Stom Glas S COBISS. SR-ID 8417026 UDC 616.31 ISSN 0039-1743

# STOMATOLOŠKI GLASNIK SRBIJE

# SERBIAN DENTAL JOURNAL

Vol. 68 • Number 4 • October-Decembar 2021

http://www.stomglas.org.rs

Stom Glas S COBISS. SR-ID 8417026 UDC 616.31 ISSN 0039-1743

# STOMATOLOŠKI GLASNIK SRBIJE

# SERBIAN DENTAL JOURNAL

**Vol. 68 • Number 4 • October-Decembar 2021**

**www.stomglas.org.rs**

**Adresa uredništva**
Srpsko lekarsko društvo
Kraljice Natalije 1
11000 Beograd
Srbija

**Telefon:** +381 (0)11 409 27 76
**Email:** stomglas@bvcom.net

**Address of the Editorial Office**
Serbian Medical Society
Kraljice Natalije 1
11000 Belgrade
Serbia

**Phone:** +381 11 409 27 76
**Email:** stomglas@bvcom.net

**Časopis izlazi četiri puta godišnje.**
**The journal is published four times a year.**

**Cene pretplate za 2021. godinu** su: 2.400 dinara za pojedince, 4.800 dinara za ustanove i 50 evra za čitaoce van Srbije. Pretplata se može uplatiti Srpskom lekarskom društvu, ul. Džordža Vašingtona 19, 11000 Beograd, na tekući račun 205-8041-21 (Komercijalna banka AD, Beograd), sa pozivom na broj 04/1710, imenom časopisa i godinom za koju se pretplata uplaćuje.
Sve dodatne informacije mogu se dobiti na telefon 011/3245-149.

**Subscriptions prices for the year 2021** are: 2,400 RSD for individuals, 4,800 RSD for institutions, and 50 Euros for readers outside Serbia. Subscription order: Serbian Medical Society, Džordža Vašingtona 19, 11000 Belgrade; details of payment: bank account number 205-8041-21 (Komercijalna banka AD, Belgrade), invoice number 04/1710, with the name of the journal and the year for which you subscribe; beneficiary: Serbian Medical Society.
For further information, please contact us on stomglas@bvcom.net.

**Finansijsku podršku izdavanju časopisa pruža** Ministarstvo prosvete, nauke i tehnološkog razvoja Republike Srbije i Stomatološka komora Srbije.

**The publishing of the Journal is financially supported by** the Ministry of Education, Science and Technological Development of the Republic of Serbia and Serbian Dental Chamber.

sciendo



**ISSN 0039-1743**
**ISSN Online 1452-3701**
**COBISS. SR-ID 8417026**
**UDC 616.31**

**www.stomglas.org.rs**

# Stomatološki glasnik Srbije
# Serbian Dental Journal

**Izdavač** Srpsko lekarsko društvo
**Publisher** Serbian Medical Society

**Osnivač** Stomatološka sekcija Srpskog lekarskog društva
**Founder** Dental Section of the Serbian Medical Society



**Prelom teksta i priprema za štampu**
**Layout & Prepress**
Jasmina Živković

**Štampa**
**Printed by**
JP „Službeni glasnik", Beograd

**Broj primeraka**
**Number of copies**
300

sciendo

# Contents / Sadržaj

Serbian Dental Journal, vol. 68, N° 4, 2021


„Ne čudim se što vidim zle ljude,
ali se čudim što se oni ničega ne stide."
*Džonatan Svift*

Prošla je još jedna „uspešna" godina u kojoj smo više puta pobeđivali „sveprisutniji" virus, gde smo značajno „unapredili" život u „zlatnom dobu", i gde smo „kreativno i sistemski" uredili „nenormalnost" i dodatno učvrstili sopstvenu nemoć.

U godini koju ispraćamo, prozaičnost svakodnevnog života uglavnom su kreirale bezumne laži, šizofreni apsurdi i medijska propaganda o svekolikom napretku i „idiličnom" životu u „falsifikovanoj" stvarnosti.

Naš aktuelni trenutak najbolje objašnjava citat irskog satiričara i esejiste sa početka ovog komentara. Naime, protagonisti društvene stvarnosti koji nam oblikuju život, bez imalo stida „poganim" jezikom i „beščasnim" postupcima nedre jedino ožiljke koje je teško ukloniti, a projekcijom sopstvene nemoći vrlo sigurno trasiraju put u bespuće. Uz to besprizorna „retorika ulice" monoumno odzvanja sa svih strana i kao eho maligno kontaminira društveni ambijent.

U atmosferi straha, surovosti i nesigurnosti koja je dodatno oplemenjena „netalentovanom patetikom" i tragikomikom, optimizam bez osnova „izvire" samo kao nasušna potreba za očuvanjem svega „trenutno postojećeg".

Idolopokloničkі hvalospevi i primitivno poltronstvo su trenutno najvažniji parametri društvenog uspeha, a Šoićevsko poimanje vlasti, kultura nasilja i primitivizma osnov bitisanja „falsifikatora stvarnosti".

Da li je bosonogim hodom po izlomljenom staklu moguće izbeći povrede?

Jasno je da je bez obuće teško izbeći povrede. U aktuelnoj svakodnevici, gde prevashodno dominiraju strah, paranoja i vrednosna inverzija, površinu „nekontaminirane" staklene podloge je jedino moguće izbeći „obućom istine" izrađenom od materijala otpornog na neistine i manipulacije.

Beg iz svekolikog posrnuća, odnosno iskorak iz „moralnog brloga", moguć je samo uz pomoć istine i nepristajanjem na laži koje kao maligni tumor prožimaju sve segmente društva. Lučonoše i nosioci istine morali bi biti pre svega učeni i moralni. Oni su dovoljno hrabri i odlučni da se odupru prostakluku i bahatosti, ali i mudri i obrazovani da „ponude" lek da „oboleli organizam" opstane, makar i na aparatima.

Nasuprot nekulturi, lažima, manipulacijama, bahatosti i poltronstvu aktuelnih „zlovremnika", sloboda i hrabrost učenih ljudi su jedini „smisleni zrak" i jedini izlaz iz kolektivnog bezizlaza.

Laž i neukus se moraju „izopštiti" iz „svekolikog" diskursa, a atmosfera „dezorijentisanog bauljanja" ka besmislu „nadvladati" znanjem i kulturom i hirurški precizno „odstraniti" iz vidika izvitoperene realnosti.

Univerzitet i članovi akademske zajednice moraju iskoračiti iz zone ravnodušnosti i postati iskra za buđenje iz „kolektivne besvesti". Poljuljani vrednosni sistem se može povratiti samo znanjem i činjenjem učenih ljudi koji slobodno i kritički misle i hrabro i odgovorno stvaraju.

Neiscrpna energija obrazovanih (nasuprot onima sa kupljenim diplomama) i njihov moralni i etički kodeks, njihova lična i unutrašnja hrabrost da stalno produbljuju sopstvena znanja i kreiraju izvesniju stvarnost – jedini su put za pristojniju budućnost.

Uz iskrene čestitke za više sreće u novoj godini, i ovaj urednički komentar ću završiti citatom velikog Gandija: „Ako činite dobro, činite ga za sebe; ako činite zlo, činite ga sebi", jer je to životna paradigma, ali istovremeno i najbolji savet za „društvenu matricu" koju živimo.

*Prof. dr Slavoljub Živković*

ORIGINAL ARTICLE
ORIGINALNI RAD

https://doi.org/10.2298/SGS2104173O
UDC: 665.52:616.314

# In vitro study of essential oils efficacy as alternative solvents in endodontic retreatment

Vanja Opačić Galić[1], Savo Adžić[2], Bojan Dželetović[1],Tamara Vlajić[3]

[1]University of Belgrade, School of Dental Medicine, Department of Restorative Odontology and Endodontics, Belgrade, Serbia;

[2]Dental Clinic Adžić, Ivanjica, Serbia;

[3]University of Belgrade, School of Dental Medicine, Belgrade, Serbia

**SUMMARY**

**Introduction** The aim of this study was to investigate the solubility of gutta-percha points and various endodontic sealants in essential oils.

**Materials and method** Ninety-six gutta-percha points were divided into the four groups of 24 samples for every essential oil and subsequently divided into the three subgroups corresponding to the immersion times (2,10 and 15 min). The post-immersion amount was obtained for each. Endodontic sealers AHplus, Acroseal, Endomethasone N were included in the research. Samples were treated with corresponding oil for 10 min. Each sample was measured and the amount was obtained.

**Results** Orange oil was the most effective in dissolving gutta-percha compared to other tested essential oils ($p < 0.05$). Eucalyptol was more effective in dissolving gutta-percha than tea tree after 10 min ($p < 0.05$). There was no statistical significance in the effectiveness of essential oils in relation to the time of action (10 or 15 minutes) ($p > 0.05$). Most weight loss was recorded with Endomethasone for all solvents, but the highest in orange oil and tea tree, followed by eucalyptus and clove oil. Tea tree dissolved AH Plus more efficiently compared to Acroseal.

**Conclusion** Essential oils showed promising results in dissolving gutta-percha and sealers.

**Keywords**: solubility; gutta-percha; essential oils; retreatment

## INTRODUCTION

Despite high success rate, some endodontic treatments do not have a successful outcome after initial endodontic procedure for various reasons. In these cases endodontic retreatment is necessary. The position of the European Association of Endodontics is that postoperative monitoring of treated teeth is necessary for at least one year, and at least four years, if there was also apical periodontitis present [1]. The most common cause of primary endodontic treatment failure is insufficiently prepared and obturated root canals, insufficient hermetic sealing of the endodontic space, which allows the growth and development of residual microorganisms, especially in dentinal tubules, ramifications and accessory canals [2]. Root canal retreatment is a known issue in modern endodontic practice due to its complexity and inferior prognosis compared to endodontic therapy, which is performed for the first time regardless of etiology [3].

Since the main cause of failed endodontic therapy is a persistent infection, it is imperative that during the root canal retreatment the previous filling is removed completely. In most cases, this means removing gutta-percha and conventional root canal sealer for better chemo mechanical irrigation of the canal in order to neutralize residual bacteria in the root canal system [4, 5].

The use of solvents during treatment is long known procedure. Experiments and later clinical studies were performed with various gutta-percha solvents. Chloroform, xylene and rectified turpentine oil proved to be the most effective [6, 7, 8]. However, their toxicity to periapical tissue, therapists, and even potential carcinogenic effects have minimized their use in modern endodontics [9, 10, 11]. In the late 80's and early 90's of the XX century, various essential oils (eucalyptus, orange) appeared as possible substitutes for these solvents [6, 12]. Although no study has shown their superiority in dissolving gutta-percha and sealers over chloroform, their biocompatibility, safety during instrumentation of curved canals still gives them an advantage [2, 6, 13].

In the XXI century development of rotary instruments for dental canal instrumentation, many NiTi instrument systems (EndoSequence rotary file, Pro Taper Universal D1-D3) have appeared, which were designed exclusively for the purpose of retreatment [1, 14]. Although they have proven to be extremely successful and convenient to use, their role is still secondary to hand instruments, as most of them involve establishing working length with hand instruments [15, 16]. The role of ultrasonic instruments as well as lasers (Nd: YAG) has also experienced development [4, 17].

**Address for correspondence:** Vanja OPAČIĆ GALIĆ, School of Dental Medicine, Department of Restorative Odontology and Endodontics, Rankeova 4, 11000 Belgrade, Serbia; *vanja.opacic.galic@stomf.bg.ac.rs*

**The aim** of this study was to investigate the solubility of gutta-percha points and various endodontic sealants in essential oils.

## MATERIAL AND METHOD

Five essential oils were used in the research: eucalyptus (*Eucalyptus globulus* essential oil) (Eucalyptol, Cerkamed, Poland), sweet orange (*Citrus aurantium*) (Davidovac Zelena Apoteka, Serbia), tea tree (*Aetheroleum melaleuca*) (Kirka, Serbia), clove (Clove essential oil) (Eterra, Serbia), neem (*Azadirachta indica*) (Eterra, Serbia) and distilled water as a negative control.

### Gutta - percha solubility test

Commercial brand gutta-percha (Diadent, South Korea) # 80 with 2% tapper was used in the research. Ninety-six gutta-percha points were standardized at 10mm in length and each one measured on an analytical scale (Acculab, USA) twice. Pre-immersion weight was measured in grams and rounded to 4 decimal places (M1). The samples were divided into the four groups of 24 samples (eucalyptol, orange, tea tree and distilled water) and subsequently divided into the three subgroups corresponding to the immersion times (2, 10 and 15 min).

Samples were placed in 96-well flat-bottomed micro titer plates into which 180 µl of solvent was poured using an automatic eight-channel pipette (BIOHIT Health Care, Finland) at the room temperature. After the measured time periods, the samples were taken out of the well using a silicone-tipped medical tweezers, rinsed with 20 ml of redistilled water and let to dry for 24 h at 37$^0$C. After drying, the samples were again measured two times and a post-immersional weight (M2) was obtained for each. To obtain the lost mass of gutta-percha (Mg), the equation used was:

$$Mg = M1-M2$$

### Sealers solubility test

Three commercial endodontic sealers were included in the research: resin-based (AHplus, Dentsply, Switzerland), calcium hydroxide-based (Acroseal, Septodont, France) and zinc oxide-eugenol (Endomethasone N, Septodont, France).

Ninety standard plastic molds 2 mm high and 5 mm in diameter were individually measured on an analytical scale in grams (Mk) and divided into the five groups for each solvent tested (eucalyptol, orange, tea tree, cloves and distilled water). Subsequently, each group of 18 was divided into 3 subgroups corresponding to a particular sealer. The sealers were mixed according to the manufacturer's instructions and poured into molds, which were stored in a water bath at 37$^0$C, at an air humidity of 80% for 72 hours. After setting, each sample was re-measured twice and the pre-immersion mass of the mold sealer (Mks1) was obtained.

In 90 plastic molds 15 mm high and 20 mm wide, 1.8 ml of a suitable solvent was poured into which the molds with sealers were immersed. After 10 min, the samples were removed (using silicone-tipped medical tweezers), rinsed with 20 ml of redistilled water and allowed to dry at 37$^0$C for 24 h. Each sample was measured and the mass Mks2 was obtained.

The following equation was used to obtain the lost mass of the sealer (Ms):

$$Ms = (Mks1-Mk) - (Mks2-Mk)$$

The arithmetic mean, median and standard deviation were calculated for each group and subgroup. The obtained results were statistically processed using two-factor analysis of variance (ANOVA); one-way ANOVA (post-hoc Bonferroni test) or Kruskal-Wallis test if data distribution was not normal. The significance level was determined to $\alpha = 0.05$.

## RESULTS

The obtained results are shown in Tables 2-3 and Figure 1. Based on a previously conducted pilot study, essential oils that did not show solubility properties, neem oil and clove oil for gutta-percha, or neem oil for sealers were eliminated.

Orange oil was the most effective in dissolving gutta-percha compared to other tested essential oils ($p<0.05$) (Table 2). After only 2 minutes, it was significantly more effective than eucalyptol and tea tree. Eucalyptol was more effective in dissolving gutta-percha than tea tree after 10 min ($p<0.05$). There is no statistical significance in the effectiveness of essential oils in relation to whether they act for 10 or 15 minutes ($p > 0.05$) (Figure 1).

**Table 1.** Composition of sealers according to the manufacturer's specification
**Tabela 1.** Kompozicija silera prema specifikaciji proizvođača

| | | |
|---|---|---|
| AH plus | Paste A: Bisphenol A epoxy resin, Bisphenol F epoxy resin, Calcium Tungstate, Zirconium oxide, Silica, Iron Oxide Pigments<br>Pasta A: epoksidna smola Bisfenol A, epoksidna smola Bisfenol F, kalcijum-volframat, cirkonijum-oksid, silicijum, pigmenti gvožđe-oksida | Paste B: Dibenzyldiamine, Amino-adamantane, Tricyclodecane-diamine, Calcium tungstate, Zirconium oxide, Silica, Silicone oil<br>Pasta B: dibenzildiamin, amino-adamantan, triciklodekan-diamin, kalcijum-volframat, cirkonijum-oksid, silicijum-dioksid, silikonsko ulje |
| Acroseal | Base: Hexamethylene tetramine, Bismut carbonate, Hydrogenated rosin, paraffin oil, Venice terentine, Enoxolone<br>Baza: heksametilen-tetramin, bizmut-karbonat, hidrogenizovana smola, parafinsko ulje, venecijanski terpentin, enoksolon | Catalyst: Bismuth carbonate, calcium hydroxide, Diglycidyl ether bisphenol A, yellow iron oxide<br>Katalizator: bizmut-karbonat, kalcijum-hidroksid, diglicidil-etar bisfenol A, žuti gvožđe-oksid |
| Endomethasone | Powder: Zinc oxide, Hydrocortisone acetat, Thymol iodid, 15% barium sulfate, Magnesium stearate<br>Prašak: cink-oksid, hidrokortizon-acetat, timol-jodid, 15% barijum-sulfat, magnezijum-stearat | Liquid: Eugenol, Pepermint oil containing (E)-anethole and dipentene<br>Tečnost: eugenol, ulje pepermenta koje sadrži (E)-anetol i dipenten |

**Table 2.** Means and standard deviation of dissolution weight loss in miligrams of gutta-percha in the respective test solvents
**Tabela 2.** Srednja vrednost i standardna devijacija gubitka mase u miligramima gutaperke u testiranim rastvaračima

| | Orange oil<br>Ulje narandže | Tea tree<br>Čajno drvo | Eucaliptol<br>Eukaliptol | Disstilled water<br>Destilovana voda |
|---|---|---|---|---|
| 2 minutes<br>2 minuta | 1.3<br>(0.513) | 0.4<br>(0.225) | 0.3<br>(0.501) | 0<br>(0.129) |
| 10 minutes<br>10 minuta | 4.1<br>(1.226) | 0.7<br>(0.507) | 1.6<br>(0.561) | 0<br>(0.126) |
| 15 minutes<br>15 minuta | 6.3<br>(1.214) | 1<br>(0.56) | 2.8<br>(1.562) | 0<br>(0.1) |

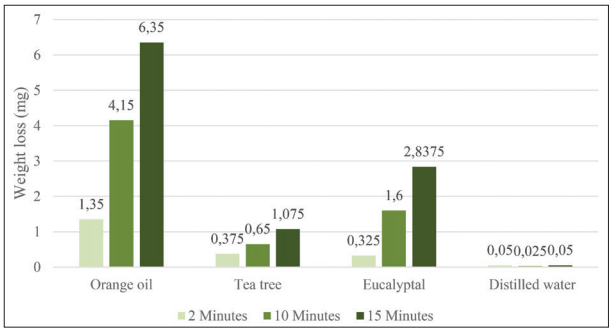


**Figure 1.** Time-dependent solubility effect of solvents on gutta-percha. Solubility is expressed as weight loss in miligrams
**Slika 1.** Efekat rastvaranja gutaperke u zavisnosti od vremena. Gubitak težine izražen u miligramima

**Table 3.** Means and standard deviation of dissolution weight loss in milligrams of different sealers in the respective test solvents
**Tabela 3.** Srednja vrednost i SD gubitka težine u miligramima različitih pasta za opturaciju u testiranim rastvaračima

| | Orange oil<br>Ulje narandže | Clove oil<br>Ulje karanfilića | Tea tree<br>Čajno drvo | Eucaliptol<br>Eukaliptol | Disstilled water<br>Destilovana voda |
|---|---|---|---|---|---|
| Endomethasone | 8.9<br>(2.52) | 1.3<br>(1.275) | 8.13<br>(1.813) | 3.9<br>(0.576) | 0<br>(0.1) |
| AH plus | 0.1<br>(0.105) | 4.3<br>(3.689) | 5.9<br>(2.533) | 0.7<br>(0.74) | 0<br>(0.1) |
| Acroseal | 0.1<br>(0.103) | 0.57<br>(1.015) | 0.1<br>(0.121) | 0.3<br>(0.197) | 0<br>(0.2) |

In all solvent groups, all three sealers showed weight loss (Table 3). Water (negative control) did not have the property on dissolving the paste. The greatest weight loss was recorded with Endomethasone for all solvents, the most in orange oil and tea tree, followed by clove and eucalyptus oil. Endomethasone dissolved in orange oil much more than AH Plus and Acroseal ($p<0.05$). Clove oil worked best on AH Plus, but without statistical significance compared to other pastes. Also, tea tree dissolved AH Plus more efficiently compared to Acroseal ($p<0.05$).

## DISCUSSION

During repeated endodontic treatment (retreatment), it is necessary to remove as much sealer and gutta-percha as possible in order to obtain clean canal walls without bacteria that are responsible for the failure of primary endodontic therapy [17]. This is most often done by applying thermal, mechanical and chemical agents or their combination [18]. Root canal retreatment is a time-consuming, complicated and uncertain procedure due to possible errors and complications: root perforation, instrument breaking, over instrumentation in which the original shape of the canal is lost, excessive removal of root dentin, difficulty in establishing the glide-path, extrusion of material and debris into the periapical area, etc. [4, 17, 18, 19]. The challenge is also presented by various sealers on the market, as well as the age of filling, which can significantly affect and change the characteristics of sealers and gutta-percha [1]. Also, different brands of gutta-percha with variations in composition (resin, wax) can affect their solubility [7].

The choice of the ideal solvent for the retreatment implies a balance between clinically safe use (substances for low toxicity and without irritation of the surrounding tissues) and high solvent capacity [2]. In general, all solvents are toxic to some degree, so their use should be limited or avoided unless necessary [20].

The use of essential oils in endodontics is growing, due to their proven safety, biocompatibility and non-carcinogenicity [8, 20]. **Neem oil** (*Azadirachta indica*) (nimbidine, nimbin, nimbolid) has the property of an anti-inflammatory agent by regulating pro-inflammatory enzymes such as cyclooxygenase (COX) and lipoxygenase (LOX), reduces the number of microorganisms in the channel roots, and is biocompatible with periodontal ligament cells [21]. **Tea Tree oil** (*Melaluca alternifolia*) is described by Aboriginal people as "the most useful medicine of nature". Its active component is terpinen-4-ol, which damages the intracellular material, disrupts homeostasis, and damages the integrity and function of the cell membrane of microorganisms. While most bacteria are sensitive to tea tree conc 1% or less, the MIC acting on *Enterococcus faecalis* is 2% [22]. **Eucalyptus oil** is distilled oil obtained from the leaves of *Eucalyptus globulus* (*Myrtaceae native* family), and the main component is 1,8-cineole. It has antibacterial and anti-inflammatory properties [8]. Eucalyptol's gutta-percha dissolution potential increases significantly if heated (37$^0$C) [23]. **Orange oil** showed the lowest concentration-dependent cytotoxicity relative to chloroform and eucalyptus [9]. The essential oil obtained from the peel of sweet orange (*Citrus aurantium*, d-Limonene 90%) is easy to obtain, has a pleasant smell and is convenient for quick coronal preparation of the canal, especially with ZOE filling with or without gutta-percha. An excellent solvent and an excellent alternative to other solvents that are much more toxic [20]. There is no evidence of carcinogenic or genotoxic effects of this essential oil [8].

In our study, orange oil dissolved gutta-percha cones significantly more than the other two solvents and water ($p < 0.05$) at all three measured times. Water has no solvent effect, as confirmed by other studies [23]. Eucalyptus was more effective than tea tree after 10 and 15 min ($p<0.05$). With the exception of orange oil, which proved to be effective after only 2 minutes, other essential oils were as

effective after 10 minutes as after 15 minutes, which should be taken into account for clinical use. The Tanomaru-Filho et al. study points out that orange oil and eucalyptol had a similar effect on conventional gutta-percha (though not as xylol), but that they dissolved thermoplastic gutta-percha much more efficiently (compared to conventional), presumably due to the increased proportion of gutta-percha's thermoplastic properties [24]. In contrast, Oyama et al. equated the efficacy of orange oil with xylol in their study [24]. Ferreira Ramos pointed out that the most effective solvent for F3 gutta-percha is xylol after 5min [25].

Although there is no international standard for the solubility of root canal sealers in organic solvents, ISO 6876: 2012 (Dental root canal sealing materials) describes a procedure that is simple, easily reproducible and economical for solubility testing [26]. Many studies indicate that it is very difficult to completely remove the filling from the main canal, and especially from ramifications [1, 27]. The duration of action of the solvent on the tested sealers in our study was 10 min, based on the collected data on the time required for retreatment of 1.5 to 10.8 min [27].

Regarding the efficiency of essential oils on dissolving ZOE-based sealant (Endomethasone N), orange oil proved to be the most efficient compared to all other oils ($p < 0.05$), followed by tea tree oil, which was more effective than cloves and eucalyptol ($p < 0.05$). Martos et al. pointed out that orange oil was more effective on ZOE sealers after only 2 minutes than xylol and eucalyptus after 10 minutes [2]. In Yadav et al. study, it dissolved the most of any sealants, mostly in xylene, followed by orange oil and eucalyptus oil [8]. In this study, endomethasone was significantly more soluble in eucalyptol than other sealants (AH plus, Acroseal) ($p<0.05$).

Resin based sealers are the least soluble in solvents (eucalyptus, orange, xylene), probably due to cross-linked structure, rigid and strong polymer [8]. AH plus dissolved almost completely in chloroform after 10 min, unlike its predecessor AH26, probably due to different resin particle sizes and other manufacturing details not listed in the specifications [28]. Bodrumlu pointed out that AH plus dissolved significantly in chloroform and eucalyptus oil after 10 min [29], contrary to our results where tea tree proved to be more effective than eucalyptol and orange oil ($p<0.05$). Clove oil was more effective than orange on AH plus, while there was no statistical significance between eucalyptol and orange. These results are in agreement with other researchers. Yadav et al. pointed out that eucalyptus and orange oil are less soluble in resin silos [8]. Tanomaru-Filho agreed with this, pointing out that eucalyptol has a weak effect on AHplus, Epiphany and similar sealers [24].

Calcium Hydroxide based sealer (Acroseal) proved to be quite resistant to the action of essential oils in this study. Eucalyptus oil had an effect on this sealer, but without statistical significance in relation to other essential oils. A similar finding was obtained by Schafer et al. that eucalyptol dissolved CH and ZOE-based sealants more efficiently than chloroform, which dissolved resins better [26]. In Calcium Hydroxide based sealers, Yadav et al. found no difference in solubility in eucalyptus and orange oil after 2 and 10 min. During the binding of the material, stable complexes were formed that were probably responsible for the lower solubility of these sealants compared to ZOE [8].

Garrib and Camilleri pointed out that in the choice of solvent, it is necessary to know the chemistry of the sealant that is being removed [18]. Organic solvents have been shown to be ineffective in hydraulic calcium silicate sealants. For them, 10% formic acid (5 minutes) is recommended, as its efficiency has been proven on Portland cement in the construction industry [18]. On the other hand, Alzraikat et al. agreed that eucalyptol had no effect on hydraulic sealer, but pointed out that ultrasonic activation of chloroform for a longer period of time could help dissolve MTA Fillapex [28]. It may be directly related to the research Topcuglu et al. who found that chloroform reduced the strength of the binding of MTA Fillapex, AH Plus and Sealapex to dentin [30]. Crozeta et al. pointed out that the application of ultrasound after establishing patency with hand instruments through endodontic filling was more efficient in removing residual material on the walls and removed it by about 18% more, compared to the GentleWave system that removed about 10% of residual material [31]. XP endo instruments were more effective in removing fillings in the mesial canals of mandibular molars than in distal ones that are oval and present a special problem and challenge for cleaning [1]. Also, the use of an adequate solvent for gutta-percha and siler can significantly reduce the amount of apically extruded debris [32]. However, Horvath et al. pointed out that solvents are not used routinely in retreatment, as greater injection of softened material into dentinal tubules has been observed, but only in cases where patency to the apex is difficult to establish [33].

