



Functional and cell surface characteristics of periodontal ligament cells (PDLCs) on RGD-synthetic polypeptide conjugate coatings

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Abstract

Background and Objective: Periodontal ligament cells (PDLCs) are an important source for periodontal tissue healing and regeneration. Proper cell adhesion is a key for survival of anchorage-dependent cells and also initiates further intracellular signals for essential cellular functions. We aimed to test 3 different synthetic conjugates with integrin-binding RGD sequence (SAK-c[RGDfC], AK-c[RGDfC], and SAK-opn on the adhesion of human PDLCs and subsequent events including proliferation, migration, behavior of cell surface molecules, and osteogenic differentiation.

Materials and Methods: Synthetic peptides were synthesized by solid-phase technique and attached to branched chain polymeric polypeptides via thioether linkage. Simple adsorption method was used to coat tissue culture plastic or electric arrays. PDLCs were isolated from 24 surgically extracted human third molars. Cell adhesion and proliferation were measured with real-time impedimetric xCELLigence SP system. Cell migration assay was performed with Ibidi® Culture inserts. Cell surface antigens were detected using flow cytometry analysis. Osteogenic differentiation was assessed with alkaline phosphatase (ALP) assay and Alizarin Red S staining, and real-time qPCR was performed to analyze the osteoblast-related gene expression. Osteogenic differentiation and adipogenic differentiation of PDLCs were monitored by real-time Electrical Cell-Substrate Impedance Spectroscopy (ECIS).

Results: Primary outcome of this study relies on that all three synthetic RGD peptides improved PDLC adhesion ($P < .05$). When animal serum is absent in culture medium, SAK-c[RGDfC] and AK-c[RGDfC] elevated cell adhesion ($P < .05$). Cell migration was enhanced by SAK-c[RGDfC] and AK-c[RGDfC] ($P < .05$). After 1-week treatment, all synthetic peptides elevated CD105 (1.7- to 2.2-fold) and CD146 (1.3- to 1.5-fold) markers and caused different integrin patterns. ALP activity (1.4-fold) and ARS (1.8- and 2.0-fold) were increased by SAK-c[RGDfC] and AK-c[RGDfC] in absence of osteogenic supplements, and all the peptides supported the mineralization



[Correction added on August 03, 2020, after initial online publication: Additional funding information has been added to the title page and Acknowledgement section.]

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Könnyek helyett...

Hatállomásos szájüregi rákszűrő program tapasztalatai, tanulságai

Dr. Mensch Károly, Dr. Czeglédy Ágota, Dr. Kollár Karolina,

Dr. Kovács Dóra, Dr. Horváth Dániel, Dr. Dombi Csaba

Semmelweis Egyetem Fogorvostudományi Kar

Orális Diagnosztika Tanszék

Könnyek helyett, tarts velünk szűrőprogramunkon! Ezen felszólítás jegyében szervez *A rák ellen, az emberért, a holnapért! Társadalmi Alapítvány* immár harmadik éve nagyszabású programsorozatot a Nemzeti Rákellenes Világnap környékén, melyen az idei évben először a Semmelweis Egyetem Orális Diagnosztika Tanszékének munkatársai, fogorvosok (a szerzők) és asszisztensek (Nagy Vivien Szandra, Dia Bettina, Lakatos Anna) is részt vettek. Ebben a publikációban szeretnénk megosztani néhány fontos gondolatot a fogorvos-társadalommal a stomatoonkológiai prevenció lehetőségeiről, jelentőségéről, valamint összegezzük a szűrővizsgáláton szerzett tapasztalatainkat.

A rák ellen, az emberért, a holnapért! Társadalmi Alapítvány 1985-ben jött létre, mint az első közadakozásból alakult magyar rákellenes civil szervezet. Küldetésük az emberek testi, szellemi és lelki egészségének helyreállítása és megóvása, egészségmegőrző, betegségmegelőző, illetve onkológiai prevenció és rehabilitációs programok szervezése, támogatása. Fontos üzenetük a társadalom felé, hogy a rák megelőzhető, illetve az, hogy a betegségből meg lehet gyógyulni.

Az idei egészségkampányhoz április 13. és május 29. között hat helyszín, Aszód, Csepel, Gyöngyös, Zugló, Pécs és Dévaványa csatlakozott. A Nemzeti Népegészségügyi Központ az alapítvány rendelkezésére bocsátotta a minden szakmai igényt kielégítő, jól felszerelt



Comparison between Micro-Computed Tomography and Cone-Beam Computed Tomography in the Assessment of Bone Quality and a Long-Term Volumetric Study of the Augmented Sinus Grafted with an Albumin Impregnated Allograft

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Abstract: The purpose of our study was to compare micromorphometric data obtained by cone-beam computed-tomography (CBCT) and microcomputed-tomography (micro-CT) of the augmented sinus and to evaluate the long-term stability of the bone gain achieved using BoneAlbumin. Sinus lifts, and after 6-months, healing bone-biopsy and implant placement were carried out. Specimens were analyzed by micro-CT. A total of 16 samples were collected from nine patients (mean age 54.7 ± 6.5 years). Pre-, postoperative, and 3-year control CBCT-data were registered to determine from where the biopsy samples were harvested. Micromorphometric variables were calculated from the micro-CT- and CBCT-data, and their correlation was determined by Spearman's test. The volume of augmented bone was calculated at the time of implant placement and after 3 years. A positive correlation was found between bone-volume fraction, trabecular-separation, open-, and total-porosity, while a negative correlation was found between trabecular-thickness obtained from CBCT- and micro-CT-data ($p < 0.05$). Mean volumetric reduction of 39.28% (11.88–60.02%) was observed. Correlation of CBCT- and micro-CT-data suggested that micromorphometric analysis of CBCT reconstructions of the augmented sinuses provided reliable information on the microarchitecture of augmented bone. CBCT as a modality might be adequate in the analysis of bone quality in the augmented sinus. At the 3-year, control sinus grafts showed volumetric stability.

Keywords: sinus floor elevation; allograft; cone-beam computed tomography (CBCT); microcomputed tomography (micro-CT); bone quality; volumetric study; 3-year follow up



THICKNESS-DEPENDENT ELECTRICAL IMPEDANCE SPECTRUM OF HUMAN DENTIN

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ABSTRACT

Utilization of impedance measuring methods in dental researches makes the determination of electrical properties of human tooth possible. Although impedance measurement forms the basis of numerous oral diagnostic methods, limited studies are available about the impedance of human dentin. In this paper the thickness dependency of the impedance of human dentin is investigated.

Dentin disks were prepared from dentin layer of the crown between the top of pulp and below dentin-enamel junction of five human wisdom teeth. Separated and isolated round shaped measurement areas were created on the surface of the specimens with diameter of 1 mm. The samples were thinned sequentially while the thickness and the complex impedance of each measurement area was recorded.

Investigation of the impedance of human dentin in the thickness range of 0.3-2.3 mm allowed us to define the thickness-impedance coefficient of human dentin, as the absolute impedance value divided by the thickness and multiplied by the area of the examined dentin. The average of the thickness-impedance coefficient is equal to $8.356 \Omega\text{m}$ at 1 kHz measurement frequency.

Approximately linear correlation between the thickness and the impedance of human dentin was revealed. These results may have significance in the field of clinical dentistry.

Keywords: bioengineering, electrical impedance spectrum, dentin thickness, human dentin

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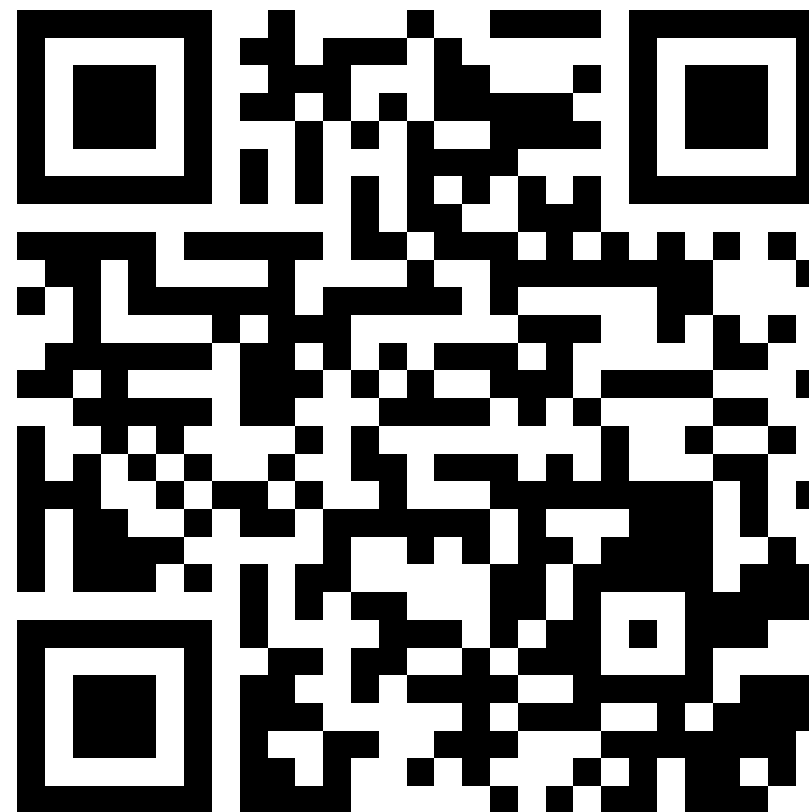


Albumin-Impregnated Allograft Filling of Surgical Extraction Sockets Achieves Better Bone Remodeling Than Filling with Either Blood Clot or Bovine Xenograft

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Purpose: The goal of this study was to compare bone graft materials in mandibular third molar extraction sockets and to monitor bone remodeling and complications. **Materials and Methods:** Patients with bilateral, impacted mandibular third molars were involved. Twenty-four patients were planned to be randomly assigned to three possible treatments: (1) the control sockets were left empty; (2) the socket was filled with bovine xenograft (Bio-Oss); or (3) the socket was filled with albumin-impregnated bone allograft (BoneAlbumin). Postoperative pain during the first week was determined with the visual analog scale. Cone beam computed tomography (CBCT) images were taken at 6 and 12 weeks and 1 year postoperatively for micromorphologic analysis and measurement of pocket depth at the second molar. Patients and image analyses were blinded toward the treatment group (randomized double-blind split-mouth design). **Results:** Postoperative pain was lowest in the allograft group (control: 5.06 ± 0.53 ; xenograft: 5.85 ± 0.42 ; allograft: 3.94 ± 0.52 ; $P < .05$). At weeks 6 and 12, early signs of remodeling were observed in the allograft group and the controls, while bone xenograft was still demarcated from the host bone. The 1-year CBCT images showed complete remodeling and integration of allograft with natural trabecular structure, while the xenograft particles were still visible. Support for the second molar was significantly better, as evidenced by less deep and prevalent pockets in the allograft-filled group compared with the controls ($P = .017$). **Conclusion:** Filling an extraction socket with albumin-integrated allografts provides superior bone regeneration compared to either native bone build-up or xenograft application or socket regeneration without bone grafting. INT J ORAL MAXILLOFAC IMPLANTS 2020;35:297–304. doi: 10.11607/jomi.7554

Keywords: 3D, albumin, biomaterials, bone graft



Continuity of bone after tooth extraction must be preserved to keep the structural and mechanical

strength of the hard tissue support, even in cases where implantation is not necessary later on.¹ After mandibular third molar removal, postoperative pain and swelling are well-known and frequent complications, especially when surgical techniques have to be applied, such as in cases of impacted or recessed teeth.² In these cases, excess bone loss is caused when drilling is applied in order to facilitate tooth removal compared with a simple extraction. The most pronounced changes of the alveolar bone loss occur in the first 6 months.³ The decreased amount of hard tissue makes it difficult to carry out both conventional and implantation treatments.⁴ Therefore, filling the iatrogenic bone loss plus the extraction socket is preferred to keep the integrity of the bone surface and to expedite healing of the bone void. Mandibular third molar sockets are considered to be useful for in vivo testing of alveolar ridge preservation techniques and graft materials.

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Cone-Beam Computed Tomography in Dentomaxillofacial Radiology

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Abstract

The daily application of cone-beam computed tomography (CBCT) has been increasing. Not only the number of referrals has been raising, but also the variety of the anatomical regions requested for imaging is also growing in the dentomaxillofacial area. Even though computed tomography (CT) has been widely used in the head and neck region, by the invention of CBCT, some of the drawbacks of CT were overcome and turned into the advantages of the CBCT appliances, such as lower patient dose. In this chapter, we provide a comprehensive picture of the everyday use of CBCT as a modality in the dentomaxillofacial region and its current limitations and expected improvements.

Keywords: cone-beam computed tomography, dental digital radiography, diagnostic imaging, dentomaxillofacial radiology, incidental findings

1. Introduction

The use of cone-beam computed tomography (CBCT) has been increasing in everyday clinical practice. The advantages of CBCT contribute to its spreading not only in the field of dentistry, but also in maxillofacial surgery, otorhinolaryngology, rheumatology, and traumatology. Conventional-computed tomography (CT) has been widely used in the head and neck and other anatomical regions; nevertheless, by the invention of CBCT device for maxillofacial imaging in the 1990s [1], some of the drawbacks of CT were overcome resulting in the application of CBCT as an alternative modality in these regions. CBCT devices offer a compact size, the ability for producing high-resolution volumetric data, and lower patient dose compared to multislice CT (MSCT) [2–4]. Nonetheless, it should be noted that CBCT devices operate in a wide range of dose values [5]; hence, in the particular clinical situation, the proper justification and optimization are crucial. In this chapter, we provide a comprehensive picture of the everyday use of CBCT as a modality in the dentomaxillofacial region and its current limitations and expected improvements.

2. Basic principles of the CBCT

2.1 Image acquisition

The CBCT device consists of an X-ray source and a flat-panel detector, which are connected by a C-arm in a fixed position, but their vertical position can be





A szájüreg leggyakoribb bakteriális eredetű kórképeinek jellegzetességei, diagnosztikája és kezelése

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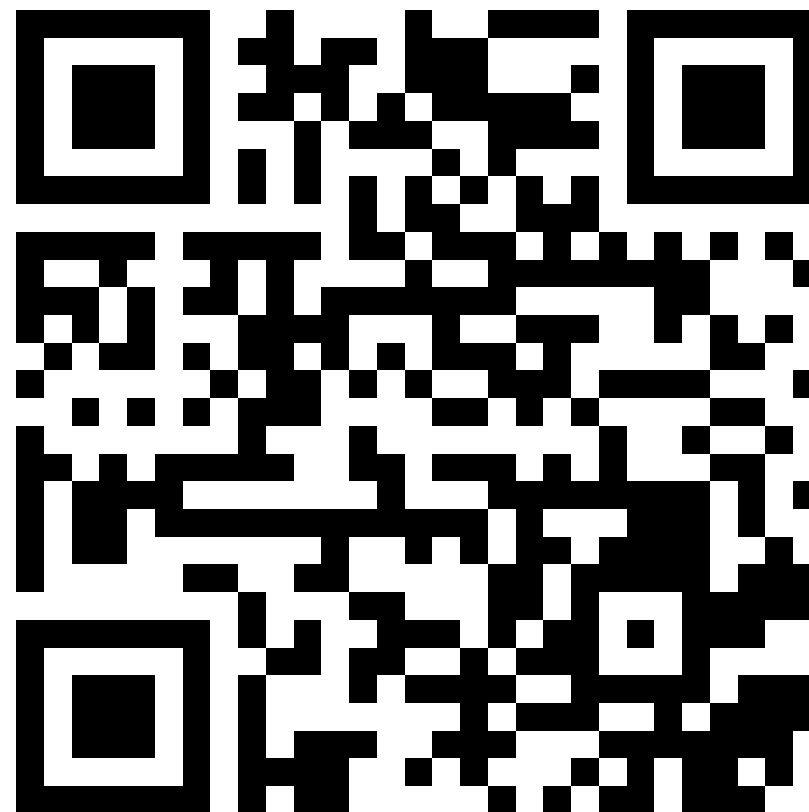
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Az emberi szájüreg mikroorganizmusok milliárdjainak élőhelye. A legnagyobb arányban baktériumok vannak jelen, több mint 600 baktériumfaj izolálható. Nagy részük ártalmatlan, némelyik kifejezetten hasznos, azonban nem megfelelő szájhigiénia, illetve legyengült immunstatus esetén számos lágy- és keményszöveti megbetegedést okozhatnak, melyeknek sok esetben szisztémás következményeik lehetnek. A szájüreg leggyakoribb bakteriális megbetegedéseként tekinthető a fogszuvasodás és a fogágybetegség. Mindkét esetben elsődleges kóroki szerepe van a nem megfelelő szájhigiénia következtében kialakult dentális biofilmmnek. A fogszuvasodás kórfolyamatában a *Streptococcus mutans*, a *S. sanguinis*, a *S. viscosus* és a *Lactobacillus acidophilus* játszik főszerepet, súlyos fogágybetegség esetén viszont az anaerob parodontopathogen kórokozók jellemzők, úgymint *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Bacteroides forsythus*, *Prevotella intermedia*, *Fusobacterium nucleatum*, *Campylobacter rectus*. A kezeletlen fogszuvasodás a fogból elhalásához vezet, s ez a fogágy irányába terjedő gyulladást okoz, amely gócnak tekintendő. A kezeletlen fogágybetegség esetén csonttasakok keletkeznek, melyek szintén gócnak minősülnek. A fogászati gócnak számos szisztémás következményük lehet, úgymint szív-ér rendszeri megbetegedések, cukorbetegség, tüdőgyulladás, izületi gyulladás, koraszülés, foltos hajhullás. Ezen betegségek esetén mindenképpen gondolni kell fogászati gócra. A tervezett műtétek előtti professzionális plakk-kontroll és klórhexidines öblögetés kiemelkedő jelentőséggel bír az aspirációs pneumonia prevenciójában. A szájüregi daganatok multikauzálisak; egyre több kutatócsoport vizsgálja az egyes baktériumok szerepét a szájüregi daganatok karcinogenezisében. Az említett kórképeken kívül a viszonylag ritka, ámde sokféle formában megjelenő, gyakran diagnosztikai kihívást jelentő bakteriális lágyrész-betegségek bemutatását egy következő közleményben tervezzük. Orv Hetil. 2019; 160(19): 739–746.

