interruption of NOAC or suspension of NOAC 24 or 36 hours before the procedure. The patients were monitored for up to 7 days for bleeding and for up to one month for thromboembolic events.

Results: There was no severe bleeding calling for re-intervention. There was one light bleeding event on day 1 reported by an NVAF patient who was easily managed with gauze compression, whose extremely high thrombotic risk (CHA2DS2-VASc 8/9) excluded any interruption in the anticoagulant therapy. No patient had thromboembolic events in the one-month period following oral surgery.

Conclusion: The indications of EHRA are a good template for dentists who must handle surgery for patients on NOAC with non-modifiable risk factors such as comorbid conditions, however, many unresolved questions on how to optimally use these drugs in specific situations remain. Most risk factors that predispose a patient to bleeding are outside the possibility of the oral surgeon to modify or decide, including comorbidities, systemic risks and, most of all, the decision about continuing or discontinuing the anticoagulant therapy, which is left to the patient's cardiologist. The oral surgeon has the responsibility for safe patient management and surgical planning, taking into consideration the lack of antidotes for NOAC that is different from conventional OAT. The collaboration between the patient's cardiologist and the oral surgeon is essential for the patient's wellbeing. Further data are needed. We hope that a wider use of these new oral anticoagulants will be accompanied by the development of institutional guidelines to efficiently guide dental health care providers in all steps, from perioperative anticoagulation management to the handling of severe bleeding emergencies. The development of such policies will be fundamental specifically for general dental practitioners who will have to plan invasive dental treatment outside the hospital structure.

Effect of a gel containing hyaluronic acid and amino acids on early wound healing of the alveolar socket after mandibular third molar extraction: a double blind RCT. Preliminary results.

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Aim: The aim of this study was to assess the effect a topical application of amino acids and sodium hyaluronate gel on early healing of alveolar socket after the surgical extraction of impacted lower third molars.

Methods: A randomized, controlled, double-blind clinical study was conducted on 136 patients between 18 and 25 years of age requiring lower third molar extraction. Immediately after the extraction in the patients of test group the post extraction socket was filled with a sterile gel containing amino acids and sodium hyaluronate while patients in control group received only a sterile saline solution socket wash. The parameters assessed at 7 and 14 post-operative days were dehiscence, exudate, mouth opening range, clinical aspect of soft tissues, alveolitis, subjective pain, NSAIDs consumption, postoperative complications. Primary (cumulative incidence of dehiscence) and secondary outcome measures were evaluated with chi-square test and bilateral confidence interval of 95% was produced. Mouth opening range modifications were evaluated with Student's t-test and pain perception was processed using repeated measures analysis of variance. The study hypothesis was that intra socket amino acids and sodium hyaluronate gel would be more effective than no treatment in terms of early wound healing, postoperative sequelae and pain perception after mandibular third molar extractions.

Results: The incidence of wound dehiscence at 7 days was 36.4% in the control group and 27.4% in the treated group with no statistically significant differences between the two treatment groups ($p = 0.28$). The rate of wound dehiscence at 14th day was 36.0% in the control and 21.4% in the treated group ($p = 0.10$). No statistically significant differences were found in comparing the two groups at the two times. Even for the other variables analyzed were not highlighted statistically significant differences. The intake of NSAIDs was higher mainly in the 3rd postoperative days and then decreased or was discontinued at the end of the post-operative week. Significant difference between groups was not shown. Pain perception during the 7 days after surgery had similar pattern in the two groups.

Conclusions: Our analyses indicate that no statistically significant differences were found between the two groups, but patients belonging to the test group showed better wound healing and perceived less postoperative pain.

Canalicular adenoma of minor salivary glands: literature review and case report

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Aim: Study and review the clinical and histological characteristics of the canalicular adenoma, evaluate its short and long-termed recurrence, its occurrence regarding ethnic groups, emphasizing the importance of the histologic analysis and the extended follow up.

Methods: Literature review regarding recurrence, locations, clinical, histological and immunohistochemical manifestations. A case report of a 73 years old female patient sought to dental care for an asymptomatic swelling in the right buccal mucosa. Visiting the patient, confirmed the presence of a nodular and floating lesion, the diagnosis was performed after surgical excision, and histological exam which confirmed a canalicular adenoma.

Results: The literature review showed a bit of disparity in the canalicular adenoma ratios regarding location, occurrence, the average age range of affection, clinical appearance and signs, but it was agreed that it is a benign tumor, its most commonly site is the upper lip then the buccal mucosa, less frequently the palate, parotid gland and extremely rare intra-mandibular (4 cases), and that it occurs mainly in elderly patients (more than 40 years) with slight predilection to females, clinically painless, slow growing, and has a tendency to present as a multifocal lesion specially in the upper lip, whom diameter is about 3 mm to 3 cm.

After continues follow ups so far our patients didn't show any signs of recurrence but its not rarely reported in the literature the recurrence on a short and long-termed distance of time (months to years).

Histologically its distinguished by the composition of layers of cells stratified in columns-like form, and immunohistochemically by the absence of protein s100, p63, ck5/6, GFAP. Its important to keep in mind that about 24% of canalicular adenoma shows foci of tumor islands micro and macroscopically which may mislead the examiner towards malignancy.

Conclusions: Despite the fact that canalicular adenoma has its clinical features that defines it from other similar lesions, its final diagnosis can't be done before or without the histological exam to eliminate any other potential more serious benign or malign lesions. Extended follow up (up to 12 years) must be performed to inspect for any potential recurrences in the prior location or any other common places, or would it be more appropriate to say that a previously diagnosed patient with canalicular adenoma should be considered more susceptible to future occurrences of it in the same or even in the contralateral side and other frequent places of appearance.

Clinical and histological evaluation of a new approach in alveolar ridge preservation

technique in the aesthetic zone: a prospective single cohort study

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Aim: Alveolar ridge resorption following tooth removal is an undesirable, but well-documented physiologic process. The reduction of the alveolar ridge width following extraction is usually greater than the loss of height in the first 6 months after extraction. Different ridge preservation or augmentation techniques have been advocated to avoid or minimize this resorptive process, using different bone grafting materials or in conjunction with barrier membranes. The purpose of this prospective single cohort study was to evaluate the use of a xenograft and a collagen matrix in treating full or partial buccal bone defects of fresh extraction sockets in the aesthetic zone.

Methods: This a prospective cohort study was conducted on 14 patients (8 males, 6 females, mean age 44.7 years old). Patients considered eligible for the study received tooth extraction and ridge preservation with a bovine derived bone (90% anorganic bovine bone in combination with 10% porcine collagen fibers) and soft tissue closure with a collagen matrix (a resorbable bilayer matrix composed of porcine collagen). Following 16 weeks of healing, clinical measurements as horizontal ridge width, vertical ridge changes and width of keratinized gingiva were recorded and a core biopsy was obtained and prepared for histologic evaluation of percentages of vital bone, residual graft, and soft tissues assessment in each patient.

Results: All treated sites allowed the placement of implants. The mean horizontal ridge width at the buccal crest for the treated patients decreased from 8.2 ± 1.1 to $7.8 - 1.2$ mm for a mean loss of 0.4 ± 0.8 mm ($P > 0.05$). The mean values of the facial soft tissue level indicated an increase over time. Moreover, the vertical change at the lingual sites was 0.5 mm and the keratinized gingiva showed a coronal shift 1.2 mm. In addition, 12% of sites required an additional bone augmentation at implant placement. The biopsies harvested from the grafted sites revealed the presence of trabecular bone, which was highly mineralized and well structured. Finally, in the palatal area no bone changes were observed. No implant failed during the

entire observation period.

Conclusion: The ridge preservation procedure allows to counteract the bone loss after tooth extraction even though the bone modelling and remodelling after a tooth extraction is not completely avoidable. The technique with xenograft and a membrane with a double layer used for ridge preservation of the extraction sockets in the aesthetic zone can be considered effective in repairing bone defects before implant placement. The secondary soft tissue healing showed a significant improvement as the soft tissue level and the width of keratinized gingiva over time and did not compromise bone formation. The results of this study demonstrated that this technique may represent an advantage in cases when aesthetic concerns are of primary interest.

