GRIGORE T. POPA UNIVERSITY OF MEDICINE AND PHARMACY IASI

HABILITATION THESIS

BEYOND THE FUNDAMENTALS: EXPLORING CURRENT TECHNIQUES IN MODERN DENTISTRY

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ABBREVIATIONS

AgP- Aggressive periodontitis
Bis-DMA- Bisphenol A dimethacrylate
Bis-GMA- Bisphenol A-glycol dimethacrylate
BOP- Bleeding on probing
BSSO- Bilateral sagittal split osteotomy
CAD- Computer aided design
CAL- Clinical attachment loss
CAM- Computer aided manufacturing
CBCT- Cone beam computed tomography
CCW- Counterclockwise
CHX- Chlorhexidine
CP- Chronic periodontitis
CR- Centric relation
Cre- Center of resistance
CRP- C-reactive protein
CT- Computed tomography
DICOM- Digital imaging and communications in medicine
DLP- Direct light processing
DNA- Deoxyribonucleic acid
Dox- Doxycycline
DUP- Direct UV printing
EDX- Energy dispersive X-ray analysis
EGDMA- Ethylene glycol dimethacrylate
FDM- Fused deposition modeling
FEA- Finite element analysis
FOV- Field of view
FP- Fixed prothesis
GCF- Gingival crevicular fluid
HBL- Extent of Periodontal Damage
Hrp -Horseradish peroxidaze conjugate
LCI- Lower central incisor
LCM- Lithography-based ceramic manufacturing
LFI- Le Fort I osteotomy
LLI- Lower lateral incisor
LLLT - Low-level light therapy
M- Dental mobility
MHP- Maximum hydrostatic pressure
MMA- Methyl methacrylate
MMP-8- Matrix metallopeptidase 8
MMP-9- Matrix metallopeptidase 9
MMPs- Metalloproteinases
MTS- Maximum tolerable stress
NHP- Natural head position
OS- Orthognathic surgery
OTM- Orthodontic tooth movement
PBMT- Photobiomodulation therapy
PD- Probing depth
PDI- Periodontal disease index
PDI- Photodynamic inactivation
PDT- Photodynamic antibacterial therapy
PEEK- Polyetheretherketone
PEKK- Polyetherketoneketone
PFEM- Probabilistic finite element method
PI- Plaque index
PMMA- Polymethyl methacrylate
PPD- Probing pocket depth
ROS- Reactive oxygen species
SARPE- Surgically assisted palatal expansion
SLA- Stereolithography
SRP- Scaling and root planning
STCA- Soft tissue cephalometric analysis
STL- Standard tessellation
TEGDMA- Triethylene glycol dimethacrylate
THL- True horizontal line
TMJ- Temporomandibular joints
TNF α- Tumour necrosis factor alpha
TSD- Tooth size differences
TVL- True vertical line parameters
UDMA- Urethane dimethacrylate
VSP- Virtual surgery planning
3DP- 3D printing

ABSTRACT

In the habilitation thesis entitled, *"Beyond the fundamentals: exploring current techniques in modern dentistry"*, personal scientific achievements from 2005 to 2023, after getting the scientific title of Professor in the domain of Dental Medicine, Technology of Dental Prostheses, are presented.

According to the recommendations of the National Council for Attestation of University Titles, Diplomas and Certificates CNATDCU, the thesis is structured into three main sections:
Section I – Scientific achievements of the post-doctoral period;
Section II – Plans for the evolution and development of one's own professional, scientific and academic career
Section III –References.

In the preamble of the first section, I resorted to a brief overview of the professional, scientific and academic research achievements obtained throughout my entire university educational career.

Section I – Scientific achievements of the postdoctoral period

Section I of the thesis is dedicated to the listing of postdoctoral scientific research, being structured into three chapters, corresponding to the main areas of research addressed. The most relevant articles published in specialized journals, indexed in the Web of Science Core Collection and in international databases are presented.

Chapter 1 of this section, entitled "*Research on computer-based technologies used for dental applications*", has as its objectives the approach of two directions of scientific research, being preceded by a literature review.

As part of the first direction of research, "*Current Trends in CAD/CAM Technologies*", emphasizes theoretical and experimental research involving digital technologies used in dental laboratories for manufacturing dental models, provisional and definitive fixed prosthetics, and partial and total prostheses. To illustrate a fully digitized workflow, a clinical case is presented, which uses a combination of three digital software tools for the purpose of correcting the defective position of the menton.

The second direction focuses on "The use of finite element analysis (FEA) of biomechanical behavior". Experimental research has been directed towards two important directions of dental medicine: prothetic appliances and ortodontics. For the field of dental prothetics, research on the biomechanical behavior of inlay-fixed dental bridges and single-element retainer dental bridges, made from titanium-based alloys, using 3D modeling and finite-element analysis is presented (FEA). In the field of orthodontics, the use of FEA will allow modeling and simulating dental movements, and highlighting the role of periodontal ligaments in producing these shifts.

Chapter 2 refers to the original scientific contributions obtained as a result of the experimental tests carried out on current direct coronal restorative materials. Composite diacrylic resins used for adhesive immobilization of periodontally damaged teeth, fabrication of inlays and permanent fixation of coronary restorations have been studied.

Chapter 3 of the first section, entitled "*Research on computer-based technologies used for dental restorations*", aimed to pursue two separate directions of scientific research.

The first direction aimeded to evaluate the periodontal inflammation produced during orthodontic and prosthetic treatments. In this sense, the evolution of doxycycline treatment used in aggressive parodontitis was followed. The focus of scientific research has been on determining the level of markers for inflammatory response, such as: matrix metaloproteinases (MMP) 8 and 9, interleukin-1beta (IL-1β) and tumor necrosis factor alpha (TNF-α).

The second direction of research addressed:
- the role of light in the treatment of periodontal diseases in patients with dental implants and prosthetic restorations,
- the effectiveness of solutions for oral rinse in oncological patients undergoing chemotherapy treatment.

Section II – Plans for the evolution and development of the professional, scientific and academic career

Section II of the qualification thesis presents the future development directions for the two components of the professional career: scientific research and personal contributions to the academic community.

The directions set for future scientific research will fall within the specifics of the discipline "Dental Protheses Technology". They will focus on the following topics:
- the continuation of the directions already addressed in the field of finite-element analysis of the biomechanical behavior of dental restorations;
- the creation of mathematical models that allow for the most perfect simulation of movements, stress states and mechanical deformations in conditions specific to the oral cavity;
- the development of research on additive technologies applied in different domains of dental medicine;
- optimization of the specific technological parameters in additive manufacturing process, in order to obtain indirect crown restorations with excellent dimensional accuracy and without plastic deformations caused by the thermo-mechanical stresses induced in the materials used;
- diversifying experimental research by involving new groups of materials intended for the realization of fixed and mobile prothetic restorations. Ceramic materials (nano-ceramic, hybrid ceramic, zirconia) and organic polymers (polieter ether ketone -PEEK, high-performance polymer reinforced with ceramic phases -BioHPPe) will be addressed.

Personal contributions to the development of the academic community will have the following priorities:
- expanding professional collaborative relationships with new teams of specialists and scientific researchers working in related fields, such as computer science, bioengineering, laboratory medicine, materials engineering;
- perfecting new educational and scientific partnerships with prestigious universities and research institutes, nationally and internationally;
- realization of collaborative partnerships with economic agents interested in application implementation by transferring the results of scientific research obtained;
- improvement of the infrastructure for teaching laboratories and multidisciplinary scientific research centres;
- the improvement of modern teaching methods based on the use of high-performance multimedia equipment;
- implementation, within the Doctoral School, of scientific research topics addressing the most current requirements in the field of modern international dentistry;
- active involvement of doctoral and master's students in scientific research projects at the faculty level;
- active participation with new proposals of advanced scientific research projects in competitions organized through national and international programs in progress;

- involvement of teachers and students in international mobility programs in order to participate in the development of the most up-to-date scientific research directions in dentistry.

Section III – References

Section III of the habilitation thesis is represented by the references used during its elaboration. The analysis of the titles of the scientific papers listed highlights the timeliness of the research topics addressed but also the importance of the future directions proposed.

The chronological systematization of the 464 cited references reveals that:

- 63% of the papers were published between 2013 and 2023;
- 37% of these papers were published before 2013.

REZUMAT

În cadrul tezei de abilitare intitulată, *“Considerații actuale asupra analizei tehnicilor inovative în medicina dentară modernă“*, sunt prezentate realizările ştiinţifice personale din perioada 2005-2023, după obţinerea titlului academic de profesor universitar, la disciplina de Tehnologia protezelor dentare.

Conform recomandărilor Consiliului Naţional de Atestare a Titlurilor, Diplomelor si Certificatelor Universitare (CNATDCU), teza este structurată pe trei secţiuni principale: Secțiunea I – Realizări științifice din perioada post-doctorală;
Secțiunea II – Planuri de evoluție și dezvoltare a propriei cariere profesionale, științifice și academice;
Secțiunea III – Referințe bibliografice.

În preambulul primei Secțiuni am recurs la o scurtă prezentare a realizărilor profesionale, de cercetare științifică și academice obținute pe parcursul întregii mele cariere educaționale universitare.

Secțiunea I – Realizări științifice din perioada post-doctorală

Secțiunea I a tezei este dedicată enumerării cercetărilor ştiinţifice postdoctorale, ea fiind structurată pe trei capitole corespunzătoare principalelor domenii de cercetare abordate. Sunt prezentate cele mai relevante articole publicate în reviste de specialitate, indexate în Web of Science Core Collection și în baze de date internaționale.

Capitol 1 al acestei secțiuni, intitulat: *"Cercetări asupra tehnologiilor bazate pe calculator utilizate pentru aplicațiile stomatologice"*,a avut ca obiectiv abordarea a două direcții de cercetare științifică, ele fiind precedate de o prezentare generală preluată din literatura de specialitate.

În cadrul primei direcții de cercetare, "*Tendințele actuale în tehnologiile CAD/CAM*", a fost acordată o atenție deosebită cercetărilor teoretice și experimentale care implică tehnologiile digitale, utilizate în laboratoarele de tehnică dentară, având ca rol fabricarea modelelor dentare, protezelor fixe provizorii și definitive, protezelor parțiale și totale. Pentru a ilustra un flux de lucru complet digitalizat, este prezentat un caz clinic, care utilizează o combinație de trei instrumente software digitale în scopul corectării poziției defectuoase a mentonului.

A două direcție se concentrează pe: *”Utilizarea analizei cu element finit (FEA) a comportamentelui biomecanic”.* Cercetările experimentale au fost orientate către două ramuri importante ale medicinei dentare: protetica dentară și ortodonția. Pentru domeniul proteticii dentare, sunt prezentare cercetări asupra comportamentului biomecanic al punților dentare fixate prin inlay și a punților dentare cu un singur element de agregare, realizate din aliaje pe bază de titan, utilizând modelare 3D și analiza cu element finit (FEA). În domeniul ortodonției, utilizarea FEA va permite modelarea și simularea mișcările dentare, și evidențierea rolului ligamentelor parodontale în producerea acestor deplasări.

Capitol 2 face referire la contribuțiile științifice originale, obținute ca urmare a încercărilor experimentale efectuate asupra materialelor restaurativ coronare directe actuale. Au fost studiate rășinile diacrile compozite utilizate pentru imobilizarea adezivă a dinților cu afectare parodontală, confecționarea incrustațiilor și fixarea de durată a restaurărilor coronare.

Capitol 3 al primei secțiuni, intitulat "Cercetări asupra tehnologiilor bazate pe calculator utilizate pentru aplicațiile stomatologice", a avut ca obiectiv urmărirea a două direcții proprii de cercetare științifică.

Prima direcție a avut ca scop evaluarea inflamației parodontale produsă în timpul tratamentelor ortodontice și protetice. În acest sens, a fost urmărită evoluția tratamentului cu doxiciclină utilizat în parodontita agresivă. Accentul cercetărilor științifice a fost pus pe determinarea nivelului markerilor pentru raspusul inflamator, precum: metaloproteinazele matriceale (MMP) 8 și 9, interleukina-1beta (IL-1β) și factorul de necroză tumorală alfa (TNF-α).

A doua direcție de cercetare a abordat:

- rolul luminii în tratamentul afecțiunilor parodontale la pacienții cu implanturi dentare și restaurări protetice,
- eficiența soluțiilor pentru clătiri orale la pacienții oncologici aflați sub tratament chimioterapeutic.

Secţiunea II- Planuri de evoluție și dezvoltare a propriei cariere profesionale, științifice și academice

Secţiunea II a tezei de abilitare prezintă direcțiile viitoare de dezvoltare pentru cele două componente ale carierei profesionale: cercetarea ştiinţifică şi contribuțiile personale aduse în cadrul comunității academice.

Direcțiile stabilite pentru cercetările științifice viitoare se vor încadra în specificul disciplinei didactice ”Tehnologia Protezelor Dentare”. Ele se vor axa pe următoarele tematici:

- continuarea direcțiilor deja abordate în domeniul analizei cu element finit a comportamentului biomecanic al restaurărilor dentare;
- crearea de modele matematice care să permită simularea cât mai perfectă a mișcărilor, stărilor de solicitări și deformații mecanice în condiții specifice cavității orale;
- dezvoltarea cercetărilor asupra tehnologiilor aditive aplicate în diferite domenii ale medicinei dentare;
- optimizarea parametrilor tehnologici specifici procesării aditive în vederea obținerii unor restaurări coronare indirecte cu o precizie dimensională excelentă și lipsite de deformațiile plastice cauzate de tensiunile termo-mecanice induse în materialele utilizate;
- diversificarea cercetărilor experimentale prin implicarea unor noi gupe de materiale destinate realizării restaurărilor protetice fixe și mobile. Vor fi abordate materiale ceramice (nano ceramica, ceramica hibridă, zirconia) și polimer organici (polieter eter cetonă -PEEK, polimer de înaltă performanță armat cu faze ceramice -BioHPPe).

