

ROMANIAN ACADEMY

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2019 VOLUME 6 ISSUE 3

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2019

CE PROGRAM FAQs



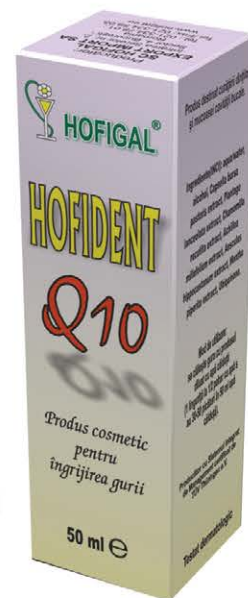
Hofident Q₁₀

Product presentation: Solution for oral hygiene.

Composition (INCI): aqua/water, alcohol, *Capsella Bursa Pastoris* extract, *Plantago Lanceolata* extract, *Chamomilla Recutita* extract, *Achillea Millefolium* extract, *Aesculus Hippocastanum* extract, *Mentha Piperita* extract, Ubiquinone.

Action: The product has antiseptic, healing, hemostatic, anti-inflammatory action, it acts as a antioxidant, detoxifier, deodorant. It is strongly recommended in gingivitis, stomatitis, thrush, compression pain caused by dental prostheses, after tooth extraction, in case of nipple lesion, bleeding gums, mouth and gum ulcers.

Recommendations: It delays dental plaque formation, it prevents bad odour and provides daily mouth hygiene.



HofImun® FORTE

Product presentation:

Chewable tablets to stimulate the immune system

Composition: Each chewable tablet contains raspberry fruit extract (*Rubii idaei fructus*), Echinacea extract (*Echinacea purpurea*), concentrated extract of licorice root (*Glycyrrhiza radix*), magnesium ascorbate and excipients.

Action: It stimulates the immune system, it is antiinflammatory, antiviral, antiseptic, it fluidifies the bronchial and pharyngeal secretions, antioxidant, cardioprotective, vasoprotective, it has antineoplastic antileukemic action, (due to the ellagic acid), it contributes to wound healing, fortifies and remineralizes (it regulates the potassium balance), it has antiulcer effects and is an overall body tonic.

Recommendations: to supplement the diet with nutrients and bioactive substances in: acute and chronic infections of the upper airways (angina, pharyngitis, laryngitis, bronchitis), prophylactic during periods with increased risk of infection with influenza viruses, it has sweating effects in fever, in recurrent herpes episodes of mucocutaneous rash, frequent urinary tract infections, inflammatory urogenital processes; immunodepression after radiotherapy or chemotherapy, bacterial skin infections, psoriasis, neurodermitis, chronic cardiovascular diseases associated with hypercholesterolemia, adjuvant in the diet indicated in the treatment of gastroduodenal ulcers, tonic during periods of physical and mental strain, exhaustion.



Bucoprotect gel

Product presentation: Gel for oral hygiene.

Composition (INCI): aqua, *capsella bursa pastoris*, *calendula officinalis*, *achillea millefolium*, *hippophae rhamnoides*, *olea europea*, *hypericum perforatum*, carbomer, triethanolamine, collagen, *foeniculum vulgare*, *mentha piperita*, *citrus amara*.

Action: Antiseptic, anti-inflammatory, healing, stimulates the inside lining of the mouth and gums trophicity, reduces pain caused by specific oral diseases (gingivitis, stomatitis, lesions of the prosthesis, thrush, periodontitis).

Recommendations: Fights against bad breath (halitosis).

Revolutionary Mouth Rejuvenation Y10



Mouth refreshing

The combination of Peppermint in Y10 toothpaste and RF current lead to mouth refreshing sensation.

Teeth whitening

provides for remarkable improvement of several shade degrees in accordance with the common shading grading.

Gums Rejuvenation

The unique combination between RF current and unique Y10 toothpaste ingredients are magnifying and accelerating these processes.

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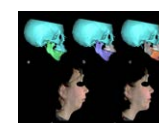
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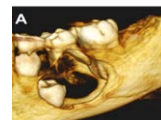
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High quality oral health – an FDI World Dental Federation objective

Michael FRANK
DDS, PhD
Associate Editor-in-Chief



Dear Readers,

It is my pleasure to write to you as the new President of the European Regional Organization of our FDI World Dental Federation, and I would like to take this opportunity to share some insights from the most recent developments in international policies for our profession. Globalization is a buzzword we have been hearing repeatedly in the media, and yes, the world is most certainly converging in terms of sharing information, data transfer, transport, trade and international financial flows. At the same time, the regions and nations of this globalized world still differ enormously in terms of their standards of living and, not in the least, their access to health care. Reducing global health inequality and tackling global health problems effectively, efficiently and sustainably were the objectives of the annual congress of the FDI World Dental Federation, held in San Francisco from 2 to 8 September, 2019. I would like to take this opportunity to tell you about the most important resolutions adopted at this meeting.

Visions for global oral health

The FDI's current strategic plan – the policy paper in which the goals of our international dental cooperation are defined – covers the years 2018 to 2021 and will therefore come to an end in two years' time. For this reason, some time ago we tasked a new working group with drawing up a new strategic plan for the FDI World Dental Federation for the period until 2030. Prof. Michael Glick (USA) and Prof. David Williams (UK) were appointed to lead this working group, and my German colleague Dr. Michael Sereny is also part of it. The key points of the plan so far are that oral health must be accessible, available and affordable worldwide. It should be integrated into the overall health agenda; this will ensure that dentists are empowered under the UN goals for sustainable development. We want to build a responsive and robust profession worldwide and we want oral health to be firmly anchored in the global discourse on health and sustainability. One point that is very important for everyone involved is to ensure that the draft of our new strategic plan, Vision 2030, is not an immutable doctrine, but instead a document that can be changed or adapted at any time. We want technical feedback and constructive criticism to be easily incorporated into the new paper, which we hope to have ready as a final draft to present to the FDI General Assembly in 2020.

New FDI policy statements

An important aspect of the work of our federation is to produce and publish information and guidelines on all aspects of oral health care and the actions of dentists worldwide. We do this with the FDI Policy Statements, which sum up our thoughts and views on a wide variety of issues and topics related to our profession, its practice and oral health. These statements are the result of long and intensive discussions and consultations with respected experts from around the world. Many of our statements are prepared by scientific committees specifically set up to debate and write them. Other statements are the result of professional collaboration between our association and other associations such as the World Health Organization (WHO).

While in San Francisco the voting delegates of the FDI member organizations adopted policy statements on the following topics:

- Access to Oral Healthcare Among Vulnerable and Underserved Populations
- Antibiotic Stewardship in Dentistry
- Continuing Education via eLearning
- Ethical International Recruitment of Oral Health Professionals (this is a revised and updated version of the 2006 statement). Updated issues included a commitment not to solicit dental professionals. As the FDI we fully align ourselves with the World Health Organization's (WHO) Code of Practice on the Ethical Recruitment of Health Professionals.
- Infection Prevention and Control in Dental Practice (revised and updated version of the 2009 state-ment)
- Malocclusion in Orthodontics and Oral Health
- Carious Lesions and First Restorative Treatment
- Repair of Restorations

Our new Policy Statements will be published shortly in English and German on the FDI website:

(<https://www.fdiworldddental.org/resources/policy-statements>).

A new President and forward-looking elections

Like most political professional bodies, the World Dental Federation has a democratic structure. Elections to the FDI Council and the standing committees on a range of topics are part of every General Assembly.

In San Francisco, the former President-elect, Dr. Gerhard Seeberger (Italy), was elected President of the FDI, leaving the post of his designated successor to be filled. The General Assembly elected Professor Ihsane Ben Yahya (Morocco) to the office of President-elect in two ballots. In accordance with the FDI constitution, she will take up the office of President of the World Federation in 2021. Dr. Jack Cottrell (Canada) and Dr. Peter Engel (Germany) had also stood for election.

Dr. Greg Chadwick (USA) took over the office of treasurer.

Dr. Julianne von Hoyningen-Huene, one of my German colleagues, was appointed chair of the FDI Women Dentists Worldwide Section.

For me personally, the congress in San Francisco marked a very fruitful and collegial cooperation of dentists from all over the world, and it was a source of pleasure and inspiration. The results of the congress encourage me to hope that in the not too distant future we will be able to work together to balance or even eliminate the dramatic differences in access to high-quality oral health care that exist around the world, and to ensure that everyone, everywhere benefits from the best possible oral health care – thus creating true globalization. I cordially invite you, dear colleagues and all readers of the Stomatology Edu Journal, to work with us to achieve this goal!

Yours sincerely,

Michael Frank, DDS, PhD

ERO President of FDI World Dental Federation

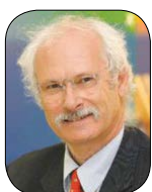
President Dental Chamber Hesse

Board of the German Dental Chamber

Associate Editor-in-Chief of the Stomatology Edu Journal

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Ways to increase the probability of acceptance of a manuscript



Jean-François ROULET
DDS, Habil, Prof hc, Dr hc, Professor
Editor-in-Chief



Nicoleta ILIE
Dipl-Eng, PhD, Professor
Co-Editor-in-Chief

Dear Authors,

You may think writing a scientific manuscript is difficult. Providing you had a well-designed experiment based on a well-thought through question, it is quite simple, since it is a standard procedure. How to get it through the review process is a vital question for you, the author. The answer is very simple: please the editor and the reviewers. There is nothing more boring for editors and reviewers to make the same corrections again and again.

Therefore, here is a list of the most common errors we see in our editorial work:

The most prominent reasons for rejection or a straight route to revision are manuscripts that have a poor language or do not comply with the instructions for authors. We ask ourselves whether it is so difficult to read instructions and follow them. Not doing so at least prolongs the review process considerably. Most of us publish not in our mother tongue but in English. Ergo have an expert in dental research and English mother tongue look over your manuscript. If you do not know any, then look for some professional scientific editing service. The internet may help.

Thinking about Materials and Methods, we are convinced that they should be described as detailed as possible so that someone could replicate the experiment. If in factorial designs the number of samples divided by the n (samples per group) does not end up in a full number, we do not know what you did and usually stop reading. The reviewers and the readers of a paper must perfectly understand the experimental design and what was done in order to judge what was done and if it was done correctly. We highly recommend to use flow charts and figures to explain the experiments performed. To disclose your sources and compositions of materials is mandatory.

Statistics are very often the reason for rejection. Please describe exactly the statistical tools you have used to analyze the data. Very often not appropriate tests are used. Furthermore, add to all tables and figures self-explanatory legends and the information about statistics. In two-way designs tell the readers about significant interactions and if needed differentiate between rows and columns. Make sure you distinguish between normally distributed data and data with skewed distributions. Do NOT mix both statistical worlds (e.g. analyze with ANOVA, but report data as box plots). Finally, strictly avoid to talk about differences between groups that are not statistically significantly different. Formulations like “group D showed the highest values, but there was no significant difference between Groups B, C, D, and E” are an absolute no go. It is also very questionable to talk about “trends” if no significant differences were found. Consulting a statistician is a very good idea that may pay off big.

Discussions are sometimes very simplistic or difficult to follow. Structuring the discussion into a discussion of the material and methods, followed by the discussion of the results helps to follow your thoughts. Try to explain why you did that,


explain what the results mean, and why they are different from the results of your peers. Please associate literature quotes to your explanations and make it clear which are facts and which are hypothetical explanations.

Finally, base your conclusions only on the results of your experiment and do not include your wishful thinking.

The references are proof that you know the actual literature and are an expert in the field. It is without question that they must be updated and complete. Furthermore, every quoted paper must be listed and every listed paper must be quoted.

It seems to us that what is said above is quite straight forward. Be assured that good editing is meticulously adhering to such facts in order to allow the readers of the Stomatology Edu Journal (Stoma Edu J) to understand what was done and to make their judgement, if it is solid and how it may influence their research or clinical practice.

Sincerely yours,

J.-F. Roulet 
Editor-in-Chief

N. Ilie 
Co-Editor-in-Chief

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The thorny road of acknowledgement

Marian-Vladimir CONSTANTINESCU
DDS, MSc, PhD, Professor
Editor-in-Chief



Dear Readers,

“Honor, Respect, Work”, the emblematic motto of the family of teachers and soldiers I was born into and where I grew up. I was raised and educated to respect all work well done, and also those who practice it joyfully.

In 2013 I was contacted by the manager of a private publishing house that publishes over 10 medical journals. He invited me to be in charge of a dental journal they did not have in their portfolio. I made an objective analysis of the needs of my colleagues and the existing quoted dental journals. I noticed the limited number of such listed journals. After about four years, with some publishing experience, and a study conducted together with some Italian colleagues, I tried to enlist the co-operation of international and then of national celebrities. I considered that the best choice for my undertaking is Prof. Jean-François Roulet, DDS, Habil, Prof hc, Dr hc, from the University of Florida, Gainesville, FL, USA, leading personality of the dental world, and editor of four quoted dental journals. After presenting to him the situation of dentists in Romania and the Republic of Moldova and their inability to publish in quoted dental journals, I asked for his support as editor-in-chief of this new journal. Although at the time we did not know each other, with generosity and readiness to give a helping hand, he accepted my request. Then, we asked for the co-operation of several major names in the dental world. Some embraced the idea, others did not respond, and one of them rejected it.

The publication of the first 2014 issue was indeed a nightmare for me. After Prof. J-F Roulet first corrected it, I felt like a boxer knocked-out during in the first seconds of the very first round! That number was revised seven times in a row! That was the defining moment for me, when I began to learn what real editorial work means. With each new issue I had something to learn. Since then, I have regularly attended all seminars organized by Clarivate Analytics, with Adriana Filip as a lecturer. In 2015, the private publishing house that initially registered the journal under an ISSN, received the money necessary to publish the 2016 numbers, money which I had managed to raise through a sponsorship contract. Nevertheless, the respective publishing house spent the money for other purposes and went into insolvency.

As I had lost all confidence in contracts signed with private companies I contacted the Romanian Academy Publishing House. The director of the publishing house told me that they only publish journals whose editors are members of the Academy. As the members of the editorial team were only members of the Academy of Medical Sciences, I had to ask for the support of two members of the Romanian Academy. The former was Prof. Constantin Ionescu-Târgoviște, MD, PhD, Acad (AR), from the “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania, President of the Romanian Medical Association, of which my company “The Association for Oral Rehabilitation and Posturotherapy in Romania-ROPOSTURO”, established in 2004, is also a member. This is the Association which, in 2005, organized the First World Congress of Posturology in the building of the Parliament Palace (www.stomaeduj.com/roposturo.ro/congres2005/en_news.htm).

I met the latter during a conference held to launch a new book at the POLITEHNICA University Bucharest. He is Prof. Adrian Bejan, Eng, PhD, J.A. Jones Distinguished Professor, Acad (AR), Duke University, Durham, NC, USA. The Board was thus strengthened by the presence of the two full members of the Academy and this played its part in securing the final acceptance of the Presidium of the Romanian Academy to publish our journal. Yet, there was another factor which was decisive, namely the consistent lobby provided by Dr. Hubert-Pierre Ouvrard, former President of the Académie Nationale de Chirurgie Dentaire (ANCD) of France, Prof. Gottfried Schmalz, member of the National Academy of Sciences Leopoldina of Germany and Prof. Vjekoslav Jerolimov, member of the Croatian Academy of Sciences and Arts (CASA). Thus, when

I applied again, I was granted approval that as of its first 2016 issue, the Stomatology Edu Journal shall be published under the auspices of the Romanian Academy (<https://acad.ro/def2002eng.htm>), while the journal has to fully cover all its publication costs. In early 2017, when the “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania awarded the title of Doctor Honoris Causa to Prof Michael L. Glick, Dean Emeritus of the School of Dental Medicine of the New York University at Buffalo and JADA editor, I presented this journal to him. I asked him to give us his approval to publish an abstract of an article with CE credits in each issue of our magazine. In this endeavor, I was supported by my good friend Prof. Adi A. Garfunkel, Dean Emeritus of the Hebrew University of Jerusalem, Israel, his master. Thus, as of the 2017 first issue, the Stomatology Edu Journal is the only journal that publishes in each issue an abstract of a JADA article with CE credits. Following Prof. J-F Roulet's constant encouragement to motivate the authors, but also our army of editors, we registered the Stomatology Edu Journal for evaluation in as many databases as possible. To provide visibility, the Stomatology Edu Journal was registered with Crossref, each article starting with the first 2014 issue received a Digital Object Identifier (DOI) and is found on Google Scholar. Also, as of 2017 the journal has been accepted by the Directory of Open Access Journals (DOAJ). Starting with the first 2017 issue, the articles are accompanied by references with active links. Yet, despite all these remarkable advances made by our journal, our editors who have assured us of all their scientific support do not really hurry to send us articles. In fact, it is easy to understand because the Stomatology Edu Journal is not rated and their articles cannot be quantified by their universities.

A few days ago, I had the opportunity to meet Prof. James R. Hupp, Founding Dean and Professor of Oral-Maxillofacial Surgery, School of Dental Medicine, Professor of Surgery, School of Medicine, East Carolina University, Greenville, NC, USA, as he was on a brief visit in Bucharest. He is Editor-in-Chief, and his wife Carmen, Managing Editor of the Journal of Oral and Maxillofacial Surgery (JOMS), a journal published by Elsevier rated IF: 1.781. During our friendly conversation, I was told they receive over 1,600 manuscripts annually, out of which only 400 are selected for publication. How wonderful it is to work for a quoted magazine that holds such a portfolio of manuscripts!

On June 13, 2018 the Stomatology Edu Journal was registered for evaluation at Clarivate Analytics. As the Clarivate Analytics Editor, Web of Science, stopped working for the company, the evaluation of the journal remained unfinished. Recently, Kathleen Michael, Manager, Editorial Selection at Clarivate Analytics was kind enough to tell us that the evaluation still continues, but under other conditions. These new conditions increase the level of requirements to be fulfilled for the evaluation. Now, the Web of Science Core Collection selection process consists of a single set of 28 criteria to evaluate journals.

That is, 24 quality criteria to select editorial rigor and best practices and 4 impact criteria to select the most influential journals, using citation activity as the main indicator (<https://clarivate.com/webofsciencegroup/solutions/editorial>).

Now, knowing these evaluation criteria, the operational editorial team must go on working with the same dedication, rigor and exigency to maintain the high quality standards of the journal out of respect for the over 280,000 readers and the international scientific community.

In 2018 I attended the spring session of the ERO-FDI in Salzburg, and Dr. Michael Frank, DDS, PhD, ERO Elect President, President of the Dental Chamber Hesse, Board of the German Dental Chamber, had a high appreciation of the quality of the Stomatology Edu Journal which made him accept to be a member of the Editorial Board as Associate Editor-in-Chief.

Now, in the current issue, as President-in-Office of ERO-FDI, he presents our readers with his first editorial entitled “High Quality Oral Health - An FDI World Dental Federation Objective”.

Moreover, as a sign of appreciation of the CE PROGRAM FAQs of the Stomatology Edu Journal, ERO-FDI and FDI intend to integrate our journal as a scientific partner for the promotion of Continuing Education in Europe and beyond.

So help us God!

Sincerely yours,

Marian-Vladimir Constantinescu 

Editor-in-Chief

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Laudatio in Celebration of Professor Zrinka Tarle on her 50th birthday

The editors of the Stomatology Edu Journal, together with its readers would like to warmly congratulate to Professor Zrinka Tarle on her 50th birthday. Her field of special expertise focuses on the properties and improvements of materials and procedures in restorative dental medicine. In spite of her comparatively young age she has already achieved quite valuable scientific experimental and clinical results in her academic career so far.

Furthermore, she has developed a very fruitful collaboration with quite a number of renowned scientists internationally (München, Zürich, Regensburg, Siena, Los Angeles), and became a name known worldwide.

Professor Tarle was born on 28th August 1969 in Osijek, Croatia, and attended primary school and grammar school in Zagreb, as well as music and ballet primary schools. She graduated from the School of Dental Medicine, University of Zagreb, Croatia (1992). During her studies she was twice declared as one of the best students of the University, and also obtained 3 Rector's Awards.

She was awarded her PhD degree from the School of Dental Medicine, University of Zagreb as one of the youngest in the University history (1995). She specialised in restorative dentistry and endodontics at the Dental Clinic, University Hospital Centre Zagreb.

Troughout her academic career she has been employed by the Dental Clinic, University Hospital Centre Zagreb, and by the Department of Restorative Dentistry and Endodontics, School of Dental Medicine in Zagreb. She became assistant professor (1997), associate professor (2002), full professor (2006), and full tenured professor (2011). She was Vice-Dean for Science and Research, and has been Head of Restorative Dental Medicine Division at the Department of Restorative Dentistry and Endodontics, Head of Postgraduate Doctoral Study of Dental Medicine, and Dean of the School of Dental Medicine University of Zagreb.

Professor Tarle authored 237 publications either as senior author or co-author (1004 citations by WoS). She has been also co-author of 4 important textbooks, and editor of one recently published (Restorative Dental Medicine, Zagreb, 2019).

She has mentored 37 theses (graduate, MSc, PhD), and was principal or assistant investigator of 9 research projects internationally or in Croatia, and was also reviewer of many other projects. She has been a member of various editorial boards and reviewer of important national and international journals. She lectured at numerous national and international meetings and organized different courses, symposia and congresses. Among other important international conferences, she organized PER IADR Conference in Dubrovnik (2014).

She is a member of many international and national scientific associations, boards and committees: e.g. member of IADR Nominating Committee and IADR Tellers Committee, PER IADR Secretary and Treasurer, CED IADR Board member and President, CED IADR Regional Development Programme President, and AODES member. Her greatest achievement has been her election as an associate member of the Croatian Academy of Sciences and Arts.



She has obtained many national and international awards and recognitions. The most important is the Croatian National Award for Science (2012). She had been educated in a family of intellectuals from whom she acquired her valuable background for her future academic life, namely from her mother Mirjana Šutalo, a grammar school teacher of Croatian language and literature, and her father Jozo Šutalo, retired eminent professor at the School of Dental Medicine in Zagreb.

Professor Tarle is married and the mother of two sons. She has enjoyed continuous and warm support for her achievements from her husband Davor Tarle, DMD, and sons Andro and Frano, students of medicine and dentistry respectively.

Furthermore, she has quite a wide range of interests, and is fluent in English and German, good in Italian.

We are very pleased wishing professor Tarle and her family a lot of pleasure and successful life !

Professor Vjekoslav Jerolimov, DMD, MSc (biol), MSc (dent), PhD
Fellow of the Croatian Academy of Sciences and Arts
Ex-Dean, Ex-Head of the Department of Prosthetic Dentistry and Ex-Chair of Dental Materials
School of Dental Medicine University of Zagreb, Zagreb, Croatia
Associate Editor-in-Chief of Stomatology Edu Journal

From The Journal of the American Dental Association



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August 2019

Hong M, Vuong C, Herzog K, Ng MW, Sulyanto R

SEALED PRIMARY MOLARS ARE LESS LIKELY TO DEVELOP CARIES

J Am Dent Assoc. 2019 Aug;150(8):641-648. doi:10.1016/j.adaj.2019.04.011.