Radiological, histological and histomorphometrical evaluation of a biomimetic nanostructured matrix as sinus augmentation graft

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Aim: Recently, oral surgery became rich with new means to improve the relationship between the bone substitutes, surrounding tissue and human organism: the regeneration led by the tissues represents one of the most encouraging examples. Many bone substitutes have been applied for sinus regeneration procedure, such as autogenous bone, inorganic bovine bone, porous and resorbable hydroxyapatite, tricalcium phosphate, bioactive glass, and blood clot. The application of bone grafts is oriented to promote bone formation with faster resorption processes and new combinations of osteoinductive scaffolds. The aim of the study was to evaluate in vivo a biomimetic nanostructured matrix composed by MgHA/collagen-based scaffold as a sinus augmentation graft.

Methods: Eleven healthy patients (mean age: 52yo; range 48–65 yo) were treated and for sinus augmentation and implant rehabilitations. The maxillary sinuses were filled with MgHA/collagen-based scaffold with a porous three-dimensional design (3D) with a composite architecture, mimicking the complex hierarchically organized bone structure. Cone Beam Computed Tomography evaluation (3D CBCT) was performed for

preoperative and post-surgical sinus augmentation. Bone specimens were obtained by trephine bur to achieve histological and histomorphometrical analysis to evaluate the residual grafted material, the percentages of newly-formed bone and marrow spaces.

Results: CBCT scans bone augmentation showed in all patients treated hyperdensity in comparison between immediate postoperative period and late postoperative period, with more density than native bone at both times (mean volume after graft elevation= 2906 mm³, min=2148.8 mm³ max= 3146.4 mm³). In the late postoperative period (6 months) the mean volume after graft elevation was 2806.7 mm³ (min=2010.9 mm³ max=3008.9 mm³). The statistical analysis demonstrated a significant difference for volume change (P <0.01%). Histological analysis shows that at low magnification trabecular mature bone was present in all specimens without any pathological inflammatory cell infiltrate. No foreign body reactions were present and the graft were completely resorbed. Mature bone deriving from the endosteal surface filled the external portion of the bone sinus, and the periphery and central portion of the cavities showed mineralized new bone formation. The sinuses were completely healed and no particles or MgHA/collagen-based scaffolds were visible. Furthermore it was observed seams of osteoblasts and unmineralized matrix with collagen fibrils at areas of new bone apposition. The tissues present in the sample were composed of 2 ± 2% of lamellar bone, 36 ± 1% of woven bone and 58 ± 4% of marrow spaces.

Conclusions: MgHA/collagen-based scaffold evaluated is an highly biocompatible bone substitute which particles have an almost complete resorbable quality; infact no residual material was found. The biomaterial which is gradually replaced by new bone apposition. The clinical and histological evidences show that MgHA/collagen-based scaffold can be used, successfully, for sinus augmentation procedures.

Histological features of bone substitutes used in GBR and socket preservation procedures: a review of the literature

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Aim: Bone regeneration in dentistry has been largely discussed throughout the years and many different bone substitutes have been studied and released on the market. The aim of this systematic review was to answer the focused questions: in humans, what are

the histologic results of these materials used in GBR and graft procedures in term of newborn formation, residual graft and bone marrow? The answer to this question is significant to understand if one material stands out compared to the others in terms of effectiveness and reliability.

Methods: We revised the literature on the subject by searching on "PubMed". and as inclusion criteria we selected "clinical trials", "humans", "histomorphometric or bioptic analysis", "GBR" and "onlay". Electronic databases were searched for human studies reporting on GBR, graft and socket preservation procedures reporting the histological results in term of newborn formation, residual graft and bone marrow.

Results: Twenty-two studies were included and from them were extracted the following parameters: n° of patients, average age, timing of the follow up, n° of samples taken for the histomorfometric evaluation, % of new vital bone, % of residual graft, % of connective tissue, side effects and failures. In general, studies presented with an unclear-to-high risk of bias. In some studies, materials were blended with other material or with PRP or with grow factors. The studies presented histological observation with a follow up included between two to nine months. The minimum and maximum observation were respectively 28% and 78 % for newbone formation, 0% and 38% for residual graft and 6% and 78% for bone marrow. The materials with larger samples were, in decreasing order, FDBA (mineralized freeze-dried bone allografts) with 149 patients, BB (bovine bone xenografts) with 91 patients and CS (calcium sulfate) with 73 patients. This review report a large variability between different bone substitutes used in GBR, grafting and socket preservation procedures.

Conclusion: From the results of this review we can not what is the perfect material, because the combination of the histological aspects does not provide an unique result. Moreover the histological observations of newborn formation, graft resorption and bone marrow quantity are not the only aspects to be taken in account to identify the best material. Other important features are the volumetric stability of the graft and the long term survival of implants placed in the graft. This review allows to compare different bone substitutes used in apposition procedures on the basis of their histological aspects. This results were important both for the clinician and for the researcher. Moreover, further studies are needed to clarify which material is the best solution in these procedures.

Maxillary sinus aspergillosis: a case report

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Aim: Approximately 10–12% of cases of maxillary sinusitis are caused by odontogenic infection, due to the proximity of the roots of posterior maxillary teeth with the maxillary sinus cavities. Apical and marginal periodontitis constitute 83% of odontogenic factors that may cause signs in maxillary sinuses. Although bacteria are the most extensively studied etiological agents in endodontic infections, fungi also can be isolated from root canals. The presence of filamentous fungi in root channels of teeth with pulp necrosis and apical periodontitis was first detected by Gomes et al. in 2010. There are several articles published in the medical literature that link the presence of filamentous fungi in the maxillary sinus with endodontically treated root canals in close contact with the maxillary sinus. Radiographically, the unique appearance of a dense opacity foreign body reaction in the maxillary sinus is considered a characteristic finding. The purpose of this article is to report a symptom-free case with the extrusion of obturation material into the maxillary sinus and its surgical management.

Methods: We reported a sinus aspergillosis case of a patient of 43 years old. The patient comes to our attention with edentulous of 1.6; is highlighted a OPT mucosal thickening of the right maxillary sinus floor, with evidence of high density nucleus, compatible with extruded endodontic material in the maxillary sinus, as a result of root canal therapy of 1.6, referred from the patient's anamnesis. A diagnosis of chronic sinusitis was made right for this case. It programs then surgical removal of the above material with simultaneous curettage of right maxillary sinus cavity. Making intrasulcular full-thickness incision up to teeth 1.7 and a full-thickness mesial incision until the alveolar mucosa; making osteotomy of the anterior wall of the maxillary sinus; making cleaning of the entire sinus cavity and removing foreign material; washing the cavity with antibiotic solution and suturing with silk points.

Results: The removed foreign material was confirmed to consist of gutta-percha and zinc oxide cement. Foreign materials were chemically fixed immediately and dehydrated; they were then embedded in epoxy resin. The histopathologic examination revealed that the lamellar keratinlike layer lay between the gutta-percha and the connective tissue, and that inflammatory cell infiltration was weak in the connective tissue. The histological diagnosis of the tissue confirmed fungal mycelium, and the mycologic analysis confirmed *Aspergillus fumigatus*.

Conclusion: In non-immunocompromised patients, aspergillosis of the paranasal sinuses is a relatively rare disease, although foreign substances in the maxillary sinus have been related to the occurrence

of aspergillosis. There are few literatures described about the extrusion cases into the maxillary sinus, and these focus on the occurrence of aspergillosis in the maxillary sinus as a complication of the extruded obturation materials, especially obturation materials that contain zinc oxide are considered to be a growth factor for *Aspergillus*. Experimental studies with fungus cultures revealed considerable acceleration of the growth of different *Aspergillus* species in the presence of zinc oxide in the culture medium. An additional role could be performed by endodontic materials made of corticosteroids, that can allow settlement and proliferation of fungi through suppression of cell-linked immunity. With this case report we want to emphasize importance of a correct root canal orthograde therapy of the posterior maxillary teeth, particularly for those whose apex, are in continuity with the sinus membrane, in order to avoid extrusion of endodontic material in the sinus cavity, able to promote the proliferation of *Aspergillus*, mainly responsible for these forms of chronic sinusitis.