Retreatment involves the synergistic use of solvents and instruments, in the same way as irrigants and instruments in primary endodontic treatment. As we expect the chemical action of irrigants in the primary endodontic procedure, so in the treatment we should think about the antibacterial potential of the solvent that would help eliminate the infection that led to the need to repeat the endodontic treatment. The essential oils used in our study (neem and tea tree) showed respectable antimicrobial potential on *Enterococcus faecalis* similar to 2% CHX (results not published).

In our *in vitro* study, some clinically important parameters such as anatomy of the canal system, approach, influence of biological fluids, influence of irrigants on solvent activity, etc. were not taken into account, so these results cannot be directly mapped into the clinical scenario. Research on an effective yet safe universal solution for softening and easier removal of the canal filling continues.

## CONCLUSION

With the limitations of this *in vitro* study it can be concluded that orange essential oil exhibited the most efficient dissolving of gutta-percha after only 2 min. There was no difference in efficiency of the essential oils after 10 and 15 min of use. Endomethason showed the highest dissolving rate in all tested essential oils. Clove and tea tree oil showed dissolving potential for AH Plus, while Acroseal dissolved the slowest in all essential oils.

## ACKNOWLEDGEMENT

This study was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia, Grant No. 175021.

## REFERENCES

1. Liu H, Lai WWM, Hieawy A, Gao Y, Haapasalo M, Tay FR, et al. Efficacy of XP-endo instruments in removing 54 monthaged root canal filling material from mandibular molars. J Dent. 2021;112:103734. [DOI: 10.1016/j.jdent.2021.103734] [PMID: 34182059]
2. Martos J, Gastal MT, Sommer L, Lund RG, Del Pino FA, Osinaga PW. Dissolving efficacy of organic solvents on root canal sealers. Clin Oral Investig. 2006;10(1):50–4. [DOI: 10.1007/s00784-005-0023-2] [PMID: 16317555]
3. Kwak Y, Choi J, Kim K, Shin SJ, Kim S, Kim E. The 5-Year Survival Rate of Nonsurgical Endodontic Treatment: A Population-based Cohort Study in Korea. J Endod. 2019;45(10):1192–9. [DOI: 10.1016/j.joen.2019.07.004] [PMID: 31439355]
4. Duncan HF. Removal of root filling materials. Endodontic Topics. 2011;19:33–57.
5. Hülsmann M, Bluhm V. Efficacy, cleaning ability and safety of different rotary NiTi instruments in root canal retreatment. Int Endod J. 2004;37(7):468–76. [DOI: 10.1111/j.1365-2591.2004.00823.x] [PMID: 15189436]
6. Kaplowitz GJ. Evaluation of Gutta-percha solvents. J Endod. 1990;16(11):539–40. [DOI: 10.1016/S0099-2399(07)80217-2] [PMID: 2084211]
7. Tamse A, Unger U, Metzger Z, Rosenberg M. Gutta-percha solvents--a comparative study. J Endod. 1986 Aug;12(8):337-9. [DOI: 10.1016/S0099-2399(86)80033-4] [PMID: 3462295]
8. Yadav HK, Yadav RK, Chandra A, Thakkar RR. The effectiveness of eucalyptus oil, orange oil, and xylene in dissolving different endodontic sealers. J Conserv Dent. 2016;19(4):332–7. [DOI: 10.4103/0972-0707.186447] [PMID: 27563181]
9. Zaccaro Scelza MF, Lima Oliveira LR, Carvalho FB, Côrte-Real Faria S. *In vitro* evaluation of macrophage viability after incubation in orange oil, eucalyptol, and chloroform. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;102(3):e24–7. [DOI: 10.1016/j.tripleo.2006.02.030] [PMID: 16920530]
10. Barbosa SV, Burkard DH, Spångberg LS. Cytotoxic effects of gutta-percha solvents. J Endod. 1994;20(1):6–8. [DOI: 10.1016/s0099-2399(06)80018-x] [PMID: 8182389]
11. WHO. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. Lyon (FR): International Agency for Research on Cancer; 1987;7:152-4.
12. Wennberg A, Orstavik D. Evaluation of alternatives to chloroform in endodontic practice. Endod Dent Traumatol. 1989;5(5):234–7. [DOI: 10.1111/j.1600-9657.1989.tb00367.x] [PMID: 2639788]
13. Karataş E, Kol E, Bayrakdar İŞ, Arslan H. The effect of chloroform, orange oil and eucalyptol on root canal transportation in endodontic retreatment. Aust Endod J. 2016;42(1):37–40. [DOI: 10.1111/aej.12126] [PMID: 26420757]
14. Ring J, Murray PE, Namerow KN, Moldauer BI, Garcia-Godoy F. Removing root canal obturation materials: a comparison of rotary file systems and re-treatment agents. J Am Dent Assoc. 2009;140(6):680-8. [DOI: 10.14219/jada.archive.2009.0254] [PMID: 19491164]
15. Xu LL, Zhang L, Zhou XD, Wang R, Deng YH, Huang DM. Residual filling material in dentinal tubules after gutta-percha removal observed with scanning electron microscopy. J Endod. 2012;38(3):293-6. [DOI: 10.1016/j.joen.2011.11.016] [PMID: 22341062]
16. Rossi-Fedele G, Ahmed HM. Assessment of Root Canal Filling Removal Effectiveness Using Micro-computed Tomography: A Systematic Review. J Endod. 2017;43(4):520–6. [DOI: 10.1016/j.joen.2016.12.008] [PMID: 28214018]
17. Mushtaq M, Masoodi A, Farooq R, Yaqoob Khan F. The dissolving ability of different organic solvents on three different root canal sealers: in vitro study. Iran Endod J. 2012 Fall;7(4):198–202. [PMID: 23130079]
18. Garrib M, Camilleri J. Retreatment efficacy of hydraulic calcium silicate sealers used in single cone obturation. J Dent. 2020;98:103370. [DOI: 10.1016/j.jdent.2020.103370] [PMID: 32387505]
19. Virdee SS, Thomas MB. A practitioner's guide to gutta-percha removal during endodontic retreatment. Br Dent J. 2017;222(4):251–7. [DOI: 10.1038/sj.bdj.2017.166] [PMID: 28232689]
20. Mushtaq M, Farooq R, Ibrahim M, Khan FY. Dissolving efficacy of different organic solvents on gutta-percha and resilon root canal obturating materials at different immersion time intervals. J Conserv Dent. 2012;15(2):141–5. [DOI: 10.4103/0972-0707.94584] [PMID: 22557812]
21. Hosny NS, El Khodary SA, El Boghdadi RM, Shaker OG. Effect of Neem (Azadirachta indica) versus 2.5% sodium hypochlorite as root canal irrigants on the intensity of post-operative pain and the amount of endotoxins in mandibular molars with necrotic pulps: a randomized controlled trial. Int Endod J. 2021;54(9):1434–47. [DOI: 10.1111/iej.13532] [PMID: 33884661]
22. Carson CF, Hammer KA, Riley TV. Melaleuca alternifolia (Tea Tree) oil: a review of antimicrobial and other medicinal properties. Clin Microbiol Rev. 2006 Jan;19(1):50-62. doi: 10.1128/CMR.19.1.50-62.2006. PMID: 16418522; PMCID: PMC1360273.
23. Magalhães BS, Johann JE, Lund RG, Martos J, Del Pino FA. Dissolving efficacy of some organic solvents on gutta-percha. Braz Oral Res. 2007;21(4):303–7. [DOI: 10.1590/s1806-83242007000400004] [PMID: 18060255]
24. Tanomaru-Filho M, Orlando Td, Bortoluzzi EA, Silva GF, Tanomaru JM. Solvent capacity of different substances on gutta-percha and Resilon. Braz Dent J. 2010;21(1):46–9. [DOI: 10.1590/s0103-64402010000100007] [PMID: 20464320]
25. Ramos TI, Câmara AC, Aguiar CM. Evaluation of Capacity of Essential Oils in Dissolving ProTaper Universal Gutta-Percha points. Acta Stomatol Croat. 2016;50(2):128–33. [DOI: 10.1564/asc50/2/5] [PMID: 27789910]
26. Schäfer E, Zandbiglari T. A comparison of the effectiveness of chloroform and eucalyptus oil in dissolving root canal sealers. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2002;93(5):611–6. [DOI: 10.1067/moe.2002.121899] [PMID: 12075213]
27. Whitworth JM, Boursin EM. Dissolution of root canal sealer cements in volatile solvents. Int Endod J. 2000;33(1):19–24. [DOI: 10.1046/j.1365-2591.2000.00266.x] [PMID: 11307469]
28. Alzraikat H, Taha NA, Hassouneh L. Dissolution of a mineral trioxide aggregate sealer in endodontic solvents compared to conventional sealers. Braz Oral Res. 2016;30:S1806–83242016000100215. [DOI: 10.1590/1807-3107BOR-2016.vol30.0016] [PMID: 26910018]
29. Bodrumlu E, Er O, Kayaoglu G. Solubility of root canal sealers with different organic solvents. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;106(3):e67–9. [DOI: 10.1016/j.tripleo.2008.05.007] [PMID: 18602299]
30. Topçuoğlu HS, Demirbuga S, Tuncay Ö, Arslan H, Kesim B, Yaşa B. The bond strength of endodontic sealers to root dentine exposed to different gutta-percha solvents. Int Endod J. 2014;47(12):1100–6. [DOI: 10.1111/iej.12257] [PMID: 24483251]
31. Crozeta BM, Chaves de Souza L, Correa Silva-Sousa YT, Sousa-Neto MD, Jaramillo DE, Silva RM. Evaluation of Passive Ultrasonic Irrigation and GentleWave System as Adjuvants in Endodontic Retreatment. J Endod. 2020;46(9):1279–85. [DOI: 10.1016/j.joen.2020.06.001] [PMID: 32553874]
32. Çanakçi BC, Er O, Dincer A. Do the Sealer Solvents Used Affect Apically Extruded Debris in Retreatment? J Endod. 2015;41(9):1507–9. [DOI: 10.1016/j.joen.2015.02.010] [PMID: 26238529]
33. Horvath SD, Altenburger MJ, Naumann M, Wolkewitz M, Schirrmeister JF. Cleanliness of dentinal tubules following gutta-percha removal with and without solvents: a scanning electron microscopic study. Int Endod J. 2009;42(11):1032–8. [DOI: 10.1111/j.1365-2591.2009.01616.x] [PMID: 19825038]

Received: 10.08.2021 • Accepted: 27.10.2021

# Ispitivanje efikasnosti eteričnih ulja kao alternativnih rastvarača u endodonciji

Vanja Opačić Galić[1], Savo Adžić[2], Bojan Dželetović[1], Tamara Vlajić[3]

[1]Univerzitet u Beogradu, Stomatološki fakultet, Klinika za bolesti zuba i endodonciju, Beograd, Srbija;
[2]Stomatološka ordinacija „Adžić", Ivanjica, Serbia;
[3]Univerzitet u Beogradu, Stomatološki fakultet, Beograd, Srbija

**KRATAK SADRŽAJ**

**Uvod** Cilj rada je bio da se ispita rastvorljivost gutaperka poena i različitih endodontskih silera u eteričnim uljima.

**Materijal i metode rada** U istraživanju je 96 gutaperka štapića podeljeno u četiri grupe od 24 uzorka za svako testirano eterično ulje i potom podeljeno u tri podgrupe za svako imerziono vreme (2, 10 i 15 min.). Za svaki uzorak je merena postimerziona težina. Paste za opturaciju AH Plus, Acroseal i Endometazon N su uključene u ispitivanje. Uzorci sa pastama su potapani u rastvarač na 10 min. Posle potapanja u testiranim eteričnim uljima, merene su težine svih uzoraka.

**Rezultati** Pomorandžino ulje je najefikasnije u rastvaranju gutaperke u odnosu na druga testirana eterična ulja ($p < 0,05$). Eukaliptol je više rastvorio gutaperku nego ulje čajevca posle 10 min. ($p < 0,05$). Nema statističke razlike u efikasnosti ulja u odnosu na to da li deluju 10 ili 15 min. ($p > 0,05$). Najveći gubitak mase je zabeležen kod paste Endometazon u svim rastvaračima, najviše u ulju pomorandže i čajevca, zatim ulju eukaliptusa i karanfilića. Čajevac rastvara AH Plus efikasnije nego Acroseal.

**Zaključak** Eterična ulja imaju potencijal za rastvaranje gutaperke i pasta za opturaciju kanala korena.

**Ključne reči:** eterična ulja; rastvorljivost; gutaperka; retretman

## UVOD

Pojedini endodontski tretmani iz različitih razloga nemaju uspešan ishod posle inicijalne endodontske terapije, pa je ponovni endodontski tretman neophodan. Stav Evropskog udruženja endodontista je da je neophodno postoperativno praćenje endodontski lečenih zuba bar jednu godinu, odnosno četiri godine, u slučaju apeksnih parodontitisa [1]. Najčešći uzrok za retretman su nedovoljno obrađeni i nedovoljno ispunjeni kanali korena, bez hermetičkog zaptivanja endodontskog prostora, što omogućava bujanje zaostalih mikroorganizama, posebno u dentinskim tubulima, ramifikacijama ili akcesornim kanalima [2]. Retretman kanalnog punjenja predstavlja posebnu problematiku u savremenoj endodontskoj praksi zbog svoje kompleksnosti i neizvesne prognoze u odnosu na endodontsku terapiju koja se prvi put radi bez obzira na etiologiju [3].

S obzirom na to da je osnovni uzrok neuspele endodontske terapije perzistentna infekcija, imperativ je da se tokom retretmana mora najpre efikasno ukloniti prethodno punjenje (gutaperka i pasta) [4], a kanal ponovo mehanički obraditi i hemijski dezinfikovati [5].

Primena rastvarača u toku retretmana je neophodna, a brojne kliničke studije su potvrdile da su najefikasniji hloroform, ksilen i obrađeno terpentinsko ulje [6, 7, 8]. Međutim, njihova toksičnost po periapeksno tkivo, terapeuta pa i potencijalni kancerogeni efekat su njihovu primenu sveli na minimum u savremenoj endodonciji [9, 10, 11]. Krajem 80-ih i početkom 90-ih godina XX veka pojavila su se razna esencijalna ulja (eukaliptusa, pomorandže) kao moguće zamene za ove rastvarače [6, 12]. Iako nijedna studija nije pokazala njihovu prednost u rastvaranju gutaperke i silera u odnosu na hloroform [2, 6], njihova biokompatibilnost i bezbednost, posebno kod povijenih kanala [13], ipak im daje prednost.

Početkom ovog veka, pored razvoja mašinskih instrumenata za obradu kanala zuba, pojavili su se i mnogi sistemi NiTi instrumenata (EndoSequence Rotary File, Pro Taper Universal D1-D3) dizajnirani samo za retretmane [1, 14]. Iako su se pokazali kao izuzetno uspešni i pogodni za primenu, njihova uloga je i dalje sekundarna u odnosu na ručne instrumente, jer najveći broj slučajeva podrazumeva uspostavljanje radne dužine upravo sa ručnim instrumentima [15, 16]. Uloga ultrazvučnih instrumenata, kao i lasera (Nd:YAG), takođe je doživela ekspanziju [4, 17].

Cilj ovog rada je bio da se ispita rastvorljivost gutaperka poena i različitih endodontskih silera u eteričnim uljima.

## MATERIJAL I METODE

U istraživanju je korišćeno pet eteričnih ulja: eukaliptus (*Eucalyptus globulus essential oil*) (Eucaliptol, Cerkamed, Poljska), kora slatke pomorandže (*Citrus aurantium*) (Zelena apoteka Davidovac, Srbija), čajevac (*Aetheroleum melaleuca*) (Kirka, Srbija), karanfilić (*Clove leaf essential oil*) (Eterra, Srbija), nim (*Azadirachta indica*) (Eterra, Srbija) i destilovana voda kao negativna kontrola.

### Ispitivanje rastvorljivosti gutaperke

U istraživanju je korišćen komercijalni brend gutaperke (Diadent, Južna Koreja) #80 i koničnosti 2%. Devedest šest gutaperka poena je standardizovano na 10 mm dužine i svaki je izmeren na analitičkoj vagi (Acculab, USA) u dubletu. Dobijena preimerziona masa je merena u gramima i zaokruživana na četiri decimale (M1). Uzorci su podeljeni u četiri grupe od po 24 uzorka (eukaliptol, pomorandža, čajevac i destilovana voda), a naknadno podeljeni u tri podgrupe koje odgovaraju vremenima imerzije (2, 10 i 15 min.).

Uzorci su postavljeni u 96-bunarne mikrotitracione pločice sa ravnim dnom u koje je uliveno po 180 µl rastvarača pomoću automatske osmokanalne pipete (BIOHIT Health Care, Finska) na sobnoj temperaturi. Nakon merenih vremenskih perioda uzorci su vađeni iz bunara uz pomoć medicinske pipete sa silikonskim vrhom, ispirani sa 20 ml redestilovane vode i ostavljeni da se suše 24 h na $37^0$ C.

Uzorci su nakon sušenja opet izmereni u dubletu i za svaki je dobijena postimerzionu masa (M2). Za dobijanje izgubljene mase gutaperke (Mg) korišćena je jednačina:

$$M_g = M_1 - M_2.$$

### Ispitivanje rastvorljivosti silera

U istraživanje su uključena tri komercijalna endodontska silera: na bazi smole (AH plus, Dentsply, Švajcarska), na bazi kalcijum-hidroksida (Acroseal, Septodont, Francuska) i cink-oksid-eugenola (Endomethasone N, Septodont, Francuska) (Tabela 1).

Devedeset standardnih plastičnih kalupa visine 2 mm i širine 5 mm su ponaosob izmereni na analitičkoj vagi u gramima (Mk) i podeljeni u pet grupa za svaki ispitivani rastvarač (eukaliptol, pomorandža, čajevac, karanfilić i destilovana voda). Naknadno je svaka grupa od 18 podeljena na tri podgrupe koje odgovaraju određenom sileru. Sileri su zamešani po uputstvu proizvođača i uliveni u kalupe, koji su čuvani u vodenom kupatilu na $37^0$ C, pri vlažnosti vazduha od 80% 72 h. Nakon vezivanja svaki uzorak je ponovo izmeren u dubletu i dobijena je preimerziona masa silera sa kalupom (Mks1). U 90 plastičnih kalupa visine 15 mm i širine 20 mm je uliveno po 1,8 ml odgovarajućeg rastvarača u koji su potapani kalupi sa silerima. Posle 10 min. uzorci su (pomoću medicinskih pinceta sa silikonskim vrhom) izvađeni, isprani sa 20 ml redestilovane vode i ostavljeni da se suše na na $37^0$ C 24 h. Svaki uzorak je izmeren i dobijena je masa $M_{ks2}$. Za dobijanje izgubljene mase silera (Ms) korišćena je sledeća jednačina:

$$M_s = (M_{ks1} - M_k) - (M_{ks2} - M_k)$$

Aritmetička sredina, mediana i standardna devijacija izračunati su za svaku grupu i podgrupu. Dobijeni rezultati su statistički obrađeni primenom dvofaktorske analize varijanse (ANOVA), One-way ANOVA (post-hoc Bonferroni test) ili testom Kruskal–Valis ukoliko raspodela nije bila normalna. Nivo značajnosti je utvrđen na $\alpha = 0,05$.

## REZULTATI

Dobijeni rezultati su prikazani u tabelama 2 i 3 i Slici 1.

Na osnovu prethodno urađene pilot studije, eliminisana su eterična ulja koja nisu pokazala svojstvo rastvorljivosti, ulje nima i karanfilića za gutaperku, odnosno nima za silere.

Pomorandžino ulje je bilo najefikasnije u rastvaranju gutaperke u odnosu na druga testirana eterična ulja ($p < 0,05$) (Tabela 2). Već posle 2 min. je značajno efikasnije od eukaliptola i čajevca. Eukaliptol je bio efikasniji u rastvaranju gutaperke od čajevca posle 10 min. ($p < 0,05$). Nema statističke značajnosti u efikasnosti eteričnih ulja u odnosu na to da li deluju 10 ili 15 min. ($p > 0,05$) (Slika 1).

U svim grupama rastvarača, sve tri paste su pokazale gubitak težine (Tabela 3). Voda (negativna kontrola) nije imala svojstvo rastvaranja pasti. Najveći gubitak težine je zabeležen kod endometazona u svim rastvaračima, a najviše u pomorandžinom ulju i čajevcu, slede ulje karanfilića i eukaliptusa. Endometazon se rastvara u pomorandžinom ulju mnogo više u odnosu na AH Plus i Acroseal ($p < 0,05$). Ulje karanfilića je najbolje delovalo na AH Plus, ali bez statističke značajnosti u odnosu na druge paste. Takođe, čajevac je efikasnije rastvorio AH Plus u odnosu na Acroseal ($p < 0,05$).

## DISKUSIJA

U toku ponovljenog endodontskog tretmana (retretmana) neophodno je ukloniti što više silera i gutaperke kako bi se dobili čisti zidovi kanala bez bakterija, koje su odgovorne za neuspeh primarne endodontske terapije [17]. To se najčešće radi primenom toplotnih, mehaničkih i hemijskih sredstava ili njihovom kombinacijom [18]. Retretman kanala korena je dugotrajan, komplikovan i neizvestan zahvat zbog mogućih grešaka i komplikacija: perforacija korena, zalamanje instrumenata, ispravljanja ili promene originalnog oblika kanala, preteranog uklanjanja dentina korena, uspostavljanja ponovne prohodnosti kanala, ekstruzije materijala i debrisa u periapeks itd. [4, 17, 18, 19]. Izazov predstavljaju i različiti sileri na tržištu kao i starost punjenja, koje može znatno uticati i izmeniti karakteristike pasti i gutaperke [1]. Takođe, i različiti brendovi gutaperki sa varijacijama u kompoziciji (smola, vosak) mogu uticati na njenu rastvorljivost [7].

Izbor idealnog rastvarača za izvođenje retretmana podrazumeva balans između klinički bezbedne upotrebe (supstance za niskom toksičnošću i bez iritacije okolnih tkiva) i velikog rastvaračkog kapaciteta [2]. Generalno, svi rastvatači su toksični u nekom stepenu, pa njihova upotreba treba biti ograničena ili izbegnuta ukoliko nije neophodna [20].

Upotreba esencijalnih ulja u endodonciji raste, zbog njihove dokazane bezbednosti, biokompatibilnosti i nekancerogenosti [8, 20]. **Nim ulje** (*Azadirachta indica*) (nimbidin, nimbin, nimbolid), poznato i kao „seoska apoteka" u Indiji, ima svojstvo antiinflamatornog agensa regulišući proinflamatorne enzime kao što su ciklooksigenaza (COX) i lipoksigenaza (LOX), smanjuje broj mikroorganizama u kanalu korena, a biokompatibilan je sa ćelijama periodontalnog ligamenta [21]. **Ulje čajevca (Tea Tree)** (*Melaluca alternifolia*) opisano je od Aboridžina kao „najraznovrsniji lek prirode". Aktivna komponenta mu je terpinen-4-ol, koja oštećuje intracelularni materijal, remeti homeostazu, oštećuje integritet i funkcije ćelijske membrane mikroorganizama. Dok je većina bakterija osetljiva na ulje čajevca koncentracije 1% i manje, MIC koja deluje na *Enterococcus faecalis* je 2% [22]. **Eukaliptusovo ulje** je destilovano ulje dobijeno iz lišća *Eucalyptusa globulusa* (familija *Myrtaceae native*), a glavna komponenta je 1,8-cineole. Ima antibakterijska i antiinflamatorna svojstva [8]. Eukaliptolov potencijal za rastvaranje gutaperke znatno raste ako se zagreje ($37^0$ C) [23]. **Pomorandžino ulje** je pokazalo najmanju citotoksičnost bez obzira na koncentraciju u odnosu na hloroform i eukaliptus, koji su zavisni od koncentracije [9]. Esencijalno ulje dobijeno iz kore slatke pomorandže (*Citrus aurantium*, d-Limonene 90%) lako se dobija, prijatnog je mirisa i zgodno je za brzo otvaranje kanala, posebno sa ZOE punjenjem sa gutaperkom ili bez nje. Odličan je rastvarač i odlična alternativa u odnosu na druge rastvarače, koji su mnogo toksičniji [20]. Ne postoje dokazi o kancerogenim ili genotoksičnim efektima ovog esencijalnog ulja [8].

U ovom istraživanju pomorandžino ulje je značajno bolje rastvorilo gutaperka konuse od druga dva rastvarača i vode ($p < 0,05$) u sva tri merena vremena. Voda nema nikakav rastvarački efekat, što su potvrdila i druga istraživanja [23]. Eukaliptus

je bio efikasniji od čajevca posle 10 i 15 min. ($p < 0,05$). S izuzetkom pomorandžinog ulja koje se pokazalo efikasno već posle 2 min., ostala etarska ulja su bila efikasna posle 10 min. jednako kao posle 15 min., što treba uzeti u obzir u kliničkoj primeni. Tanomaru-Filho i sar. u svojoj studiji ističu da su pomorandžino ulje i eukaliptol imali sličan efekat na konvencionalnu gutaperku (ipak ne kao ksilol), ali da mnogo efikasnije rastvaraju termoplastičnu gutaperku (u odnosu na konvencionalnu), pretpostavlja se zbog povećanog udela gutaperke, koja poboljšava njena termoplastična svojstva [24]. Suprotno njima, Oyama i sar. su u svom istraživanju [24] izjednačili efikasnost pomorandžinog ulja sa ksilolom. Ferreira Ramos ističe da je ipak najefikasniji rastvarač za F3 gutaperku ksilol, nakon 5 min. [25].

Iako ne postoji internacionalni standard za rastvorljivost kanalnih silera u organskim rastvaračima, ISO 6876:2012 (Dental root canal sealing materials) opisuje proceduru koja je jednostavna, lako ponovljiva i ekonomična za ispitivanje rastvorljivosti [26]. Mnoga istraživanja ukazuju da je veoma teško kompletno ukloniti punjenje iz glavnog kanala, a posebno iz ramifikacija [1, 27]. Vreme delovanja rastvarača na ispitivane silere u ovom istraživanju je 10 min., na osnovu prikupljenih podataka o vremenu potrebnom za retretman, koje iznosi od 1,5 do 10,8 min. [27].

Što se tiče efikasnosti eteričnih ulja na rastvaranje silera za opturaciju na bazi ZOE (Endomethasone N), najefikasnije se pokazalo pomorandžino ulje u odnosu na sva druga ulja ($p < 0,05$), zatim ulje čajevca, koje je bilo efikasnije od karanfilića i eukaliptola ($p < 0,05$). Martos i sar. ističu da je pomorandžino ulje već posle 2 min. bilo efikasnije na ZOE silere od ksilola i eukaliptusa posle 10 min. [2]. Kod Yadava i sar. se najviše rastvara od svih silera i to najviše u ksilenu, pa pomorandžinom ulju i eukaliptusovom ulju [8]. Endometayon se u ovom istaživanju značajno više rastvorio u eukaliptolu od ostalih silera (AH plus, Acroseal) ($p < 0,05$).

Sileri sa smolom se najmanje rastvaraju u rastvaračima (eukaliptus, pomorandža, ksilen). Verovatno je reč o jako umreženom, krutom i jakom polimeru [8]. AH plus se skoro potpuno rastvara u hloroformu nakon 10 min., za razliku od njegovog prethodnika AH26, verovatno zbog različite veličine čestica smole i drugih proizvođačkih detalja koji se ne navode u specifikacijama [28]. Bodrumlu ističe da se AH plus značajno rastvara u hloroformu i eukaliptusovom ulju posle 10 min. [29], što je suprotno našim rezultatima, gde se čajevac pokazao kao efikasniji od eukaliptola i pomorandžinog ulja ($p < 0,05$). Ulje karanfilića je bilo efikasnije od pomorandže na AH plus, dok između eukaliptola i pomorandže nije bilo statističke značajnosti. Ovi rezultati su u saglasnosti sa drugim istraživačima. Yadav i sar. ističu da eukaliptusovo i pomorandžino ulje slabije rastvara silere sa smolom [8]. Sa ovim se slaže i Tanomaru i Filho, koji ističu da eukaliptol slabo deluje na AH plus, Epiphany i slične silere [24].