[https://jada.ada.org/article/S0002-8177\(19\)30291-0/fulltext](https://jada.ada.org/article/S0002-8177(19)30291-0/fulltext)

This article has an accompanying online continuing education activity available at:

<http://jada.ada.org/ce/home>.

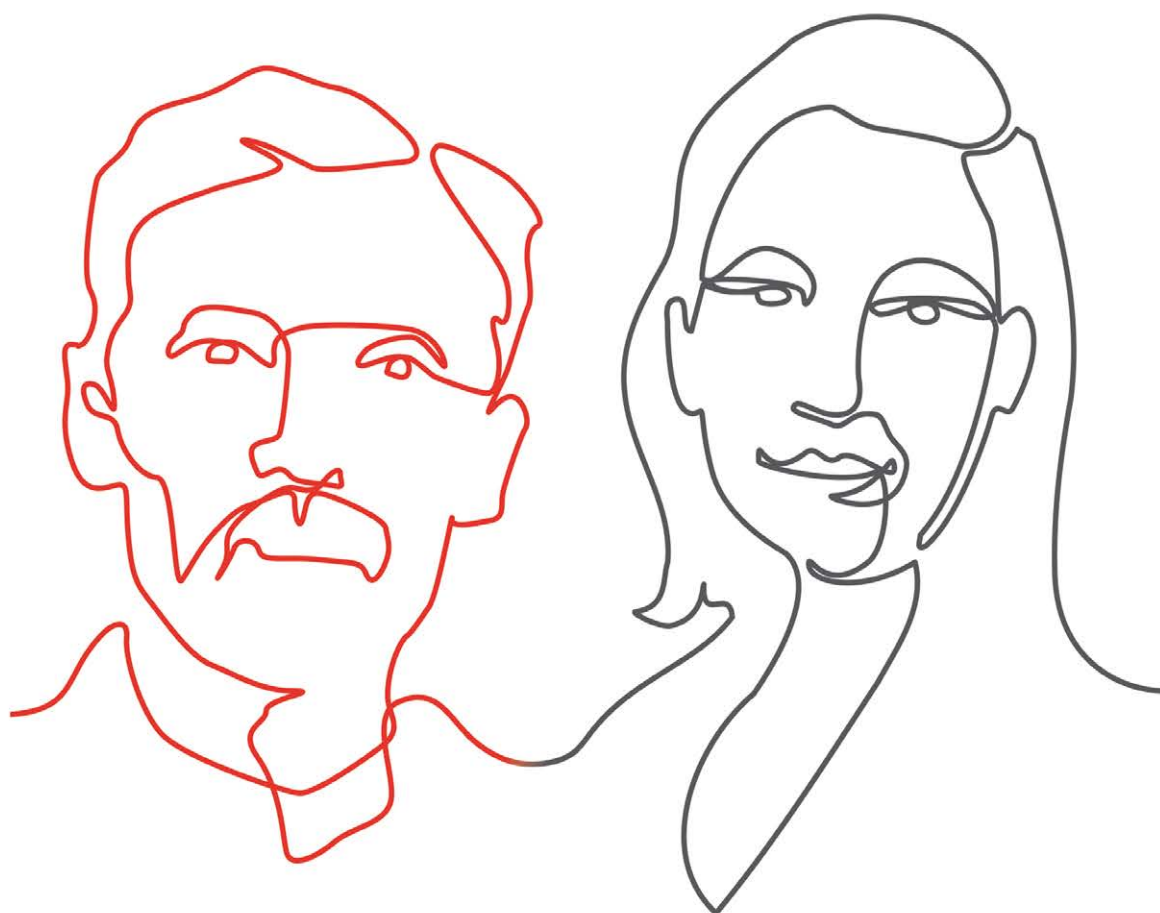
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Continuity by Innovation



Auguste Maillefer **1889**
2019 130 years anniversary

IMPACT OF PERIODONTITIS ON THE ECG DISPERSION MAPPING OF THE MYOCARDIAL TISSUES

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^aDMD, PhD, MSc, Assistant Professor, Head of the Department of Therapeutic Dentistry

^bDMD, PhD, Academician, Professor

^cDMD, PhD, Professor, Dean of the Faculty of Stomatology

^dDMD, University Assistant

ABSTRACT

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Introduction: The periodontal disease is considered to have an *epidemic* reach in the general population. The impact of the periodontal disease on the general health is studied from the perspective of the existence of complex interrelationships, especially with respect to the cardiovascular system. The aim of the study was the assessment of the correlation between the clinical signs of the chronic periodontitis and the changes in the ECG dispersion of the myocardial tissues and the analysis of the efficiency of the masticatory test and full mouth disinfection procedure for recording these signs in patients with chronic periodontitis.

Methodology: 92 patients with chronic periodontitis without the clinical manifestations of the cardiovascular disease and pathological signs on standard ECG were included in the study. Periodontitis was diagnosed based on the clinical and radiological exams. The ECG dispersion mapping technology was used to identify changes in the myocardial tissues, under various conditions.

Results: The pathological system of *periodontitis-target organ (heart)*, its elements and the pathways of interaction were described. The research outlined the diagnostic value of the masticatory test and of the full mouth disinfection procedure in the process of identifying the changes in ECG dispersion of the myocardial tissues in patients with chronic periodontitis. It also proposed an algorithm for the interdisciplinary management of patients with chronic periodontitis, based upon the *periodontitis-target organ (heart)* concept.

Conclusion: The *periodontitis-target organ (heart)* concept represents a cumulative synthesis of the available data from literature and of our investigations, and it may prove as a step towards an integrative medicine approach in periodontology.

Keywords: Interdisciplinary management; Index myocardium; Periodontal index; Periodontics; Target organ.

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Peer-Reviewed Article

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1. Introduction

According to the epidemiological studies published by WHO, gingivitis and periodontitis can be classified as presenting epidemic traits, even in highly developed countries – severe chronic periodontitis affects about 35% of the US population and it is forecast that by 2030, the number of individuals with chronic periodontitis in the US will reach 71 million (1 in 5 individuals) [1,2]. Chronic periodontitis is a public health issue, not only based on the dramatic increase in the number of patients, but also due to serious medical, social and economic consequences. Currently, the relationship between the periodontal disease and general health is being thoroughly studied [3,4]. The notion of *periodontal medicine* has

emerged, which refers to the multiple and complex interrelationship between periodontal diseases and general health. In 1891, W. D. Miller described the oral cavity as the *infection foci*, by which bacteria and their products enter adjacent or remote parts of the body. There are three ways of interaction between the affected periodontium and non-oral organs: bacteremia, systemic inflammation (interleukins, etc.) and endotoxemia caused by swallowed bacteria [5].

Hypothesis: For patients with chronic periodontitis, ischemic myocardial disorders develop gradually, and at the initial stages they may be asymptomatic, afterwards they intensify with the increase in the disease's duration and severity.

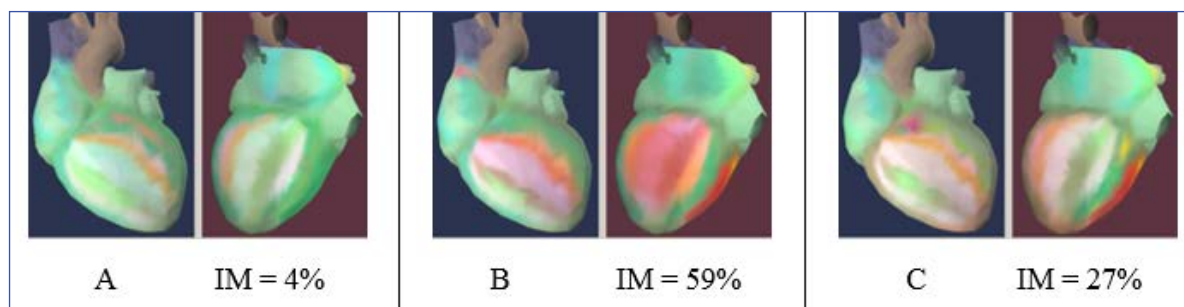


Figure 1. Values of the Index Myocardium before and after the masticatory test on a patient with chronic periodontitis (48 yr. old).

A – before the masticatory test, IM has a normal value ($IM < 15$);

B – 20 minutes after the masticatory test, IM has a pathological value ($IM > 15$);

C – 60 minutes after the masticatory test, IM has a pathological value ($IM > 15$).

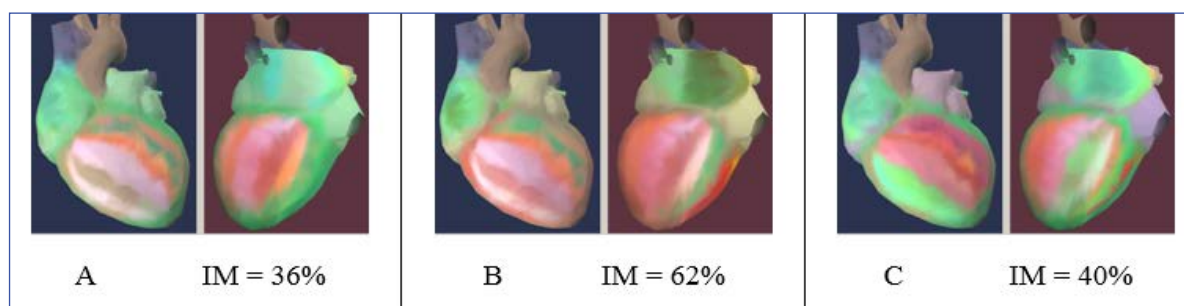


Figure 2. Values of the Index Myocardium before and after the masticatory test on a patient with chronic periodontitis (52 yr. old).

A – before the masticatory test, IM has a pathological value ($IM > 15$);

B – 20 minutes after the masticatory test, IM has a pathological value ($IM > 15$);

C – 60 minutes after the masticatory test, IM has a pathological value ($IM > 15$).

Aim of the study: Assessment of the correlation between the clinical signs of the chronic periodontitis and the changes in ECG dispersion of the myocardial tissues and analysis of the efficiency of the masticatory test and full mouth disinfection procedure for recording these signs in chronic periodontitis.

2. Materials and Methods

92 patients with chronic periodontitis (aged between 25-58 years) without clinical manifestations of cardiovascular disease and pathological signs on standard ECG analysis (after a prior exam at the cardiologist) were selected for this study. Periodontitis was diagnosed following the clinical and radiological exam. The ECG dispersion mapping [1,6] was used to identify changes in the ECG dispersion of the myocardial tissues, under various conditions (relaxed state, mastication test – during 2 minutes, full mouth disinfection procedure (FMDP) in 2 stages/24h).

2.1. ECG dispersion mapping

Currently, electrocardiography (ECG) is one of the most widespread medical methods, with wide application not only in cardiology and although there is still an ongoing development of standard ECG methods, they still have a low specificity and sensitivity (30-40%) to identify myocardial ischemia [7]. This means that in 60% of cases, the clinical forms of myocardial ischemia will remain undiagnosed.

The ECG dispersion mapping technology is based on

the analysis and visualization of the electromagnetic radiation of the myocardium, with the recording of the small amplitudes fluctuations. The quantitative and qualitative characteristics of the amplitude fluctuations were analyzed using the CardioVisor-06s device (Medical Computer Systems, Russian Federation). The technology allows recording multiple indices, including the Index Myocardium (IM), which quantitatively reflects the myocardial ischemic processes in a range between 0-100%. In healthy individuals, the Index Myocardium does not exceed 15%. A higher value of the index translates into more pronounced myocardial ischemic disorders. It is to be noted that the ECG dispersion mapping technology is much more informative compared to the standard ECG – myocardial ischemic disturbances can be detected in individuals who show normal values of the standard ECG indices. The diagnostic value of this method for identifying myocardial ischemic disturbances is very high – sensitivity $>80\%$ [7].

3. Results

The ECG dispersion mapping makes it possible to identify not only the organic, but also the functional disturbances of the myocardium. This has provided the opportunity to highlight ischemic disorders at a preclinical level. We have determined that in 85% cases of patients with chronic periodontitis, preclinical ischemic myocardial disorders were present (Index Myocardium > 15).

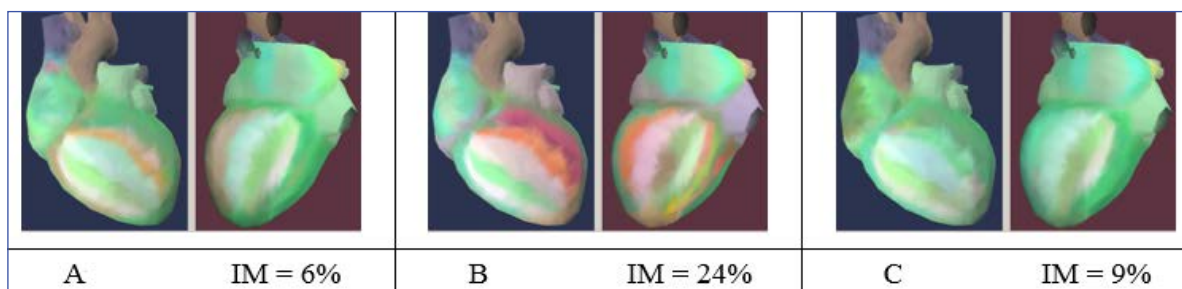


Figure 3. Values of the Index Myocardium (normal initial IM value) before and after the full mouth disinfection procedure (1st phase – mandible).

A - before FMDP (IM < 15);
B - 20 minutes after FMDP (IM > 15);
C - 12 h after FMDP (IM < 15).

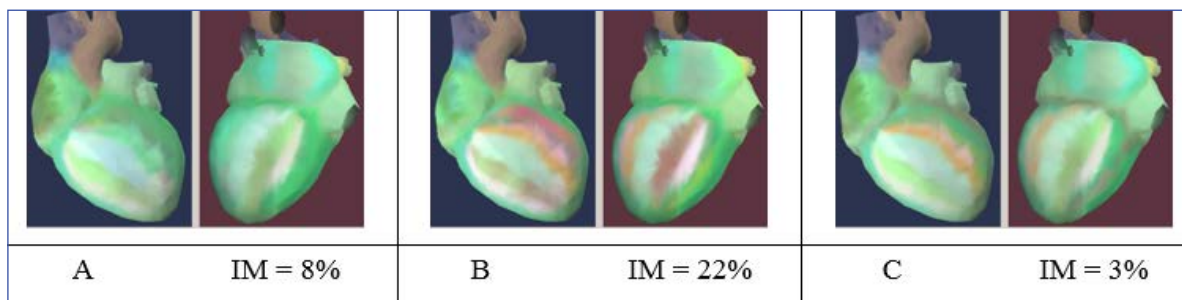


Figure 4. Values of the Index Myocardium (normal initial IM value) before and after the full mouth disinfection procedure (2nd phase – maxilla).

A - before FMDP (IM < 15);
B - 20 minutes after FMDP (IM > 15);
C - 12 h after FMDP (IM < 15).

We have studied the correlation between the Index Myocardium (IM) and the Integrative Periodontal Index (IPI – synthesis of common periodontal indices – PMA, OHI-S, PI, PBI, TM), disease duration, patient's age and systolic blood pressure (SBP).

The correlation analysis has shown that with the increase in the severity of the periodontitis, the value of the Index Myocardium (ischemic signs) will be higher; the duration of the chronic periodontitis has a stronger correlation with the Index Myocardium ($r_{xy} = 0.59$, $p < 0.01$) in comparison to the age factor ($r_{xy} = 0.42$, $p < 0.05$), which demonstrates that the duration of pathological periodontal process has a more negative impact on the ischemic myocardial disorders. Although in this study, patients without pathological values of SBP were included, statistically significant correlations were observed between SBP and the Index Myocardium ($r_{xy} = 0.46$, $p < 0.05$). This demonstrates that the SBP variations, even if they are within the normal range, have a significant influence upon the ischemic myocardial disorders – with the increase of the SBP values, the preclinical ischemic myocardial signs are more expressed.

3.1. ECG dispersion mapping dynamics under the influence of the **masticatory test** on patients with chronic periodontitis

The analysis of data from patients with chronic periodontitis and initial normal values of the Index Myocardium (IM<15) has shown the following changes in comparison with the values observed in a relaxed state (48 patients/100%):

- for 10 patients (20.8%), the Index Myocardium

has increased 20 minutes after conducting the masticatory test;

- for 38 patients (79.2%), the Index Myocardium has deviated ~1-2% (without significant changes).

The analysis of the data from patients with chronic periodontitis with initial pathologic values of the Index Myocardium (IM>15), has shown the following changes in comparison to the values observed in a relaxed state (46 patients/100%):

- for 17 patients (37%), the Index Myocardium has increased 20 minutes after the masticatory test;
- for 29 patients (63%) the Index Myocardium has deviated ~1-2% (without significant changes).

3.2. ECG dispersion mapping dynamics under the influence of the **full mouth disinfection procedure** (FMDP) on patients with chronic periodontitis

Preclinical ischemic changes in the myocardium (IM index) in patients with chronic periodontitis under the influence of the full mouth disinfection procedure appear in 2 variants – monophasic or biphasic. The first phase – *IM-aggravation phase* (worsening of the preclinical ischemic signs) starts within the first minutes and hours after the full mouth disinfection procedure; and is probably caused by transitory bacteremia. The second phase – *IM-reduction phase* (mitigation of preclinical ischemic signs) starts after several more hours, after the full mouth disinfection procedure, possibly due to the elimination of the periodontal foci, with a reduction in the degree of bacterial invasion

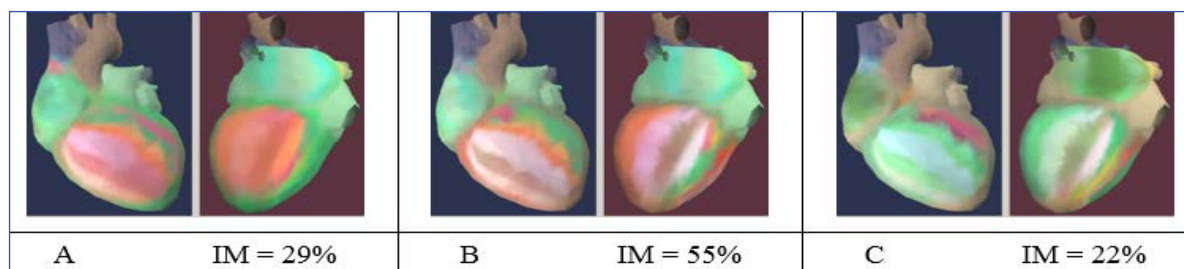


Figure 5. Values of the Index Myocardium (pathological initial IM value) before and after the full mouth disinfection procedure (1st phase – mandible).
A - before FMDP (IM > 15);
B - 20 minutes after FMDP (IM > 15);
C - 12 h after FMDP (IM > 15).

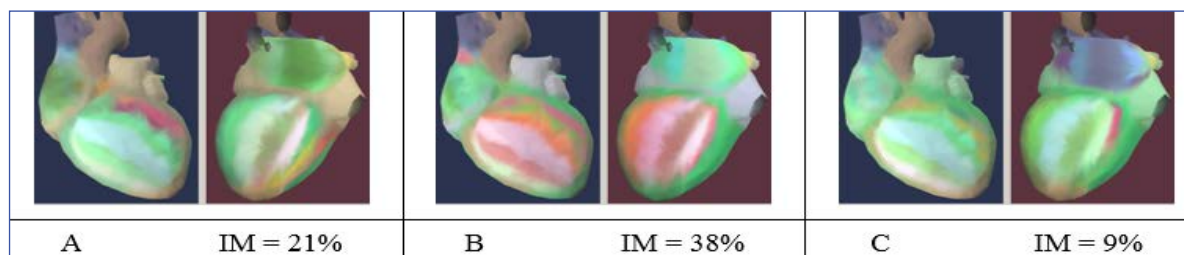


Figure 6. Values of the Index Myocardium (pathological initial IM value) before and after the full mouth disinfection procedure (2nd phase – maxilla).
A - before FMDP (IM > 15);
B - 20 minutes after FMDP (IM > 15);
C - 12 h after FMDP (IM < 15).

and dissemination into the bloodstream. In 79.8% cases, during FMDP, both phases can be observed (a *biphasic response* – *aggravation/reduction*). In 20.2% cases, the aggravation phase is maintained for a longer time, without transitioning to the reduction phase (*monophasic response*). It is to be noted that when the values of the Index Myocardium are higher than 50% or if FMDP induces only a monophasic response, it is advised to conduct the consequent dental treatment under the surveillance of a cardiologist.

4. Discussion

Numerous studies have been published in the last decade, that indicate a close relationship between periodontal disease and systemic diseases (cardiovascular diseases, diabetes mellitus, low-preterm birth-weight, osteoporosis, etc.), especially highlighting the more profound impact in regard to the cardiovascular system. The analysis of the data from the literature and of our own results enabled us to identify a pathological system – the *periodontitis-target organ (heart)* (Fig. 7).