Influence of PRF membrane in the healing of bone and gingival tissues in post-extractive dental implants. Clinical evaluations

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Aim: The aim of this study is to evaluate a predictable protocol in order to increase the peri-implant tissues maintenance around post-extractive dental implants, thanks to the use of platelet rich fibrin membrane (PRF).

Methods: Atraumatic dental extraction and flapless implant surgery was performed in this study. After placing implant we have filled the surgical site with PRF membrane, so as to fill the gap between bone tissue and the implant surface, then we have covered the surgical site with another PRF membrane, so as to coat the gap between alveolar crest and implant.

Results: We observed the complete covering of dental implants, with newly formed soft tissue of variable thickness between 1 and 3 mm.

Conclusion: Long term maintenance of crestal bone and the rapid healing of soft tissue dimension with the support of peri-implant site were observed as outcomes after post-extractive implant insertion. PRF is considered a healing biomaterial, and it has a robust stimulating effect on various aspects including angiogenesis, immune control, harnessing the circulating stem cells, and may be used alone or in combination with bone grafts, promoting hemostasis, bone growth and maturation. PRF membrane helps in wound healing, protecting the surgical site promoting

soft tissue repair; when mixed with bone graft, it may act as a "biological connector", which attracts stem cells, favors the migration of osteoprogenitor cells to the center of the graft, and provides a neo-angiogenesis.

Comparative study between sinus floor elevation and tilted implant in the atrophic posterior maxilla

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Aim: Owing to mechanical and anatomic difficulties, implant treatment in the atrophic maxilla represents a challenge. The purpose of this study was to compare two rehabilitation techniques: the maxillary sinus and the tilted implants.

Methods: Have been selected 10 patients with the same inclusion and exclusion criteria which included age, the absence of systemic diseases, absence of bisphosphonate therapy, the absence of allergies, reduced minimum height of the residual edentulous ridge of 3mm. They were divided into two groups: the test group was made of the breast upward and control group were inserted tilted implants, mesial to the anterior wall of the maxillary sinus whose platform is placed at the level of the first molar, to allow a prosthetic rehabilitation fixed from 1.2 to 1.6 without cantilever distal. Information about the quantity and quality of bone, the system characteristics (shape, diameter and length), the presence of dehiscence and fenestrations and torque implant insertion were recorded on special forms at the time of surgery, both for reasons legal doctor of the final prosthetic management. The patients were followed weekly for the first month to evaluate the healing of the peri-implant soft tissue and the prosthetic functionality. Subsequent check-ups are carried out on the basis of Implant maintenance protocol and when requested by the patient. During the entire observation period it was recorded the plaque index and bleeding index every six months, using a predefined scheme. Every six months for the first two years and then annually up to five years from the load must be carried out individual radiographs with individual centering technique and the long cone for accurate assessment of changes in the peri-implant bone level through computer analysis.

Results: Monitoring visits were found a plaque and bleeding index in the standard (20-25%) and a low percentage of implant loss. There is no statistically significant superiority between the two techniques. The tilted implant offer the possibility of an immediate

aesthetic while for sinus lift you must wait a period of between 4-6 months for the bone healing and proceed to the case of the prosthesis. Also in two of 10 patients it manifested a sinus complication.

Conclusions: Results indicate that the use of tilted implants is an effective and safe alternative to maxillary sinus floor augmentation procedures.

Titanium mesh: early exposure managing proposal

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Aim: Alveolar bone regeneration by means of titanium meshes is a widespread procedure, however only few relevant studies were reported in literature concerning this technique (1). Titanium mesh is a space maintaining device used in conjunction with horizontal and vertical ridge reconstruction for implant placement purposes. The aim is to maintain the desired shape of the graft dissipating the mechanical forces acting against the first phases of bone formation (2). Literature shows that the scaffold choice is mainly autologous or a mixed compound of at least 50% of autologous and anorganic bone (3). This surgical technique is shown not to be free of complications (4). The exposure of the Mesh is evaluated to be a possible event, and is related to the flap's passivation, the surgical site, the mesh geometry, suture technique and multiple addictive factors well described in literature (4). This event is reported with an average frequency of 22,2% (range 5.3% 5.-80% 6.) on 231 cases analyzed (4). Most of the authors reporting exposures assess that ridges were augmented even when this complication occurred, but no managing protocols are described.

Methods: This case report presents a bone regeneration by the use of Ti-mesh filled with 50% of autologous bone and 50% of inorganic bovine bone all covered by a collagen membrane. Twenty days after the surgical procedure is shown an extended exposure of both titanium mesh membrane. The patient is prescribed the following hygienic protocol: chlorhexidine 0.12% rinsing every eight hour and gentle cleaning with a soft post-surgical toothbrush. The mesh is left on site for four months with the aim of waiting for a mechanically stable immature bone formation. New re-epitelization was observed under the mesh during the follow-up time.

Results: After 4 months following the given instruction, frequent control checks and hygienist support, no signs of inflammation around the area is noticed. At x-ray control radiopacity is observed compatible with a bone growth. The resorption of the graft is estimated to be less than 10% of the original volume. Therefore the mesh is removed with minimal mechanical traumas to tissues and, at six months post-op, implants are placed in a prosthetically driven position. At nine years follow up bone and tissue stability is judged optimal.

Conclusion: The exposure of the titanium mesh is a complication that can occur, it nevertheless seems to jeopardize the final outcome (4.) as this event is only associated to a reduction of the graft volume (4.). Comparing the use of the mixed graft with the 100% autogenous, it appears that the remodeling rate of the first is reduced. In the presented case report the maintenance protocol applied in the event of an early exposure achieved a good result, with a long term success of the therapy at 9 years follow up.

Aromatherapy in dentistry. Reassessment over distance of two domestic hygiene maintenance methods, in patients with overdentures on implants: a randomized clinical trial

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Aim: The main aim of this clinical study was to evaluate the greater method to maintain optimal oral hygiene in special implant patients rehabilitated with overdenture retained by four implants splinted by milled bar. This purpose has been pursued by a comparison of effectiveness of the most used principals in this patient's category.

Methods: The study sample involved 18 subjects including 9 women and 9 men aged between 44 and 72 and with a mean age of 62. The treated patients has such implant rehabilitation only in one arch, 11 subjects presented maxillary overdenture and 7 mandibular one. The first step was a registration of main parameters of oral health, including BOP, PI, PPD, and PI on prosthesis attachments to rate periodontal and prosthetics conditions. After this registration patients were subjected to an oral hygiene seat and randomly divided in 2 groups, called group A and group B. The two groups were differently instructed about oral hygiene and different principals were handed them. However in both groups intensive instruction and motivation in oral hygiene were carried out. Group A was instructed to use superfloss and an implant soft toothbrush on implant component; to



brush the prosthesis was use the same toothbrush with any polishing paste. Instead patients of group B used pipe cleaner with plastic core and manual soft toothbrush on implants and the same toothbrush with degreasing soap on the prosthesis. Three weeks later patients were recalled and were re-recorded all parametres considered at the first seat (BOP, PI, PPD, PI on prosthesis attachments).

Results: After two sessions, data of first seat and new data collected were compared with each others and subjected to statistical analysis. The primary outcome is the improvement of each parameter in both groups from T0 (first seat) to T1 (second seat). However this improvement appeared greater in group B than in group A. Statistical analysis confirmed the significance of better results exhibited by group B onlhy for BOP and PI. The minimal improvement of PPD from T0 to T1 was not significant probably due to the short time interval considered; about PI of prosthesis attachments was not found any difference between the two groups.

