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Веће научних области медицинских наука, на XIII седници одржаној дана 22. маја 2012. године, донело је

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ДАЈЕ СЕ сагласност на предлог теме докторске дисертације:

Кандидат

Јелена Нешковић

Назив теме: "Клиничка и микробиолошка анализа неуспеха ендодонтског лечења зуба".

ПРЕДСЕДНИК ВЕЋА

Проф. др Нада Ковачевић



Доставити:

- Факултету
- секретару Већа
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**БЕОГРАДСКИ УНИВЕРЗИТЕТ
СТОМАТОЛОШКИ ФАКУЛТЕТ
СЕКРЕТАРИЈАТ**

ПРИМЉЕНО: 24-05-2012

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POTVRDA

U Centralnoj biblioteci Stomatološkog fakulteta urađena je kategorizacija objavljenih radova JELENE NEŠKOVIĆ, indeksiranih u Web of Science bazi.

Na osnovu Pravilnika o postupku i načinu vrednovanja, i kvantitativnom iskazivanju naučnoistraživačkih rezultata istraživača ("Službeni glasnik RS", br. 38/08) utvrđeno je da je Jelena Nešković publikovala rad u časopisu sa impakt faktorom (*Journal Citation Reports* lista).

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Ružica Petrović

U Beogradu, 21.04.2016. godine

Nastavno - naučnom veću Stomatološkog fakulteta Univerziteta u Beogradu

Na sednici Nastavno – naučnog veća Stomatološkog fakulteta Univerziteta u Beogradu od 26. 04. 2016. godine, imenovana je komisija u sastavu:

Prof. dr Đurica Grga, Stomatološki fakultet, Beograd

Prof. dr Branka Popovic, Stomatološki fakultet, Beograd

Prof. dr Snježana Čolić, Stomatološki fakultet, Beograd

Prof. dr Aleksandar Mitić, Medicinski fakultet u Nišu, odsek stomatologija

za ocenu završene doktorske disertacije pod nazivom: **„KLINIČKA I MIKROBIOLOŠKA
ANALIZA NEUSPEHA ENDODONTSKOG LEČENJA ZUBA“**

Kandidat: Mr sci dr Jelena Nešković

Mentor: Prof. dr Slavoljub Živković

Imenovana komisija je proučila tekst doktorske disertacije i Nastavno – naučnom veću Stomatološkog fakulteta Univerziteta u Beogradu podnosi sledeći

IZVEŠTAJ

A. Prikaz sadržaja doktorske disertacije

Doktorska disertacija dr Jelene Nešković pod nazivom: „KLINIČKA I MIKROBIOLOŠKA ANALIZA NEUSPEHA ENDODONTSKOG LEČENJA ZUBA“ je napisana na 133 strane i sadrži 25 tabela, 35 slika i 214 referenci iz savremene naučne literature.

Tekst disertacije uključuje: sažetak na srpskom i engleskom jeziku, uvod, pregled literature, radnu hipotezu, ciljeve istraživanja, materijal i metode, rezultate, diskusiju, zaključke i literaturu.

U **Uvodu** je kratko predstavljena naučna problematika ove teze koja se odnosi na pojedina nerešena pitanja, vezana za uzroke i kriterijume neuspeha primarne endodontske terapije kao i mogućnosti i prognoze ponovljenog terapijskog zahvata.

U **Pregledu literature** su navedena savremena istraživanja o mogućim uzrocima neuspeha endodontske terapije i mogućnostima i kliničkim ishodima konzervativnog tretmana kod dijagnostikovanih neuspeha primarnog endodontskog lečenja. Jasno i pregledno su opisana i dosadašnja ispitivanja o mikrobiološkom statusu predhodno endodontski lečenih kanala korena. Predstavljena su i mnogobrojna istraživanja o ishodu ponovljene endodontske terapije. Imajući u vidu da se presudnim kriterijumom neuspeha endodontske terapije smatra pojava ili perzistiranje radiografskog rasvetljenja u periradikularnim koštanim strukturama, postavljena je i radna hipoteza ove doktorske disertacije da su osnovni uzročnici neuspeha endodontskog lečenja mikroorganizmi bez čijeg prisustva u kanalu korena nema ni patoloških promena u periapexnom parodonticijumu.

Ciljevi istraživanja su jasno i precizno definisani: klinički i radiografski analizirati uzrok neuspeha primarnog endodontskog tretmana; utvrditi eventualno prisustvo mikroorganizama *Enterococcus faecalis*, *Peptostreptococcus micros*, *Prevotella intermedia*, *Porphyromonas endodontalis* i *Actinobacillus Actinomicetemcomitans* neposredno nakon uklanjanja materijala za opturaciju iz kanalnog sistema zuba primenom PCR metode; mikro-CT analizom ekstrahovanih endodontski lečenih zuba proceniti razloge neuspeha endodontskog lečenja; klinički i radiografski proceniti uspeh ponovljenog endodontskog lečenja zuba posle perioda od 2 godine.

U poglavlju **Materijal i metode**, u delu koji se odnosi na laboratorijsku studiju detaljno je opisana priprema uzoraka i svi eksperimentalni postupci. Jasno je opisan postupak pripreme kanala i procedura uzimanja uzoraka za PCR-analizu. Detaljno je predstavljena PCR-metoda identifikacije mikroorganizama. Opisan je postupak skeniranja mikrokomputerizovanom tomografijom.