Siler na bazi CH (Acroseal) u ovom se istraživanju pokazao kao dosta rezistentan na delovanje eteričnih ulja. Eukaliptusovo ulje je delovalo na ovaj siler, ali bez statističke značajnosti u odnosu na druga eterična ulja. Sličan nalaz je dobio i Schafer sa sar., gde eukaliptol efikasnije rastvara silere na bazi CH i ZOE u odnosu na hloroform, koji je bolje rastvorio smole [26]. Kod silera na bazi CH Yadav ne nalazi razliku u rastvorljivosti u eukaliptusovom i pomorandžinom ulju posle 2 i 10 min. U toku vezivanja materijala stvaraju se stabilni kompeksi, koji su verovatno odgovorni za nižu rastvorljivost ovih silera u odnosu na ZOE [8].

Garrib i Camilleri ističu da je u izboru rastvarača ključno poznavati hemizam silera koji se uklanja [18]. Organski rastvarači su se pokazali neefikasni kod hidrauličnih kalcijum-silikatnih silera. Za njih se preporučuje 10% mravlja kiselina (5 minuta), čija je efikasnost dokazana na cementu Portland u građevinskoj industriji [18]. S druge strane, Alzraikat i sar. se slažu da eukaliptol nema efekta na hidraulični siler, ali ističu da ultrazvučna aktivacija hloroforma duže vreme može pomoći u rastvaranju MTA Fillapexa [28], što je možda u direktnoj vezi sa istraživanjima koja su sproveli Topcuglu i sar., koji nalaze da hloroform smanjuje jačinu veze MTA Fillapexa, AH Plusa i Sealapexa sa dentinom [30]. Crozeta i sar. ističu da je primena UZ posle uspostavljanja prohodnosti ručnim instrumentima kroz endodontsko punjenje bilo efikasnije u uklanjanju zaostalog materijala na zidovima i uklonilo ga je za oko 18% više u odnosu na sistem GentleWave, koji je uklonio oko 10% zaostalog materijala [31]. XP endo instrumenti su efikasniji u uklanjanju punjenja u mezijalnim kanalima mandibularnih molara nego u distalnim, koji su ovalni i prestavljaju poseban problem i izazov za čišćenje [1]. Takođe, upotreba adekvatnog rastvarača za gutaperku i siler može znatno smanjiti količinu apikalno ekstrudiranog debrisa [32]. Ipak, Horvath i sar. ističu da se rastvarači ne koriste rutinski u retretmanu, jer je uočeno veće utiskivanje razmekšanog materijala u dentinske tubule, već samo u slučajevima kad je teško uspostaviti prohodnost do apeksa [33].

Retretman uključuje sinergičnu upotrebu rastvarača i instrumenata, na isti način kao i iriganasa i instrumenata u primarnom endodontskom tretmanu. Kao što očekujemo hemijsku akciju od irigansa u primarnom endodontskom zahvatu, tako bi i u retretmanu trebalo razmišljati o antibakterijskom potencijalu rastvarača koji bi pomogao u eliminaciji infekcije koja je dovela do potrebe za ponavljanjem endodontskog tretmana. Esencijalna ulja korišćena u ovom istraživanju su pokazala respektabilan antimikrobni potencijal na *Enterococcus faecalis*, i to ulje nima i čajevca slično 2% CHX (rezultati nisu publikovani).

U ovoj *in vitro* studiji nisu uzeti u obzir neki klinički važni parametri kao što su anatomija kanalnog sistema, pristup, uticaj bioloških fluida, uticaj iriganasa na aktivnost rastvarača i sl., tako da se ovi rezultati ne mogu direktno preslikati u klinički scenario. Istraživanja o efikasnom a bezbednom univerzalnom sredstvu za razmekšavanje i lakše uklanjanje kanalnog punjenja nastavljaju se dalje.

## ZAKLJUČAK

Uz ograničenja ove *in vitro* studije može se zaključiti da esencijalno ulje pomorandže najefikasnije rastvara gutaperku već posle dva min. Nema razlike u efikasnosti eteričnih ulja između 10 i 15 min. delovanja. Endometazon se najviše rastvara u svim testiranim eteričnim uljima. Ulje karanfilića i čajevca su pokazali rastvaračkи potencijal na AH Plus, dok se Acroseal najslabije rastvara u testiranim esencijalnim uljima.

**Zahvalnica**

Istraživanje je podržano od strane Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije, br. 175021.

sciendo

Serbian Dental Journal, vol. 68, N° 4, 2021 | 181

ORIGINAL ARTICLE
ORIGINALNI RAD

https://doi.org/10.2298/SGS2104181A
UDC: 616.314.17-085:615.246

# Clinical effects of local use of probiotics as an adjunct to non-surgical periodontal therapy

Tijana Adamović[1], Nataša Trtić[1], Ognjenka Janković[1], Valentina Veselinović[1], Mirjana Umićevic-Davidović[1], Igor Đukić[1], Verica Pavlić[1,2]

[1]University of Banja Luka, Faculty of Medicine, Banja Luka, Republika Srpska, Bosnia and Herzegovina;
[2]Institute of Dentistry Banja Luka, Republika Srpska, Bosnia and Herzegovina

## SUMMARY

**Introduction** Periodontal disease is a chronic inflammatory disease caused by pathologic microorganisms/periopathogens from oral biofilm. Standard periodontal therapy consists of scaling and root planing (SRP). Probiotics can be used as an adjunctive to standard periodontal therapy, since it is known that probiotics can modify pathogenic potential of biofilm by suppressing the colonization of periopathogens.

The aim of this study was to assess the clinical effect of *Bifidobacterium* and *Lactobacillus* probiotic lozenges, probiotic mouthwash, as an adjuvant to SRP in the treatment of initial to moderate chronic periodontitis.

**Material and methods** Thirty patients with initial to moderate chronic periodontitis were recruited and monitored clinically at baseline (before SRP) and 60 days following SRP. All patients were randomly assigned to experimental group: SRP + probiotic (n = 15) and control group: SRP only (n = 15). The probiotic mouthwash was used twice a day for 60 days. Clinical parameters: the probing pocket depth (PPD), clinical attachment level (CAL) and bleeding on probing (BOP) were measured at baseline and 60th day following SRP. Data were statistically analyzed using the one-way Anova test and SPSS 19 software (IMB Company, New York, U.S.). The Friedman and Mann Whitney tests were used as a post hoc test for intergroup analysis. Statistical significance was set at $p < 0.05$.

**Results** After 60 days of treatment, the clinical parameters PPD, CAL and BOP were significantly lower in both groups compared to the baseline. In the experimental group, the clinical parameters PPD, CAL and BOP were significantly reduced after 60 days of treatment compared to the initial measurements ($p < 0.05$). In the control group, statistically significant decrease after 60 days of treatment was recorded only for BOP parameter, while there was no statistically significant decrease of PPD and CAL values ($p > 0.05$).

**Conclusion** The results of the present study demonstrated clinical benefits of adjunctive use of probiotics to SRP in terms of pocket depth reduction in initial to moderate periodontal disease.

**Keywords**: probiotics; periodontitis; scaling and root planning

## INTRODUCTION

Periodontitis is a chronic destructive inflammatory disease of the teeth' supporting tissues caused by a specific microorganisms or group of microorganisms, characterized by a disturbance of homeostatic balance necessary for an efficient host immune response [1, 2]. Even though periodontal disease is considered a multifactorial disease, oral biofilm plays the primary etiological role in the initial development of periodontitis. The golden standard of periodontal therapy is removal of etiological factors, namely oral biofilm. Therefore, the ideal goal of periodontal therapy is decreasing the periodontal pocket depth (PPD) and clinical attachment level (CAL) [3].

To date, ensuring excellent oral hygiene, frequent monitoring for progression or recurrence of periodontal disease and removal of oral biofilm by non-surgical and surgical treatment are considered conventional treatment approaches. Despite widespread clinical advantages of conventional periodontal treatment, it does not always lead to clinical improvement, especially in patients with deep periodontal pockets and patients with comorbidities (diabetes mellitus, obesity, cardiovascular diseases). In these cases, selective use of antibiotics and antiseptics has remained the cornerstone of periodontal treatment [4]. Systemic antibiotic therapy is used to enhance the effects of non-surgical and surgical periodontal treatment and serves to support the host immune system to eliminate subgingival pathogens that remain after SRP. However, antibiotics have many side effects and can cause bacterial resistance. As a result of these limitations, efforts have been made to investigate the use of alternatives, such as probiotics as adjunctive to conventional periodontal treatment [3, 5].

According to the definition of the Food and Agriculture Organization of the United Nations and the World Health Organization, probiotics are living microorganisms (so-called "good" bacteria) that, when applied in adequate quantities, have beneficial effects on the health of a host [6]. Probiotics are natural microorganisms that have great potential in suppressing the reproduction of microorganisms in the oral biofilm without exhibiting side

**Address for correspondence:** Tijana ADAMOVIĆ, Bulevar Petra Bojovića bb,78 000 Banja Luka, Republika Srpska, BiH; *tijana.adamovic@med.unibl.org*

effects. Recent studies demonstrated that probiotics have a beneficial effect on human health leading to several new recommendations to encourage the use of probiotics to improve the immune system, including oral health [7, 8, 9].

The effects of probiotics on oral health may be a result of local and/or systemic action. Indirectly, probiotics compete with pathogens for essential nutrients; they can also limit the ability of pathogens to adhere by changing the pH of the medium. By binding to dental tissues, they become part of the biofilm and act as a protective coating for oral tissues against oral diseases. Such biofilm keeps bacterial pathogens away from oral tissue by filling a space that could serve as a niche for pathogens in future [1, 10].

Several studies have examined the adjuvant use of probiotics in the treatment of chronic periodontitis [11–16]. Different outcomes have been observed as a result of probiotic therapy, although most studies suggested beneficial clinical results in the form of decreased PPD, CAL and bleeding on probing (BOP) [17, 18]. However, a study by Morales et al. showed that adjuvant use of probiotics in the treatment of chronic periodontitis does not necessarily lead to an improvement in clinical parameters [11]. Therefore, this randomized placebo-controlled clinical study aimed to evaluate the effect of application of probiotic capsules with *Bifidobacterium* and *Lactobacillus* strain as adjuvants to SRP in the treatment of initial to moderate forms of periodontal disease, measured by clinical parameters (PPD, CAL, BOP).

## MATERIAL AND METHODS

The study involved 30 systemically healthy patients, aged 20 to 65 years, with an initial to moderate form of chronic periodontitis who had at least three natural teeth in each quadrant, not counting the third molars. Criteria for exclusion from the study were: presence of systemic diseases, periodontal treatment in the last six months, use of antibiotics or probiotics in the last three months, and pregnant and lactating women. Before the beginning of the study, all subjects were informed in details about the procedures required to perform this study and only those who gave written consent were included in the study.

All patients were randomly assigned to the experimental group: SRP + probiotic (n = 15) or the control group: SRP + placebo (n = 15). Initially, all patients underwent SRP, 7 days prior to the probiotic administration. During that visit, the patients received instructions on maintaining adequate oral hygiene.

Clinical parameters PPD, CAL and BOP were measured at the beginning of the study (7 days following SRP) and on the 60th day (end of study). All clinical measurements were recorded by one investigator, periodontist (T.A.). At the same visit, patients received the instructions of how to use probiotic/placebo capsules. Each patient was given 120 capsules to use twice per day for 60 consecutive days, precisely after waking up and at bedtime following oral hygiene. The content of the capsule would be emptied into 10 ml of distilled water and then vigorously shaken into the oral cavity for 60 seconds, then spit out.

Data were statistically analyzed using one-way ANOVA in SPSS 19 software (IMB Company, New York, USA). The Friedman and Mann-Whitney test were used as post hoc tests for intergroup analysis. The results were presented as mean and standard deviation. Statistical significance was set at $p < 0.05$.

## RESULTS

All participants remained until the end of the study and during the study no adverse events were registered. Thirty patients participated in the study, 15 in the experimental group and 15 in the control group. The mean age of the patients in the experimental group was 44.11 ± 4.57 and 43.21 ± 5.43 for the control group. The male/female ratio was approximately the same in both groups. There were 4 smokers in the control group, and 3 in the experimental group (Table 1).

**Table 1.** Demographic characteristics
**Tabela 1.** Demografske karakteristike

| VARIABLE<br>VARIJABLA | CONTROL GROUP<br>KONTROLNA GRUPA | EXPERIMENTAL GROUP<br>EKSPERIMENTALNA GRUPA | p-value<br>vrednost p |
|---|---|---|---|
| Number of patients<br>Broj pacijenata | 15 | 15 | NS<br>NZ |
| Number of men<br>Broj muškaraca | 8 | 7 | NS<br>NZ |
| Number of women<br>Broj žena | 7 | 8 | NS<br>NZ |
| Number of smokers<br>Broj pušača | 4 | 3 | NS<br>NZ |
| Years<br>Godine | 43.21 ± 5.43 | 44.11 ± 4.57 | NS<br>NZ |

Significance of the difference between the groups: $p < 0.05$ is significant (bold), NS – is not significant
Značaj razlike između grupa: $p < 0,05$ je značajno (podebljano), NZ – nije značajno

In the control group, PPD at the beginning of therapy was 3.21 mm and at the end 3.20 mm and this difference was not statistically significant. The mean value of CAL was initially 2.84 mm and after two months 2.82 mm and this difference was not statistically significant. The mean value of BOP at the beginning of treatment was 58.42% and at the end 4.13% and this difference were statistically significant (Table 2). In the experimental group, the PPD at the beginning of therapy was 3.51 mm and at the end 3.00 mm and this difference was statistically significant. The mean value of CAL was initially 2.67 mm and after two months 2.33 mm and this difference was statistically significant. The mean value of BOP at the beginning of therapy was 60.72% and at the end 3.48% and this difference were statistically significant (Table 2).

The results demonstrated that topical application of probiotic capsules with *Bifidobacterium* and *Lactobacillus* strain as adjuvants to conventional therapy of periodontal disease lead to a statistically significant decrease in PPD and CAL values in the experimental group ($p < 0.05$), while PPD and CAL values in the control group did not show statistically significant difference ($p > 0.05$). A

**Table 2.** The comparison of clinical parameters of periodontal disease within and between groups (mean ± SD)
**Tabela 2.** Poređenje kliničkih parametara parodontopatije unutar i između grupa (srednja vrednost ± SD)

| | CONTROL GROUP<br>KONTROLNA GRUPA | | | EXPERIMENTAL GROUP<br>EKSPERIMENTALNA GRUPA | | |
|---|---|---|---|---|---|---|
| | At the beginning of therapy<br>Na početku terapije | Two months later<br>Posle dva meseca | p-value<br>vrednost p | At the beginning of therapy<br>Na početku terapije | Two months later<br>Posle dva meseca | p-value<br>vrednost p |
| PPD (mm)<br>DPDŽ (mm) | | | | | | |
| Mean value<br>Srednja vrednost | 3.21 ± 0.52 | 3.20 ± 0.46 | 0.58 | 3.51 ± 0.52 | 3.00 ± 0.46 | 0.03* |
| Mean value of the difference<br>Srednja vrednost razlike | | 0.01 ± 0.06 | | | 0.51 ± 0.06 | |
| CAL (mm)<br>NPE(mm) | | | | | | |
| Mean value<br>Srednja vrednost | 2.84 ± 0.68 | 2.82 ± 0.45 | 0.63 | 2.67 ± 0.68 | 2.33 ± 0.45 | 0.01* |
| Mean value of the difference<br>Srednja vrednost razlike | | 0.02 ± 0.23 | | | 0.34 ± 0.23 | |
| BOP (%)<br>KPS (%) | | | | | | |
| Mean value<br>Srednja vrednost | 58.42 ± 5.12 | 4.13 ± 3.51 | 0.02* | 60.72 ± 9.98 | 3.48 ± 2.21 | 0.03* |
| Mean value of the difference<br>Srednja vrednost razlike | | 54.29 ± 1.61 | | | 57.24 ± 7.77 | |

Comparison within the group with the Friedman test ($p < 0.05$). Significant values are indicated with star.
Intergroup comparison by Mann Whitney test ($p < 0.05$).
PPD – depth of the periodontal pocket
CAL – level of attachment epithelium
BOP – bleeding during probing
SD – standard deviation
Poređenje unutar grupe korišćenjem Fridmanovog testa ($p < 0,05$). Značajne vrednosti su označene zvezdicom.
Poređenje među grupama pomoću testa Mena i Vitnija ($p < 0,05$).
DPDŽ – dubina parodontalnog džepa
NPE – nivo pričvrsnog epitela
KPS – krvarenje prilikom sondiranja
SD – standardna devijacija

statistically significant difference (decrease) in BOP values was observed in both groups at the end of the treatment (Table 2).

## DISCUSSION

The results of our study showed the benefits of adjuvant use of probiotic capsules with *Bifidobacterium* and *Lactobacillus* strain in the treatment of periodontal disease, measured through clinical parameters: PPD, CAL and BOP (Table 2).

The growing prevalence of antimicrobial resistance has encouraged the development of new antimicrobial therapeutic approaches in the treatment of biofilm-related oral diseases [17]. Probiotics are living microorganisms that, when given in adequate amounts, provide a health benefit to the host by preventing the adhesion of pathogenic species, inhibiting bacterial growth, modulating the mucosal immune response, cell proliferation, and improving intestinal barrier integrity. Probiotic species mainly belong to the genera *Bifidobacterium* and *Lactobacillus* and are commonly used to treat various diseases of the gastrointestinal tract, urogenital infections, eczema, and oropharyngeal infections [19]. The main property of probiotics used in the oral cavity is their ability to adhere to the surface of oral structures and colonization [20]. Previous research suggested that probiotics cannot replace destroyed natural flora, but as temporary colonies can help body by performing the same functions as natural flora, giving natural flora enough time to recover [21].

Also, several clinical studies have been conducted with the aim to assess the impact of probiotics in the treatment of oral diseases. It has been shown that probiotics can successfully manipulate the microbiological composition and improve clinical condition of oral diseases such as bad breath, candidiasis and periodontal disease [4, 7, 22–27].

The results of this research are in accordance with the results of the research that examined the activity of *Bifidobacterium lactis* HN019 strain in 41 patients with chronic periodontitis [17]. All subjects were first given total disinfection of the mouth and SRP and they were randomly divided into the two groups: experimental group (probiotics + SRP) and control group (SRP + placebo). Clinical follow-up began at the first visit (before SRP) and then 30 and 90 days of treatment, and in addition to clinical evaluation (PPD and CAL), immunological and microbiological tests were performed. Subjects used probiotic or placebo capsules twice daily for 30 days. The study showed that after 90 days the clinical parameters were improved in the experimental group compared to the control group ie. significantly higher reduction in PPD and CAL was observed in the group that used probiotics [17].

Similarly, Vicario et al. examined the action of *Lactobacillus reuteri* lozenge in systemically healthy subjects, non-smokers, with an initial or moderate form of

periodontitis. Subjects in this double-blind, randomized clinical study were divided into the two groups, experimental and control. The experimental group took one lozenge of *Lactobacillus reuteri* per day for 30 days while the control group used a placebo. Clinical parameters were registered at the beginning and 30 days after the beginning of the treatment. After 30 days, the experimental group showed a statistically significant decrease in all periodontal parameters monitored in this study (plaque index, BOP, PPD). The placebo-treated control group showed no statistically significant changes in periodontal parameters [28].

In a study by Ince et al. the use of probiotic capsules based on *Lactobacillus reuteri* as adjuvant to SRP in the treatment of moderate forms of periodontitis showed excellent results. Subjects used probiotic capsules twice daily for three weeks. As a result of the use of probiotic capsules, there was a decrease in the values of clinical parameters that were monitored: gingival index, plaque index, BOP, PPD and CAL [18].

Contrary to our results are the findings of Morales et al. in whose study the use of probiotic capsules based on *Lactobacillus rhamnosus* did not lead to a significant reduction of clinical parameters (PPD, CAL, plaque index and BOP). Patients used a placebo or probiotic capsules once daily for three months [11].

Data obtained in the literature indicated that different probiotic cultures, as well as the manner and time of their application in the treatment of periodontitis, result in variable outcomes. Despite the literature showing mostly encouraging results, further research is needed to elucidate the potential use of probiotics in the prevention and treatment of periodontitis. A combination of conventional periodontal treatment and probiotics has not yet been introduced into the protocol for the treatment of periodontal patients.

## CONCLUSION

The use of probiotic capsules as an adjunct to SRP in the treatment of patients with initial to moderate periodontitis lead to statistically significant improvement in the mean PPD, CAL and BOP values in the observed period of two months. The use of probiotics could bring additional clinical benefits to classical periodontal treatment during the maintenance phase, in terms of reducing PPD, CAL and BOP. However, more studies with larger number of patients and longer observation period in order to assess the ideal method use of probiotics are necessary.

## REFERENCES


1. Mani A, Saini R, Saini SR. Efficacy of oral probiotics as an adjunct to scaling and root planing in nonsurgical treatment outcome of generalized chronic periodontitis patients: A clinico-microbiological study. Int J Experiment Dent Sci. 2017;6(1):6–13. [DOI 10.5005/jp-journals-10029-1145]
2. Theodoro LH, Cláudio MM, Nuernberg MAA, Miessi DMJ, Batista JA, Duque C, et al. Effectsof Lactobacillus reuteri as an adjunct to the treatment of periodontitis in smokers: randomised clinical trial. Benef Microbes. 2019;10(4):375–84. [DOI: 10.3920/BM2018.0150]
3. Nguyen T, Brody H, Guo-Hao L, Rangé H, Kuraji H, Changchang Y, et al. Probiotics, including nisin-based probiotics, improve clinical and microbial outcomes relevant to oral and systemic diseases. Periodontol 2000. 2020;82(1):173–85. [DOI: 10.1111/prd.12324] [PMID: 31850634]
4. Penala S, Kalakonda B, Pathakota KR, Jayakumar A, Koppolu P, Lakshmi BV, et al. Efficacy of local use of probiotics as an adjunct to scaling and root planing in chronic periodontitis and halitosis: A randomized controlled trial. J Res Pharm Pract. 2016;5(2):86–93. [DOI: 10.4103/2279-042X.179568] [PMID: 27162801]
5. Cobb CM. Clinical significance of nonsurgical periodontal therapy: an evidence based perspective of scaling and root planing. J Clin Periodontol 2002;29:6–16. [PMID: 12010523]
6. Adamović T, Trtić N, Pavlić V. Probiotics in dentistry. Contemporary materials. Academy of Sciences and Arts of the Republic of Srpska. 2018;35:427–34.
7. Laleman I, Teughels W. Probiotics in the dental practice: a review. Quintessence Int. 2015;46(3):255–64. [DOI: 10.3290/j.qi.a33182] [PMID: 25485319]
8. Matsubara VH, Bandara HM, Ishikawa KH, Mayer MP, Samaranayake LP. The role of probiotic bacteria in managing periodontal disease: a systematic review. Expert Rev Anti Infect Ther. 2016;14(7):643–55. [DOI: 10.1080/14787210.2016.1194198] [PMID: 27224284]
9. Gruner D, Paris S, Schwendicke F. Probiotics for managing caries and periodontitis: Systematic review and meta-analysis. J Dent. 2016;48:16–25. [DOI: 10.1016/j.jdent.2016.03.002] [PMID: 26965080]
10. Gatej S, Gully N, Gibson R, Bartold M. Probiotics and periodontitis-A literature review. J Int Acad Periodontol. 2017;19(2):42–50. [PMID: 31473722]
11. Morales A, Carvajal P, Silva N, Hernandez M, Godoy C, Rodriguez G, et al. Clinical effects of Lactobacillus rhamnosus in non-surgical treatment of chronic periodontitis: a randomized placebo-controlled trial with 1-year follow-up. J Periodontol. 2016;87(8):944–52. [DOI: 10.1902/jop.2016.150665] [PMID: 26944407]
12. Ikram S, Hassan N, Baig S, Borges KJJ, Raffat MA, Akram Z. Effect of local probiotic (*Lactobacillus reuteri*) vs systemic antibiotic therapy as an adjunct to non-surgical periodontal treatment in chronic periodontitis. J Investig Clin Dent. 2019;10(2):e12393. [DOI: 10.1111/jicd.12393] [PMID: 30663271]
13. Liu J, Liu Z, Huang J, Tao R. Effect of probiotics on gingival inflammation and oral microbiota: A meta-analysis. Oral Dis. 2021. [DOI: 10.1111/odi.13861] [PMID: 33772970]
14. Vohra F, Bukhari IA, Sheikh SA, Albaijan R, Naseem M, Hussain M. Effectiveness of scaling and root planing with and without adjunct probiotic therapy in the treatment of chronic periodontitis among shamma users and non-users: A randomized controlled trial. J Periodontol. 2020;91(9):1177–85. [DOI: 10.1002/JPER.19-0464] [PMID: 31985066]
15. Butera A, Gallo S, Maiorani C, Molino D, Chiesa A, Preda C, et al. Probiotic alternative to chlorhexidine in periodontal therapy: Evaluation of clinical and microbiological parameters. Microorganisms. 2020;9(1):69. [DOI: 10.3390/microorganisms9010069] [PMID: 33383903]
16. Pelekos G, Acharya A, Eiji N, Hong G, Leung WK, McGrath C. Effects of adjunctive probiotic L. reuteri lozenges on S/RSD outcomes at molar sites with deep pockets. J Clin Periodontol. 2020;47(9):1098–107. [DOI: 10.1111/jcpe.13329] [PMID: 32511775]
17. Invernici MM, Salvador SL, Silva PHF, Soares MSM, Casarin R, Palioto DB, et al. Effects of *Bifidobacterium* probiotic on the treatment of chronic periodontitis: A randomized clinical trial. J Clin Periodontol. 2018;45(10):1198–210. [DOI: 10.1111/jcpe.12995] [PMID: 30076613]
18. Ince G, Gursoy H, Ipci SD, Cakar G, Emekli-Alturfan E, Yilmaz S. Clinical and biochemical evaluation of lozenges containing *Lactobacillus reuteri* as an adjunct to non-surgical periodontal therapy in chronic periodontitis. J Periodontol. 2015;86(6):746–54. [DOI: 10.1902/jop.2015.140612] [PMID: 25741580]

19. Martin-Cabezas R, Davideau JL, Tenenbaum H, Huck O. Clinical efficacy of probiotics as an adjunctive therapy to non-surgical periodontal treatment of chronic periodontitis: a systematic review and meta-analysis. J Clin Periodontol. 2016;43(6):520–30. [DOI: 10.1111/jcpe.12545] [PMID: 26970230]
20. Deepak T, Manjunath M, Pewa S. Antibiotics are passe: take a look at probiotcs. WJD. 2010;1:109–11. [DOI: 10.5005/jp-journals-10015-1022]
21. Oyetayo VO, Oyetayo FL. Potental of probiotcs as biotherapeutc agents targetng the innate immune system. AJB. 2005;4:123–7.
22. Burton JP, Chilcott CN, Moore CJ, Speiser G, Tagg JR. A preliminary study of the effect of probiotic Streptococcus salivarius K12 on oral malodour parameters. J Appl Microbiol. 2006;100(4):754–64. [DOI: 10.1111/j.1365-2672.2006.02837.x] [PMID: 16553730]
23. Masdea L, Kulik EM, Hauser-Gerspach I, Ramseier AM, Filippi A, Waltimo T. Antimicrobial activity of Streptococcus salivarius K12 on bacteria involved in oral malodour. Arch Oral Biol. 2012;57(8):1041–7. [DOI: 10.1016/j.archoralbio.2012.02.011] [PMID: 22405584]
24. Hatakka K, Ahola AJ, Yli-Knuuttila H, Richardson M, Poussa T, Meurman JH, et al. Probiotics reduce the prevalence of oral Candida in the elderly – a randomized controlled trial. J Dent Res. 2007;86(2):125–30. [DOI: 10.1177/154405910708600204] [PMID: 17251510]
25. Jiang Q, Stamatova I, Kari K, Meurman JH. Inhibitory activity in vitro of probiotic lactobacilli against oral Candida under different fermentation conditions. Bene Microbes. 2015;6(3):361–8. [DOI: 10.3920/BM2014.0054] [PMID: 25380800]
26. Zahradnik RT, Magnusson I, Walker C, McDonell E, Hillman CH, Hillman JD. Preliminary assessment of safety and effectiveness in humans of ProBiora, a probiotic mouthwash. J Appl Microbiol. 2009;107(2):682–90. [DOI: 10.1111/j.1365-2672.2009.04243.x] [PMID: 19486429]
27. Teughels W, Durukan A, Ozcelik O, Pauwels M, Quirynen M, Haytac MC. Clinical and microbiological effects of Lactobacillus reuteri probiotics in the treatment of chronic periodontitis: a randomized placebo-controlled study. J Clin Periodontol. 2013;40(11):1025–35. [DOI: 10.1111/jcpe.12155] [PMID: 24164569]
28. Vicario M, Santos A, Violant D, Nart J, Giner L. Clinical changes in periodontal subjects with the probiotic *Lactobacillus reuteri* Prodentis: a preliminary randomized clinical trial. Acta Odontol Scand. 2013;71(3–4):813–9. [DOI: 10.3109/00016357.2012.734404] [PMID: 23176716]