Kulcsszavak: fogszuvasodás, fogágybetegség, gócbetegség, szájüregi rák

Characteristics, diagnosis and treatment of the most common bacterial diseases of the oral cavity

Billions of microorganisms can be found in the oral cavity, from which bacteria are the most frequent. More than 600 bacterial species can be isolated. Most of them are harmless, moreover, some species prove themselves to be specifically useful. However, in the case of a weakened immune status or inappropriate oral hygiene, they may cause many types of soft and hard tissue disorders. Caries and periodontal diseases are the most common bacterial diseases of the oral cavity. In both cases, the dental biofilm gives rise to the disorder, which is caused by the insufficient oral hygiene. Dental caries are mainly caused by cariogenic streptococci and lactobacilli. In the case of serious periodontal diseases, anaerob parodontopathogen microorganisms play the major role. Untreated caries may result in the necrosis of the pulp, which can cause an inflammation expanding towards the parodontium. This can be characterized as a focal infection, like the untreated periodontal pockets. Dental foci may have lots of systemic consequences such as cardiovascular diseases, diabetes, pneumonia, arthritis, preterm birth and alopecia areata. When these diseases occur, dental foci should always be considered. The professional plaque control and chlorhexidine rinsing before the proposed surgeries have an outstanding role in the prevention of ventilator-associated pneumonia. Oral cancer is multicausal; more and more researchers are analyzing the role of certain bacteria in the carcinogenesis of oral cancer. In addition to the mentioned clinical aspects, we are planning to describe the relatively rare, but diverse and diagnostically challenging bacterial soft tissue disorders in another publication.



Modulation transfer function evaluation of cone beam computed and microcomputed tomography by using slanted edge phantom

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ABSTRACT

Modulation transfer function (MTF) is a well known and widely accepted method for evaluating the spatial resolution of a digital radiographic imaging system. In the present study our aim was to evaluate the MTF obtained from CBCT and micro-CT images. A cylinder shaped phantom designed for slanted-edge method was scanned by a CBCT device at a 100 μm isometric voxel size and by a micro-CT device at a 20 μm isometric voxel size, simultaneously. The MTF curves were calculated and the mean spatial resolutions at 10% MTF were 3.33 ± 0.29 lp/mm in the case of CBCT images and 13.35 ± 2.47 lp/mm in the case of micro-CT images. The values showed a strong positive correlation regarding the CBCT and the micro-CT spatial resolution values, respectively. Our results suggests that CBCT imaging devices with a voxel size of 100 μm or below might aid the validation of fine anatomical structures and allowing the opportunity for reliable micromorphometric examinations.

Keywords: Modulation transfer function; Cone-beam CT; Micro-CT; 3-D imaging; Imaging phantom

1. Introduction

Numerous publications have been investigated the use of cone beam computed tomography (CBCT) for evaluating small anatomical structures in dentistry e.g. root canal morphology in endodontics [1-10] or bone quality assessment in maxillofacial surgery [11-20]. It is essential to visualize these details to set up the proper diagnosis and treatment plan, hence clinicians need to select the adequate imaging technique with the appropriate resolution. Among the currently available "high resolution" CBCT equipments the voxel size are 100 μm or even smaller [21], which are comparable with the size of a root canal's apical constriction [22-24] or bone trabeculae [25, 26]. Due to the main advantages of CBCT, namely the higher spatial resolution and lower patient dose compared to medical computed tomography CBCT modality has an increasing interest in the dental practice [27], nevertheless inaccurate image quality can lead to misdiagnosis and unnecessary radiation dose for the patient. Thus it is worthwhile to assess the image quality of the CBCT device and other radiographic imaging system quantitatively to ensure the diagnostic accuracy of the chosen modality [28].

Spatial resolution, which is related to the ability of distinguishing two adjacent structures on a radiograph, is one of the parameters, which can be measured objectively allowing us to estimate the imaging performance of an X-ray based medical system [29, 30]. There are two main methods for determining the spatial resolution, namely visual resolution assessment test and MTF determination. In general both methods are evaluated in line-pairs per millimeter (lp/mm). MTF is a well known and widely accepted method for evaluating the spatial resolution of a digital radiographic imaging system [31, 32]. To calculate the MTF of a computed tomography device thin wire, narrow slit or slanted edge phantom - among others -



CASE REPORT

Open Access



Difficulties in the diagnosis of periapical translucencies and in the classification of cemento-osseous dysplasia

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Abstract

Background: Cemento-osseous dysplasia is a benign fibro-osseous lesion of the tooth-bearing region of the jaws with a periodontal ligament origin. It appears predominantly in Black and Asian middle-aged females. Its importance is that it could mimic a periapical lesion in the early, translucent stage.

Case presentation: In this report a rare case of familial cemento-osseous dysplasia is presented: a 50-years old Caucasian woman with labial paraesthesia and radiological translucency around the roots of the mandibular incisors and the first molar teeth. The lesion around the first molar was diagnosed as periapical granuloma and a root canal treatment was carried out. The diagnosis of florid cemento-osseous dysplasia and the treatment plan based on two- and three-dimensional radiographic examinations were certified histologically after surgical removal of the lesion. We screened the family members - including the patient's mother, daughter and son - and identified a periapical version of cemento-osseous dysplasia in the daughter. Our case highlights the difficulties of differential diagnosis of cemento-osseous dysplasia and other periapical pathologies. The inconsistencies in the present classification of cemento-osseous dysplasia are also discussed with a proposal for a different classification based on new aspects that would be very helpful in setting up a correct treatment plan.

Conclusion:

- Differentiation of endodontic and non-endodontic origin of radiolucency and distinguishing it from anatomical landmarks by appropriate clinical evaluation and using vitality testing can give an opportunity to prevent unnecessary endodontic treatment.
- The current categories of cemento-osseous dysplasia classification do not cover the early stage of a hereditary florid form of cemento-osseous dysplasia.
- Instead of anatomical location of the lesion, clinical and genetic features may be recommended as parameters of cemento-osseous dysplasia classification.

Keywords: Cemento-osseous dysplasia, Classification, Differential diagnosis, Familial form of COD, Florid, Misdiagnosis, Periapical translucencies



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Hematopoietic or Osteoclast-Specific Deletion of Syk Leads to Increased Bone Mass in Experimental Mice

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Syk is a non-receptor tyrosine kinase critically involved in signaling by various immunoreceptors including B-cell-receptors and activating Fc-receptors. We have previously shown that Syk also mediates immunoreceptor-like signals required for the *in vitro* development and function of osteoclasts. However, the perinatal lethality of Syk^{-/-} mice precluded the analysis of the role of Syk in *in vivo* bone metabolism. To overcome that problem, we generated mice with osteoclast-specific (Syk^{ΔOC}) or hematopoietic (Syk^{ΔHemo}) Syk deficiency by conditional deletion of Syk using Cre recombinase expressed under the control of the Ctsk or Vav1 promoter, respectively. Micro-CT analysis revealed increased bone trabecular density in both Syk^{ΔOC} and Syk^{ΔHemo} mice, although hematopoietic Syk deficiency caused a more severe phenotype than osteoclast-specific Syk deficiency. Osteoclast-specific Syk deficiency reduced, whereas hematopoietic Syk deficiency completely blocked *in vitro* development of osteoclasts. Both interventions inhibited the resorptive activity of osteoclasts and osteoclast-specific gene expression. Kinetic analysis of Syk protein levels, Cre expression and the genomic deletion of the Syk^{fllox} allele revealed complete and early deletion of Syk from Syk^{ΔHemo} osteoclasts whereas Syk was incompletely deleted at a later stage of osteoclast development from Syk^{ΔOC} cultures. Those results provide an explanation for the *in vivo* and *in vitro* difference between the Syk^{ΔOC} and Syk^{ΔHemo} mutant strains and suggest late activation of, and incomplete target gene deletion upon, osteoclast-specific Cre expression driven by the Ctsk promoter. Taken together, our results indicate that Syk plays an indispensable role in osteoclast-mediated *in vivo* bone resorption and suggest that Syk-specific inhibitors may provide therapeutic benefit in inflammatory and other diseases characterized by excessive osteoclast-mediated bone resorption.

Keywords: SYK (spleen tyrosine kinase), tyrosine kinase, osteoclasts, Cre-Lox, *in vivo*, mice



Intelligent Assisting Tools for Endodontic Treatment

Csaba Dobo-Nagy and Balazs Benyo

Abstract

The integration of image processing in novel systems bids fair to significantly improve the endodontic practice in the near future. Also, the attempt to automatically locate and classify the root canals may result in significantly decreased chair time for both the patient and the practitioner. We focus on the shapes of human root canals and their automatic classification, methods for automatic processing, and center line identification of tooth root canal as defined previously. We introduce some micro-computed tomography image analysis methods possible for clinical implementation of cone beam computed tomography image analysis in endodontics and limitations of novel techniques. In this chapter, we present our results of segmentation and root canal identification of cone beam computed tomography images.

Keywords: image processing, skeleton extraction, cone beam computed tomography, human root canal geometry, fuzzy relations

1. Introduction

Tooth development is a more complex biological process moderated by a series epithelial and mesenchymal interactions [1]. Every developed root canal has its own individual form; therefore, visualizing and understanding root canal systems are essential for successful root canal treatment (Figure 1). Classifications were formulated on basis of: number and relations of canals in a single root, cross-sectional forms, and the curvature along the long axis of the main root canal [2]. Alteration of normal odontogenesis causes developmental anomalies in roots. Depending on the stage of tooth development, various anomalies either in root or root canal number or size or shape can occur [1]. The most common human root malformations include: dilacerations, taurodontism, root fusion, dens invaginatus, and C-shape canals. A new complex system has been developed for classifying root morphology, the main root canal system in relation to accessory canals and root canal anomalies [3]. A new coding system was also introduced to provide more comprehensive information on the morphological features of a specific tooth, root, and canal within a single code.

These complex data characterizing roots' inner and outer forms were provided by micro-computed tomography (μ CT) technology. This technology opens a new world for fine visualization and micro-morphological characterization of dental root canals for endodontists. All of the aforementioned necessary morphological information was gained from μ CT image set collected from extracted teeth scans.





Development of a quantitative preclinical screening model for implant osseointegration in rat tail vertebra

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Abstract

Objectives Functional tooth replacement and bone regeneration are parts of the daily practice in modern dentistry, but well-reproducible and relatively inexpensive experimental models are still missing. We aimed to develop a new small animal model to monitor osseointegration utilizing the combination of multiple evaluation protocols.

Material and methods After cutting the tail between the C4 and C5 vertebrae in Wistar rats, custom made, parallel walled, non-threaded implants were placed into the center of the tail parallel with its longitudinal axis using a surgical guide. Osseointegration of the titanium implants was followed between 4 and 16 weeks after surgery applying axial extraction force, and resonance frequency analysis as functional tests, and histomorphometry and micro-CT as structural evaluations.

Results In functional tests, we observed that both methods are suitable for the detection of the time-dependent increase in osseointegration, but the sensitivity of the pull-out technique (an approximately five times increase with rather low standard error) was much higher than that of the resonance frequency analysis. In structural evaluations, changes in the detected bone implant contact values measured by histomorphometry (yielding 1.5 times increase, with low variations of data) were more reliable than micro-CT based evaluations to screen the developments of contact between bone and implant.

Conclusion Our results provide evidence that the caudal vertebrae osseointegration model is useful for the preclinical evaluation of implant integration into the bone.

Clinical relevance The combination of the biomechanical and structural tests offers a well-reproducible small animal system that can be suitable for studying the integration of various implant materials and surface treatments.

Keywords Osseointegration · Implant · Micro-CT · Pull-out test · Resonance frequency analysis · Histomorphometry

GW and GV equally contributed to the project; therefore, they both should be considered as the last authors of this paper.

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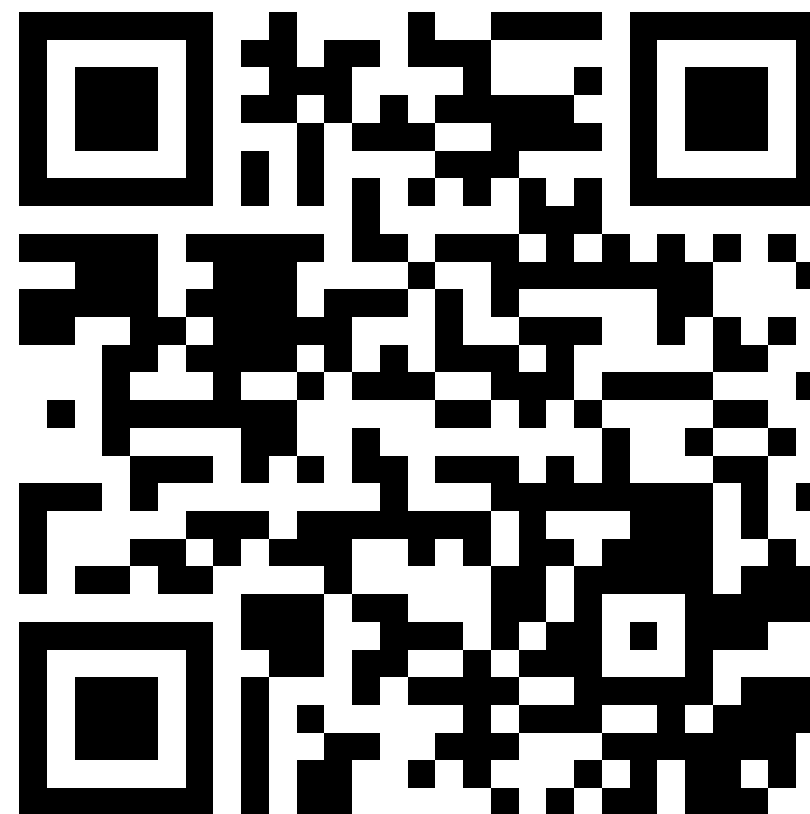
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Introduction

Since osseointegration was introduced by Branemark as a rigid fixation of an implant within bone tissue more than half a century ago [1], numerous in vitro, preclinical and clinical studies have been carried out to investigate this process. Osseointegration is defined as the direct structural and functional contact between the artificial implant surface and the living bone tissue [2]. Furthermore, the term also refers to the process of forming this direct fixation which has high dependency on the preceding surgical procedure and preoperative circumstances [3]. The process starts when the primary stability of the implant is achieved by mechanical fixation [4]. Then, bone regeneration and remodeling proceed continuously, which finally leads to a rigid and stable fixation of the implant into the surrounding bone tissue. After the initial bone healing around titanium implants, bone remodeling is



Serum albumin-coated bone allograft (BoneAlbumin) results in faster bone formation and mechanically stronger bone in aging rats

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Abstract

Serum albumin-coated bone allografts (BoneAlbumin) have successfully supported bone regeneration in various experimental models by activating endogenous progenitors. However, the effect of tissue aging, linked to declining stem cell function, has yet to be explicitly examined within the context of BoneAlbumin's regenerative capacity. Stem cell function was tested with an in vitro attachment assay, which showed that albumin coating increases stem cell attachment on demineralized bone surfaces in an aging cell population. Bone regeneration was investigated in vivo by creating critical size bone defects on the parietal bones of aging female rats. Demineralized bone matrices with and without serum albumin coating were used to fill the defects. Bone regeneration was determined by measuring the density and the size of the remaining bone defect with computed tomography (CT). Microcomputed tomography (MicroCT) and mechanical testing were performed on the parietal bone explants. In vivo CT and ex vivo microCT measurements showed better regeneration with albumin-coated grafts. Additionally, the albumin-coated group showed a twofold increase in peak fracture force compared with uncoated allografts. In the present study, serum albumin-coated demineralized bone matrices successfully supported faster and functionally superior bone regeneration in aging rats. Because stem cell function, a key contributor of bone remodelling, decreases with age and serum albumin is an effective activator of endogenous progenitor cells, this method could be an effective and safe adjuvant in bone regeneration of aging adult and osteo-compromised populations.