U delu koji se odnosi na kliničko istraživanje na zubima pacijenata, detaljno su opisani kriterijumi za uključivanje ispitanika u istraživanje, kao i detaljan klinički postupak. Predstavljena je kontrolisana, nestratifikovana i balansirano randomizovana studija koja je obuhvatila pacijente oba pola starosti od 24 do 79 godina. U studiju su uključeni pacijenti kod kojih je indikovana ponovljena endodontska terapija. Objašnjena im je klinički protokol sprovođenja tretmana i kontrolnih pregleda nakon 12 i 24 meseca. U statističkoj obradi podataka navedeni su svi racionalno upotrebljeni statistički testovi.

Rezultati su prikazani u tri poglavlja koja se odnose na klinička istraživanja, PCR-analizu i mikro-CT analizu. U prvom delu su tabelarno opisani rezultati kliničkih istraživanja sa periodom praćenja od 2 godine o ishodu ponovljenog endodontskog tretmana dokumentovani radiografskim slikama kliničkih slučajeva. U drugom delu su prikazani rezultati PCR identifikacije 5 vrsta mikroorganizama u korelaciji sa pojavom periapikalnih lezija i kliničkih simptoma. U delu koji se odnosi na skeniranje mikrokompjuterizovanom tomografijom prikazani su slučajevi predhodno endodontski lečenih ekstrahovanih zuba i kvaliteta obturacije njihovih kanala korenova u korelaciji sa mikrobiološkim statusom.

U **Diskusiji** su naučnom analizom dobijenih rezultata objašnjeni uzroci neuspeha endodontskog lečenja kao i brojni faktori u endodontskoj proceduri koji utiču na konačan ishod terapije. Detaljnom analizom uzroka i posledica neadekvatnog endodontskog lečenja napravljena je klinička korelacija rezultata mikrobioloških ispitivanja i mikro-CT analize endodontski lečenih zuba. Ukazano je da prisustvo samo prisustvo mikroorganizama u kanalu korena dovode do patoloških promena u periapikalnim tkivima, a dobijeni rezultati su povezani i analizirani sa nalazima dosadašnjih istraživanja iz dostupne literature sa sličnom problematikom.

Na osnovu iznetih i diskutovanih rezultata izneti su **Zaključci** koji predstavljaju jasne odgovore na postavljene ciljeve.

Korišćena **Literatura** sadrži spisak od 214 referenci iz savremene i značajne naučne literature vezane za ovu oblast, a koja je citirana u rukopisu teze.

B. Kratak opis postignutih rezultata

Dobijeni rezultati ove doktorske teze su pokazali da na ishod endodontskog lečenja značajno utiču kvalitet (hermetičnost) obturacije kanala korena kao i prisustvo i kvalitet koronarne restauracije, te da uzroke njegovog neuspeha pre svega treba tražiti u neadekvatno sprovedenom endodontskom tretmanu. Najčešći radiografski nalaz u momentu dijagnostikovanja neuspeha primarnog endodontskog lečenja bio je nedovoljno ekstenzirano kanalno punjenje (kratko), odnosno „zaboravljeni“ kanali.

Jedan od faktora koji onemogućava adekvatno sprovođenje svih faza endodontske terapije jeste komplikovana kanalna anatomija koja se ne može u potpunosti i adekvatno detektovati radiografijom, dok se mikrokomjuterizovanom tomografijom može precizno registrovati prisustvo akcesornih kanala i apeksnih ramifikacija.

Prisustvo periapikalnih lezija značajno utiče na mikrobiološki status kanala korena endodontski lečenih zuba. Kod svih uzoraka uzetih iz kanala korena endodontski lečenih zuba sa hroničnim periapikalnim lezijama registrovano je prisustvo bakterija. Najzastupljeniji je bio *E.faecalis* (94%) i *P.intermedia* (82,3% kanala). Korenovi endodontski lečenih zuba u čijim kanalima prisustvo bakterija nije potvrđeno, imali su zdrava parodontalna tkiva u predelu vrha korena.

Prisustvo periapikalnih promena iznad vrha korena zuba pre otpočinjanja retreatmana značajno utiče na ishod ponovljenog endodontskog tretmana. Ponovljena endodontska terapija kod zuba sa zdravim parodontalnim tkivima nakon 24 meseca bila je upešna u 93,3% slučajeva, dok je kod zuba sa prisutnim hroničnim periapikalnim lezijama uspeh registrovan u 67,6% slučajeva. Potuno izlečenje (restitutio ad integrum) nakon retreatmana kod postojanja perzistirajućih periapikalnih lezija iznad vrha korena postignuto je u 52,9% slučajeva.

Ukupni rezultati ove doktorske disertacije ukazuju na činjenicu da je retreatman težak i komplikovan endodontski postupak ali sa velikim šansama za uspeh. Osnovni preduslovi za uspešnost endodontskog tretmana u ponovljenom zahvatu vezani su za pravilnu dijagnozu endodontskog neuspeha (Rtg, CBCT), adekvatnu dezohturaciju i preparaciju u ponovnom

čišćenju i oblikovanju kanala (stručnost terapeuta, instrumentarijum, materijali), odnosno kvalitetnu trodimenzionalnu hermetičnu opturaciju kanalskog sistema i kvalitetnu, pravovremenu i adhezivnu restauraciju endodontski lečenog zuba u ponovljenom tretmanu.