Contribuțiile personale aduse la dezvoltarea comunității academice vor avea următoarele priorități:

- extinderea relațiilor de colaborare profesională cu noi colective de specialiști și cercetători științifici care activează în din domenii conexe, precum informatica, bioingineria, medicina de laborator, ingineria materialelor;
- perfectarea unor noi parteneriate educaționale și științifice cu universități și institute de cercetare de prestigiu, la nivel național și internațional;
- realizarea parteneriatelor de colaborare cu agenții economici interesați de implementarea aplicativă prin transferul rezultatelor cercetărilor științifice obținute;
- îmbunătățirea infrastructurii destinată laboratoarelor pentru activități didactice și a centrelor de cercetare științifică multidisplinară;
- perfecționarea metodelor moderne de predare, bazate pe utilizarea echipamente multimedia performante;
- implementarea, în cadrul Școlii Doctorale, a temelor de cercetare științifică care să abordeze cele mai actuale tendințe din domeniul stomatologiei moderne internaționale;

- implicarea activă a studenților doctoranzi și masterazi în proiectele de cercetare științifică la nivelul facultății;
- participarea activă cu noi propuneri de proiecte de cercetare științifică avansată în cadrul competițiilor organizate prin Programe Naționale și Internaționale aflate în derulare;
- implicarea cadrelor didactice și a studenților în programe de mobilități internaționale pentru a cunoaște și participa la dezvoltarea celor mai actuale direcții de cercetare științifică în stomatologie.

Secțiunea III – Referințe bibliografice

Secţiunea III a tezei de abilitarea este reprezentată prin referințele bibliografice folosite pe parcursul elaborării ei.

Analiza titlurilor lucrărilor științifice enumerate, evidențiază actualitatea temelor de cercetare abordate dar și importanța direcțiilor de viitor propuse.

Sistematizarea calendaristică a celor 464 de indicațiilor bibliografice menționate, arată faptul că:

- 63% dintre lucrări au fost publicate în perioada anilor 2013-2023;
- 37% dintre lucrări au fost publicate înainte de anul 2013.

OVERVIEW OF ACADEMIC, PROFESIONAL AND SCIENTIFIC ACHIEVEMENTS

ACADEMIC ACTIVITY

Following the completing the internship medical period, in 1991 I successfully passed the assistant exam, marking the beginning of my teaching journey at the Faculty of Stomatology Iasi.

I joined the Technology of Dental Prostheses discipline, under the guidance of Prof. Dr. Panaite Stefan.

To provide a chronological overview of my academic progress, the timeline is as follows:

1991-1997	Assistant – Technology of Dental Prostheses discipline Faculty of Dental Medicine, „Grigore T Popa” University of Medicine and Pharmacy, Iași
1997-2001	Lecturer – Technology of Dental Prostheses discipline Faculty of Dental Medicine, „Grigore T Popa” University of Medicine and Pharmacy, Iași
2001-2005	Associate Professor- Technology of Dental Prostheses discipline Faculty of Dental Medicine, „Grigore T Popa” University of Medicine and Pharmacy, Iași
2005- present	Professor- Technology of Dental Prostheses discipline Faculty of Dental Medicine, „Grigore T Popa” University of Medicine and Pharmacy, Iași

Over 32 years, my teaching activities have been consistently focused on advancing the field of Dental Prostheses Technology. This commitment is reflected in my participation in over 40 postgraduate professional development courses conducted by prominent lecturers from both national and international communities.

In the organization of teaching activities (practical works and courses), I have considered the use of modern teaching methods. The course content has encompassed up-to-date documentation in the field, while practical works have been updated through the utilization of new materials and technologies. The presentation of theoretical and practical concepts is in accordance with the new technologies specific to the field, incorporating an interactive approach in course delivery

Motivated by my desire to provide to our students with well-structured and current information that aligns with accredited programs, I have developed manuals and educational materials specifically tailored to their needs. These resources have been made available on E-learning platforms and Microsoft Teams directories for easy and open access.

The most representative achievements are listed below:

Books	1. Dana Gabriela Budala, ***Monica Silvia Tatarciuc.*** Complete denture Practical Guide, Ed. Pim, Iasi, 2022, ISBN978606-13-7180-8

	2. Diana Antonela Diaconu, ***Monica Silvia Tatarciuc.*** Éleménts de morphologie de l'appareil dento-maxillaire, Ed. Pim, Iași 2021, ISBN 978-606-13-56152-6 3. ***Monica Silvia Tatarciuc***, Ioana Martu, Andra Aungurencei-La technologie de realization des prostheses fixes plurielle, Editura GR.T. Popa, Iasi,2021, ISBN 978-606-544-735-6 4. ***Monica Silvia Tatarciuc***, Diana Antonela Diaconu, Diana Tatarciuc. Elemente de morfologie a sistemului stomatognat, Ed. Pim, Iași 2020, ISBN 978-606-13-5468-9 5. Diana Diaconu-Popa, ***Monica Silvia Tatarciuc***, Anca Vițalariu. Technologie de la protheses totale, Ed. Performantica Iaşi 2019, ISBN 978-606-685-661-4 6. Diana Antonela Diaconu, ***Monica Tatarciuc.*** Particularitati tehnologice in realizarea puntilor ceramice, Ed. Performantica Iasi 2015, ISBN 978-606-685-241-8 7. Diana Antonela Diaconu, ***Monica Silvia Tatarciuc***. Technologies des prostheses unidentaires, Ed. Performantica Iasi, 2012, ISBN 978-973-730-948-8 8. Anca Mihaela Viţalariu, Radu Comăneci, ***Monica Tatarciuc***. Reconstituirile corono-radiculare. Casa de editură Venus, Iaşi, 2007, ISBN: 978-973-756-049-0 9. Diana Diaconu, Monica Tatarciuc. Tehnologia protezelor metalo-ceramice, Ed. Junimea Iasi, 2006, ISBN 978-973-37-1216-9
Book chapters	1. Anca Vitalariu, Cristina Masgras, Irina Chonta, Diana Diaconu-Popa, ***Monica Tatarciuc***. Impactul local şi sistemic al refacerii morfologiei ocluzale şi a funcţiei masticatorii, Cap.II.15, 2017, p.163-173, Vol. Sănătatea orală în contextul sănătăţii generale, Ed. Grigore T. Popa, ISBN: 978-606-544-402-7. 2. Monica Tatarciuc, Diana Diaconu-Popa, Anca Vitalariu-Prevenirea afecţiunilor orale determinate de coroziunea aliajelor dentare, Cap.III.11, 2017, p.266-273, Vol. Sănătatea orală în contextul sănătăţii generale, Ed. Grigore T. Popa, ISBN: 978-606-544-402-7. 3. Anca Vitalariu, Diana Diaconu, Irina Chonta, Monica Tatarciuc-, Gutierele pentru protecție în activitățile sportive, Cap. IV.7, p.259-273, Vol. Managementul preventiv și interceptiv al afecțiunilor stomatologice la copii și adultul tânăr, Ed. Grigore T. Popa, 2016, ISBN 978-606-544-392-1 4. Diana Diaconu, Anca Vitalariu, ***Monica Tatarciuc***. Prevenirea afectarii starii de sanatate generala in medicina dentara- Posibilitati si mijloace de prevenire a infectiei incrucisate in laboratorul de tehnica dentara, Cap.4 in *Prevenirea afectiunilor stomatologice*, 2014, p.183-187, Ed. Grigore T. Popa, ISBN 978-606-544-229-0 5. ***Monica Tatarciuc*** Formare formatori /specialisti in reabilitarea orala-Modulul III Aspecte clinice si tehnologice ale reabilitarii orale Protetica si tehnologia protezelor, Capitolul IV Aspecte practice actuale in algoritmul tehnologic specific protezarii fixe, 2013, p.266-293, Casa Editoriala Demiurg, ISBN 978-973-152-271-5 6. ***Monica Tatarciuc***. Formare formatori/specialisti in reabilitarea orala-Modulul III Aspecte clinice si tehnologice ale reabilitarii orale Protetica si

	tehnologia protezelor, Capitolul IV Aspecte practice actuale in algoritmul tehnologic specific protezarii fixe, 2013, p.266-293, Casa Editoriala Demiurg, ISBN 978-973-152-271-5

In addition to my involvement in the didactic activities with the students from the bachelor program (first, third and fourth-year students of the Faculty of Dental Medicine; first and second-years students of the College of Dental Technology), I am also actively engaged in the coordination of master's students. As part of my involvement in the master's program "Modern Techniques in Aesthetics and Technological Rehabilitation in Specific Edentulous Situations," I provide professional support to the students.

Since 2019 I became Coordinator within the newly established residency program of General Dentistry. In this position, I was able to guide the practical and theoretical activities of resident doctors, in the field of Prosthetics. I have been actively involved in providing my expertise to resident doctors undergoing training in General Dentistry, offering lectures, case presentations, and intensive practical training. To further support their development, I have encouraged resident doctors to engage in personal research and documentation, participate in specialization courses both domestically and internationally, attend specialized congresses, and pursue continuous professional training. Resident doctors who have demonstrated a keen interest in scientific and research activities have been integrated into the clinic's research team. As a result, they have had the opportunity to become co-authors of specialized articles or studies presented at scientific events.

I had the honour and consistent responsibility to extend the didactic activity by including the managerial and professional tasks related to the position of Head of Dental Prostheses Technology Discipline (2005 – 2023) and Dean of the Faculty of Dental Medicine, „Grigore T. Popa” University of Medicine and Pharmacy, Iași, since 2020.

Overall, my contributions as a member of the academic community have been recognized in numerous ways, including:

- Membership in the Central Committee of the Dental Medicine Admission;
- Membership in the Committee for Bachelor's Degree Examinations for graduates of Dental Technology Colleges and the Faculty of Dental Medicine;
- Membership in the Committee for the presentation of master's dissertations
- Membership in the Professional Committee for the development strategy of the faculty;
- Membership in the Doctoral Admission Committees;
- Membership in the Committees for the examinations and projects presentation within the doctoral program
- Referee in Committees for the presentation of doctoral theses;
- President of the Public Presentation Committee for the doctoral thesis;
- Membership of Admission Committees for the recruitment of teaching positions such as Assistant, Lecturer, Associate Professor;
- Expert evaluator for the Romanian National Council for Academic Evaluation and Accreditation (ARACIS);
- Membership in the Evaluation Committee for the professional activities of the teaching staff in the Faculty of Dental Medicine - "GrigoreT.Popa" University of Medicine and Pharmacy, Iași;
- Member of the working team for the revision of Procedures for PP-07 "Undergraduate Studies" and PP-09 "Organization of Teaching Activities for Master's Degree Education";
- Organizer and member in various scientific committees for national and international congresses, conferences.

PROFESSIONAL DENTAL PRACTICE

The significant milestones in my professional development are closely connected to my successful completion of high school and university studies. I started working as a dentist in The Dental Gnathoprosthetics Clinic of Universitary Clinic no.1, Iași (1985-1988)
and later I provided medical assistance at the conty practice Miroslăveşti, Iaşi (1988-1991).

With a specific focus on prosthodontics, I obtained certification as a Senior Specialist in General Dentistry. Furthermore, with the establishment of the new specialty of Prosthodontics, I pursued additional certification in this specialized field as well.

1975-1980	High-school diploma, No. 60146/5.07.1980, Physics-Chemistry profile „Emil Racoviţă” High School, Iaşi
1980-1985	Doctor - dentist, Bachelor's degree No. 1195/28.10.1985 Faculty of Dental Medicine, „Grigore T Popa” University of Medicine and Pharmacy, Iași
1985-1988	Trainee in Dentistry - University Dental Polyclinic The Dental Gnathoprosthetics Clinic of Universitary Clinic no.1, Iași
1991	Specialist in General Dentistry, confirmed by the Order of the Minister of Health no. 939/2.07.1991
1996	Senior specialist in General Dentistry, confirmed by the Order of the Minister of Health no. 1376/19.06.1996
2012	Specialist in Prosthodontics, confirmed by the Order of the Minister of Health no. 786/03.08.2012

In addition to my continued dedication to improving my knowledge and abilities in dentistry, shown by my active participation in national and international scientific meetings and post-graduate courses, my interests also included the membership in The College of Stomatologists from Romania (CMSR).

SCIENTIFIC RESEARCH ACTIVITY

In May 1993, I successfully competed for admission to the Doctoral School of the Faculty of Dental Medicine at "Grigore T Popa" University of Medicine and Pharmacy in Iași. Under the guidance of Professor Dr. Valentina Dorobăţ, I embarked on my doctoral journey. After 6 years of dedicated research and study, I was awarded the title of Doctor in Dental Medicine in 1999. This achievement was officially recognized through the Doctor's Degree Series R No. 0004903 on 10.06/1999 and confirmed by the Order of the Minister of Education and Research No. 3772/5.05.1999.