Other organs may serve as target organs for periodontitis (liver, lungs, pancreas, kidneys, etc.). Currently, most data, however, are related to the relationship between chronic periodontitis and heart disease [3,8,9,10], and may be summarized as follows:

- the presence of common risk factors for chronic periodontitis and cardiovascular diseases (smoking, stress, etc.);
- frequent association of chronic periodontitis

with various cardiac conditions (stenocardia, myocarditis, atherosclerosis, etc.);

- the presence of certain bacterial agents (*T. forsythensis*, *T. denticola*, *P. gingivalis*, *A. actinomycetemcomitans*), simultaneously in the periodontal tissues and in the endothelium of the cardiac vessels;
- experimental administration of *Porphyromonas gingivalis* in animals leads to the occurrence of myocarditis and myocardial infarction and induces a pro-coagulant response to the vasculopathic effects; a simultaneous worsening of the inflammation degree of the periodontium and myocardium, at the injection of certain pro-inflammatory factors;
- bacteremia in patients with chronic periodontitis leads to the thickening of the heart valves;
- acceleration of atherogenic processes due to periodontal pathogens; followed by the destabilization of atherosclerotic plaques under the influence of periodontal bacteria that enter the endothelium and the vascular myocytes; exacerbation of inflammation with a progression of the atherosclerotic plaque, based on immune mechanisms, under the influence of periodontal bacterial products (molecular mimicry);
- the existence of common toxic factors in chronic periodontitis and cardiovascular diseases;
- the existence of common mechanisms in the process of diminishing dento-periodontal support and bone resorption, with the occurrence of cardiovascular disturbances – each 20% bone loss is associated with an increase in

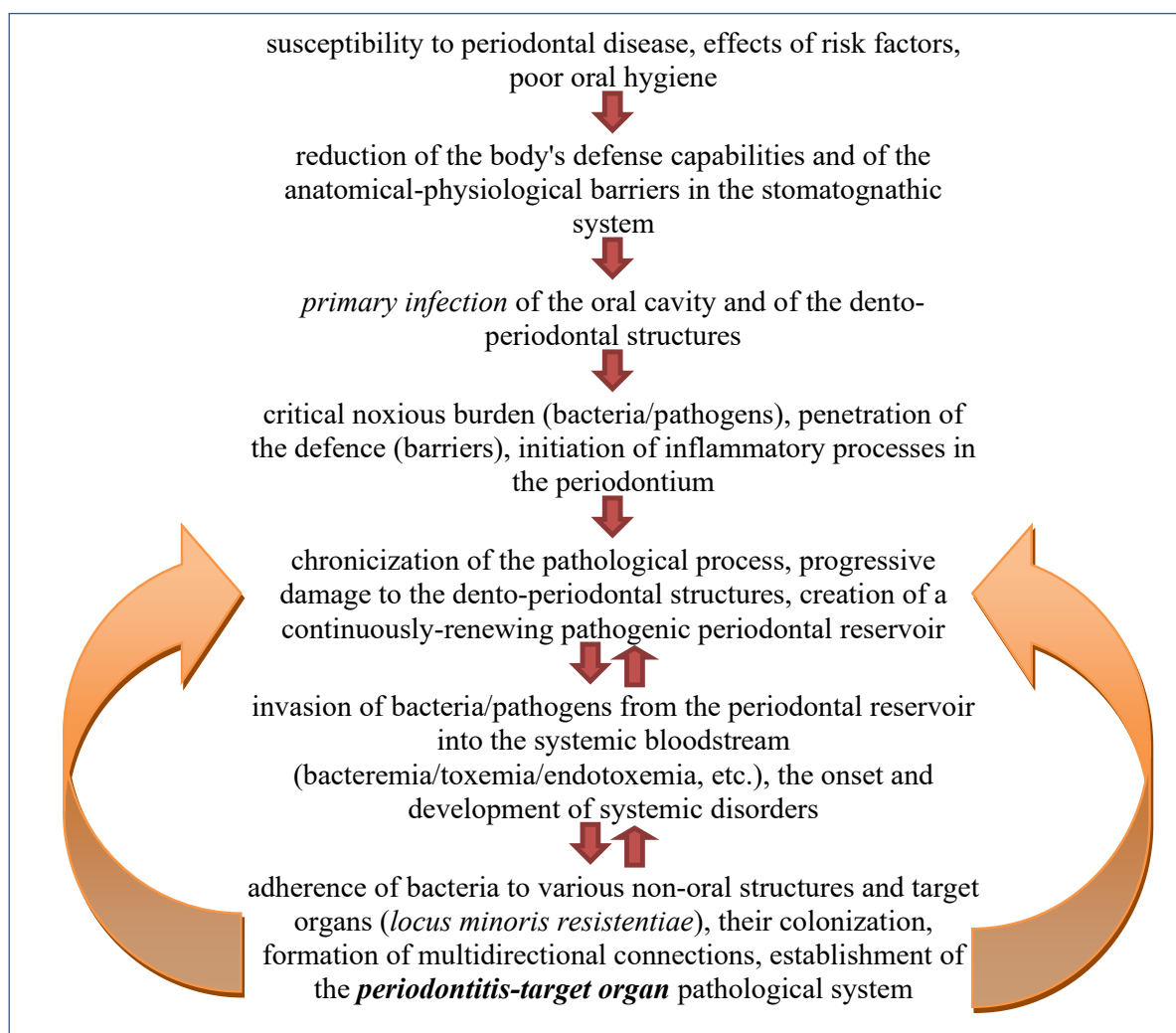


Figure 7. The periodontitis-target organ (heart) pathological system.

the incidence of cardiovascular diseases by 40%; chronic periodontitis and tooth loss increases the risk of fatal events in cardiac patients;

- diminishing the severity of the pathological manifestations of chronic periodontitis under the influence of treatment, simultaneously with the reduction of the morpho-functional disorders in the cardiovascular system;
- existence of a common genetic predisposition for periodontal and heart disease; the genes for the immune and inflammatory response inter-penetrates and influence the expression of a hyper-inflammatory phenotype, that predisposes both to coronary atherosclerosis and to periodontal disease.

Our own investigations revealed the presence of preclinical ischemic myocardial disturbances (PIMD), evidenced by changes in ECG dispersion of the myocardial tissues in patients with chronic periodontitis, which demonstrates the role of the heart as a target organ for periodontitis at a preclinical level: the frequent occurrence of PIMD in patients with chronic periodontitis (85% of cases); diminution/disappearance of PIMD after efficient treatment of chronic periodontitis; reduction/

disappearance of PIMD after the removal of occlusal trauma in patients with chronic periodontitis; aggravation of PIMD in patients with chronic periodontitis under the influence of the masticatory test and the professional oral hygiene procedure (microtrauma, transient bacteremia); the positive correlation between the severity of the chronic periodontitis and the duration of the disease with the PIMD expression.

The analysis of the results obtained in combination with the data from the literature allowed us to highlight the main ways of interaction in the periodontitis-target organ (heart) pathological system: interaction based on the infectious factor (bacteremia); neurogenic interaction; humoral-metabolic interaction, immune and toxic factors; interaction based on genetic determinism.

The bacterial factor is one of the most important in the periodontitis-target organ (heart) system.

Actinobacillus actinomycetemcomitans, *Campylobacter rectus* and *Eikenella corrodens* are most commonly found in periodontal processes, but under various pathological conditions, the role of major bacteria can be played by various species. In patients with chronic periodontitis, more than 700

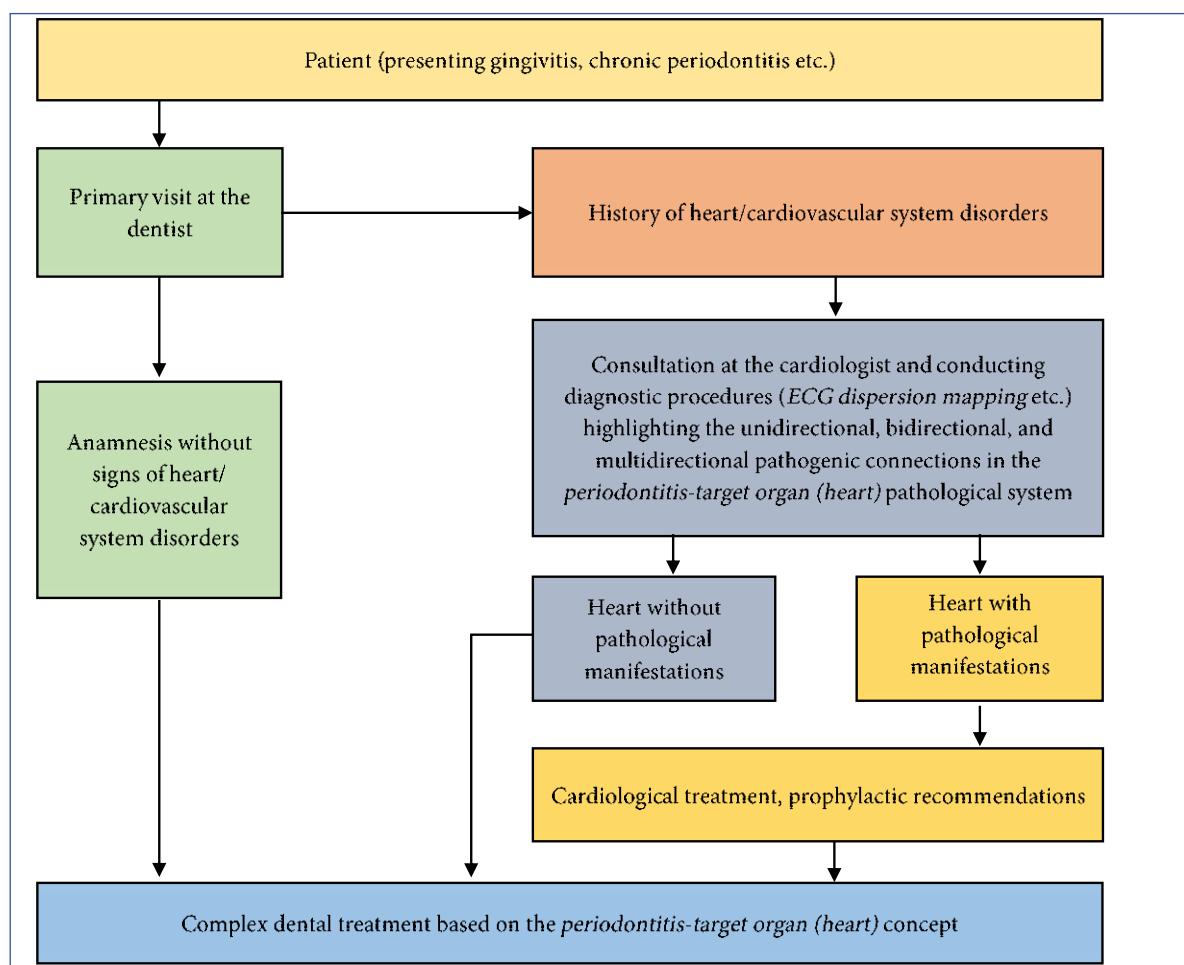


Figure 8. Algorithm of the interdisciplinary management of patients with chronic periodontitis (in the vision of the *periodontitis-target organ (heart)* concept).

bacterial species have already been detected [11]. Periodontal bacteria can induce proliferation of smooth muscle cells in the vessels of the heart, causing destruction and endothelial damage, vasomotor functional disorders [7]. In our studies, we highlighted the distinct phases of the changes in ECG dispersion of the myocardial tissues, under the effect of the FMDP, associated with the occurrence of transient bacteremia: the *worsening phase* (the first minutes and hours, during and after the procedure) and the *mitigation phase* of the ischemic disturbance (hours and days after the procedure).

In 79.8% cases, both phases (*worsening/mitigation*) are manifested, and in 20.2% cases the worsening stage persists without a transition to the mitigation phase, which is an indication for additional investigations/monitoring by the cardiologist. Therefore, the dentist, based on the peculiarities of the chronic periodontitis management, may be the first specialist to detect the presence of preclinical ischemic myocardial disorders associated with chronic periodontitis, based on the detection of changes in the ECG dispersion of the myocardial tissues.

Another point is represented by the neurogenic interaction, which is fundamental in achieving sanogenic and pathogenic connections, which are

present in the case of chronic periodontitis. The afferent part of the trigeminal-cardiac reflex consists of the somatosensory trigeminal terminations, the Gasser node, and the trigeminal sensory nuclei. Afterwards, via interconnecting short internuclear fibers, there is a link established with the structures of the reticulated formation and with the motor nuclei of the *vagus* nerve.

Various pathological irritations, dental manipulations in the area innervated by the trigeminal nerve can cause the trigeminal-cardiac reflex [12]. In recent years, the maxillo-mandibulo-cardiac reflex has been described, with pronounced bradycardic effects. Arakeri et al. describes the dento-cardiac reflex, which is manifested at the irritation of the maxillary jaw (hypotension, syncope, hyperhidrosis, bradycardia) [13]. This reflex may be observed in patients without cardiovascular disease.

The *interaction of humoral-metabolic, immune and toxic factors* is another important component in the *periodontitis-target organ (heart)* pathological system. There is a strong interaction between periodontal metabolic disorders and the cardiovascular pathology – IL-1 β , IL-6, TNF- α , PGE2 and other pro-inflammatory factors produced in the affected periodontal tissues, may enter the bloodstream and cause various infections at remote

sites, including in the heart [3,14].

A series of *endocrine-like substances* [15] are produced in the periodontal foci, with immune complexes being formed, that amplify the inflammation, both in the dento-periodontal region and in the tissues of the heart [10,20].

The affected marginal periodontium represents a continuously-renewing reservoir with a permanent secretion of toxic substances into the bloodstream, inducing and perpetuating the pathological effects and systemic disorders of the internal organs, including the heart.

In patient with periodontitis, even mild mastication already releases bacterial endotoxins from the oral cavity into the bloodstream with harmful effects on the cardiovascular system.

Applying *ECG dispersion mapping* as a screening test for the preclinical myocardial ischemic disorders by detecting changes in ECG dispersion of the myocardial tissues, in patients with chronic periodontitis has allowed us to highlight the diagnostic value of this method: Se (*sensitivity*) – 36.9%, Sp (*specificity*) – 79.1 %, +PV (*positive predictive value*) – 62.9%, -PV (*negative predictive value*) – 43.2%. These data demonstrate that the masticatory test and the ECG dispersion mapping can be applied first of all, in order to exclude ischemic processes involving the myocardium in patients with periodontitis.

Genetic factors are studied insufficiently, although the DNA of the microbiota represents 99% of the collective genome of the human body [16]. The first to demonstrate the association between periodontitis and genetic determinism was Michalowicz et al. [17]. In heterozygous and homozygous mice with a congenital apolipoprotein-E deficit, there was a high risk of atherosclerosis of the aortic and cardiac vessels at the intravenous administration of *P. gingivalis* [6]. A relationship between a specific polymorphism of the IL-1 genotype and the phenotypic expression of the marginal periodontitis was detected.

The increased risk for severe periodontitis in individuals with a positive genotype (*periodontitis susceptibility test*) is estimated to be 6.8 times higher compared to subjects with a negative genotype. It is estimated that about 30% of the population may be positive for this genetic marker [4]. There is a common genetic predisposition for periodontitis and heart disease [18].

Highlighting these interactions based on the *periodontitis-target organ (heart)* concept – provides the opportunity to monitor the patient's condition and to optimize the complex personalized treatment programs in accordance with an interdisciplinary algorithm for the management of patients with chronic periodontitis (Fig. 8).

The first results in regard to the optimization of the diagnosis and complex treatment based on the proposed concept seem to be promising. Thus,

in order to act on the interaction pathways in the *periodontitis-target organ (heart)* system, we applied biologically active preparations (BioR[®]), the pituitary neuropeptide – oxytocin, transcranial direct-current stimulation, transcutaneous electric nerve stimulation (TENS) [8,19,20].

Based on the *periodontitis-target organ (heart)* concept, it is recommended to monitor the risk factors of cardiovascular disorders during dental treatment; the dental consultation should include gathering information on cardiovascular system diseases and disorders, the medications prescribed by the cardiologist, etc.

Dental treatment of chronic periodontitis based on the proposed concept is a paradigm that opens new perspectives in the development of interdisciplinary and personalized dentistry, based on principles that emphasize the fundamental relationships between dental diseases, the general condition of the organism, metabolism and the internal organs that are multidirectionally involved in pathological processes.

5. Conclusions

The Index Myocardium (ECG dispersion mapping) positively correlates with the severity and duration of the periodontal disease, patient's age and the systolic blood pressure level. Around 85% of patients with chronic periodontitis had preclinical ischemic signs, revealed by changes of the ECG dispersion mapping of myocardial tissues.

The subsequent dental treatment for patients with high initial values of the Index Myocardium (IM > 50) or with an aggravation of the preclinical ischemic signs during dental procedures will require the surveillance of the cardiologist.

The *periodontitis-target organ (heart)* concept represents a cumulative synthesis of the available data from literature and our investigations, and it may prove as a step towards an integrative medicine approach in periodontology.

Author Contributions

VF: Idea, experimental design, performed investigations, data analysis, manuscript writing. VL: Idea, experimental design, data gathering, analysis and interpretation, manuscript writing. SC: Data analysis, manuscript proofreading. GB: Data analysis, manuscript proofreading.

Acknowledgments

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CV

Author of more than 55 inventions in the field of dentistry. Participant at national and international invention fairs (Moldova, Romania, Ukraine, USA, Belgium, Switzerland, China, Poland, Germany, Czech Republic, Spain), awarded with 61 medals, including 26 gold, 19 silver and 11 bronze medals and others.

In 2010, his practice received WIPO (World Intellectual Property Organization) Award for Innovative Enterprises. In 2018, he has received the WIPO Award for Innovative Activity. Author of more than 92 scientific articles in national and international journals. Author of clinical guidebooks and monographs. Double champion (2001, 2004) of the International Contest for Restorative Dentistry "Prisma Championship" (Poltava, Ukraine). 1st place at the International Dental Contest of Clinical Cases, Moscow, Russia, 2004. Vice-president of Association of Stomatologists of Republic of Moldova (ASRM).

Questions

1. How many individuals are forecasted to have periodontitis in US population in 2030?

- ☐ a. One in ten;
- ☐ b. One in two;
- ☐ c. One in three;
- ☐ d. One in five.

2. What does a high value of MI (myocardial index) mean?

- ☐ a. A high value means less myocardial ischemic disorders;
- ☐ b. A low value means higher myocardial ischemic disorders;
- ☐ c. A high value means higher myocardial ischemic disorders;
- ☐ d. A low value means less myocardial ischemic disorders.

3. What is the sensitivity of the ECG dispersion mapping?

- ☐ a. 78%;
- ☐ b. 80%;
- ☐ c. 99%;
- ☐ d. 26%.

4. How big is the risk for developing severe periodontal disease in individuals with a positive genotype (detected on periodontitis-susceptibility test)?

- ☐ a. 2 times higher;
- ☐ b. 6,8 times higher;
- ☐ c. 4 times higher;
- ☐ d. It is the same as in individuals with negative genotype.



STUDYING DENTINE CARIES IN THE FIRST PERMANENT MOLARS IN CHILDREN

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ABSTRACT

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Introduction: Caries in permanent teeth most often start from the occlusal surfaces of the first molars, soon after eruption at the age of six. At that point the occlusal surfaces are at risk due to the presence of many retentive areas.

Aim – To study the spread and characteristics of cavitated dentine caries in the first permanent molars after eruption.

Methodology: 351 children, distributed into two groups were subjected to the study: the first group - 6 to 9-year olds, and the second group - 10 to 12-year olds. The registration of the oral status was carried out with an epidemiological card for oral health assessment - brief bio, dental status and description of the cavitated carious lesions in the dentine. The clinical description of the D3 carious lesions present was determined according to the localization of the carious lesions (occlusal, approximal, cervical), the color and the consistency of the carious dentine, via the Bjørndal et al scale.

Results: The results of this study show that children aged 6 to 12 have on average three to four carious teeth. Dentine carious lesions D3 with occlusal localization in the first permanent molars are plausibly more numerous than the carious lesions with approximal and cervical localization. In the first permanent molars, the dentine carious lesions with occlusal localization are characterized by darker colors of carious dentine and a relatively hard consistency.

Conclusions: In the first permanent molars the more slowly progressing carious lesions are predominant.

Keywords: Caries; Dental decay; Dentine; Occlusal surfaces; Permanent first molar.

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 **Peer-Reviewed Article**

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1. Introduction

Caries formation is a dynamic process of imbalances in the oral environment that lead to the development of carious lesions, on predisposed surfaces in the primary and permanent teeth in children [1]. The progression of the carious lesion may be influenced in its early stages of development by modeling the oral environment and remineralization [2-4]. Despite the indisputable successes and the increased scientific interest with respect to improving children's dental health, the problem of reducing the frequency and severity of caries remains relevant [5-7]. On a world scale, 60-90% of school-age children suffer from caries (WHO, 2012). The disease also leads to serious economic consequences for society as a whole [8]. According to the data from the last epidemiological study conducted in Bulgaria in 2011, approximately 71% of the six-year-old children in the country have caries, with the most frequently affected temporary teeth numbering three or four. In the 12-year-olds group, 79% of them had caries of the permanent teeth, with an average of three permanent teeth being affected, and in the 18 year-olds group the same held true for 92% of the teeth, with the number

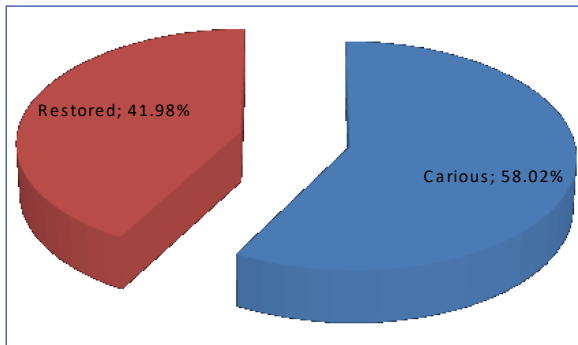
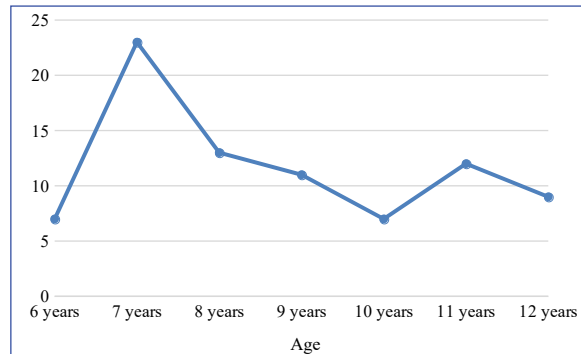
of affected permanent teeth reaching six. Every fourth 18-year-old already has one extracted tooth. Only 30% of the six-year-olds in the country are caries free, and with the 12-year-olds the percentage drops further down to 22% [6,7].

Caries in permanent teeth most often start from the occlusal surfaces of the first permanent molars, soon after their eruption at the age of six. At that point the occlusal surfaces are at risk due to the presence of many retentive areas. The mineralization of the enamel at that place is not complete. Difficulty in early diagnosing of the initial carious lesions present on the occlusal surfaces of the permanent first molars and the lack of regular prophylactic examination leads to the quick development of cavitated dentine lesions during the first years after eruption. This requires their early inclusion in the restoration cycle, and not infrequently leads to their early loss.

Raising awareness for the spread and characteristics of dental caries in the permanent first molars, conducting effective prophylactics or timely microinvasive treatment of already developed lesions could lead to a significant decrease of occlusal caries in children with a mixed dentition.

Table 1. Visual-tactile criteria. (Bjørndal et al.)

Visual criteria – dentine color	Tactile criteria (with probe) - dentine consistency
black	Code 1 (very soft) – the probe penetrates and peels parts of it away easily;
dark brown	Code 2 (soft dentine) – probe can easily penetrate and exit the dentine;
light brown	Code 3 (moderately hard) – light resistance during probing;
yellow	Code 4 (hard dentine) – the probe moves over the dentine with light resistance leaving a white trail;
light yellow	Code 5 (hard non-carious) – soft squeaking and resistance during probing.

**Figure 1.** Ratio between carious and restored permanent first molars. $t=5,00$ $p<0,05$ **Figure 2.** Spread of D3 lesions in first permanent molars.

Aim – To study the spread and characteristics of cavitated dentine caries in the permanent first molars, immediately after eruption.

Tasks

1. To study the general cariousness and the relative portion of occlusal caries in the permanent first molars in children aged 6 – 12.
2. To provide a clinical description of the registered cavitated dentine carious lesions in the permanent first molars of the children tested.

2. Materials and Methods

351 children, distributed into two groups were the subject of the study, as follows: group one - 6 to 9-year-olds; group two - 10 to 12-year-olds. We had received an ethical approval from KENIMUS – Ethical commission of the Medical University of Sofia – 24/07.12.2018.