C. Uporedna analiza doktorske disertacije sa rezultatima iz literature

Rezultati ove doktorske disertacije, proistekli iz eksperimentalne i kliničke studije, pokazali su da ishod endodontskog lečenja značajno utiču kvalitet (hermetičnost) obturacije kanala korena kao i prisustvo i kvalitet koronarne restauracije, te da uzroke njegovog neuspeha pre svega treba tražiti u insuficijentnoj instrumentaciji, što za posledicu ima neadekvatnu obturaciju koja se radiografski može verifikovati (Pecora i sar 2015). Najčešći radiografski nalaz u momentu dijagnostikovanja neuspeha primarnog endodontskog lečenja bio je nedovoljno ekstenzirano kanalno punjenje (kratko), odnosno „zaboravljeni“ kanali.

Među zubima sa promenama u apeksnom parodoncijumu bilo je 84% neadekvatnih restauracija, od čega je 50% imalo izraženu simptomatologiju što takođe ukazuje na značaj dobrog rubnog zatvaranja. Činjenica je da izgledi za uspeh endodontske terapije rastu ukoliko su i endodontski tretman i krunična restauracija sprovedeni adekvatno. (Gillen i sar 2011). U situacijama gde je obturacija adekvatna, krunično zaptivanje ne utiče značajno na ishod endodontskog tretmana, ali ukoliko nedostaje, šanse za uspeh dobro ispunjenih kanala se značajno smanjuju. (Siqueira i sar 2005) Među četiri odlučujuća faktora za uspešan ishod endodontske terapije: postojanje periapikalne lezije pre intervencije, gustina i apikalna ekstenzija kanalnog punjenja i kvalitet koronarne restauracije (Ng, Gulabibala 2002) najnovijim istraživanjima CBCT-jem je pokazano da su presudni gustina kanalnog punjenja i kvalitet kruničnog zaptivanja. (Liang, Wesselink 2011)

Interseansna medikacija u ovim istraživanjima je sprovedena u dve faze primenom 2% rastvor hlorheksidina u trajanju od 2 dana i vodene suspenzije $\text{Ca}(\text{OH})_2$ u trajanju od dve nedelje, uz privremenu restauraciju glasjonomer cementom kako bi se maksimalno redukovalo

mikrocurenje tokom perioda medikacije. Savremena istraživanja potvrđuju superiornost CHX nad Ca(OH)_2 , kad je u pitanju antimikrobno dejstvo na *E.faecalis* (Delgado i sar 2010). Ca(OH)_2 je efikasan u borbi sa obligatnim anaerobima ali je protiv gram-pozitivnih fakultativnih anaeroba i *Candide albicans* neophodno pomešeti ga sa hlorheksidinom (Sinha i sar 2013).

Rezultati ove studije pokazuju da je ponovljena endodontska terapija bila uspešna u **75,5%** slučajeva (bez obzira na periapikalni status), u observacionom periodu od 24 meseca. Ukoliko se uzme u obzir i periapeksni parodontalni status pri postavljanju indikacije za ponovljenu endodontsku intervenciju, uspeh preduzete terapije iznosi **93,3%** u grupi zuba sa zdravim parodontcijumom, dok je procenat uspeha u grupi sa prisutnim periapikalnim lezijama značajno manji i iznosi **67,6%**. Prognostički faktori koji statistički značajno doprinose periapikalnom izlečenju su: odsustvo preoperativne periapikalne lezije (ukoliko je manjeg promera bolja je prognoza), mogućnost upostavljanja apikalne prohodnosti i čišćenja kanala, odsustvo perforacije zidova kanala korena, izostanak pojave interseansnih bolova ili otoka i prisustvo adekvatne koronarne restauracije (Ng, Mann i Gulabivala su 2011)

Svi uzorci uzeti iz kanala korena zuba sa hroničnim periapikalnim lezijama su bili pozitivni na prisustvo bakterija (100%). Takođe, svi negativni uzorci su uzeti iz kanala korena zuba sa zdravim parodontcijumom. Na taj način je potvrđena hipoteza da bez bakterija nema infekcije u periapikalnim tkivima a samim tim ni neuspeha endodontskog lečenja. Indirektan dokaz da je perzistirajuća infekcija odgovorna za neuspeh je i taj da je učestalost periapikalnih oboljenja značajno veća u slučajevima gde je već ranije postojala periapikalna lezija (Siqueira i sar 2005)

Najprisutniji mikroorganizam u kanalima sa pozitivnim bakteriološkim nalazom bio je *E. faecalis* koji je identifikovan u 83,3% kanala, zatim *P.inermedia* sa 75% i *P.micros* sa zastupljenošću od 58,3%. *E. faecalis* je identifikovan u 94% kanala korena zuba sa hroničnim periapikalnim lezijama što se slaže sa nalazima drugih autora koji su analizirali mikrobiološki status sekundarno inficiranih kanala PCR-metodom (Sedgley i sar 2006, Gomes i sar, 2008)

Kod pacijenata sa simptomima uglavnom su postojale promene u apeksnom parodontijumu endodontski lečenih zuba. Kod svih pacijenata sa izraženim simptomima (bol, osetljivost na perkusiju), kao i kod polovine uzoraka uzetih iz kanala korena pacijenata sa prisutnim otokom i fistulom registrovani su *E.faecalis* i *P.intermedia* (Rôças i Siqueira, 2010.) dok je *P. micros* identifikovan u 66,6% pacijenata sa bolom. (Pinheiro i sar 2003, Gomes i sar 2008)

Kada je u pitanju kvalitet obturacija koje su analizirane mikro-CT-om u ovom istraživanju, potvrđeno je da su bile nezadovoljavajućeg kvaliteta. Kanal koji je hermetički „zapečaćen“ i apikalno i koronarno je ideal kome teže svi endodontisti. Međutim, mnogi autori su pomoću mikro-CT-a dokazali da ga je nemoguće dostići, tj, da još uvek ne postoji materijal ni tehnika obturacije kojom se može dobiti kanalno punjenje bez poroznosti (Zogheib i sar 2013)