Received: 24.08.2021 • Accepted: 19.10.2021

# Klinički efekti lokalne primene probiotika kao adjuvantne mere nehirurškom lečenju parodontopatije

Tijana Adamović[1], Nataša Trtić[1], Ognjenka Janković[1], Valentina Veselinović[1], Mirjana Umićević-Davidović[1], Igor Đukić[1], Verica Pavlić[1,2]

[1]Univerzitet u Banjoj Luci, Medicinski fakultet, Banja Luka, Republika Srpska, Bosna i Hercegovina;
[2]Zavod za stomatologiju Banja Luka, Republika Srpska, Bosna i Hercegovina

**KRATAK SADRŽAJ**

**Uvod** Parodontopatija je hronična inflamatorna bolest prouzrokovana patološkim mikrorganizmima. Mogući mehanizmi delovanja probiotika u terapiji parodontopatije zasnivaju se na modifikacijama patogenog potencijala mikrobnog biofilma. Probiotici pomažu u stimulisanju rasta zdrave flore i time suzbijaju rast i kolonizaciju patoloških mikroorganizama u toku parodontopatije.
Cilj ove studije je da se proceni klinički efekat primene probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* kao adjuvantima kauzalnoj terapiji parodontopatije (čišćenje i poliranje površine korena zuba, SRP) u lečenju početnog ili umerenog oblika hronične parodontopatije.
**Materijal i metode rada** Trideset pacijenata sa početnim do umerenim oblikom hronične parodontopatije je regrutovano u ovu studiju i praćeno klinički na početku (pre SRP-a) i 60 dana nakon SRP-a. Svi pacijenti su nasumično raspoređeni u eksperimentalnu grupu: SRP + probiotik (n = 15) ili kontrolnu grupu: SRP + placebo (n = 15). Ispiranje usne duplje rastvorom sa probiotičkim kapsulama je vršeno dva puta dnevno tokom uzastopnih 60 dana. Klinički parametri, dubina parodontalnog džepa (DPDŽ), nivo pripojnog epitela (NPE) i krvarenje prilikom sondiranja (KPS) mereni su na početku lečenja i 60. dana. Podaci su statistički analizirani uz pomoć one-way Anova testa i softvera SPSS 19 (IMB Company, New York, U.S.). Fridmanov test i test Man–Vitni su korišteni kao post hock testovi za međugrupnu analizu. Statistička značajnost je postavljena na $p < 0,05$.
**Rezultati** Nakon 60 dana terapije, klinički parametri DPDŽ, NPE i KPS bili su značajno niži u obe grupe u poređenju sa početnim vrednostima. U eksperimentalnoj grupi klinički parametri DPDŽ, NPE i KPS su se statistički značajno smanjili posle 60 dana terapije u poređenju sa početnim merenjima ($p < 0,05$). U kontrolnoj grupi statistički značajno smanjenje posle 60 dana terapije zabeleženo je samo za parametar KPS, dok za vrednosti DPDŽ i NPE nije došlo do statistički značajnog smanjenja ($p > 0,05$).
**Zaključak** Ovo istraživanje je pokazalo da adjuvantna upotreba probiotika u terapiji hronične parodontopatije pruža kliničku korist u smislu smanjenja dubine parodontalnog džepa, nivoa pripojnog epitela i krvarenja prilikom sondiranja.
**Ključne reči:** probiotici; parodontopatija; obrada parodontalnog džepa

## UVOD

Parodontopatija je hronična destruktivna inflamatorna bolest potpornih tkiva zuba uzrokovana specifičnim mikroorganizmom ili grupom specifičnih mikroorganizama koji izazivaju disbiozu, koja se karakteriše poremećajem homeostatske ravnoteže neophodne za efikasan imuni odgovor domaćina, što dovodi do neregulisane upale i gubitka alveolarne kosti [1, 2].

Uprkos tome što se smatra multifaktornom bolešću, oralni biofilm je primarni etiološki faktor nastanka parodontopatije.

Delovanje na primarni etiološki faktor je glavni cilj lečenja parodontopatije. Idealan rezultat terapije parodontopatije predstavlja smanjenje dubine parodontalnog džepa sa smanjenjem nivoa pripojnog epitela [3].

Različiti terapijski modaliteti, koji uglavnom uključuju savete o održavanju oralne higijene i nehirurško terapiju (čišćenje i poliranje površine korena zuba) (SRP), hirurška terapija i u pojedinim slučajevima selektivna primena antibiotika i antiseptika do danas su ostali kamen temeljac terapije parodontopatije [4].

Uprkos široko rasprostranjenim kliničim prednostima, nehirurška terapija parodontopatije ne dovodi uvek do poboljšanja, posebno kod pacijenata sa dubokim parodontalnim džepovima i pacijenta sa komorbiditetima (dijabetes melitus, gojaznost, kardiovaskularne bolesti). U ovim situacijama se adjuvantna primena antibiotika ili probiotika u terapiji može pokazati korisna.

Sistemska antibiotska terapija se koristi za pojačanje delovanja nehirurške i hirurške terapije parodontopatije, služi kao podrška imunom sistemu domaćina za eliminaciju subgingivalnih patogena koji ostaju nakon SRP-a.

Uz SRP, sistemski antibiotici mogu da ponude dodatne pogodnosti; međutim, antibiotici nisu bezopasni lekovi jer je njihova primena praćena pojavom neželjenih efekata i stvaranjem rezistentnih sojeva mikroorganizama. Kao rezultat ovih ograničenja, uloženi su napori da se istraži upotreba probiotika kao druge metode za modulaciju sastava oralnog biofilma u kombinaciji sa SRP-om [3, 5].

Prema definiciji organizacije za hranu i poljoprivredu Ujedinjenih naroda te Svetske zdravstvene organizacije, probiotici su živi mikroorganizmi (tzv. „dobre" bakterije) koji kada se primene u adekvatnoj količini imaju povoljne učinke na zdravlje domaćina [6].

Probiotici su prirodni mikroorganizmi koji imaju veliki potencijal u suzbijanju razmnožavanja mikroorganizama u oralnom biofilmu bez ispoljavanja neželjenih efekata.

Nedavne studije su pokazale da probiotici imaju blagotvoran učinak na zdravlje čoveka, što dovodi do nekoliko novih preporuka za podsticanje upotrebe probiotika u cilju poboljšanja imunog sistema, uključujući i oralno zdravlje [7, 8, 9].

Efekti probiotika na oralno zdravlje mogu proisteći iz lokalnog i sistemskog načina delovanja. Indirektno, probiotici se takmiče sa patogenima za neophodne hranljive sastojke; takođe mogu ograničiti sposobnost adhezije patogena promenom pH sredine. Vezujući se za dentalna tkiva, postaju deo biofilma i deluju kao zaštitna obloga za oralna tkiva protiv oralnih bolesti. Takav biofilm drži bakterijske patogene dalje od oralnog tkiva popunjavanjem prostora koji je mogao da posluži kao niša za patogene u budućnosti [1, 10].

Nekoliko studija je ispitivalo adjuvantnu primenu probiotika u terapiji hronične parodontopatije [11–16].

Različiti ishodi su primećeni kao rezultati terapije probioticima, mada većina studija pokazuje pozitivne kliničke rezultate u vidu smanjenja dubine parodontalnog džepa (DPDŽ), nivoa pripojnog epitela (NPE) i krvarenja prilikom sondiranja (KPS) [17, 18].

Za razliku od studija koje pokazuju pozitivan efekat primene probiotika, studija Moralesa i saradnika je pokazala da adjuvantna primena probiotika u terapiji hronične parodontopatije ne dovodi uvek do poboljšanja kliničkih parametara [11].

Stoga je ova randomizirana placebo kontrolisana klinička studija imala za cilj da proceni klinički efekat (DPDŽ, NPE, KPS) lokalne primene probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* kao adjuvantima kauzalnoj terapiji parodontopatije (SRP) u lečenju početnog do umerenog oblika parodontopatije.

## MATERIJAL I METOD RADA

Kriterijumi za učešće u studiji su bili: da su pacijenti muškog ili ženskog pola, starosti od 20 do 65 godina, da imaju najmanje tri prirodna zuba u svakom kvadrantu ne računajući treće molare, da se prethodno nisu lečili od parodontopatije. Kriterijumi za isključenje iz studije su bili: sistemske bolesti, pacijenti koji su u zadnja tri meseca koristili antibiotike ili probiotike, trudnice i dojilje.

Pre samog početka studije svi ispitanici su bili detaljno informisani o procedurama potrebnim za izvođenje ovog istraživanja i samo oni koji su dali pismenu saglasnost su bili uključeni u ovo istraživanje.

U studiji je učestvovalo 30 sistemski zdravih pacijenata sa početnim do umerenim oblikom hronične parodontopatije.

Svi pacijenti su nasumično raspoređeni u eksperimentalnu grupu: SRP + probiotik (n = 15) ili kontrolnu grupu: SRP + Placebo (n = 15). Na početku, svi pacijenti su podvrgnuti SRP-u.

SRP je izveden sedam dana pre početka primene probiotika ili placeba, korišćenjem ručnih i ultrazvučnih instrumenata. U istoj poseti pacijenti su takođe dobili i uputstva o održavanju adekvatne oralne higijene.

Klinički parametri DPDŽ, NPE i KPS mereni su na početku lečenja (sedam dana posle SRP-a) i 60. dana (završetak studije). Sva klinička merenja su zabeležena od strane jednog ispitivača.

Posle registrovanja kliničkih parametara (DPDŽ, NPE, KPS) svakom pacijentu je detaljno objašnjen način primene probiotičkih kapsula ili placeba.

Pacijenti su dobili po 120 kapsula koje su koristili odmah posle obavljanja oralne higijene, dva puta dnevno (posle buđenja i pre spavanja).

Sadržaj kapsule bi ispraznili u 10 ml destilovane vode i zatim energično mućkali usnu duplju 60 sekundi, zatim ispljunuli. Placebo ili probiotičke kapsule sa sojevima *Bifidobacterium* i *Lactobacillus* korišćene su tokom uzastopnih 60 dana.

Podaci su statistički analizirani korištenjem one-way ANOVA testa uz pomoć softvera SPSS 19 (IMB Company, New York, U.S.). Fridmanov i test Man–Vitni korišćeni su kao post hock testovi za međugrupnu analizu. Rezultati su predstavljeni u vidu srednje vrednosti i standardne devijacije. Statistička značajnost je postavljena na $p < 0,05$.

## REZULTATI

U studiji je učestvovalo 30 pacijenata – 15 u eksperimentalnoj grupi i 15 u kontrolnoj grupi, koja je primala placebo. Svi učesnici su ostali u studiji do samog završetka studije i nisu registrovani neželjeni događaji. Prosečna starost pacijenata u eksperimentalnoj grupi je bila 44,11 ± 4,57 i 43,21 ± 5,43 za kontrolnu grupu. Procenat muškaraca/žena (8/7) bio je približno jednak u obe grupe. U kontrolnoj grupi je bilo četiri pušača, dok je u eksperimentalnoj bilo tri (Tabela 1).

U kontrolnoj grupi DPDŽ na početku terapije je iznosila 3,21 mm, a na kraju 3,20 mm i ova razlika nije bila statistički značajna. Srednja vrednost NPE je na početku iznosila 2,84 mm, a posle dva meseca 2,82 mm i ova razlika nije bila statistički značajna. Srednja vrednost KPS na početku terapije je iznosila 58,42%, a na kraju 4,13% i ova razlika je bila statistički značajna (Tabela 2).

U eksperimentalnoj grupi grupi DPDŽ na početku terapije iznosila je 3,51 mm, a na kraju 3,00 mm i ova razlika je bila statistički značajna. Srednja vrednost NPE je na početku iznosila 2,67 mm, a posle dva meseca 2,33 mm i ova razlika je bila statistički značajna. Srednja vrednost KPS na početku terapije je iznosila 60,72%, a na kraju 3,48% i ova razlika je bila statistički značajna (Tabela 2).

Rezultati istraživanja su pokazali da lokalna primena probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* kao adjuvantima kauzalnoj terapiji parodontopatije dovodi do statistički značajnog smanjenja vrednosti DPDŽ i NPE kod eksperimentalne grupe ($p < 0,05$), dok se vrednosti DPDŽ i NPE kod kontrolne grupe nisu statistički značajno promenile ($p > 0,05$). Statistički značajno smanjenje vrednosti KPS je primećeno u obe grupe na kraju terapije (Tabela 2).

## DISKUSIJA

Ovo istraživanje je imalo za cilj da proceni klinički efekat lokalne primene probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* kao adjuvantima kauzalnoj terapiji parodontopatije u lečenju početnog ili umerenog oblika parodontopatije.

Rezultati istraživanja su pokazali da adjuvantna primena probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* može imati pozitivan efekat u terapiji parodontopatije, odnosno da dolazi do smanjenja vrednosti DPDŽ, NPE i KPS (Tabela 2).

Rastuća prevalencija antimikrobne rezistencije podstaknula je razvoj novih antimikrobnih terapijskih pristupa u lečenju oralnih bolesti povezanih sa biofilmom [17].

Probiotici predstavljaju žive mikroorganizme koji kada se daju u adekvatne količine pružaju zdravstvenu korist za domaćina sprečavanjem adhezije patogenih vrsta, inhibicijom rasta bakterija, modulacijom imunog odgovora sluznice, ćelijske proliferacije i poboljšanjem integriteta crevne barijere. Probiotičke vrste uglavnom pripadaju rodovima *Bifidobacterium* i *Lactobacillus* i obično se koriste za lečenje različitih bolesti gastrointestinalnog trakta, urogenitalnih infekcija, ekcema i orofaringealnih infekcija [19].

Glavno svojstvo probiotika koji se koriste u usnoj šupljini je njihova sposobnost adheriranja za površinu struktura usne šupljine i kolonizacija [20].

Dosadašnja istraživanja naučnika upućuju da probiotici ne mogu zameniti uništenu prirodnu floru, nego kao privremene kolonije mogu pomoći organizmu obavljajući iste funkcije kao prirodna flora, dajući prirodnoj flori dovoljno vremena da se oporavi [21].

Na kliničkom nivou, nekoliko studija je sprovedeno sa ciljem procene uticaja probiotika u lečenju oralnih oboljenja. Pokazalo se da probiotici mogu uspešno manipulisati mikrobiološkim sastavom i poboljšati kliničko stanje kod oralnih oboljenja kao što su neugodan zadah, kandidijaza i bolesti parodoncijuma [4, 7, 22–27].

Rezultati ovog istraživanja su u skladu sa rezultatima istraživanja koje su realizovali Invernici i sar. Oni su ispitivali delovanje soja *Bifidobacterium lactis HN019* na 41 pacijentu sa hroničnom parodontopatijom. Svim ispitanicima je prvo izvršena totalna dezinfekcija usta te SRP. Slučajnim odabirom su podeljeni su u dve grupe. Eksperimentalna grupa: probiotici + SRP i kontrolna grupa: SRP + placebo. Kliničko praćenje započelo je pri prvoj poseti (pre SRP-a) te zatim 30 i 90 dana terapije, a osim kliničke evaluacije (DPDŽ i NPE) vršena su imunološka i mikrobiološka ispitivanja. Ispitanici su koristili kapsule sa probiotikom ili placebom dva puta na dan, kroz 30 dana. Istraživanje je pokazalo da su nakon 90 dana klinički parametri bili poboljšani kod eksperimentalne grupe u poređenju sa kontrolnom grupom. Odnosno, primećena je značajno veća redukcija DPDŽ i NPE kod grupe koja je koristila probiotik [17].

Rezultati studije španskih naučnika Vikarija i saradnika takođe su u skladu sa ovim nalazima. Oni su ispitivali delovanje pastila *Lactobacillus reuteri* kod sistemski zdravih ispitanika, nepušača, s početnim ili umerenim oblikom parodontopatije. Ispitanici su u ovoj, dvostruko slepoj, randomiziranoj kliničkoj studiji, bili podeljeni u dve grupe – eksperimentalnu i kontrolnu. Eksperimentalna grupa je uzimala jednu pastilu *Lactobacillus reuteri* na dan tokom 30 dana, dok je kontrolna koristila placebo. Klinički parametri su registrovani na početku i 30 dana posle početka terapije. Eksperimentalna grupa je posle 30 dana pokazala statistički značajno smanjenje svih parodontoloških parametara praćenih u ovoj studiji (plak indeks, KPS, DPDŽ). Kontrolna grupa tretirana s placebom nije pokazala statistički značajne promene parodontoloških parametara [28].

U studiji Ince i saradnika primena probiotičkih kapsula na bazi *Lactobacillus reuteri* kao adjuvantne mere u terapiji umerenih oblika parodontopatije pokazala je odlične rezultate. Ispitanici su koristili probiotičke kapsule dva puta dnevno tri sedmice. Kao rezultat primene probiotičkih kapsula došlo je do smanjenja vrednosti kliničkih parametara koje su pratili: gingivalnog indeksa, plak indeksa, KPS, DPDŽ i NPE [18].

U suprotnosti sa našim rezultatima su saznanja do kojih su došli Morales i saradnici, u čijem istraživanju primena probiotičkih kapsula na bazi *Lactobacillus rhamnosus* nije dovela do značajnog smanjenja kliničkih parametara (DPDŽ, NPE, plak indeks i KPS). Pacijenti su koristili placebo ili probiotičke kapsule jednom dnevno tri meseca [11].

Podaci do kojih se dolazi u literaturi ukazuju na činjenicu da odabir različitih probiotičkih kultura kao i način i vreme njihove primene u terapiji parodontopatije rezultiraju promenjivim rezultatima.

Uprkos tome što literatura pokazuje uglavnom ohrabrujuće rezultate, potrebna su dodatna istraživanja kako bi se rasvetlila moguća upotreba probiotika u prevenciji i lečenju parodontopatije. Još uvek kombinacija mehaničke terapije (SRP) i probiotika nije uvedena u protokol za lečenje parodontoloških pacijenata.

## ZAKLJUČAK

U skladu sa ograničenjima ove studije možemo da zaključimo da adjuvantna upotreba probiotičkih kapsula kao dodatak SRP-u u lečenju pacijenata sa početnim do umerenim oblikom parodontopatije dovodi do statistički značajnog poboljšanja prosečnih vrednosti DPDŽ, NPE i KPS tokom dvomesečnog praćenja. Upotreba probiotika mogla bi doneti dodatne kliničke prednosti klasičnoj terapiji parodontopatije tokom faze održavanja, u smislu smanjenja DPDŽ, NPE i KPS, ali je za potvrdu potrebno više studija sa većim brojem pacijenata i duže praćenje ovih rezultata za procenu idealnog načina primene probiotika.

ORIGINAL ARTICLE
ORIGINALNI RAD

https://doi.org/10.2298/SGS2104189D
UDC: 615.463:616.314-7

# Radiopacity of calcium silicate-based endodontic sealers using digital imaging

Bojan Dželetović, Ivana Bošnjak, Đorđe Antonijević, Jovan Badnjar, Zoran Petrov, Vanja Opačić-Galić

University of Belgrade, School of Dental Medicine, Department for Restorative Dentistry and Endodntics, Belgrade, Serbia

**SUMMARY**

**Introduction** Adequate radiopacity of endodontic sealers allows radiographic visualization, assessment of root canal filling quality and its clinical follow-up after obturation. The aim of our study was to evaluate the radiopacity of Bio-Root RCS, MTA Fillapex, Bioceramic Root Canal Sealer, GuttaFlow Bioseal in comparison to AH Plus sealer, as a gold standard in clinical practice.

**Material and methods** Sealer specimens, 2 mm thick and 5 mm in diameter, were radiographed with an aluminum stepwedge using digital imaging system. Radiographic densities of the specimens were shown as mean greyscale values (Adobe Photoshop CS4 software) and expressed as mmAl/mm of the material. ANOVA with a post hoc Tukey test was used, significance was set at 0.05.

**Results** Differences in radiopacity between tested endodontic sealers were statistically significant except the difference between BioRoot RCS and GuttaFlow Bioseal.

**Conclusion** Radiopacities of all evaluated calcium silicate-based sealers were higher than minimal values recommended by standards. AH Plus sealer had the highest radiopacity, while calcium silicate-based sealers showed lower values, from BioRoot RCS, followed by GuttaFlow Bioseal, to MTA Fillapex, in descending order, and Bioceramic Root Canal Sealer with the lowest values.

**Keywords:** radiopacity; calcium silicate; root canal sealer

## INTRODUCTION

Obturation, that follows adequate cleaning and shaping of the root canal, should seal the canal apically and laterally and prevent potentional microleakage, avoiding possible reinfection. Root canal filling consists of solid gutta-percha cone and endodontic sealer that fills spaces between gutta-percha and dentin walls of the root canal [1].

Since root canal sealer is in contact with periapical tissues its biological properties should be favorable for reparation/regeneration proceses in alveolar bone, cementum or periodontal ligament. Calcium silicate-based sealers have bioactive properties related to ions release and hydroxyapatite crystals formation on their surface after contact with phosphate containing body fluids [2]. Calcium hydroxide formed during calcium silicate materials hydration results in high pH that changes alkalinity in the adjacent promoting healing, hard tissue formation and interference with osteoclastic activity [3]. These materials show antimicrobial activity through neutralization of lipopolysaccharides that are present in the membrane of gram-negative bacteria and through irreversible reaction with bacterial enzymes [4, 5].

In order to assess endodontic filling quality and follow-up its long-term efficiency, endodontic materials should have sufficient radiopacity. Namelly, radiopacity enables clear distinction between endodontic filling and surrounding dental and periapical tissues [6]. Adequate radiopacity of endodontic materials allows radiographic visualization of voids in the canal obturation that can be formed by air bubbles entrapment during the mixing of two-component sealers or during gutta-percha cones insertion in the canal [7]. On the other hand, empty spaces in endodontic filling cause inadequate seal and could be created by sealer dissolution. These voids are difficult to spot and could, particularly, be masked by strong radiopacity of obturation materials [8].

New calcium silicate-based sealers became available on the market but independent research on some of their physical properties are still lacking. On the other hand, there are discrepancies in results of studies examining radiopacity of calcium silicate-based sealers that probably could be explained by differences in experimental designs used [9, 10]. In order to obtain evidence-based recomendations for clinical practice it is important to perform scientific research on newly developed sealers and compare them with currently widely used materials.

**The aim** of our study was to evaluate radiopacities of calcium silicate-based sealers BioRoot RCS, MTA Fillapex, Bioceramic Root Canal Sealer and GuttaFlow Bioseal in comparison to AH Plus sealer that is a gold standard in clinical practice.

**Address for correspondence:** Bojan DŽELETOVIĆ, Rankeova 4, 11000 Belgrade, Serbia; *dzeletovicbojan6@gmail.com*

**Table 1.** Sealers, manufacturers and composition of the tested materials
**Tabela 1.** Naziv paste, proizvođač i sastav

| Sealer | Manufacturer | Composition |
|---|---|---|
| BioRoot RCS | Septodont, Saint Maur-des-Fosses, France | **Powder:** tricalcium silicate, zirconium oxide and excipients<br>**Liquid:** aqueous solution of calcium chloride and excipients<br>**Prašak:** trikalcijum-silikat, cirkonijum-oksid i pomoćne supstance<br>**Tečnost:** vodeni rastvor kalcijum-hlorida i pomoćnih supstanci |
| MTA Fillapex | Angelus, Londrina, Brazil | **Base paste:** salicylate resin, natural resin, calcium tungstate, nanoparticulated silica, pigments<br>**Catalyst paste:** diluting resin, mineral trioxide aggregate, nanoparticulated silica, pigments<br>**Osnovna pasta:** salicilatna smola, prirodna smola, kalcijum-volframat, nanočestice silicijum-dioksida, pigmenti<br>**Katalizatorska pasta:** smola za razređivanje, mineralni trioksid |
| Bioceramic Root Canal Sealer | SSWhite, Lakewood, New Jersey, USA | **Base paste:** salicylate resin, natural resin, calcium tungstate, nanoparticulated silica, pigments<br>**Catalyst paste:** diluting resin, mineral trioxide aggregate, nanoparticulated silica, pigments<br>**Osnovna pasta:** salicilatna smola, prirodna smola, kalcijum-volframat, nanočestice silicijum-dioksida, pigmenti<br>**Katalizatorska pasta:** smola za razređivanje, mineralni trioksid |
| GuttaFlow Bioseal | Coltène/Whaledent, Langenau, Germany | Gutta-percha powder, polydimethylsiloxane, platinum catalyst, zirconium dioxide, silver (preservative), coloring, bioactive glass ceramic<br>Prah gutaperke, polidimetilsiloksan, katalizator platine, cirkonijum-dioksid, srebro (konzervans), boje, bioaktivna staklokeramika |
| AH Plus | Dentsply, DeTrey GmbH, Konstanz, Germany | **Paste A:** Bisphenol epoxy resin–A, Bisphenol epoxy resin–F, calcium tungstate, zirconium oxide, silica, iron oxide pigments<br>**Paste B:** Dibenzyldiamine, aminodiamantana, tricyclodecane–diamine, calcium tungstate, zirconium oxide, silica, silicone oil<br>**Pasta A:** bisfenol-epoksidna smola-A, bisfenol-epoksidna smola-F, kalcijum-volframat, cirkonijum-oksid, silicijumdioksid, gvožđe-oksidni pigmenti<br>**Pasta B:** dibenzildiamin, aminodiamantana, triciklodekan-diamin, kalcijum-volframat, cirkonijum-oksid, silicijum-dioksid, silikonsko ulje |

## MATERIAL AND METHODS

The following materials were evaluated in the study: BioRoot RCS (Septodont, St Maur-des-Fosses, France), MTA Fillapex (Angelus, Londrina, Brazil), Bioceramic Root Canal Sealer (SS White, New Jersey, USA), GuttaFlow Bioseal (Coltene Whaledent, Langenau, Germany) and AH Plus (Dentsply DeTrey Gmbh, Konstanz, Germany) (Table 1). Endodontic sealers were mixed according to the manufacturers instructions and placed in teflon molds, 2 mm thick and 5 mm in diameter. Specimens were placed in an incubator at 37°C and 95% relative humidity and following complete setting, thickness of the specimens was checked using a digital caliper. If necessary, specimens were ground wet with carbide paper (P600) to reach the thickness of 2±0.1 mm.