Conclusions: Search results suggest that apparently instruments given to group B for the implants care have greater efficiency of those used by group A and in particularly highlight the superiority of pipe cleaner than superfloss. However this conclusions must be learned considering the short period considered, low sample number and the dexterity of each individual subject.

Split crest technique in the atrophic maxilla: indication for the treatment

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Aim: Various treatment strategies and techniques have been proposed to perform alveolar bone augmentation; the most common of all is the split crest. In this study, we describe the indication for the bone augmentation techniques in order to optimize the regenerative bone conditions in a bone augmentation technique. In order to plan an intervention with crestal expansion technique it is essential to obtain as much information as possible regarding the actual structural characteristics of the bone residue, both qualitatively and quantitatively. It becomes necessary a presurgical study for three-dimensional evaluating regarding the amount and morphology of the residual ridge, the bone quality, and the relationship with the opposing arch and the prosthesis elements programmed. Objective examination and palpation of the edentulous areas, as well as the radiological study represent the most suitable a diagnostic tools for

obtaining a complete diagnosis of the bone segment to be expanded.

Methods: Cone Beam Computed Tomography is the most appropriate exam for the analysis radiographic investigation of the edentulous alveolar ridge. Thanks to the ridge expansion techniques is possible the dislocation of the buccal bone plate in a labial direction and simultaneous implant insertion in single-stage surgery, abbreviating overall treatment time. The piezoelectric ridge expansion technique permits to obtain the expansion of very mineralized bone crests without excessive traumas or the risk of ridge fractures. The fundamental idea on which is based the piezoelectric surgery is the use of a surgical force able to cut the bone according to the needs of the case. It transmits energy in a controllable way, it minimize the surgical trauma and the reduction of ridge's fracture risk, while stimulating a favorable response of tissue healing.

Results: In base of the result obtaining by the measurement and anatomical variations of CBCT it is possible determine the degree of surgical difficulty in each case and choose the most appropriate surgical technique. Through the analysis of cross-sectional images and their three-dimensional processing, is possible an accurate picture of the actual thickness of the atrophic ridge.

Conclusion: The split crest technique appears to be a promising and effective one to gain bone width. When the pre-surgical study by Cone Beam images shows a triangular shaped ridge, with vestibular cortical thin and poor cancellous bone density, surgical difficulty will be modest. It is not possible having predictable results by using the conventional mechanical method of expansion in front of the present of a very mineralized bone crest that is seen in the edentulous jaws of old date.

Conservative surgical treatment of MRONJ lesions in patients affected by osteoporosis exposed to oral bisphosphonates: 24 months follow-up

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Aim: Purpose of the present study was to evaluate the efficacy of localized surgical treatment of MRONJ lesions in a coorte affected by osteoporosis and exposed to BPS.

Methods: The study included all consecutive subjects

diagnosed with MRONJ that had undergone localized surgery in the Department of Dentistry and Oral Surgery of the University Hospital of Pisa from January 2008 to December 2014. The inclusion criteria were patients affected by osteoporosis exposed with oral bisphosphonates, with MRONJ who had undergone surgical treatment, with at least 24 months follow-up. The exclusion criteria were exposure to radiation focused in head and neck region and treatment with zoledronic acid or other endovenous bisphosphonates. The surgical outcome according to MRONJ stage was evaluated at least 24 months after conservative surgical treatment. After surgery, the patients were seen every week for the first month, and every 3 months up to year. At annual control all the patients were prescribed an OPT in order to evaluate bone healing.

Results: The fifty-three patients revealed 55 lesions; 71% (39 lesions) of the lesions were located in the mandible. Bone exposure was detected in 73% of the cases (72,7%) and MRONJ lesions were mainly symptomatic (50 lesions, 90,9%). Five lesions were associated with hemimandibular paraesthesia and two lesions with oro-antral communication. The most frequent stage at presentation, according to the AAOMS 2014 guidelines, were stage II (41 lesions, 66,6%), followed by stage I and III, which presented the same number of lesions (7 lesions, 16,7%). In 53% of lesions the triggering event leading to MRONJ was dental extraction, in 18% prosthetic trauma, in 16% dental abscess and in 11% periodontal/peri-implant disease; in one case the lesions was triggered by dysodontiasis of mandibular third molar. During the two years' follow-up four patients died. Forty-eight lesions (87,3%) show complete healing after surgical treatment. However, seven lesions (22,7%) do not completely recuperate and required further surgical management to treat the relapsed lesion. Stratification indicated 100% total disease resolution for all stage I lesions, 90,2% of improvement for stage II (37 lesions) and 57% for stage III (4 lesions).

Conclusion: This is the first prospective cohort study that analyse the effect of surgical treatment on MRONJ lesions in patients exposed to oral bisphosphonate. Our data suggest that patients with MRONJ lesions may benefit from local surgical treatment. Patients affected by rheumatoid arthritis with severe MRONJ stage seem to present an increased risk of surgical treatment failure.

Oral metastasis of a bladder primitive cancer firstly diagnosed through an oral biopsy: case report

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Aim: Aim of this report is to describe an extremely rare case of a secondary oral metastasis due to a primitive bladder cancer, firstly diagnosed through an oral biopsy.

Methods: The patient is a 69 years old man, smoker, and has a history of hypertension and poor oral compliance; he went to his dentist for a single tooth extraction due to coronal fracture and dental mobility of element 3.5. A week after the extraction of the tooth he came back to his dentist with an exophytic lesion in the surgical site. The first diagnostic hypotheses made was a hypertrophied clot, the dentist made a surgical debridement of the clot. Less than a week after the first surgical debridement the patient came back with the same exophytic lesion. The patient was scheduled for an oral pathology visit and the oral surgeon decided to make a biopsy of the lesion.

Results: the histological diagnosis was a carcinoma with a papillary aspect. A metastasis of this lesion was suspected. According with the physician an abdominal and chest CT scan was prescribed and a bladder carcinoma was detected. The oncology specialist provides a T3N1M1 staging of the primary bladder carcinoma. A week later the oral lesion grew up and more than doubled its size. Chemotherapy and radiotherapy were started with positive results. After 6 months since the diagnosis, the patient is still alive despite the low rating survival, below the 15%.

Conclusion: Metastasis to the oral cavity generally is not common and far more uncommon are oral metastasis from bladder cancers which usually gives metastasis to breast, lung and kidney. The most common cancers types metastasizing to the oral cavity include lung and breast carcinomas. On the contrary, distant metastases, that are the far more unusual form of bladder cancer (4% of cases), involves usually lung (33-72%), infra-abdominal lymph nodes (3-35%), bone (21-25%), brain (7-13%) and liver (5-10%). The literature reviews identified the gingiva and alveolar mucosa as the commonest site for intraoral metastasis (54.8%) followed by the tongue (27.4%). It forms about 1-3% of all malignant oral neoplasms. The purpose of this study is to show an extremely rare metastatic mandibular tumour and the correct practitioner behaviour. It was quite difficult to make a first diagnostic decision due to the similar aspect of the metastatic lesion to a hypertrophied clot. Only after the relapse, the malignancy of the lesion was suspected. It becomes mandatory to make a biopsy due to obtain the correct diagnosis. The growth of this lesion was impressive; it doubled its size in a month since the first debridement. One of the most frequent complication referred by the patient was the inability to feed himself. The focus point of this study is to suggest every clinician to suspect something different



from a bad healing when a lesion recurs after a surgical wound debridement.

Evaluation of combined surgical approach in sinonasal complications of dental disease or treatment

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Aim: To evaluate the outcomes of combined surgical approach in sinonasal complications of dental disease or treatment (SCDDT) such as periapical granulomas, chronic oral antral fistula (OAF), foreign bodies (endodontics material, dental implants, teeth roots, parts of broken instruments), odontogenic tumors or odontogenic cysts.