D. Objavljeni rad koji čini deo doktorske disertacije

1. Nešković J, Živković S, Medojević M, Maksimović M. Outcome of orthograde endodontic retreatment-two-year follow up, Srp Arh Celok Lek. 2016 Mar-apr; 144 (3-4):174-180

E. Zaključak (obrazloženje naučnog doprinosa)

Doktorska disertacija „Klinička i mikrobiološka analiza neuspeha endodontskog lečenja zuba“ dr Jelene Nešković predstavlja značajan i originalan naučni doprinos u rasvetljavanju problematike faktora koji utiču na ishod primarnog i ponovljenog endodontskog tretmana. Izabranim naučnim metodom daje bliži uvid u faktore koji utiču na ishod endodontske terapije. U radu su primenjene savremene eksperimentalne i kliničke metode za analizu navedenih uzročnika neuspeha endodontskog tretmana.

Ova doktorska disertacija je urađena prema svim principima naučnog, kliničkog i eksperimentalnog istraživanja, sa precizno definisanim ciljevima, originalnim naučnim pristupom, savremenom metodologijom rada, adekvatno prikazanim i diskutovanim rezultatima i jasno uobličenim zaključcima.

Na osnovu svega napred navedenog, i imajući u vidu dosadašnji naučni rad kandidata, Komisija predlaže Nastavno-naučnom veću Stomatološkog fakulteta Univerziteta u Beogradu da prihvati pozitivan izveštaj Komisije za ocenu doktorske disertacije dr Jelene Nešković i odobri njenu javnu odbranu.

U Beogradu, 27.aprila 2016.

Članovi Komisije:

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Outcome of orthograde endodontic retreatment – A two-year follow-up

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SUMMARY

Introduction Endodontic retreatment is a complex intervention that requires detailed analysis of possible reasons for failure, and flawless practical execution of the procedure.

Objective The aim of the study was to assess the outcome of endodontic retreatment based on clinical and radiographic criteria after a two-year observation period.

Methods Clinical study included 49 teeth indicated for endodontic retreatment based on periapical index (PAI). All teeth were divided into two groups. Group I comprised teeth without any periapical lesion (PAI score of 1 and 2) while Group II consisted of teeth with visible periapical radiolucency (PAI score of 3, 4, and 5). Endodontic retreatment was completed in two visits with inter-appointment medication of 2% chlorhexidine and calcium hydroxide for two weeks. Outcome of endodontic retreatment was evaluated 12–24 months after final obturation.

Results Endodontic retreatment was successful in 93.3% in Group I after 24 months. In Group II, successful treatment and complete healing was found in 52.9% of teeth, whereas 14.7% of teeth showed only partial healing. However, clinical symptomatology was not present in any of the cases. Considering the absence of clinical signs and subjective symptoms, retreatment was successful in 67.6% of cases where chronic periapical inflammation was present.

Conclusion Endodontic retreatment was successful in high percentage in teeth with and without periapical lesions.

Keywords: endodontic retreatment; endodontic failure; apical periodontitis

INTRODUCTION

Contemporary endodontic therapy aims to preserve functionality and aesthetics of teeth with diseased pulp and/or periapical tissue. Root canal treatment is currently one of the most efficacious dental interventions with high success rate [1–4]. Endodontic treatment is affected by anatomical and morphological complexity of root canal system, diagnosis, and periradicular tissue state before the intervention. Also, equipment and materials, operator experience, and the presence of infection at the time of obturation play an important role [5,6].

In certain cases endodontic treatment may fail. One of the most common reasons is inability to eliminate microorganisms from the root canal. Some of the reasons for microorganism survival after endodontic procedure are inaccessibility to all parts of the canal system during chemo-mechanical instrumentation, or procedural errors such as root perforations, ledge formation, and transportation or separated instruments [6]. Procedural errors by themselves are not direct cause of endodontic treatment failure but indirectly they pose risk due to incomplete chemo-mechanical debridement or inadequate obturation of the root canal system [4–7]. It has been confirmed that presence of root canal infection at the time of obturation and preoperative presence of periapical

lesion significantly reduce chance for successful outcome of endodontic treatment [5, 6]. In addition to the persistence of intraradicular infection, some possible causes for failure of endodontic treatment are extraradicular infection in the form of actinomycosis, true cysts (in which lumen does not communicate with the apex of the root canal), foreign body reaction in the presence of cholesterol crystals or endodontic materials extruded in periapical tissue or fibrous scar tissue [8].

There is no exact definition of failure of endodontic treatment among endodontists. Many clinicians would agree that the absence of pain and other clinical symptoms, or even more precise – preservation of function of an endodontically treated tooth can be considered successful endodontic treatment [1, 9]. However, the existence of inflammatory lesion in periapical tissue that previously did not exist, its persistence or even increased size after endodontic treatment is a definite sign of failed endodontic treatment [6, 8, 9].

Radiographic evaluation of endodontic treatment is main method of monitoring outcome of the treatment [10, 11]. It is, however, limited by visual interpretation that is not objective but depends on the observer [12]. Epidemiological studies on large number of samples showed that most failures have occurred within two years of the treatment, whereas

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sometimes it takes four to five years for complete healing of bone defect [4, 7, 12–16].