Three specimens of each sealer were radiographed with an aluminum stepwedge (99.6 % pure, 10 mm thickness, in steps of 1 mm each) using a Radiovisiography (RVG-4) CCD-based digital sensor (Trophy Radiology, Cedex, France). X-ray generator (Trophy Radiology) operating at 70 kVp and 7 mA was used with a source-to-object distance of 30 cm and exposure of 0.07 s. Radiographic densities of the specimens were expressed as mean greyscale values using Adobe Photoshop CS4 software (Adobe Systems, San Hose, CA). Each sealer specimen was read three times as well as each step of the aluminum stepwedge. Regions containing iregularities such as air bubbles were avoided. For radiopacity determination, graph for the logarithm of aluminum thickness versus the corresponding radiographic density was plotted with the best-fitting logarithmic trend line. After that, the radiographic density of the material was used to calculate the radiopacity from the graph. Radiopacities were expressed as mmAl/mm of the material (mmAl).

The normality of data distribution was tested by Kolmogorov–Smirnov test. Analysis of variance (ANOVA) with a post hoc Tukey test was used for comparison of the differences between the sealers. We used SPSS 16.0 for Windows (SPSS Inc., Chiago, IL, USA) statistical program for all analyzes and significance was set at 0.05.

## RESULTS

Figure 1 shows digital radiograph of GuttaFlow Bioseal and aluminium stepwedge. Table 2 shows mean values and standard deviations of the radiopacities of investigated endodontic sealers in millimetres of aluminium (mm Al). The highest average radiopacity was observed for AH Plus paste (11.22 mmAl), followed by decreasing values: BioRoot RCS (8.32 mmAl), GuttaFlow Bioseal (7.64 mmAl), MTA Fillapex (5.58 mmAl), while the lowest values were shown for Bioceramic Root Canal Sealer paste (3.4 mmAl). The statistical analysis revealed significant difference in mean radiopacity between MTA Fillapex and all other sealers, Bioceramic Root Canal Sealer and all other sealers, as well as GuttaFlow Bioseal and all other sealers. There was no significant difference only between BioRoot RCS and GuttaFlow Bioseal.

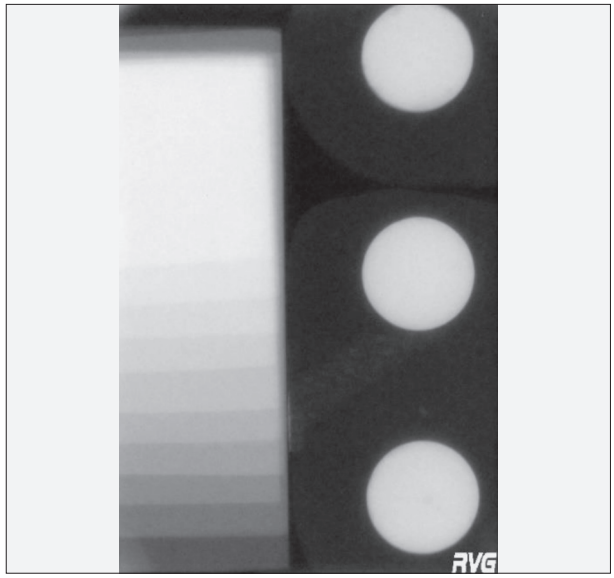


**Figure 1.** Digital radiographic image of GuttaFlow Bioseal and aluminium stepwedge
**Slika 1.** Digitalni radiogram paste GuttaFlow Bioseal i aluminijumskog etalona

**Table 2.** Radiopacity values of calcium silicate-based endodontic sealers, expressed in millimetres of aluminium equivalent
**Tabela 2.** Vrednosti rendgenkontrastnosti kalcijum-silikatnih pasta izražene u ekvivalentnim milimetrima aluminijuma

| Calcium silicate-based sealers<br>Kalcijum silikatne paste | Radiopacity (mmAl) (mean ± SD)<br>Rendgenokontrast (mmAl)<br>(srednja vrednost ± SD) |
|---|---|
| BioRoot RCS | 8.32 ± 0.7 |
| MTA Fillapex | 5.58 ± 0.37 |
| Bioceramic Root Canal Sealer | 3.4 ± 0.25 |
| GuttaFlow Bioseal | 7.64 ± 0.5 |
| AH Plus | 11.22 ± 0.43 |

## DISCUSSION

It is established by International Organization for Standardization (ISO) that the root canal sealers, at a thickness of 1 mm, should have a radiopacity equivalent to at least 3 mm of aluminum. All endodontic sealers evaluated in our study had a greater radiopacity than the minimum recommended by the ISO specified standards. Although the examined sealers are calcium silicate-based, significant differences in radiopacity, observed in this study, could be the consequence of type and percentage of radiopacifying agents in these materials.

Namelly, it was found by Duarte et al. in 2009 that different radiopacifiers had decreasing radiopacity: bismuth oxide, lead oxide, bismuth subnitrate, iodoform, zirconium oxide, bismuth carbonate, calcium tungstate, barium sulphate, and zinc oxide [11]. Bioceramic Root Canal Sealer and MTA Fillapex have calcium tungstate as opacifying agent and that could be the reason for their lower radiopacity in comparison to other sealers [11].On the other hand, BioRoot RCS and AH plus contain zirconium oxide in its composition that increases their radiopacity more [11]. GuttaFlow Bioseal has several components that increase its radiopacity: zirconium dioxide, silver and gutta-percha [12]. Beside zirconium oxide, AH plus contains calcium tungstate and iron oxide which contribute to the highest raiopacity value obsearved for this sealer [13].

Scientific literature showed large variety of radiopacity values reported for calcium silicate-based sealers evaluated in the present study. Radiopacity of BioRoot RCS ranged from 5.2 to 8.3 mmAl [14, 13], while values reported for GuttaFlow Bioseal were between 3.94 and 7.44 mmAl [15, 16]. Results for MTA Fillapex reported in previous studies ranged from 3.01 to 9.4 mmAl [17, 18]. It is important that the composition of MTA Fillapex was changed by the manufacturer and instead of bismuth oxide calcium tungstate was added as radiopacifying agent which further complicated comparisons between studies [19]. Bioceramic Root Canal Sealer is a product relatively recently introduced and we found no data in literature regarding its radiopacity, so it was not possible to compare our results with the ones from previous examinations. Epoxy-based sealer AH Plus was a control material in the majority of studies on sealers and showed significant variability in radiopacity values, from 5.9 to 18.4 mmAl [13, 20].

This diversity in experimental results could partially be explained by various methodological approaches and different radiographic systems, conventional or digital, used in mentioned studies [9]. Namelly, according to international standards for radiopacity of endodontic sealers radiographic visualization must be obtained through chemical processes of conventional radiographic film developing, fixation, rinsing and drying. All these procedures may negatively interfere with radiographic image quality and are time consuming [21]. In order to minimize the influence of radiographic film processing and X-ray exposure conditions on measurement accuracy, aluminium wedge, which is chosen as a reference since aluminum roentgenographic contrast is very similar to dentin, is radiographed on the same film with examined samples [22]. After film processing, the amount of light transmitted by the sample image should be measured using an optical densitometer and translated in thickness of aluminum step-wedge image that transmits equivalent amount of light. On the other hand, as digital radiography became more widely used in dental practice, this motivated new examinations on radiopacity of dental materials based on digital systems [23].

Wide adoption of digital radiography systems made them more clinically relevant than conventional film radiography. As well, computer-based digital image processing and analysis make data acquisition easier, excludes errors with film processing and uses lower radiation dose since digital sensors are more sensitive than conventional films [24]. Having in mind widespread usage and advantages of digital radiography over film some authors proposed that new, modified protocols should be revised by standardization organizations [25, 26].

Different examinations on radiopacity of endodontic materials comparing conventional and digital radiography demonstrated that the choice of imaging system might significantly affect radiopacity measurements [27, 28]. In these studies, the authors concluded that it is difficult

to compare their results with the results of other studies due to different methodological approaches to radiopacity measurement. This suggests that when obtaining radiopacity values for different endodontic sealers it would be important to use the same experimental design and radiographic system in order to reliably compare them. It is interesting that radiopacity values for BioRoot RCS were very close to our results in previous studies (7.96 and 8.3 mmAl) which, similarly to our study, used digital radiography systems [13, 29]. Likewise, our findings for GuttaFlow Bioseal were quite consistent with radiopacities reported in two studies (7.02 and 7.44 mmAl) that also used similar digital radiography systems [15, 30].

Another possible cause for various radiopacity values of endodontic sealers reported in literature could be the variations in the ratio of components of two-component endodontic sealers, during its preparation, that could substantially alter materials properties [31]. This was shown for different physicochemical properties such as setting time, flow, solubility or radiopacity values, even when used methodology was the same [31]. Similarly, the authors who evaluated radiopacity of endodontic materials assumed that the manipulation with the material during the mixing process could be the reason for observed diversity of results [32]. Additionally, it was shown that the quantity of radio-opacifiers could be different in two ends of the packing tube, and that the radiopacifying agent could be deposited at the lower end, while the upper portions of the tube could present lower quantity of radio-opacifier [33].

## CONCLUSION

Endodontic sealers examined in the present study showed different radiopacity values that could be the consequence of type and amount of radiopacifying agents in its composition. AH Plus sealer had the highest radiopacity, while calcium silicate-based sealers showed lower values, from BioRoot RCS, followed by GuttaFlow Bioseal, to MTA Fillapex, in descending order, and Bioceramic Root Canal Sealer with the lowest values.

## ACKNOWLEDGES

This study was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia, record number: 451-03-9/2021-14/ 200129.

## REFERENCES

1. Chen B, Haapasalo M, Mobuchon C, Li X, Ma J, Shen Y. Cytotoxicity and the Effect of Temperature on Physical Properties and Chemical Composition of a New Calcium Silicate-based Root Canal Sealer. J Endod. 2020;46(4):531–8. [DOI: 10.1016/j.joen.2019.12.009] [PMID: 32081458]
2. Kaup M, Schäfer E, Dammaschke T. An *in vitro* study of different material properties of Biodentine compared to ProRoot MTA. Head Face Med. 2015;11:6. [DOI: 10.1186/s13005-015-0074-9] [PMID: 25934270]
3. Guo J, Yang D, Okamura H, Teramachi J, Ochiai K, Qiu L, Haneji T. Calcium hydroxide suppresses *Porphyromonas endodontalis* lipopolysaccharide-induced bone destruction. J Dent Res. 2014;93(5):508–13. [DOI: 10.1177/0022034514526886] [PMID: 24603641]
4. Tanomaru JM, Leonardo MR, Tanomaru Filho M, Bonetti Filho I, Silva LA. Effect of different irrigation solutions and calcium hydroxide on bacterial LPS. Int Endod J. 2003;36(11):733–9. [DOI: 10.1046/j.1365-2591.2003.00717.x] [PMID: 14641436]
5. Estrela C, Sydney GB, Bammann LL, Felippe Júnior O. Mechanism of action of calcium and hydroxyl ions of calcium hydroxide on tissue and bacteria. Braz Dent J. 1995;6(2):85–90 [PMID: 8688662]
6. Katz A, Kaffe I, Littner M, Tagger M, Tamse A. Densitometric measurement of radiopacity of Gutta-percha cones and root dentin. J Endod. 1990;16(5):211–3. [DOI: 10.1016/S0099-2399(06)81671-7] [PMID: 2074412]
7. Tagger M, Katz A. Radiopacity of endodontic sealers: development of a new method for direct measurement. J Endod. 2003;29(11):751–5. [DOI: 10.1097/00004770-200311000-00016] [PMID: 14651284]
8. Gambarini G, Testarelli L, Pongione G, Gerosa R, Gagliani M. Radiographic and rheological properties of a new endodontic sealer. Aust Endod J. 2006;32(1):31–4. [DOI: 10.1111/j.1747-4477.2006.00005.x] [PMID: 16603043]
9. Zamparini F, Siboni F, Prati C, Taddei P, Gandolfi MG. Properties of calcium silicate-monobasic calcium phosphate materials for endodontics containing tantalum pentoxide and zirconium oxide. Clin Oral Investig. 2019;23(1):445–57. [DOI: 10.1007/s00784-018-2453-7] [PMID: 29737429]
10. Prüllage RK, Urban K, Schäfer E, Dammaschke T. Material Properties of a Tricalcium Silicate-containing, a Mineral Trioxide Aggregate-containing, and an Epoxy Resin-based Root Canal Sealer. J Endod. 2016;42(12):1784–8. [DOI: 10.1016/j.joen.2016.09.018] [PMID: 27769676]
11. Húngaro Duarte MA, de Oliveira El Kadre GD, Vivan RR, Guerreiro Tanomaru JM, Tanomaru Filho M, de Moraes IG. Radiopacity of portland cement associated with different radiopacifying agents. J Endod. 2009;35(5):737–40. [DOI: 10.1016/j.joen.2009.02.006] [PMID: 19410095]
12. Camargo RV, Silva-Sousa YTC, Rosa RPFD, Mazzi-Chaves JF, Lopes FC, Steier L, et al. Evaluation of the physicochemical properties of silicone- and epoxy resin-based root canal sealers. Braz Oral Res. 2017;31:e72. [DOI: 10.1590/1807-3107BOR-2017.vol31.0072] [PMID: 28832718]
13. Khalil I, Naaman A, Camilleri J. Properties of Tricalcium Silicate Sealers. J Endod. 2016;42(10):1529–35. [DOI: 10.1016/j.joen.2016.06.002] [PMID: 27523906]
14. Siboni F, Taddei P, Zamparini F, Prati C, Gandolfi MG. Properties of BioRoot RCS, a tricalcium silicate endodontic sealer modified with povidone and polycarboxylate. Int Endod J. 2017;50 Suppl 2:e120–e136. [DOI: 10.1111/iej.12856] [PMID: 28881478]
15. Tanomaru-Filho M, Torres FFE, Chávez-Andrade GM, de Almeida M, Navarro LG, Steier L, et al. Physicochemical Properties and Volumetric Change of Silicone/Bioactive Glass and Calcium Silicate-based Endodontic Sealers. J Endod. 2017;43(12):2097–101. [DOI: 10.1016/j.joen.2017.07.005] [PMID: 29032816]
16. Lopes FC, Zangirolami C, Mazzi-Chaves JF, Silva-Sousa AC, Crozeta BM, Silva-Sousa YTC, et al. Effect of sonic and ultrasonic activation on physicochemical properties of root canal sealers. J Appl Oral Sci. 2019;27:e20180556. [DOI: 10.1590/1678-7757-2018-0556] [PMID: 31508791]
17. Lee JK, Kwak SW, Ha JH, Lee W, Kim HC. Physicochemical Properties of Epoxy Resin-Based and Bioceramic-Based Root Canal Sealers. Bioinorg Chem Appl. 2017;2017:2582849. [DOI: 10.1155/2017/2582849] [PMID: 28210204]
18. Marciano MA, Duarte MA, Camilleri J. Calcium silicate-based sealers: Assessment of physicochemical properties, porosity and hydration. Dent Mater. 2016;32(2):e30–40. [DOI: 10.1016/j.dental.2015.11.008] [PMID: 26727694]
19. Kebudi Benezra M, Schembri Wismayer P, Camilleri J. Interfacial Characteristics and Cytocompatibility of Hydraulic Sealer Cements.

J Endod. 2018;44(6):1007–17. [DOI: 10.1016/j.joen.2017.11.011] [PMID: 29398087]
20. Almeida LHS, Moraes RR, Morgental RD, Cava SS, Rosa WLO, Rodrigues P, et al. Synthesis of silver-containing calcium aluminate particles and their effects on a MTA-based endodontic sealer. Dent Mater. 2018;34(8):e214–e223. [DOI: 10.1016/j.dental.2018.05.011] [PMID: 29789161]
21. Syriopoulos K, Sanderink GC, Velders XL, van der Stelt PF. Radiographic detection of approximal caries: a comparison of dental films and digital imaging systems. Dentomaxillofac Radiol. 2000;29(5):312–8. [DOI: 10.1038/sj/dmfr/4600553] [PMID: 10980568]
22. Antonijevic D, Jevremovic D, Jovanovic S, Obradovic-Djuricic K. An *in vitro* radiographic analysis of the density of dental luting cements as measured by CCD-based digital radiography. Quintessence Int. 2012;43(5):421–8. [PMID: 22536594]
23. Rasimick BJ, Shah RP, Musikant BL, Deutsch AS. Radiopacity of endodontic materials on film and a digital sensor. J Endod. 2007;33(9):1098–101. [DOI: 10.1016/j.joen.2007.05.005] [PMID: 17931942]
24. Cutajar A, Mallia B, Abela S, Camilleri J. Replacement of radiopacifier in mineral trioxide aggregate; characterization and determination of physical properties. Dent Mater. 2011;27(9):879–91. [DOI: 10.1016/j.dental.2011.04.012] [PMID: 21571361]
25. Carvalho-Junior JR, Correr-Sobrinho L, Correr AB, Sinhoreti MA, Consani S, Sousa-Neto MD. Radiopacity of root filling materials using digital radiography. Int Endod J. 2007;40(7):514–20. [DOI: 10.1111/j.1365-2591.2007.01246.x] [PMID: 17511790]
26. Baksi BG, Sen BH, Eyuboglu TF. Differences in aluminum equivalent values of endodontic sealers: conventional versus digital radiography. J Endod. 2008;34(9):1101–4. [DOI: 10.1016/j.joen.2008.06.004] [PMID: 18718374]
27. Akcay I, Ilhan B, Dundar N. Comparison of conventional and digital radiography systems with regard to radiopacity of root canal filling materials. Int Endod J. 2012;45(8):730–6. [DOI: 10.1111/j.1365-2591.2012.02026.x] [PMID: 22458866]
28. Antonijević D, Ilić D, Medić V, Dodić S, Obradović-Djuričić K, Rakočević Z. Evaluation of conventional and digital radiography capacities for distinguishing dental materials on radiograms depending on the present radiopacifying agent. Vojnosanit Pregl. 2014;71(11):1006–12. [DOI: 10.2298/vsp1411006a] [PMID: 25536802]
29. Antunes TBM, Janini ACP, Pelepenko LE, Abuna GF, Paiva EM, Sinhoreti MAC, et al. Heating stability, physical and chemical analysis of calcium silicate-based endodontic sealers. Int Endod J. 2021;54(7):1175–88. [DOI: 10.1111/iej.13496] [PMID: 33577106]
30. Camargo RV, Silva-Sousa YTC, Rosa RPFD, Mazzi-Chaves JF, Lopes FC, Steier L, et al. Evaluation of the physicochemical properties of silicone- and epoxy resin-based root canal sealers. Braz Oral Res. 2017;31:e72. [DOI: 10.1590/1807-3107BOR-2017.vol31.0072] [PMID: 28832718]
31. Camps J, Pommel L, Bukiet F, About I. Influence of the powder/liquid ratio on the properties of zinc oxide-eugenol-based root canal sealers. Dent Mater. 2004;20(10):915–23. [DOI: 10.1016/j.dental.2004.02.002] [PMID: 15501319]
32. Vivan RR, Ordinola-Zapata R, Bramante CM et al. Evaluation of the radiopacity of some commercial and experimental root-end filling materials. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108(6):e35–8. [DOI: 10.1016/j.tripleo.2009.07.037] [PMID: 19913718]
33. Baldi JV, Bernardes RA, Duarte MA, Ordinola-Zapata R, Cavenago BC, Moraes JC, et al. Variability of physicochemical properties of an epoxy resin sealer taken from different parts of the same tube. Int Endod J. 2012;45(10):915–20. [DOI: 10.1111/j.1365-2591.2012.02049.x] [PMID: 22486920]

Received: 08.09.2021 • Accepted: 09.11.2021

# Ispitivanje rendgenkontrastnosti kalcijum-silikatnih pasta digitalnim radiografisanjem

Bojan Dželetović, Ivana Bošnjak, Đorđe Antonijević, Jovan Badnjar, Zoran Petrov, Vanja Opačić-Galić

Univerzitet u Beogradu, Stomatološki fakultet, Klinika za bolesti zuba i endodonciju, Beograd, Srbija

**KRATAK SADRŽAJ**

**Uvod** Adekvatna rendgenkontrastnost pasta za punjenje kanala korena omogućava radiografsku vizuelizaciju, procenu kvaliteta kanalnog punjenja i kliničko praćenje nakon opturacije.

Cilj ovog rada je bio da se ispita rendgenkontrastnost pasta BioRoot RCS, MTA Fillapex, Bioceramic Root Canal Sealer, GuttaFlow Bioseal i da se uporede sa rendgenkontrastnošću paste AH Plus, koja se smatra zlatnim standardom u kliničkoj praksi.

**Materijal i metode** Uzorci pasta promera 5 mm i debljine 2 mm radiografisani su, zajedno sa stepeničastim etalonom, digitalnim radiografskim sistemom. Radiografske gustine uzoraka, prikazane kao srednje vrednosti tona sivo-bele skale (Adobe Photoshop CS4), izražene su u mm Al/mm materijala. Korišćena je jednofaktorska analiza varijanse sa testom Tukey post hoc i nivoom značajnosti od 0,05.

**Rezultati** Razlike u rendgenkontrastnosti su bile statistički značajne između svih ispitivanih pasta osim između BioRoot RCS i GuttaFlow Bioseal.

**Zaključak** Rendgenkontrastnost svih ispitivanih pasta je bila veća od minimuma propisanog standardom. Najveću rendgenkontrastnost imala je pasta AH Plus, dok su kalcijum-silikatne paste pokazale manje vrednosti, po opadajućem redosledu od BioRoot RCS, preko GuttaFlow Bioseal, zatim MTA Fillapex i Bioceramic Root Canal Sealer, kod koje su uočene najmanje vrednosti.

**Ključne reči:** rendgenkontrastnost; kalcijum-silikati; pasta za punjenje kanala

## UVOD

Opturacija, koja sledi posle adekvatnog čišćenja i oblikovanja kanala korena, treba da omogući apeksno i lateralno zaptivanje kanala i prevenciju mogućeg mikrocurenja, čime bi se sprečila moguća reinfekcija. Kanalno punjenje se sastoji od gutaperka poena i paste za punjenje kanala, koja popunjava prostor između gutaperke i dentinskog zida kanala korena [1].

S obzirom na to da je pasta za punjenje kanala u kontaktu sa periapikalnim tkivom, njegova biološka svojstva bi trebalo da omoguće stimulaciju reparatornih/regeneracionih procesa u alveolarnoj kosti, cementu i periodontalnom ligamentu. Kalcijum-silikatne paste imaju bioaktivna svojstva koja se vezuju za oslobađanje jona i formiranje kristala hidroksiapatita na njihovoj površini nakon kontakta sa tkivnim tečnostima bogatim fosfatima [2]. Kalcijum-hidroksid, koji nastaje hidratacijom kalcijum-silikatnih materijala, dovodi do povećanja pH vrednosti, čime se povećava alkalnost u okolnim tkivima, što stimuliše zarastanje, formaciju tvrdih tkiva i smanjenje osteoklastne aktivnosti [3]. Antimikrobna aktivnost ovih materijala se ostvaruje neutralizacijom lipopolisaharida prisutnih u membrani gram-negativnih bakterija i ireverzibilnom reakcijom sa bakterijskim enzimima [4, 5].

Da bi se procenio kvalitet kanalnog punjenja i pratio uspeh endodontske terapije, endodontski materijali bi trebalo da imaju odgovarajuću rendgenkontrastnost. Naime, rendgenkontrastnost omogućava jasno razlikovanje endodontskog materijala od okolnih zubnih i periapikalnih tkiva [6]. Adekvatna rendgenkontrastnost endodontskih materijala omogućava vizuelizaciju pora u kanalnom punjenju, koje mogu nastati kao posledica mešanja dvokomponentnih pasta ili tokom unošenja gutaperka poena u kanal [7]. Sa druge strane, nepopunjeni prostori unutar kanalnog punjenja uzrokuju neadekvatnu hermetičnost i mogu biti posledica rastvaranja paste. Ovi prostori se teško uočavaju i mogu biti zamaskirani naročito kod pasta sa izrazitom rendgenkontrastnošću [8].

Na tržištu su se pojavile nove kalcijum-silikatne paste, ali u literaturi još uvek nedostaju nezavisna istraživanja o svim njihovim fizičkim svojstvima. Takođe, postoji neusaglašenost u rezultatima studija koje su ispitivale rendgenkontrastnost kalcijum-silikatnih pasta, što je najverovatnije posledica korišćenja različitih eksperimentalnih modela [9, 10]. Da bismo dobili, na dokazima zasnovane, preporuke za kliničku praksu, važno je sprovesti naučna ispitivanja novih endodontskih pasta i uporediti ih sa materijalima koji su već u širokoj upotrebi.

Cilj ovog rada je bio da se ispita rendgenkontrastnost kalcijum-silikatnih pasta BioRoot RCS, MTA Fillapex, Bioceramic Root Canal Sealer i GuttaFlow Bioseal i uporedi sa rendgenkontrastnošću paste AH Plus, koja je zlatni standard u kliničkoj praksi.

## MATERIJAL I METOD

U ovoj studiji su korišćene sledeće paste: BioRoot RCS (Septodont, St Maur-des-Fosses, Francuska), MTA Fillapex (Angelus, Londrina, Brazil), Bioceramic Root Canal Sealer (SS White, Nju Džerzi, SAD), GuttaFlow Bioseal (Coltene Whaledent, Langenau, Nemačka) i AH Plus (Dentsply DeTrey Gmbh, Konstanz, Nemačka) (Tabela 1). Paste su zamešane prema uputstvu proizvođača i ulivene u teflonske kalupe debljine 2 mm, promera 5 mm. Uzorci su inkubirani na 37° C i 95% relativne vlažnosti do potpunog vezivanja pasta. Debljina uzoraka je proverena digitalnim mikrometrom i ukoliko je bilo potrebno, oni su polirani abrazivnim papirom (P600) da bi se osigurala ujednačena debljina od 2 ± 0,1 mm.

Od svake paste napravljena su po tri uzorka koji su radiografisani zajedno sa aluminijumskim etalonom (čistoće 99,6%, 10 stepenika debljine od po 1 mm) radiovizijskim sistemom (RVG-4) sa CCD digitalnim senzorom (Trophy Radiology, Cedex, Francuska). Korišćen je radiografski aparat (Trophy Radiology) koji je radio na 70 kVp i 7 mA, sa rastojanjem od

objekta radiografisanja 30 cm i vremenom ekspozicije od 0,07 s. Radiografska gustina uzoraka je izražena srednjim vrednostima tona sivo-bele skale korišćenjem programskog paketa Adobe Photoshop CS4 (Adobe Systems, San Hose, Kalifornija). Merenja su ponavljana tri puta za svaki uzorak i za svaki stepenik aluminijumskog etalona. Delovi uzoraka na kojima su uočene nepravilnosti, kao što su mehurići vazduha, nisu bili podvrgnuti merenju. Za određivanje rendgenkontrastnosti napravljen je grafikon logaritamske zavisnosti debljine aluminijuma od tona sivo-bele skale. Zatim su radiografske gustine materijala korišćene za određivanje rendgenkontrastnosti sa grafikona. Rendgenkontrastnost je bila izražena u mmAl/mm materijala (mmAl).

Normalnost distribucije podataka ispitana je testom Kolmogorov–Smirnov. Urađena je jednofaktorska analiza varijanse sa testom Tukey post hoc za poređenje razlika među silerima. Statistička analiza je urađena u programskom paketu SPSS 16.0 za Windows (SPSS Inc., Chiago, IL, SAD), nivo značajnosti je bio $\alpha = 0,05$.

## REZULTATI

Na Slici 1 prikazan je digitalni radiogaram paste GuttaFlow Bioseal i stepeničastog etalona. U Tabeli 2 su prikazane srednje vrednosti i standardne devijacije rendgenkontrastnosti ispitivanih pasta u milimetrima aluminijuma (mm Al). Najveća prosečna rendgenkontrastnost uočena je kod AH Plus paste (11,22 mmAl), a zatim, po opadajućim vrednostima: BioRoot RCS (8,32 mmAl), GuttaFlow Bioseal (7,64 mmAl), MTA Fillapex (5,58 mmAl), dok je najmanje vrednosti pokazala pasta Bioceramic Root Canal Sealer (3,4 mmAl). Statistička analiza je pokazala značajne razlike u vrednostima rendgenkontrastnosti između MTA Fillapex i svih ostalih pasta, zatim Bioceramic Root Canal Sealer i svih ostalih pasta, kao i GuttaFlow Bioseal i svih ostalih pasta. Jedino između pasta BioRoot RCS i GuttaFlow Bioseal nije bilo značajne razlike.