My doctoral thesis, titled "Bioengineering in Orthodontic Treatment," explored the application of bioengineering principles in the field of orthodontics. This research delved into the utilisation of advanced techniques, materials, and computer-assisted methods to improve orthodontic treatment outcomes.

The most part of my research is carried out in the field of Dental Medicine in the following research directions:
- Metallo-Ceramic Technology;
- Biocompatibility of Materials;
- Orthodontic Appliance Technology;
- Mathematical Modeling of Orthodontic Tooth Movements;
- Alternative Techniques for Aesthetic Rehabilitation;
- Minimally Invasive Prosthodontics;

- Implications of Bivalent Cations in Oral Health.

From the beginning, I joined the research team associated with this discipline and actively contributed to collaborative projects. This involvement led to my initial presentations of research findings at conferences and congresses related to the discipline profile. In total, I have delivered 271 oral or poster presentations (218 in Romanian and 53 abroad congresses) and published over 230 articles that have been published in prestigious journals indexed in the Web of Science Core Collection, in ISI proceedings volumes, in International database listed journals and in the volumes of national and international conferences.

I have participated in several research contracts:

- Member of a complex project carried out in a CDI consortium: “Obtaining and expertise of new biocompatible materials for medical applications, no. 63/19.03.2018, (MedicalMetMat), type grant PN III – PCCDI, project director Forna Norina Consuela
- Member in the group of experts COST Action TD1408 "Interdisciplinarity in Research Programming and Funding Cycles" (INTREPID)"- duration: 2015-2019
- Member of Internal UMF Iasi grant, No. 31588/23.12.2015, ”Effect of silver nano-particles on the properties of acrylic dental resins”- duration: 2015-2017
- Member in the project CEEX 181/2006, ”Regional network of excellence in micro-nano-biotehnologies and textile materials for medical use”- duration: 2006-2008
- Member in the grant CNCSIS Type A No. 841/16.05.2006 „ The evaluation of the longevity of post and core reconstructions by testing the rezistance to thermo-mechanical fatigue into the artificial oral environment ” - duration: 2006-2007

In summarised form, the following indices indicate my research's overall international scientific visibility:

Clarivate Analytics Web of Science Hirsch-Index	11
Scopus Hirsch Index	9
Google Scholar Hirsch Index	11
Number of publications in Clarivate Analytics database	95
Total number of citations without self-citations (Clarivate Analytics)	209
Average citation per item	3.72
In extenso ISI scientific articles in Clarivate Analytics database	39
In extenso IDB scientific papers in Clarivate Analytics database	66
Number of publications in Scopus database	59
Number of publications in Google Scholar database	145
ORCID: 0000-0002-7178-8283	

SECTION I

SCIENTIFIC ACHIEVEMENTS FROM THE POSTDOCTORAL PERIOD

CHAPTER 1
RESEARCH ON THE COMPUTER-BASED TECHNOLOGIES FOR DENTAL APPLICATIONS

1.1. CURRENT TRENDS IN CAD/CAM TECHNOLOGIES

1.1.1. State of art

In the past three decades, Computer-Aided Design/Computer-Aided Manufacturing (CAD/CAM) has gained significant popularity and trust from both dental professionals and patients alike. It has facilitated ease, comfort, and high-quality restoration to dentists and dental laboratory technicians. Furthermore, CAD/CAM restorations are more durable, have better marginal adaptation, are aesthetically more pleasing, and are faster to fabricate when compared to conventional restorations.

CAD/CAM has its roots into ancient civilizations like Egypt, Rome, and Greece, where evidence suggests that the technology was used in various forms. Euclid of Alexandria was the mathematician, who laid the foundation for modern CAD software by establishing the axioms and postulates of Euclidian geometry that underlie contemporary CAD software.

The development of CAD software accelerated in the early 1960s when Ivan Sutherland created Sketchpad. However, before this, Dr. Patrick J. Hanratty had already designed the first numerically controlled CAM, called Pronto, earning him the title "Father of CAD/CAM."

The introduction of CAD/CAM technology in dentistry can be traced back to the pioneering work of Dr. Duret, who, in 1971 (Duret, Preston, 1991), developed a method for fabricating a crown using a numerically controlled machine and an optical impression of an abutment tooth. Although Dr. Duret's Sopha system was not widely adopted, Dr. Mormann introduced the first commercially designed CAD/CAM system, called CEREC, in 1985 (Mormann et al., 1989). This system allowed for the fabrication of inlays, onlays, and crowns from a ceramic block using a digital impression taken with an intraoral camera. Another important development in the CAD/CAM field was the Procera system, which was developed in the mid-1980s by Dr. Andersson.

In 1994, Siemens revealed the CEREC 2 system, which utilised two-dimensional principles and had the ability to manufacture various dental restorations such as inlays, onlays, veneers, partial and full crowns, and copings. The third generation of CEREC technology, which was unveiled by Sirona in 2005. This system is capable of producing the same restorations as the previous model, but with the added feature of virtual automatic occlusal adjustment (Miyazaki et al., 2009).

CAD/CAM systems typically consist of three essential components. The first component is a digitalization tool or scanner that captures the geometry of an object or structure and transforms it into digital data that can be processed by the computer. The second component is the software that processes the digital data and generates a data set that specifies how the product will be fabricated. The software can vary depending on the application, but it is responsible for designing and creating the final product. The third component is the production technology, which transforms the data set into the desired product. This can involve different techniques such a subtractive process (milling) or additive processes (3D printing), depending on the specific application and material being used (Aslam, Nadim, 2015).

In the field of dentistry, CAD/CAM systems can be categorized into three different production concepts (Beuer et al., 2008; Freedman et al., 2007) based on their location of components:

1. *Chairside production:* All the CAD/CAM system components are located in the dental surgery, allowing for the fabrication of dental restorations at the chairside without the need for a laboratory procedure. The intra-oral camera serves as the digitalisation instrument, replacing conventional impressions in most clinical situations.

2. *Laboratory production:* This production variant is equivalent to the traditional working sequence between the dentist and laboratory. The dentist sends the impression to the laboratory where a master cast is fabricated. The remaining CAD/CAM production steps are carried out completely in the laboratory, where a scanner generates three-dimensional data based on the master die. Dental design software is then used to process the data and send it to a milling device or a 3D printer, that produce the real geometry.

3. *Centralised production:* Satellite scanners in the dental laboratory can be connected to the production centre via the internet, with data sets produced in the dental laboratory sent to the production centre for CAD/CAM device restoration production. The prosthesis is then sent back to the responsible laboratory. This procedure allows for greater independence and requires smaller investment but limits access to a particular production technology, and almost all CAD/CAM systems are only available as closed systems. Additionally, the dental laboratory loses the income from producing the framework, as it is fabricated in the production centre.

Computer-Aided Design (CAD)

The integration of data from various sources, along with advancements in user-interface and CAD software capabilities, has led to significant improvements in the field. The CAD software allows the user – the dentist or the dental technician - to interactively manipulate the data obtained from the scan. The interactive data manipulation functions include pre-processing, visualizing the scanned areas, virtual editing, measurements, reconstructions design, and virtual simulation of functions (Rekow, 2018).

The utilisation of digital technology in dentistry has led to the development of digital smile design (DSD) which involves the use of digital photographs of the patient's face and software analysis to facilitate the creation and planning of a treatment regimen by practitioners and laboratory technicians. The virtual simulation of the final aesthetic outcomes is a valuable tool, especially in intricate and interdisciplinary restorative procedures. The system facilitates communication between healthcare providers and laboratory personnel, as well as streamlines pre-treatment consultations with patients (Charavet et al., 2019). Several recent case reports and studies have documented the effective implementation of the DSD method in the field of dentistry (Garcia et al., 2018; Lin et al., 2018; Pozzi et al., 2018).

Tooth form libraries offer comprehensive tooth form and proportion data, facilitating the partial automation of restoration design and expediting the digital 'waxing' procedure.

The satisfaction of patients is contingent upon both the shape and shade of their teeth. Digital photography can be adjusted for colour and white balance and subsequently superimposed onto the virtual image produced by intraoral scanning (Sampaio et al., 2019; Lam et al., 2018). The utilisation of virtual teeth models that incorporate enhanced photograph-based colour information can enhance the accuracy of shade matching and promote collaborative decision-making between patients and clinicians regarding the ultimate restoration.

The extent to which computer-aided design (CAD) software can effectively account for shade variations resulting from manufacturing processes, cement selection, or underlying tooth structure remains uncertain (Rekow, 2020).

The consideration of occlusion is a crucial aspect in the design of restorations, impacting their durability and the contentment of patients. The utilisation of cone beam computed tomography (CBCT) or an intraoral scanner can facilitate the capture of jaw dynamics, thereby enabling the creation of a virtual articulator. This virtual articulator is capable of capturing a comprehensive range of static and dynamic jaw movements and occlusion. The integration of this data has the potential to enhance various dental procedures such as smile design, computer-assisted implant planning, and digital maxillofacial surgery planning (Seay, 2018).

Virtual surgery planning (VSP) is a computer-assisted process that uses cone beam computed tomography (CBCT) images of a patient's face and jaw to create a virtual model of the patient. This virtual model can then be used to simulate orthognathic sur-gical procedures, allowing the surgeon to evaluate the feasibility of different treatment plans and provide the patient with a more precise description of the possible outcomes. Thanks to these developments, the communication and understanding between patients and medical teams have been improved (Lai et al., 2022).

In the current literature, the most listed commercially available VSP software is Dolphin Imaging (Dolphin Imaging & Management Solutions, Los Angeles, CA, USA), Maxilim (Medicim NV, Mechelen, Belgium), SimPlant OMS (Materialise NV, Leuven, Belgium), and Mimics (Materialise NV, Leuven, Belgium) (Lin, Lo, 2015; Alkhayer et al, 2020). A large number of surgeons, each with their own unique approaches, puts substantial pressure on software companies to address both general and individual needs.

One of the biggest benefits of VSP is the improved visualization of craniofacial deformities, such as occlusal canting and asymmetries (Quast et al., 2021; Hsu et al., 2020; Liao et al., 2020). In addition, the surgeon can have an accurate image of the relationship between bony fragments concerning want-ed/unwanted gaps, interferences, and steps along the position of the central upper inci-sor, the inclination of the occlusal plane, cant, and yaw. VSP is believed to be less time-consuming (Alkaabi et al., 2022), less expensive, and with lower complication incidence than conven-tional surgery planning, based on 2D cephalometric and patient images, face-bow, articulators, and mounted dental models (Hurst et al., 2007; Kusnoto, 2007; Hsu et al., 2020).

Despite advancements in data integration, the process of seamlessly integrating data from multiple sources remains incomplete. This necessitates the interactive transfer of files between systems, as well as user interactions for superimpositions.

Computer-Aided Manufacturing (CAM)

Subtractive machining (milling)

Milling devices can be categorized based on the number of milling axes they possess, which include: 3-axis devices, 4-axis devices, 5-axis devices.

The 3-axis milling devices have limited movement capabilities along the X, Y, and Z axes. However, milling of complex shapes, such as sections, axis divergences, and convergences, may not be possible without virtual blocking in such areas. In dental applications, all 3-axis devices can also rotate the component by 180° to mill the inside and outside. These devices have the advantages of shorter milling times and simplified control, resulting from the three axes. Consequently, they are usually less expensive than those with more axes. Examples of 3-axis devices in dentistry include inLab (Sirona), Lava (3M ESPE), and Cercon Brain (DeguDent).

A 4-axis milling device adds another rotational axis to the three spatial axes. This allows for the tension bridge of the component to be continuously rotated, allowing for adjustments to be made to fit bridge constructions with large vertical height displacement into typical mold dimensions. This can save time and material during the milling process. One example of a 4-axis milling device is the Zeno, manufactured by Wieland-Imes.

A 5-axis milling device offers the additional capability of rotating the milling spindle (5th axis), in addition to the three spatial dimensions and the rotatable tension bridge (4th axis). Some examples of 5-axis milling devices include the Everest Engine (KaVo) in the laboratory area, and the HSC Milling Device (etkon) in the production center. It is important to note that the quality of the restoration is not solely determined by the number of processing axes, but rather by the accuracy and precision of the digitalization, data processing, and production process.

There are two main types of milling processes: dry and wet. Dry processing is commonly used for zirconium oxide blanks with low pre-sintering levels. This process has advantages such as lower investment costs and no initial drying times for the ZrO2 frame prior to sintering. However, it also has the disadvantage of higher shrinkage values for the frameworks due to the lower pre-sintering level. Some manufacturers offer the option of dry milling resin material as well. Wet milling, on the other hand, is necessary for all metals and glass ceramic materials to avoid damage from heat development. A spray of cool liquid protects the milling diamond or carbide cutter. Wet processing is recommended for zirconium oxide ceramic with a higher degree of pre-sintering, which results in a reduction of shrinkage factor and less sinter distortion. Wet processing milling devices such as Everest (KaVo), Zeno 8060 (Wieland-Imes), and inLab (Sirona) are among the available options.

Additive manufacturing (AM)

Additive manufacturing, also known as 3D printing (3DP), is now an entirely integrated option in CAM hardware, offering a viable alternative to subtractive machining (milling). The solid block is no longer required as the starting point for manufacture. Instead, products are built layer by layer, allowing for geometric complexity.