Prior to retreatment it is important to consider all options in relation to the time, cost and prognosis of therapy, and to decide between nonsurgical (orthograde) retreatment, surgical retreatment, or extraction[17]. Endodontic retreatment includes removal of material from the root canal space, detection of all deficiencies, and repair of pathological or iatrogenic defects, followed by shaping and cleaning, and finally obturation[18]. Decision for retreatment is directly related to reduced percentage of success in repeated interventions [7, 12, 13, 15, 19, 20].

OBJECTIVE

The aim of this study was to assess the outcome of endodontic retreatment based on clinical and radiographic criteria during a two-year period.

METHODS

Clinical study included 37 patients and 49 teeth (28 multirooted and 21 single-rooted teeth) indicated for retreatment. Endodontic treatment was done in a period of less than one year in two cases, a period of one to five years in 17 cases, while 30 teeth were treated more than five years before diagnosis of endodontic failure. Adequate prosthetic restoration was observed in 17 teeth, five teeth no longer had definitive filling material, and 27 teeth did not have proper restoration. Retreatment was done at the Department of Restorative Dentistry and Endodontics, Faculty of Dental Medicine in Belgrade by one therapist while two therapists assessed the outcome of retreatment.

All patients were clinically and radiographically examined in order to establish diagnosis and indications for conventional retreatment. Patients also signed informed consent for voluntary participation in the clinical study. Teeth with extensive carious destruction, severe periodontal disease and patients who didn't sign the consent were excluded from the study. Teeth that had blocked canals or separated instruments were indicated for surgical retreatment.

Retreatment decision was based on detailed analysis of initial endodontic treatment failure, analysis of intraoral radiography, clinical examination of teeth and periodontal tissues, possible success of retreatment and adequate reconstruction afterwards.

Periapical tissue was assessed radiographically using periapical index (PAI) system [21]:

PAI 1 – normal periapical structure;

PAI 2 – small changes in the structure of bone not pathognomonic of apical periodontitis;

PAI 3 – changes in bone structure with mineral loss characteristic for apical periodontitis;

PAI 4 – well defined apical radiolucency characteristic for apical periodontitis, and

PAI 5 – severe periodontitis with exacerbating features and bone expansion.

Based on radiographic assessment of periapical tissue, the teeth were divided into two groups. Group I included teeth without periapical changes (PAI score of 1 and 2) where retreatment was indicated due to the poor quality of root canal filling. The teeth with visible signs of damage in periapical tissue (PAI score of 3, 4, and 5) were assigned to Group II. For the evaluation of multirooted teeth, the greatest damage of periapical tissue around roots was considered. The second parameter for analysis was the presence of clinical symptoms where Group I included teeth with no clinical symptoms (diagnosed accidentally) and Group II consisted of teeth with clinical symptoms (pain, swelling, sensitivity to bite or presence of sinus tract) (Table 1).

Endodontic retreatment was conducted according to contemporary standards of endodontic therapy. After the access cavity preparation, root canal material was removed from root canal space. Gates Glidden instruments were used to remove gutta-percha from the coronal two thirds of the canal, while Hedstrom files with copious irrigation with 1% sodium hypochlorite solution were used to remove obturation materials from the apical third. In some cases Gutasolv and Endosolv (Septodont, Saint-Maur-des-Fossés, France) were used to dissolve gutta-percha. Working length was determined using apex locator. Complete material removal and working length were also verified using X-rays. Access cavity was thoroughly examined to find missed canals. All canals were instrumented using “crown-down” technique with Gates Glidden and K-files and K-flex hand instruments to full working length using 17% EDTA or Canal + (Septodont). After copious irrigation with 1% sodium hypochlorite solution, canals were irrigated with 10% citric acid and saline. After drying with paper points, 2% chlorhexidine (R4, Septodont) solution was placed in the canal for inter-appointment medication. The teeth were temporarily closed with glass ionomer cement (Alfagal, Galenika, Belgrade, Serbia) for two days. In the next visit, after removing medication, the canals were irrigated and suspension of calcium hydroxide was placed in the canals using lentulo spiral. The teeth were again temporarily restored with glass ionomer cement for two weeks. If symptoms still persisted, medication was repeated for two more weeks. Obturation was done using

Table 1. Distribution of teeth in relation to the presence of clinical symptoms in the group of teeth with healthy periapical tissues and the group with present periapical lesions.

Clinical symptoms		Teeth with healthy periapical tissue		Teeth with periapical lesion	
		N	%	N	%
Symptoms	Yes	0	0	9	36%
	No	15	100%	25	64%
Pain	Yes	0	0	6	24%
	No	15	100%	28	76%
Sensitivity to bite	Yes	0	0	3	12%
	No	15	100%	31	88%
Swelling	Yes	0	0	3	12%
	No	15	100%	31	88%
Sinus tract	Yes	0	0	3	12%
	No	15	100%	31	88%

lateral compaction of gutta-percha and sealer (Acroseal, Septodont). The teeth were permanently restored by sandwich technique using glass ionomer cement (Fuji VIII and Fuji IX, GC, Tokyo, Japan) and composite material (Filtek, 3M ESPE, Saint Paul, MN, USA) or they received prosthetic restoration.

Periapical X-rays were taken before, during and immediately after obturation and permanent restoration. Follow-up was scheduled for two years after retreatment. All X-rays were blind-coded and organized randomly. To avoid subjectivity, two dentists carried out the analysis. X-rays were analyzed in the light box with the use of magnification ($\times 2$). In order to minimize false-positive results, in cases of disagreement, radiographic analysis was repeated until consensus was reached.