## DISKUSIJA

Međunarodna organizacija za standardizaciju (ISO) propisala je da bi paste za punjenje kanala korena, pri debljini od 1 mm, trebalo da imaju rendgenkontrastnost ekvivalentnu debljini od minimalno 3 mm aluminijuma. Sve paste testirane u ovoj studiji ostvarile su rendgenkontrastnost veću od standardom propisane. Iako su sve ispitivane paste na bazi kalcijum-silikata, značajne međusobne razlike u rendgenkontrastnosti uočene u ovoj studiji mogu biti posledica vrste i procentualne zastupljenosti rendgenkontrastnog sredstva u ovim materijalima.

Naime, Duarte i sar. 2009. su utvrdili da različita rendgenkontrastna sredstva imaju opadajuću rendgenkontrastnost: bizmut-oksid, olovo-oksid, bizmut-subnitrat, jodoform, cirkonijum-oksid, bizmut-karbonat, kalcijum-tungstat, barijum-sulfat i cink-oksid [11]. Bioceramic Root Canal Sealer i MTA Fillapex kao rendgenkontrastna sredstva imaju kalcijum-tungstat, što može biti uzrok njihove niže rendgenkontrastnosti u odnosu na ostale paste [11]. Sa druge strane, BioRoot RCS i AH Plus sadrže cirkonijum- oksid u svom sastavu, koji uslovljava veću rendgenkontrastnost [11]. Pasta GuttaFlow Bioseal ima više komponenti koje povećavaju njenu rendgenkontrastnost: cirkonijum- dioksid, srebro i gutaperka [12]. AH Plus, pored cirkonijum-oksida, sadrži i kalcijum- tungstat i fero-oksid, koji dodatno doprinose najvećoj rendgenkontrastnosti zabeleženoj kod ove paste [13].

U literaturi se nailazi na različite vrednosti rendgenkontrastnosti za kalcijum-silikatne paste koje su predmet ovog istraživanja. Rendgenkontrastnost BioRoot RCS varira od 5,2 do 8,3 mmAl [14, 13], dok se vrednosti zabeležene za GuttaFlow Bioseal kreću od 3,94 do 7,44 mmAl [15, 16]. Vrednosti za pastu MTA Fillapex u prethodnim studijama kreću se od 3,01 do 9,4 mmAl [17, 18]. Važno je naglasiti da je proizvođač menjao sastav paste MTA Fillapex, tako što je bizmut-oksid zamenjen kacijum-tungstatom, što dodatno usložnjava poređenje među studijama [19]. Kako je Bioceramic Root Canal Sealer relativno nov proizvod na tržištu, u literaturi nismo pronašli podatke koji se tiču njegove rendgenkontrastnosti, pa nije bilo moguće uporediti naše sa rezultatima drugih istraživanja. U većini studija o endodontskim pastama, AH Plus pasta, na bazi epoksi smole, bila je kontrolni materijal i pokazala izraženu varijabilnost u vrednostima rendgenkontrastnosti od 5,9 do 18,4 mmAl [20, 13].

Varijabilnost navedenih rezultata se delimično može objasniti različitim metodološkim pristupima i različitim radiografskim sistemima, konvencionalnim ili digitalnim, koji su korišćeni u pomenutim studijama [9]. Naime, prema međunarodnom standardu za rendgenkontrastnost pasta za punjenje kanala, ispitivanje radiografske vizuelizacije ostvaruje se hemijskim procesom razvijanja, fiksacije, ispiranja i sušenja konvencionalnog rendgen filma. Sve ove procedure mogu negativno uticati na kvalitet rendgen filma i vremenski su zahtevne [21]. Da bi se umanjio uticaj procesa razvijanja filma i uslova radiografisanja na preciznost merenja, na istom filmu sa uzorkom radiografiše se i aluminijumski etalon, koji je izabran kao referentan jer aluminijum ima sličnu rendgenkontrastnost kao dentin [22]. Nakon razvijanja filma potrebno je optičkim denzitometrom meriti količinu svetlosti koju propusti film i prevesti je u debljinu aluminijuma koja na filmu propusti istu količinu svetlosti. Sa druge strane, sve veća upotreba digitalne radiografije u kliničkoj praksi pokrenula je nova istraživanja rendgenkontrastnosti stomatoloških materijala uz upotrebu digitalizovanih sistema [23].

Široka upotreba ovih sistema ih je načinila i klinički relevantnijim u odnosu na konvencionalnu radiografiju. Takođe, kompjuterska obrada i analiza digitalne slike omogućavaju da se lakše dođe do podataka, isključuje greške koje se vezuju za razvijanje filmova i koristi manje doze zračenja, s obzirom na to da su digitalni senzori osetljiviji od konvencionalnih filmova [24]. Imajući u vidu široku rasprostranjenost i prednosti digitalne radiografije u odnosu na konvencionalnu, neki autori su smatrali da bi trebalo usvojiti nove, modifikovane protokole od strane organizacija za standardizaciju [25, 26].

Različita istraživanja o rendgenkontrastnosti endodontskih materijala, poredeći konvencionalnu i digitalnu metodu, pokazala su da izbor metode za radiografisanje može značajno uticati na dobijene vrednosti rendgenkontrastnosti [27, 28]. U ovim istraživanjima autori su zaključili da je teško poredити njihove rezultate sa rezultatima drugih studija zbog različitih metodoloških pristupa merenju rendgenkontrastnosti. Ovo dalje implicira da je pri određivanju rendgenkontrastnosti različitih pasta za punjenje kanala važno da se primeni isti eksperimentalni dizajn studije i isti radiografski sistem da bi rezultati bili

uporedivi. Interesantno je što je u prethodnim studijama koje su, slično našoj, koristile digitalne radiografske sisteme, BioRoot RCS pasta imala slične vrednosti rendgenkontrastnosti (7,96 i 8,3 mmAl) [29, 13]. Takođe su rezultati rendgenkontrastnosti za GuttaFlow Bioseal u našem istraživanju saglasni sa rezultatima iz dve studije (7,02 i 7,44 mmAl) koje su koristile digitalne radiografske sisteme slične našim [30, 15].

Drugi mogući uzrok za veliki raspon u vrednostima rendgenkontrastnosti pasta za punjenje kanala korena opisan u literaturi mogle bi biti varijacije u odnosu pojedinačnih komponenti dvokomponentnih pasta, tokom njihove pripreme, koje mogu značajno da promene svojstva materijala [31]. Ovo je pokazano za različita fizičko-hemijska svojstva, kao što su vreme vezivanja, tečljivost, rastvorljivost ili rendgenkontrastnost, čak i kada je korišćena ista metodologija [30, 32]. Isto tako, autori koji su ispitivali rendgenkontrastnost endodontskih materijala smatrali su da manipulacija materijalom tokom procesa mešanja može uzrokovati razlike u rezultatima [33]. Takođe je pokazano da količina rendgenkontrastnog sredstva može biti različita na dva kraja tube sa endodontskom pastom, kao i da se rendgenkontrastno sredstvo može nataložiti na donjem kraju tube, dok gornji delovi mogu sadržati manju količinu rendgenkontrastnog sredstva [32].

## ZAKLJUČAK

Paste za punjenje kanala korena ispitane u ovoj studiji pokazale su različite vrednosti rendgenkontrastnosti, koje mogu biti posledica vrste i količine rendgenkontrastnih sredstava u njihovom sastavu. Najveću rendgenkontrastnost imala je pasta AH Plus, dok su kalcijum-silikatne paste pokazale manje vrednosti, po opadajućem redosledu, od BioRoot RCS, preko GuttaFlow Bioseal, zatim MTA Fillapex i Bioceramic Root Canal Sealer, kod koje su uočene najmanje vrednosti.

## ZAHVALNICA

Istraživanje je podržano od strane Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije, evidencioni broj: 451-03-9/2021-14/200129.

sciendo

Serbian Dental Journal, vol. 68, N° 4, 2021 | 197

REVIEW ARTICLE
PREGLED LITERATURE

https://doi.org/10.2298/SGS2104197M
UDC: 616.31-006.04-085:615.849; 617.56-006.04-085:615.849

# The role of radiotherapy in the treatment of malignant tumors of the oral and maxillofacial region

Nikola Milošević[1], Srđan Milanović[1], Suzana Stojanović-Rundić[1,2], Marko Dožić[1]

[1]Institute of Oncology and Radiology of Serbia, Belgrade, Serbia;
[2]University of Belgrade Faculty of Medicine, Belgrade, Serbia

**SUMMARY**

Malignant tumors of the maxillofacial and oral region are relatively rare and form a very heterogeneous group of tumors whose incidence is constantly increasing. It is a disease of the elderly population, with a slight prevalence of males. The most common histological type is squamous cell carcinoma, and the most common localization of the tumor is on the skin and mucous membranes of this region. In the treatment of these tumors, the cooperation of different specialties is necessary. According to all modern recommendations for treatment, surgery is the first method of treatment, and radiotherapy has its place in both adjuvant and definitive approaches. Chemotherapy with limited effect is used for disseminated disease. The aim of the study was to present the role of radiotherapy in multidisciplinary treatment of malignant tumors of the oral and maxillofacial region.

**Keywords:** malignant tumors of maxillofacial and oral regions; squamous cell carcinomas; radiotherapy

## INTRODUCTION

The maxillofacial and oral region encompasses all structures of the face and jaw, ie. includes the space between the frontal line of the hair (forward up) and the hyoid bone (forward down), and posteriorly from the ramus of the mandible. It includes the following regions: frontal, orbital, infraorbital, zygomatic, nasal, lip and mouth region, cheek, parotidomaseteric, auricular, temporal, submental, and submandibular region [1].

Malignant tumors of the maxillofacial and oral regions are highly heterogeneous group of tumors that differ in primary origin, risk factors, histology, clinical appearance and biological behavior. They can arise from malignantly transformed cells of all types of tissue in this region (skin, melanocytes, subcutaneous and connective tissue, fat and muscle tissue, mucous membranes, blood vessels, glandular tissue, lymphatic system, bones, cartilage and teeth). The most common localizations of these tumors are gingiva, tongue, buccal mucosa, mouth, palate, maxilla, parotid gland and sinuses. Histological types represented in this region are squamous cell and mucoepidermoide carcinoma, osteosarcoma, lymphoma, and melanoma [2]. The current WHO (World health organisation) classification divides them into benign and malignant odontogenic tumors, benign and malignant tumors of bone and cartilage, benign and malignant soft tissue tumors, fibrose and bone tumors and hematolymphoid tumors [3].

## EPIDEMIOLOGY, CLINICAL DATA AND DIAGNOSIS

Malignant tumors of the maxillofacial and oral regions make about 10% of all malignant solid tumors [4]. They occur in both children and adults. Data has shown that it is a disease of the elderly population, with a slight prevalence of males [5]. There is no clearly defined cause of these tumors, but there are certain risk factors: socioeconomic (these tumors usually occur in underdeveloped countries), tobacco use, alcohol consumption, oral hygiene, food and viral infections [6]. The symptoms of these tumors are various such as swelling, pain, bleeding, problems with chewing, swallowing, speech, nose, eyes, and teeth.

The diagnosis includes anamnesis, clinical examination (the role of the dentist and maxillofacial surgeon is especially important), CT and MRI of the splanchnocranium (according to symptoms and CT of endocranium), and CT of the neck and thorax. They are usually detected in the locally advanced stage of the disease.

## TREATMENT OF MALIGNANT TUMORS OF THE MAXILOFACIAL AND ORAL REGION

The treatment is multimodal and individualized, including surgery, radiotherapy and chemotherapy.

## SURGERY

Surgery is the primary approach in the treatment of tumors of the maxillofacial and oral regions, especially in the early stages of the disease. There are many challenges in the surgical treatment of these tumors because they are located near sensitive areas of this region. Which modality of surgery will be applied is determined by the maxillofacial surgeon according to clinical examination and additional diagnostic image, taking into account the

**Address for correspondence:** Nikola MILOŠEVIĆ, Institute of Oncology and Radiology of Serbia, Pasterova 14, Belgrade, Serbia; *milosevicnikola43@gmail.com*

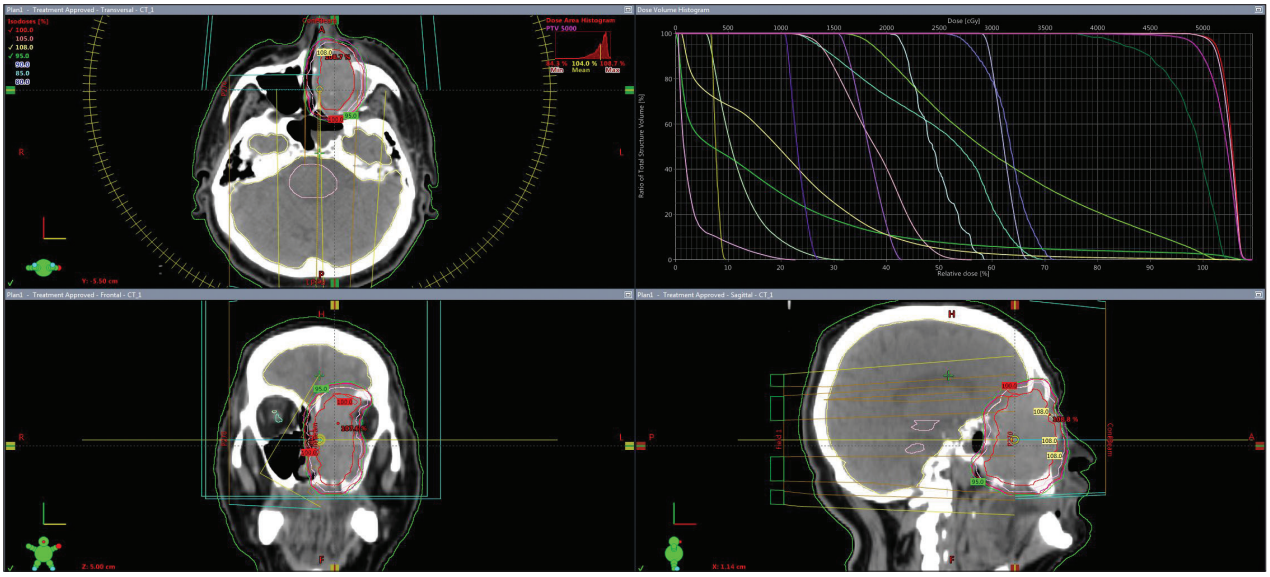

**Figure 1.** Irradiated volumes, dose distribution and radiation fields arrangement in definitive radiotherapy of paranasal cavity cancer
**Slika 1.** Zračni volumeni, dozna distribucija i raspored zračnih polja kod definitivne zračne terapije karcinoma paranazalnih šupljina

formation of the smallest deformity with minimal scarring [7]. Surgical methods include enucleation, drainage, surgical excision, resection, and if possible, reconstructive procedures are performed.

## RADIATION

Radiotherapy is a treatment modality that is used in the treatment of malignant tumors of the maxillofacial and oral regions, usually as postoperative (adjuvant), definitive and palliative. The most widely used oncology guides in the treatment of these tumors are NCCN (National Comprehensive Cancer Network) [8] and ESMO (European Society for Medical Oncology).

Adjuvant radiotherapy (radiochemotherapy) is indicated in patients who have a high risk of disease relapse (positive surgical margin, extracapular nodal extension, involvement of multiple lymph nodes, perineural and lymphatic invasion).

Definitive radiotherapy (radiochemotherapy) is used in the early stages if there are contraindications for surgery, and in the locally advanced cases if the tumor is unresectable [9].

Palliative radiotherapy is used to control local symptoms such as pain, bleeding and airway obstruction.

In terms of treated volume, radiation therapy can be local and locoregional. Locoregional radiotherapy implies that regional lymph nodes are included in the planned volume.

Radiation treatment for these tumors encompasses a wide range of techniques that can be applied: ortho-voltage, 3D conformal (3D CRT), intensity-modulated radiotherapy (IMRT), and volumetrically modulated arc therapy (VMAT). The choice and decision on how to plan and conduct radiation therapy depends on the location of the tumor and the stage of the disease.

Orthovoltage radiotherapy is a simple technique that is mostly used in the treatment of malignant tumors of the skin of the maxillofacial and oral region, and its advantage over other radiation techniques is reflected in the dose distribution, so that the maximum dose is on the skin surface or tumor lesion. Due to availability of lesions, the arrangement of radiation fields is simple (from one direct field) with collimation with lead protections.

3D conformal, IMRT and VMAT radiotherapy are modern radiation techniques that enable significant saving of organs at risk, while reducing toxicity and giving higher doses of radiation onto tumor volume. 3D CRT means the distribution of the radiation dose that is adapted to the irregular shape of the target volume, and IMRT means the controlled inhomogeneous dose distribution, whose inhomogeneity is adjusted to the variations of the shape of the target volumes and/or organs at risk. VMAT is a novel radiation therapy technique that continuously delivers a dose of radiation as the radiation treatment machine rotates. Similar to IMRT, this technique precisely shapes the dose distribution over a given radiation volume, while minimizing the dose to surrounding organs that are in the immediate vicinity of tumor. Radiation therapy is performed with doses of 60–66 Gy in the adjuvant and 66–72 Gy in the definitive approach, with a standard fractionation regimen, 2 Gy daily, 5 days weekly [10] (Figures 1, 2).

The toxicity of radiotherapy in the treatment of malignant tumors of the maxillofacial and oral region can be acute and late and occurs on the skin and mucous membranes of this region.

Acute toxicity develops during radiation therapy and occurs on mucosa as mucositis, dysgeusia, and xerostomia. Mucositis is radiation damage to the mucous membrane, it is the most common acute toxicity of radiotherapy and it is developed by all patients who irradiate this region. There are 4 degrees of mucositis: I (erythema), II (plaques) , III (ulcerations), and IV (necrosis). Dysgeusia is a loss of taste sensation and occurs in the initial phase of radiation therapy as an acute reaction of the mucosa, due to the damage of receptor cells and usually precedes the development of mucositis. Xerostomia is dry mouth and occurs as a consequence of salivary glands damage by radiation therapy. All

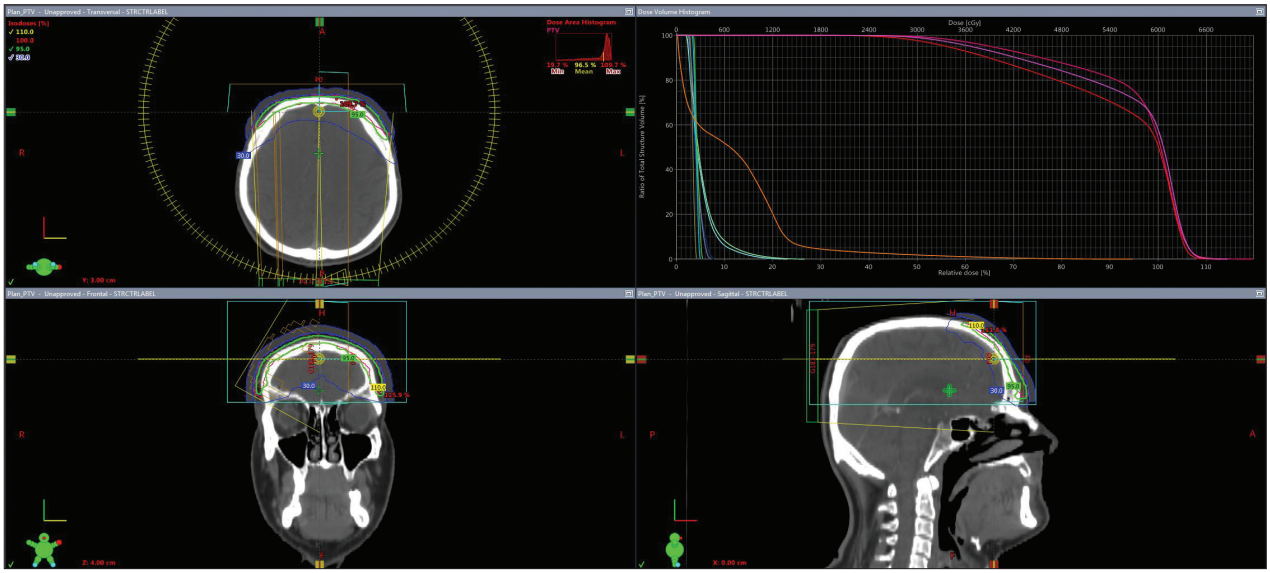

**Figure 2.** Irradiated volumes, dose distribution and radiation fields arrangement in postoperative radiotherapy of skin cancer
**Slika 2.** Zračni volumeni, dozna distribucija i raspored zračnih polja kod postoperativne zračne terapije karcinoma kože

these changes are reversible except for xerostomia. Acute skin toxicity also occurs during radiation therapy such as dermatitis and it is radiation damage to the skin. There are four degrees of dermatitis: I (erythema), II (dry desquamation), III (wet desquamation), and IV (ulceration and necrosis) [11].

Late toxicity occurs several months after radiation therapy. These changes are all irreversible. Atrophy occurs on the mucosa and atrophy, telangiectasia, induration, and edema occur on the skin. Teeth can be damaged by painless radiation caries, and due to fibrous changes in the masseter muscles trismus occurs. Osteoradionecrosis of the mandible is the most serious late complication of radiation therapy [12].

## CHEMOTHERAPY

Chemotherapy in the treatment of malignant tumors of the maxillofacial and oral region is usually used in combination with radiotherapy in the postoperative approach in patients with locally advanced disease and risk factors for relapse or definitive radiochemotherapy and is used alone in disseminated disease. Platinum-based cytostatics are most commonly used.

## CONCLUSION

Malignant tumors of the maxillofacial and oral regions are a major global health problem, and their incidence is increasing. In order to choose the optimal method of treatment, a multidisciplinary approach is necessary, which includes a team of specialists from various fields: radiology, medical and radiation oncology, maxillofacial surgery and dentistry. Surgical treatment is the first therapeutic choice (especially in the early stages), but radiotherapy (especially in the locally advanced stages) certainly plays a significant role in the treatment of these diseases. Unfortunately, the use of cytostatics in the disseminated phase of the disease does not give the expected effect.

## REFERENCES


1. Iwanaga J, Tubbs RS. Atlas of Oral and Maxillofacial Anatomy. 1st ed. Springer; 2021. [DOI: 10.1007/978-3-030-78327-3]
2. Alotaibi ON. Oral and maxillofacial cancer: A 35-year retrospective analysis at a referral dental hospital in Saudi Arabia. Saudi Dent J. In Press. 2021. [DOI: 10.1016/j.sdentj.2021.10.001]
3. El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ. WHO classification of head and neck tumours. 4th edn. Lyon: IARC; 2017. p. 205–60.
4. Rolski D, Kostrzewa-Janicka J, Zawadzki P, Życińska K, Mierzwińska-Nastalska E. The Management of Patients after Surgical Treatment of Maxillofacial Tumors. Biomed Res Int. 2016;2016:4045329. [DOI: 10.1155/2016/4045329] [PMID: 27747229]
5. Ariyoshi Y, Shimahara M, Omura K, Yamamoto E, Mizuki H, Chiba H, et al. Epidemiological study of malignant tumors in the oral and maxillofacial region: survey of member institutions of the Japanese Society of Oral and Maxillofacial Surgeons, 2002. Int J Clin Oncol. 2008;13(3):220–8. [DOI: 10.1007/s10147-007-0756-9] [PMID: 18553231]
6. Rao SVK, Mejia G, Roberts-Thomson K, Logan R. Epidemiology of Oral Cancer in Asia in the Past Decade – An Update (2000–2012). Asian Pac J Cancer Prev. 2013;14(10):5567–77. [DOI: 10.7314/APJCP.2013.14.10.5567] [PMID: 24289546]
7. Aldelaimi AA, Enezei HH, Aldelaimi TN, Mohammed KA. Tumors of Craniofacial Region in Iraq (Clinicopathological Study). J Res Med Dent Sci. 2021;9(1):66–71.
8. National Comprehensive Cancer Network. 2021. Head and neck cancer (version 3.2021).
9. Lu JJ, Brady LW. Decision Making in Radiation Oncology. Volume 1. Springer; 2011. [DOI 10.1007/978-3-642-13832-4]
10. Mileusnić D, Marošević G, Durbaba M. Radijaciona onkologija. Medicinski fakultet Univerziteta u Banja Luci, 2020.
11. Halperin EC, Wazer DE, Perez CA, Brady LW. Perez & Brady's Principles and Practice of Radiation Oncology. 7th ed. Wolters Kluwer; 2019.
12. DeVita VT, Lawrence TS, Rosenberg SA. DeVita, Hellman, and Rosenberg's Cancer Principles & Practice of Oncology. 10th ed. Wolters Kluwer; 2015.


Received: 20.09.2021 • Accepted: 22.11.2021

# Uloga radioterapije u lečenju malignih tumora oralne i maksilofacijalne regije

Nikola Milošević[1], Srđan Milanović[1], Suzana Stojanović-Rundić[1,2], Marko Dožić[1]

[1]Institut za onkologiju i radiologiju Srbije, Beograd, Srbija;
[2]Univerzitet u Beogradu, Medicinski fakultet, Beograd, Srbija

**KRATAK SADRŽAJ**

**Uvod** Cilj ovog rada bio je da istraži savremene metode primene veštačke inteligencije u dijagnozi virusa SARS Cov-2 i da predvidi razvoj potencijalnih hitnih stanja.

**Metode** Pretražene su najčešće korišćene elektronske baze podataka, npr. Scopus i Medline, tokom 2020. godine. Za sintezu dobijenih podataka korišćen je narativni pristup.

**Rezultati** U ovom preglednom radu pokazalo se da primena veštačke inteligencije igra veoma važnu ulogu u dijagnozi i prognozi virusa u kliničkim ispitivanjima. Omogućava da se resursi (kao što su respiratori u bolnicama) koriste mnogo racionalnije tokom lečenja SARS Cov 2 i predviđanje mogućeg mortaliteta. Rezultati su dobijeni nakon analize izvedene na 120 radova i studija koje su elektronski preuzete iz radova objavljenih u bazama podataka Scopus i Pub Medline. Najčešće korišćene tehnike veštačke inteligencije su konvolucione neuronske mreže i učenje uz pomoć računara.

**Zaključci** Obuhvaćene studije pokazale su da veštačka inteligencija ima potencijal da značajno poboljša lečenje SARS Cov-2, iako mnoge od predloženih metoda još uvek nisu klinički prihvaćene. Iz toga sledi da je potrebno mnogo više napora za razvijanje standardizovanih protokola izveštavanja ili smernica o tome kako primeniti veštačku inteligenciju na konvencionalnu kliničku praksu. Ova tehnologija je pogodna za brzu i tačnu dijagnozu, predviđanje i praćenje pacijenata, odnosno prognozu razvoja bolesti kod budućih pacijenata.

**Ključne reči:** učenje uz pomoć računara; veštačka inteligencija; snimanje; RTG snimanje grudnog koša; CT

## UVOD

Maksilofacijalna i oralna regija obuhvata sve strukture lica i vilica, tj. uključuje prostor između frontalne linije kose (napred gore) i hiodne kosti (napred dole), a pozadi posteriorno od ramusa mandibule. Uključuje sledeće regije: frontalnu, orbitalnu, infraorbitalnu, zigomatičnu, nazalnu, regiju usne i usta, regiju obraza, parotidomaseteričnu, aurikularnu, temporalnu, submentalnu i submandibularnu [1].