Registration of the oral status of the children was carried out with an epidemiological card for oral health assessment, which includes a brief biography, dental status and description of the cavitated carious lesions in the dentine present – D3 according to the locally adopted Peneva et al. classification [9]. All surfaces of a tooth were cleaned of debris and plaque, the teeth were dried using an air syringe and visually examined without magnification. If there were suspicious areas, then an explorer – a blunt probe (periodontal probe) was used to check for the surface texture and to remove plaque from fissures using a dredging motion.

The carious status of the children was diagnosed and registered in teeth with a D1b diagnostic threshold

– enamel carious lesion visible after drying. Further noted were D2, D3a, D3b and D4 carious lesions. The DMFT index was used, and while registering it, for the purposes of this study, DMF(T+t) was also registered, due to the fact that part of the children were with a mixed dentition [9]. The fissure sealants were included in the number of restorations. The clinical description of the D3 carious lesions present was determined according to the location of the carious lesions (occlusal, approximal, cervical), the color and consistency of the carious dentine, via the Bjørndal et al scale [10].

The statistical processing of the data was carried out with the statistical program SPSS (version 19, SPSS Inc. USA). A 95% interval of plausibility ($p<0.05$) was chosen as a level of significance at which the null hypothesis is rejected.

3. Results

3.1. Cariousness of the children tested:

- General cariousness

The results obtained in determining the cariousness – DMF(T+t) of the children tested, are presented in the following table.

The results show that the general cariousness (DMF(T+t)) in all children is between three and four carious teeth. A plausible decrease in cariousness is observed in temporary teeth, due to their replacement, while an increase in cariousness is observed in permanent teeth with age ($p<0.05$).

- Relative portion of carious and restored permanent first molars

The following diagram presents the results, obtained

Table 2. Cariousness of the children tested – DMF(T+t) as grouped by ages.

Children gr.	DMFT		DMFt	DMF(T+t)	Ind t-test
	N children	Mean ± SD (teeth)	Mean ± SD (teeth)	Mean ± SD (teeth)	
1 st gr.– 6 to 9	201	0.60 ± 0.87	3.60 ± 2.24	4.20 ± 2.31	$T_{T,t} = -17.05$ (P=0.00) $T_{T,T+t} = -22.78$ (P=0.00) $T_{t,T+t} = -9.87$ (P=0.00)
2 nd gr. -10 to 12	150	2.42 ± 1.76	0.99 ± 1.30	3.42 ± 1.74	$T_{T,t} = 6.80$ (P=0.00) $T_{T,T+t} = -9.20$ (P=0.00) $T_{t,T+t} = -10.87$ (P=0.00)
Ind T-test	T=-12.73 P=0.00		T= 12.7 P=0.00	T=-1.61 P=0.11	

Table 3. Distribution of the carious lesions in the permanent first molars.

Diag. T-hold	D1b		D2		D3		D4		total	
Children group	n	% ± Sp	n	% ± Sp	n	% ± Sp	n	% ± Sp	n	%
1 st gr–6 to 9	12	12.90±3.48	27	29.04±4.71	54	58.06±5.12	0		93	100
2 nd gr–10 to 12	73	40.11±3.63	76	41.76±3.66	28	15.38±2.67	5	4.12±1.34	182	100
total	85		103		82		5		275	100
T test	$T = 5.41$		$T = 2.14$		$T = 7.39$					

in determining the relative portion of carious and restored permanent first molars of the children tested. The data in the diagram show that the carious permanent first molars are plausibly predominant over the restored ones in both age groups ($p < 0.05$). The data gathered in determining the severity of the registered carious lesions in the first molars are presented in the table 3. The data presented in the table show that in the permanent first molars in the first age group, D1b take up only 12.9%, D2 carious lesions are 29%, and over a half (58%) of the registered carious lesions are irreversible – D3 in the period immediately after eruption of the examined teeth ($p < 0.05$). In the second age group the portion of reversible carious lesions plausibly increases, while the irreversible ones plausibly decrease, which is probably due to the restoration of the cavitated lesions ($p < 0.05$). The higher relative portion of irreversible carious lesions in the children of the first age group (6-9 years) could be explained by the specificities of the carious pathology of the fissures of these teeth in cases where adequate preliminary prophylactics are lacking. The data gathered in this study regarding the spread of cavitated dentine carious lesions (D3) in first molars according to the age of the children are presented in the following diagram. The graph shows that the peak of registered D3 carious lesions in the sixth teeth of the children tested can be observed as early as after the first or second year of their eruption. A quick progression of the occlusal caries is present in the seven to eight year period and development of D3 carious lesions. Past eight years of age a significant decrease in the cases of D3 lesions is observed, probably due to an increase in the number of restored teeth.

3.2. Clinical description of the registered dentine carious lesions (D3) in the permanent first molars of the children tested.

- Localization of the carious lesions

The data are presented in the table 4.

Between the ages of 6 and 12, the D3 carious lesions with occlusal localization in the first molars are 72% and are significantly more than those with approximal (14.6%) and cervical (13.4%) localization in both age groups ($p < 0.05$). As the children grow in age, the caries with occlusal, approximal and cervical localization remain within close parameters ($p > 0.05$). The anatomical peculiarities of the permanent first molars are a primary risk factor for the onset of an occlusal caries, immediately after eruption. They have a highly characteristic occlusal surface (narrow and deep fissures), thin to non-existent enamel at the bottom of the fissures, significantly lower mineralization, insufficient self-cleaning of these surfaces, absence of established oral hygiene habits and lack of motivation for early control. Early diagnostics in such cases is more difficult which leads to the development of cavitated dentine carious lesions in the molars [6,9].

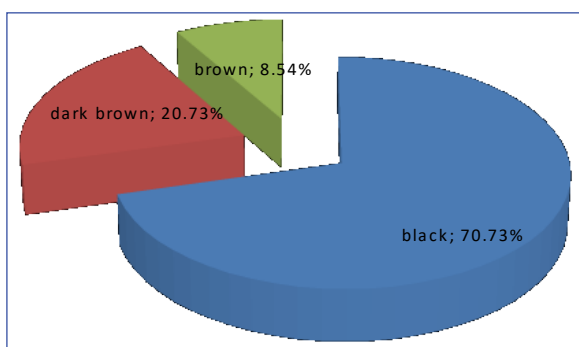
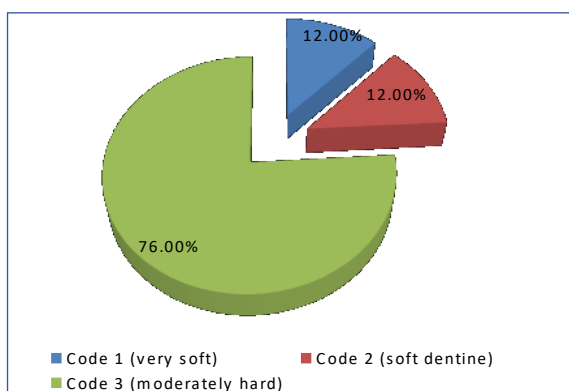
- Color and consistency of the carious lesions

The color of the carious dentine of the D3 lesions in the permanent first molars is predominantly black, followed by dark brown carious dentine, while the lowest is the number of registered D3 carious lesions which are light brown in color ($p < 0.05$).

The predominant darker colors in the carious dentine may be due to delayed pigments and this is an indicator for a slower developing carious process, which is conducive to microinvasive treatment. The aim is to further slowdown or arrest the development

Table 4. Distribution of D3 lesions in permanent first molars according to localization.

Children group	total	occlusal		approximal		cervical		
	n	n	% ± sp	n	% ± sp	n	% ± sp	
1 st gr – 6 to 9	54	40	74.1 ± 5.96	8	14.8 ± 4.83	6	11.1 ± 4.28	$T_{1,2}=6.08$ $T_{1,3}=6.66$ $T_{2,3}=0.56$
2 nd gr – 10 to 12	28	19	67.9 ± 8.83	4	14.3 ± 6.61	5	17.8 ± 7.24	$T_{1,2}=3.50$ $T_{1,3}=3.19$ $T_{2,3}=0.34$
total	82	59	72.0 ± 4.96	12	14.6 ± 3.90	11	13.4 ± 3.76	$T_{1,2}=6.08$ $T_{1,3}=6.66$ $T_{2,3}=0.56$
		$t_{2,3}=0.58$		$t_{2,3}=0.06$		$t_{2,3}=0.80$		

**Figure 3.** Color of the carious dentine in the first molars with D3 carious lesions. Pearson Chi Square = 12,468 Sig = 0,000**Figure 4.** Consistency of the dentine in the D3 carious lesions of the first molars. Pearson Chi Square = 14,732 Sig = 0,000

of the dentine caries and provide conditions for activating the natural defence mechanisms of the pulp-dentine complex.

The diagram shows that in over 3/4 of the cases the consistency of the carious dentine of the registered D3 carious lesions is that of a moderately hard dentine (76%), while the remaining 1/4 of cases are distributed equally between soft (12%) and very soft dentine (12%) ($p < 0.05$).

The data show that the consistency of the carious dentine of the D3 carious lesions in permanent teeth is predominantly code 3 – moderately hard ($p < 0.05$). Soft and very soft consistency (code 2 and code 1) of the carious dentine is found in a smaller percentage of the cases of the registered D3 carious lesions. If we adopt the notion that the consistency of the carious dentine depends on the speed of the carious process and is indicative of this, we could reach the conclusion that in the D3 carious lesions of the first permanent molars, registered in this study, the caries with a slower development speed are predominant, which confirms the conclusion reached regarding the color of the dentine.

- The study of the interdependency of the research parameters – color, consistency DMFT+t – is presented via the Pearson correlation index at a plausibility level of $p < 0.05$ and $p < 0.01$. The data in the table show that the color of the carious dentine correlates with the consistency and the DMFT+t

index. The data are supported by high statistical plausibility ($p < 0.01$). Higher values of the DMFT+t index are observed in the children with darker and relatively hard carious dentine in the cavitated dentine lesions. In the first permanent molars of the children covered in this study, the cases of relatively hard, dry carious dentine with dark coloration are predominant.

4. Discussion

The results of this study show that children between aged 6 to 12 have on average three to four carious teeth. The general cariousness (DMFT+t) is higher between the ages of 6-9 (4.20), while in older children it decreases slightly (3.42). The results of this study show that the ratio between carious and restored teeth of the children studied changes in the separate age groups, with the cases of carious teeth (D) decreasing at the expense of increasing the relative proportion of restored teeth (F) as the age of the children increases.

The data gathered in this study match that of the last national epidemiological study of the spread of dental caries in children in 2011, which showed that in six-year-old children between three to four carious teeth can be found, and three carious teeth in 12-year-olds. The epidemiological study conducted in the Ruse region in 2010 shows that six-year-old children have an average of six carious teeth [6,7].

Table 5. Correlation between color, consistency and DMFT in the children studied.

indicators	Pearson Correlation index		
	color	const.	DMFT+t
color		-0.767**	-0.682**
consistency	-0.767**		0.673**
DMFT+t	-0.682**	0.673**	

A2008 study by M. Peneva shows that DMFT is 4.3, which includes only dentine carious lesions. If we add enamel caries, which are reversible, the data will show an average of seven carious teeth [11].

The first permanent molars erupt in early childhood and carry a maximal occlusal load as the main chewing teeth. They are among the most affected form of dentine caries due to their morphological and functional characteristics, which is the motivation behind this study of the spread and characteristics of the dentine caries in this tooth group.

The higher relative portion of irreversible carious lesions, established in this study, of first permanent molars in the children of the first age group (6-9 year old) could be explained by the specificities of the carious pathology of the fissures of these teeth in cases where adequate preliminary prophylactics are lacking. The stages conducive for non-operative treatment in these instances pass quickly and can easily be missed, which leads to the development of dentine caries in the permanent teeth immediately after their eruption, with a high risk of affecting the highly exposed pulp. As to avoiding potential complications in the treatment of such carious lesions, the efforts of a number of authors are dedicated toward the development and application of methodologies for minimally invasive operative treatment of dentine lesions, with the aim of optimally preserving the structures of the recently erupted permanent children's teeth [12-15].

Similar to our study some authors have reported high scores of cavitated dentine carious lesions in children in Canada (between 38% to 44.1%) and Thailand - in 3-year-olds [16,17].

The levels of cavitated dentine carious lesions increase with age and they remain problematic in adults [18]. The cohort study reported that over a period of 38 years, an annual increase in number of tooth surfaces affected by cavitated dentine carious lesions [19]. The results of this study show that D3 carious lesions with occlusal localization in the first permanent molars are plausibly more numerous than the carious lesions with approximal and cervical localization in both age groups. According to a study, the occlusal surfaces are only 6% of all dental surfaces, while occlusal caries account for 60% of all caries. It is considered that this is due primarily to the plaque retentive anatomy of these surfaces [20]. According to studies, most frequent are occlusal caries in molars, followed by approximal caries in molars, while least carious are the approximal surfaces of the front teeth [21,22].

The rapid development of occlusal caries in the dentine of newly erupted permanent molars has steered numerous researchers in the direction of applying treatment methodologies that provide an optimally non-invasive excavation, leading to a minimal loss of hard dental structures. Careful excavation would allow for the preservation of dentine, which is partially demineralized, but with preserved regeneration capabilities, which are highly expressed in the permanent teeth of children [23,24]. This study has concluded that in the first molars, the dentine carious lesions with occlusal localization are characterized by darker colors of carious dentine and a relatively hard consistency. The results of this study confirm the idea that darker color and harder dentine consistency are probable indicators of a more slowly developing carious lesion, while lighter color and softer consistency – of a faster developing carious lesion [25].

In our study we found that the newly erupted permanent first molar evince high prevalence of cavitated carious lesion, which means that there is a significant risk of affecting the highly exposed pulp. The features of the carious process in these teeth makes them especially appropriate for applying the minimal invasive methods of treatment. The analysis of the results shows that in the first permanent molars the more slowly progressing carious lesions are predominant. This circumstance has been the basis for trying to develop methodologies for a minimally-invasive treatment of these carious lesions, with data being found in scientific literature in recent years about a number of authors working in this direction [26-28]. The aim is to develop alternative methods and methodologies for a treatment which will lead to an additional slowdown and/or arrest of the carious process in the dentine and provide conditions for the activation of the natural defense mechanisms of the pulp-dentine complex [29,30]. The prevalence of occlusal dentinal caries lesion in the newly erupted permanent molars and their early inclusion in the cycle of "caries-restoration-replacement of restoration" draws our attention to the need of an application of new therapeutic methods of minimally-invasive treatment. The aim is to ensure the preservation of integrity of the pulp and apply the biological approach.

5. Conclusions

1. Dentine carious lesions D3 with occlusal localization in the permanent first molars are plausibly more numerous than the carious lesions

with approximal and cervical localization;
2. In the permanent first molars, the dentine carious lesions with occlusal localization are characterized by darker colors of carious dentine and a relatively hard consistency;
3. The more slowly progressing carious lesions are predominant in the permanent first molars.

Author Contributions

NM: contributed to formulating the concept, protocol, data gathering, analysis and interpretation

of the data. NI: contributed to the analysis, interpretation of the data and critically revised the manuscript. Both authors agree to be accountable for the content of the work.

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CV

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Questions

1. What is the most common location of caries in the permanent first molars?

- ☐ a. Approximal;
- ☐ b. Cervical;
- ☐ c. Occlusal;
- ☐ d. Other.

2. Which of the following most fully and accurately describes the causes of occlusal caries in the first permanent molars?

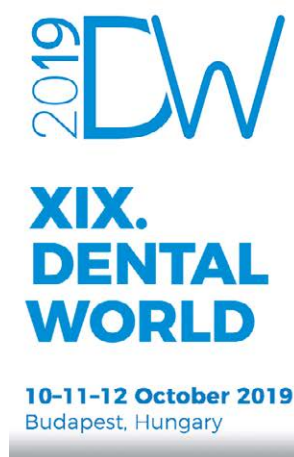
- ☐ a. Deep and retentive fissures; unsatisfactory oral hygiene habits;
- ☐ b. A thin and slightly mineralized layer of enamel; unsatisfactory oral hygiene habits; difficult diagnosis;
- ☐ c. Deep and retentive fissures; a thin and slightly mineralized layer of enamel; unsatisfactory oral hygiene habits; availability of timely and adequate prevention;
- ☐ d. Deep and retentive fissures; a thin and slightly mineralized layer of enamel; difficult diagnosis; unsatisfactory oral hygiene habits; lack of timely and adequate prevention.

3. What is the characteristic of carious dentine in the occlusal caries of the permanent first molars?

- ☐ a. Dark and relatively hard dentine;
- ☐ b. Dark and soft dentine;
- ☐ c. Light and soft carious dentine;
- ☐ d. Light and relatively hard dentine.

4. Which type of lesions prevails according to the speed and nature of the carious process in the occlusal caries of the permanent first molars?

- ☐ a. Rapidly progressing carious lesions;
- ☐ b. Slowly progressing carious lesions;
- ☐ c. Both;
- ☐ d. Neither.



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ALTERNATIVE METHODS FOR ACCELERATING THE RATE OF ORTHODONTIC TOOTH MOVEMENT: LITERATURE REVIEW

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ABSTRACT

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Background: The rate of orthodontic tooth movement depends on two general factors: the forces used in order to cause orthodontic tooth movement and respectively the individual (biological) response of the body to these forces.

Objective: The aim of this review is to offer an overview of the factors that has been mentioned in literature to accelerate the biologic response to orthodontic forces.

Data Sources: PubMed, Google Scholar and Scopus databases were used.

Study selection: We included in our study controlled clinical trials, but also randomized controlled trials and even cases series with more than 5 subjects that aimed to evaluate alternatives methods in accelerating the rate of orthodontic tooth movement. Publications published until April 2018 were included.

Data Extraction: All the factors that had been mentioned in literature to have a positive influence on the rate of orthodontic tooth movement were synthesized and described as a review. These methods are the followings: physical, surgical and chemical agents. Physical factors are easy to apply, surgical factors are invasive and the pharmacological agents we described in this article are: prostaglandin E2 (PGE2) and vitamin D3.

Data Synthesis: The alternatives methods that accelerate the rate of orthodontic tooth movement modulate the biologic response of the periodontal ligament to the mechanical forces. Vitamin D3 was mentioned as the most biopotential agent in accelerating the rate of orthodontic treatment. Although it has biomodulator effect on bone tissue, supplementary studies are needed in order to clarify what is the exact reduction of orthodontic treatment period.

Keywords: Accelerated orthodontic tooth movement; Rate of orthodontic tooth movement; Orthodontic treatment; Biologic response.

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 **Peer-Reviewed Article**

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1. Introduction

Recently, it has been mentioned in literature many methods for accelerating the rate of orthodontic tooth movement. The rate of orthodontic tooth movement depends on the forces used in order to cause orthodontic tooth movement and the individual response (the biological response) of the body to these forces.

Regarding the optimal forces used in order to determine the orthodontic tooth movement, Schwarz established that the forces used to move the teeth must be equal to the capillary pressure on the periodontal ligament. The forces situated below this threshold do not cause any tooth movement, while the forces that exceed this level cause avascular area on the periodontal ligament. While the forces

are applied on the tooth, the resorption process is directly influenced by the number of the recruited osteoclasts in the local area [1].

Secondary, the cell response of the body to orthodontic tooth movement can be accelerated by many factors.

The aim of this article was to update the information mentioned in literature regarding the possibilities to accelerate orthodontic tooth movement.

2. Methodology

A literature search in PubMed, Google Scholar and Scopus databases was performed in order to find randomized controlled trials, controlled clinical trials, clinical cases with at least 5 subjects that aimed to evaluate the alternatives methods that accelerate the

rate of orthodontic tooth movement. Publications published until April 2018 were included. We used the following keywords: (drugs OR medicaments OR pharmacological agents OR vibratory stimulation OR surgical methods) and (accelerated orthodontic tooth movement OR increased orthodontic tooth movement). The factors that can influence positively the rate of orthodontic tooth movement are presented in a form of literature review.

3. Results

3.1. Physical stimuli

Physical stimuli used in association with active orthodontic tooth movement in order to accelerate the rate of orthodontic tooth movement are the following: photobiomodulation, low level laser therapy, low frequency electromagnetic fields, vibrations, low-intensity pulsed ultrasound.

Low level laser therapy and low-intensity pulsed ultrasound were used in order to accelerate orthodontic tooth movement because they have bio-stimulatory effects [2]. In cell-culture experiments, it has been shown that low-intensity pulsed ultrasound application cause an effect on osteoblastic cells. These osteoblastic cells respond by producing local factors: bone morphogenetic proteins (BMP), growth factors (FGF, TGF-beta), and cytokines (IL). These local factors trigger new osteoblastic cells. Also, it has been shown that low-intensity pulsed ultrasound application has an effect on osteoclastic cells in cell-culture experiments. Moreover, the studies that were done on animals, shown that the application of low-intensity pulsed ultrasound caused an acceleration of the process that lead to new bone formation.

The pulsed electromagnetic fields (PEMFs) application influence bone metabolism [3]. Several studies demonstrated that electromagnetic fields accelerate the bone formation.

3.2. Surgical procedures

Several surgical procedures were performed in order to reduce the rate of orthodontic treatment: corticotomy, dental distraction, piezocision, section of the periodontal ligament.

Alternatives methods used in association with conventional orthodontic therapy cause an augmentation of the rate of orthodontic tooth movement compared with orthodontic treatment only. This phenomenon is related to the effect of stimulation of bone turnover and also to accelerated cellular activity in the periodontal ligament [4].

3.3. Pharmacological agents

Regarding the pharmacological agents that contribute to the acceleration of the rate of orthodontic treatment mentioned in literature we cite: PGE2, vitamin D, parotid hormone, and thyroxine.

Prostaglandin E2 (PGE2) is one of the most studied pharmacological agent implicated in bone turnover which has an important role in the inflammatory

process. Their effect on the rate of orthodontic tooth movement was studied by various researchers using animals like monkeys or rats [5-8]. The results of their studies shown that experimental tooth movement was greater compared with the rate of control tooth after one single application or after multiple application, the rate of the tooth movement of the experimental tooth being depended of the administrated dose of PGE2 [5-8]. The action mechanism of the PGE2 is explained through the stimulation process of bone resorption acting directly on osteoclastic cells [9].

Vitamin D3 (calcitriol or 1,25 dihydroxycalciferol) is the active form of the vitamin D which is formed on dermis or it is obtained from alimentary sources and after the two hydroxylation on the liver and kidney respectively convert into the active form of vitamin D3 (calcitriol or 1,25 dihydroxycalciferol). Vitamin D3 in association with calcitonin and parotid hormone are implicated in regulation of the fosfo-calcic homeostasis. Moreover, vitamin D3 in its active form stimulates bone apposition and it has been shown that vitamin D receptors present both the osteoblastic and osteoclastic cells [8].