KEYWORDS

aging, bone, bone substitute, BoneAlbumin, serum albumin, stem cells

1 | INTRODUCTION

Endogenous stem cell function is one of the most important factors contributing to proper tissue healing. Mesenchymal stem cells (MSCs)

are essential to the bone regenerative cascade, with the localization of these cells appearing paramount (Gibson, Lu, & Goodman, 2016). Periosteal and endosteal tissue is the most abundant source of MSCs after bone injury, highlighting the role of local progenitors in bone

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Research Article

Effectiveness of Parameters in Quantifying Root Canal Morphology Change after Instrumentation with the Aid of a Microcomputed Tomography

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The objective of this study was to analyse the effectiveness of some parameters which characterise the change in morphology in human root canals subjected to ProTaper rotary enlargement with the help of an X-ray microfocus computed tomography (MCT) and to introduce a novel parameter that is effective in quantifying changes in root canal morphology. Ten each straight and curved root canals with mature apices chosen from extracted human upper incisor and canine teeth were scanned with MCT before and after canal shaping using ProTaper rotary instruments in order to facilitate three-dimensional digital reconstruction and quantitative gauging of relevant instrumental parameters and changes therein (surface area and volume). Root canal geometry change and the effectiveness of shaping were quantified with Structure Model Index change (ΔSMI) and surface area change to volume change ratio ($\Delta SA/\Delta V$). These two parameters were also tested on simulated canals. Postinstrumentation cross-sectional changes were also analysed, but only on the plastic blocks. Statistical analysis of parameters was carried out to verify the significance of results. Analysis of cross-sectional shape of postinstrumented resin simulated canals showed statistically significant decrease in Form Factor ($p < 0.05$) and statistically significant increase in Eccentricity ($p < 0.005$). ΔSMI did not show significant difference between straight and curved canals. SMI values showed bidirectional change during root enlargement which questions the reliability of this metric in analysing instrumentation. Statistically significant ($p < 0.005$) deviations in $\Delta SA/\Delta V$ were quantified as 1.92 and 3.22 for straight and curved human canals, respectively. Instrumentation-induced canal geometry change was determined to be more pronounced in curved canals using the novel parameter $\Delta SA/\Delta V$. This has been proven as being a statistically accurate and reproducible parameter for quantitative characterisation of root canal geometry change and differentiation of preparational efficacy for both straight and curved root canals.

1. Introduction

Root canal instrumentation is strongly affected by canal configuration [1] with studies showing morphology to be highly

influential on the efficacy of canal preparation. Frequency and magnitude of canal aberrations (e.g., zip, elbow, perforations, and asymmetric preparation) have been proven as being more prominent in curved root canals than straight ones [2].



Áttörésben visszamaradt bölcsességfogak ellátása az ambuláns szájsebészeti gyakorlatban egy év adatai alapján

DR. GYULAI-GAÁL SZABOLCS, DR. MINYA FANNI

Az áttörésben visszamaradt fogak között a leggyakoribbak a bölcsességfogak, amelyek számos patológiás elváltozást, illetve orthodonciai problémát okozhatnak. Osztályunkon egy év alatt sebészi feltárással 1048 db bölcsességfogot távolítottunk el, melyek közül 700 esetben részletes radiológiai elemzést és statisztikát készítettünk. A terápiás, preventív és orthodonciai okból eltávolított fogak száma közel megegyező volt, a terápiás indikációk közül leggyakoribb a perioronitis és caries volt. A preventív és orthodonciai célú bölcsességfog-eltávolítás ideális ideje 16–23 éves kor, amikor még a gyökerek kevesebb mint 2/3-a fejlődött ki. Az esetek 20%-ában ebben az időpontban történt a fogeltávolítás, ami a preventív szemlélet terjedését támasztja alá. Posztoperatív szövödmény az esetek 6%-ában fordult elő, köztük leggyakoribb a hosszabb ideig fennálló duzzanat és fájdalom. Súlyosabb szövödmény, mint sebszétnyílás és idegsérülés csak 1-1 esetben történt. A posztoperatív szövödmények előfordulása preoperatív radiológiai kiértékeléssel minimalizálható, illetve nehezebb esetekben CBCT-felvétel készítése is javasolt.

Kulcsszavak: bölcsességfog, retenció, impakció, prevenció, röntgendiagnosztika

Bevezetés

A dento-alveoláris sebészetben az egyik leggyakoribb ambuláns beavatkozás az áttörésben visszamaradt fogak eltávolítása. Az állcsontok méretének csökkenése, a fogív rövidülése miatt gyakori probléma, hogy nincs elég hely az állcsontban a fogaknak. Torlódás miatt bizonyos fogak egyáltalán nem mutatnak előtörési hajlamot, vagy beékelődnek és nem tudják elfoglalni helyüket a fogsorban, így részben vagy teljesen áttörésben visszamaradtok maradnak [25, 10]. Ezek közül a leggyakoribbak az alsó, majd a felső bölcsességfogak, ezeket követik a felső szemfogak [11, 12], a kisírlők és a számfeltti mesiodensek.

A részben előtört bölcsességfogak gyakran okoznak problémát. A körülöttük lévő fog eredetű follicularis térbe ételmaradványok kerülnek és a felszaporodó baktériumok fájdalmas lágyrészgyulladást, pericoronitist okoznak [23]. A nehéz hozzáférés miatt általában kevésbé sikerül tisztán tartani ezeket a bölcsességfogakat, ami nemcsak a pericoronitisnek, hanem a cariesnek is kedvez. A retineált bölcsességfog további patológiás folyamatok forrása lehet, amelyek az előtte lévő moláris fogat is érinthetik [3, 8]. A szomszédos moláris fog gyökéresorptiója is előfordulhat [2].

A teljesen impaktált fogak körül kialakulhat follicularis cysta [30], ritkán odontogén tumor [29, 13], pl. ameloblastoma, ami állcsontduzzanatot és arcfájdalmakat okozhat. A bölcsességfogak, késői előtörésük során az előtűntük lévő fogakra kifejtett nyomással azok torlódását

okozhatják [7, 26]. Emiatt gyakran nemcsak terápiás, hanem preventív és orthodonciai okkal is eltávolítjuk a bölcsességfogakat.

Vizsgálatainkat a Semmelweis Egyetem Orális Diagnosztikai Tanszék Dento-alveoláris Sebészeti Osztályán végeztük, ahol összesen 1048 db bölcsességfog műtéti eltávolítása történt 2016. 12. 01. és 2017. 12. 31. között.

Vizsgálati anyag és módszer

A vizsgálatban 483 páciens vett részt, amely során összesen 700 bölcsességfog eltávolítást értékeltünk ki részletesen. A páciensek átlag életkora 25 év (13–83 év). Egyetlen páciens sem került kizárára általános sebészi kontraindikáció miatt [20]. Az anatómiai képletek sérülésének veszélye miatt 3 esetben döntöttünk a fog megtartása mellett, ami egyébként nem okozott panaszt.

A sebészi feltárás előtt minden esetben panorámafelvétel készült, szükség esetén, összesen 17-szer CBCT-felvétellel kiegészítve. A fogak formáját, helyzetét ezek alapján értékeltük és soroltuk nehézségi fokozatba a műtét megtervezéséhez.

Minden esetben sebészi feltárás történt, a hazai és nemzetközi útmutatással megegyező módon [5, 9, 18]. L-alakú mucoperiosteális lebeny képzésével, vagy sulcusban vezetett, segédmetszés nélküli lebennnyel kerültek a fogak feltárára [31]. Szükség esetén a környező csont eltávolítását és a fog darabolását követően a fogak eltávolítása fogóval vagy emelővel történt. A fog-



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Az implantológia helye a fogcsírahiányos esetek ellátásában

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A fogcsírahiányos páciensek ellátása komplex, multidiszciplináris feladat, amely során kiemelten fontos a korai diagnózis és a megfelelő kezelési terv felállítása. Ideiglenesen célszerű lehet a perzisztáló tejfog megtartása az aplasiás maradó fog helyén esztétikai és helyfenntartó céllal. A foghiányból adódó rés záródása történhet spontán, irányított fogváltással, vagy pedig orthodonciai kezeléssel. Ha a hiányzó fogat pótoljuk, szükség lehet helyteremtés céljából preprotetikai-orthodonciai kezelésre. Ebben a kezelési szakaszban kell megoldanunk a résnyitás mellett a szomszédos fogak tengelyállásának és occlusiós anomáliáinak korrekcióját is. A protetikai ellátás során, főleg fiatal páciensek esetében, fontos a minimál invazív szemlélet. A konvencionális fogpótlások mellett egyre nagyobb szerep jut az adhezív és kompozit hidaknak, hégaknak. Előnyös lehet a hiányzó fog pótlása implantátummal, valamint az arra készülő koronával. Ehhez többnyire keskeny átmérőjű implantátumokat használunk, szükség esetén előzetes csontpótló beavatkozással kombinálva. Az implantációs műtét kivitelezhetősége szempontjából a megfelelő csontmennyiség és hely megteremtése, az implantációs fogpótlás hosszú távú stabilitása érdekében az esetleges parafunkciós mozgások kiküszöbölése elengedhetetlen. A fogcsírahiányos esetek sikeres ellátásának legfontosabb feltétele a szájsebész és a fogszabályozó orvos együttműködése a kezelés teljes időtartama alatt.

Kulcsszavak: aplasia, hypodontia, csírahiány, implantológia, multidiszciplináris terápia

Bevezetés

A fogak fejlődési rendellenességei közé tartoznak a számbeli eltérések, amelyek lehetnek foghiányok vagy számfelletti fogak. Csírahiány esetén a fogívben a szabályszerűen kevesebb fog található, ami egyaránt előfordulhat a tej- és maradó fogazatban. A fogcsírahiány előfordulása tejfogazatban ritka (1% alatti), viszont a maradó fogazatban a leggyakoribb fejlődési rendellenesség [19]. A hazai és nemzetközi irodalom alapján előfordulása nagyon változó, 2,7–16% közötti, a bölcsességfogak hiányát figyelmen kívül hagyva [5, 19]. A férfiak és nők közötti megoszlásban nincs jelentős eltérés, férfiaknál 6,5%, nőknél 7,5% a csírahiány előfordulásának aránya [13]. A Bolk-féle terminális redukcióelmélet szerint az egyes fogcsoportok utolsó tagjai, vagyis a kismetsző, a második premoláris és a bölcsességfogak csírahiánya a leggyakoribb [8]. Nagy esetszámú klinikai megfigyelések alapján leggyakrabban az alsó második premoláris hiányával találkozhatunk, ezt követi a felső kismetsző, a felső második premoláris és végül az alsó metszők [12]. Egy fog hiánya esetén aplasiáról, 6-nál több csírahiány esetén oligodontiáról beszélünk. Ha csupán néhány fog jelenik meg, anodontia partialis, teljes fogatlanság esetén pedig anodontia totalis a diagnózis [7].

A fogcsírahiány lehet genetikailag meghatározott, öröklődő fejlődési zavar, vagy szerzett rendellenesség, amikor környezeti ártalmak okozzák a foghiányt [2]. Ilyen környezeti ártalom lehet a terápiás dózisú röntgensugárzás az arc területén a fogak fejlődésének ideje alatt [17].

A fogcsírahiány ellátásának lehetőségei

Maradó fogazatban a csírahiány ellátásának célja a funkció és a megfelelő esztétika megteremtése, valamint a kiegyensúlyozott occlusio helyreállítása. Fontos továbbá a foghiányból adódó káros következmények megelőzése is. Az ellátás során figyelembe kell venni a páciens életkorát, a hiányzó fogak számát, elhelyezkedését, a harapási formát és a helykinálatot. A sikeres rehabilitáció mindenképp multidiszciplináris feladat, csapatmunkát igényel, melyhez a korai diagnózis és a megfelelő kezelési terv felállítása a legelső lépés.

Gyermekeknél célszerű a csírahiány helyén az analóg tejfog megtartására törekedni, amíg annak gyökere nem szívódik fel, átmenetileg betöltve a hiányzó fog szerepét. A tejfog helyfenntartóként szolgál, megakadályozza az antagonista fog elongációját és az alveoláris csont felszívódását a maradó fog végleges pótlásáig [3].





Cell physiological effects of glass ionomer cements on fibroblast cells

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ABSTRACT

The cytotoxicity of glass ionomer cements (GICs) was investigated using a novel, cost-effective, easy-to-perform and standardized test. GIC rings were made using in-house designed, custom-made moulds under sterile conditions; 10 with Fuji Equia and 10 with Fuji Triage capsules, placed in direct contact with primary human gingival fibroblasts (HGF) and immortalized human fibroblasts (HFF1). On day 1, 4, 14 and 21, an AlamarBlue® (resazurin) assay was completed towards determining the effects of the GICs on metabolic activities of the cells, whilst cell morphology was examined by light microscopy. The influence of the compounds released from the GIC rings on cell physiological effects (viability, proliferation and adhesion) during 24 h incubation was further investigated by impedimetry.

Result trends obtained from this battery of techniques were complementary. At 100 v/v% concentration, the released compounds from Equia were strongly cytotoxic, while at lower concentration (0, 4, 20 v/v%) they were not cytotoxic. In contrast, Triage elicited only slightly transient cytotoxicity.

The method proposed has been proved as being efficient, reliable and reproducible and may be useful in quick testing of the cytotoxicity of similar biomaterials by using an immortalized cell line.

1. Introduction

Since mercury was recognised as a global threat to human and environmental health, reduction of its use and disposal has been on the agenda of major health and environmental organisations (European Commission: Scientific Committee on Health and Environmental Risks (SCHER), n.d). However, the complete removal of existing dental amalgam has not been enacted since it is an effective filling material with infinitesimal adverse effects and it is unnecessary to remove clinically satisfactory restorations (European Commission: Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), n.d). Nonetheless, the design and optimisation of alternative dental materials remain a key area of growth, as dental amalgam lacks aesthetics and has poor tooth adhesion. Mercury-free restorative dental materials likewise present challenges, particularly with respect to their potential cytotoxicity, a problem compounded by the commercial secrecy withholding their full chemical specifications. Hence, testing

cytotoxicity of these restoratives is requisite in the development of highly biocompatible restorative dental materials.

In the search and optimisation of alternatives to dental amalgam, glass ionomer cements (GICs) have shown great potential. GICs, in general, have sound biocompatibility, good aesthetics, natural adhesion to tooth structures and anticariogenic property due to their sustained fluoride release (Wilson and Kent, 1972; Forsten, 1998; Nicholson, 1998).