Methods: 35 patients affected by SCDDT were included in this study. All of them presented chronic maxillary sinusitis of dental origin. 16 patients presented OAF after dental extractions, 4 patients presented periapical granulomas, 4 patients presented foreign bodies into the sinus (1 dental implant and 3 dental fillings), 5 patients presented odontogenic cysts and 6 patients were affected by odontogenic tumors. Preoperative orthopantomography and computed tomography scans in axial, sagittal and coronal plane were evaluated for precise diagnosis of the location. 17 patients were treated under local anesthesia plus conscious sedation and 18 patients were treated under general anesthesia. The protocol consisted of: antibiotic therapy (Amoxicillin – Clavulanic Acid 1 g/2 times per day orally) plus oral steroid therapy 1 week before surgery; one stage surgical procedure with the treatment of the odontogenic source (closing the OAF with a Rehrmann's buccal advancement flap, removal of cysts, tumors and foreign bodies and surgical endodontic treatment of the teeth affected by the lesion) and the endoscopic sinus surgery (ESS) with opening the maxillary natural ostium; antibiotic therapy (Amoxicillin – Clavulanic acid 1 g/2 times per day orally) 1 week after surgery. Patients were followed up weekly for the first month.

Results: At the 1 week, 2 weeks, 3 weeks and 6 month follow - up no endoscopic and radiological evidences of maxillary sinusitis were observed. The complete closure of the OAF was always obtained. After this combined surgical approach, 2 patients presented a post operative bleeding and 1 patient presented a synechia that necessitated a sinus revision surgery

under local anesthesia. The rest of the patients were completely symptom – free.

Conclusion: This study showed that with a combined surgical approach, intraoral and endoscopic, there is a successful closure of OAF and a complete disappearance of SCDDT. This treatment represents a reliable and easily applicable method; not too much invasive for the patients, with less morbidity and lower incidence of complications.

Aesthetic issues about the implant-prosthetic rehabilitation of the hard and soft tissues in case of agenesis of anterior teeth

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Aim: The post implant surgery evaluation of hard and soft tissues healing in patients with agenesis in maxillary aesthetic areas.

Methods: For this study were identified three patients with agenesis of the maxillary lateral incisors between the ages of 18 and 24 years in whom the correct useful space for an implant-prosthetic rehabilitation was kept or obtained orthodontically. In these patients an expansion of alveolar ridge technique was performed because of the vestibule-palatal deficits that often recurs in cases of agenesis. So, after a careful radiographic evaluation of the available mesio-distal and buccal-palatal spaces, the surgical approach has involved the design of a paracrestal flap with a primary palatal incision and a total thickness dissection. With a beaver and a firing pin it is provided to create a bone incision in order to insert scalpels of increasing thickness, until it had recreated a correct expansion of the alveolar process of the edentulous site. Then the surgical site was created using dedicated burs at low speed to avoid any fractures of the vestibular cortical bone. The site preparation was completed with the use of an osteotome. By setting implant motor at 20 rpm and a torque of 35 N implants BioSafin Winsix were placed with a diameter of: Case 1: Two 3.3 x 13mm TTX implants – Case 2: Two 3.3 x 13mm K implants – Case 3: a 3.3 x 13mm TTX implant. Immediately after placement the fixtures were provisionally prosthodontized with PMMA single crowns. We preferred to use screwed crowns in case 2 and 3 because, despite the higher cost, it's easier to manage any complications and they have an higher biocompatibility (operator dependent); in the case 1 we chose to cement the crowns for a particular inclination of the implants, due to the anatomy of

the patient (which would not be easily managed with a screw technique). The finishing of provisional prosthetic element played an important role because a careful and meticulous polishing, especially in its transmucosal portion, allowed a drastic reduction of bacterial plaque film. In this way the maturation of the peri-implant soft tissues was facilitated. In the early stages of tissue maturation it is unavoidable notice a tissue retraction that can cause imperfections which are being reduced thanks to the modeling of the resin provisional element emergence profile by the addition of composite resin. Another key element for proper healing was the occlusion of the provisional and the patient's motivation and its compliance about it (soft diet for the first few months). The healing of hard and soft tissues was assessed radiographically and clinically. Cases 1 and 2 were evaluated with follow-up at 3 months and the case 3 at one year.

Results: The healing of hard tissues and the correct conditioning of the soft ones was highlighted at 3 months. In case 3 specifically (at one year) it was possible to establish the correct integration of both bone and aesthetics of the implant.

Conclusion: The expected aesthetic result was reached by a correct implant placement and a proper prosthesis. A big advantage was given by the not functionalized (out of occlusion) immediate loaded implant because, compared to delayed technique, it gave aesthetic function and phonetics, managing immediately the soft tissues and avoiding orthodontics maintenance, without forgetting of the "positive psychological impact" on the patient.

Treatment of patients undergoing hematopoietic stem cells transplantation: analysis of logistic aspects and systemic and oral complications

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Aim: The aim of this study is to analyse the influence of surgical and non-surgical dental treatment in patients undergoing Hematopoietic Stem Cells Transplantation (HSCT) through the identification and treatment of oral infectious foci before transplantation, and post-transplant complications evaluating clinical signs and oral conditions. These complications were registered during and after the recovery in order to identify if oral foci could be cause of infection and to propose a valid management protocol for those patients.

Methods: The sample includes 139 patients treated for HSCT in the Bone Marrow Transplant Centre, Haematology Departments, and visited for evaluation of oral cavity work up in the Oral Surgery

Departement, Dental School, Turin. Protocol: Treat all symptomatic lesions with the most conservative treatment; Resend in post-transplant asymptomatic lesions, such as initial caries with radiographic distance from the pulp ≥ 2 mm; periapical lesions ≤ 5 mm in endodontically treated teeth with intact coronal seal; periodontal pockets with PD (probing depth) ≤ 5 mm. Treat asymptomatic diseases as deep caries (distance < 2 mm from the pulp); periapical lesions > 5 mm or coronal seal leakage in endodontically treated teeth; periodontal pockets with PD > 5 mm. Treat partially erupted third molars if symptomatic. Do not treat not erupted or asymptomatic third molars. The management of these patients involves three steps: I) First visit, with physical examination and analysis of the X-rays; II) Treatment of infectious foci, with surgical, conservative, endodontic and periodontal treatments; III) Post-transplant follow-up: after 30 days, 100 days (with new x rays) and 6 months.

Results: The average time between diagnosis and transplantation was 699 days (23 months). The average time between diagnosis and dental examination was of 609 days (20 months). The average time for dental treatment was 47 days. The average time of hospitalization after transplant was 37 days. There were performed 412 oral treatments: 128 professional oral hygiene sessions, 23 root planing, 41 caries fillings, 16 root canal therapy, 214 extractions. The sample was divided, for the statistical analysis, in the following groups: • Group A: 46 patients (34%) treated according to the research protocol of this study; • Group B: 39 patients (27%) not treated for asymptomatic lesions due to lack of time before the transplantation; • Group C: 54 patients (39%) that received a radical treatment, with the elimination of all the infectious foci. The analysis of the data underline how there was no difference in post-transplant complications between patients who received a total elimination of all foci and patients not treated for chronic lesion deemed to be free of infectious risk: I) At 30 days fever ($p=0,18$), mucositis ($p=0,99$), GVHD ($p=0,11$), death from toxicity ($p=0,99$); II) At 30 days fever ($p=0,99$), GVHD ($p=0,51$), death from toxicity ($p=0,99$).

Conclusions: It has to be noted that dental extraction is still the more frequent oral treatment before HSCT due to the short interval from the first dental visit and the day of transplantation (only 47 days average). There is no statistically difference from very strict protocol and a more conservative one. Following the protocol proposed by this study is possible to preserve dental elements, which previously would have been extracted, and to simplify the plans of pre-transplant treatment, not only to improve the mastication function, phonetics and aesthetics; but also the psychological and social aspects, in order to improve patients' quality of life after transplantation.