Studies in vivo shown an augmentation of orthodontic tooth movement after local administration of vitamin D3 [10,11,12]. These augmentations is related to both the role of the vitamin D3 in inducing osteoblastic cells proliferation [13] and stimulating osteoclastic cells activity [13]. The rate of orthodontic tooth movement for the experimental tooth was 60% greater than the rate of orthodontic tooth movement measured on control tooth.

Humans studies that demonstrate the clinically efficiency of locally administration of calcitriol in acceleration the rate of orthodontic tooth movement are reduced and inconclusive. In this regard, the only article one humans which evaluates the clinical efficacy of locally administrated calcitriol in accelerating the rate of orthodontic tooth movement is the article published by Al Hasani et al in 2011. The results of their study shown a rate of tooth movement grater with a percentage equal of 51% for the experimental tooth compared to the controls tooth [14].

The association of alternatives methods with conventional orthodontic therapy benefits of some advantages like: accelerated tooth movement, reduced treatment period time and even greater stability of the results obtained after orthodontic treatment. Physical stimuli are easy the applicate but necessitate special devices. Surgical procedures determine rapid tooth movements, but are invasive methods. As regarding the pharmacological agents, they are easy to administrate. Of all the pharmacological agents mentioned in this article, locally administration of calcitriol is the promissive way to reduce orthodontic treatment time. Vitamin D3 in its active biological form has several benefits when

is locally administrated: stimulates bone resorption inherent for any therapeutic tooth movement and promote bone apposition, helping optimizing the ratio between resorption and apposition in the periodontal ligament. In this way, the biological response to the biomechanical forces is optimized. Other agents, like prostaglandin E2 has an important effect in accelerating orthodontic tooth movement even when it is administrated on a single dose mode, but it has also a secondary effects, being responsible for inducing root resorption on experimental tooth. That's why the studies were reduced only to animals and were not been extended to humans beings.

4. Limitations of the current analysis

The articles that met the inclusion criteria were few because the randomized controlled trials, controlled clinical trials and respectively clinical cases with more than 5 subjects included that aimed to accelerate the orthodontic tooth movement are few.

5. Conclusions

Of all the alternatives methods presented in this article, locally administrated calcitriol (vitamin D3)

seems to be the most promissive way to accelerate the orthodontic treatment: it is an easy method to realize, it has no secondary effect. Although the results of previous study mentioned its important role in the biology of orthodontic tooth movement, the information regarding the overall reduced treatment period are absents. It will be interesting studying the amount of reduced orthodontic treatment period caused by locally administration of vitamin D3 and comparing this period to the one in which patients are following orthodontic treatment only.

Conflict of interest statement

The authors declare no conflict of interest.

Author Contributions

MDC, OND, LZ: wrote the manuscript. RMV, INZ: critically revised the manuscript.

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Questions

1. The most biopotent agent in accelerating the rate of orthodontic treatment is:

- ☐ a. Vitamin D3;
- ☐ b. Vitamin C;
- ☐ c. Vitamin D;
- ☐ d. Vitamin A.

2. The surgical procedures performed in order to reduce the rate of orthodontic treatment are the following, with one exception:

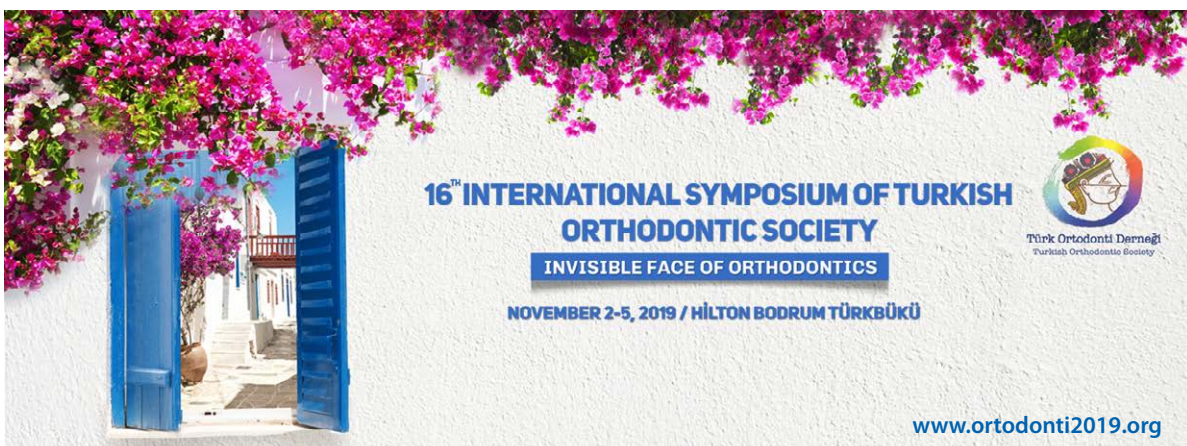
- ☐ a. Corticotomy;
- ☐ b. Administration of calcium;
- ☐ c. Piezocision;
- ☐ d. Dental distraction.

3. The pharmacological agents that contribute to the acceleration of the rate of orthodontic treatment are following, with one exception:

- ☐ a. PGE2;
- ☐ b. Vitamine D;
- ☐ c. Vitamin B;
- ☐ d. Parotid hormone.

4. The association of alternatives methods with conventional orthodontic therapy benefits have the following advantages, with one exception:

- ☐ a. Increased treatment period time;
- ☐ b. Accelerated tooth movement;
- ☐ c. Reduced treatment period time;
- ☐ d. Greater stability of the results obtained after orthodontic treatment.



THREE DIMENSIONAL PLANNING OF ORTHOGNATHIC SURGERY: A NARRATIVE REVIEW OF THE LEUVEN PROTOCOL

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Background & Objective: The aim of this paper was to present the virtual surgical planning (VSP) protocol for orthognathic surgery used in daily practice in the department of Oral and Maxillofacial surgery, University Hospitals of Leuven, Leuven, Belgium.

Data Sources: The different steps are presented in details explaining the protocol and showing an example of a bimaxillary case.

Data Synthesis: A variety of aspects have been discussed including the different possibilities with respect to the software used and their limitations. The pros and cons of that software compared to other commercial software tools have been highlighted.

Keywords: 3D planning; Orthognathic surgery; Virtual planning; Surgical planning; Virtual surgical planning (VSP).

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1. Introduction

Surgical virtual planning is currently possible due to the recent developments in maxillofacial radiology with the introduction of low dose cone beam computer tomography (CBCT) especially with CBCT systems scanning the full skull. The added value of virtual planning of orthognathic surgery has been proven which include a better and more accurate outcome as stated by Stokbro et al in their systematic review [1]. The virtual planning is significantly faster for single- and double-jaw surgery compared to the conventional method [2]. Moreover, Scheinder et al. recommended the use of virtual model surgery and the prefabricated three dimensionally (3D) printed splints to replace traditional orthognathic surgery as it becomes cost-effective [3]. Several virtual planning protocols have been published in the recent years [4-9]. One protocol was called the triple scan CBCT protocol [9] as it relied on 3 CBCT scans: first the patient is scanned with a thin wax bite in the mouth, which is followed by a limited dose scan with a tray of impression in the mouth. Then the last step is a high resolution scan of the patient's tray of impression. That protocol had the privilege of automating some preprocessing steps to allow for faster planning. However, this protocol has been replaced with the commonly used protocol with only one CBCT of the patient's full skull with a thin wax bite. A variety of software programs are available commercially implementing the one-scan protocol,

commonly known as Virtual Surgical Planning (VSP), but with different algorithms and tools whether semi or fully automated. In this paper, we present the VSP protocol used in University Hospitals of Leuven to virtually plan orthognathic surgery in daily practice after introducing improvements.

2. Methodology

The VSP protocol can be divided into 10 steps which will be explained in details in this section based on the Proplan software (Materialise, Leuven, Belgium) as used in the department of Oral and Maxillofacial surgery, University Hospitals of Leuven, Leuven, Belgium. There is a wizard specifically made for orthognathic VSP. An example is shown in Fig. 1. Ethical approval was obtained from the Ethical Review Board of the University Hospitals Leuven (S58253).

3. Results

1. Segmentation

The Digital Imaging and Communications in Medicine (DICOM) images of the patient are imported into the Mimics Inprint software (Materialise) for the segmentation step. Image segmentation is the process of assigning voxels with shared characteristics to an object. For VSP, the segmented objects are typically the full skull, the airway and the soft tissue and the segmentation is threshold based. The software tools allow separating the mandible

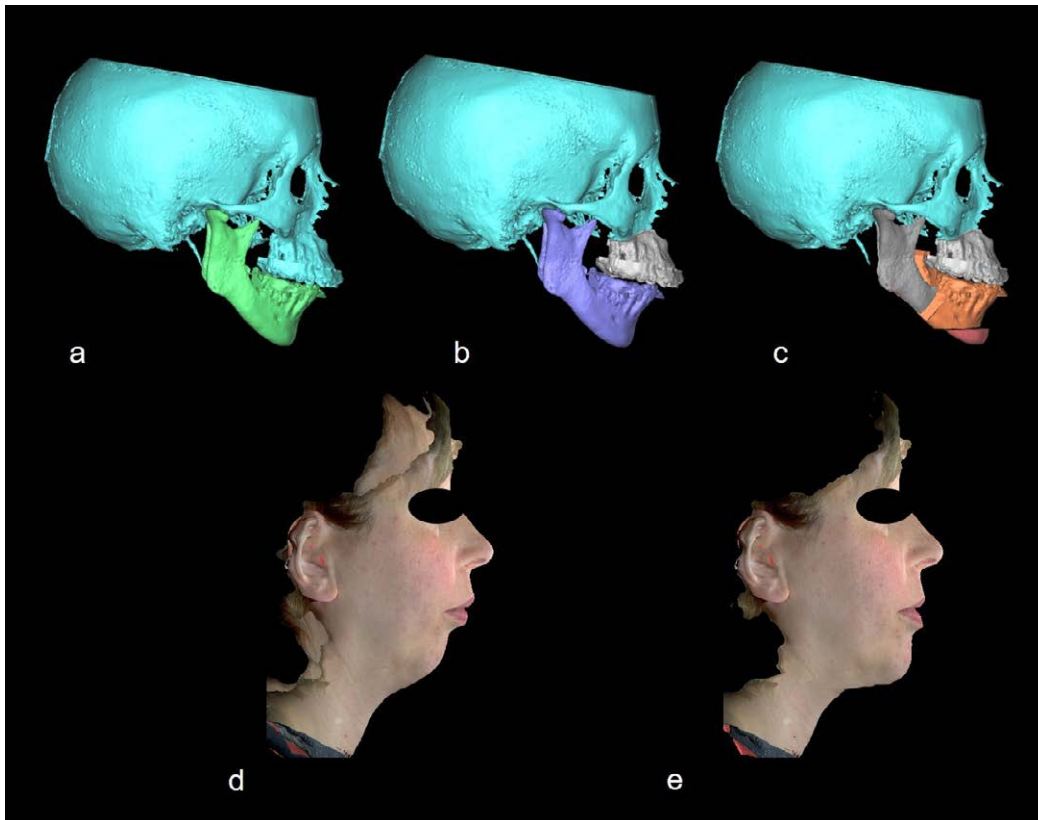


Figure 1. An example of a patient undergoing bimaxillary orthognathic surgery: a) the preoperative situation (steps 1 to 3); b) the intermediate situation (clinical plan was: Le Fort I advancement 1mm and translation 2 mm to the left); c) the final situation with registered BSSO and genioplasty advancement 6mm; d) the preoperative 3D photo; e) the soft tissue simulation (step 9).

from the rest of the skull semi-automatically and also refining the segmentation of each object as needed. For example when the condyles are not fully segmented, 3D interpolation tools can be applied to add the missing parts or when some artifacts are presented in the segmented objects, these can be manually removed. 3D models are then reconstructed and exported to the Proplan software.

1. Augmented models

Since the slice thickness of CBCT scans of a full skull is typically within the range of 0.3 – 1 mm, along with the artefacts introduced into the images due to the orthodontic brackets, the teeth cannot be used later for the fabrication of the splints. Therefore, high resolution scans of the upper and lower teeth are superimposed on the maxilla and the mandible respectively to create augmented models (maxillary and mandibular). The high resolution scans of the teeth can either be the plaster models scanned or direct scan using an intra oral scanner. Either way the output has to be 2 stereolithography (STL) files that are imported into the software and superimposed on the CBCT teeth using surface based registration (Fig. 1a).

2. Natural Head Position (NHP)

NHP is allowed in the software using three possibilities: manually, Frankfurt horizontal plane (FHP) or occlusal plane. In our protocol, we start with FHP then manually adjusted according to the clinical images of the patient.

3. Cephalometric analysis

The Leuven cephalometric analysis is used which is based on selected measurements of different analyses to analyze the hard tissue, soft tissue, proportions, angular and linear measurements. This analysis was previously developed in 2D and called Genk Surgical then adopted and extended into 3D. The landmarks, planes and measurements are once created. The software guides the user to place the landmarks then the measurements are automatically calculated and shown on the 3D models.

4. Nerve tracing

For patients undergoing a bilateral sagittal split osteotomy (BSSO), the mandibular inferior alveolar nerves are traced to assist the surgeon with the decision of handling the nerve during the surgery [10].

5. Osteotomy simulation

In the orthognathic wizard, the commonly used osteotomies such as Le Fort 1, BSSO, genioplasty are implemented with a user friendly guide to place specific points then press apply and your objects are cut according to the chosen osteotomy. Furthermore, other osteotomies are allowed using the curve tool in which the user can draw curved planes. This is commonly used for multiple pieces Le Fort 1 or any type of segmental osteotomies.

6. Occlusion registration

The STL of the occlusion cast is then imported into the software and registered using surface based registration on the maxilla then the BSSO mandibular

segment is registered onto the registered cast as explained by Shaheen et al. [11,12]. This order is followed for BSSO and bimaxillary cases. As for a single Le Fort 1 operation, the registration of the cast starts with the mandible then the maxilla is registered to the registered cast. The occlusion cast is the final required occlusion defined and set by the surgeon which can be the plaster cast models in final occlusion scanned by a high resolution CBCT or the printed models from the intra oral scanner scanned once more in final occlusion.

1. Virtual planning

For bimaxillary surgery, 3 objects are moved together (Le Fort 1, BSSO and registered occlusion cast). Manual or defined translations and rotations are allowed. Choices of rotations around cephalometric points are also possible. There is freedom of choice while visualizing the amount of movements on the selected cephalometric points (Fig. 1b,c).

2. Soft tissue simulation

Once the bony parts are displaced, the soft tissue simulation can be activated and immediately shown. The software allows visualizing the changes occurring on the soft tissue live while changing the bony structures which facilitates updating or improving the final plan. The soft tissue simulation algorithm is based on an improved finite element model [13]. Another advantage is the possibility to visualize the soft tissue simulation on a 3D photo which is superimposed on the soft tissue segmented object using a combination of landmarks followed by surface based registration (Fig. 1d,e).

3. Splints design

The final step of the orthognathic wizard is to design the splints. For single jaw operation, one final splint is needed. For double jaw surgery, a final and an intermediate splints are needed. The splint is designed by means of placing minimum three points on the upper jaw and three on the lower jaw. Then a first design is presented that can be further refined according to the need of the surgeon. Holes and different inclinations can also be implemented. The splints are then labeled and exported as STL files to be 3D printed.

4. Discussion

In this paper, we presented the protocol used in Leuven for VSP of orthognathic surgery which is also in line with the general VSP protocol recently used worldwide. Proplan is our choice for VSP but there are other software available on the market that follow the same protocol. However, in some detailed steps some software could be faster/slower, more or less accurate, etc. Some software tools limit the user to specific scanning protocols to automate the preprocessing steps for faster use, but, with more complex situations it could ask the user to manually interfere to solve some problems. Other software allow exporting the STL files to only the splints which limits the ability of the user to 3D print other

objects or to experiment with other technologies such as pre-bended metal plates. Soft tissue simulation is an important tool even though still not completely accurate especially around the nose and lips regions. However, it provides an estimate of what the patient will look like postoperatively, especially patients with obvious facial asymmetry. Some software does not allow superimposing 3D photos which makes it difficult to show the patients the simulation of their postoperative approximate situation due to lack of reality. A software without a clear wizard of the steps is not a strong user friendly tool. A wizard decreases human error as the user follows instructions. The less interference from the user, the more accurate the results will be therefore, more automated tools are needed but refinement tools are strongly recommended to overcome complex situations. Automatic final occlusion should also be implemented in the software but again with the possibility to perform manual corrections. Unfortunately not all software tools allow more than the predefined osteotomies which limits the use of the software for complex cases. Moreover, the lack of segmentation and only allowing visualization threshold restricts the capabilities of the software. After two validation studies [11,12] introducing improvements into the protocol, this specific protocol was implemented on 500 orthognathic patients from 2016. Prior to 2016, another software was used for only simulation purposes without using 3D printed splints and preoperative scans were CT based. An in-house tool was implemented to evaluate the accuracy of the achieved outcome versus the virtually planned maxilla for bimaxillary cases [14]. After testing on 55 skeletal class III patients, we concluded that our 3D VSP of maxilla was generally accurate when compared to the outcome achieved [15]. Both advantages and disadvantages need to be recognized. According to our experience in over 500 patients, the following advantages are clinically relevant:

- the 3D-reconstructed virtual head set is a great communication tool to be used when explaining the planned movements to the patient
- the introduction of the virtual planning process has profoundly influenced the life-cycle of the learning process in orthognathic surgery. The ease of superimposition allows the surgeon quickly to understand which distances and which directions of change are difficult to deliver preoperatively.
- postoperative problems with wafers can easily be solved by reprinting the stored STL-file of the wafer
- as the original position of the ascending ramus can be visualized during the entire planning process, lingual bony interferences distal to the tooth bearing area can be readily identified and anticipated, mainly during rotations of the lower jaw, as well as any bone grafting needs in the osteotomy gaps.
- the influence of the surgical plan on the airway can

- readily be predicted during the planning process
- refinements to the planning concerning pitch, roll and yaw are taken more often into consideration in the digitized planning process.
- it is the only way towards waferless planning with preprinted osteosynthesis plates and it allows the surgeons the freedom to choose between wafer and waferless transfer of the virtual surgical planning to the operating room
- the planning process allows mirroring techniques in hemimandibular or hemifacial hypoplasia to predict the amount of bone/soft tissue needed to reach symmetry.
- severe asymmetry cases are poorly planned in conventional planning tools where the lateral cephalogram remains the main starting file; VSP eliminates this shortcoming as the frontal plane is equally visualized as the sagittal plane
- cutting guides can be designed in delicate surgical osteotomy lines where the inferior alveolar nerve could be compromised.
- during the VSP the position of the condyles is checked and compared, readily identifying incongruences

According to our experience the following disadvantages need to be recognized:

- since the soft tissue changes at the area of the nose are poorly predicted, the amount of advancement of the maxilla remains a decision of mere clinical judgement
- the sagittal position of the maxilla remains as accurate as the initial waxbite. If the waxbite which had been used during planning was erroneous, the sagittal position of the maxilla will be erroneous too if wafers are used
- mild canting of the occlusal plane or upper midline deviations tend to be corrected in respect of the bony 3D reference lines instead of being judged against the soft tissues of the upper lip and nose.
- in multisegmental osteotomies of the upper jaw this digital planning process in no way facilitates designing transpalatal arches in order to stabilize the transverse dimension.
- the cost of software purchase, maintenance and upgrade is considerable and limits its in-house use only to high volume orthognathic practices.
- the workflow does not allow anticipating nor predicting postoperative condylar resorption, nor temporomandibular joint dysfunction

- presurgical planning with plaster casts allows the surgeon to easily identify which teeth need to be ground during or before surgery. This is a far more difficult exercise with VSP.
- if scanning of dental casts is used, the errors of plaster dental casts will be transferred into the VSP Virtual surgical planning is also prone to intrinsic weaknesses which urge for validation of methods used:
- 3D-CBCT superimposition algorithms are based on a variety of methods, each with their advantages and disadvantages, but hardly any of them can be considered accurate in growing individuals; different segmentation techniques can result in significant variances [16].
- the resulting differences in volume usually are depicted in color-maps, representing color-coded surface distances, allowing a qualitative interpretation of the changes but hardly any robust volumetric changes.
- many methods of superimposition using other anatomical structures than the mandible to study condylar resorption after orthognathic surgery fail to be accurate due to possible changes of condylar position between the two measurements.

A number of advantages of the availability of CBCT-data should not be attributed to VSP, such as the traceability of the inferior alveolar nerve, the positioning of the condyle in the fossa, the follow-up of qualitative changes of the condyle.

5. Conclusion

Virtual Surgical Planning can safely replace Custom Manual Surgical Planning but does not constitute a major advantage if its use is limited to digital splint design and production. It is a necessary step towards a renewed orthognathic planning process where the bony changes are reliably deducted from the desired functional and esthetic orthognathic outcome using validated processes and methods.

Author contributions

All authors contributed to reporting the case, performing literature review and drafting the manuscript.

Conflict of interest

No conflict of interest to declare.

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Questions

1. The software used by UZ Leuven for VSP is:

- ☐ a. Proplan;
- ☐ b. Simplant O&O;
- ☐ c. IPS;
- ☐ d. Mimics.

2. The UZ Leuven protocol was implemented on over:

- ☐ a. 50 patients;
- ☐ b. 150 patients;
- ☐ c. 300 patients;
- ☐ d. 500 patients.

3. One of the following is considered an advantage of VSP:

- ☐ a. Dependency on initial waxbite;
- ☐ b. Registering occlusion casts;
- ☐ c. Reprint of STL of wafers;
- ☐ d. Nerve tracing.

4. One of the following is considered a disadvantage of VSP:

- ☐ a. Dependency on initial waxbite;
- ☐ b. Registering occlusion casts;
- ☐ c. Reprint of STL of wafers;
- ☐ d. Nerve tracing.



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AGGRESSIVE DENTIGEROUS CYST IN A 9-YEAR CHILD: A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

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Aim: To report a case of aggressive dentigerous cyst associated with unerupted mandibular 2nd premolar.


Summary: Dentigerous cyst (DC) is a developmental odontogenic cyst, commonly occurs between the 2nd and 3rd decade and is associated with the crown of unerupted tooth. Unless infected, these cysts usually remain asymptomatic. However, they may develop as a result of apical spread of inflammation from primary teeth causing pain, swelling and bone destruction.

A 9-year-old child presented to the pediatric clinic with pain and swelling for 3 weeks. Clinical examination revealed endodontically treated lower left primary 2nd molar with slight mobility. Also, there was an obvious expansion of the buccal plate. The radiographs and CBCT revealed large cystic lesion around the crown of unerupted mandibular left 2nd premolar causing massive destruction of the buccal and lingual plates. The cystic lesion was treated by enucleation and removal of the unerupted 2nd premolar tooth. The histopathology confirmed a diagnosis of dentigerous cyst. The follow-up demonstrated uneventful healing and good prognosis.

Key learning points:

- It is crucial to follow-up any pulpally treated primary teeth.
- There is a potential Infection spread from infected primary roots to the follicular tissues of permanent teeth that could instigate unexpected pathology.