AM technologies are classified into the following categories: powder bed fusion, material jetting, vat photopolymerization, directed energy deposition, material extrusion, binder jetting, and sheet lamination (Najmon et al., 2019). However, four 3DP technologies are most commonly used in dentistry: stereolithography (SLA), digital light processing (DLP), material jetting (MJ) and material extrusion (MD) (Revilla-León et al., 2017, 2019; Galante et al., 2019).

Depending on the system, materials employed for 3D printing include polymers (vinyl polymer -Polymethyl methacrylate/PMMA, styrene polymers, polyesters), metal-based materials (titanium and its alloys, cobalt-based alloys), ceramics (zirconia, alumina) and smart materials (shape-memory materials and shape-changing materials) (Khorsandi et al., 2021; Rekow, 2018; Galante et al., 2019).

In dentistry, 3D printers that utilize vat polymerization to produce 3D objects utilise different types of light sources for polymerization (International Organization for Standardization, 2015; Methani et al., 2020). Stereolithography (SLA) technology, which uses lasers to polymerize resin, was one of the earliest types of printers utilized in dentistry, even though the term SLA generally refers to 3D printing itself. Meanwhile, digital light processing (DLP) technology is used in some printers, which dramatically reduces printing time (Hornbeck, 2009). Liquid crystal display (LCD) can also serve as a light source, which is less costly and less complex than the other methods (Methani et al., 2020).

Regardless of the type of light source, every 3D printing process begins with slicing the 3D design of an object into different layers digitally. The layers are then individually polymerized by the light source and co-polymerize with the adjacent superimposed layers to form the desired object. Every 3D printer has a distinct set of printing parameters that can be modified and are usually outlined by the manufacturers of 3D resins (Revilla-León et al., 2019).

However, certain parameters can be adjusted in any 3D printer, regardless of its light-curing technology. These parameters include the build orientation of the object, the object's location on the platform, and the thickness of the printed layer. The build orientation is commonly altered to minimize printing time (Rubayo et al., 2021) or allow for improved resin flow or better object distribution within the printer platform.

Although some studies have confirmed that the build orientation can impact the accuracy of an object (Rubayo et al., 2021; Osman et al., 2017; Derban et al., 2021; Park et al., 2019; Ryu et al., 2020; Yu et al., 2021; McCarty et al., 2020; Shim et al., 2020) and the mechanical properties of some resins (Shim et al., 2020; Derban et al., 2021; Keβler et al., 2021), its influence on the 3D printing of dental provisional resins (3DRs) is not fully explored (Osman et al., 2017; Park et al., 2019; Ryu et al., 2020; Yu et al., 2021; Derban et al., 2021; Keβler et al., 2021), particularly in 3D printers that use different light source technologies, such as LCD SLA and DLP.

Additive manufacturing has found a wide range of applications in the field of dentistry. Some of the major applications include the fabrication of dental crowns, bridges, dentures, dental implants, aligners and orthodontic brackets, surgical guides and templates, dental replica models, bites (Makvandi et al., 2018), mouth guards, and oral drug delivery devices (Liang et al., 2018). Additionally, additive manufacturing technology has also been utilized for research and development as well as education and training purposes in the dental industry (Javaida, Haleemb, 2019; Jawahar, Maragathavalli, 2019).

Among other studies, 3DP interim crowns fit better (Bae et al., 2017; Eftekhar et al., 2018), drill guides are accurate to within 0.25 of expected implants (Neumeister et al., 2017), and occlusal splints have comparable polished surfaces and wear (Huettig et al., 2017). The trueness of the outer surface, intaglio surface, marginal area, and intaglio occlusal surface of 3D zirconia printed crowns was determined to be" no worse than matching milled crowns" (Wang et al., 2019). Custom-made templates and craniofacial prosthesis outperform standard techniques in terms of aesthetics and fit (Thakur et al., 2019).

The main focus of research in this area has been on digital technologies used in dental laboratories for fabricating dental models, provisional and definitive fixed prostheses, removable partial dentures, and complete dentures. This research aims to improve the accuracy and efficiency of the fabrication process, while also improving patient outcomes. Furthermore, a case report has been presented to demonstrate a fully digitized workflow that uses a combination of three digital software tools to correct predicted post-upward sliding genioplasty defects.

	The following are the most significant personal scientific contributions in this field
Published articles in ISI journals	1*. Onică N, Onică CA, **Tatarciuc M**, Baciu E-R, Vlasie G-L, Ciofu M, Balan M, Gelețu GL. Managing Predicted Post-Orthognathic Surgical Defects Using Combined Digital Software: A Case Report. Healthcare. **2023**; 11(9): art. no 1219. IF=3.160 2*. Elena-Raluca Baciu, Carmen Nicoleta Savin, **Monica Tatarciuc**, Ioana Mârtu, Oana Maria Butnaru, Andra Elena Aungurencei, Andrei-Marius Mihalache, Diana Diaconu-Popa. Experimental Study on Mechanical Properties of Different Resins Used in Oral Environments, Medicina 2023, 59, 1042. https://doi.org/10.3390/medicina5906104 2*. Baciu ER, Budala DG, Vasluianu RI, Lupu CI, Murariu A, Geletu GL, Zetu IN, Diaconu-Popa D, **Tatarciuc M**, Nichitean G, Luchian I. A Comparative Analysis of Dental Measurements in Physical and

	Digital Orthodontic Case Study Models, Med Lith, **2022**, 58(9): art. no 1230. IF=2.948 3*. Martu I, Murariu A, Baciu ER, Savin CN, Foia I, **Tatarciuc M**, Diaconu-Popa D. An Interdisciplinary Study Regarding the Characteristics of Dental Resins Used for Temporary Bridges, Med Lith, **2022**, 58(6): art. no 811. IF=2.948 4*.Ioana Mârtu, Alice Murariu, Elena Raluca Baciu, Carmen Nicoleta Savin, Iolanda Foia, Monica Tatarciuc, Diana Diaconu-Popa. An Interdisciplinary Study regarding the Characteristics of Dental Resins Used for Temporary Bridges, Medicina 2022, 58, 811. https://doi.org/10.3390/medicina58060811 5*.Monica Tatarciuc, George Alexandru Maftei, Anca Vitalariu , Ionut Luchian, Ioana Martu, Diana Diaconu-Popa -Inlay-Retained Dental Bridges—A Finite Element Analysis, Appl. Sci. 2021, 11, 3770, 1-17, https://doi.org/10.3390/app11093770
Published articles in BDI journals	1. Diaconu-Popa D, **Tatarciuc M**, Vitalariu A. Digital technology for removable partial denture realization. case report, Med-Surg J, **2021**, 125(1): 170-174 (ESCI-WSCC) 2. Diaconu-Popa D, Vitalariu A, Martu I, Luchian I, Luca O, **Tatarciuc M**. Full dentures realization -conventional vs digital technologies, Rom J Oral Rehabil, **2021**, 13(4): 160-173 (ESCI-WSCC) 3. **Tatarciuc M**, Luchian I, Vitalariu A, Martu I, Diaconu-Popa D. Study regarding the technologies for complete dentures realization, Rom J Oral Rehabil, **2021**, 13(3): 200-211 (ESCI-WSCC) 4. **Tatarciuc M**, Vitalariu A, Diaconu-Popa D. Digital technologies in dental laboratory, Rom J Oral Rehabil, **2021**, 13(2): 122-131 (ESCI-WSCC) 5. Diaconu-Popa D, **Tatarciuc M**, Vitalariu A, Pacuraru I, Luca O. Direct digital technology for ceramic dental bridge realization, Rom J Oral Rehabil, **2021**, 13(2): 218-222 (ESCI-WSCC) 6. Diaconu-Popa D, Vitalariu A, Matei D, Matei A, Tatarciuc M. Digital technologies in fixed prostheses, Rom J Med Dent Educ, **2021**, 10(1): 113-122 (DOAJ) 7. Diaconu-Popa D, Vitalariu A, **Tatarciuc M**. Digital technologies for complete dentures realization, Rom J Med Dent Educ, **2020**, 9(3): 43-49 (DOAJ) 8. **Tatarciuc M**, Diaconu-Popa D, Vitalariu A. Digital dentistry, Med-Surg J, **2019**, 123(4): 735-738 (ESCI-WSCC) 9. Diaconu-Popa D, Tatarciuc M, Vitalariu A. Esthetic rehabilitation through cad/cam technology - case report, Rev Med Chir Soc Med Nat Iasi, **2016**, 120(3): 711-714 (Pubmed, ESCI-WSCC)

**Publications described in detail in the next subchapters*

1.1.2. Fixed prostheses- An Interdisciplinary Study Regarding the Characteristics of Dental Resins Used for Temporary Bridges

Aim of the study

The attention was focused on the analysis of surfaces roughness, before and after finishing and polishing, and the mechanical strength of polymethyl methacrylate materials (used for temporary bridges), following whether there is a significant difference between the devices obtained by conventional technology, which uses heat curing resins and the samples obtained by subtractive and additive digital technologies.

The null hypothesis in the statistical analysis was that there is no difference between the characteristics of the samples obtained by the three types of technologies.

Materials and Methods

In order to analyze the characteristics of temporary prostheses materials, we realized 60 samples, 30 for the tensile tests and 30 the surface roughness analysis (figure 1).

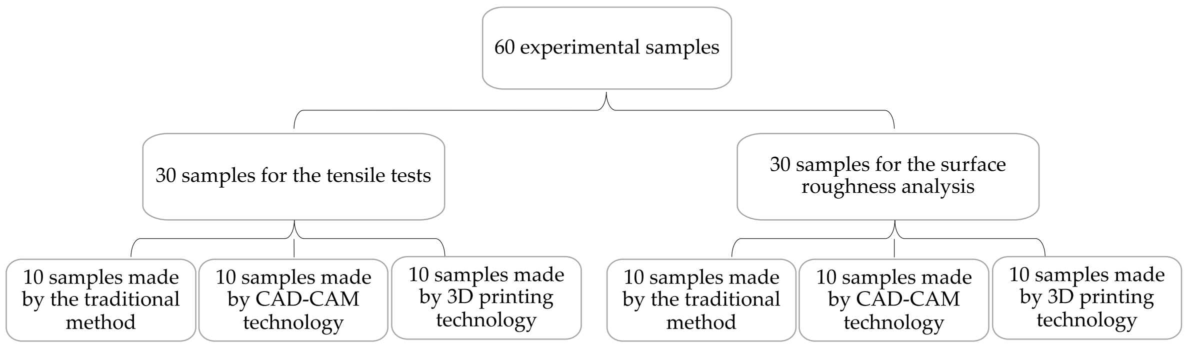


Figure 1. Experimental samples

20 samples were made by the traditional method, using the heat-curing acrylic resin Superpont C+B (SpofaDental, Jicin, Czech Republic), 20 were performed by subtractive CAD/CAM technology, using Zotion dental milling PMMA block (Zotion, Chongqing, China) and 20 by additive digital technology, using Freeprint Temp (Detax GmbH & Co. KG, Ettlingen, Germany) resin.

The first step was to make two different shapes of wax pattern: for the traction tests measures 2 mm thickness dumbbell-shaped wax patterns, having the following dimensions: 75 mm length, 12.5 mm width, at the extremities and 4 mm in the central area; for the roughness tests, the wax patterns were rectangular shape, also 2 mm thick, 70 mm length and 30 mm width. The dimensions chosen were in accordance with ASTM D-638 (and ISO 527-2 standards) and are adapted to the requirements of the device used in the analysis of mechanical characteristics.

For the analysis of the surface condition, the sample sizes were also chosen according to the standards imposed by the roughness tester used.

For conventional resin samples the wax patterns, made of pink wax, 2 mm thick (DistriWax-DinstridentPlus, Suceava, Romania) were transformed into acrylic specimens according to the same technology used for temporary acrylic dental bridges. They were first invested in dental stone (Elite Rock class IV gypsum-Zhermack, Badia Polesine, Italy) in order to obtain a mold (figure 2).

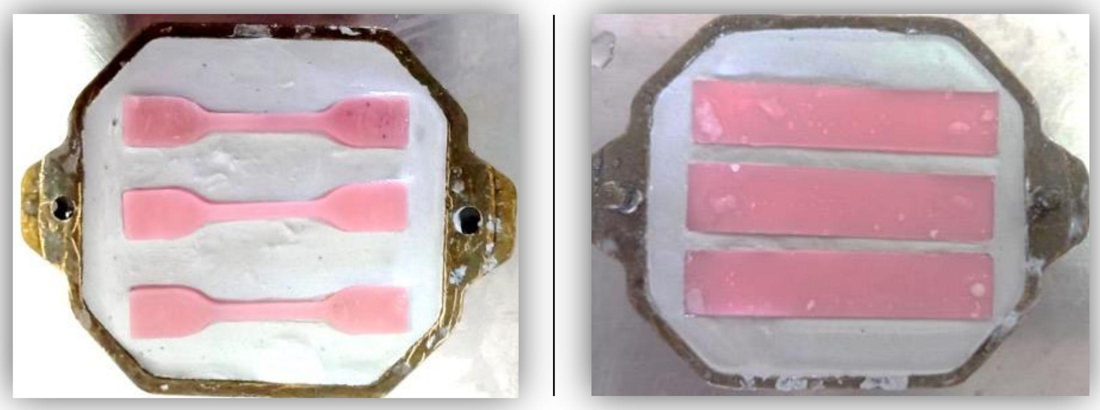


Figure 2. Investing wax pattern and mold realization

After the mold isolation with a separating agent (Isodent/ SpofaDental, Jicin, Czech Republic), the acrylic resin was prepared, following the producer's indications: mix 2 g of powder with 1 gram of liquid (or in units of volume 3 parts powder to 1 part liquid), the mixing time being 1.5 minutes.