Follow-up included the assessment of subjective symptoms (if any, before treatment) and objective signs after the retreatment, after 12 months, and two years. In the group of teeth where periapical radiolucency was present, radiographic evaluation of healing process after retreatment was done based on the following criteria [22]:

1. Unchanged – no changes in the periapical area after completion of retreatment and follow up visits;
2. Improvement – reduced radiolucency in alveolar bone with bone forming or partial repair of damaged cementum;
3. Complete healing – disappeared periapical radiolucency and bone formation, re-establishment of the lamina dura and cementum apposition (*restitutio ad integrum*), and
4. Deterioration – persistence of radiolucency and alveolar bone resorption with the same or larger lesion or dulled apex.

Table 2. Distribution of teeth in relation to periapical index (PAI) value before retreatment and on the follow-ups.

PAI	Before retreatment		After 12 months		After 24 months	
	N	%	N	%	N	%
1	8	16.3	10	20.4	22	44.9
2	7	14.3	20	40.8	15	30.6
3	16	32.7	15	30.6	7	14.3
4	12	24.5	2	4.1	1	2.0
5	6	12.2	2	4.1	4	8.2

The results were statistically analyzed using appropriate statistical tests (Man–Whitney U-test).

RESULTS

On follow-up examination after 12 months there was major improvement of apical periodontitis. PAI score of 4 was initially found in 24.5%, and after 12 months in only 4.1% of the cases. At the end of the observation period of 24 months, PAI score of 1 and 2 (successful retreatment) was observed in 44.9% (score 1) and 30.6% (score 2) of the teeth. This means that retreatment was successful in 75.5% of the cases (37 of total of 49 teeth). PAI index 3, 4, and 5 (unsuccessful retreatment) was found in 24.5% of the cases (14.3% for score 3, 2% for score 4, and 8.2% for score 5) (Table 2).

Retreatment in the group of teeth with healthy periapical tissue was successful in 93.3% of the cases after 24 months (Figures 1, 2; Table 3). Partial improvement was observed in 14.7%, and complete healing in 52.9% of the cases (Figures 3, 4, 5). Statistically significant difference in treatment outcome was found between the two studied groups ($U=158$, $Z=2.485$; $p=0.013$). Considering the absence



Figure 1. a) Periapical radiography of the right maxillary first molar with forgotten buccal canals, b) Obturation after retreatment, c) Prosthetic reconstruction with post and metal-ceramic crown – complete healing after two years.



Figure 2. a) Periapical radiography of the left maxillary first molar with inadequate obturation and without changes in the periapical tissue, b) Obturation after retreatment, c) Complete healing after two years.

Table 3. Outcome of repeated endodontic treatment in relation to the existence of periapical (PA) lesion.

Follow-up			Treatment outcome				Total
			Deterioration	Status quo	Improvement	Complete healing	
After 12 months	Without PA	N	0	0	0	15	15
		%	0%	0%	0%	100%	100%
	With PA	N	2	9	8	15	34
		%	5.9%	26.5%	23.5%	44.1%	100%
After 24 months	Without PA	N	1	0	0	14	15
		%	6.7%	0.05%	0%	93.3%	100%
	With PA	N	4	7	5	18	34
		%	11.8%	20.6%	14.7%	52.9%	100%

**Figure 3.** a) Periapical radiography of the left first and second maxillary premolars. No. 24 was sensitive to palpation and with inadequately filled root canals, No. 25 had inhomogeneous filling with periapical radiolucency, b) Obturation after retreatment, c) Complete healing after two years.**Figure 4.** a) Periapical radiography of the left mandibular first molar. No. 36 was painful and swelling was present, b) Obturation after retreatment, c) Complete healing after two years.**Figure 5.** a) Periapical radiography of the left mandibular first molar with short filling in the distal canal and forgotten mesial canals, b) Obturation after retreatment, c) Complete healing after two years.

of clinical signs and subjective symptoms, retreatment was successful in 67.6% of cases where chronic periapical inflammation was present.

DISCUSSION

Repeated endodontic treatment is a very interesting endodontic problem that requires complex analysis of indications and perfect practical execution of the procedure.

Torabinejad et al. [23] conducted comprehensive review of literature on clinical studies that assessed success and failure of endodontic treatment in the period 1970–2004. They analyzed 31 original articles and six review articles. Only a few studies had high level of evidence (level 2). Also, even though all studies examined causes of endodontic treatment failure and outcome of retreatment, they all had different design and performance [7, 8, 11, 12, 13, 15, 19, 20].

Ørstavik et al. [21] introduced PAI system for radiographic assessment of periapical status that was used in

our study. This system allows easier tracking of periapical changes and purposeful comparison of outcome of conventional endodontic retreatment in clinical studies. Radiographic evaluation is the main method to monitor outcome of endodontic treatment. It is however limited by visual interpretation, which is not an objective method and depends on the observer. Disagreement between observers in the interpretation of radiographs is very common. Therefore, “strategies of observation” increase the degree of compliance among observers, minimizing subjectivity in interpretation [24]. Another limitation is that radiography shows only two dimensions. A lesion is radiographically visible if there is significant bone destruction. This means that a lesion in reality is bigger than on a radiographic view. Bender et al. [25] indicated that changes in X-ray beam angulation might increase or reduce the size of the lesion. Furthermore, differences in exposition and conditions for X-ray developing can affect the assessment of treatment outcome. Some anatomical structures (maxillary sinus, mental foramen, inferior alveolar nerve canal, zygomatic bone...) can also make the interpretation of intraoral radiography difficult.