Keywords: Dentigerous Cyst; Enucleation; Marsupialization; Unerupted premolars.

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1. Introduction

Dentigerous cyst (DC) is the most common developmental odontogenic cyst that invariably occurs between the second and third decade and its incidence is second to the radicular cyst [1,2]. The incidence of the DC in young individual is quite low; less than 10% within the first 10 years of life [3]. The most common site for DC is the mandibular third molar region followed by maxillary canine region. Nevertheless, they may develop in association with unerupted mandibular premolars or supernumerary teeth, with a slight male predominance [4]. The pathogenesis of these cystic lesions is not fully understood. However, it is believed that the accumulation of fluids between the enamel surface and the reduced enamel epithelium (epithelial remnants of tooth-forming organs) leading to separation of the latter and cyst formation. The cyst encloses the crown of the involved tooth and is attached to the cemento-enamel junction. DCs are considered developmental in origin, from a

tooth follicle; however, there is a strong association between DC development and inflammation spreading from nonvital predecessor teeth [5-7]. Generally, DCs are presented with no symptoms and in many occasions are discovered during routine radiographic examination. Radiographically, they are presented as a unilocular radiolucency around the crown of unerupted tooth with a well-defined sclerotic border. In other instances, they may be symptomatic causing swelling, mobility of teeth, and delay in eruption or pain if it is infected [8]. Diagnosis of DCs is mostly based on the radiographic examination, however, a set of differential diagnosis need to be made in cases with aberrant presentation. Various treatment options of DCs have been advocated, including surgical removal of the cyst and associated tooth, elimination of damage to the affected permanent teeth and marsupialization. Nevertheless, complete removal of the pathological cyst lining along with the involved tooth is preferred to avoid any future recurrence [3,8,9]. The aim of this



Figure 1. Shows expansion of the buccal cortex.



Figure 2. Shows oval-shaped radiolucency and mesial root resorption of the left mandibular 2nd primary molar.

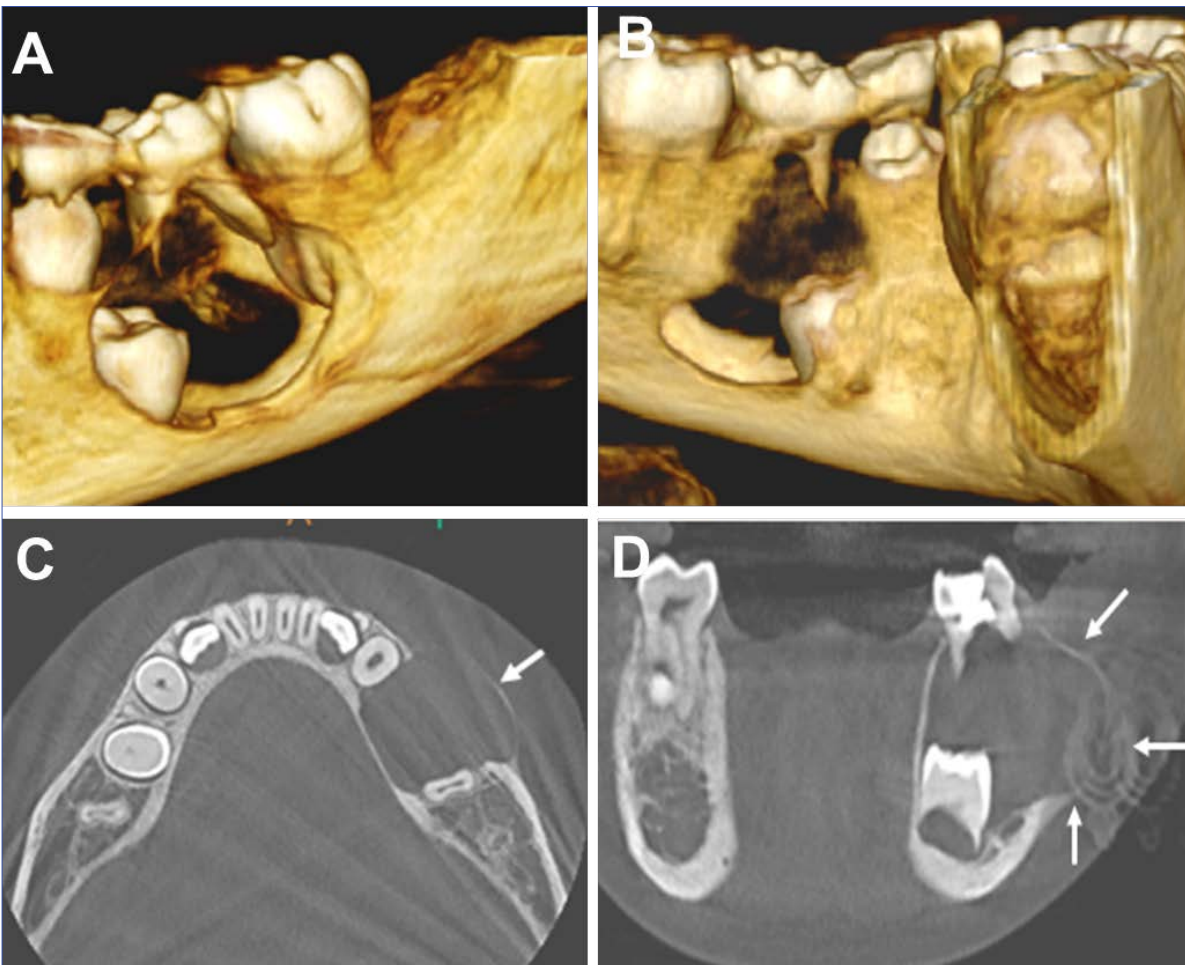


Figure 3. CBCT images (3D reconstruction) demonstrating massive destruction of the buccal cortex (A) and lingual cortex (B). CBCT axial view (C) and coronal view (D) demonstrating expansion of the buccal cortex and thinning of the lingual cortex.

report is to present a case of aggressive DC involving unerupted lower left second premolar causing massive bone resorption in a young female child.

As a routine procedure, all patients or their guardians attending RAKCODS clinic are required to electronically sign a consent form before launching any treatment procedure. Also, they are aware that any tissues taken from patients or a performed procedure may be utilized for teaching and

knowledge dissemination without any details that may identify individuals.

2. Case report

A 9-year-old female patient presented to the Pediatric Dentistry Department, RAKCODS clinic complaining of severe pain and swelling on the left side of the mandible for the last 4 weeks. On examination, the patient was healthy and the past medical history

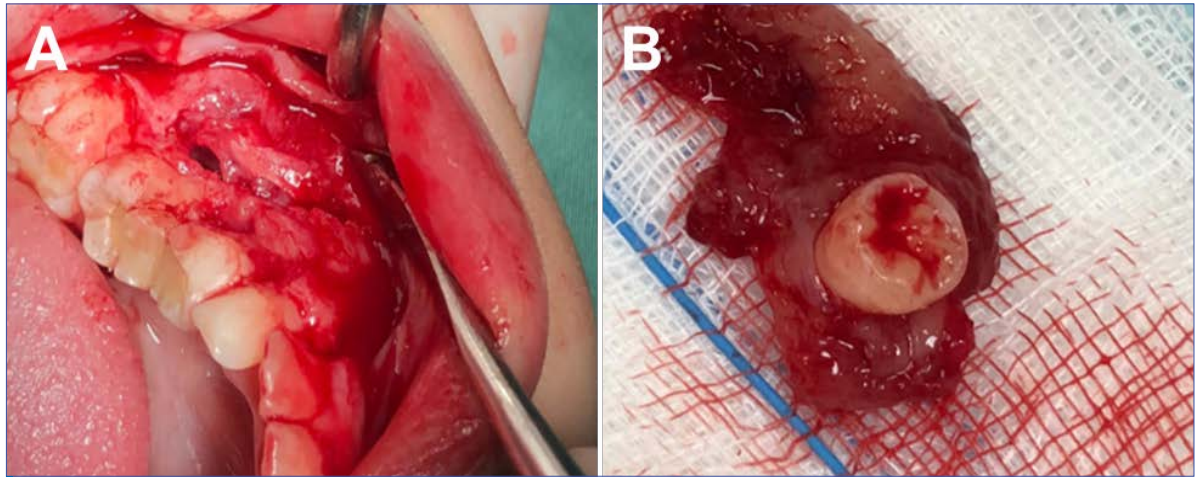


Figure 4. A - shows reflection of the buccal flap and exposure of the lesion; B - shows the attachment of the cystic lining to the cervical margin of the tooth.

revealed no relevant illnesses and the routine blood investigations were within the normal ranges. There was no history of hospitalization or trauma to the jaw. Extra-oral examination revealed a single diffuse swelling on the left side of the face with no sinus or active discharges. Intra-oral examination, showed a hard swelling in the 74, 75 regions with obliteration of the buccal vestibule (Fig. 1). The swelling was bony hard with expansion of the buccal cortex, with no evidence of the lingual cortex expansion. The primary left 2nd mandibular molar tooth was nonvisual, showing evidence of pulp therapy and composite filling. The tooth showed slight mobility and the adjacent soft tissues were normal with no signs of inflammation. The permanent first molar (36) was sound and the pulp vitality was not compromised. Orthopantomograph (OPG) revealed an oval-shaped unilocular radiolucency around the developing second premolar with partial sclerotic border. The mesial root of 74 showed resorption with loss of bone in the bifurcation area (Fig. 2). The cone beam computed tomography (CBCT) images revealed thinning of the buccal and lingual cortex (Fig. 3 A-D). Based on the clinical, radiographical and CBCT examination, a provisional diagnosis of dentigerous or bifurcation cyst was made. After consultation with the oral surgeon, it was decided to enucleate the cystic lesion surgically. A surgical incision extending from the distal aspect of 32 to the mesial aspect of 36 was established to expose the involved area. The primary molars (74 & 75) were removed and the area was explored. The cystic lining of the lesion was found attached to the cervical margin of the 2nd premolar crown revealing a DC (Fig. 4 A, B). Enucleation of the DC was established with extraction of the unerupted mandibular 2nd premolar, followed by primary closure of the wound. The whole specimen was kept in 10% buffered formalin and sent for histopathology examination. The histopathology examination reported a cystic fibrous wall lined by non-keratinized stratified squamous epithelium. Epithelial hyperplasia was noticed in many areas of the lining. The lamina



Figure 5. The radiograph demonstrates the regeneration of bone and the temporary space maintainer in place.

propria showed heavy infiltrates of acute and chronic inflammatory cells. These appearances are consistent with DC. The sutures were removed after one week, and the healing was uneventful. Soon after full eruption of 34 crown a space maintainer (band and loop) was fitted in place until further treatment (Fig. 5). Three months radiographic follow up demonstrated progressive bone regeneration filling the cavity and excellent soft tissue healing.

3. Discussion

DC is a benign developmental cyst associated with the crown of un-erupted tooth and is the second most common odontogenic cyst [10]. Radiographically, it appears as a solitary, well demarcated radiolucency enclosing a crown of impacted tooth. The hallmark of the cyst is the attachment of the follicular epithelium to the cemento-enamel junction. According to Zhang, et al. [11] the peak incidence is in the second and third decade. In contrast to this finding, Shibata, et al. [12] showed that the age range of discovery of the DC was 9-11 years. In the current case the child age was also 9-year-old. The noticed discrepancy may be attributed to the various studied ethnic groups of population.

DC is commonly associated with mandibular 3rd mandibular molar [13]. However, in the current case the cyst was associated with the unerupted mandibular 2nd premolar. Although such cases are relatively rare, a few cases have been reported [14]. Shibata et al. [12] studied the occurrence of DCs in association with succedaneous teeth during the transitional dentition phase and reported 77.1% prevalence in the premolar region. There have been several explanations for the development of DC. The experimental and clinical observations propose two types of DCs; inflammatory and non-inflammatory, instigated by different causes and develop at different stages of tooth development [15]. Three pathways were suggested for histogenesis of the DC. In the first scenario, the developmental DC forms from dental follicle and becomes secondarily infected as a result of a non-vital tooth. The second type occurs when a permanent successor erupts into radicular cyst that forms at apex of a non-vital deciduous resulting into a DC that is extra follicular in origin. Nevertheless, a radicular cyst developing at apex of primary tooth is extremely rare. The third possible cause is due to spread of peri-apical inflammation from a non-vital deciduous tooth to follicle of permanent successor [7].

Two main surgical approaches are usually followed for management of such cystic lesions; either enucleation or marsupialization. Several factors are taken into consideration, such as the size and location of the lesion, the amount of bone loss, integrity of the cystic wall, and its relation to vital structures. Conservative approach, the marsupialization has been advocated for management of DC in children to provide a chance for the unerupted tooth to erupt [16]. Nevertheless, it has a disadvantage that the pathology of the cystic lining is left behind and remains without thorough histopathological

examination. In our case, enucleation of the cyst including the unerupted tooth approach was chosen. Radiographically, there was substantial bone destruction and examination of the entire cystic tissues was deemed necessary. It was obvious that the cystic lining was attached to neck of the tooth and the histopathology report showed severe inflammation masking the classical microscopic appearance. Three months post-operative follow-up showed uneventful healing. The radiograph showed that the cystic cavity is completely filled with bone. The band and loop space maintainer was provided until further orthodontic treatment is instituted.

4. Conclusion

Development of DC in association with an unerupted successor due to inflammatory change at the apex of a deciduous tooth is not uncommon. Although, DCs are asymptomatic, they may cause pain, swelling and massive bone destruction. Therefore, close monitoring of pulpally treated primary molars is crucial to prevent or reduce the potential morbidity associated with the same.

Acknowledgments

We would like to appreciate the help of the of oral surgery department team in Saqr hospital, RAK for accommodating the case in spite of the busy oral surgery schedule.

Disclosure statement

The authors report no conflict of interest

Ethical Issue

The guardian of the patient has signed a consent form in his mother's tongue language with translation and understood that no identifying details would be declared in any form.

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Questions

1. A classical dentigerous cyst is classified as:

- ☐ a. Inflammatory;
- ☐ b. Developmental;
- ☐ c. Hereditary;
- ☐ d. Reactive.

2. Diagnosis of dentigerous cyst is mainly based on:

- ☐ a. Clinical examination;
- ☐ b. Biopsy;
- ☐ c. Radiographic examination;
- ☐ d. History taken.

3. Which of the following is a primary differential diagnosis of a dentigerous cyst associated with unerupted premolar tooth?

- ☐ a. Bifurcation cyst;
- ☐ b. Radicular cyst;
- ☐ c. Paradental cyst;
- ☐ d. Periodontal cyst.

4. A dentigerous cyst can be treated conservatively by:

- ☐ a. Cyst enucleation;
- ☐ b. Surgical extraction;
- ☐ c. Orthodontic;
- ☐ d. Marsupialization.

DOWNGRADING ADVANCED STAGE MEDICATION RELATED OSTEONECROSIS OF JAW (MRONJ) USING PEDICLED FLAP- TECHNICAL REVIEW WITH CASE REPORT

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Introduction: Medication related osteonecrosis of the jaw (MRONJ) is a locally destructive, and potentially devastating disease process that occurs in patients with a history of antiresorptive or antiangiogenic therapy. A widely accepted practice of surgical intervention in the management of advanced stage MRONJ involves segmental resection of the affected bone.

Aim: We propose to downgrade the stage with pedicled flaps for eradication of biofilm and vascular coverage with load sharing or load bearing constructs of the skeleton. As patients that receive antiresorptive or antiangiogenic therapy often have multiple medical comorbidities, this limits their surgical options and precludes them from being able to undergo expansive segmental resections or microvascular free tissue transfers and are left with palliative measures, thus compromising their care.

Summary: Either concept of MRONJ progression- bone metabolism or vascular breakdown is treated with immediate advancement of a pedicled local tissue flap and is performed for soft tissue coverage, thus providing a new vascular envelope and decreasing soft tissue toxicity to halt furtherance of the disease. Submental island flaps, nasolabial flaps, pedicled buccal fat pad flaps, and facial artery musculomucosal flaps have demonstrated success for longer than two years. This technique addresses downgrading MRONJ stage II and III in the mandible as a possible long-term treatment. This unreported innovative approach consists of marginal resection of the involved alveolar bone, while preserving the affected basal bone and subsequently provides reinforcement with a titanium bone plate, decreasing the chance of pathologic fracture.

Keywords: MRONJ; Flap; Pedicled flap; Medication related osteonecrosis of the jaw; Bisphosphonate related osteonecrosis of the jaw.

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1. Introduction

Medication related osteonecrosis of the jaw (MRONJ) is defined as exposed or probable bone in the maxillofacial region without resolution in 8-12 weeks in persons with a history of treatment with an antiresorptive or antiangiogenic therapy who have not received radiation therapy to the jaws [1]. This is an iatrogenic process with an elevated potential for morbidity and decreased quality of life. MRONJ typically occurs in patients with a history of long-term bisphosphonate, RANK ligand inhibitor, or angiogenesis inhibitor use with

a precipitating trauma to the maxilla or mandible, such as a dentoalveolar procedure [1,2]. MRONJ has a spectrum of presentation, as represented in its staging [1]:

MRONJ Staging

At Risk: No apparent necrotic bone in patients who have been treated with oral or IV bisphosphonates.

Stage 0: No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms

Stage 1: Exposed and necrotic bone for more than 8 weeks, or fistulae that probes to bone in patients

Table 1. Summary of the stages 0-3 on the left column; middle column is the current and the right column proposes the modification in management especially in the stage 2 & 3.

MRONJ Staging	Standard Treatment Strategies	Proposed Treatment Strategies
At Risk: No apparent necrotic bone in patient who have been treated with oral or IV bisphosphonates.	- No Treatment indicated - Patient education	No changes
Stage 0: No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms	Systemic management - Analgesics - Antibiotics	No changes
Stage 1: Exposed and necrotic bone, or fistulae that probe to bone in patients who are asymptomatic and have no evidence of infection	- Antibacterial mouth rinse - Clinical follow-up - Patient education and review of indications for antiresorptive and antiangiogenic therapies.	No changes
Stage 2: Exposed and necrotic bone, or fistulae that probe to bone, associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage	- Symptomatic treatment with oral antibiotics - Oral antibacterial mouth rise - Pain control - Debridement to relieve soft tissue irritation and infection control	- Symptomatic treatment with oral antibiotics - Oral antibacterial mouth rise - Pain control - Debridement of alveolar bone and immediate advancement of a pedicled local tissue flap
Stage 3: Exposed and necrotic bone or fistula that probes to bone in patients with pain, infection, and one or more of the following: exposed or necrotic bone extending beyond the region of the alveolar bone, resulting in pathologic fracture, extra-oral fistula, oroantral/ oronasal communication, or osteolysis extending to the inferior boarder of the mandible or sinus floor.	- Antibacterial mouth rinse - Antibiotic therapy and pain control - Surgical debridement /resection for longer term palliation of infection and pain	- Antibacterial mouth rinse - Antibiotic therapy and pain control - Surgical debridement / resection of alveolar bone, leaving basilar bone intact, placement of a supra or subperiosteal titanium bone plate and immediate advancement of a pedicled local tissue flap

Table 2. The table highlights the advantages to the vascular flap coverage to MRONJ management.

Advantages of Vascular Coverage
1. Improved blood supply to underlying bone
2. Improved medication delivery to underlying bone
3. Eradication of chronic biofilm colonization
4. Decreased inflammation
5. Halts disease progression

Table 3. Key notable points prior to sequestrum removal and vascular coverage of MRONJ.

Critical Steps Prior to Vascular Soft Tissue Coverage
1. Obtain cultures
2. Review imaging to determine the presence of pathologic fracture or need for internal fixation
3. Biopsy for recurrence of neoplastic process. Example- recurrence of multiple myeloma

who are asymptomatic and have no evidence of infection

Stage 2: Exposed and necrotic bone, or fistulae that probe to bone, associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage

Stage 3: Exposed and necrotic bone or fistula that probes to bone in patients with pain, infection, and one or more of the following: exposed or necrotic bone extending beyond the region of the alveolar bone, resulting in pathologic fracture, extra-oral fistula, oroantral/oronasal communication, or osteolysis extending to the inferior boarder of the mandible or sinus floor.

To date, there is no consensus on the MRONJ stage III treatment protocol.

The current management options range from the non-invasive, antibacterial mouth rinse, systemic treatment with oral antibiotics, and close follow up, to invasive management of potentially extensive debridement/resection of the maxilla or mandible. Conservative therapy is defined as no surgical intervention. This category includes the use of antibacterial mouth rinses and antibiotics and the removal of sequestra without local anesthetics. Ozone therapy and hyperbaric oxygen therapy are considered conservative therapeutic approaches, even though for neither of these evidence-based



Figure 1. MRONJ and bony sequestrum of right mandible in patient with history of antiangiogenic therapy.



Figure 2. Resection of necrotic alveolar bone is done, basal bone retained can be reinforced by plating (load bearing or sharing as needed) and submental island flap harvested using the same neck incision.

proof of benefit is available. Conservative surgical therapy is defined as a sequestrectomy, without resection or removal of non-sequestered bone. Whenever no mucoperiosteal flap is used a sequestrectomy is considered limited surgical therapy. Invasive surgical treatment includes anything from a sequestrectomy (starting with the use of mucoperiosteal flaps), with a resection of the affected bone up to the bleeding margins of bone, to segmental mandibulectomies and reconstructions with pedicled or microvascular free flaps.

Conservative management alone is insufficient to achieve full mucosal healing, but can be useful to stabilize disease progression in patients unfit for surgery. The use of hyperbaric oxygen therapy has no role in MRONJ grade III. The conservative surgical approach provides better results than a purely conservative approach: 75% achieve an improved condition, and of these, 54% achieve full mucosal healing. However, this group consists of a relatively small number of patients (n=48, distributed over four studies) [3,4,5]. The best treatment results for MRONJ stage III are observed in patients treated with invasive surgery. Invasive surgery without microvascular flap reconstruction yields a full mucosal healing rate of 85%, when six studies are combined [6-11]. This approach outperforms the 54% healing rate achieved with the limited surgical approach. This finding suggests that extensive bony resection up to the bleeding margins is more efficient than a sequestrectomy to achieve full mucosal healing in MRONJ stage III. Invasive surgery with microvascular flap reconstruction yields even better results, with a full mucosal healing rate of 97% [12,13]. However, many patients cannot undergo this kind of procedure, due to underlying comorbidity [14]. Bisphosphonate, RANK ligand inhibitor, and angiogenesis inhibitors are most commonly used for cancer-related conditions, and thus these patients

typically have numerous medical co-morbidities that often do not allow them to undergo extensive debridement/resection of the affected bone and reconstruction. Patients who are not able to undergo their indicated surgical treatment typically suffer deterioration of MRONJ and their antiresorptive or antiangiogenic therapy is often discontinued. This leaves the patient vulnerable to advancement of their cancer-related condition and their inadequate treatment allows for progression of MRONJ leading to involvement of previously unaffected bone, pathologic fractures and extra-oral and oronasal/oroantral fistula development. Soft tissue toxicity has been proposed in the pathogenesis of MRONJ. The mechanism is thought to involve the toxic effects of deposited bisphosphonates to local soft tissue and this might contribute to osteonecrosis of the jaw (ONJ) [2,15,16]. The inhibition of a variety of cell types to grow on bone surfaces previously treated with bisphosphonates has been demonstrated [17]. However, no tissue toxicity has been reported with RANK-L inhibitors. Given these considerations, we have developed a less invasive technique for the treatment of MRONJ while providing a vascularized soft tissue envelope and down grading the disease, irrespective of the cause of MRONJ.