When the resin has a plastic consistency, it is introduced into the mold, and pressed with the help of the hydraulic press. The curing process is performed in a thermo-polymerization chamber, at a temperature of 100°C, pressure 2-4 bar, for 40 minutes (Tatarciuc, Panaite, 2001; Zafar, 2020). The technological steps are identical to those of the algorithm for making interim bridges from heat cured resin in dental laboratories.

After cooling, the samples were removed from the mold (figure 3), verified and sandblasted.

Figure 3. Divesting resin samples

Digital samples were realized in a private practice dental laboratory (Draghici Dental, Iasi, Romania). For the subtractive method, the dental milling machine with 5 Axes VHF K5 Plus (VHF, Ammerbuch, Germany) was used; the wax pattern was initially scanned (Swing DOF Scanner, DOF Inc., Seoul, South Korea) in order to obtain their virtual image using the scanning and modeling EXOCAD system (Darmstadt, Germania) (figure 4).

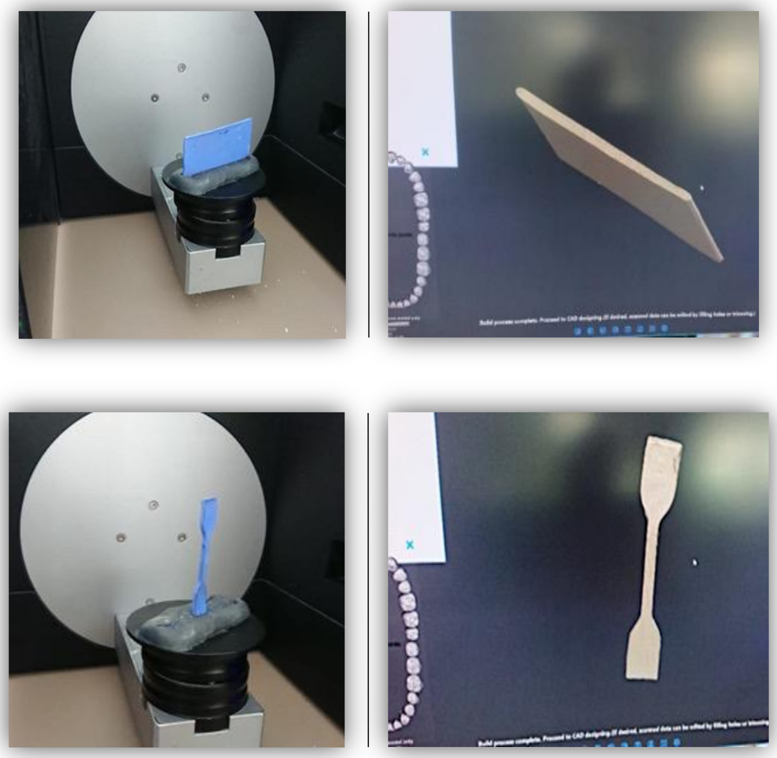


Figure 4. Wax patterns scanning

A large disk of PMMA A1 monochrome acrylic resin was chosen, with a diameter of 98 mm and a thickness of 20 mm, used for temporary long-term crowns or bridges. The disk was fixed on the plate of the milling machine and based on the information transmitted by the CAD unit, the two types of samples were performed (figure 5). Then the samples were finished and polished.

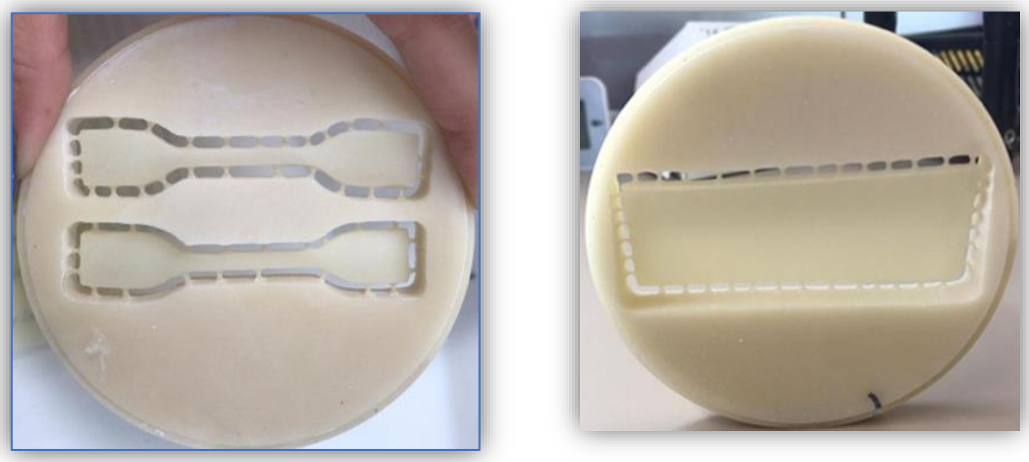


Figure 5. CAD/CAM samples

For the additive technology, data on the shape and size of the wax patterns were acquired using the same scanning system and then the information were transmitted to the Asiga MAX 3D printer (Asiga, Alexandria NSW, Australia) (figure 6).

Figure 6. 3D Printing samples

The printed samples were removed from the build platform, and it was used a hand-piece with a cutting disk, to separate the supports and the raft from printed parts; the devices were washed with Isopropyl Alcohol (IPA≥99%)) and dry with the steamer.

The final step was the post-polimerization using Asiga Flash Post Curing Unit (Asiga, Alexandria NSW, Australia), performing a light curing process, for 20 minutes.

All the samples were processed on one surface, according to the same protocol for finishing and polishing temporary bridges, using Acrylic Contouring & Finishing Kit HP (Shofu Dental GmbH, Ratingen, Germany). The surfaces was first adjusted with dark gray AcryPoint Coarse Grit BP1 tooll, mounted in a hand-piece at low speed (10,000 rpm), followed by finishing with brown AcryPoint Medium Grit BP1 (10,000 rpm); for polishing it was used fine AcryPoints (light grey) tool (5,000rpm) and soft Circular Goat Hair Brush (90 mm diameter) at a maximum speed of 4,000 rpm, and for the final gloss we used Buffing Wheel and Universal polishing paste (Ivoclar Vivadent AG, Schaan, Liechtenstein) (4,000rpm).

The mechanical tests were performed in collaboration with Gheorghe Asachi Technical University of Iaşi, Faculty of Materials Science and Engineering. Tensile tests were carried out at room temperature, according to the ISO 527-1: 2000 standard, using a computer-controlled testing machine, with a dynamic clip-on strain gauge extensometer Dynamic Extensometer Instron 2716-002 (Instron, Norwood, United States) for direct strain measurement. The rectangular specimens were placed and fixed between the grips of the testing machine (figure 7).

Figure 7. Samples and Instron testing machine.

The tensile load was applied at a crosshead speed of 1 mm/min (Atash et al., 2015). Young's modulus (the slope of a secant line between 0.05% and 0.25% strain on a stress-strain plot), tensile yield (tensile stress at yield) and tensile strength (maximum tensile stress during the test) were determined.

To determine the surface roughness, the R_a, R_z and R_q parameters were recorded for each sample. R_a represents the arithmetical mean of the absolute values of the profile deviations from the mean line of the roughness, R_z is the average of all values represented by the maximum height between the maximum and the minimum profile within the assessment length, for each sample and R_q represent the root mean square of the surface roughness.

Three roughness measurements were made on the surface of each sample and the data was recorded with Form Talysurf roughness tester (Taylor Hobson, Leicester, England), whose peak radius of the cantilever is r = 2 µm (figure 8).

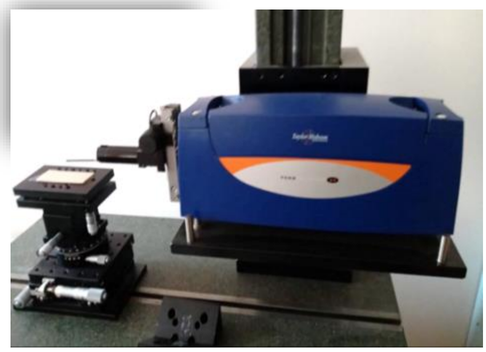


Figure 8. Roughness registration.

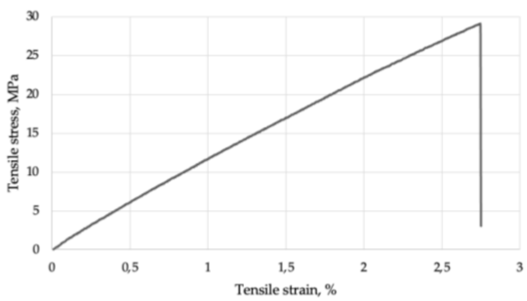
The roughness of the test surfaces was investigated on unfinished and unpolished surface and on the finished and polished, surface according to the protocol to see if the same processing technique, for all samples, generates significant differences in surface characteristics.

The statistical analyses were employed using Stata 16.1 software (StataCorp, Texas, United States). The two-way ANOVA analysis for the two paired samples, before and after the finishing and polishing procedures.

Results

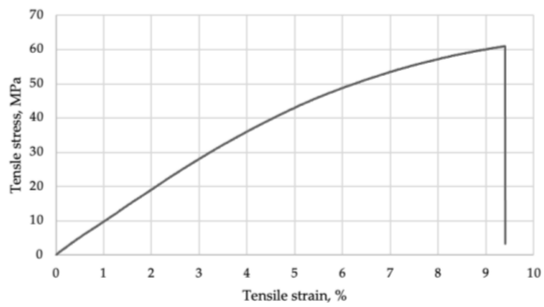
Tensile stress and tensile strain were calculated for the three categories of samples and the diagrams (figure 9.a-c) illustrate that the best resistance to fracture load has been registered for milled samples, followed by the heat –cured samples; the lowest values of mechanical resistance was found for the 3D printed specimens. The tensile behavior of the materials is similar, observing a reversible stage of elastic deformation, followed by an irreversible plastic deformation, up to the maximum limit, when material fracture occurs.

a)

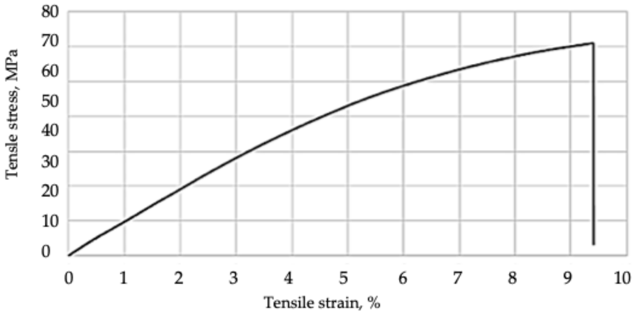


F_{max}, N	E, Mpa	$R_{p0.2}$, Mpa	R_m, MPa	Au, %
310.84	1239.31	27.93	28.83	2.76

b)



F_{max}, N	E, Mpa	$R_{p0.2}$, Mpa	R_m, MPa	Au, %
630.14	1035.17	35.34	60.98	9.38



F_{max}, N	E, Mpa	$R_{p0.2}$, Mpa	R_m, MPa	Au, %
520.14	987.17	35.34	40.93	6.37

c)

Figure 9. Tensile tests vs tensile strain diagrams: a) Milled samples; b) 3D printed samples; c) Cured samples.

In our study, following the statistical analysis of the results it can be seen that statistically speaking there are no significant differences between the values of mechanical strength parameters (figure 10). So, temporary bridges made by digital methods are not significantly different, in terms of fracture strength, of those performed by conventional methods.

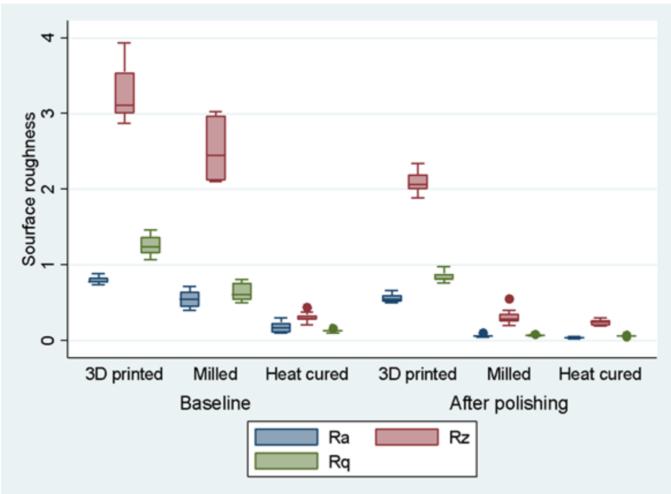


Figure 10. Box plot of surface roughness by resin, before/after polishing

Notes: The distribution of rugosity coefficients for each of the three raisins (different colors), both before (baseline) and after polishing are displayed on the Y axis. Three measurements for surface rugosity were used: R_a - arithmetical mean of the absolute values of the profile deviations from the mean line of the roughness; R_z - average of all values represented by the maximum height be-tween the maximum and the minimum profile within the assessment length; R_q - the root mean square of the surface roughness.

Roughness is an important characteristic of surface quality and can be assessed by determining the micrometric profile of the finished and polished samples.

Surface roughness is quantified by the deviations in the direction of the normal vector of a real surface from its ideal form. If these deviations are large, the surface is rough and if they are small, the surface is smooth. In surface metrology, roughness is typically considered to be the high-frequency, short-wavelength component of a measured surface. However, in practice it is often necessary to know both the amplitude and frequency to ensure that a surface is fit for a purpose.