To achieve a perfect balance between biocompatibility and physical and mechanical properties appears to be the main theme throughout the development of GICs (Smith, 1998; Mohd Zainal Abidin et al., 2015; Goldberg, 2008; Silva et al., 2016; Najeeb et al., 2016; Moshaverinia et al., 2016; Kim et al., 2017; Senthil Kumar et al., 2017; Noorani et al., 2017). However, the changing atomic cohesion and fluctuating interfacial configurations during setting of GICs result in their falling short of the fracture toughness requisite for universal permanent restoration (Tian et al., 2012, 2015), though they are acceptable for niche

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Research Article

Development and Characterisation of Gastroretentive Solid Dosage Form Based on Melt Foaming

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Abstract. Dosage forms with increased gastric residence time are promising tools to increase bioavailability of drugs with narrow absorption window. Low-density floating formulations could avoid gastric emptying; therefore, sustained drug release can be achieved. Our aim was to develop a new technology to produce low-density floating formulations by melt foaming. Excipients were selected carefully, with the criteria of low gastric irritation, melting range below 70°C and well-known use in oral drug formulations. PEG 4000, Labrasol and stearic acid type 50 were used to create metronidazole dispersion which was foamed by air on atmospheric pressure using in-house developed apparatus at 53°C. Stearic acid was necessary to improve the foamability of the molten dispersion. Additionally, it reduced matrix erosion, thus prolonging drug dissolution and preserving hardness of the moulded foam. Labrasol as a liquid solubiliser can be used to increase drug release rate and drug solubility. Based on the SEM images, metronidazole in the molten foam remained in crystalline form. MicroCT scans with the electron microscopic images revealed that the foam has a closed-cell structure, where spherical voids have smooth inner wall, they are randomly dispersed, while adjacent voids often interconnected with each other. Drug release from all compositions followed Korsmeyer-Peppas kinetic model. Erosion of the matrix was the main mechanism of the release of metronidazole. Texture analysis confirmed that stearic acid plays a key role in preserving the integrity of the matrix during dissolution in acidic buffer. The technology creates low density and solid matrix system with micronized air-filled voids.

KEY WORDS: solid foam; lipid matrix; PEG 4000; gastric retention; solid dispersion.

INTRODUCTION

Several drugs display site-specific absorption in the gastrointestinal tract (1). Contribution of numerous factors, such as site specific, environmental pH and/or intestinal enzyme activity, could lead to low bioavailability (2). The gastrointestinal motility determines the residence time of the formulation in its absorption window (3).

Gastric retention is a promising mechanism for the oral modified-release drug products (4). These delivery systems provide sustained drug release coupled with resistance against the gastric milling (5,6) and emptying motions (7,8) and show prolonged residence time in the stomach. On the other hand, when localised therapy of the stomach or the duodenum is preferred, these delivery platforms may provide site-specific drug release for a longer time (9).

To achieve gastric retention, several technologies are available. Expanding devices increases their size upon or followed by the contact with gastric juice to inhibit transit through the pyloric sphincter. Hydrogels (5,10), and other unfolding technologies, such as the Accordion Pill® (7,11,12), are formulations with prolonged residence time in the stomach. Mucoadhesive formulations containing hydrophilic polymers adhere to the gastric mucosa (13) and release their drug in sustained manner.

Floating or low-density formulations remain on the top of the gastric content (14), thus avoiding passage to the duodenum. Gas-generating platforms usually contain carbonates (15–17) and polymers to entrap the formed gas or a

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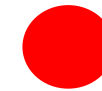
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SCIENTIFIC REPORTS



OPEN

Significance of the Tks4 scaffold protein in bone tissue homeostasis

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The main driver of osteoporosis is an imbalance between bone resorption and formation. The pathogenesis of osteoporosis has also been connected to genetic alterations in key osteogenic factors and dysfunction of bone marrow mesenchymal stem/stromal cells (BM-MSCs). Tks4 (encoded by the *Sh3pxd2b* gene) is a scaffold protein involved in podosome organization. Homozygous mutational inactivation of *Sh3pxd2b* causes Frank-ter Haar syndrome (FTHS), a genetic disease that affects bone tissue as well as eye, ear, and heart functions. To date, the role of Tks4 in adult bone homeostasis has not been investigated. Therefore, the aim of this study was to analyze the facial and femoral bone phenotypes of *Sh3pxd2b* knock-out (KO) mice using micro-CT methods. In addition to the analysis of the *Sh3pxd2b*-KO mice, the bone microstructure of an FTHS patient was also examined. Macro-examination of skulls from Tks4-deficient mice revealed craniofacial malformations that were very similar to symptoms of the FTHS patient. The femurs of the *Sh3pxd2b*-KO mice had alterations in the trabecular system and showed signs of osteoporosis, and, similarly, the FTHS patient also showed increased trabecular separation/porosity. The expression levels of the *Runx2* and osteocalcin bone formation markers were reduced in the bone and bone marrow of the *Sh3pxd2b*-KO femurs, respectively. Our recent study demonstrated that *Sh3pxd2b*-KO BM-MSCs have a reduced ability to differentiate into osteoblast lineage cells; therefore, we concluded that the Tks4 scaffold protein is important for osteoblast formation, and that it likely plays a role in bone cell homeostasis.

Osteoporosis is a globally distributed, multifactorial metabolic bone disease characterized by dysregulation of bone tissue remodeling. Bone homeostasis is maintained via a fine balance between bone formation and bone resorption. Although the mechanisms of these osteoporotic processes have been extensively studied, the genetic factors^{1,2} and molecules that influence bone homeostasis are still under investigation^{3–5}.

Scaffold proteins modulate cellular signaling by bringing regulatory proteins, enzymes or actin-organizing structures into close proximity⁶. The Tks protein family consists of large, multidomain scaffold proteins that are phosphorylated by the Src kinase, hence the acronym Tyrosine kinase substrate (Tks)⁸. Tks4 contains four Src Homology 3 (SH3) domains, one Phox Homology domain (PXD) and several conserved linear motifs, e.g., proline-rich regions⁹. The Tks4-encoding gene was named *Sh3pxd2b* based on this domain structure. The primary function of the PX domain is to directly bind to membrane-associated phosphoinositides to tether Tks4 to the cell membrane. The SH3 domains mediate protein-protein interactions and are docking sites for other signaling components. Tks4 is involved in signal transduction in the EGFR pathway¹⁰. When Tks4 is phosphorylated by the EGFR-activated Src kinase, it interacts with cortactin to regulate the actin cytoskeleton. Tks4 is a key scaffold protein during podosome formation¹¹; furthermore, it participates in reactive oxygen species (ROS) production by tumor cells¹² and is necessary for mesenchymal stem/stromal cell (MSC) differentiation¹³.

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A novel hydrogel scaffold for periodontal ligament stem cells

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Abstract: Periodontal ligament stem cells (PDLSCs) possess extensive regeneration potential. However, their therapeutic application demands a scaffold with appropriate properties. HydroMatrix (HydM) is a novel injectable peptide nanofiber hydrogel developed recently for cell culture. Our aim was to test whether HydM would be a suitable scaffold for proliferation and osteogenic differentiation of PDLSCs. PDLSCs were seeded on non-coated or HydM-coated surfaces. Both real-time impedance analysis and cell viability assay documented cell growth on HydM. PDLSCs showed healthy, fibroblast-like morphology on the hydrogel. After a 3-week-long culture in osteogenic medium, mineralization was much more intense in HydM cultures compared to control. Alkaline phosphatase activity of the cells grown on the gels reached the non-coated control levels. Our data provided evidence that PDLSCs can adhere, survive, migrate, and proliferate on HydM and this gel also supports their osteogenic differentiation. We first applied impedimetry for dental stem cells cultured on a scaffold. HydM is ideal for *in vitro* studies of PDLSCs. It may also serve not only as a reference material but also in the future as a promising biocompatible scaffold for preclinical studies.

Keywords: stem cell, HydroMatrix, periodontal ligament, cell proliferation, impedimetry, osteogenic differentiation

Introduction

Dental stem cell (SC)-based therapies could provide new opportunities in the field of regenerative medicine. The fact that SCs exist in periodontal tissues became evident in 2004 when Seo et al. [1] first succeeded in isolating periodontal ligament stem cells (PDLSCs). This mesenchymal SC type possesses multipotent differentiation capacities including osteogenic [1], adipogenic [1], chondrogenic [2], and myogenic [3] ones. Beyond these mesenchymal lineages, PDLSCs can also be differentiated into neuronal phenotype [3] due to their ectomesenchymal origin. The wide spectrum of their regeneration potential makes these cells ideal candidates for regeneration therapy.

To be useful for tissue regeneration therapy, an ideal scaffold should fulfill the following three criteria:

(1) biocompatibility, (2) biodegradability, and (3) three-dimensional structure similar to the natural environment of the cells, e.g., extracellular matrix (ECM) [4]. Intensive research to find structures for biomedical application found that hydrogels are the most promising scaffolds [4–6]. Hydrogels are cross-linked, three-dimensional hydrophilic polymer networks that are insoluble in water but can absorb large amounts of water or biological fluids [7]. Among hydrogels, increasing attention is paid to *in situ* gelling hydrogels. The great advantage of these gels is that they are injectable and spontaneous gel formation occurs under physiological conditions [8]. Due to the chemical similarity to ECM proteins, self-assembling peptide hydrogels are the most suitable for mimicking the natural ECM [9]. However, for clinical application of periodontal SCs, a scaffold with appropriate properties is also required. In the preclinical studies of dental SCs, investigations are



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Microarchitecture of the Augmented Bone Following Sinus Elevation with an Albumin Impregnated Demineralized Freeze-Dried Bone Allograft (BoneAlbumin) versus Anorganic Bovine Bone Mineral: A Randomized Prospective Clinical, Histomorphometric, and Micro-Computed Tomography Study

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Abstract: Serum albumin has been identified as an endogenous protein that is integral to early bone regeneration. We hypothesized that albumin addition to allografts may result in better bone remodeling than what can be achieved with anorganic xenografts. Sinus elevations were performed at 32 sites of 18 patients with the lateral window technique. Sites either received filling with an anorganic bovine bone mineral (ABBM, BioOss, Geistlich, CH) or albumin impregnated allograft (BoneAlbumin, OrthoSera, AT). After 6-months patients received dental implants and 16 bone core biopsy samples were obtained from the ABBM filled, and 16 from the BoneAlbumin augmented sites. The biopsies were examined by histomorphometry and μ CT. Percentage of the residual graft in the BoneAlbumin group was 0–12.7%, median 5.4% vs. ABBM 6.3–35.9%, median 16.9%, $p < 0.05$. Results of the μ CT analysis showed that the microarchitecture of the augmented bone in the BoneAlbumin group resembles that of the native maxilla in morphometric parameters Trabecular Pattern Factor and Connectivity. Our data show that while ABBM successfully integrates into the newly formed bone tissue as persisting particles, BoneAlbumin is underway towards complete remodeling with new bone closely resembling that of the intact maxilla.





Study on process parameters and optimization of microencapsulation based on phase separation

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ABSTRACT

As surfactants are capable of influencing the droplet formation, our study primarily aims the investigation of the effect of a nonionic surfactant e.g. Polysorbate 80 on the formation of microspheres on the course of vibrating nozzle method with coacervation. The experiments also concern the impact of the different process parameters (e.g. vibration frequency, feed rate and voltage) on the shape and size distribution of microspheres characterized by laser diffraction size determination completed with particle image analysis. The calcium-alginate microspheres were processed using freeze-drying to ensure solid state with better drug carrier capability.

Addition of isomalt was advantageous in the formation of freeze-dried microspheres at low alginate concentration, which was explained by micro-CT analysis of the constructed particle structure. The internal three-dimensional network of calcium alginate demonstrated a more cancellous architecture ameliorating the roundness of microparticles.

1. Introduction

Alginates are in focus of drug formulation for decades. This natural polysaccharide of an α -L-guluronic acid and β -D-mannuronic acid chain has a hydrogel-forming ability with Ca^{2+} and other divalent cations Sr^{2+} (Thu et al., 1996), Ba^{2+} (Tønnesen and Karlsen, 2002), Zn^{2+} (Pistone et al., 2017). Its water solubility, plant origin, biocompatibility and pH-sensitive swelling potential are beneficial in drug formulations and also in functional food products. Sodium alginate is successfully administered using ionotropic gelation for the entrapment of compounds of broad scale to protect their original character: flavonoids (Aizpurua-Olaizola et al., 2016; Wang et al., 2016; Nori et al., 2011) oil-soluble compounds (Chew and Nyam, 2016), and proteins (Thu et al., 1996).

Microencapsulation via coacervation using the vibrating nozzle method is a complex physicochemical procedure, which supports the production of spherical beads, as the extruded solution lands separated by vibrational frequencies in a curing liquid. There are a great number of influential factors affecting the morphology of the eventuated particles, i.e. viscosity, surface tension, feeding rate of polymer, gelling time (Razga, 2014; Lotfipour et al., 2012; Martins, 2012). Recent studies underline the observation that drug release depends on the shape

of gel beads. Higher drug release rate is seen from oblate than from spherical particles, since an oblate particle is of a larger surface area than a spherical one. Alginate particle shape is characterized as a significant parameter in pharmaceutical drug release profile kinetics (Chuang et al., 2017). The thickness of the shell in microcapsules also has an effect on the release rate under conditions where the materials show swelling, so the diffusion through the gel layer determines the release rate (McClements, 2017).

Alginate hydrocolloid ageing is manifested in syneresis after production depending on their Ca^{2+} concentration, gelling time, alginate molecular weight and alginate concentration (Rehm, 2009). The shrinkage and concomitant water loss can compromise the inclusion efficiency of microparticles and their spherical shape as well. Latter corresponds with flowability when the particles are aimed to be applied in a dried form.

The release of the active ingredient from the microcapsule during gel solidification can be prevented by the elevation of the osmotic pressure of the coacervation liquid. For this reason glycerol was administered (Davarci et al., 2017).

Isomalt, a sugar alcohol carrying many positive characteristics as being nonacidogenic, non-hygroscopic, resistant to acidic and enzymatic hydrolysis was successfully administered in coating procedures



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PCR Technique Assisting the Early Diagnosis of Human Papillomavirus

A retrospective clinical study

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The number of oral cancers associated with Human Papillomavirus (HPV) infection is increasing worldwide. The purpose of this retrospective clinical trial is to investigate the relationship between genital and oral HPV infection and to observe the possibilities of polymerase chain reaction (PCR) technique and the limitations for oral HPV infection. The results of genital and oral HPV screening of 34 female patients and their partner, and 14 single female patients were processed in a private practice in Budapest between 2012 and 2015. After brush-biopsy sampling, HPV DNA identification and typing were performed using PCR technique. All in all 164 samples were typed. HPV DNA was detected in 76 cases (48.20%). HPV was detected in 55 cases from the genital samples (67%), and in 21 cases from the oral samples (25.6%). Genital HPV infection was statistically significantly higher in women (79.2% vs 22.9%, $p < 0.001$). Gender comparison of genital HPV infection showed a statistically significant difference (79.2% for women, 50% for men, $p = 0.006$). In case of genital HPV infection, the oral HPV infection of the same person is more frequent. In this study, the above mentioned difference is significant for women and not significant for men. HPV16 is the HPV genotype which was identified in the highest ratio (47.2%). PCR technique is capable of the detection of oral HPV infection, but follow-up studies with higher case number, and questionnaire studies are needed to understand HPV transmission more accurately.

Keywords: polymerase chain reaction, oral cancer, human papillomavirus

Human papillomavirus (HPV) infection is the most common sexually transmitted disease in the world [1]. HPV infection is diagnosed in approximately 6 million cases annually and 9.0-13.0 per cent of the world population are infected. More than 100 genotypes of HPV are known. There are low-risk groups (Low-Risk HPV, LR HPV), such as HPV 6,11, which play a role in the aetiology of benign lesions such as papilloma or condyloma acuminatum. There are high-risk, oncogenic genotypes (High-Risk HPV, HR HPV), such as HPV16,18 and 31, which are responsible for the development of malignant lesions (e.g., cervix carcinoma, oropharyngeal tumours). Worldwide 6.7 per cent of all malignant tumours is due to oncogenic HPV infection [2]. Malignant tumours associated with HPV have a highest incidence on the cervix, there 99.7 per cent of malignant lesions have oncogenic HPV infection in the background [3]. Oncogenic genotypes have been isolated from cancers of the vulva, vagina, penis, anus and oropharyngeal and oesophageal cancers. Low-risk genotypes HPV6 and HPV11 are most often present in the mucus membranes causing papilloma and condyloma acuminatum [4].

In Hungary according to the data of the Hungarian Central Statistical Office the incidence of cervix carcinoma is around 1500 cases per year and around 500 patients die annually [3]. Hungary is the leader in incidence and mortality in oropharyngeal cancer in Europe and is second in the world in terms of men [5]. In terms of the numbers in 2014 according to the National Cancer Registry 3765

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new cases of head and neck cancer have been registered, 2688 men and 1077 women. According to data from the Hungarian National Statistical Office in 2015 1157 male and 303 female patients died of head and neck cancer.