Bone regeneration induced by bone porcine block with bone marrow stromal stem cells in a mini-pig model of mandibular "critical size" defect

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Aim: Biomaterials' effectiveness has greatly confirmed in recent years. To increase bone regeneration potential of biomaterials had to add with stem cells with osteoblastic-like activity. In the present study bone scaffold, with and without Bone Marrow Stromal Stem Cells (BMSSCs), were inserted in critical size defects to evaluate quantity and quality of regenerated bone.

Methods: Six adult mini pigs (mean age 2 years; mean weight 29kg \pm 4 kg) were used. Bone marrow was extracted from tibiae and humeri. BMSSCs were isolated and seeded on BPB (Bone Porcine Block). BPB presented a cylindrical shape, 5mm in diameter and 5 mm in length. They were rigid cancellous blocks, thus able to maintain in time the original graft volume. In each mandibula 3 defects were created. The defects were filled in following way: one with BPB added to BMSSCs, one with BPB without BMSSCs and one was left empty as control. Cone Beam Computed Tomography (CBCT) and standard RX 55x75 mm films were executed on retrieved mandibulae. After three months histomorphometric analysis were performed on the specimens dehydrated, embedded in a glycolmethacrylate resin and then sectioned in slides of 50 μ m.

Results: Histomorphometric analysis provided percentages of the three groups. In the control group regenerating osseous tissue extending from the margin of the axial walls was observed. Tissues present in control defects were 23 \pm 2% lamellar bone, 28 \pm 1% woven bone and 56 \pm 4% marrow spaces. In BPB defects the regenerated bone tissue extended to approximately all of the bone defects except in the central area, where the fibrous tissue still occupied part of the interparticular spaces. The percentages were 20 \pm 5% BPB, 32 \pm 2% lamellar bone, 24 \pm 1% woven bone and 28 \pm 2% marrow spaces. In BPB/BMSSCs defects was observed new bone extended to the basal third from the margin of the bone defect and partially surrounded the BPB block. New bone extended also in the central part of the bone defects. The percentages were 17 \pm 4% BPB/BMSSCs, 42 \pm 2% lamellar bone, 12 \pm 1% woven bone and 22 \pm 3% marrow spaces.

Conclusions: This study demonstrates that BPB when used as a scaffold to induce bone regeneration may benefit from the addition of BMSSCs in the tissue-

engineered constructs. Our data shows the healing pattern in a mini-pig model, but further research is needed for human applications.

The soft tissue healing through the use of Mucograft® in oral surgery: a clinical study

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Aim: Nowadays, the soft tissue management in oral surgery concern periodontal and implant plastic surgery procedures, such as grafts of keratinized mucosa, connective grafts, or transposition of flaps. Nevertheless, these methods are not always effective or feasible. Thus, especially as a result of more invasive interventions, the need to resort to the aid of alloplastic materials to increase the soft tissues where, as a result of large excisions, considerable gap still resulted. Hence the desire to carry out a pilot clinical study to assess the efficacy of a collagen matrix, the Mucograft®.

Methods: The object of our study came to our observation with a hyperkeratotic lesion of considerable size at the level of the right buccal mucosa. The treatment plan includes a complete excision of the lesion extending in clinically healthy tissue. According to the extension of the defect, 3 porcine collagen matrices Mucograft® were used in order to correct the remaining gap avoiding a withdrawal of autologous tissue in place extraoral, and also to ensure a less bothersome post-operative for the patient. Mucograft® is a 3D matrix of purified collagen type I and III, deriving from porcine origin, which is developed on the model of a free gingival graft. An open healing was adopted, i.e. the matrix was sutured to the edge of the defect and then left exposed to the oral cavity, surgical procedure justified by the innovative design of this biomaterial that allows an excellent healing even when exposed.

Results: No post surgical complications were recorded and the patient's post operative was comfortable. After two weeks since the surgery, a site which was still in the process of healing was appreciated with formation of a granulation tissue; at four weeks good tropism of the neo-epithelium was observed; at eight weeks, the site was almost fully healed, then mucosa very similar to that surrounding the mucosal lesion was noted. Finally, at six months in addition to a satisfactory healing of the site, the absence of dyskeratosis areas was observed. No relapse was observed at 24 months follow-up.

Conclusion: Despite Mucograft® is a latest generation material, it is supported by a good scientific

literature. From our clinical experience Mucograft® is an extremely effective product when positioned at the level of post-biopsy defects: it ensures a faster and more aesthetically acceptable healing, as well as a quite comfortable post-operative. This matrix was created as a substitute for soft tissue autogenous graft; as a matter of fact, the withdrawal of a donor site is avoided which is a traumatic procedure causing an increase in surgical time, greater technical difficulties for the operator and especially a longer and painful post-operative for the patient. Although the results of this matrix are satisfactory a more large series are required in order to be able to determine the actual effectiveness of Mucograft® and its predictability in different oral surgery treatments.

Carcinomas of oral cavity sites in Eastern Sicily: an epidemiological survey

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Aim: The aim of the study was to do an epidemiological survey about malignant tumors of oral cavity sites in Eastern Sicily. For this purpose all cases of malignant tumors, extracted from the Integrated Tumors Registry (R.T.I.) of Eastern Sicily (covered provinces Catania - Messina - Siracusa - Enna), were observed over a period ranged from 2003 to 2013. These tumors belonged to specific oral sites: Gum (C03), Floor of mouth (C04), Palate (C05), Cheek mucosa (C06.0), Vestibule of mouth (C06.1), Retromolar area (C06.2), Overlapping lesion of other and unspecified parts of mouth (C06.8/C06.9). Particular attention has been given to sex, age, diagnosis, annual distribution, grading and morphology. Besides it has been possible to obtain the cancer incidence rates to make regional (Sicily), national (Italy) and European matching.

Methods: The observed period of time extends from 2003 to 2013. Three hundred eighty-three cases of oral cavity carcinoma are analyzed. The cancer age-standardized incidence rates (European standard) obtained, were compared with regional (Atlante Sanitario della Sicilia 2016), national (Database of the Italian Association of Cancer Registries AIRTUM) and European (International Agency for Research on Cancer IARC) data.

Results: Results show that in Eastern Sicily, among the 383 examined cases, 62% are males (237 cases) and 38% are females (146 cases). The distribution in the years examined, changes from a minimum of 28 cases in 2006 and a maximum of 44 cases in 2007, and is uniform over the period (2003-2013). The most affected

decades are 60s in males with 71 cases out of 237 (30%) and 70s in females with 41 cases out of 146 (28,1%). As for histologic grading and differentiation, 118 cases are not determined, 152 moderately differentiated, 68 well differentiated and 45 poorly differentiated. It has been noted that the most prevalent morphologies are: squamous cell carcinoma (66,06%), squamous cell carcinoma keratinizing and squamous cell carcinoma with horn formation (9,14% and 5,22%), adenoid cystic carcinoma and verrucous carcinoma (4,70% and 4,44%). It has been observed that on 383 cases, the percentage of affected oral sites are: Gum (C03) 13,6%, Floor of mouth (C04) 14,9%, Palate (C05) 18,5%, Cheek mucosa (C06.0) 15,4%, Vestibule of mouth (C06.1) 1,6%, Retromolar area (C06.2) 3,9%, Overlapping lesion of other and unspecified parts of mouth (C06.8/C06.9) 32,1%. Carcinomas of oral cavity represent 0,26% of all malignant tumors in the R.T.I. The cancer age-standardized incidence rates obtained from R.T.I. (2003-2013) is 1,7 per 100.000 person-year (male) and 0,8 per 100.000 person-year (female). The cancer age-standardized incidence rates obtained from regional registries (Atlante Sanitario della Sicilia 2016 - database from 2003 to 2011) is 1,8 per 100.000 person-year (male) and 1,0 per 100.000 person-year (female). National Italian data, obtained from Database of the Italian Association of Cancer Registries AIRTUM (2006-2009), show (on 38 registries) an incidence of 2,6 per 100.000 person-year (male) and 1,2 per 100.000 person-year (female). European data show that Eastern Sicily, if compared with other nations, occupies the lower positions in the country ranking, like Portugal for females and Sweden for males.