The shape and dimensions of the micrometric profile have an influence on the adherence and development of the bacterial biofilm at the surfaces of the acrylic prostheses.

The values recorded for the surface roughness analysis were centralized, to compare the data and establish statistically significant differences. Figure 10 displays an overview on our samples by the three materials used (different colors), before and after polishing procedures. Each sample distribution is reflected by a plot with the following landmarks: the upper and the bottom of the box indicate the values marking the first and third quartiles (Q1 and Q3); the median of the sample is represented by the horizontal line; the whiskers display the minimum and maximum values of the sample. First, it is interesting to observe that polishing procedures seems to induce a decrease of coefficients for all the three resins. Secondly, the output in figure 10 suggests that the 3D printed sample displays, on average, the highest coefficients, being followed by the milled and heat-cured ones. The same ranking also applies after polishing. Finally, the highest variation of coefficients is captured when the R_z measure is used.

To materialize even more eloquently the differences of the parameters that characterize the surface condition of the three categories of materials, a two way-ANOVA analysis was carried out. In order to check the robustness of our results, the analysis was performed for each of the three rugosity measurements. The normality of data for each sample by treatment, material used, and rugosity measure was initially tested in order to make sure series are normally distributed. Finally, post hoc multiple comparisons were performed using Tukey's test.

Table I summarizes the results of the two-way ANOVA analysis that was employed on a sample of 30 observations, 10 for each of the materials used. The results revealed that surface roughness was significantly influenced by both the type of resin used ($p<0.001$) and the treatment induced by finishing and polishing ($p<0.001$). Similar p-values were obtained for each of the three resins.

Table I. Means (±SEM) of surface roughness parameters by resin used, before and after polishing

Surface roughness	3D printed			Milled			Heat cured		
	Baseline	After polishing	ΔR%	Baseline	After polishing	ΔR%	Baseline	After polishing	ΔR%
R_a	0.80(0.02)^a	0.56(0.02)^b	-15.10	0.55(0.04)^b	0.06(0.00)^d	-44.61	0.17(0.02)^c	0.04(0.00)^d	-38.78
R_z	3.26(0.12)^a	2.08(0.04)^c	-18.07	2.51(0.13)^b	0.32(0.03)^d	-43.73	0.31(0.02)^d	0.24(0.01)^d	-10.28
R_q	1.26(0.04)^a	0.86(0.02)^b	-15.75	0.64(0.04)^c	0.07(0.00)^d	-44.60	0.13(0.00)^d	0.06(0.00)^d	-26.51

Note: n = 10 obs. per sample $^{a-d}$ Means in a row without a common superscript letter are different ($p < 0.05$) as evidenced by two-way ANOVA and the Tukey's test. R_a: arithmetical mean of the absolute values of the profile deviations from the mean line of the roughness; R_z: average of all values represented by the maximum height between the maximum and the minimum profile within the assessment length; R_q: the root mean square of the surface roughness.

It is important to note that there was also a significant interaction between the type of resin used and the polishing treatment on coefficients assessing the surface roughness (R_a: F(df 2, 54) = 41.46, $p<0.001$; R_z: F(df 2, 54) = 97.32, $p<0.001$ R_q: F(df 2, 54) = 55.82, $p<0.001$).

Discussion

The mechanical characteristics of the materials that are used for prosthetic constructions are influenced by the technological steps. The conventional method described in our study, which uses heat-curing resins, involves a large number of laboratory steps, which leads to a longer working time, a longer number of treatment sessions, but also an increased risk of technological errors. On the other hand, this method allows greater control over the morphology and marginal adaptation of the temporary bridges.

Previous clinical studies have yielded conflicting results regarding the effects of fixed interim restorations on periodontal tissues (Skorulska et al., 2021; Lambert et al., 2017; Al Jabbari et al., 2013). However, the conventional wisdom is that fixed interim restorations featuring adequate marginal adaptation and proper finishing and polishing do not induce gingival inflammation, and this was supported by the present results (Jabbari et al., 2013).

Digital technologies substantially reduce the workflow, which is a great advantage for both the dental team and the patient. Several studies show that polymers used in digital technologies exhibit optimal mechanical parameters than conventional PMMA interim resin material, therefore, these resins are indicated for long-term temporary bridges. The resins for digital technologies are fabricated under controlled industrial conditions and presenting improved mechanical properties, reduced residual monomers, and, due to the milling fabrication, they show no heat of reaction (Regish et al., 2011; Fasbinder, 2011; Tatarciuc et al., 2021).

Digholkar et al. (2016) compared samples from conventional resins and samples obtained by milling and printing methods. The authors concluded that milled samples had the highest flexural strength and 3D printed samples had the highest microhardness.

The study of Pascutti et al. (2017) emphasize that temporary bridges obtained by CAD/CAM methods provided the highest flexural strength values being followed by the heat-curing acrylic resin, that in turn was significantly superior to cold curing resins.

Çakmak et al. (2020) found that the flexural strength of CAD/CAM PMMA-based polymers was higher than the flexural strength of conventional resin.

Pantea et al. (2022) observed that the additive manufactured samples exhibited higher elastic moduli (2.4 ± 0.02 GPa and 2.6 ± 0.18 GPa) than the conventional samples (1.3 ± 0.19 GPa and 1.3 ± 0.38 GPa), as well as a higher average bending strength (141 ± 17 MPa and 143 ± 15 MPa) when compared to the conventional samples (88 ± 10 MPa and 76 ± 7 MPa); the results also suggested that the materials were more homogenous when produced via additive manufacturing.

Rayyan et al. (2015) showed that that CAD/CAM interim crowns presented stable physical and mechanical properties and may be used for long-term interim restorations.

On the other hand, despite their many benefits, computer technologies are still the most expensive way to make interim crowns and bridges, according to Güth et al. (2012).

The results of this study reveal that there are no significant differences between the mechanical characteristics of heat-curing resin samples and those obtained by subtractive and additive digital methods.

Other authors reported small differences in fracture force, wear, and roughness between conventional and digital materials for temporary bridges. In vivo and in vitro aging led to comparable results in SEM evaluation. No significant differences in fracture force and wear but differences in roughness, heat of reaction, and thermal weight loss were found in extensive analyses, including simulation of aging processes and mechanical stability (Sari et al., 2020).

Of course, the strength of temporary bridges is an important quality but not essential for these prosthetic constructions. In contrast, surface characteristics have a much greater impact on the longevity of these prostheses.

Surface roughness enhances plaque retention, promoting bacterial colonization, especially at the restorative margins, resulting in periodontal inflammation and infection. These drastic changes contribute to pulpal sensitivity, gingival recession, tissue inflammation and complicate the challenge of restorative rehabilitation (Abdullah et al., 2018; Abdulmohsen et al., 2016; Hahnel et al., 2019). Thus, to all these side effects, which would compromise the final therapeutic solution and preserve the periodontal restorative interface, an optimal quality of the interim restoration is desired.

The surface roughness of a restoration alters under the influence of multiple factors, which include the fabrication technique, oral conditions, opposite dentition load, diet, material composition, and polishing techniques (Digholkar et al., 2016; Alp et al., 2018; Beuer et al., 2008). In the present study, the surface roughness was assessed according to the fabrication technique CAD/CAM subtractive method, 3D printing, and the conventional technique. The highest surface roughness was observed in 3D printing, with a similar outcome to the CAD/CAM milling technique. Nevertheless, the lowest roughness value was observed using the conventional samples. This indicates that conventional heat-cured materials can be successfully used in the long-term temporary restoration.

Roughness, especially in the subgingival area, is considered the major cause of plaque buildup and the subsequent inflammatory response. Several sources of the roughness have been described: strips and scratches on the surface of carefully polished acrylic resin, separation of the cervical crown margin, and the cervical margin of the finishing line by the luting material exposing the rough surface of the prepared tooth, dissolution and disintegration of the luting material causing crater formation between the preparation and the restoration and inadequate marginal fit of the restoration (Sari et al., 2020).

The undersurface of pontics in fixed bridges should barely touch the mucosa and plaque formation determines gingival inflammation and even pseudo pocket formation. The preservation of periodontal health around the crown's margins is a serious challenge for a dentist and detecting the restoration margin relative to the neighboring bone is a significant factor when providing for the long-lasting health of the gingival tissues (Alt et al., 2019; Riccitiello et al. 2018).

The final finishing of the prosthetic restoration affects the development of the microbial biofilm, as increased surface roughness creates a favorable environment for bacterial growth. So, a prosthetic surface finish from proper manufacturing technique is important (Rayyan et al., 2015; Perea-Lowery et al., 2020; Karaokutan et al., 2015). Most comparative studies have been performed on self-curing resins and resins used in digital technologies; indeed, these resins, used in the conventional technology, may undergo polymerization contractions, and may have a rougher surface; but heat-cured resins, used in our study, allow strict control over each stage, so these drawbacks can be removed. Additionally, further studies are needed in order to test also other materials used for provisional prostheses, such as nanofilled composites (Montero et al., 2021), and fiber reinforced materials (Scribante et al., 2018).

However, under the conditions of correct preparation of the resin and strict observance of all stages of the polymerization reaction, there is no risk of volumetric changes, and the mechanical parameters have optimal values.

Our results confirm that there is a statistically significant difference in terms of surface condition between the baseline values and the values after polishing ($p<0.001$). The statistically significant difference was confirmed for each of the three resins, with similar p-values.

This is in line with the results suggested by the descriptive statistics, which revealed a sizeable downward trend. The same result holds true for all the three resins investigated in our study. On needs to mention that, for the heat cured sample, the difference is only statistically significant when looking at the R_a coefficients, but not for the other two measurements. The sharpest reduction is displayed by the milled raisin which displayed average reductions of more than 44% for each of the three measurements investigated. It is also interesting to add that the highest coefficients values are shown, on average, in the 3D printed samples. The means for this material was also confirmed to be statistically different from the means displayed by the other two resins used. The same results hold true after the polishing process. At the other end lies the heat-cured samples which reports the lowest averages.

It was shown that CAD/CAM temporary restorations have superior mechanical properties and superior surface quality, compared with their conventional counterparts (Aldahian et al., 2021; Sadighpour et al., 2021; Rosentritt et al., 2020; Ibrahim et al., 2020), as evidenced by our study.

The temporary prosthesis should not be considered as a useless stage with uncertain indications but as a way of transition from disability to functionality. Materials and methods which were used to make interim bridges are of a major importance for achieving this type of prosthesis.

The direct technique in the dental office is an alternative which is used in practice for temporary bridge fabrication. In this technique, the patient undergoes interim prosthesis in the same stage as the abutment preparation, which is an advantage because intermediate laboratory procedures are eliminated. However, the direct technique has significant disadvantages such as poorer marginal fit, pulpal damage due to the temperature released by the resin polymerization reaction, lower mechanical strength, and and inaccurate dental morphological rehabilitation.

Therefore, the routine use of directly formed interim restoration is not recommended when indirect techniques (conventional or digital) are feasible (Regish et al., 2011; Ozcelik et al., 2008).

One of the study's limitations includes a limited number of materials and mechanical tests investigated. However, we believe it is essential to examine these three types of resins, which are commonly used in dental laboratories. Further research is needed on over a wider range of materials and possibly extending it with other methods of analysis that more accurately reflect the mechanical parameters.

The fact that the printed samples were obtained exclusively through digital light processing is another limitation. Future studies should focus on the behaviour of samples made with stereolithography (SLA) and material jetting (Polyjet).

Conclusions

Within the limitations of this study, we can conclude that temporary bridges made using the subtractive technology can allow obtaining resistant devices with low roughness structure. At the same time, we can, ensure an optimal restoration of the teeth morphology and a correct functional rehabilitation.

Therefore, these methods can be used to make long-term interim prosthodontics restorations.

In this stage of the research, we focused on the analysis of some frequently used resins in the dental laboratory for temporary bridges realization. In order to obtain even more relevant results, the study will be continued, taking into account other resins used for these prosthetic constructions.

In the current era, conventional methods, using heat-curing resins are still a viable alternative and these materials can be successfully used for short-term temporary prosthetic restorations.

1.1.3. Orthodontics - Comparative Analysis of Dental Measurements in Physical and Digital Orthodontic Case Study Models

Aim of the study

The purpose of the present study was to compare the values obtained by traditional and digital orthodontic measurements on physical and digital case study models.

In order to achieve the proposed objective, we formulated two null hypotheses:

- The linear measurement values are not influenced by the method, the material, or the obtainment technique used in the case study models.

- The lack of space is undisturbed by the obtained values using various measurement techniques and dental study models.

Materials and Methods

Patient selection and impression recording

The study protocol (figure 11) was approved by the Ethics Committee of “Grigore T. Popa” University of Medicine and Pharmacy of Iasi (No. 196/03.06.2022), and the included participants consented to the procedures.