The aetiology of oral cancer is multicausal. A distinction between HPV positive and HPV negative tumours is made in the literature. Classic etiologic factors include smoking, excessive alcohol consumption, male gender, old age, poor oral hygiene and mechanical irritation [6]. Due to current sexual behaviour oral HPV infection is becoming more and more common [7]. In the past 30 years the number of HPV positive oral cancers has been on the rise [8, 9], especially in the case of tonsil tumours, in 70 per cent of which oncogenic HPV can be detected [10, 11]. The prevalence of smoking has a decreasing tendency worldwide as well as in Hungary, but the incidence of oral cancer is stagnating. Oncogenic HPV-positive tumours are probably the explanation for this discrepancy [8, 12]. Characteristics of HPV related tumours include: location in the posterior segment of the mouth (posterior tongue, soft palate, tonsils, mesopharynx), the male:female ratio is typically 1:1, patients are younger, presence of precancerous lesion is rare. The prognosis of HPV-positive cancers is better, recurrence is less frequent and they respond better to radiotherapy [13]. The etiologic role of the oncogenic HPV 16 genotype is proven in oral cancer. HPV 16 isolated from the back of the mouth can be considered a 13 fold risk factor [14].



Fibrosus dysplasia differenciál-diagnózisa

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A tanszékünkön megjelent 69 éves nőbeteg anamnézisének felvétele és stomato-onkológiai szűrése után panoráma(OP) felvétel készült, amelyen multiplex szklerotikus, cystosus felritkulások láthatók a mandibulán. A tapasztalt elváltozások alapján további képalkotó modalitások alkalmazása vált indokolttá, így posteroanterior (PA) és oldalirányú (LAT) koponya-, illetve cone beam CT (CBCT) felvételeket készítettünk. A PA és LAT koponyafelvételeken kóros eltérés a mandibulán kívül egyéb területen nem ábrázolódt. Minthogy a páciens ötében belül nem jelent meg tüdőszűrő vizsgálaton, ezért nem rendelkezünk PA-mellkasfelvétellel. A páciens képanyaga alapján megerősítettük a fibrosus dysplasia radiológiai diagnózisát.

Kulcsszó: orthopantomographia, cone beam computed tomography, csont fibrosus dysplasia, monostoticus fibrosus dysplasia, differenciál diagnózis

Bevezetés

A fibrosus dysplasia (FD) a csontszövet többnyire jóindulatú tumorszerű fejlődési rendellenessége [1–4]. A csontvelő helyén fibrosus és éretlen osteoid szövet képződik („woven bone”) [4–6]. Weinstein és munkatársai leírták, hogy a zavart csontéresi folyamat hátterében a Gsa fehérje alegységet kódoló GNAS1 génaktiváló mutációja áll [7], ami az osteoblastok differenciálódásának gátlásához és azok abnormális proliferációjához vezet [7, 8]. Az elváltozás a benignus csontdaganatok 2,5–7%-át adja [2, 3]. A FD irodalmában többféle csoportosítási rendszer ismert [1, 3, 7], amelyekben közös, hogy a FD-t megjelenési helye szerint rendszerezik. A monostoticus FD, amelynek során csak egy csont érintett, sokkal gyakoribb (az összes FD esetek 70–80%-a), mint a több csontra kiterjedő polyostoticus forma [2, 9, 10], amely gyakran tovább növekszik a csontok érésének befejeződése után, és csontfájdalomhoz, súlyos deformitásokhoz vezethet, növelve a patológiás fractura kockázatát [2]. A FD leggyakrabban a hosszú csöves csontokban [2, 10, 11], a craniofaciális területen [2, 4, 11], illetve a bordákon alakul ki [2, 10, 11]. A monostoticus FD-s esetek 10–25%-ában, a polyostoticus esetek 50%-ában koponya- vagy arckoponyacsont érintett [12], de bármely csontban kialakulhat [4]. A monostoticus forma egyenletes eloszlást mutat mindkét nemből, a polyostoticus forma viszont többnyire fiatal nők körében gyakoribb [9]. A polyostoticus formához társulhat McCune Albright vagy Mazabraud szindróma [10]. Előbbi esetben az FD mellett fellép endocrinopathia, leggyakrabban pubertás praecox, illetve café au lait pigmentáció; utóbbi esetben pedig a polyostoticus FD intramuscularis myxomákkal

társul [2, 9, 10, 13]. Egyes szerzők külön tárgyalják a craniofaciális FD-t [1, 3], ugyanis az itt kialakuló elváltozás radiológiai képe gyengén körülhatárolt és bizonyos esetekben tartalmazhat lamelláris csontot, míg az axiális csontok esetében inkább radiolucens és nem tartalmaz lamelláris csontot [9, 14].

A pontos diagnózis felállításához gyakran nem elegendő pusztán szövettani diagnózis megállapítása, hanem megfelelő radiológiai modalitás is szükséges [1]. A radiológiai kép változatos megjelenésű, amely a FD korai fázisában – tekintve a lítikus folyamatokat – inkább a radiolucens területek, míg a későbbi, a FD laesio érettebb állapotában a denzebb területek dominánsabbak [13, 15]. A monostoticus FD többnyire tünetmentes és egyéb indikációjú radiológiai vizsgálat során derül rá fény [2]. A röntgenképe az alábbi három jellegzetességet mutathatja: 56%-ban tejüvegszerű, 23%-ban homogén denz és 21%-ban cystosus (egy vagy többrekeszes) mintázatot [10, 12, 16]. Utóbbi esetben jellemző a héjszerű sclerotikus szél, amely az axiális csontokon detektálva fontos diagnosztikus értékkel bír [14, 17]. Az állcsontok esetén ez a sclerotikus határ lehet vékony, jól körülírt, ténylegesen cystát körülhatároló; gyakrabban bár vékony, de szabálytalan lefutású, illetve vastagabb, sávszerű opacitást mutathat többrekeszes radiolucens területek körül [1]. A homogén denz formára jellemző lehet a narancshéj- vagy ujjlenyomat-szerű rajzolat [14], amely fiatalabb korban és főleg a maxillán figyelhető meg és más elváltozásra nem jellemző, azaz csak a FD-ra specifikus [1]. A tejüvegszerű megjelenés gyakoribb felnőtt pácienseknél, lokalizációját tekintve inkább a maxillán jellemző, viszont hiányzik a narancshéj rajzolatnál jellemző szemcsézettség [13]. Az irodalomban fellelhető adatok alapján a legjellem-



Clinical Paper
Dental Implants

Microarchitectural study of the augmented bone following ridge preservation with a porcine xenograft and a collagen membrane: preliminary report of a prospective clinical, histological, and micro-computed tomography analysis

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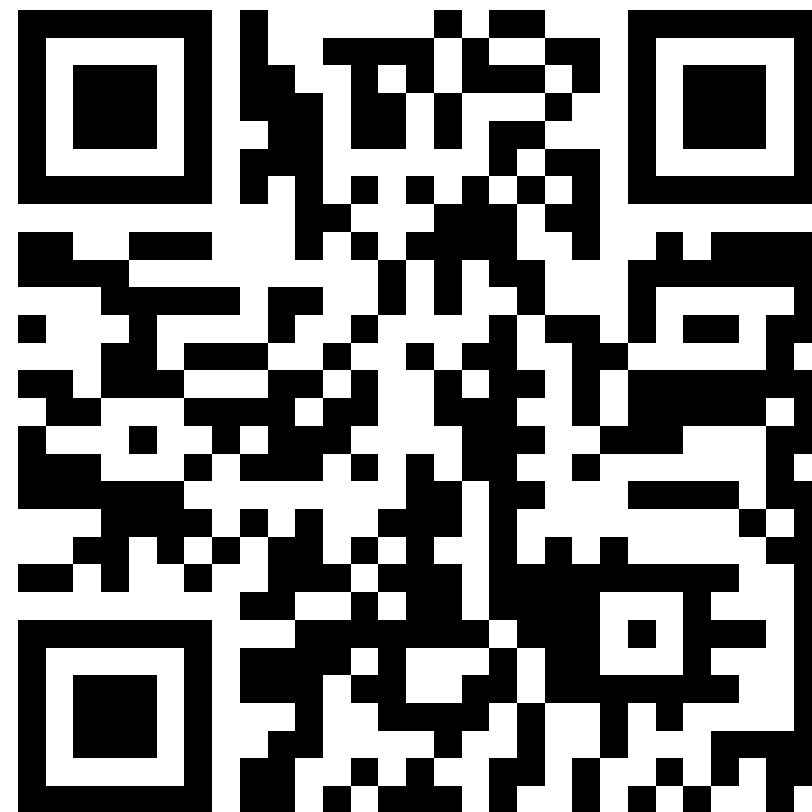
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M. Kivovics, B.T. Szabó, O. Németh, N. Tari, F. Dóri, P. Nagy, C. Dobó-Nagy, G. Szabó: Microarchitectural study of the augmented bone following ridge preservation with a porcine xenograft and a collagen membrane: preliminary report of a prospective clinical, histological, and micro-computed tomography analysis. *Int. J. Oral Maxillofac. Surg.* 2017; 46: 250–260. © 2016 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. Socket preservation using a combination of porcine xenograft and collagen membrane maintains the vertical and horizontal dimensions of the ridge. The aim of this study was to evaluate the microarchitecture of the grafted area by histological analysis and micro-computed tomography. Patients in the test group (group 1; nine patients) underwent socket preservation, while the sockets in the control group (group 2; eight patients) were allowed to heal without preservation. After a 6-month healing period, bone core biopsy samples were obtained and implants were placed in the augmented sites in the test group (12 biopsy samples) and the non-augmented



Endodontic and microsurgical treatments of maxillary lateral incisor dens invaginatus in combination with cone-beam-computed tomography fusion imaging

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Abstract In this case report, we present the endodontic treatment and microsurgical intervention of dens invaginatus affecting a lateral incisor using cone-beam-computed tomography (CBCT). A 26-year-old woman visited us with a diagnosis of acute apical periodontitis in the upper right lateral incisor (tooth 12). Endodontic treatment of the tooth was carried out. Intraoral radiography provided limited information on the unusual anatomy of the pulp chamber and root canal system; therefore, preoperative CBCT was performed. At the 3-month recall, a radiograph revealed a 5-mm-diameter lateral transparency, and CBCT was, therefore, repeated to facilitate microsurgery treatment planning. A medical image-processing program was used to demonstrate the changes between the CBCT images obtained before and after root canal preparation. In conclusion, endodontic treatment of dens invaginatus is challenging even for endodontic specialists, because the therapy sometimes requires surgical intervention. The currently available novel three-dimensional imaging modalities may have importance in planning and following

up the root canal treatment in such cases, especially when unforeseen complications arise.

Keywords Cone-beam CT · Dens in dente · Fused image · Microsurgery

Introduction

Dens invaginatus is a common malformation of permanent teeth [1]. Patients with this disorder show radiographic deepening or invagination of the enamel and dentin into the pulp chamber, sometimes into the root, and rarely into the periapical space of the apical foramen [2]. The most frequently affected tooth is the permanent maxillary lateral incisor [2]. Patients with dens invaginatus are at higher risk of caries formation as well as pulpal and periodontal disease development. Furthermore, the higher variability in the coronal pulp and root canal anatomy often poses difficulties for dentists [3–7]. This is reflected by the survey results reported by Hommez et al. [8], who found that 38.4 % of 307 general dental practitioners considered that if a tooth with dens invaginatus required root canal treatment, they would refer the patient to an endodontic specialist.

Several classifications of dens invaginatus have been described. The first was published by Hallet [9] in 1953. The most widely used classification was proposed by Oehlers [3]. It is important to recognize dens invaginatus before dental treatment is needed; imaging of the affected teeth is especially important in patients requiring root canal treatment. Both plain X-ray images and cone-beam-computed tomography (CBCT) are currently available for this purpose; the latter shows the three-dimensional (3D) morphology of the pulp and root canal system.

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Comparison of hand and semiautomatic tracing methods for creating maxillofacial artificial organs using sequences of computed tomography (CT) and cone beam computed tomography (CBCT) images

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ABSTRACT

Introduction: The aim of this study was to compare the paranasal sinus volumes obtained by manual and semi-automatic imaging software programs using both CT and CBCT imaging.

Methods: 121 computed tomography (CT) and 119 cone beam computed tomography (CBCT) examinations were selected from the databases of the authors' institutes. The Digital Imaging and Communications in Medicine (DICOM) images were imported into 3-dimensional imaging software, in which hand mode and semiautomatic tracing methods were used to measure the volumes of both maxillary sinuses and the sphenoid sinus. The determined volumetric means were compared to previously published averages.

Results: Isometric CBCT-based volume determination results were closer to the real volume conditions, whereas the non-isometric CT-based volume measurements defined coherently lower volumes. By comparing the 2 volume measurement modes, the values gained from hand mode were closer to the literature data. Furthermore, CBCT-based image measurement results corresponded to the known averages.

Conclusions: Our results suggest that CBCT images provide reliable volumetric information that can be depended on for artificial organ construction, and which may aid the guidance of the operator prior to or during the intervention.

Keywords: 3-D imaging, Cone-beam CT, Paranasal sinuses, Spiral CT

Introduction

Success in treating sinonasal disorders requires comprehensive knowledge and the proper visualization of the anatomic conditions of the osteomeatal complex and the paranasal sinuses, which is crucial in head and neck surgery, especially in otolaryngology, skull base surgery and maxillofacial surgery (1-7). As an additional examination to the clinical investigations to confirm the anatomical landmarks and the diagnosis, to localize and measure the extensions of the pathologic lesions (2, 8), computed tomography (CT) is widely

used as the "gold standard" method (2, 9). Currently, cone-beam computed tomography (CBCT) also seems to be a reliable imaging technique in these fields, thanks to its lower radiation dose and higher resolution and quality (1, 4, 10-13). The use of CBCT was first reported by Mozzo et al (14) and has been proposed in the last decade for maxillofacial imaging (15, 16). A CBCT scan uses a different type of acquisition than that used in medical CT (MDCT). Rather than capturing an image as separate slices as in MDCT, CBCT produces a cone-shaped X-ray beam that allows an image to be captured in a single shot. The resultant volume can be reformatted to provide multiple reconstructed images (e.g. sagittal, coronal, and axial) that are similar to traditional MDCT images (17, 18). CBCT thus offers the distinct advantage of a lower radiation dose than MDCT and the possibility of importing and exporting individualized, overlap-free reconstructions. Moreover, these possibilities and increasing access to CBCT imaging for surgeons are enabling the movement from 2-dimensional (2D) analysis to 3-dimensional (3D) analysis prior to any kind of surgery. Studies of CBCT applications in dentistry have determined that they provide a reliable and accurate tool

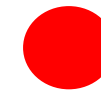
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Serum albumin coating of demineralized bone matrix results in stronger new bone formation

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Abstract: Blood serum fractions are hotly debated adjuvants in bone replacement therapies. In the present experiment, we coated demineralized bone matrices (DBM) with serum albumin and investigated stem cell attachment *in vitro* and bone formation in a rat calvaria defect model. In the *in vitro* experiments, we observed that significantly more cells adhere to the serum albumin coated DBMs at every time point. *In vivo* bone formation with albumin coated and uncoated DBM was monitored biweekly by computed tomography until 11 weeks postoperatively while empty defects served as controls. By the seventh week, the bone defect in the albumin group was almost completely closed (remaining defect $3.0 \pm 2.3\%$), while uncoated DBM and unfilled control groups still had significant defects (uncoated: $40.2 \pm 9.1\%$, control: $52.4 \pm 8.9\%$). Higher density values were also observed in the albumin coated DBM group. In addition, the serum albumin enhanced

group showed significantly higher volume of newly formed bone in the microCT analysis and produced significantly higher breaking force and stiffness compared to the uncoated grafts (peak breaking force: uncoated: 15.7 ± 4 N, albumin 46.1 ± 11 N). In conclusion, this investigation shows that implanting serum albumin coated DBM significantly reduces healing period in nonhealing defects and results in mechanically stronger bone. These results also support the idea that serum albumin coating provides a convenient milieu for stem cell function, and a much improved bone grafting success can be achieved without the use of exogenous stem cells. © 2015 Wiley Periodicals, Inc. *J Biomed Mater Res Part B: Appl Biomater*, 104B: 126–132, 2016.