2. Technique

The current standard practice in the treatment of MRONJ is to resect the affected portion of the jaws until the necrotic portion has been removed and bleeding bone is encountered [18]. As MRONJ is

a generalized affliction of the skeleton, the idea of debridement is to eradicate the biofilm of the exposed bone and aid in soft tissue coverage. In patients with progressive or advanced stages of the disease, large amounts of the supporting basilar bone is often removed, creating a loss of structure and scaffolding for the surrounding soft tissues. In these cases, we propose solely removing the affected alveolar portion of the bone, leaving the affected portions of basilar bone intact (Table I). Due to the inherent lack of strength of the necrotic basilar bone, a supra or subperiosteal titanium bone plate is placed spanning the length of the affected portion of the jaw.

This plate is anchored with bicortical locking screws on the proximal and distal aspects of the span. From there, soft tissue coverage is provided by way of a pedicled local flap (Table II). Depending on the location and size of the soft tissue defect, a flap is raised and rotated over the soft tissue defect, creating a tension-free closure. Submental island flaps, nasolabial flaps, pedicled buccal fat pad flaps, and facial artery musculomucosal flaps can be used to cover the defect.

Local pedicled flaps also help in oroantral fistulas and tori coverage. So far three patients with stage III MRONJ have been treated with this technique with a minimum follow-up of 13 months. All patients kept the necrotic basilar bone, protected by a lower border reconstruction plate, and no intraoral fistula recurred during the follow-up period. The technique is depicted in Figures 1-2.

3. Discussion

MRONJ has several proposed hypotheses of pathophysiology, including bone remodeling inhibition, inflammation and infection, angiogenesis inhibition, and immunity dysfunction.

Given the fact that MRONJ occurs in patients with a history of antiresorptive and antiangiogenic therapies and a host of different backgrounds most authors agree that the MRONJ pathogenesis is likely multifactorial.

One of the earlier noted hypotheses was that bisphosphates, especially nitrogen-containing bisphosphonates, caused direct soft tissue toxicity, inducing apoptosis and decreased proliferation of oral epithelial cells [2,15]. Invitro studies demonstrate that nitrogen containing bisphosphonates localize to epithelial tissue and bone and that alendronate is associated with esophageal irritation, requiring

special precautions during administration [19]. One of the facets to our proposed technique is to provide a new soft tissue envelope by way of advancing a pedicled flap. This not only provides a more robust blood supply to the underlying bone, but it allows for increased delivery of medications. It also eradicates the chronic colonization of debris and biofilm that causes persistent inflammation. Our observations show that this technique has been able to halt furtherance of the disease.

As previously discussed, MRONJ has a spectrum of presentation, as represented in its staging. Multiple studies have suggested treatment of the early stage MRONJ as more significant debilitation to the quality of life and pathological fractures happen in advanced stages of MRONJ. By removing the overlying infected soft tissue, debriding the alveolar bone and providing a new soft tissue coverage, this technique successfully downgrades MRONJ to a less severe state so that local measures, such as antibacterial mouth wash, are able to keep the symptom manageable.

Several other authors agree that a new vascular soft tissue coverage is essential to the long-term treatment of MRONJ (Table III) [20]. Commonly clinic based plain panoramic imaging in outpatients and cone beam computed tomographic imaging may be adequate to monitor bone status if there is appropriate soft tissue coverage.

Bone isotope studies are more specific for the turnover with biocontamination of the exposed bone. Additionally, osteoporosis from bacterial biofilm burden of the area is reduced from good vascularized soft tissue coverage as proposed here.

4. Conclusion

This technique demonstrates a novel approach to MRONJ treatment. Our more conservative technique of alveolar bone debridement, leaving the basilar bone intact, placement of a titanium bone plate for reinforcement and advancement of a local tissue flap for soft tissue coverage is ideal for patients who are unable to undergo a microvascular free tissue transfer or who should not terminate their antiresorptive or antiangiogenic therapy.

Conflict of Interest

All authors have no conflict of interest to declare.

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Dr. Srinivasa Rama Chandra is a Maxillofacial Surgery Specialist in Seattle, Washington. Having more than 24 years of wide experience, especially in Maxillofacial Surgery, Dr. Srinivasa Rama Chandra is affiliated with the Head and Neck Oncological and Microvascular reconstructive surgery at the Fred and Buffett Cancer Center and collaboratively operates with surgical oncologists, neurosurgeons and dermatologists.

Srinivasa Rama Chandra currently works at the Head and Neck Oncology and Reconstructive Microvascular- Oral and Maxillofacial Surgery, University of Nebraska Medical Center. Srinivasa conducts research in Head and Neck Oncology, Oral and Maxillofacial Surgery and Pathology. He specializes in Reconstructive, open skull base access and reconstruction, dermatological pathology and has additional appointment in dermatology.

Questions

1. MRONJ in which there is exposed and necrotic bone, or fistulae that probes to bone, associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage is:

- ☐ a. MRONJ stage 0;
- ☐ b. MRONJ stage 1;
- ☐ c. MRONJ stage 2;
- ☐ d. MRONJ stage 3.

2. Denosumab (monoclonal antibody) inhibits maturation of osteoclasts by binding to and inhibiting:

- ☐ a. RANK-Ligand;
- ☐ b. Osteoprotegerin;
- ☐ c. WNT-ligand;
- ☐ d. Sclerostin.

3. One of following treatments does not belong to the standard of care in MRONJ:

- ☐ a. Hyperbaric oxygen;
- ☐ b. Antibiotics;
- ☐ c. Sequestrectomy;
- ☐ d. Regional or distant soft tissue flaps.

4. XGEVA® is a:

- ☐ a. Nitrogen containing bisphosphonate;
- ☐ b. Non-nitrogen nitrogen containing bisphosphonate;
- ☐ c. Diphosphonic acid;
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The gold standard of removable dental appliances care - Dr. Mark's HyGenie® ergonomic oral hygiene device

This spring, while attending the 38th International Dental Exhibition (IDS), Cologne, Germany, I came across Dr. Mark's HyGenie® ergonomic oral hygiene device as a first innovation. Despite innovations dedicated to mobile dental devices, their care has remained unchanged.

Dr. Mark's HyGenie®, a simple solution to a common problem, has been created by an Australian, Dr. Mark Woakpoon, BDSc, who, after four years and thousands of hours of work dedicated to the creation process, has made the device available to the consumers as part of a project supported by the Australian Government Department of Industry, Innovation and Science based on marketing grant under the Entrepreneurs' Programme. In addition to Dr. Mark's HyGenie® device, Dr. Woakpoon has also developed Dr. Mark's SureGrip SureGrip® and Dr. Mark's DentalFresh.

Dr. Mark's HyGenie device is multifunctional, serves all types of removable dental appliances, cleans, stores and protects them.

The device made of durable materials lasts up to two years in daily use, proving its efficiency, accessibility and elegance. Each component was designed, and each material was chosen for the purpose of high-performance care of all types of removable dental devices.

The ergonomic device fits all ages, has a set of *clustered brushes* that rotate effortlessly in opposite directions. After inserting the removable dental device into the oral hygiene device, apply two to three drops of DentalFresh, pass the device under a stream of running water, make about 15-20 turns, and then flush it.

The rotating action causes the brushes to clean all surfaces of the removable dental device simultaneously.

The cleaned dental device can be worn immediately or stored in the oral hygiene device.

Dr. Mark's DentalFresh is a product designed to keep your dental device clean and fresh. The solution is a formula with pure peppermint oil, paraben- and alcohol-free, designed for daily use with a pH set to 5.0, which dissolves calculus accumulation, without affecting the dental apparatus.

I use and recommend Dr. Mark's HyGenie® multifunctional ergonomic device for clean, store, and protect purposes, to all my patients who carry different removable dental devices from sports mouthguards, orthodontic aligners, night guards, splints, retainers, to full dentures, overdentures, and partial dentures.

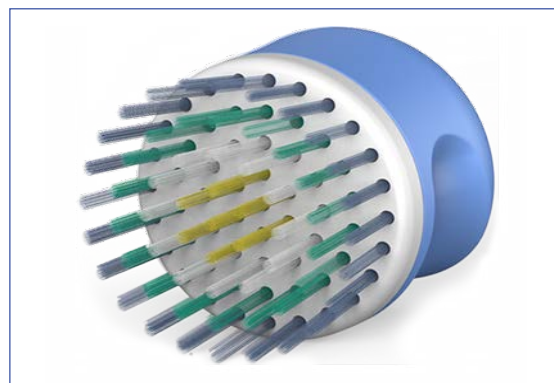
Let me also take this opportunity to warmly recommend it to you.



Dr. Mark's HyGenie device (Dr. Mark's HyGenie Pty Ltd., Perth, Wa 6000, Australia) <https://drmarkshygenie.com/>.



Dr. Mark's DentalFresh (Dr. Mark's HyGenie Pty Ltd., Perth, Wa 6000, Australia) <https://drmarkshygenie.com/>.



Dr. Mark's SureGrip Denture Brush (Dr. Mark's HyGenie Pty Ltd., Perth, Wa 6000, Australia) <https://drmarkshygenie.com/>.

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Editorial Director, Product News

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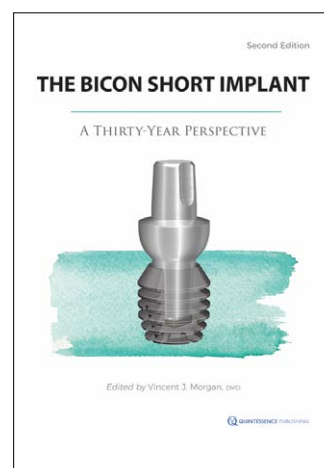
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The Bicon Short Implant **A Thirty-Year Perspective**

Editor: Vincent J. Morgan
Publisher: Quintessence Publishing Co. Inc,
Hanover Park, IL 60133, USA
Language: English
ISBN: 978-0-86715-781-9
Edition: 2/e
Publish Year: 2018
Pages: 325, illustrated
Price: 192.00 €



Thomas Driskell's Bicon dental implant design has proven to be effective due to the prosthetic restorations performed on this model over a period of more than 30 years. Additionally, the success of this design has been recognized by various dental implant manufacturers in Asia and Europe who have "assimilated" the design. Dr. Vincent J. Morgan has compiled a presentation of the Bicon system for a period of over 30 years which he called *The Bicon Short Implant*. In this book, the editor as well as 47 of the most experienced contributors describe their experience in using Bicon implants. The book is divided into 20 chapters with an index.

After a brief presentation of the history of dental implants we are presented with the Bicon system and the characteristics of implant-abutment prosthetic systems. Updating the data on the biological response to dental implants are updated so as to support the understanding of the engineering aspects of Bicon implants and the influence of the implant-abutment interface on peri-implant health.

In order to assess the performance of short implants, the five-year clinical experience of a novice Bicon clinician is analyzed (different locations of mandibular or molar application), compared with radiographic studies for 15 years and longer, concluding that short implants can solve many clinical situations, remaining a reliable and predictable solution over time.

Treatment planning and surgical protocols for this type of implant are described in detail, and then suggestive examples are given for different placement. To better understand the surgical techniques that aid oral implantology, the sinus lift techniques (internal, crestal window, lateral), the ridge splitting and the split-thickness flap are clearly described and illustrated suggestively. Also, the surgical techniques to approach atrophic ridges, as well as the maxillary and mandibular approach are given a detailed presentation supported by explicit iconography.

The factors that can affect the bone levels in short implant restorations are analyzed by exploring the limits of tolerable forces regarding crown-to-implant ratios (CIRs), excessive loading, bone gain or loss, abutment design and NSAIDs.

The clinical capabilities of the Bicon system in different compromised bone and soft tissues are exemplified in ameloblastoma, epidermolysis bullosa, type 2 diabetes mellitus, bone marrow transplantation, denosumab, bisphosphonate therapy, bilateral cleft palate, mandibular squamous cell carcinoma, irradiated bone, and bone voids. In addition to the incursion into the possibilities of restorations on short implants, we are offered a synthesis of the materials and techniques used in bone regeneration.

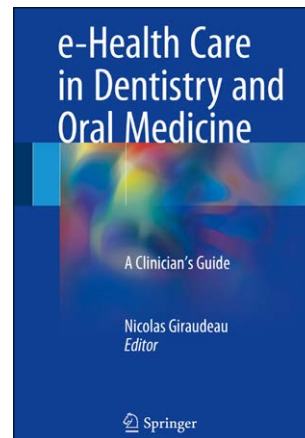
Dr. Vincent J. Morgan's book, *The Bicon Short Implant* is a compelling plea addressed to all clinicians and dental technicians who wish to provide patients with clinically limited situations the opportunity for a simple, predictable and effective dental implant system.

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The Books Review is drafted in the reviewer's sole wording and illustrates his opinions.

e-Health Care in Dentistry and Oral Medicine A Clinician's Guide

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AG, Switzerland
Language: English
ISBN: 978-3-319-69450-4
Edition: 1/e
Publish Year: 2018
Pages: 154, illustrated
Price: 140,39 €



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Dr. Nicolas Giraudeau of the University of Montpellier, France, managed to gather together the most famous specialists in *e-health* in the field of dentistry and oral medicine. The book he coordinated as editor, *e-Health Care in Dentistry and Oral Medicine* is divided into three parts and 12 chapters.

Part I, General Aspects of e-Oral Health, defines teledentistry and e-oral health tools, and then discusses the development of teledentistry from pilot projects to implementation, as well as the ethics and economics of teledentistry.

The second part, e-Health Care in Oral Medicine, presents in turn the fields of application of teledentistry, Oral Health Promotion, Implantology, Orthodontics and Oral Cancer, introduction, materials and methods, results, discussion and conclusion.

Part III, a global view on teledentistry, is a brief overview which presents the current state of e-health in different countries of the world: United States of America, Brazil and France.

This book argues in favour of e-oral health, which sums up information on information and communication technologies for oral health care. This book can be considered as an useful guide not only for dentists, but also for dental hygienists, dental assistants and professionals in other medical fields.

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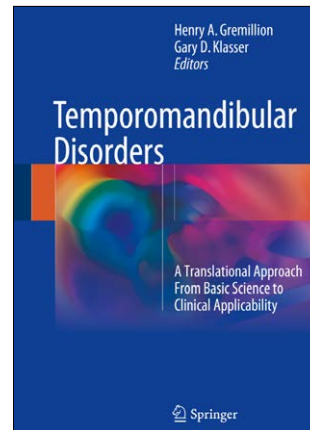
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Temporomandibular Disorders A Translational Approach from Basic Science to Clinical Applicability

Editors: Henry A. Gremillion, Gary D. Klasser
Publisher: Springer International Publishing AG,
Switzerland
Language: English
ISBN: 978-3-319-57247-5
Edition: 1/e
Publish Year: 2018
Pages: 217, illustrated
Price: 145,59 €



Lately, in current practice, clinicians have been increasingly dealing with the treatment of signs and symptoms of temporomandibular dysfunction. The book entitled *Temporomandibular disorders* seeks to cover topics from basics and principles to management principles in the treatment of TMD disorders.

The book is divided into 4 parts and 10 chapters.

Part I, *Fundamentals and Principles*, after presenting the embryology of the masticatory system, as a synthesis of the latest data from the literature, describes the anatomy of the masticatory system, on the osteology, myology, nerves and vessels at this level. Finally, the physiology of the masticatory system from its periphery to the central aspects is made.

Part II, *Normal Function of the Masticatory System* describes information regarding the masticatory and cervical muscles which contribute to the functions of chewing, swallowing and speaking, and the temporomandibular joint, so as to better understand the anatomy and physiology of this joint.

Part III, *Disfunction of the Masticatory System* first presents the myogenous disorders, starting from the explanatory models of muscle pain and diagnostic classification, and then the arthrogenous disorders, taking into consideration intraarticular consideration, inflammatory models of pain development, diagnostic classification, arthralgia and degenerative joint disease.

Part IV, *Management Principles*, discusses muscle-based conditions, temporomandibular joints and psychosocial considerations in TMD. To exemplify muscle-based conditions and temporomandibular joints specific management strategies are presented: patient education, physical therapy, pharmacotherapy, oral appliances, and finally psychosocial considerations on TMD treatment.

The book coordinated by Henry A. Gremillion and Gary D. Klasser, renowned specialists in Orofacial Pain, manages to gather the most relevant information from various disciplines of dental medicine, physical therapy, pharmacology and psychology, regarding temporomandibular disorders.

This book is useful to students, residents, academic and clinical care providers and in the library of every practitioner to treat TMD patients.

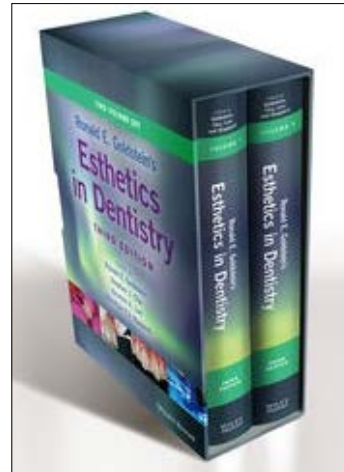
DOI: <http://www.stomaeduj.com> 10.25241/stomaeduj.2019.6(3).bookreview.3

The Books Review is drafted in the reviewer's sole wording and illustrates his opinions.

Ronald E. Goldstein's *Esthetics in Dentistry*

A Thirty-Year Perspective

Editors: Ronald E. Goldstein, Stephen J. Chu,
Ernesto A. Lee, Christian F.J. Stappert
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Language: English
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Pages: 1576, illustrated
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More and more frequently, in their daily activity, dentists are increasingly being asked to perform cosmetic and esthetic treatments.

Ronald E. Goldstein's *Esthetics in Dentistry*, Third Edition seeks to meet these requirements by providing an up-to-date reference to esthetic and cosmetic dentistry.

This edition is improved by twenty-three new chapters containing clinical cases and treatment protocols.

The book consists of two volumes divided in nine parts and forty-seven chapters accompanied by an index

The first volume has three parts.

Part 1, *Principles of Esthetics* introduces us to the field, presenting aesthetic concepts, the management of common psychological challenges, skills in esthetic treatment planning, digital smile design, dentistry marketing, legal considerations, practical clinical photography, proportional smile design and understanding color.

Based on these notions, in Part 2 we move on to *Esthetic Treatments*, details and aspects regarding cosmetic contouring, bleaching discolored teeth, adhesion to hard tissue, composite resin bonding, ceramic veneers, partial-coverages restorations and crown restoration.

Part 3, *Esthetic Challenges of Missing Teeth*, highlights the possibilities of prosthesis with the help of fixed partial dentures, removable partial dentures, complete dentures and dental implants.

The first volume is accompanied by several appendices: aesthetic evaluation form, functional aesthetic analysis, laboratory checklist, and Pincus principles.

The second volume consists of six parts.

Part 4, *Esthetic Problems of Individual Teeth*, informs us on the management of stained and discolored teeth, abfraction, abrasion, attrition, and erosion, chipped, fractured or endodontically treated teeth.

Part 5 talks about aesthetic challenges of malocclusion like: oral habits, diastema, crowded teeth, adult orthodontics and surgical orthodontic correction of dentofacial deformity.

Part 6 familiarizes us with aesthetic problems of special populations such as: child patients and older adults, appearance enhancement, plastic surgery, cosmetic adjuncts, and periodontal plastic surgery.

Part 7 discusses traumatic emergencies and aesthetic failures. Part 8 addresses the issues of chairside procedures, tooth preparation, impressions, esthetic temporization, try-in and cementation. Part 9 discusses aspects regarding aesthetic principles in building ceramic restorations, digital impression devices, CAD-CAM systems, and maintenance of esthetic restorations.

Each chapter of this book is accompanied by numerous illustrations and the latest references in the field. The book has over 3700 photographs that help the reader to better understand the concepts presented.

In conclusion, this new edition presents the golden rules in aesthetic and cosmetic dentistry, constituting a guide that should not be missing from the library of any practitioner and especially of those who focus specifically on dental esthetics.

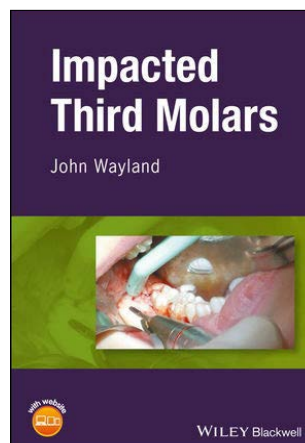
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The Books Review is drafted in the reviewer's sole wording and illustrates his opinions.

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Impacted Third Molars

Author: John Wayland
Publisher: Wiley-Blackwell, Hoboken,
NJ 07030, USA
Language: English
ISBN: 978-1-119-11835-0
Edition: 1/e
Publish Year: 2018
Pages: 266, illustrated
Price: \$130.00



Dr. John Wayland, founder of the Western Surgical and Sedation, has a mobile third molar practice in the San Francisco Bay Area, California, USA, and has authored the book entitled *Impacted third molar*, a surgical guide that provides all the information needed to remove the impacted third molars efficiently.

The book is divided into 10 chapters, followed by an index. It provides step-by-step procedures for removing impacted third molars and also includes practice management, legal aspects, and marketing advice.

After presenting the anatomy data of the two fossa, submandibular and infratemporal, we are introduced to the data regarding case selection and possible complications. We are acquainted with the equipment, instruments and materials, as well as the surgical principles and techniques.

Separate chapters present the pharmacokinetics and pharmacodynamics, sedation and emergency techniques in sedation and their monitoring. The book insists on the informed consent and describes possible cases of malpractice which are. The last chapter presents the author's experience regarding the mobile third molar practice, highlighting the benefits, promotion, IV sedation, guidelines, instruments, medical history, pre and postsurgical instructions and consent.

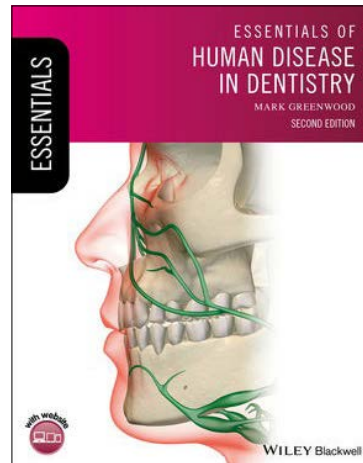
Each chapter is accompanied by compelling radiological drawings, photographs and images and up-to-date references in the specialized literature. This book is a beneficial surgical reference for a general dentist, specialist or resident, being accompanied by video support on the publisher's website.