Conclusion: Our data demonstrate that males are most affected than females at a younger age. Squamous cell carcinoma, according to what has been reported in literature, is the most represented morphology. In the end, the cancer age-standardized incidence rates of Eastern Sicily are below the regional, national and European values, both for males and females.

1,5 mm of buccal bone width prevents recession: perspective evaluation on 84 consecutive cases

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Aim: This perspective study is aimed to evaluate the soft-tissue maturation around titanium implants at three years follow-up. In detail, is monitored the influence of the residual facial bone thickness at implant placement time on the buccal gingival zenith stability.

Methods: The study includes 84 consecutively enrolled implants. The total follow-up time is 3 years with a planned evaluation at provisional placing (baseline) and 1,2,3 years. All implants were clinically and radiologically monitored at each year follow-up and data regarding facial mucosa height (HG, the distance between the gingival zenith and the incisal edge of the prosthetic restoration) and 4 points probing depth were collected. Buccal bone width (BBW) value was evaluated during surgery and was recorded after implant placement not deeper than 1,5 mm from the implant shoulder. All data were then inserted in a statistical software (SPSS 20, IBM) and processed. Afterwards delta, mean and statistical correlation results were analyzed (Pearson Two-Tailed 95% Conf. Int.).

Results: At the third year follow up, it is observed that for a buccal bone width $\geq 1,5$ mm the buccal zenith of the corresponding implant creeps by an average of +0,59 mm. For a buccal bone width from 0,6 to 1,4 mm the average gingival zenith value results -0,78 mm shrunk and when buccal bone width is $< 0,5$, the zenith recedes by an average -1,13 mm. Results were observed to be statistically significant ($p=0,002$) (Pearson Two-Tailed 95% Conf. Int.).

Conclusions: Whenever a correct treatment plan is applied, patient's domiciliar maintenance is observed and good prosthetic design is reached, the buccal bone width at implant placement plays a cutting edge role on gum parable stability over the time. In the 84 considered cases the relation is confirmed and a wider buccal bone width results favorable whenever is possible. Implant designs that preserve bone width should be the first choice and wherever buccal bone width is below 1,5 mm guided bone regeneration techniques are mandatory to overcorrect the buccal plate in order to achieve a highly predictable tissue stability around implants.

Long-term evaluation of autologous extraoral bone grafts as bone substitute in maxillary vertical augmentation procedure

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Aim: The aim of this study was to evaluate from a

microscopic and morphostructural point of view and at different time point, the integration of extraoral autologous bone grafts from calvaria used as bone substitute in maxillary vertical augmentation procedure.

Methods: Bone samples, obtained 4 months (T1), 10 years (T2) and 15 years (T3) since their grafting in edentulous sites of posterior maxilla were analyzed by light microscopy after hematoxylin-eosin staining, to evaluate morphostructural differences and to compare them with samples obtained from the donor site at the time of withdrawal (T0).

Results: T1 samples showed remodeling phenomena typical of the integration phase of a grafted tissue. In fact, a mostly compact structure and the presence of vascular neoformation and new bone apposition could be noticed after 4 months from grafting, together with extensive remodeling areas with welding lines and resorption margin between the graft and the newly formed bone tissue. In T2 samples, microscopic observation revealed a morphological and structural appearance of the grafted tissue very similar to native bone. After a long observation time (T3), microscopically the graft assumed very similar characteristics to native bone, as highlighted from the disappearance of welding lines. Interestingly, small polygonal cells resembling the osteoblasts could be noticed around the Haversian channel, thus making it possible to hypothesize that not only the graft is perfectly integrated but that it is a vital bone with active bone remodeling phenomena.

Conclusions: The microscopic observation of samples obtained at different experimental times from maxillary grafted area, confirmed the presence of remodeling phenomena. These phenomena, strongly represented in the T1 samples, are essential for the integration of the grafted bone. Conversely, after 10 years, the microscopic appearance of the graft, as well as expected accordingly the good clinical results, appears to be indistinguishable from native bone. This data, combined with clinical observations and the results obtained after 15 years, suggest that extraoral autologous bone grafts, and in particular those from calvaria are particularly suitable as a biomaterial for the vertical augmentation in posterior maxilla prior an implant-supported rehabilitation.

Metastasis to the oral cavity in Eastern Sicily

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Aim: The present study refers about the epidemiology of metastatic formations in the oral cavity. As literature documents, they are quite rare. In fact

they represent only 1% of malignant tumors of the oral cavity. The majority of primary tumors which metastasize in oral cavity are: Lung cancer, Breast cancer, Prostate cancer, Kidney cancer and Colon cancer. As reported in literature, the most affected metastasized sites are: jaw and retromolar area (as for hard tissues), and tongue, cheek and gum (as for soft tissues). The aim of this study is to verify, through the data obtained from the Integrated Tumors Registry (R.T.I.) of Eastern Sicily (covered provinces Catania - Messina - Siracusa - Enna), if what literature reports can be confirmed.

Methods: For this study, the Integrated Tumors Registry (R.T.I.) of Eastern Sicily (covered provinces Catania - Messina - Siracusa - Enna) was examined. We used the Identification Code ICD9 198.89 to find these cases. Many difficulties were found due to the Identification Code because there isn't an exclusive code for metastatic injuries in the oral cavity, unlike other tumors. A subselection was done to restrict the analytical field, so we could analyze only potential cases of oral metastasis, considering only cases which presented a diagnostic - instrumental examination of the head. Whereas, as for salivary glands, there is a specific Identification Code for the registration of metastatic injuries. Besides, since lymph node route is one of the most important and most frequent metastatic spreads of oral cavity region, we evaluated all metastatic cases of the lymph nodes in the Head-Neck region that were diagnosed and by the following 6 months from the diagnosis. The cases grouped are those that presented primary tumor in the 5 sites which more probably metastasized to the oral cavity.

Results: All cases that correspond to the Identification Code ICD9 198.89 were obtained. A subselection of cases about the head was done, restricting the field only to cases which presented a diagnostic - instrumental examination of the head and obtaining 348 cases. These cases were analyzed individually and carefully, examining anatomic pathology reports and HDF (Hospital Discharge Form). Indeed only 2-3 cases out of 348 gave answer to requirements of metastasis. As for salivary glands, on 348 cases of metastasis in the Head-Neck region, 17 presented metastasis diagnosis to the submandibular glands. As for lymph nodes of the Head-Neck region, 2166 cases were found.

Conclusion: This study confirms, as literature says, that it is not possible to diagnose a metastatic injury just by histological slide, but we necessarily need to evaluate and study patient's clinical history in detail. In fact metastatic injuries to the oral cavity are often registered as simple primary tumors. In the end, the obtained results confirm literature data, showing that in Sicily the percentage is a little bit lower than in other Italian countries.

Management of a 12-years old patient with complex odontoma, impacted first molar, pericoronal dentigerous cyst and involvement of inferior alveolar nerve

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Aim: Tooth impaction is a relatively rare condition in children, the incidence rate is estimated to be around 0.38% (excluding third molars and maxillary canines), according to the Literature. Many causes are recognized for tooth impaction, but in most cases this condition suggests the presence of an obstacle to the eruption path. The aim of this case presentation is to report on the management of a complex Odontoma, associated to an impacted inferior first molar, dentigerous cyst and inferior alveolar nerve involvement.