Key Words: serum albumin, bone, DBM, calvaria defect, stem cells

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INTRODUCTION

Allogeneic bone substitutes are extensively used in bone replacement interventions, such as, fresh-frozen, freeze-dried or demineralized bone. Although, allografts are generally safe, every step of the preparation process was shown to compromise bone-forming capacity.¹ For example, the harsh physico-chemical methods needed to remove antigens and reduce contamination, which also results in the reduction in osteogenic response of demineralized bone matrix (DBM).² One way of tackling this issue is to replace the missing ossification factors in the bone grafts before implantation. Recombinant bone morphogenic proteins

(BMPs) can be loaded onto the surface of various bone substitutes and faster ossification can be observed in animal studies.^{2–4} Although there is no question about the strong bone-inducing ability of BMPs, recent data gained from clinical use pointed out safety issues of these proteins.^{5,6} Some of these issues may be related to the fact that BMPs are typically applied as single proteins, much like a classical drug; while optimal proliferation in the tissues normally requires several factors with varying concentrations. A balanced mixture of such growth factors is present in blood activated by an injury. Based on this idea, serum fractions, such as platelet rich plasma, are also



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Semmelweis Egyetem, Fogorvostudományi Kar, Orális Diagnosztika Tanszék

A fogorvosok vélekedése szerint a rendelőben többnyire – fogászati problémájuktól eltekintve – egészséges emberek fordulnak meg. Ez a megállapítás már évtizedekkel ezelőtt sem volt érvényes, manapság pedig a sebészeti és a gyógyszeres kezeléseknek, valamint a növekvő általános életkornak köszönhetően egyre több beteg él túl, egyre hosszabban életveszélyes betegségeket.

Elméresek szerint a fogorvosi rendelőben megforduló páciensek mintegy 30%-ának van valamilyen egészségügyi problémája. A fogorvosi ellátást nem csak a háttérben meghúzódó betegség, de a kezelésére kapott gyógyszerek is befolyásolhatják. Ugyanakkor helytelen és szabálytalan az az általánosan elterjedt gyakorlat, hogy valamilyen kockázati tényező felszínre kerülésekor a beteget „pánikszerűen” továbbküldjük, szinte mindegy, hogy hová, csak el. Különleges ellátást a betegeknek csak kis hányada igényel, egy krónikus hepatitiszes vagy HIV-fertőzött beteg gyakorlatilag kockázat nélkül kezelhető az infektológusok szabályainak szigorú betartásával, és a véralvadástól szedő beteg is ellátható a szakmai szabályok mentén. HIV-fertőzött betegnél expozíció esetén – például tűszúrásos baleset – a fertőződés kockázata 0,3%, míg a gyógyszeres terápiával kezelt esetekben gyakorlatilag 0%, mivel a kezelés eredményeképpen a betegek gyakorlatilag nem fertőzőek, a vírus nem mutatható ki szervezetükből.

Hepatitis B hordozóknál expozíció esetén a fogékony alany esetében a kockázat elérheti a 30%-ot is, de az egészségügyi dolgozók oltást kapnak, és védettségük a munkavállalás feltétele, így nem fertőződhetnek meg. Hepatitis C esetén a legnagyobb kockázat, tüszúrás kapcsán 1,8%, amennyiben a beteg ürít vírust, ami a korszerű kezelésnek köszönhetően ritka. Egyébként is, minden beteg potenciálisan fertőző betegnek kell tekinteni, ezért minden egészségügyi beavatkozásnál be kell tartani a fertőzések átvitelét megakadályozó higiénés szabályokat, mivel éppen a fel nem ismert, és így kezeletlen esetek jelentik a nagyobb veszélyt. Az indokolatlan átirányítások elkerülhetetlenül oda vezetnek, hogy a beteg nem tájékoztatja a sokadik orvost problémájáról, aki így nem tud felkészülni egy váratlan szövődés bekövetkeztére. Figyelni kell a betegjogokra is, a fertőző betegsége miatt elutasított beteg jogorvoslatot kereshet. Az ombudsmani állásfoglalás szerint „vét az ellátás szakmai szabályai ellen, sérti a hátrányos megkülönböztetés tilalmát és az emberi méltósághoz való jogot az az egészségügyi



Remineralization of demineralized bone matrix in critical size cranial defects in rats: A 6-month follow-up study

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Abstract: The key drawback of using demineralized bone matrix (DBM) is its low initial mechanical stability due to the severe depletion of mineral content. In the present study, we investigated the long-term regeneration of DBM in a critical size bone defect model and investigated the remineralization after 6 months. Bone defects were created in the cranium of male Wistar rats which were filled with DBM or left empty as negative control. *In vivo* bone formation was monitored with computed tomography after 11, 19, and 26 weeks postoperatively. After 6 months, parietal bones were subjected to micro-CT. Mineral content was determined with spectrophotometric analysis. After 11 weeks the DBM-filled bone defects were completely closed, while empty defects were still open. Density of the DBM-treated group increased significantly while the controls remained unchanged. Quantitative analysis

by micro-CT confirmed the *in vivo* results, bone volume/tissue volume was significantly lower in the controls than in the DBM group. The demineralization procedure depleted the key minerals of the bone to a very low level. Six months after implantation Ca, P, Na, Mg, Zn, and Cr contents were completely restored to the normal level, while K, Sr, and Mn were only partially restored. The remineralization process of DBM is largely complete by the 6th month after implantation in terms of bone density, structure, and key mineral levels. Although DBM does not provide sufficient sources for any of these minerals, it induces a faster and more complete regeneration process. © 2015 Wiley Periodicals, Inc. *J Biomed Mater Res Part B: Appl Biomater* 104B: 1336–1342, 2016.

Key Words: DBM, bone, mineralization, critical size defect

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INTRODUCTION

Demineralized bone matrix (DBM) is a well-known bone substitute that is gaining popularity in orthopedic and spinal surgery indications. Even though autografting is still the gold standard method for bone substitution, DBM has been developed to increase the availability and to avoid donor site morbidity. It is also safe to use due to the elimination of immunogenic surfaces.¹ The other key feature of DBM is also its key drawback: the lack of mineral content. The demineralization process unmasks the osteoconductive and osteoinductive extracellular matrix factors such as collagen and bone morphogenic proteins at the expense of losing

mechanical strength.^{2–4} Indeed, this is still the main concern among surgeons who use DBM that initial strength is negligible and it is largely unknown when and to what extent shall the mineral structure build-up to load-bearing levels. Until regenerated bone is readily recognizable with imaging techniques by virtue of its opacity, its functional value will always be questioned by surgeons. In other words, if it looks different on radiographs, it cannot be fully relied on. Meta-analyses of studies in spinal fusion showed that DBM in various formats can significantly improve fusion rates when combined with autografts, but its effect is less convincing when applied alone.^{5–7} Thus, the current clinical

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A SZIVACSOS CSONT MECHANIKAI ANIZOTRÓPIÁJÁNAK MÉRÉSE MIKROSZERKEZETI VÉGESELEMES SZIMULÁCIÓ SEGÍTSÉGÉVEL, A SZERKEZETI ANIZOTRÓPIA FIGYELEMBE VÉTELÉVEL

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Absztrakt

Jelen vizsgálat célja a foggyökér környezetében, a terhelések hatására kialakuló anizotrópia mérése volt. A vizsgálatokhoz 10 különböző korú férfi és nő állcsontjából származó 10 darab mintát vetettünk alá mikro-CT vizsgálatnak. A szerkezeti anizotrópia mérését beillesztett ellipszoidok – a csontállomány belső pontjai környezetében a legnagyobb olyan ellipszoid, ami úgy írható a pont köré, hogy belsejében csak csontanyagot tartalmaz, és felülete érinti a velőüreget – segítségével végeztük. Feltételezve, hogy a szerkezeti és mechanikai anizotrópia főirányai megközelítőleg egybeesnek, a kapott domináns irányokban kivágott csontkockákra mikroszerkezeti végeselemes modellt generálva lehetővé vált a szivacsos állcsont mechanikai anizotrópiájának közelebbi megismerése. A mikroszerkezet végeselemes szimulációja segítségével mérhető volt a foggyökér környezetéből származó csontminták esetén a mechanikai anizotrópia foka és becsülhető a három domináns iránybeli rugalmassági modulus.

Kulcsszavak: szivacsos csont, anizotrópia, μ FEM

Micro-FEM based mechanical anisotropy measurement of the trabecular bone, in view of the structural anisotropy

Abstract

The present study aimed to determine the anisotropy around the tooth root, resulting from the loads of the jaw. 10 specimens from 10 patients were submitted to micro-CT scanning. The measurement of the structural anisotropy was conducted by means of inserted ellipsoids – the largest ellipsoids around certain points in the material, which contain bone and their surfaces touch the medullary cavity. Assuming that the principal directions of the structural and mechanical anisotropy approximately coincide with each other, conclusions could be drawn about the mechanical anisotropy of the trabecular bone, by generating a microstructural finite element model of bone cubes cut in the dominant directions. By means of the finite element simulations of the microstructure, the degree of the anisotropy could be measured and an estimation of the Young moduli in the three dominant directions could be given.

Keywords: trabecular bone, anisotropy, FEM





Phase separation in an ionomer glass: Insight from calorimetry and phase transitions

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ABSTRACT

The G338 ionomer glass is a fluoro-alumino-silicate system, which is used as the powder component of glass ionomer cements (GICs) in dental applications. However, despite progress in understanding the nature of this glass, chemical identity of its separated amorphous phases has not yet been conclusively determined. In this work, we identify these phases by performing differential scanning calorimetry (DSC) and X-ray diffraction (XRD) analyses on both the as-received glass and heat-treated samples. We detected three glass transitions in the as-received G338 glass during DSC upscanning, implying the co-existence of three amorphous phases. Towards resolving the chemical identity of the three phases, we performed XRD analyses on samples subjected to dynamic heating, while further DSC and XRD analyses were performed on samples subjected to isothermal treatment. The results suggest that the three amorphous phases in G338 are Ca/Na–Al–Si–O, Ca–Al–F and Ca–P–O–F phases, respectively. However, the exact chemical compositions of the three phases still require further exploration. The results of this work are important for understanding the impact of phase separation within ionomer glasses on the setting behavior of GICs, and hence improving performances of GICs by optimizing the glass production conditions.

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1. Introduction

Many glass-forming melts exhibit liquid–liquid immiscibility, and when cooled the resulting glasses will be phase-separated [1]. Phase separation in these glass melts is a favorable thermodynamic process due to the decrease in the free energy. The ionomer glasses with composition ranges (wt.%) of ~20–36 SiO₂, ~15–40 Al₂O₃, ~0–35 CaO, ~0–10 AlPO₄, ~0–40 CaF₂, ~0–5 Na₃AlF₆, ~0–6 AlF₃ [2] are typical systems exhibiting metastable immiscibility [3]. They are used primarily to produce glass ionomer cements (GICs) and glass-ceramics. GICs, also called glass polyalkenoate cements, have been widely used in dentistry as luting cements and filling materials since their invention in the early

1970s. Their extraordinary properties, especially good biocompatibility and natural adhesion to the teeth and bone – amongst other advantages [4], have helped expand their applications to other fields of medicine, including otorhinolaryngological (ear–nose–throat) and maxillofacial augmentation and surgeries, use in orthopedic surgeries as bone cements and the potential use as bone graft substitutes [5–8].

Ionomer glasses appear opal, due to light scattering from the different phases, giving GICs a tooth-color like appearance; significant for dental use. According to an early study [9] on the glass microstructure, another version of ionomer glass, i.e., the G200 glass with a nominal composition (mol%) of 38.52 SiO₂, 12.97 Al₂O₃, 35.07 CaF₂, 1.89 Na₃AlF₆, 5.04 AlF₃, and 6.51 AlPO₄ has a tendency to be separated into two phases: a continuous calcium alumino-silicate matrix and partly crystalline calcium fluoride-rich droplets (sphere in matrix morphology). Controlled acid-etching experiments show the acids selectively attacking the amorphous phase of the droplets, the extent of which depends on the melting temperature [9]. It has been postulated that the setting reactions contain two overlapping stages: i) the rapid leaching of calcium cations from the droplets and ii) the subsequent slower

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Atomic and vibrational origins of mechanical toughness in bioactive cement during setting

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Bioactive glass ionomer cements (GICs) have been in widespread use for ~40 years in dentistry and medicine. However, these composites fall short of the toughness needed for permanent implants. Significant impediment to improvement has been the requisite use of conventional destructive mechanical testing, which is necessarily retrospective. Here we show quantitatively, through the novel use of calorimetry, terahertz (THz) spectroscopy and neutron scattering, how GIC's developing fracture toughness during setting is related to interfacial THz dynamics, changing atomic cohesion and fluctuating interfacial configurations. Contrary to convention, we find setting is non-monotonic, characterized by abrupt features not previously detected, including a glass-polymer coupling point, an early setting point, where decreasing toughness unexpectedly recovers, followed by stress-induced weakening of interfaces. Subsequently, toughness declines asymptotically to long-term fracture test values. We expect the insight afforded by these *in situ* non-destructive techniques will assist in raising understanding of the setting mechanisms and associated dynamics of cementitious materials.



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ORIGINAL ARTICLE

Immunolocalization of AQP5 in resting and stimulated normal labial glands and in Sjögren's syndrome

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OBJECTIVE: In our current work, *in vivo* examination of AQP5 distribution in labial salivary glands following stimulation of secretion has been carried out in normal individuals and in patients with Sjögren's syndrome.

SUBJECTS AND METHODS: For this study, we selected five patients with primary Sjögren's syndrome (mean age 62.4 ± 10.6 s.d. years) diagnosed in accordance with the European Cooperative Community classification criteria. There were five patients (mean age 27 ± 2.5 s.d. years) in the control group. The subcellular distribution of AQP5 in human labial gland biopsies was determined with light and immunoelectron microscopy before and 30 min after administration of oral pilocarpine.

RESULTS: In unstimulated control and Sjögren's labial glands, AQP5 is about 90% localized in the apical plasma membrane, with only rarely associated gold particles with intracellular membrane structures. We have found no evidence of pilocarpine-induced changes in localization of AQP5 in either healthy individuals or patients with Sjögren's syndrome.

CONCLUSIONS: Our studies indicate that neither Sjögren's syndrome itself, nor muscarinic cholinergic stimulation *in vivo* caused any significant changes in the distribution of AQP5 in the labial salivary gland cells.

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Keywords: aquaporin-5; oral pilocarpine; salivary secretion; Sjögren's syndrome

Introduction

Sjögren's syndrome (SS) is an autoimmune disease characterized by progressive infiltration of exocrine glands by

mononuclear cells, mainly resulting in decreased secretions of salivary glands (xerostomia) and lacrimal glands (xerophthalmia) (Carpenter *et al.*, 2000; Jonsson *et al.*, 2001; Fox, 2005). In human minor and major salivary glands, AQP5 is abundantly localized to the apical plasma membrane domains of acinar cells and not detected in the duct cells (Gresz *et al.*, 2001).

In the symptomatic treatment for xerostomia, oral pilocarpine has been used to increase salivary secretion (Fox *et al.*, 1991, 2001; Rhodus, 1997; Vivino *et al.*, 1999; Nyarady *et al.*, 2006). At 30, 60, and 90 min after drug intake, salivary flow rate significantly increased with a peak salivary flow occurring approximately 60 min after drug intake. The main adverse effect was sweating. Five-milligram pilocarpine tablets/day improved symptoms significantly.

Examination of AQP5 distribution in intracellular structures and apical plasma membrane of the human labial salivary gland cells following stimulation of secretion have not previously been performed *in vivo*. Discrepancies in the literature regarding AQP5-localization in human salivary tissue were challenging to us (Ishikawa *et al.*, 1998, 1999, 2000, 2002, 2004, 2005; Tada *et al.*, 1999; Ishikawa and Ishida, 2000; Beroukas *et al.*, 2001; Steinfeld *et al.*, 2001, 2002; Steinfeld and Delporte, 2002; Waterman *et al.*, 2002, 2003; Matsuzaki *et al.*, 2003; Gresz *et al.*, 2004; Li *et al.*, 2004, 2006; Delporte and Steinfeld, 2006; Xiao *et al.*, 2011). The aim of this study was to determine the effect of oral pilocarpine on the localization of AQP5 in human labial minor salivary glands of normal and patients with SS using light microscopy and immunogold electron microscopy with different types of anti-human AQP5 antibodies. To show the earliest events in salivary secretion, a stimulation time of 30 min was chosen. According to the data in the literature, in our current work, we chose a time point where the concentration of AQP5 is the highest at the place of its basic function, that is, at the place of water secretion, namely at the apical membrane. This was 30 min after stimulation with pilocarpine. At 90 min, a decrease in secretion has already



Távoktatás

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Szájüregi gombás fertőzések a mindennapi praxisban

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Az emberi szervezetben kialakuló gombás fertőzéseket leggyakrabban *Candida* törzsek okozzák. A bőr, és különösen a nyálkahártyák gombás fertőzéseinek gyakorisága – és ennek következtében az iránta megnyilvánuló figyelem is – világszerte nő, ami több okra vezethető vissza, például az immundeficiens betegek növekvő száma, a súlyos háttérbetegséggel rendelkezők egyre hosszabb túlélése, a széles spektrumú antibiotikum-kezelések terjedése és a növekvő átlagéletkor. A fogorvosi rendelőben leggyakrabban előforduló, nem-immunhiányos betegek oropharingeális candidiasisa annak ellenére, hogy az egyik legtöbbször előforduló gombás fertőzés – a tanulmányok szerint az akrilát fogsort viselők 50–70%-a érintett –, az esetek nagy számában felismeretlen és kezeletlen marad. Bár tünetei többnyire jellegzetes képet mutatnak, potenciálisan veszélyeztethetik a beteget, és jelentősen ronthatják életminőségét, mégis, több szakma határterületévé amolyan mostohagyereknek számít.