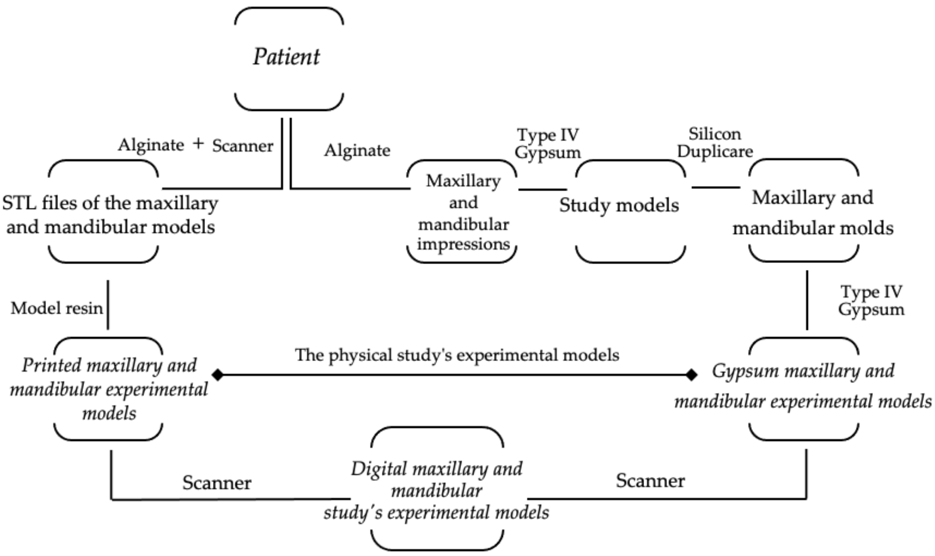


Figure 11. The study protocol's design: from patient to digital case study models.

To perform the experimental models, alginate maxillary and mandibular impressions were taken from patients.

Patients had to meet the following criteria in order to be included in the study: over 18 years of age; cooperative; no general diseases; no previous experience of anaphylactic reactions; completely erupted permanent dentition from the first molar; no interproximal caries or fillings, prosthetic crowns, or bridges; no teeth anomalies, edentation, orthopedic, or orthodontic treatments in their history; diagnosed with Class I malocclusion.

The impressions were registered at the Faculty of Dentistry, Iasi, Romania. To achieve this stage, medium-sized plastic–steel impression trays (Guangzhou Aurora Health Products Company, Hunan, China), perforated for a better retention of the impression material, together with Orthoprint (Zhermack SpA, Badia Polesine, Italy) alginate material, were used. After the appropriate amount of powder with water was measured out and prepared in accordance with the manufacturer's recommendations, the final impressions were transported to the dental laboratory, in a 100%-humidity medium, within 30 minutes, and then poured (Wadhwa et al., 2013).

The methods of producing the case study models.

The physical models

Traditional pouring and additive manufacturing/digital light processing were used to create 4 sets of experimental models. Each set (using same material and method) included 4 study models—2 maxillary and 2 mandibular; therefore, a total of 16 models were obtained (figure 12).

Figure 12. Experimental case study models**.**

Dental stone models

Silicon Duplicate Elite Double 22 (Zhermack SpA, Badia Polesine, Italy) was used to duplicate the models. When using Type IV gypsum powder, the manufacturer's recommended dosage of water was followed. For 30 seconds, the gypsum paste was molded under vacuum to produce a homogenous paste with a semi-fluid consistency, free of air inclusions, after it had been spatulated. The gypsum material was gradually poured in the mold placed on the vibration table. After 60 minutes, the models were removed from the molds and stored for 48 hours, at room temperature (Millstein, 1992). All models were poured by the same dental technician.

Three-dimensionally printed models

The scanned images (Swing DOF Scanner- DOF, Seoul, Korea) of the recorded impressions were automatically converted to standard tessellation language (STL) format by the dedicated scanner software. The files were then imported using the AsigaComposer software (ASIGA, Alexandria, NSW, Australia) to be manufactured on a digital light processing printer, 3D MAX UV Asiga (ASIGA, Alexandria, NSW, Australia).

The following settings were used:

- Support scripts: contact with the model—0.5 mm; height leveling—2 mm; support spacing—2 mm; material strength—40x; torsion tolerance—0.
- Thickness layer—0.05 mm.
-" Fast print" mode with separation detection and anti-aliasing.

At each printing cycle, two models in a series were printed in a horizontal position (figure 13). Each cycle lasted for approximately one hour. The printed models were stored for 24 hours at room temperature (Joda et al., 2020).

Figure 13. The 3D-printed models: from STL files to printed models**.**

The digital models

The digital models were created by scanning the physical ones, using a white light LED source and an L-shaped dental scanner—Swing DOF (DOF, Seoul, Korea). The data were saved in an .STL-format file.

Dental measurement

We evaluated the reproducibility of dental arch characteristics, such as mesiodistal widths of incisors, canines, premolars, and first molars, as well as interpremolar and molar widths, using manual and digital linear measurements as follows:

-The upper arch interpremolar width was measured between central grooves on the occlusal surface of the first premolars;

-The superior intermolar distance was measured between mesial pits on the occlusal surface of first molars;

-The distance between contact points of the lower premolars was assessed for the lower premolar diameter;

-The distance between the tips of the distobuccal cusps of the first lower molar was used as the point of measurement for the lower molar diameter (Rykman, Smailiene, 2015; Domenyuk et al., 2016; Bolton, 1962).

Traditional dental measurement

The measurements were taken with a portable digital caliper Gedore No. 711 (GEDORE Austria GmbH, Österreich, Austria) with 0.01 mm accuracy, which was previously calibrated. Each measurement was performed twice, at one-day intervals, by the same operator. The operator was instructed to measure a maximum of 8 dental study models in a single day so that fatigue-related to errors may be reduced. The procedure was repeated in order to include all of the models, and a Microsoft Excel spreadsheet was used to record the results of the measurements that were taken in millimeters. A total of 448 manual measurements were performed.

Modern dental measurement

The digital measurements made on the scanned experimental dental models followed the same guidelines. The digital models were analyzed using DentalCAD 3.0 Galway (exocad GmbH, Darmstadt, Germany). The three-dimensional images were rotated and enlarged on screen to facilitate measurements (figure 14).

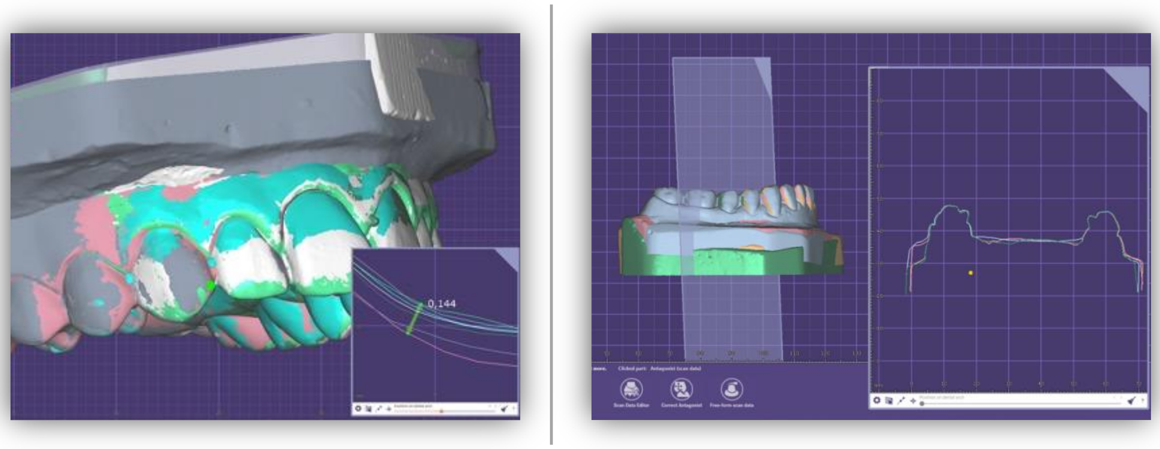


Figure 14. DentalCAD 3.0 Galway (exocad GmbH, Darmstadt, Germany) measurements on the digital study models**.**

A total of 14 measurements were made on each dental digital model by the same operator.

Orthodontic model analysis

Using these measured values for the orthodontic model analysis, the Pont and Linder–Harth indices, Bolton's anterior, and the overall ratio were calculated (table II).

Table II. The formulas used to calculate the development of the arches (Rykman, Smailiene, 2015; Domenyuk et al., 2016; Bolton, 1962).

Methods	Equations
Pont Index	SI = sum of mesio-distal width of the maxillary incisors
	Interpremolar arch widths $= \frac{\text{sum of the widths of the maxillary incisors} \times 100}{80}$
	Intermolar arch widths $= \frac{\text{sum of the widths of the maxillary incisors} \times 100}{64}$
Linder–Harth Index	Interpremolar arch widths $= \frac{\text{sum of the widths of the maxillary incisors} \times 100}{85}$
	Intermolar arch widths $= \frac{\text{sum of the widths of the maxillary incisors} \times 100}{65}$
Bolton's analysis	Anterior ratio $= \frac{\text{sum of the widths of the 6 mandibular anterior teeth}}{\text{sum of the widths of the 6 maxillary anterior teeth}} \times 100$
	Overall ratio $= \frac{\text{sum of the widths of the 12 mandibular teeth}}{\text{sum of the widths of the 12 maxillary teeth}} \times 100$

Statistical analysis

Statistical analysis was performed using SPSS, version 20 (SPSS Inc., Chicago, IL, USA). The obtained data were subjected to multiple Mann–Whitney U tests for pairwise comparisons among groups represented by manual and digital measurements on physical and digital models. The statistical analysis was conducted at a significance level of $p<0.05$.

Results

Evaluation of the first hypothesis

The following data were compared in order to test the first study hypothesis:

- The average values obtained by manual measurements of the mesiodistal widths of the incisors, canines, premolars, and first permanent molars, as well as the interpremolar and molar widths at the level of the traditionally models (type IV gypsum) versus 3D-printed models (resins).
- The average values acquired by digital measurements of the mesiodistal widths of the incisors, canines, premolars, and first permanent molars, as well as the interpremolar and molar widths at the level of scanned models: type IV gypsum digital model versus resin (3D printing) digital model.
- The average values produced by manual measures as opposed to digital measurements of the mesiodistal widths of the incisors, canines, premolars, and first permanent molars, as well as the interpremolar and molar widths at the level of the traditional models (type IV gypsum).
- The average values obtained by manual measurements, as opposed to digital measurements, of the mesiodistal widths of the incisors, canines, premolars, and first permanent molars, as well as of the interpremolar and molar widths at the level of the additive processing models (resins).

The findings from the statistical analysis for the maxillary and mandibular arches are shown in Tables III and IV.

Table III. Maxillary pairwise comparison of the 14 studied diameters using the Mann–Whitney U test.

Pairwise Comparison		Mean Rank	*p*-Value[a]
Type IV Gypsum versus Resin DigitalCalliper	S1.1+ S1.3+ S2.1+ S2.3 DigitalCalliper	28.45	*.980*
	R1.1+ R1.3+R2.1+R2.3 DigitalCalliper	28.55	
Type IV Gypsum versus Resin Exocad	S1.1+ S1.3+ S2.1+ S2.3 Exocad	28.75	*.909*
	R1.1+ R1.3+R2.1+R2.3 Exocad	28.25	
DigitalCalliper versus Exocad Type IV Gypsum Products	S1.1+ S1.3+ S2.1+ S2.3 DigitalCalliper	28.50	*1.000*
	S1.1+ S1.3+ S2.1+ S2.3 Exocad	28.50	
DigitalCalliper versus Exocad Resins	R1.1+ R1.3+R2.1+R2.3 DigitalCalliper	28.70	*.928*
	R1.1+ R1.3+R2.1+R2.3 Exocad	28.30	

[a] The Mann–Whitney U test was used. The significance level was set at 0.05.
S1.1—maxillary stone (GC FUJIROCK EP Premium—GC, Tokyo, Japan) model, no.1; S1.3—maxillary stone (GC FUJIROCK EP Premium—GC, Tokyo, Japan) model, no.3; S2.1—maxillary stone (GC FUJIROCK EP Classic—GC, Tokyo, Japan) model, no.1; S2.3—maxillary stone (GC FUJIROCK EP Classic—GC, Tokyo, Japan) model, no.3; R1.1—maxillary resin (ASIGA SuperCAST V3—ASIGA, Alexandria, NSW, Australia) model no.1; R1.3—maxillary resin (ASIGA SuperCAST V3—ASIGA, Alexandria, NSW, Australia) model no.3; R2.1—maxillary resin (ASIGA DentaModel—ASIGA, Alexandria, NSW, Australia) model no.1; R2.3—maxillary resin (ASIGA DentaModel—ASIGA, Alexandria, NSW, Australia) model no.3.

Table IV. Mandibular pairwise comparison of the 14 studied diameters using the Mann–Whitney U test.