Maligni tumori maksilofacijalne i oralne regije su izrazito heterogena grupa tumora koji se razlikuju prema primarnom poreklu, faktorima rizika, histologiji, kliničkoj slici i biološkom ponašanju. Oni mogu nastati iz maligno transformisanih ćelija svih vrsta tkiva u ovoj regiji (kože, melanocita, potkožnog, vezivnog, masnog i mišićnog tkiva, sluznica, krvnih sudova, žlezdanog tkiva, limfnog sistema, kostiju, hrskavice i zuba). Najčešće lokalizacije ovih tumora su gingiva, jezik, bukalna sluznica, usta, nepce, maksila, parotida i sinusi. Histološki tipovi koji su zastupljeni u ovoj regiji su skvamocelularni i mukoepidermiodni karcinom, osteosarkom, limfom i melanom [2]. Savremena klasifikacija SZO (Svetska zdravstvena organizacija) deli ih na: benigne i maligne odontogene tumore, benigne i maligne tumore kostiju i hrskavice, benigne i maligne tumore mekih tkiva, fibro-koštane i hematolimfoidne tumore [3].

Cilj rada je da se prikaže uloga radioterapije u multidisciplinarnom lečenju malignih tumora oralne i maksilofacijalne regije.

## EPIDEMIOLOGIJA, KLINIČKA SLIKA I DIJAGNOZA

Maligni tumori maksilofacijalne i oralne regije čine oko 10% svih malignih solidnih tumora [4]. Javljaju se i kod dece i odraslih. Podaci govore da se radi o bolesti starije populacije, sa blagom prevalencijom muškog pola [5]. Ne postoji jasno definisan uzrok nastanka ovih tumora, ali postoje određeni faktori rizika: socioekonomski (ovi tumori se javljaju obično u nerazvijenim zemljama), upotreba duvana, konzumacija alkohola, oralna higijena, hrana i virusne infekcije [6].

Simptomi ovih tumora su različiti, a mogu biti otok, bol, krvarenje, problemi sa žvakanjem, gutanjem, govorom, nosem, očima i zubima.

Dijagnoza obuhvata anamnezu, klinički pregled (posebno naglašena uloga stomatologa i maksilofacijalnog hirurga), KT i MR splanhnokranijuma (prema simptomima i endokranijuma) i KT vrata i toraksa. Obično se otkriju u lokalno odmaklom stadijumu bolesti.

## TERAPIJA MALIGNIH TUMORA MAKSILOFACIJALNE I ORALNE REGIJE

Lečenje je multimodalno i individualizovano, uključuje hirurgiju, radioterapiju i hemioterapiju.

## HIRURGIJA

Hirurgija je primarni pristup u lečenju malignih tumora maksilofacijalne i oralne regije, posebno kod ranih stadijuma bolesti. Brojni su izazovi u hirurškom lečenju ovih tumora zato što se oni nalaze u blizini osetljivih područja ove regije, a koji će se modalitet hirurgije primeniti donosi maksilofacijalni hirurg prema kliničkom pregledu i dopunskom dijagnostičkom imidžingu, uzimajući u obzir formiranje najmanjeg deformiteta sa minimalnim ožiljkom [7]. Hirurške metode obuhvataju enukleaciju, drenažu, hiruršku eksciziju i resekciju, a ako postoji mogućnost, rade se i rekonstruktivni zahvati.

## RADIOTERAPIJA

Radioterapija je modalitet lečenja koji se primenjuje u lečenju tumora maksilofacijalne i oralne regije obično kao postoperativna (adjuvantna), definitivna i palijativna. Najšire korišćeni onkološki vodiči u lečenju ovih tumora su NCCN (National Comprehensive Cancer Network) [8] i ESMO (European Society for Medical Oncology).

Adjuvantna radioterapija (radiohemioterapija) indikovana je kod pacijenata koji imaju visok rizik od relapsa bolesti (pozitivna hirurška margina, ekstrakapsularna nodalna ekstenzija, zahvaćenost multiplih limfnih nodusa, perineuralna i limfatična invazija).

Definitivna radioterapija (radiohemioterapija) koristi se kod ranih stadijuma ako postoje kontraindikacije za operaciju, a kod lokalno odmaklih ako je tumor neresektabilan [9].

Palijativna radioterapija se primenjuje u cilju kontrole lokalnih simptoma kao što su bol, krvarenje i opstrukcija disajnih puteva.

U pogledu tretiranog volumena, zračna terapija može biti lokalna i lokoregionalna. Lokoregionalna radioterapija podrazumeva da su u planirani zračni volumen obuhvaćeni i regionalni limfni čvorovi.

Zračna terapija ovih tumora obuhvata širok spektar tehnika koje se mogu primeniti: ortovoltažna, 3D konformalna (3D CRT), intenzitetom modulisana radioterapija (IMRT) i volumetrijski modulisana lučna terapija (VMAT). Izbor i odluka o načinu planiranja i sprovođenja zračne terapije zavisi od lokalizacije tumora i stadijuma bolesti.

Ortovoltažna radioterapija je jednostavna tehnika, koja se najviše koristi u lečenju malignih tumora kože maksilofacijalne i oralne regije, a čija se prednost u odnosu na druge tehnike zračenja ogleda u doznoj distribuciji, tako što je maksimum doze upravo na površini kože, to jest, na površini tumorske lezije. S obzirom na dostupnost lezija, aranžman zračnih polja je jednostavan (iz jednog direktnog polja) uz kolimaciju olovnim zaštitama.

3D konformalna, IMRT i VMAT radioterapija su savremene tehnike zračenja koje omogućavaju značajniju poštedu organa od rizika uz smanjenje toksičnosti i davanje većih doza zračenja na tumorski volumen. 3D CRT podrazumeva distribuciju doze zračenja koja je svojim oblikom prilagođena nepravilnom obliku ciljnog volumena, a IMRT podrazumeva kontrolisano nehomogenu distribuciju doze, čija je nehomogenost prilagođena varijacijama oblika ciljnih volumena i/ili organa od rizika. VMAT je novija tehnika zračne terapije kojom se kontinuirano isporučuje doza zračenja dok se glava aparata za zračenje rotira. Slično kao i kod IMRT, ovom tehnikom se precizno oblikuje distribucija doze na zadati zračni volumen, dok se minimizira doza na okolne organe koji su u neposrednoj okolini tumora.

Zračna terapija se sprovodi dozama od 60 do 66 Gy u adjuvantnom, a 66–72 Gy u definitivnom pristupu, standardnim režimom frakcionisanja, 2 Gy dnevno, pet dana nedeljno [10] (slike 1 i 2). Toksičnost radioterapije u lečenju malignih tumora maksilofacijalne i oralne regije može biti akutna i kasna i javlja se na koži i sluzokoži ove regije.

Akutna toksičnost se javlja tokom zračne terapije i na sluznici se javlja kao mukozitis, disgeuzija i kserostomija. Mukozitis je radijaciono oštećenje sluznice, predstavlja najčešću akutnu toksičnost radioterapije i razviju je svi pacijenti koji zrače ovu regiju. Postoje četiri gradusa mukozitisa: I (eritem), II (plakovi), III (ulceracije) i IV (nekroza). Disgeuzija je gubitak osećaja ukusa i nastaje u početnoj fazi zračne terapije kao akutna reakcija mukoze, zbog oštećenja receptorskih ćelija i obično prethodi razvoju mukozitisa. Kserostomija je suvoća usta i nastaje kao posledica oštećenja pljuvačnih žlezda pod dejstvom zračne terapije. Sve ove promene su reverzibilne osim kserostomije. Akutna toksičnost kože se takođe javlja tokom zračne terapije kao dermatitis i predstavlja radijaciono oštećenje kože. Postoje takođe četiri gradusa dermatitisa: I (eritem), II (suva deskvamacija), III (vlažna deskvamacija) i IV (ulceracije i nekroze) [11]. Kasna toksičnost se javlja nekoliko meseci posle zračne terapije. Sve ove promene su ireverzibilne. Na sluznici se javlja atrofija, a na koži atrofija, teleangiektazije, induracija i edem. Zubi mogu biti oštećeni bezbolnim radijacionim karijesom, a usled fibroznih promena mišića žvakača (m. massetera) nastaje trizmus. Osteoradionekroza mandibule je najozbiljnija kasna komplikacija zračne terapije [12].

## HEMIOTERAPIJA

Hemoterapija u toku lečenja malignih tumora maksilofacijalne i oralne regije primenjuje se obično u kombinaciji sa radioterapijom u postoperativnom pristupu kod pacijenata sa lokalno odmaklim stadijumima bolesti i prisutnim faktorima rizika za relaps bolesti ili kod definitivne radiohemioterapije, a samostalno se primenjuje u diseminovanoj bolesti. Najčešće se koriste citostatici na bazi platine.

## ZAKLJUČAK

Maligni tumori maksilofacijalne i oralne regije su veliki globalni zdravstveni problem, a

njihova incidenca raste. Radi izbora optimalnog načina lečenja, neophodan je multidisciplinarni pristup koji uključuje tim specijalista iz različitih oblasti, kao što su radiolog dijagnostičar, medikalni i radijacioni onkolog, maksilofacijalni hirurg i stomatolog. Hirurško lečenje je prvi terapijski izbor (posebno kod ranih stadijuma), ali značajnu ulogu u terapiji ovih oboljenja svakako zauzima radioterapija (posebno kod lokalno odmaklih stadijuma). Primena citostatika u diseminovanoj fazi bolesti, nažalost, ne daje očekivani efekat.

Serbian Dental Journal, vol. 68, N° 4, 2021

CASE REPORT
PRIKAZ BOLESNIKA

https://doi.org/10.2298/SGS2104202L
UDC: 616.288-77; 616.28-089.843

# Auricular prosthesis retained with implants – a case report

Vojkan Lazić[1], Ana Todorović[1], Marko Lazić[2], Vitomir Konstantinović[2]

[1]University of Belgrade, Faculty of Dental Medicine, Department of Prosthodontics, Belgrade, Serbia;
[2]University of Belgrade, Faculty of Dental Medicine, Department of Maxillofacial Surgery, Belgrade, Serbia

**SUMMARY**

Maxillofacial defects create physical, emotional and mental problems for the patient. The task of surgical-prosthetic rehabilitation is to provide best possible functional and esthetic solution. The aim of this paper was to present a modern approach to auricular defect rehabilitation. A 24-year-old patient with a lack of the right ear lobe due to trauma was admited for aesthetic rehabilitation. Implant-retained ear prosthesis was indicated. Three implants were placed into mastoid region of the temporal bone, and after the period of osseointegration, an individualized bar was attached to them for the retention of an auricular prosthesis made out of silicone. Prosthetic rehabilitation, in this case, achieved excellent retention and restored the appearance as well as self-confidence of the patient.

**Keywords:** ear prosthesis; silicone prosthesis on implants; maxillofacial implants

## INTRODUCTION

The success of a facial prosthesis largely depends on retention. This task becomes more complex with advances both in techniques and materials. The concept of surgical implantation of smaller implants for the retention of auricular prostheses, first presented by Branemark et al. in 1977, has been improved several times to date [1]. Extraoral implants are shorter than intraoral ones, and therefore can be implanted in the pericranial bone [2, 3]. Rehabilitation of patients with implant-supported prostheses has several advantages over the conventional method, where the use of skin adhesives for retention is necessary. In particular, they eliminate the separation caused by the movement of the surrounding soft tissue or sweating, which can lead to loss of contact between the edges of the silicone prosthesis [4]. Adhesives can cause skin irritation, allergic reactions, discoloration of prosthetic material and separation of prosthesis from skin [5, 6].

Several factors should be considered when designing an implant-supported prosthesis retention system with in the area of the face in order to avoid possible complications or implant loss. It is necessary to connect all implants with a rigid-bar-type connection. Consequently, the stress transfered on implants will be distributed equally among them. The retention bar must rest passively on the implants, and the retention system must fit within the margins of the prosthesis without affecting its contours or symmetry. Retention must be adequate in order to prevent accidental separation of the prosthesis.

The aim of this paper was to present clinical and laboratory procedures in the process of making auricular prosthesis for a patient with unilateral deformity of the auricle.

## CASE REPORT

In this case, a decision was made on surgical-prosthetic therapy of ear shell defect caused by ablation in a car accident. A 24-year-old patient was referred to the Clinic for Maxillofacial Surgery at the Faculty of Dentistry, University of Belgrade, with a unilateral ear lobe deficiency (Figure 1). CT of the temporal bone showed the existence of the bone of sufficient quality for the implantation of endosseous implants. Three Straumann SP short implants were placed (2 RN Ø 4.1 mm × 4 mm and 1 VN Ø 4.8 mm × 6 mm, Straumann, AG, Switzerland) in the auricle area (Figure 2). After a period of osseointegration of three months, all implants were well integrated, based on radiological criteria and clinical stability (Figure 3). After the period of osseointegration, the impression was done using the method of individual open tray and polyvinyl siloxanes (A-silicone). Before taking the impression of the defect, the implant position tranfers were placed and the impression was done at the implant level with addition silicone. A bar with matrices was planned and modeled on the working model. Based on the selected position of the ear prosthesis and the position of the bar, the base was modeled in wax and later made of thermally polymerized acrylate and used as a base for modeling the earlobe in wax. The epithesis was anchored using Hader bars, made to provide better retention and stability of the prosthesis. The Hader bar was cast from cobalt-chromium alloy using prefabricated plastic models (CEKA, Netherlands) (Figure 4). The acrylic base with plastic retention matrices was designed and manufactured to better support silicone dentures. Wax prosthesis model was prepared and evaluated on the patient, to ensure that the model faithfully restores contour and symmetry (Figure 5). After modeling, the wax ear prosthesis was made out of addition silicone using intrinsic and extrinsic

**Address for correspondence:** Vojkan LAZIĆ, Faculty of Dental Medicine, Department of Prosthodontics, Dr Subotića 8, 11000 Belgrade, Serbia; *vojkan.lazic@stomf.bg.ac.rs*

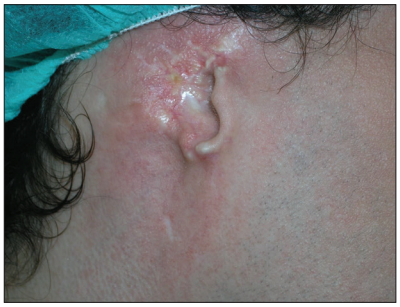

**Figure 1.** The auricular defect before implant placement
**Slika 1.** Izgled aurikularnog defekta pre ugradnje endosealnih implantata

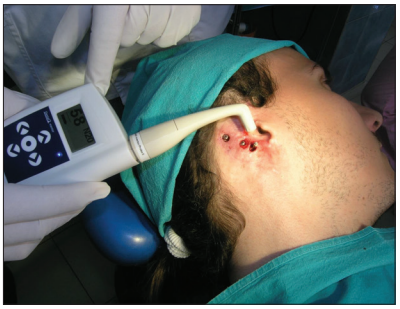

**Figure 2.** Checking the primary stability of the implant during placement using an Osstell Mentor (Ostell, Sweden)
**Slika 2.** Provera primarne stabilnosti implantata tokom ugradnje pomoću Osstell Mentora (Ostell, Sweden)

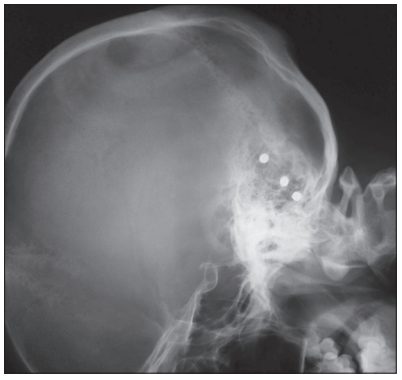

**Figure 3.** Control X-ray image
**Slika 3.** Kontrolni RDG snimak implantata

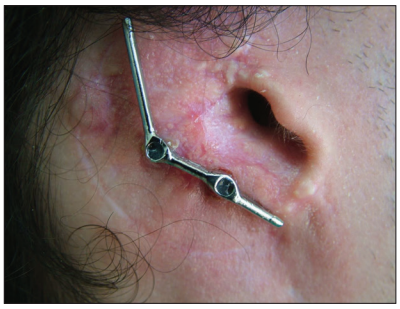

**Figure 4.** Individualized bar placed on the implants
**Slika 4.** Postavljena individualizovana prečka na implantate

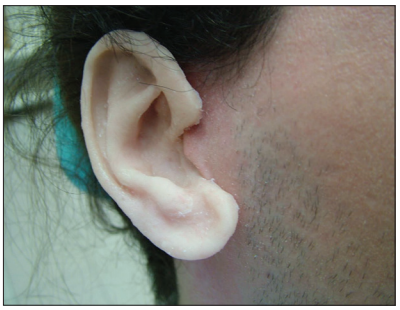

**Figure 5.** Auricular prosthesis model try in
**Slika 5.** Proba modela aurikularne proteze

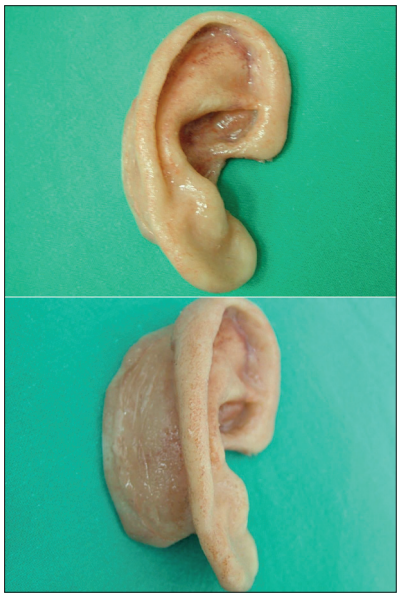

**Figure 6.** Auricular prosthesis after intrinsic and extrinsic staining procedures
**Slika 6.** Izgled aurikularne proteze posle intrinzičkih i ekstrinzičkih procedura bojenja

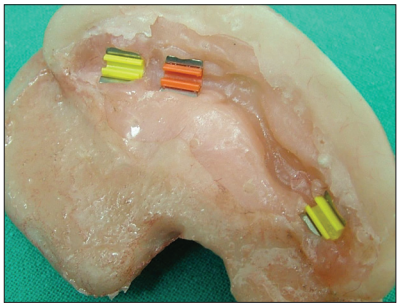

**Figure 7.** Acrylic base of auricular prosthesis with clips
**Slika 7.** Akrilatna baza aurikularne proteze sa matricama

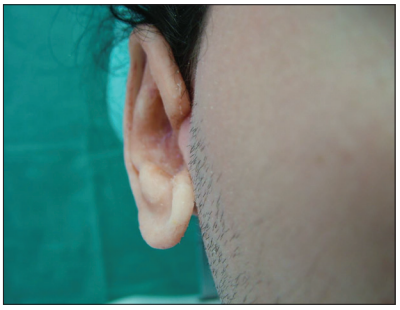

**Figure 8.** Finished auricular prosthesis
**Slika 8.** Izgled završene aurikularne proteze

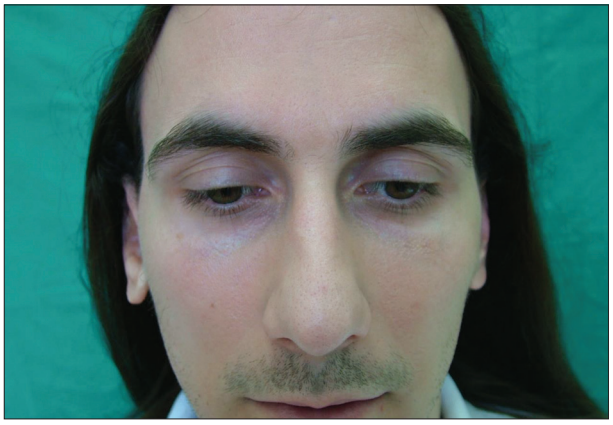

**Figure 9.** The patient after delivery of the auricular prosthesis
**Slika 9.** Izgled pacijenta po predaji aurikularne proteze

staining procedures (Epithetik Set; Bredent, Germany) (Figure 6). The intrinsic color was derived to match the color of the surrounding skin. After polymerization, the external dyeing was performed with the appropriate technique of applying color and adhesion. The silicone prosthesis was retained with plastic matrices on the acrylic substructure of the bars screwed on the implants (Figure 7). Metal housings were attached to the acrylic housings on the base before the prosthesis was implanted. The prosthesis was handed over to the patient and he was given instructions for hygiene maintenance (Figure 8). After 3, 6 and 12 months, at follow-up examinations, the patient was satisfied both with aesthetics and functional characteristics of the prosthesis (Figure 9).

## DISCUSSION

Extraoral implants in the mastoid region have very high success rate, close to 100% [7, 8]. Implant-retained auricular prosthesis provides more satisfaction to patients compared to adhesive, due to the ease of use and good retention in daily activities [9]. Clinical and biomechanical studies have shown that two implants are sufficient for retention of an ear prosthesis. The two primary retention systems used in the auricular region are magnet and bar based [10, 11]. The bar system ensures good retention of the prosthesis, however, it can be difficult for hygiene maintenance.

## CONCLUSION

Although there are obvious differences in the color and texture of skin and prosthesis, it can be concluded that this is currently the most up-to-date solution in maxillofacial-prosthetic rehabilitation of the auricular region and thus improves the "quality of life" of our patients. Implant-retained ear prosthesis provides multiple benefits for the patient: convenience, safety, consistent retention and positioning, eliminating the need for adhesive and maintaining marginal integrity and long-lasting.

## REFERENCES

1. Branemark PI, Albrektsson T. Titanium implants permanently penetrating human skin. Scand J Plast Reconstr Surg. 1982;16(1):17–21. [PMID: 7112035]
2. Tjellstrom A, Jacobsson M, Albrektsson T, Jannson K. Use of tissue integrated implants in congenital aural malformations. Adv Otorhinolaryngol. 1988;40:24–32. [PMID: 3389230]
3. Tjellstrom A, Yontchev E, Lindstrom J, Branemark PI. Five years' experience with bone-anchored auricular prostheses. Otolaryngol Head Neck Surg. 1985;93(3):366–72. [DOI: 10.1177/019459988509300315] [PMID: 3927232]
4. Lemon JC, Chambers MS. Locking retentive attachment for an implant-retained auricular prosthesis. J Prosthet Dent. 2002;87(3):336–8. [DOI: 10.1067/mpr.2002.122016] [PMID: 11941364]
5. Cantor R, Hildestad P. A material for epitheses. A preliminary report. Odontol Tidskr. 1966;74(1):32–40. [PMID: 5326048]
6. Chang TL, Garrett N, Roumanas E, Beumer J 3rd. Treatment satisfaction with facial prostheses. J Prosthet Dent. 2005;94(3):275–80. [DOI: 10.1016/j.prosdent.2005.06.002] [PMID: 16126080]
7. Aydin C, Karakoca S, Yilmaz H, Yilmaz C. Implant-retained auricular prostheses: an assessment of implant success and prosthetic complications. Int J Prosthodont. 2008;21(3):241–4. [DOI: 10.5772/27030] [PMID: 18548964]
8. Wazen JJ, Wright R, Hatfield RB, Asher ES. Auricular rehabilitation with bone-anchored titanium implants. Laryngoscope. 1999;109(4):523–7. [DOI: 10.1097/00005537-199904000-00001] [PMID: 10201734]
9. Sencimen M, Bal HE, Demirogullari M, Kocaoglu M, Dogan N. Auricular episthesis retained by an attachment system (2 case reports). Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;105(2):e28–34. [DOI: 10.1016/j.tripleo.2007.08.016] [PMID: 18230374]
10. De Vale V, Faulkner MG, Wolfaardt JF, Rangert B, Tan HK. Mechanical evaluation of craniofacial osseointegration retention systems. Int J Oral Maxillofacial Implants. 1995;10(4):491–8. [PMID: 7672853]
11. Wolfaardt JF, Wilkes GH, Anderson JD. Craniofacial osseointegration: Prosthodontic treatment. In: Taylor TD, editor. Clinical maxillofacial prosthetics. Chicago: Quintessence; 2000. p. 285–7.
12. Chauhan D, Roy ID, Viswamnara M, Thakur A, Athwale R. Rehabilitation of Auricular Defect with Implant-Retained Auricular Prosthesis – A Case Report. Ann Maxillofac Surg. 2021;11(1):164–8. [DOI:10.4103/ams.ams_343_20] [PMID: 34522676]

Received: 01.10.2021 • Accepted: 30.11.2021

# Aurikularna proteza retinirana implantatima – prikaz slučaja

Vojkan Lazić[1], Ana Todorović[1], Marko Lazić[2], Vitomir Konstantinović[2]

[1]Univerzitet u Beogradu, Stomatološki fakultet, Klinika za stomatološku protetiku, Beograd, Srbija;
[2]Univerzitet u Beogradu, Stomatološki fakultet, Klinika za maksilofacijalnu hirurgiju, Beograd, Srbija

**KRATAK SADRŽAJ**

Maksilofacijalni defekti predstavljaju fizičke, emocionalne i psihičke probleme za pacijenta. Zadatak hirurško-protetske rehabilitacije je da obezbedi najbolje moguće funkcionalno i estetsko rešenje.
Cilj ovog rada je da se prikaže savremeni pristup rehabilitacije aurikularnog defekta.
Pacijent starosti 24 godine sa nedostatkom desne ušne školjke usled traume javlja se radi estetske rehabilitacije.
Planirana je ušna proteza retinirana implantatima. Hirurškim putem su u mastoidnu kost postavljena tri implantata, a nakon perioda oseointegracije za njih je pričvršćena individualizovana prečka za retenciju aurikularne proteze izrađene od silikona.
Protetskom rehabilitacijom u ovom slučaju postignuta je odlična retencija i vraćen izgled i samopouzdanje pacijenta.
**Ključne reči:** ušna proteza; silikonska proteza na implantatima; maksilofacijalni implantati

## UVOD

Uspeh facijalne proteze uglavnom zavisi od retencije. Ovaj zadatak postaje složeniji sa napredovanjem tehnika i materijala. Koncept hirurške ugradnje implantata manjih dimenzija radi retencije aurikularne proteze, koji prvi put predstavljaju Branemark i saradnici 1977. godine, do danas je više puta unapređivan [1]. Ekstraoralni implantati su kraći nego intraoralni i zato ih je moguće ugraditi u perikranijalnu kost [2, 3]. Rehabilitacija pacijenata implantatno-nošenim protezama ima nekoliko prednosti u odnosu na kovencionalni metod, gde je neophodna upotreba adheziva za kožu radi retencije. Konkretno, eliminišu odvajanje uzrokovano pomeranjem okolnog mekog tkiva ili znojenjem, što može dovesti do gubitka kontakta ivica silikonske proteze [4].

Adhezivi mogu izazvati iritaciju kože, alergijske reakcije, diskoloraciju protetskog materijala i odvajanje proteze od kože [5, 6].

Nekoliko faktora treba uzeti u obzir pri dizajniranju retencionog sistema proteza u predelu lica nošenim implantatima kako bi se izbegle moguće komplikacije gubitka implantata. Neophodno je povezati sve implantate pomoću rigidne konekcije tipa prečke. Posledično, stres koji prihvataju implantati će se distribuirati podjednako između implantata. Retenciona prečka mora nalegati pasivno na implantate, a retencioni sistem se mora uklopiti u okviru granica proteze bez uticaja na njene konture ili simetriju. Retencija mora biti odgovarajuća kako bi se sprečilo akcidentalno odvajanje proteze.

Cilj ovog rada bio je da se prikažu klinički i laboratorijski postupci u izradi aurikularne proteze za pacijenta sa jednostranim deformitetom ušne školjke.