A gombák csoportosítása

A gombák eukarióta szervezetek, a szaporodó alakok morfológiailag két típusba sorolhatók: sarjadzó és fonalas gombák.

A fonalas gombák 2–10 μ átmérőjű, csőszerű, elágazó, apicalis irányban folyamatosan növekedő fonalakat

képeznek, melyeket pórusokkal megszakított szeptumok osztanak cellákra.

A sarjadzó gombák egysejtű, blastosporákból álló szervezetek, melyek sarjadzással szaporodnak: A blastosporákból pseudohypha jöhet létre, mely az osztódás során egymástól el nem vált sejtekből áll. A pseudo-





Távoktatás

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Szisztémás betegségekhez kapcsolódó szájüregi gombafertőzések a fogorvosi gyakorlatban

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Cikkünk előző részében a nem-immunhiányos betegek orális gombafertőzéseit, annak felismerését, tüneteit és terápiáját elemeztük ki. A betegek másik, növekvő számú csoportját azok képezik¹, akiknek egy szisztémás betegség következtében meggyengült az immunrendszerük, így esetükben a gombás fertőzések más, súlyosabb formában jelentkeznek.

Ezeknek a betegeknek egy része súlyos általános állapotú, és olyan kórházi osztályok kezelése alatt áll, ahol felkészültek az ilyen fertőzések terápíjára, így a gyakorló fogorvos nem találkozik velük. Azonban a gyógyítás hatékonyságának növekedésével, új, hatásos gyógyszeres terápiák egyre szélesebb körben történő alkalmazásával, és a betegek ennek következtében egyre hosszabb túlélésével nő azok száma, akik jó általános állapotuk eredményeképpen járóbetegként keresik fel a fogorvosi rendelőt. Ezért fontosnak tartjuk, hogy a fogorvosok felismerjék és kezelni tudják az ilyen betegeknek kialakuló szájüregi gombás fertőzéseket is, melyeknek a megjelenési formája és a terápiája eltérhet az egészséges immunrendszerű betegektől. Ugyancsak fontos az ilyen állapothoz vezető, a háttérben meghúzódó betegségek ismerete, mert ezek befolyásolják a választott terápiát (a kezelésre alkalmazott gyógyszerek fajtája, dózisa, alkalmazásuk hossza, gyógyszerkölcsonhatások stb.), de előfordulhat az is, hogy a fogorvosnál

jelentkező beteg panasza egy súlyos betegség első tünete, vagy romlásának jele.

Szoros összefüggés ismerhető fel az általános állapot és a szájüreg elváltozásai között.² A következőkben azokat a legfontosabb szisztémás betegségeket tekintjük át a teljesség igénye nélkül, amelyek maguk, vagy éppen a kezelésükre alkalmazott gyógyszerek növelik egy orális gombafertőzés kialakulásának esélyét. Ezen fertőzések súlyossága nagyon széles skálán mozog az alapbetegségnek megfelelően, de még a legenyhébb is fokozott kockázatot hord magában egy súlyos, disszeminált fertőzés kialakulásának szempontjából, ezért az adekvát terápia alkalmazása nagyon fontos.

Allergia

Bizonyos esetekben a mucosa régóta fennálló allergiás irritációja talaján is megtelepedhetnek a gombatörzsek. Például a szájban hosszú ideje meglévő amalgámtömés okozhat ilyen, az alkalmazott gombaellenes terápia csak részleges javulást hoz, a teljes gyógyulás a



Multiple microlithiasis in bilateral parotid glands as the initial clinical manifestation of primary Sjögren's syndrome

Adrienn Dobai¹ · Levente Pataky¹ · József Barabás¹

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Abstract We report a rare case of Sjögren's syndrome (SS) with multiple microliths in the bilateral parotid glands. A 41-year-old man presented to our department with mild pain in the region of the right parotid gland. The dental examination was negative except for the parotid regions. The right region was moderately swollen and the left mildly swollen. Plain radiography revealed multiple calculi in the bilateral parotid glands. Ultrasonography showed heterogenic parenchyma, with microliths and cystic lesions in the parotid glands and heterogenic echotexture in the submandibular glands. Immunologic tests and the Schirmer test confirmed the diagnosis of SS. As the patient had no classic symptoms of SS, the bilateral multiple microliths were the first sign, facilitating the final diagnosis. Early diagnosis of SS is highly relevant because the proper therapy can be initiated. Adequate follow-up and, especially, control of the disease activity by identifying the predictive factors, are the primary objectives of SS management, enabling personalized treatment of this malignant disease. This case is a good example of how detection of calcifications in the bilateral parotid glands by plain radiography can help diagnose SS at an early stage.

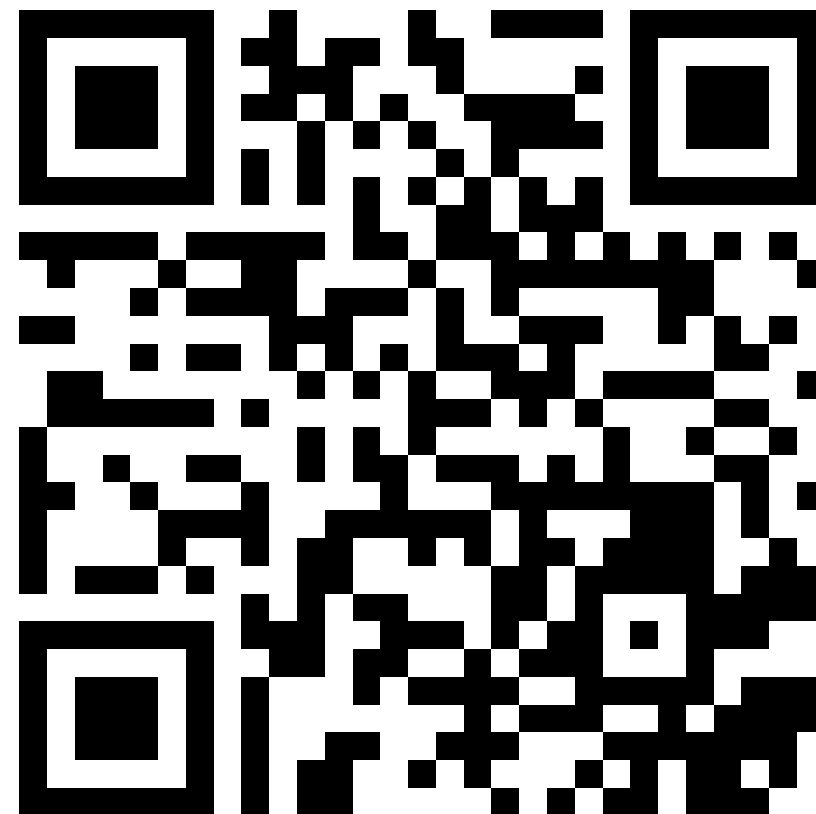
Keywords Sjögren's syndrome · Microlithiasis · Parotid gland · Ultrasonography · Plain radiography

Introduction

Sjögren's syndrome (SS) is the second most common chronic autoimmune disease [1]. It can be an individual entity (primary SS) or associated with other autoimmune disorders (secondary SS), such as systemic lupus erythematosus, rheumatoid arthritis, or scleroderma. Primary SS presents with sicca symptoms (e.g., xerophthalmia, xerostomia) and is more common in women than in men [2, 3]. The female/male ratio is 9:1 [4, 5]. Although the frequency of primary SS increases with age, the mean age of onset is usually during the fourth to fifth decades [5]. The reported prevalence of primary SS varies but has been reported at 3.0–4.5% in those >50 years of age [4, 5].

Primary SS is characterized clinically mostly by dryness of the eyes (xerophthalmia) and mouth (xerostomia) [2], although 25–66% of patients with primary SS have major salivary gland enlargement [6]. Additionally, in some cases, primary SS is associated with sialolithiasis of the major salivary glands [7–9]. Although calculi in the bilateral parotid glands are uncommon, their appearance is highly relevant because they usually occur in severe cases [grade 4 SS based on the ultrasonography (US) score] [10, 11]. Because patients with SS are at a higher risk of developing lymphoproliferative disorders [12], the treatment, routine follow-up, and, especially, control of the disease activity based on predictive factors are the primary management objectives for SS patients to repress chronic B-cell stimulation [13].

Here, we report a patient who presented only with right parotid area pain and no history of an autoimmune disorder. The radiologic examination revealed multiple calculi in the bilaterally enlarged infiltrative parotid glands. Immunologic tests confirmed the presence of SS. To date, no other case has been published in which multiple



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Statistics based landmark selection model for cone-beam CT derived three-dimensional cephalometry

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Abstract: Although some articles have already assessed the reliability of three dimensional (3D) cephalometric landmarks, but the results were questionable because most of them analyzed the landmarks using linear or angular measurements instead of the coordinates. Therefore, the aim of this study was to eliminate the mistakes of the 3D landmark selection by the means of statistics based landmark selection model and a practically useable decision tree. In our study three medical doctors – the “examiners” – identified 55 particular landmarks on 30 non-orthodontic Cone Beam Computed Tomography (CBCT) scans using the Cranioviewer software. The identification process has been done three times in order to increase the accuracy. Intraclass correlation coefficient and analysis of variance were applied to decrease the intra- and inter- examiner variability, while standard deviation (SD) and mean absolute difference (MAD) were used for characterization of landmark locations. Inaccurate coordinates were grouped according to both the intra- and the inter-examiner deviation of ≥ 1 mm and the difference between the two statistical methods (SD vs. MAD). The intra-examiner identification errors were ≤ 1 mm. The inter-examiner SD and MAD were ≥ 1 mm except in cases of four landmarks with MAD and in cases of two with SD. Inter-examiner deviations were always higher than intra-examiner deviations. Standard deviation distorted more than mean absolute difference. Based on these result we have created a decision tree for landmark selection. Most of the coordinates belong to the landmarks can be reliably adapted to 3D cephalometric, but the statistics based decision model could be useful to eliminate mistakes in landmark selection as well. Since, the statistical rules are summarized like a decision tree it can be easily used in practice.

Keywords: Cephalometry, Planning Techniques, Computer-Generated 3D Imaging, Cone-Beam Computerized Tomography, Dimensional Measurement Accuracy





Landmark-based midsagittal plane analysis in patients with facial symmetry and asymmetry based on CBCT analysis tomography

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Abstract

Purpose Reconstruction of the facial midplane is relevant in anthropometry, orthodontics, maxillofacial surgery, and the accurate measurement of symmetry deviation is relevant in many fields of medicine especially when planning surgical treatment. In the literature, three different means of midplane generation have been published; however, there is currently no consensus regarding the approach to use. Morphometric methods are used to determine the true midsagittal plane (MSP), but its use in clinical practice is difficult. A regression plane based on N-ANS-PNS landmarks reportedly approximates the morphometric MSP. As these points are vulnerable, we investigated which combination of landmarks can be substituted in symmetric and asymmetric faces.

Patients and methods Thirty symmetric and 30 asymmetric faces were analyzed on cone-beam computed tomography scans. A total of 50 regression planes were generated based on three unpaired landmarks and 35 regression planes were generated based on the midpoints of paired landmarks. The Na-ANS-PNS plane was used as reference plane, and the mean angle between it and each generated MSP was calculated. The differences from the reference plane were compared by t-test between the groups.

Results In the symmetric group, 86% of angles deviated by $<5^\circ$ using unpaired points, whereby 74% of angles deviated by $<5^\circ$ for paired points. Between the two groups 50% of planes from midline points, and 77% of planes from paired points were significantly different. All planes deviated more in the asymmetric group.

Conclusions The N-ANS-PNS reference plane can be substituted with the following combinations: ANS-G-Ba, ANS-G-S, ANS-S-De, PNS-G-Ba, PNS-S-Ba, PNS-ANS-G, and PNS-N-Ba.

Keywords CBCT analysis · Midsagittal plane · Facial symmetry · Facial asymmetry · Orthognathic surgery

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Arcrekonstrukciós és orthognath műtétek tervezési lehetőségei háromdimenziós képalkotói módszerekkel

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Munkánkban irodalmi adatok és néhány saját eset bemutatásán keresztül foglaljuk össze az orthognath és arcrekonstrukciós sebészet területén alkalmazható tervezési lehetőségeket, melyek a háromdimenziós (3D-) képalkotás megjelenésével váltak elérhetővé. Az arcrekonstrukciós és orthognath műtétek sokszor az egyetlen megoldást jelentik a fejlődési rendellenesség, trauma vagy tumor okozta arcdeformitások kezelésekor. Ezeknek a szakterületeknek nélkülözhetetlen eszköze a radiológiai képalkotás, mely nemcsak a diagnosztikában, hanem a kezelés megtervezésében is fontos szerepet játszik. A műtéti tervezések során korábban rutinszerűen használt oldalirányú telerröntgen-felvételre végzett kétdimenziós analíziseket a cone-beam számítógépes tomográfia (CBCT) megjelenésével fokozatosan a három dimenzióban végezhető mérések váltották fel. Az analízisek adaptálásának első lépését a CBCT-adatállományból származtatott röntgenképek jelentették, majd a renderelt felszínen alkalmazott szegmentációs technikák létrejöttével az arckoponya csontjai már három dimenzióban is mozgathatóvá váltak, így az úgynevezett virtuális műtéti modellezések is kialakultak. A CAD/CAM technika és a 3D-nyomatók fejlődésével pedig megjelentek a preoperatív nyomtatott sín, lemezek és az úgynevezett kézzel fogható modellműtétek kivitelezései is. A képalkotás fejlődése mindezek által elősegítette a személyre szabott, pontos és megbízhatóbb tervezést, mely jelentősen meghatározza a kezelés sikerességét.

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Kulcsszavak: cone-beam CT, cefalometria, CAD/CAM, 3D-nyomatás

Planning options of reconstructive and orthognathic operation by means of three-dimensional imaging

We summarize up-to-date planning technics of orthognathic and reconstructive surgery operation which appeared with three-dimensional imaging, using literature data and some clinical examples. In many cases, orthognathic and reconstructive operations mean the only treatment of facial deformity caused by tumour, traumatic injury or congenital anomaly. In this field, radiology plays an important role not only in the diagnosis but also in the planning of the treatment. With the appearance of cone-beam computed tomography (CBCT), the previously used two-dimensional cephalometric analysis on lateral cephalogram was changed for three-dimensional cephalometric measurements. The first step of the adaptation was the lateral and frontal x-ray images generated from the CBCT database and later the volume rendered surface and segmentation technics provided the moving of the facial bones in three dimensions which meant virtual surgical planning. With the development of CAD/CAM technic and the three-dimensional printing, many opportunities became available, such as preoperative bending splints and plates and printed surgical model for the tangible planning. The progress of imaging facilitated the individual, accurate, and reliable planning which significantly determines the success of the treatment.

Keywords: cone-beam computed tomography, cephalometry, CAD/CAM, 3D printing

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Lower face cephalometry based on quadrilateral analysis with cone-beam computed tomography: a clinical pilot study

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Abstract

Objective As most orthognathic surgeries focus on the lower face, the aim of this study was to transfer previously developed two-dimensional cephalometry—which is useful for surgeons in the orthognathic surgery of the lower face—to three-dimensional (3D) cephalometry by using cone-beam computed tomography (CBCT). We selected the quadrilateral lower face analysis developed by the surgeon Di Paolo, who focused only for the lower face and mentioned that data in millimeters are more easy to use than angles for surgeons. Additionally, we wanted to create a 3D lower face analysis approach based on quadrilateral analysis and establish a reference table for surgical planning.

Study design Three investigators assigned 16 landmarks on CBCT images from 30 patients with normocclusion. Intra-class correlation coefficients (ICCs) and standard deviations (SDs) were calculated according to each landmark. The maxillary and mandibular lengths and widths and the anterior and posterior lower facial heights (ALFH and PLFH) are presented as means and SDs. The asymmetry of the face was calculated with paired *t* test, and the coherence of the lower face was assessed with correlation coefficients (*r*) and regression models.