DOI: <http://www.stomaeduj.com> 10.25241/stomaeduj.2019.6(3).bookreview.5

The Books Review is drafted in the reviewer's sole wording and illustrates his opinions.

Essentials of Human Disease in Dentistry

Author: Mark Greenwood
Publisher: Wiley-Blackwell, Hoboken,
NJ 07030, USA
Language: English
ISBN: 978-1-119-25185-9
Edition: 2/e
Publish Year: 2018
Pages: 376, illustrated
Price: \$83.25



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In current practice, a dentist has the opportunity to provide specialized care to patients with various general diseases.

Dr. Mark Greenwood, author of the second edition of *Essentials of Human Disease in Dentistry*, improved the first edition, namely *Textbook of Human Disease in Dentistry*, adding aspects related to general medicine and surgery, pharmacy, pathology and microbiology.

The book is an accessible guide on human disease for dentistry divided in 21 chapters, accompanied by an appendix and an index.

First of all, it presents the areas that need to be covered in the medical history, and then, the book presents the clinical observations and the examination of the hands, face, cardiovascular system, respiratory system, and vital signs.

The potential consequences of tissue injury, inflammation and anti-inflammatory drugs are then described. The author presents an overview of infection and infection control, methods of infection control, clinical examples of bacterial, viral and fungal infections and their management, and then an overview of abnormal immune response, abnormalities in the immune response, immunodeficiency, autoimmunity, and allergy.

The area of major cardiovascular disorders is accompanied by an overview of the main drugs used to treat risks from bacteremia-producing dental procedures and their impact on the practice of dentistry.

The impact of respiratory disorders, gastrointestinal disorders, kidney disorders, neurology disorders and muscular-skeletal disorders on dentistry is further explained.

Major dermatological disorders and their oral manifestations, major endocrine glands disorders, dental aspects of endocrine disorders, and implications for patient management are covered in the following chapters.

In describing pain and anxiety control we become acquainted with local anesthesia and adverse effects, vasoconstrictors, commonly used analgesics, drugs used in conscious sedation, adverse drug reactions, and their interactions.

The author also covers various aspects related to general oncology and oral complications of malignancy, child development, infections in childhood, medicine for the elderly patients, common psychiatric disorders, general aspects of hematology and hemostasis, and management of medical emergencies in dental practice. Each chapter is accompanied by suggestive schemes and figures, which can be accessed on the Internet, on the companion website of the publisher, multiple choice questions, together with relevant references on the topics covered. This second edition of *Essentials of Human Disease in Dentistry* is an invaluable resource for undergraduate dentistry students, for dentists preparing for the MFDS exam, and for all dental practitioners.

DOI: <http://www.stomaeduj.com> 10.25241/stomaeduj.2019.6(3).bookreview.6

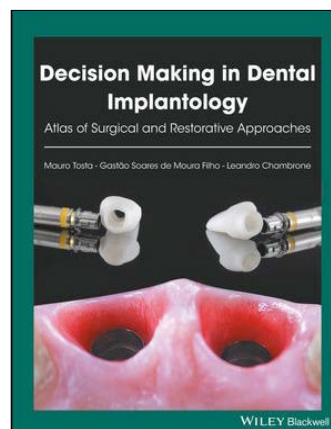
The Books Review is drafted in the reviewer's sole wording and illustrates his opinions.

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Decision Making in Dental Implantology

Atlas of Surgical and Restorative Approaches

Authors: Mauro Tosta, Gastão Soares de Moura Filho, Leandro Chambrone
Publisher: Wiley-Blackwell, Hoboken, NJ 07030, USA
Language: English
ISBN: 978-1-119-22594-2
Edition: 1/e
Publish Year: 2018
Pages: 410, illustrated
Price: \$187.25



The success of the management of patients requiring treatment with dental implants depends on how we think and put the decisions into practice.

The book entitled *Decision Making into Dental Implantology: Atlas of Surgical and Restorative Approaches* is the result of over 20 years of study in dental implantology, in private practice, as well as in clinical education.

The book is divided in 6 chapters accompanied by an index.

We are introduced to the current status of clinical practice with dental implants for completely and partially edentulous patients. The evidence quality rating / strength of recommendation of procedures proposed by the US Preventive Services Task Force (USPSTF) is described.

For the treatment plan of bone defects in the alveolar ridge we are presented with the characteristics of the most frequent osseous defect, the use of bone grafting materials for bone filling and the mechanism of osseous repair.

The rationale and clinical use of different treatment modalities in esthetically compromised areas is described suggestively with the help of 12 cases.

Clinical treatment alternatives for the posterior areas of the mandible and the maxilla are presented and illustrated by 15 cases.

The role of certain phases of performing successful implant-supported oral rehabilitation of completely and partially edentulous patients is exemplified by 8 cases.

Finally, we are presented with suggestions for the multidisciplinary construction of treatment approaches for cases evincing high esthetic and functional complexity based on 6 cases.

The book covers the latest concepts for implant dentistry, treatment planning for alveolar bone defects, esthetic areas, areas posterior and oral rehabilitation based on the latest references in the scientific literature. Decision making in dental implantology is a useful reference, illustrated with over 2000 color images, being a guide for periodontists, oral surgeons, prosthodontists, implant dentists and dental residents.

DOI: <http://www.stomaeduj.com> 10.25241/stomaeduj.2019.6(3).bookreview.7

The Books Review is drafted in the reviewer's sole wording and illustrates his opinions.

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Built-in smartness

The Xive S implant system is as individual as each patient. Its flexibility and ease-of-use have set the bar in dental practices and their laboratories for more than two decades.

Prefabricated and patient-specific components give you the greatest possible restorative freedom, enabling you to confidently and cost-effectively restore smiles. The unique TempBase concept, included with every Xive S implant, facilitates immediate temporary restorations. Convenient for you, even better for your patients. So, isn't it time you too experienced how Xive can simplify your everyday work?

Smartness in practice.

Xive by Dentsply Sirona Implants.



19th Biennial ESE Congress

Date: 12-14 September 2019
 Location: Vienna, Austria
 Event types: Conference, Exhibition, Workshops
 Visit event website: <https://www.e-s-e.eu/e-se-biennial-congress/vienna2019/index.html>

ICDO 2019 - 3rd Edition of International Conference on Dentistry and Oral Health

Date: 16-18 September 2019
 Location: London, UK
 Event types: Conference, Exhibition, Workshops
 Visit event website: <https://dental-conferences.magnusgroup.org/>

Annual OSHA Training and Compliance Seminars for Dental Professionals

Date: 25 September 2019
 Location: Denver, CO, USA
 Event type: Conference, Exhibition
 Visit event website: <https://kimlaudenslager.com/>

EAO 28th Annual Scientific Meeting

Date: 26-28 September 2019
 Location: Lisbon, Portugal
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://www.dds.world/event/eao-28th-annual-scientific-meeting/>

Implants Fixed and Removable Course

Date: 30 September 2019
 Location: Seattle, WA, USA
 Event type: Course, Exhibition, Workshops
 Visit event website: <https://www.koiscenter.com/courses/275-implants-course-fixed-and-removable/>

Implementing Complete Care Dentistry

Date: 03-04 October 2019
 Location: St. Petersburg, FL, USA
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://thedawsonacademy.com/event/implementing-complete-care-dentistry-4/>

Dentinal Tubules Congress 2019

Date: 03-04 October 2019
 Location: Oxford, UK
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://www.dentinaltubules.com/congress>

Bucharest Dentistry Summit 2019

Date: 03-05 October 2019
 Location: Bucharest, Romania
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://bds.dentaleaders.com/bucharest-dentistry-summit-2019-homepage-ro/>

Dentsply Sirona World 2019

Date: 03-05 October 2019
 Location: Las Vegas, NV, USA
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://www.dentsplysirona.com/en/news-article.html/content/newsroom/en/corporate-news/2019/dentsply-sirona-world-2019--a-unique-experience-for-dental-profe.html>

Sofia Dental Meeting 2019

Date: 03-06 October 2019
 Location: Sofia, Bulgaria
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://www.dds.world/event/sofia-dental-meeting-2019/>

World Congress of Esthetic Dentistry

Date: 10-12 October 2019
 Location: Barcelona, Spain
 Event type: Conference, Exhibition, Workshops
 Visit event website: http://www.sepes-ifed2019.sepes.org/w_eng_info_sede.php

Periodontal disease management

Date: 11 October 2019
 Location: Cardiff, UK
 Event type: Conference, Exhibition
 Visit event website: <https://www.bda.org/events/seminars/periodontal-disease-management-11-october-2019-cardiff>

European Congress for Ceramic Implant Dentistry – ESCI

Date: 11-12 October 2019
 Location: Horgen, Switzerland
 Event type: Conference, Exhibition, Workshops
 Visit event website: www.esci-online.com

Global Summit on Dentistry & Integrated Medicine

Date: 16-18 October 2019
 Location: Tbilisi, Georgia
 Event type: Conference, Exhibition
 Visit event website: <https://www.coalesceresearchgroup.com/conferences/dentistry/>

2nd Annual Congress on Orthodontics and Endodontics

Date: 21-22 October 2019
 Location: Melbourne, Australia
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://orthodontics-endodontics.dentalcongress.com/>

2019 ACP Annual Session

Date: 30 October-02 November 2019
 Location: Miami, FL, USA
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://www.prosthodontics.org/continuing-education/2019-annual-session/>

DenTech China 2019

Date: 30 October-02 November 2019
 Location: Shanghai, China
 Event type: Conference, Exhibition, Workshops
 Visit event website: <https://www.dentech.com.cn/en-us/index>

Botulinum Toxins and Dermal Fillers for Every Dental Practice

Date: 01-02 November 2019
 Location: Chicago, IL, USA
 Event type: Conference, Workshops
 Visit event website: https://www.ada.org/en/education-careers/continuing-education/ada-ce-live/2019-botox-course?utm_source=ADAorg&utm_content=livece&utm_medium=rotator&utm_term=botoxnov

16th International Symposium of Turkish Orthodontic Society

Date: 02-05 November 2019

Location: Bodrum, Turkey

Event type: Conference, Exhibition, Workshops

Visit event website: <http://ortodonti2019.org/eng/>**Preservation of Alveolar Bone in Extraction Sockets**

Date: 02 November 2019

Location: San Francisco, CA, USA

Event type: Conference, Exhibition, Workshops

Visit event website: https://reg.abcsignup.com/reg/event_page.aspx?ek=0036-0020-53cdc4011710471da3a3fbb42fe1e267**ID Infotage Dental Frankfurt 2019**

Date: 08-09 November 2019

Location: Frankfurt, Germany

Event type: Conference, Exhibition, Workshops

Visit event website: https://www.infotage-dental.de/id_m_home_de**11th Dental Facial Cosmetic International Conference**

Date: 08-09 November 2019

Location: Dubai, UAE

Event type: Conference, Exhibition, Workshops

Visit event website: <https://www.cappmea.com/aesthetic-dentistry>**EDAD 2019 - 23rd International Congress of Esthetic Dentistry**

Date: 08-10 November 2019

Location: Istanbul, Turkey

Event type: Conference, Exhibition, Workshops

Visit event website: <http://www.edad2019.org/en>**Powerlooking: Anterior Direct Composite Course**

Date: 14-15 November 2019

Location: Chicago, IL, USA

Event type: Conference, Exhibition

Visit event website: <https://dentaleventscalendar.com/event/powerlooking-anterior-direct-composite-course/>**28th Portuguese Dental Association Annual Meeting**

Date: 14-16 November 2019

Location: Lisbon, Portugal

Event type: Conference, Exhibition, Workshops

Visit event website: <https://www.ond.pt/congresso/2019>**SAO 2019 - Southern Association of Orthodontists Annual Meeting**

Date: 14-16 November 2019

Location: Orlando, FL, USA

Event type: Conference, Exhibition, Workshops

Visit event website: <https://www.saortho.org/current-meeting>**World Congress on Dentistry and Oral Health**

Date: 21-22 November 2019

Location: Kuala Lumpur, Malaysia

Event type: Conference, Exhibition, Workshops

Visit event website: <https://oralhealthconferences.org/>**ADF 2019 – The French Dental Association Annual Meeting**

Date: 26-30 November 2019

Location: Paris, France

Event type: Conference, Exhibition, Workshops

Visit event website: <https://www.adfcongres.com/en/>**20th SIOI National Congress**

Date: 29-30 November 2019

Location: Milan, Italy

Event type: Conference, Exhibition, Workshops

Visit event website: <https://www.sioi.it/evento/20-congresso-nazionale-sioi-a-milano-il-29-e-30-novembre-2019/>**Greater New York Dental Meeting 2019**

Date: 29 November-04 December 2019

Location: New York City, NY, USA

Event type: Conference, Exhibition, Workshops

Visit event website: <https://www.gnydm.com/>**Trends in Minimally Invasive Dentistry**

Date: 5 December 2019

Location: Lakewood, CA, USA

Event type: Conference, Exhibition

Visit event website: <https://www.harbordentalsociety.org/continuingeducation/course/77>**2019 Dental Implant Conference**

Date: 05-07 December 2019

Location: Chicago, IL, USA

Event type: Conference, Exhibition, Workshops

Visit event website: <https://www.aaoms.org/meetings-exhibitions/2019-dental-implant-conference>**CIDAE 2019 – 6th International Congress of Adhesive & Aesthetic Dentistry**

Date: 12-14 December 2019

Location: Brussels, Belgium

Event type: Conference, Exhibition, Workshops

Visit event website: <https://cidae.be/>**AEEDC Cairo 2019 - Dental Conference & Exhibition**

Date: 12-14 December 2019

Location: Cairo, Egypt

Event type: Conference, Exhibition, Workshops

Visit event website: www.index.ae

The Stomatology Edu Journal (Stoma Edu J) is a quarterly international journal, double blind peer-reviewed, open access journal to be database indexed, which accepts original articles for publication in all aspects of dental development and research. It addresses those interested in oral and maxillofacial sciences including students, graduates, postgraduates, educators, researchers, dental practitioners, those involved in dental industry and policy-makers relevant to the practice of dentistry.

1. Submission Instructions

The Stomatology Edu Journal (Stoma Edu J) publishes articles written only in English. All articles will be accompanied by the signed copyright form which can be returned by e-mail, fax (as scanned documents). All the responsibility for the originality of the material sent belongs to the author(s) alone. Each article will be evaluated by the peer-review committee composed of two independent peer-reviewers, in a blinded fashion, according to the peer-review protocol. All manuscripts must be original and exclusive. The Stomatology Edu Journal Editor will consider only articles that are original, have not been published elsewhere and have been submitted exclusively to the Stomatology Edu Journal. The manuscripts should be submitted online at www.ManuscriptManager.net/stom.

2. Ethics in publishing

The Stomatology Edu Journal (Stoma Edu J) and its editorial board fully adhere and comply to the policies and principles of Committee on Publication Ethics (COPE) (https://publicationethics.org/files/2008_Code_of_Conduct.pdf). Your manuscript should not contain any information that has already been published. If you include already published figures or images, please obtain the necessary permission from the copyright holder to publish under the CC-BY license. Plagiarism, data fabrication and image manipulation are not tolerated. Plagiarism is not acceptable in the Stomatology Edu Journal (Stoma Edu J) submissions. Plagiarism includes copying text, ideas, images, or data from another source, even from your own publications, without giving any credit to the original source. Reuse of text that is copied from another source must be between quotes and the original source must be cited. If a study's design or the manuscript's structure or language has been inspired by previous works, these works must be explicitly cited.

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3. Articles sent for publishing

The Stomatology Edu Journal (Stoma Edu J) publishes: original articles; reviews; case reports; technical procedures; consensus declaration coming from an association or from a group of specialists; letters to the editor. All articles must be up to 3,000 and 5,000 words for meta-analysis (the word count is for the manuscript text only). Letters to the editor must not exceed 400 words of text and have no more than 3 authors. Letters to the editor can be related to an article already published in the journal or it can represent original scientific contributions or events news/presentations etc. of interest for the reader.

4. Permissions and Ethics

For citations, tables, figures etc. which are not original, these must be accompanied by the written permission for their use and the full reference must be provided. Photographs of identifiable persons must be sent alongside the written permission of the person(s) and all regions that may allow the identification of the subject must be covered. The author must have obtained, for all studies including human subjects, the permission of the subjects to be part of the study whilst keeping their anonymity. By sending the article, the author declares that

he obtained this permission from all his subjects. All studies must respect the Helsinki Declaration (1975). For human and animal studies, the authors must have obtained the approval of the ethics committee from the University/Institute/etc. where the study was done. Consent for publication is required for studies involving human subjects - ALL case reports, letters that describe cases and some original articles. Cohort studies are exempt; instead evidence of IRB approval (name of IRB, date of approval and approval code/reference number) must be provided.

5. Manuscript preparation

The article must be written in conformity with the general recommendations of the International Committee of Medical Journal Editors. <http://www.icmje.org/icmje-recommendations.pdf>

The Stomatology Edu Journal (Stoma Edu J) uses double-blind review, which means that both the reviewer and author name(s) are not allowed to be revealed to one another for a manuscript under review. The identities of the authors are concealed from the reviewers, and vice versa. To facilitate this, please include the following separately:

Title page (with author details): This should include the title, authors' names and affiliations, and a complete address for the corresponding author including an e-mail address, Author Contributions, Acknowledgements and Curriculum Vitae.

Blinded manuscript (no author details): The main body of the paper (including the references, figures, and tables) should not include any identifying information, such as the authors' names or affiliations.

The articles must be sent either as a Microsoft Word 2000 document (*.doc) or as a Microsoft Word 2003 document (*.docx). The article will be written using Times New Roman font, size 12 for the characters with one and half (1 1/2) spaces between paragraphs. The manuscript must be sent in its final form. The pages will be numbered with the manuscript containing the following sections: title, authors, abstract, keywords, the text of article, contributions, acknowledgments, references, the figures and the tables legend.

A. The title of the manuscript will have a maximum of 100 characters without spaces, written in title case, centered capitals, and in 12 point bold Times New Roman font at the top of page. Abbreviations should be avoided within the title.

B. The author(s) will send their full name(s) and surname(s), the highest academic position, their full titles and their affiliations. All names are listed together and separated by commas. Provide exact and correct author names as these will be indexed in official archives. Affiliations should be keyed to the author's name with superscript numbers and be listed as follows: Laboratory, Department, Institute, Organization, City, State abbreviation (USA, Canada, Australia), and Country (without detailed address information such as city zip codes or street names).

The correspondent author will send his/her full name and surname, the highest academic position, his/her full title, his/her affiliation, his/her institution address, his/her telephone, fax and e-mail. The authors will send this information in the same format as that in the published articles.

C. The Structured Abstract

The abstract can have a maximum of 250 words. After the abstract, the author(s) must mention a maximum of 5 keywords. Keywords must be selected from **Medline Mesh**. Abbreviations are not accepted in the title or the abstract.

The abstract for Original Scientific Articles should be no more than 250 words using the following structure: Introduction; Methodology; Results; Conclusion.

The abstract for Review Articles should be no more than 250 words with the authors covering all the following information regarding the subject presented under the following subheadings: Background, Objective, Data Sources, Study Selection, Data Extraction, Data Synthesis.

The abstract for Case Reports should be no more than 250 words using the following structure: Aim, Summary and Key learning points: provide up to 5 short statements of the report.

The abstract for Clinical Articles should be no more than 250 words using the following structure: Aim, Methodology, Results and Conclusions.

D. The Article Text

Headings and Sub-headings

Except for special names (e.g. GABAergic), capitalize only the first letter of headings and subheadings. Headings and subheadings need to be defined in Times New Roman, 12, bold. You may insert up to 5 heading levels into your manuscript (not more than for example: 3.2.2.1.2 Heading title).

For original articles:

1. Introduction - a presentation of the most important aspects in the studied domain without doing a review of the literature. The purpose of this part is to present and backup the hypothesis on which the study was based.

2. Material and Methods - this section will include all required information so that the reader can verify the validity of the study including, but not limited to, subjects, measurements, statistics and ethics. The methods used should be discussed (why the methods have been chosen, which the limitations/advantages). A paragraph about the statistical analysis is required as well.

3. Results - the results of the study will be presented in a descending order of importance. An interpretation of the results will not be done in this section.

4. Discussion - the authors will present the way the results backup the original hypothesis, as well as the way in which the results are backed up or contradicted by the published literature. A paragraph must be dedicated to presenting the limitations of the study.

5. Conclusion - The conclusion presents the implications of this latest work. In addition, authors may consider discussing future plans or recommendations for future research etc. For all other types of articles, we recommend the use of a clear structure based on sections and sub-sections.

E. Author Contributions

The Author Contributions section is mandatory for all articles, including articles by sole authors. The Author Contributions statement must describe the contributions of individual authors and, in doing so, all authors agree to be accountable for the content of the work. Please list only 2 initials for each author, without periods, but separated by commas (e.g. AC, AS). In the case of two authors with the same initials, please use their middle initial to differentiate between them (e.g. AEC, ASC). Each author must be able to prove his active participation in the study by contributing to the concept, protocol, data gathering or analysis, their interpretation or by critically revising the manuscript.

F. Acknowledgments

Acknowledge persons who have made substantive contributions to the study. Specify grant or other financial support, citing the name of the supporting organization and grant number.

G. References

- The references will be written using the Vancouver style (<https://www.imperial.ac.uk/media/imperial-college/administration-and-support-services/library/public/vancouver.pdf>). All references that are identified with DOI (Digital Object Identifier) must be mentioned.

- For each reference use active links to the full text (DOI link), free PMC article, PubMed, Google Scholar, and Scopus pages, were they exist:

- For all references identified with DOI the full-text link must be the CrossRef hyperlink

Examples

Articles with DOI

Singbartl G. Pre-operative autologous blood donation: clinical parameters and efficacy. *Blood Transfus.* 2011;9(1):10-18.

[CrossRef] [Free PMC Article] [PubMed] Google Scholar Scopus

Articles without DOI

Mehta H, Shah S. Management of Buccal Gap and Resorption of Buccal Plate in Immediate Implant Placement: A Clinical Case Report. *J Int Oral Health.* 2015;7(Suppl 1):72-75.

[Full text links] [PubMed] Google Scholar

- The references will be numbered, in the order they appear in the text, in square brackets, as such: [3], [5,7-9].

- All sources found in the text must be present in the bibliography and all the papers mentioned in the bibliography must appear in the text.

- For references with more than 5 authors, list the first 3 authors followed by "et al."

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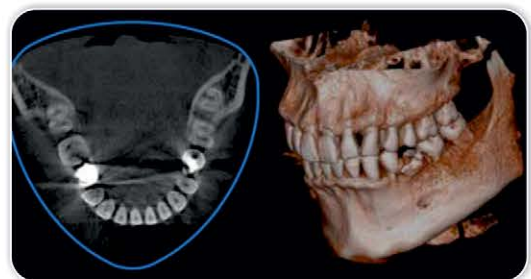
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