## PRIKAZ BOLESNIKA

U ovom slučaju doneta je odluka o hirurško-protetskoj terapiji nedostatka ušne školjke nastalog posle ablacije u saobraćajnoj nesreći. Pacijent, star 24 godine, upućen je na Kliniku za maksilofacijalnu hirurgiju Stomatološkog fakulteta Univerziteta u Beogradu sa jednostranim nedostatkom ušne školjke (Slika 1). KT temporalne kosti je pokazala postojanje dovoljno kvalitetne kosti za ugradnju endosealnih implantata. Tri Straumann SP kratka implantata su postavljena (2 RN Ø 4,1 mm k 4 mm i 1 VN Ø 4,8 mm k 6 mm, Straumann, AG, Švajcarska) u predelu aurikule (Slika 2). Posle perioda oseointegracije od tri meseca, svi implantati su bili dobro integrisani na osnovu radioloških kriterijuma i kliničke stabilnosti (Slika 3). Nakon perioda oseointegracije, otisak je realizovan metodom individualne otvorene kašike i polivinil-siloksanima (A-silikon). Pre uzimanja otiska defekta postavljeni su prenosnici položaja implantata i realizovan je otisak na nivou implantata adicionim silikonom. Na radnom modelu je planirana i modelovana prečka sa matricama. Na osnovu izabranog položaja ušne proteze i položaja prečke, modelovana je baza u vosku i kasnije napravljena od toplotno polimerizovanog akrilata i korišćena kao baza za modelovanje ušne školjke u vosku. Epiteza je usidrena pomoću prečki Hader, koje su proizvedene da obezbede bolju retenciju i stabilnost proteze (Slika 4). Prečka Hader je izlivena od legure kobalt–hrom pomoću prefabrikovanih plastičnih modela (CEKA, Netherlands). Akrilatno kućište sa plastičnim matricama za retenciju je dizajnirano i proizvedeno za bolju potporu silikonske proteze. Modelacija proteze u vosku je pripremljena i evaluirana na pacijentu, kako bi se obezbedilo da model verno restauriše konturu i simetriju (Slika 5). Nakon modelovanja, ušna proteza u vosku je izrađena od adicionog silikona uz korišćenje intrinzičkih i ekstrinzičkih procedura bojenja (Epithetik Set; Bredent, Germany). Intrinzična boja je izvedena tako da odgovara boji okolne kože (Slika 6). Nakon polimerizacije izvedeno je spoljašnje bojenje odgovarajućom tehnikom nanošenja boje i adhezije. Proteza od silikona je retinirana plastičnim matricama na akrilnoj substrukturi prečki ušrafljenih na implantatima (Slika 7). Za akrilna kućišta na bazalnoj strani pričvršćena su metalna kućišta pre ugradnje proteze. Proteza je predata pacijentu i data su mu uputstva za održavanje higijene (Slika 8). Nakon tri, šest i 12 meseci, na kontrolnim pregledima, pacijent je bio zadovoljan i estetskim i funkcionalnim karakteristikama proteze (Slika 9).

## DISKUSIJA

Ekstraoralni implantati u mastoidnom regionu imaju veoma visoku stopu uspeha od blizu 100% [7, 8]. Aurikularna proteza retinirana implantatima pruža više zadovoljstva pacijentima u odnosu na adheziv zbog lakoće upotrebe i dobre retencije u svakodnevnim aktivnostima [9].

U kliničkim i biomehaničkim studijama pokazano je da su dva implantata dovoljna za retenciju ušne proteze. Dva pri-

marna sistema retencije koji se koriste u aurikularnoj regiji su pomoću magneta i prečke [10, 11]. Sistem retencije pomoću prečke i matrica obezbeđuje dobru retenciju proteza. Međutim, prečke mogu otežati održavanje higijene.

Iako postoje očigledne razlike u boji i teksturi kože i proteze, može se zaključiti da je ovo za sada najsavremenije rešenje u maksilofacijalno-protetičkoj rehabilitaciji aurikularne regije i na taj način se poboljšava „kvalitet života" pacijenata.

Ušna proteza retinirana implantatima pruža višestruke prednosti za pacijenta: pogodnost, sigurnost, doslednu retenciju i pozicioniranje, eliminisanje potrebe za lepkom, održavanje marginalnog integriteta i dugovečnost.

# Da li ste pažljivo čitali radove?

1. Maligni tumori maksilofacijalne i oralne regije su:
   a) relativno česti
   b) relativno retki
   c) izuzetno retki

2. U istraživanju rastvorljivosti gutaperka poena i pasti korišćene su:
   a) dve paste
   b) tri paste
   c) četiri paste

3. U kliničkoj studiji primene probiotika je učestvovalo:
   a) 20 pacijenata
   b) 30 pacijenata
   c) 40 pacijenata

4. Primena probiotika:
   a) smanjuje krvarenje prilikom sondiranja
   b) povećava krvarenje prilikom sondiranja
   c) ne utiče na krvarenje

5. Pasta koja se koristi kao zlatni standard za rengenkontrastnost je:
   a) ENDOMETAZON
   b) AH PLUS
   c) ACROSEAL

6. Primarni pristup u lečenju malignih tumora oralne i maksilofacijalne regije je:
   a) radioterapija
   b) hirurgija
   c) hemioterapija

7. Adhezivi kao retenciona sredstva u predelu lica:
   a) mogu izazvati iritaciju kože
   b) ne mogu izazvati iritaciju kože
   c) utiču na bolju vezu

8. Incidenca malignih tumora maksilofacijalne regije je:
   a) u stalnom porastu
   b) u konstantnom opadanju
   c) poslednjih godina nepromenjena

9. Rastvorljivost gutaperke i endodontskih silera je proveravana kod:
   a) eteričnih ulja
   b) hlorfenola
   c) EDTA

10. Primena probiotika
    a) smanjuje dubinu parodontalnog džepa
    b) povećava dubinu parodontalnog džepa
    c) ne utiče na parodontalni džep

11. Uzorci pasti su analizirani u kalupima promera:
    a) 2 mm
    b) 4 mm
    c) 5 mm

12. Radioterapija se u lečenju malignih tumora maksilofacijalne regije primenjuje kao:
    a) osnovni vid lečenja
    b) kao postoperativna
    c) kao terapijski postupak pre hirurške intervencije

13. Pacijenti sa implantatima reteniranim protezama su:
    a) efikasniji od konvencionalnih
    b) manje efikasni od konvencionalnih
    c) iste efikasnosti kao i konvencionalni

14. U istraživanju rastvorljivosti uzorci sa pastama su potopljeni u rastvor:
    a) tokom pet minuta
    b) tokom 10 minuta
    c) tokom 20 minuta

15. Klinička studija primene probiotika je trajala:
    a) 15 dana
    b) 30 dana
    c) 60 dana

16. Primena probiotika u terapiji hronične parodontopatije:
    a) pruža kliničku korist
    b) pogoršava stanje
    c) nema nikakvog efekta

17. Rengenkontrastnost je proveravana kod:
    a) pet pasti
    b) šest pasti
    c) osam pasti

18. Najmanja rengenkontrastnost je uočena kod
    a) AH PLUS
    b) MTA G
    c) Bioceramic Root CANAL SEALER

19. Zračna terapija u definitivnom pristupu se sprovodi u dozama od:
    a) 60–66 Gy
    b) 62–68 Gy
    c) 66–72 Gy

20. Ekstraoralni implantati su:
    a) duži nego intraoralni
    b) kraći nego intraoralni
    c) iste dužine kao intraoralni

21. Rastvorljivost gutaperka poena je ispitivana na:
    a) 36 gutaperka poena
    b) 66 gutaperka poena
    c) 96 gutaperka poena

22. Klinički parametri (DPDŽ, NPE, KPS) na kraju su bili:
    a) značajno viši nego na početku
    b) značajno niži nego na početku
    c) identični kao na početku

23. Rengenkontrastnost je proveravana kod pasti:
    a) na bazi kalcijum-sulfata
    b) na bazi kalcijum-aluminata
    c) na bazi kalcijum-silikata

24. Maligni tumori maksilofacijalne regije su:
    a) bolest mladih
    b) bolest starije populacije
    c) bolesti mladih i starih

25. Hemioterapija se u lečenju malignih tumora maksilofacijalne regije primenjuje:
    a) kao osnovni vid
    b) u kombinaciji sa radioterapijom
    c) samo u kombinaciji sa hirurgijom

26. Retencioni sistem proteza u predelu lica treba povezati:
    a) rigidnom vezom
    b) elastičnom vezom
    c) poluelastičnom vezom

27. Gutaperka štapići su potopljeni u eterično ulje:
    a) 1, 3 i 5 minuta
    b) 2, 5 i 10 minuta
    c) 2, 10 i 15 minuta

28. Klinički efekat probiotika je proveravan primenom kapsula:
    a) samo BIFIDOBACTERIUM
    b) samo LACTOBACILLUS
    c) BIFIDOBACTERIUM I LACTO BACILLUS

29. Rengenkontrastnost pasti za opturaciju obezbeđuje:
    a) bolju vizuelizaciju
    b) bolji kvalitet punjenja
    c) bolje hermetičko zaptivanje

30. Primena citostatika u diseminovanoj fazi bolesti kod tumora maksilofacijalne regije:
    a) daje očekivane rezultate
    b) ne daje očekivane rezultate
    c) izuzetno se retko primenjuje

31. U rastvaranju gutaperke najefikasnije je bilo:
    a) pomorandžino ulje
    b) eukaliptus
    c) ulje od karanfilića

32. Probiotici:
    a) pomažu rast i kolonizaciju patoloških mikroorganizama
    b) suzbijaju rast i kolonizaciju patoloških mikroorganizama
    c) suzbijaju rast zdrave flore kod parodontopatija

33. Uzorci pasti su analizirani u kalupima debljine:
    a) 1 mm
    b) 2 mm
    c) 3 mm

34. Uspeh facijalne proteze uglavnom zavisi od retencije?
    a) Da
    b) Ne
    c) Samo kod proteze nosa

35. Retenciona prečka mora:
    a) aktivno nalegati na implantate
    b) pasivno nalegati na implantate
    c) da odstoji od implantata

36. Eterična ulja se mogu koristiti za rastvaranje gutaperke i masti za opturaciju kanala?
    a) Da
    b) Ne
    c) Nemaju rastvarački efekat

37. Rengenkontrastnost pasti je bila:
    a) veća od minimuma propisanog standardom
    b) manja od minimuma propisanog standardom
    c) identična sa minimumom propisanog standarda

38. Maligni tumori maksilofacijalne regije su sa:
    a) blagom prevalencom kod žena
    b) blagom prevalencom kod muškaraca
    c) blagom prevalencom kod mlađih žena

39. Aurikularna proteza na implantatima je prikazana kod pacijenata:
    a) sa jednostranim deformitetom ušne školjke
    b) sa obostranim deformitetom
    c) sa delimičnim jednostranim deformitetom

40. Najveću rengenkontrastnost je pokazala pasta:
    a) AH PLUS
    b) MTA G
    c) BIO ROOT

41. Najveći gubitak mase endodontskih pasti je zabeležen kod:
    a) ENDOMETAZONA
    b) ACROSEAL
    c) AH PLUS

42. Dubina parodontalnog džepa je merena:
    a) na početku i na kraju kliničke studije
    b) samo na početku kliničke studije
    c) samo na kraju kliničke studije

43. Koncept hirurške ugradnje implantata manjih dimenzija radi retencije aurikularne proteze predstavio je:
    a) BRENEMARK
    b) ŠTRAUMAN
    c) BRANOVAČKI

44. Histološki maligni tumori maksilofacijalne regije su najčešće:
    a) skvamocelularni karcinomi
    b) sarkomi donje vilice
    c) sarkomi gornje vilice

45. Nivo pripojnog epitela je parametar koji je meren na početku i na kraju kliničke studije?
    a) Da
    b) Ne
    c) Meren je samo na početku kliničke studije

46. Najčešća lokalizacija malignog tumora maksilofacijalne regije je:
    a) koža
    b) gornja i donja vilična kost
    c) parotidna žlezda

47. Ulje čajevca rastvara AH PLUS:
    a) efikasnije nego ACROSEAL
    b) efikasnije nego ENDOMETAZON
    c) efikasnije nego ACROSEAL i ENDOMETAZON

48. Ispiranje usta rastvorom sa probiotičkim kapsulama je rađeno:
    a) jednom dnevno
    b) dva puta dnevno
    c) tri puta dnevno

49. Maligni tumori maksilofacijalne regije čine:
    a) 5% svih malignih tumora
    b) 7% svih malignih tumora
    c) 10% svih malignih tumora

50. Najveći gubitak mase kod Endometazona je uočen u ulju:
    a) eukaliptusa
    b) karanfilića
    c) pomorandže i čajevca

**Odgovore slati na email adresu Uredništva časopisa „Stomatološki glasnik Srbije“ ili na adresu Stomatološke komore Srbije (Uzun Mirkova 3/3). Tačni odgovori na pitanja će se vrednovati u skladu s Pravilnikom o kontinuiranoj medicinskoj edukaciji zdravstvenih radnika.**

# Uputstvo autorima za pripremu rada

**Stomatološki glasnik Srbije** je časopis Srpskog lekarskog društva osnovan 1953. godine. Časopis objavljuje: originalne naučne i stručne radove, prikaze iz prakse, pregledne radove, saopštenja, istoriografske radove, prikaze knjiga, komentare i pisma uredništvu, društvenu hroniku.

Svi rukopisi se podvrgavaju recenziji. Radove recenziraju dva anonimna stručnjaka i, ukoliko je potrebno, statističar. Konačnu odluku o prihvatanju rada za štampu donosi glavni i odgovorni urednik. Autori se obaveštavaju o prijemu ili odbijanju rada najkasnije osam nedelja od podnošenja rukopisa.

Za objavljene radove se ne isplaćuje honorar, a autorska prava se prenose na izdavača. Rukopisi i prilozi se ne vraćaju. Za reprodukciju ili ponovno objavljivanje nekog segmenta rada publikovanog u „Stomatološkom glasniku Srbije" neophodna je saglasnost izdavača.

Radovi se štampaju na engleskom i srpskom jeziku.

**Opšta uputstva** Tekst rada treba da bude otkucan u programu za obradu teksta *Word*, sa dvostrukim proredom, isključivo fontom Times New Roman i veličinom slova 12 pt. Sve margine treba podesiti na 25 mm, veličinu stranice na A4 format, a tekst kucati s levim poravnanjem i uvlačenjem svakog pasusa za 10 mm, bez deljenja reči. Ako se u tekstu koriste specijalni znaci (simboli), koristiti font Symbol. Podaci o korišćenoj literaturi u tekstu označavaju se arapskim brojevima u uglastim zagradama – npr. [1, 2], i to redosledom kojim se pojavljuju u tekstu. Stranice se numerišu redom u okviru donje margine, počev od naslovne strane.

**Naslovna strana** Na posebnoj, prvoj strani rukopisa treba navesti sledeće: naslov rada bez skraćenica, puna imena i prezimena autora bez titula, zvaničan naziv ustanova u kojima autori rade, mesto i državu; na dnu stranice navesti ime i prezime, adresu za kontakt, broj telefona i e-mail adresu autora zaduženog za korespondenciju.

**Kratak sadržaj i ključne reči** Druga strana treba da sadrži kratak sadržaj rada obima 100–250 reči. Kratak sadržaj originalnog rada treba strukturirati na sledeće delove: Uvod (u okviru kojeg se navodi cilj rada), Materijal i metode rada, Rezultati i Zaključak. Navode se najvažniji rezultati, numeričke vrednosti, statističke analize i nivo značajnosti. Ispod kratkog sadržaja navesti od tri do šest ključnih reči. U izboru ključnih reči koristiti *Medical Subject Headings – MeSH* (*http://www.nlm.nih.gov/mesh*).

**Struktura rada** Originalni rad treba da sadrži sledeće podnaslove: Uvod (sa ciljem rada), Materijal i metode rada, Rezultati, Diskusija, Zaključak i Literatura. Prikaz iz prakse čine: Uvod, Prikaz bolesnika, Diskusija i Literatura. Ne treba koristiti imena bolesnika, inicijale ili brojeve istorija bolesti. Pregledni i informativni rad čine Uvod, odgovarajući podnaslovi, Zaključak i Literatura. Pregledni rad mogu objaviti samo autori koji su izuzetno uspešni u oblasti kojom se bave i koji navedu najmanje pet autocitata radova publikovanih u časopisima s recenzijom.

**Tekst rukopisa** Koristiti kratke i jasne rečenice, bez stranih reči i neadekvatnih pojmova iz prevoda iz strane literature. Za nazive lekova koristiti generička imena. Skraćenice koristiti samo kada je to neophodno, a ne koristiti ih u naslovu. Za svaku skraćenicu pun termin treba navesti pri prvom pojavljivanju u tekstu, sem ako to nije standardna jedinica mere. Decimalne brojeve u engleskom tekstu pisati sa tačkom, a u srpskom sa zarezom. Kad god je to moguće, broj zaokružiti na jednu decimalu. Sve rezultate hematoloških, kliničkih i biohemijskih merenja navoditi u metričkom sistemu prema Međunarodnom sistemu jedinica (SI).

**Obim rukopisa** Celokupni rukopis rada – koji čine naslovna strana, kratak sadržaj, tekst rada, spisak literature, svi prilozi, potpisi za njih i legenda (tabele, slike, grafikoni, sheme, crteži) – mora iznositi za pregledni rad do 7.000 reči, za originalni rad do 5.000 reči, a za informativni rad i prikaz iz prakse do 3.000 reči. Provera broja reči u dokumentu može se izvršiti kroz podmeni Tools–Word Count ili File–Properties–Statistics.

**Tabele** Tabele se označavaju arapskim brojevima prema redosledu navođenja u tekstu, a moraju biti urađene u programu *Word*, kroz meni Table–Insert–Table, uz definisanje tačnog broja kolona i redova koji će činiti mrežu tabele. Korišćene skraćenice u tabeli treba objasniti u legendi ispod tabele.

**Grafikoni** Grafikoni treba da budu urađeni i dostavljeni u programu *Excel*, da bi se videle prateće vrednosti raspoređene po ćelijama.

**Slike** Slike se označavaju arapskim brojevima prema redosledu navođenja u tekstu. Primaju se isključivo digitalne fotografije (crno-bele ili u boji) rezolucije 300 dpi i formata zapisa .tiff ili .jpg. Ukoliko autori ne poseduju ili nisu u mogućnosti da dostave digitalne fotografije, onda originalne slike treba skenirati kao Grayscale (ili u boji) u rezoluciji 300 dpi i snimiti ih u originalnoj veličini.

**Sheme** Sheme crtati i dostaviti u programu *CorelDraw* ili *Adobe Illustrator*. Podatke u shemi kucati fontom Times New Roman i veličinom slova 10 pt.

**Zahvalnica** Navesti sve one koji su doprineli stvaranju rada, ali ne ispunjavaju merila autorstva. Finansijska i materijalna pomoć u obliku sponzorstva, stipendija, poklona, opreme, lekova, materijala i drugog takođe treba da bude navedena.

**Literatura** Spisak referenci je odgovornost autora, a citirani članci treba da budu lako pristupačni čitaocima časopisa. Stoga uz svaku referencu obavezno treba navesti DOI broj članka (jedinstvenu nisku karaktera koja mu je dodeljena) i PMID broj ukoliko je članak indeksiran u bazi PubMed/MEDLINE.

Reference numerisane arapskim brojevima navoditi prema redosledu citiranja u tekstu. Broj referenci u originalnim radovima ne bi trebalo da bude veći od 30, osim kod preglednih i informativnih radova, gde broj referenci nije ograničen. Izbegavati korišćenje apstrakta kao reference, a apstrakte starije od dve godine ne citirati. Reference članaka koji su prihvaćeni za štampu treba označiti kao „u štampi" (*in press*) i priložiti dokaz o prihvatanju rada.

Reference se citiraju prema Vankuverskom stilu (jednoobraznim zahtevima za rukopise koji se predaju biomedicinskim časopisima), koji je uspostavio Međunarodni komitet urednika medicinskih časopisa (*http://www.icmje.org*), čiji format koriste U.S. National Library of Medicine i baze naučnih publikacija. Primeri navođenja publikacija (članaka, knjiga, monografija, elektronskog, neobjavljenog i drugog objavljenog materijala) mogu se naći na internet-stranici *http://www.nlm.nih.gov/bsd/uniform_requirements.html*.

**Propratno pismo** Uz rukopis obavezno priložiti pismo koje su potpisali svi autori, a koje treba da sadrži: izjavu da rad prethodno nije publikovan i da nije istovremeno podnet za objavljivanje u drugom časopisu, te izjavu da su rukopis pročitali i odobrili svi autori koji ispunjavaju merila autorstva.

**Autorstvo** Autorstvo se zasniva na bitnom doprinosu koncepciji rada, dobijanju rezultata ili analizi i tumačenju rezultata, planiranju rukopisa ili njegovoj kritičkoj reviziji od znatnog intelektualnog značaja, te doprinosu u završnom doterivanju verzije rukopisa koji se priprema za štampanje. Finansiranje, sakupljanje podataka ili generalno nadgledanje istraživačke grupe sami po sebi ne mogu opravdati autorstvo.

**Slanje rukopisa** Rukopis rada i svi prilozi uz rad mogu se dostaviti imejlom (*stomglas@bvcom.net*), preporučenom pošiljkom ili lično, dolaskom u Uredništvo. Ukoliko se rad šalje poštom ili donosi u Uredništvo, rukopis se dostavlja odštampan u dva primerka i narezan na CD (snimljeni materijal treba da je istovetan onom na papiru).

**Važna napomena** Svi autori i koautori radova moraju biti članovi Srpskog lekarskog društva i pretplatnici na časopis za godinu u kojoj predaju rad za publikovanje.

**Adresa:**
Srpsko lekarsko društvo
Uredništvo časopisa „Stomatološki glasnik Srbije"
Ul. kraljice Natalije 1
11000 Beograd
Srbija

**Telefon:** +381 (0)11 409 27 76
**E-mail:** stomglas@bvcom.net
**Internet-adresa:** http://www.stomglas.org.rs

# Instructions for Authors

**Serbian Dental Journal** is the journal of the Serbian Medical Society, founded in 1953. The journal publishes original scientific and professional papers, case reports, review articles, preliminary research reports, historical papers, book review, comments and letters to the Editor, social chronicle.

All manuscripts are peer-reviewed. Manuscripts are reviewed by two anonymous referees and, if necessary, a statistician. The final decision on paper acceptance for publishing is made by the Editor-in-Chief. Authors are informed of acceptance or rejection of the paper within eight weeks after manuscript submission.

Copyright is transferred from the author(s) to the publisher upon paper acceptance and no fees are paid for papers to be published. Manuscripts are not returned to the author. For any reproduction and repeated publishing of part or the whole paper, written consent from the publisher is requested.

The journal is published in English and Serbian.

**General instructions** The manuscript should be typed in MS Word, with double line spacing, only in Times New Roman font and letters size 12 pt. Page margins should be 25 mm, page size set to A4 format, and text typed aligned left with paragraph indentations of 10 mm. Words should not be hyphenated. If special symbols are used in the text, preferred font is Symbol. References should be marked with Arabic numbers in brackets, e.g. [1, 2], in the order of appearance in the text. Page numbers should be inserted at the bottom of the page, starting from the title page.

**Title page** The first page should contain: the title of the paper without abbreviations, authors' names without professional titles, authors' affiliations; the exact postal address of the corresponding author, telephone number and e-mail address must be given at the bottom of the title page.

**Summary and keywords** The second page should contain a structured summary of the paper with Introduction (with the aim), Material and Methods, Results and Conclusion with up to 250 words. Each of these segments should be written as a new paragraph with bold subtitles. Only the most important results should be indicated with the statistical level of significance. Following summary it is recommended to list 3 to 6 keywords related to the paper. Keywords should be chosen according to the Medical Subject Headings – MeSH (*http://www.nlm.nih.gov/mesh*).

**Structure of the manuscript** Original paper should have the following subheadings: Introduction (with the aim), Material and Methods, Results, Discussion, Conclusion and References. Case report should contain: Introduction, Case Report, Discussion, Conclusion and References. No patients' names, initials or record numbers should be indicated. Review and informative article consists of Introduction, subheadings, Conclusion and References. Only distinguished authors with at least five citations of their published papers are eligible to publish review articles.

**Text of the manuscript** Text should be written in short and clear sentences, avoiding foreign language words and inadequate terms and interpretation from the literature. Medications should be indicated by their generic names. For each abbreviation, full term should be indicated when first mentioned in the text, except for standard measuring units. Decimals should be separated with a comma in Serbian, and with a dot in English. Numbers should be approximated to one decimal place. All results of hematological, clinical and biochemical measurements should be quoted in the metrical system according to the International Unit System (SI).

**Length of the manuscript** The entire manuscript (title page, summary, the whole text, list of references, all enclosures including captions and legends) should not exceed 7,000 words for a review article, 5,000 words for an original paper, and 3,000 words for an informative article and case report. The number of words can be checked in MS Word using Tools–Word Count or File–Properties–Statistics options.

**Tables** Tables should be marked in Arabic numbers in the order of appearance in the text, and should be prepared in MS Word using Table–Insert–Table, with clearly defined number of columns and rows. Abbreviations used in a table should be explained in the legend under the table.

**Graphs** Graphs should be prepared in MS Excel, in order to maintain a clear view of all values within the cells.

**Photographs** Photographs should be marked in Arabic numbers in the order of appearance in the text. Only original digital photographs (black-and-white or color), resolution of 300 dpi, and .tiff or .jpg format, are acceptable. If authors do not posses or are not able to provide digital photographs, then the original photos should be scanned as Grayscale (or RGB color) with resolution of 300 dpi, and saved in original size.

**Schemes** Schemes should be drawn in CorelDraw or Adobe Illustrator programmes. The text in the scheme should be typed in Times New Roman, font size 10 pt.

**Acknowledgment** All contributors to the paper who are not named as authors should be acknowledged. Financial and other material support, like sponsorship, grants, gifts, medical supplies, etc., should also be mentioned.

**References** The reference list is the responsibility of the authors. Cited articles should be readily accessible to the journals readership. Therefore, following each reference, its DOI number and PMID number (if the article is indexed for MEDLINE/PubMed) should be typed.

References must be marked in Arabic numbers and cited in the order of appearance in the text. The number of references should not exceed 30, except in review and informative articles, when no limits are established. The use of abstracts as references should be avoided and an abstract more than two years old should not be quoted by any means. When citing accepted papers, these should be indicated as "in press" and a proof of acceptance should be provided.

References are cited according to the Vancouver style (*Uniform Requirements for Manuscripts Submitted to Biomedical Journals*), rules and formats established by the International Committee of Medical Journal Editors (*http://www.icmje.org*), used by the *U.S. National Library of Medicine* and scientific publications databases. Examples of citing publications (journal articles, books and other monographs, electronic, unpublished and other published material) could be found on the web site *http://www.nlm.nih.gov/bsd/uniform_requirements.html*.

**Cover letter** A cover letter should be signed by all authors and with the following content: written consent that the paper was not previously published and is not simultaneously submitted to publication in other journals, and written consent that the paper was reviewed and approved by all other co-authors.

**Authorship** Authorship is based only on: crucial contribution to the article conception, obtaining of results or analysis and interpretation of results; design of the manuscript or its critical review of significant intellectual value; final revision of the manuscript being prepared for publication. Funding, collection of data or general supervision of the research group alone cannot justify authorship.

**Submission** Manuscript and all enclosures can be sent by e-mail (*stomglas@bvcom.net*). If sent by registered mail or delivered in person at the Editorial Office in Belgrade, it should contain two printed copies and a CD with the version identical to that on paper.

**Important notice** All authors and co-authors must be members of the Serbian Medical Society and subscribers to the journal for the year in which the manuscript is being submitted.

**Address:**
Serbian Medical Society
Editorial Board of the Serbian Dental Journal
Ul. kraljice Natalije 1
11000 Belgrade
Serbia

**Phone:** +381 (0)11 409 27 76
**E-mail:** stomglas@bvcom.net
**Web site:** http://www.stomglas.org.rs

CIP - Каталогизација у публикацији
Народна библиотека Србије, Београд

616.31

**STOMATOLOŠKI glasnik Srbije** = Serbian
Dental Journal / glavni i odgovorni urednik
Slavoljub Živković. - God. 1, br. 1 (1955)-
. - Beograd (Džordža Vašingtona 19) :
Srpsko lekarsko društvo, 1955- (Beograd :
Službeni glasnik). - 29,5 cm

Dostupno i na: http://www.stomglas.org.rs - Tromesečno

ISSN 0039-1743 = Stomatološki glasnik Srbije
(Štampano izd.)
COBISS.SR-ID 8417026