Results The ICCs were ≥ 0.90 , and the SDs of the landmarks were lower than 1.00 mm, except for the J-point, which was located at the junction of the anterior border of the ramus and the corpus of the mandible. The SDs of linear measurements were 3.06–5.20 mm, and there was no significant facial asymmetry. The *r* among the structures was greater than 0.3 in 13 of 15 assessments. Based on these values, we could establish a floating norm of the lower face using the following five regressions: one linear regression for the mandibular length, two quadratic models for the ALFH and PLFH, and two multivariate regressions for the posterior widths of the maxillae and mandible.

Conclusion The adaptation of quadrilateral analysis can provide accurate 3D characterization of the morphology of the lower face and the floating norm based on millimeter values, which is practical for surgeons. As the 3D extension of quadrilateral analysis could provide references of the lower face, which might be an accurate 3D approach for presurgical planning, the further investigation in bigger sample would be relevant in the practice.

Keywords Cephalometry · Facial asymmetry · Computer-assisted three-dimensional imaging · Biostatistics

Introduction

Presently, the incidences of oral cancer, traumatic casualties, and congenital oral anomalies are high, and therefore, many patients require orthognathic surgery. In these cases, cone-beam computed tomography (CBCT)-based cephalometry can be used for accurate presurgical planning. CBCT-based cephalometry has several advantages over conventional lateral cephalometry. CBCT-based cephalometry provides distortion-, magnification-, and summation-free isometric images

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Az alsó archarmad Di Paolo-féle vizsgálata Cone-Beam CT adatállományon

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A rekonstruktív sebészet területén gyakran Cone-Beam CT által megvalósítható 3D kefalometria az egyetlen lehetőség a pontos kezelési terv elkészítéséhez. A valódi háromdimenziós normarendszer kidolgozásához első lépésként célul tűztük ki a Di Paolo által leírt analízis 2D vizsgálatát volumentomogrammon és ezt követően 3D adaptációját. 30 Angle I. osztályú okklúzióval rendelkező páciensről készült felvételt válogattunk ki három év alatt azon betegek közül, akikről nem ortodanciai célból készült CBCT volumentomogram. A vizsgálati csoport tagjairól készült $0,4 \times 0,4 \times 0,4$ mm voxelméretű volumentomogramokon a referenciapontokat három vizsgáló, egymástól függetlenül, három alkalommal jelölte ki a Cranio Viewer szoftver segítségével. Meghatároztuk a mandibula és a maxilla vetületi hosszát, szélességét (milliméterben és szögértékben kifejezve), illetve az alsó elülső és hátulsó arcmagasságot. Az anatómiai struktúrák alacsony szórásértékeinek és a közöttük fellépő, nagyrészt szoros korrelációknak köszönhetően a 2D adatállományban megfogalmazott geometriai elképzelés adaptálható a 3D adatállományra, így lehetővé teszi az alsó archarmadot leíró 3D kefalometria létrehozását, amely által a transzverzális aszimmetria is pontosan kiértékelhetővé válik.

Kulcsszavak: Cone-Beam CT, kefalometria, malocclusio, Angle I Oszály, anatómiai referenciapont, 3D megjelenítés

Bevezetés

A kefalometria nemcsak az ortodanciai eltérések diagnosztikájában és a kezeléstervezésben játszik meghatározó szerepet, hanem az arc-rekonstrukciós műtétek tervezésében is. A Cone-Beam CT elterjedése lehetővé teszi a koponyaméretnek nemcsak kettő, hanem három dimenzióban történő elemzését egy adatállományon, ezáltal lehetőséget biztosítva az esetleges transzverzális irányú arc-aszimmetriák vizsgálatára is, melyek a régen használt frontális röntgenképeken a nagyfokú egymásra vetülések miatt nehezen voltak értékelhetőek. A CBCT előnyeinek – a torzítás-, nagyítás- és szummációmentes izometrikus ábrázolásának – köszönhetően a mindennapi diagnosztikában is egyre nagyobb jelentőséggel bír [1]. Legfőbb hátránya a relatív nagy sugárdózis [2–4], mely azonban a technika fejlődésének eredményeként folyamatosan csökken. Azt a tényrt figyelembe véve, hogy egy komplexebb ortodanciai kezeléshez egy laterális, egy frontális teleröntgen, egy panorámafelvétel és esetlegesen még további kiegészítő (okklúziós, periapikális) felvételek szükségesek, több vizsgálat is igazolta, hogy a röntgenfelvételek összdózisa gyakran meghaladja a CBCT vizsgálat effektív dózisát [5]. Ennek következtében a nemcsak dentális, hanem szkeletális abnormalitással járó traumás és fejlődési rend-

ellenességek diagnosztikája során ma már a CBCT az ajánlott vizsgálati módszer [3, 6]. A fejlesztéseknek köszönhetően, napjainkban már léteznek kifejezetten ortodanciai célokra használható modulok (pl. Planmeca Low-dose), melyek alkalmasak a CBCT rutinszerű alkalmazására a szkeletális eltérések diagnosztikájában és a műtéti tervezések során.

Az archhelyreállító műtétek nagy része csak az alsó archarmadot érinti, így az diagnosztikában és kezeléstervezésben kiválóan alkalmazható az 1962-ben Di Paolo által leírt Quadrilaterális analízis, amely az alsó archarmadon mért elülső és hátulsó arcmagasságot, valamint a maxilláris és a mandibuláris alveolus hosszát hasonlítja össze (1. ábra). Ideális arcviszonyoknak 1:1 arány áll fenn a maxilláris alveoláris csontív nyílirányú vetülete és a mandibuláris alveoláris csontív szagittális irányú vetületének hossza között, valamint az elülső alsó arcmagasság [ALFH] és a hátulsó alsó arcmagasság [PLFH] átlaga és az alveoláris csontív-vetületek hossza között.

Azaz Maxilla vetülethossz = Mandibula vetülethossz = (Anterior + Posterior alsó arcmagasság) / 2.

Az elülső és hátulsó arcmagasság átlaga az alsó átlagos arcmagasság [LFH]. Ezen kapcsolat figyelembevételével Di Paolo 1969-ben harminckét ortodanciailag kezeletlen, normál okklúzióval rendelkező 10,7–13,6 éves fiatal páciensen, majd 1984-ben már összesen 245 nem-





Article

Composition—Nanostructure Steered Performance Predictions in Steel Wires

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Abstract: Neutron scattering in combination with scanning electron and atomic force microscopy were employed to quantitatively resolve elemental composition, nano- through meso- to metallurgical structures and surface characteristics of two commercial stainless steel orthodontic archwires—G&H and Azdent. The obtained bulk composition confirmed that both samples are made of metastable austenitic stainless steel type AISI 304. The neutron technique's higher detection sensitivity to alloying elements facilitated the quantitative determination of the composition factor (CF), and the pitting resistance equivalent number (PREN) for predicting austenite stability and pitting-corrosion resistance, respectively. Simultaneous neutron diffraction analyses revealed that both samples contained additional martensite phase due to strain-induced martensite transformation. The unexpectedly high martensite content (46.20 vol%) in G&H was caused by combination of lower austenite stability (CF = 17.37, $p = .03$), excessive cold working and inadequate thermal treatment during material processing. Together, those results assist in revealing alloying recipes and processing history, and relating these with corrosion resistance and mechanical properties. The present methodology has allowed access to unprecedented length-scale (μm to sub-nm) resolution, accessing nano- through meso- scope properties. It is envisaged that such an approach can be extended to the study and design of other metallic (bio)materials used in medical sciences, dentistry and beyond.

Keywords: steel; wire; martensite; work hardening; gamma energy; neutron; alloying; structure; corrosion; surface

1. Introduction

Ideally, medical (arch)wires are designed to support, retain or move bone and/or tooth positions with light and continuous force towards a pre-planned final alignment. The associated force vectors can be optimized to reduce patient discomfort, prevent tissue hyalinisation and undermine resorption [1]. When in service, archwires should behave elastically for a period of weeks to months, dependent on




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Compositional studies of functional orthodontic archwires using prompt-gamma activation analysis at a pulsed neutron source

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Prompt-gamma activation analysis (PGAA) measurements were carried out at the ISIS Spallation Neutron Source on two sets of functional commercial stainless steel orthodontic archwires, aiming at providing insights into the elemental and isotopic composition differences of two nominally equivalent archwires. The results were compared to those obtained from parallel cold neutron PGAA measurements on the same samples at the Budapest Neutron Centre in order to test the current status of PGAA at a pulsed neutron source and eventually to inform improvement in set-up and acquisition methods. In addition, time-resolved PGAA (T-PGAA) that combines PGAA and neutron time-of-flight methods was applied to the present set of samples, allowing the measurement of the neutron energy dependence of the PGAA spectra. The advantages of this technique were demonstrated to be that through incident neutron energy selection, spanning 0.07–67.94 eV, enhancement or decrease of specific gamma lines associated with isotopes of interest could be achieved. These were shown to reduce peak interference and to increase the signal-to-background ratio for certain species in order to facilitate accurate elemental identification. Suggestions for potential performance improvement for this evolving technique are proposed.

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Introduction

Elemental analysis, both qualitative and quantitative, is widely applied to the investigation of normal and pathological tissues and to the development of new bio- and medical materials. Non-

destructive and non-invasive techniques are of particular relevance in the characterization of functional materials. X-rays and electrons are generally used as laboratory probes for elemental analysis. Neutrons, with the advantages of deeper penetration ranges into the bulk of materials,¹ higher sensitivity to light elements² and improved capability to differentiate elements of similar mass or even isotopes,³ represent unique probes for non-destructive and non-invasive multi-elemental analysis.⁴

Prompt-gamma activation analysis (PGAA)⁵ is one of the most accurate and efficient non-destructive techniques,⁶ which makes use of the (n,γ) reaction, where a nucleus de-excites with the prompt emission of γ radiation after neutron capture.^{7,8} The energy of the γ emission is characteristic of each nucleus and the intensity of the γ peak is proportional to the number of the radiating nuclei in the sample.^{5,7–9} Compared to traditional Instrumental Neutron Activation Analysis (INAA), which measures delayed γ emission,¹⁰ PGAA can measure samples in the intact form and the reduced irradiation time eliminates radiation damage.⁴ Thus PGAA excels in the study of metal-containing cultural-heritage samples. Unfortunately, access to PGAA has been limited due to the need for dedicated stations at thermal or cold neutron sources, e.g. the PGAA facility at the Budapest Neutron Centre (BNC), operated by the Centre of Energy Research, Hungarian Academy of Sciences.

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Periodic vs. molecular cluster approaches to resolving glass structure and properties: Anorthite a case study



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ABSTRACT

Periodic and molecular cluster models are presented for anorthite ($\text{CaAl}_2\text{Si}_2\text{O}_8$), a cement forming glass with desirable thermal and mechanical properties also tested in dental applications. Both the crystalline and amorphous structures were characterised by ab initio molecular dynamics and found to be in good agreement with experiment. Additional investigations of the elongation and fracture of the glass were also made. The recovery of material properties signaled the failure of the periodic method to generate acceptable fracture surfaces to model cement forming-sites. Isolated molecular cluster models of anorthite were therefore investigated with electronic structure methods and showed sound structural matches with the traditional periodic structures. The equilibrated glass clusters were used to develop cement models, through binding of short acid oligomers to selected Al-centres, simulating the glass-polymer interface. Overall, the anorthite glass structures emerging from periodic and cluster models were in close agreement. Results suggest that bare molecular cluster models represent an alternative avenue for accurately investigating amorphous systems, providing more realistic descriptions of edge and corner sites, as well as interfaces.

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1. Introduction

Anorthite (An), a calcium rich compositional variety of plagioclase feldspar minerals found in the lower crust of the earth and igneous rocks [1], is also the main component of the lunar highlands [2]. Its calcium aluminosilicate composition ($\text{CaAl}_2\text{Si}_2\text{O}_8$) equilibrates in both crystalline and amorphous forms [3]. Glasses based on anorthite are widely used for display screens, while An-glass-ceramic systems find specific medical function as implants [4] and tooth/bone restorations [5], as well as in technological applications including insulators [6] and electronic substrates (low temperature co-fired ceramic substrate) [7] due to low dielectric constants, good co-fireability with other materials, and low cost [7,8]. Of particular interest is the cement-forming properties of anorthite glasses, having been trialled in biocompatible ionomer cements for dental use [9] and cements with reduced CO_2 emission

relative to traditional binder materials (i.e. Portland) [10]. Anorthite is also used in temperature stable geothermal cements for high temperature applications [11,12] and in firebrick [13], due to its potential for ultra-low thermal conductivity [12]. It is used in geologic CO_2 sequestration to reduce anthropogenic CO_2 emission and mitigate global climate change [14]. Further, it serves as an ethical replacement for natural bone-ash in superior whitewares such as bone china [15].

However, An is a relatively rare mineral outside of the Earth's mantle and lower crust due to its relatively low weathering potential. Although limited amounts are sourced from volcanic sources for study [16], synthetic forms are most often employed [1]; often prepared via sol gel processing [17] and firing at 1250 °C [18], or from waste materials, such as a combination of spent hydroprocessing catalysts and furnace slag [19]. Deviations in mechanical, optical and electrical properties of synthetic An relative to natural forms are of historic and continuing interest [15, 20–25].

For earth science purpose, An crystals are usually examined under compression to reveal their polymorphs [26–28]. The structure of An glass has been studied with X-ray diffraction [29], Raman spectroscopy

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Simulations reveal the role of composition into the atomic-level flexibility of bioactive glass cements†

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Bioactive glass ionomer cements (GICs), the reaction product of a fluoro–alumino–silicate glass and polyacrylic acid, have been in effective use in dentistry for over 40 years and more recently in orthopaedics and medical implantation. Their desirable properties have affirmed GIC's place in the medical materials community, yet are limited to non-load bearing applications due to the brittle nature of the hardened composite cement, thought to arise from the glass component and the interfaces it forms. Towards helping resolve the fundamental bases of the mechanical shortcomings of GICs, we report the 1st ever computational models of a GIC-relevant component. *Ab initio* molecular dynamics simulations were employed to generate and characterise three fluoro–alumino–silicate glasses of differing compositions with focus on resolving the atomic scale structural and dynamic contributions of aluminium, phosphorous and fluorine. Analyses of the glasses revealed rising F-content leading to the expansion of the glass network, compression of Al–F bonding, angular constraint at Al-pivots, localisation of alumino–phosphates and increased fluorine diffusion. Together, these changes to the structure, speciation and dynamics with raised fluorine content impart an overall rigidifying effect on the glass network, and suggest a predisposition to atomic-level inflexibility, which could manifest in the ionomer cements they form.

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Introduction

Bioactive glasses and related glass cements have drawn attention for their potential use as synthetic bone graft substitutes as well as in the repair and replacement of damaged bones and teeth.^{1,2} Glass ionomer (or polyalkenoate) cements (GICs), have been successfully used in dentistry as luting cements and anterior restorative materials since their introduction in the early 1970s by the British Technology Group^{3,4} – and remain their 2nd biggest earner for chemical technology. As a mercury (Hg) free alternative to dental amalgams these glass–polymer composites are specifically highlighted in the EU commission report: Study on the Potential for Reducing Mercury Pollution from Dental Amalgam and Batteries, as being “cost-effective and environmentally-friendly Hg-free restoration”.⁵ With strict regulations and actions recently coming into effect (1st January, 2014)

short- and long-term future growth is assured, particularly in combination with the rapid developments in bone-remineralisation and hydroxyapatite-coated implantation.⁶ This is further buoyed by GICs being ideally suited for and extensively used in atraumatic restorative treatment (ART), in developing nations in particular, with tooth fillings being prepared and completed without requirement of electric instruments or anesthetic.^{7–9}

The pervasive use of GICs is due to the following desirable properties: good biocompatibility,^{10,11} tooth-like colour appearance, antibacterial and anticariogenic properties *via* lasting fluoride release,^{12–15} minimised microleakage attributed to low setting shrinkage and thermal expansion coefficient similar to that of tooth,¹⁶ and direct durable bonding to tooth and bone¹⁷ through development of a dynamic interfacial “ion-exchange” layer containing ions both from the tooth and the GICs.^{18,19}

With some of these properties transferable to other fields of medicine, for example, successful applications in various otorhinolaryngological and maxillofacial reconstructive surgeries and augmentation,^{20–22} much attention was focused on developing an *in situ* setting glass ionomer bone cement in the 1990s.²³ The initial positive *in vivo* biocompatibility and bone tissue responses have confirmed their osteoconduction and osteo-integration.^{23–25} Studies have found GICs to be bioactive in the bone environment *via* the persistent release of Ca²⁺, PO₄^{3–} and

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