Methods: A healthy 12-years-old chinese patient was referred to the Dental clinic, Padua University hospital, in February 2014, because of the appearance of swelling, charged to the posterior side of the left mandible. The clinical examination showed an unresectable lesion on the buccal side of the left mandible associated to the absence of first and second left molars. The orthopantomography showed a wide radiodense lesion with a lucent rim and an impacted tooth, surrounded by a radiolucent lesion. The radiodense lesion was surgically removed. It is demonstrated that a tooth tends to erupt spontaneously after having enucleated an obstructive lesion, regardless of the degree of root formation, but four months after surgery the inferior first molar was still impacted in the initial position, whereas the radiolucent lesion around its crown had increased its size. A Computer Tomography showed that the roots of the impacted inferior first molar surrounded the mandibular canal. The patient was subjected to another surgery under conscious sedation and local anesthesia, to extract the tooth and enucleate the lesion. The surgeon elevated a mucoperiosteal intrasulcular flap, from the mesial side of the lower canine to the distal side of the lower second premolar a disto-vestibular and a mesio-vestibular release cuts. A bony window (15x10mm) was set up using a piezoelectric device (Piezosurgery, Mectron SpA, Carasco, Italy) irrigated with sterile saline solution, to guarantee the most atraumatic detachment of the vestibular cortical of the mandible. The tooth was sectioned with the same device and extracted in pieces, together with the lesion, in order to avoid nerve injury. The bony window was repositioned and fixed by osteosynthesis screws and the flap was sutured using a mid-term absorbable synthetic suture. The following

medications were prescribed: Amoxicillin as antibiotic and Acetaminophen as painkiller.

Results: The histological examinations confirmed the diagnosis of odontoma and odontogenic cyst with a disepithelization and chronic inflammation (compatible with follicular cyst). The one-week follow-up visit showed a mucosa in phase of healing. Another orthopantomography was taken in December 2015, showing a quite complete ossification. At the one-year follow-up visit another orthopantomography was taken. The healing of soft and hard tissues was complete and the patient reported no paresthesia.

Conclusion: The use of conscious sedation had helped the patient feeling neither anxiety nor agitation, it had improved on the contrary her cooperation, avoiding the risks of general anesthesia. A minimally invasive surgical approach with the use of piezosurgery proved to be effective for the management of young patients affected by wide oral lesions. No postoperative complications, such as mandibular fracture nor bleeding, have occurred. A mild anesthesia charged to the mental nerve's innervation area was recorded at the beginning, but it was related to the first surgery, and no paresthesia was reported at the one-year follow-up visit.

Surgical decompression of mental nerve to treat altered sensation secondary to dental extraction: a case report

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Aim: The aim of the present study is to report on a case of mental nerve altered sensation completely recovered after surgical approach under intraoperative microscope.

Methods: A healthy 57-year-old female patient was subjected to the extraction of a crown-fractured right first premolar performed by her dental practitioner. The day after, the patient was referred to the Dental Clinic, Padua University Hospital, because of altered sensation which consisted of anesthesia and dysesthesia charged to the chin, unbearable burning sensation and numbness of the lower right lip. Thinking about mental nerve shear during osteotomy, local anesthesia injection or the flap elevation, the clinicians decided to explore the post-extractive site according to the patient. After local anesthesia (inferior alveolar nerve block, buccal nerve block and paraperiosteal injections with Mepivacaine Hydrochloride with 2% epinephrine and Bupivacaine Hydrochloride), an intrasulcular incision with two release cuts was performed and a mucoperiosteal flap

was elevated. The mental nerve, isolated with under intraoperative microscope (Leica, Wetzlar, Germany, 5 to 40x magnification), appeared undamaged but extremely hypertrophic, strangled close to the mental foramen. Two small reddish roundish extroflexions have been identified mesiovestibularly and distally to the main trunk. The mental foramen was enlarged using a piezoelectric device (Piezosurgery, MectronSpA, Carasco, Italy), in order to reduce the compression exerted on the hypertrophic nerve. After the nerve isolation, a solution of Betamethasone 8mg was injected directly inside the main trunk and irrigation with sterile saline solution was performed. A multifilament absorbable suture was applied, seeking a first intention healing. Antibiotic therapy (Amoxicillin/Clavulanate 1g orally every 8hrs), antalgic treatment (Acetaminophen 1000mg orally every 8hrs), steroid treatment (Prednisone 25mg daily, for 4 days) and Acetylcarnitinehydrochloride (Nicetile 500mg daily) have been prescribed after surgery.

Results: At the one-month follow-up visit, the altered sensation was fully recovered. The soft and hard tissues healing was excellent.

Conclusion: Iatrogenic injuries of neuro-vascular bundles are not rare occurrences, but they fortunately have a relatively low incidence rate, estimated at around 3% according to the Literature. Injuries can affect the inferior alveolar, lingual, mental, grater palatine, nasopalatin and infraorbital nerves. Altered sensation may result into different degrees including allodynia, hyperalgesia, dysesthesia, paresthesia, sensory disturbance, numbness. Altered sensation charged to the distribution area of the mental nerve can be caused by local anesthesia, overfilling of root canals, mandibular fracture, dental extractions, inflammatory or neoplastic lesions, orthognathic surgery and improper implant placement. The diagnosis of neurological lesions of the oral cavity requires the exploration of the patient's past medical history, the analysis of signs and symptoms, a careful physical examination and imaging techniques or other tests, depending upon the clinical situation. The Sensitivity disorders are not objectively quantifiable and their manifestations are quite heterogeneous: burning, tightness, heaviness, electric shocks, tingling. The prognosis for recovering depends upon the cause and degree of damage, if the spontaneous regeneration does not take place, only a surgical revision could be effective. Literature describes two possible treatment approaches once the sensitivity disorder has been diagnosed: an immediate intervention or the follow-up. In this case the patient underwent to an immediate surgical treatment, due to the severity of symptoms.

Utility of blood components for non-transfusional use to prevent bisphosphonate

related osteonecrosis of the jaw

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Aim: Biphosphonates are drugs widely used against diseases which affecting bones mostly such as: Osteoporosis, Paget's Disease, Multiple Myeloma, Bone Metastasis. Inhibition of osteoclasts and anti angiogenic capacity of biphosphonates can lead to the event of Osteonecrosis of the Jaw after oral surgery treatment. The aim of our study is to establish the possibility to prevent Osteonecrosis of the jaw when the surgical extraction treatment is necessary.

Methods: At the Odontostomatological Special Needs department of Policlinico Tor Vergata we selected 51 patients in therapy with Biphosphonates. We assigned to all of them a risk class depending on the value of serum CTX. We assigned a peculiar antibiotic therapy based on Amoxicillin + Clavulanic ac. and Metronidazole. Patients were divided into 2 groups: patients of the study group were treated using autologous Platelet Rich Plasma (PRP) after the surgical extractions, those of the control group were treated without using PRP. We have chosen to use PRP cause by platelet degranulation we get antibacterial action, immediate stabilization of the clot and liberation of large amounts of Growth Factors

such as PDGF (Platelet-derived growth factor), VEGF (Vascular endothelial growth factor), TGF β (Tumor growth factor), FGF (Fibroblast growth factor), EGF (Epidermal growth factor) which are very important in tissue healing process.

Results: After the surgical extractions among 27 patients of the control group we detected 4 cases of bone exposure, they have all been detected within 4 weeks after surgery. Instead among 24 patients of the work group we didn't noticed signs of bone exposure in any of the protracted follow up visits to 3 months after surgery. We also recorded more comfortable postoperative course and shorter healing times in the work group. Then the 4 cases of bone exposure of the control group were treated, this time using the PRP that led to complete healing and re-epithelialization of tissues already after 2 weeks from surgical treatment.

Conclusion: According to the results obtained following this experimental study it can be stated that intra operative use of Platelet Rich Plasma produces great benefits such as faster healing time, more comfortable postoperative course and it gives more guarantees in prevention of Osteonecrosis of the Jaws related to Biphosphonates drug therapy, especially in patients with high-risk category which is determinate by CTX serum. Due to the limited number of patients we can only talk about clinical evidence for now, it will be necessary to broaden the sample of patients and further studies to obtain statistical evidence.