Cone beam computed tomography (CBCT) represents the most modern, three-dimensional diagnostic system and has been specially designed for use in maxillo-facial region. Regardless of its superiority compared to traditional two-dimensional intraoral radiography, CBCT is not yet in widespread clinical use due to its cost and significant radiation dose [26, 27].

Microbiological status of endodontically treated teeth is significantly different compared to untreated infected root canal. Gram-positive cocci, bacilli and filaments with equal distribution of facultative and obligate anaerobes *Enterococcus* and *Streptococcus*, *Actinomyces*, *Peptostreptococcus*, *Propionibacterium* (previously *Arachnia*) and *Lactobacillus* are most commonly found in endodontically treated teeth [28, 29].

Enterococcus faecalis is a microorganism that is not present in the initial periapical infection but is associated with asymptomatic, persistent endodontic infections after endodontic treatment in high percentage (24–77%) [29, 30]. *E. faecalis* has a variety of mechanisms to survive in extreme conditions, different virulence factors, potency to invade dentinal tubules and is difficult to eliminate from the canal system. Aseptic technique and intracanal medication with calcium hydroxide must be complemented with 2% chlorhexidine solution to reduce the number of microorganisms [30]. Zerella et al. [31] demonstrated that combination of chlorhexidine and calcium hydroxide was significantly more effective in retreatment compared to calcium hydroxide only. Yoldas et al. [32] conducted a clinical study in order to compare the efficiency of one-visit vs. two-visit retreatment using medication that combines calcium hydroxide and 2% chlorhexidine solution. The results showed that two-visit retreatment was more effective in reducing postoperative pain and potential flairs-ups.

The results of the current study indicate that after 24 months repeated endodontic treatment was successful in 75.5% regardless of the periapical status. The criteria for

evaluating success were the absence of clinical signs and symptoms and radiographical findings that show healthy periodontal tissue or minor radiolucency (PAI index ≤ 2). During the two-year observational period, four teeth were extracted, two because of pain, and two because of uncertain prognosis in terms of prosthetic rehabilitation plan. The reason for the treatment failure of one of the two teeth was vertical root fracture that was diagnosed during the extraction. The only case of failure after repeated therapy in teeth with previously healthy periodontal tissue could be attributed to delayed prosthetic reconstruction of more than three months and inadequate coronal seal during that period.

Our study showed that 93.3% of teeth with no signs of periapical radiolucency had successful outcome of endodontic retreatment while this percentage was 67.6% for teeth that showed signs of periapical radiolucency before retreatment. High success rate of endodontic retreatment in the current study could be explained by the fact that treatment was conducted in adequate conditions with appropriate instrumentation and medication after detailed analysis of causes of failure. The most common causes of failure were incomplete or delayed conservative or prosthetic reconstruction, inadequate occlusal relationship with other teeth, as well as individual oral hygiene. The results of our study are in agreement with results of other studies that have investigated outcomes of nonsurgical endodontic retreatment [7, 11, 13, 15, 19, 20].

Gorni and Gagliani [20] investigated the success of endodontic retreatment over a period of two years. They analyzed 452 teeth divided into two categories. The first one comprised teeth with modified anatomy where initial endodontic treatment altered morphology of the canal system. In this group retreatment was successful in 47%. In the second group, where there were no significant anatomical changes and morphology of canals was respected, success rate was 86.8% [20]. Fristad et al. [19] conducted a long-term study where they performed radiographical evaluation of 112 retreated teeth after 20–27 years. They found that asymptomatic periapical radiolucency should not be considered a failure because in 95.5% of cases they remain asymptomatic. Also many of them (especially those that were adequately restored) showed delayed healing after a prolonged period of time [19].

Friedman et al. [7, 13] conducted extensive epidemiological study in Toronto to evaluate successful outcome of repeated conventional nonsurgical endodontic treatment and factors that influence it. During the observation period of four to six years in four stages of research, they examined 126 retreated teeth and found that 81% of them had absence of periapical inflammation and signs and symptoms of periapical inflammation. They concluded that the most important factors to determine successful outcome of endodontic retreatment are the quality of canal filling, the existence of preoperative perforation, and preoperative status of periapical tissue [7, 13].

Salehrabi and Rotstein [15] assessed 4,744 non-surgically endodontically retreated teeth during an observation period of five years. They found that 89% of teeth were still present in the oral cavity while 11% were extracted. Dur-

ing the first two years, 4% of the retreated teeth underwent surgical intervention (apicoectomy). This high success rate is related to criteria that exclusively analyze survival and function of teeth and ignore radiographical findings.

CONCLUSION

Retreatment of previously endodontically treated teeth for various endodontic indications during an observation

period of two years was successful in high percentage in teeth with and without clinical symptoms and radiographic signs of periapical lesion.

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Исход поновног третмана ендодонтски лечених зуба након две године

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КРАТАК САДРЖАЈ

Увод Ендодонтски ретретман је комплексна интервенција која захтева детаљну анализу индикација, односно перфектну практичну реализацију оваквог захвата.

Циљ рада Циљ овог рада је био да се на основу клиничких и радиографских критеријума процени исход поновљене ендодонтске терапије након периода од две године код пацијената са различитим ендодонтским индикацијама.

Методе рада Клиничка студија је обухватила 49 зуба индикованих за поновљени ендодонтски третман, који су на основу ПАИ (периапикални индекс) скоро подељени у две групе. У прву групу су сврстани зуби без периапикалних промена (ПАИ скор 1 и 2), док су другу групу чинили зуби са видљивим знацима оштећења апексног пародонцијума (ПАИ скор 3, 4 и 5). Поновљено ендодонтско лечење подразумевало је медијацију 2% раствором хлор-хексидина и суспензијом калцијум-хидроксидом у трајању од две не-

деље у обе групе зуба. Исход предузете терапије процењиван је на клиничким и радиографским контролама 12–24 месеца након дефинитивне оптурације.

Резултати Поновљена ендодонтска терапија у групи зуба са здравим пародонталним ткивима након 24 месеца била је успешна у 93,3% случајева. У групи са периапикалним променама радиографски делимично побољшање забележено је у 14,7%, а потпуно излечење у 52,9% случајева. С обзиром на одсуство клиничких знакова и субјективних симптома, поновљена терапија сматрана је успешном у оба случаја, дакле у укупно 67,6% зуба код којих су постојале хроничне периапикалне лезије.

Закључак Поновљена ендодонтска терапија је била успешна у високом проценту и код зуба без изражених клиничких и радиографских симптома и са њима.

Кључне речи: ендодонтски ретретман; ендодонтски неуспех; апијални периодонтитис

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O D L U K U

Usvaja se pozitivan izveštaj Komisije za ocenu završene doktorske disertacije **mr sc. dr Jelene Nešković**, pod nazivom „KLINIČKA I MIKROBILOŠKA ANALIZA NEUSPEHA ENDODONTSKOG LEČENJA ZUBA“

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1. prof. dr Đurica Grga
2. prof. dr Branka Popović
3. prof. dr Snježana Čolić
4. prof. dr Aleksandar Mitić, Medicinski fakultet u Nišu

O b r a z l o ž e n j e

Veće naučnih oblasti medicinskih nauka, na sednici od 22.05.2012. godine, dalo je saglasnost na predlog teme doktorske disertacije mr sc. dr Jelene Nešković, pod nazivom KLINIČKA I MIKROBILOŠKA ANALIZA NEUSPEHA ENDODONTSKOG LEČENJA ZUBA“

Imenovani/a je objavio/la:

- u časopisu „Srpski arhiv za celokupno lekarstvo“, rad pod nazivom: „Outcome of orthograde endodontic retreatment – A two-year follow-up“ (2016)

Imajući u vidu napred navedeno, Nastavno naučno veće Stomatološkog fakulteta Univerziteta u Beogradu, rešilo je kao u dispozitivu.

Odluku dostaviti: Imenovanom/oj, Univerzitetu u Beogradu, Odseku za nastavu, Veću, Komisiji (4) i Pisarnici.

Referent kadrovskog odseka
Violeta Rastović

Dekan
Stomatološkog fakulteta

Prof. dr Miroslav Vukadinović

Fakultet STOMATOLOŠKI

UNIVERZITET U BEOGRADU

Stručno veće za medicinske nauke

Broj zahteva _____

(naziv stručnog veća kome se zahtev upućuje, shodno
čl.6 Statuta Univerziteta u Beogradu i čl. 7. st.1
ovog pravilnika)

_____.god.
(Datum)

ZAHTEV

za davanje saglasnosti na izveštaj o urađenoj doktorskoj disertaciji

Molimo da, shodno članu 68. st.3. Zakona o univerzitetu ("Službeni glasnik RS" br. 20/98), date saglasnost na

izveštaj o urađenoj doktorskoj disertaciji kandidata

MR JELENE ZORAN NEŠKOVIĆ

(ime, ime jednog od roditelja i prezime)

KANDIDAT MR JELENE ZORAN NEŠKOVIĆ

prijavila je doktorsku disertaciju pod nazivom

(ime, ime jednog od roditelja i prezime)

„KLINIČKA I MIKROBIOLOŠKA ANALIZA NEUSPEHA ENDODONTSKOG LEČENJA ZUBA“

Univerzitet je dana 22.05.2012. svojim aktom pod br. 18704/10-12 dao saglasnost na predlog teme doktorske disertacije koja je glasila _____

„KLINIČKA I MIKROBIOLOŠKA ANALIZA NEUSPEHA ENDODONTSKOG LEČENJA ZUBA“

Komisija za ocenu i odbranu doktorske disertacije kandidata

MR JELENE ZORAN NEŠKOVIĆ

(ime, ime jednog od roditelja i prezime)

obrazovana je na sednici održanoj 26.04.2016 odlukom fakulteta pod br. _____

u sastavu:

ime i prezime člana komisije:	zvanje:	naučna oblast:
<u>ĐURICA GRGA</u>	<u>PROFESOR</u>	<u>KLINIČKE STOM. NAUKE</u>
<u>BRANKA POPOVIĆ</u>	<u>PROFESOR</u>	<u>BAZIČNE STOM. NAUKE</u>
<u>SNJEŽANA ČOLIĆ</u>	<u>PROFESOR</u>	<u>KLINIČKE STOM. NAUKE</u>
<u>ALEKSANDAR MITIĆ</u>	<u>PROFESOR</u>	<u>KLINIČKE STOM. NAUKE</u>

Nastavno-naučno veće fakulteta prihvatilo je izveštaj Komisije za ocenu i odbranu doktorske
disertacije na sednici održanoj dana 07.06.2016.

DEKAN FAKULTETA

Prof. dr Miroslav Vukadinović

- Prilog:
1. Izveštaj komisije sa predlogom
 2. Akt Nastavno-naučnog veća fakulteta o usvajanju izveštaja
 3. Primedbe date u toku stavljanja izveštaja na uvid javnosti, ukoliko je takvih primedbi bilo.