Pairwise Comparison		Mean Rank	*p*-Value[a]
Type IV Gypsum versus Resin DigitalCalliper	S1.2+ S1.4+ S2.2+ S2.4 DigitalCalliper	28.71	*.922*
	R1.2+ R1.4+R2.2+R2.4 DigitalCalliper	28.29	
Type IV Gypsum versus Resin Exocad	S1.2+ S1.4+ S2.2+ S2.4 Exocad	29.09	*.787*
	R1.2+ R1.4+R2.2+R2.4 Exocad	27.91	
DigitalCalliper versus Exocad Type IV Gypsum Products	S1.2+ S1.4+ S2.2+ S2.4 DigitalCalliper	27.95	*.799*
	S1.2+ S1.4+ S2.2+ S2.4 Exocad	29.05	
DigitalCalliper versus Exocad Resins	R1.2+ R1.4+R2.2+R2.4 DigitalCalliper	28.23	*.902*
	R1.2+ R1.4+R2.2+R2.4 Exocad	28.77	

[a] The Mann–Whitney U test was used. The significance level was set at 0.05.
S1.2—mandibular stone (GC FUJIROCK EP Premium—GC, Tokyo, Japan) model no.2; S1.4—mandibular stone (GC FUJIROCK EP Premium—GC, Tokyo, Japan) model no.4; S2.2—mandibular stone (GC FUJIROCK EP Classic—GC, Tokyo, Japan) model no.2; S2.4—mandibular stone (GC FUJIROCK EP Classic—GC, Tokyo, Japan) model no.4; R1.2—mandibular resin

(ASIGA SuperCAST V3—ASIGA, Alexandria, NSW, Australia) model no.2; R1.4—mandibular resin (ASIGA SuperCAST V3—ASIGA, Alexandria, NSW, Australia) model no.4; R2.2—mandibular resin (ASIGA DentaModel—ASIGA, Alexandria, NSW, Australia) model no.2; R2.4—mandibular resin (ASIGA DentaModel—ASIGA, Alexandria, NSW, Australia) model no.4.

Even if there were differences in the mean ranks of the obtained results (with greater values recorded in digital measurements), they were not statistically significant (p>0.05).

Evaluation of the second hypothesis

In order to evaluate the second hypothesis, the following values were compared:

- The values obtained by manual and digital measurements of the Pont index, the Linder–Harth index, and Bolton's analysis on traditionally poured versus 3D-printed models.
- The values obtained by manual versus digital measurements of the Pont index, the Linder–Harth index, and Bolton's analysis on physical and digital models.

A similar result for excessive mesiodistal mandibular teeth (Bolton's overall ratio >91.3%) was noticed from a comparative examination of the average values obtained in the case of the investigated indices (figure 15 and figure 16).

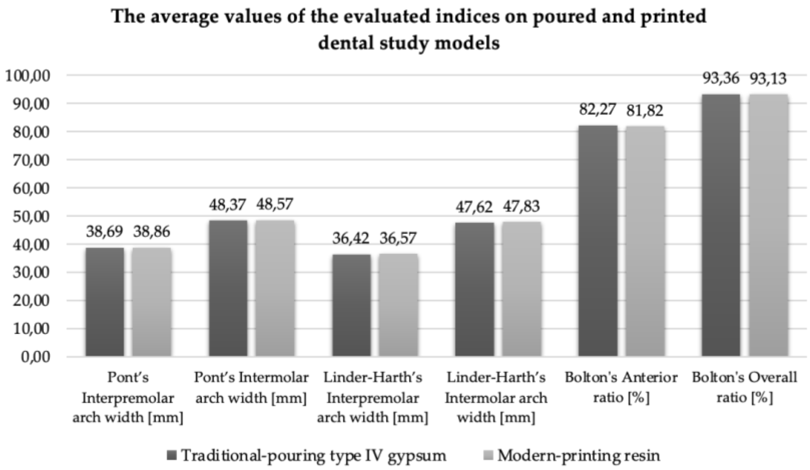


Figure 15. The average values of the evaluated indices on the experimental case study models.

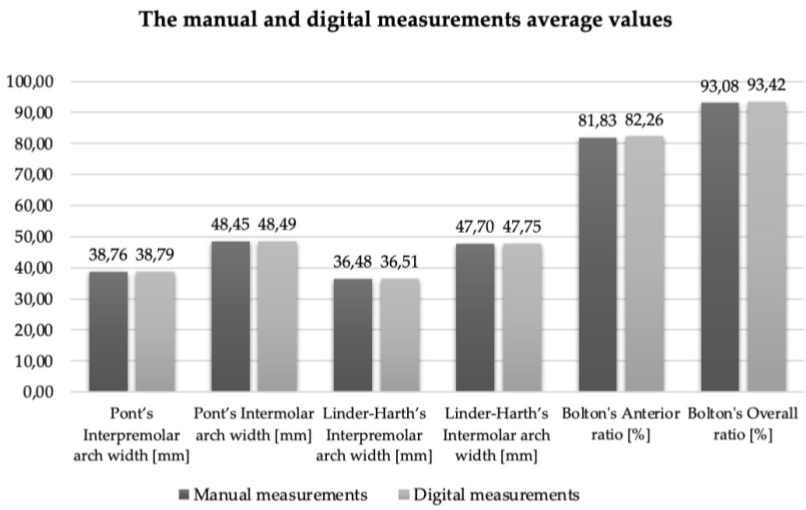


Figure 16. The average values of the evaluated indices by manual and digital measurements.

Table V shows statistically significant values for the measured indices: Pont interpremolar and intermolar arch widths (p<0.05) and Linder-Harth interpremolar and intermolar arch widths (p< 0.05) at the level of printed models versus traditional ones. When the difference between the calculated and the measured values was evaluated, a statistically insignificant result (p = 0.83-Pont's and Linder-Harth's interpremolar arch widths; p = 0.59-Pont's and Linder–Harth's intermolar arch widths) was obtained.

Table V. Traditional pouring versus 3D printing comparison of the analyzed indices using the Mann–Whitney U test.

Orthodontic analysis		Traditional pouring versus 3D printing	Mean Rank	*p*-Value[a]
Pont Index	Interpremolar arch widths	Traditional pouring	2.50	*.020*[*]
		3D printing	6.50	
	Intermolar arch widths	Traditional pouring	2.50	*.020*[*]
		3D printing	6.50	
	The difference between the calculated and the measured interpremolar arch widths values	Traditional pouring	6.00	*.083*
		3D printing	3.00	
	The difference between the calculated and the measured intermolar arch widths values	Traditional pouring	6.00	*.059*
		3D printing	3.00	
Linder–Harth Index	Interpremolar arch widths	Traditional pouring	2.50	*.021*[*]
		3D printing	6.50	
	Intermolar arch widths	Traditional pouring	2.50	*.020*[*]
		3D printing	6.50	
	The difference between the calculated and the measured interpremolar arch widths values	Traditional pouring	6.00	*.083*
		3D printing	3.00	
	The difference between the calculated and the measured intermolar arch widths values	Traditional pouring	6.13	*.059*
		3D printing	2.88	
Bolton's analysis	Anterior ratio	Traditional pouring	5.75	*.149*
		3D printing	3.25	
	Overall ratio	Traditional pouring	5.63	*.189*
		3D printing	3.38	

[a] The Mann–Whitney U test was used. [*] The significance level was set at 0.05.

In the case of the overall ratio (Bolton's analysis, p<0.05), a statistical significance between the mean ranks of manual versus digital measurements (table VI) was established. However, the difference between average values was 0.34 mm, which is considered to have no clinical significance.

Table VI. Manual versus digital measurements comparison of the analyzed indices using the Mann–Whitney U test.

Orthodontic analysis		Manual versus Digital measurements	Mean Rank	*p*-Value[a]
Pont Index	Interpremolar arch widths	Manual measurements	4.50	*1.000*
		Digital measurements	4.50	
	Intermolar arch widths	Manual measurements	4.50	*1.000*

		Digital measurements	4.50	
	The difference between the calculated and the measured interpremolar arch widths values	Manual measurements	5.75	*.149*
		Digital measurements	3.25	
	The difference between the calculated and the measured intermolar arch widths values	Manual measurements	4.63	*.885*
		Digital measurements	4.38	
Linder–Harth Index	Interpremolar arch widths	Manual measurements	4.50	*.885*
		Digital measurements	4.50	
	Intermolar arch widths	Manual measurements	4.50	*1.000*
		Digital measurements	4.50	
	The difference between the calculated and the measured interpremolar arch widths values	Manual measurements	5.75	*.149*
		Digital measurements	3.25	
	The difference between the calculated and the measured intermolar arch widths values	Manual measurements	4.63	*.885*
		Digital measurements	4.38	
Bolton's analysis	Anterior ratio	Manual measurements	3.00	*.083*
		Digital measurements	6.00	
	Overall ratio	Manual measurements	2.63	*.028**
		Digital measurements	6.38	

[a] The Mann–Whitney U test was used. * The significance level was set at 0.05.

Discussion

Numerous authors have highlighted dental digital models as beneficial. Some of these advantages include simpler data transmission, reduced treatment planning, and shorter diagnostic time when compared with traditional model setups and reconstruction (Shastry, Park, 2014; Palmer et al., 2005; Kuroda et al., 1996). However, when considering the usefulness of digital models, the following question arises: are they reliable?

Two previous systematic reviews, by Fleming et al. (2011) and Luu et al. (2012) respectively, compared the validity of digital model measurements with those from plaster models. According to the authors' findings, the digital model evaluations were correct.

The study results showed that there were no statistically significant differences in the mean rank of the obtained linear measurement values on the physical and digital case study models, which means that the first null hypothesis was verified.

Similar findings were obtained by Sousa et al. (2012) who evaluated the reliability of measurements made on 3D digital models obtained by scanning plaster models with laboratory scanners. The authors emphasized the increased ability to enlarge and rotate the pictures of the digital model image, as well as the software's simplicity of use in detecting landmarks.

Abizadeh et al. (2012) found a statistically significant difference between model analysis on plaster models and digital models created by model scanning. Measurements of plaster models were more accurate than measurements of digital models due to the fact that the digital model scans were not a true 1:1 replica of the plaster ones.

The current investigation included study models obtained by full dental arch impressions with alginate material. The results indicated that printed and traditional models both properly reproduce dental arch details. In contrast, a recent study conducted by Sayed et al. (2022) concluded that stone casts generated using polyvinyl siloxane and alginate impression and pouring type IV die stone have a higher linear dimensional accuracy than 3D-printed casts.

According to Nestler et al. (2021) both extrusion-based and photopolymerization-based printers were precise, although Asiga MAX UV (ASIGA, Alexandria, NSW, Australia) had the highest accuracy. In contrast, Sayed et al. (2022) found that the greatest number of distortions above 0.5% were produced by the digital model with full-arch-prepared abutment teeth obtained using the same printer.

Choi et al. (2022) and Jin et al. (2019) found no statistically significant differences between measurements taken from the physical plaster and printed models using the stereolithography method.

In a systematic review of the literature, Etemad-Shahidi et al. (2020) evaluated the accuracy of full-arch dental models manufactured using different 3D-printing technologies and concluded that other factors such as the layer thickness, base design, postprocessing, and storage can equally influence the accuracy of the resultant 3D-printed models.

It is well documented in the literature that tooth size differences (TSD) play an important role in orthodontic finalization, particularly in the front area. Knowing about TSD and other variables provides the practitioner an advantage when making a final treatment selection to achieve great results.

The existing studies on TSD used traditional measuring compasses or digital calipers to estimate mesiodistal tooth widths using plaster or digital models (Tomassetti et al., 2001; Zilberman et al., 2003).

Furthermore, it has been demonstrated that measurements taken from 3D digital models are a viable alternative to those taken from physical models, since storing records is faster, more reliable, and easier to complete. Accuracy has been measured using digital calipers, which are widely regarded to be the gold standard (Zilberman et al., 2003; O'Mahony et al., 2011; Zerouaoui et al., 2014; Stevens et al., 2006; Naidu, Freer, 2013; Bowes et al., 2017).

According to the "clinically acceptable" term (Naidu, Freer, 2013; Wan Hassan et al., 2017; Hirogaki et al., 2001; Bell et al., 2003), the results of the present study revealed that the values had differences of less than 0.5 mm between traditional and 3D-printed models, as well as between manual and digital measurement methods. On the other hand, for prosthodontic applications, the accuracy requirements for dental models are often greater, and a measurement discrepancy less than 0.2 mm was shown to be clinically acceptable in (Papaspyridakos et al., 2020).

Despite minor differences in the measurements of mesiodistal tooth width and arch length on digital models, Leifert et al. (2009) found that digital models were clinically acceptable and repeatable when compared to traditional models.

Wan Hassan et al. (2017) questioned the accuracy of dental measurements in various degrees of crowded dentitions when measuring stone casts and reconstructed rapid prototyping models.

The findings of the current study showed greater mesiodistal teeth width values recorded in digital rather than manual measurements. Similar results were also obtained by Cuperus et al.'s (2012) research using an intraoral scanner to create the digital models.

The difference between manual and digital recordings, according to Naidu et al. (2013) is explained by the absence of a physical barrier when placing measurement points on virtual models; the difficulty in scanning the contact points, which results in small amounts of missing data that must be interpolated by a computer algorithm; and the operator's training and proficiency, which can cause minor variations in contact point locations between the stone and digital models.

Even if—in the case of Pont and Linder–Harth interpremolar and intermolar arch widths ($p<0.05$) and Bolton's overall ratio ($p<0.05$)—a statistically significant difference between the manual and digital measurements was observed, the discrepancies were deemed to have no clinical implications. In this context, the second null hypothesis must also be accepted.

The reasons for the significant differences between physical and digital study models could be a highlighted correction of tooth position, the increased accuracy of the virtual setup compared with the manual one, and the superimposition of moving objects that may affect the geometry of digital models (Naidu et al., 2013; Rossini et al., 2016).

Similar to other in vitro studies, this research had several limitations. One limitation was that only one laboratory scanner, one type of 3D printer, and one software for digital measurements were employed. Another limitation was the difficulty of measuring tooth widths with a digital caliper on physical mandibular models due to access and the difficulty of resting at the exact mesial and distal landmarks in crowded areas.

Digital technology limitations were represented by the scanning procedure (the accuracy of physical models may be affected when imaging powder is applied to them before scanning), the "shape assumption" problem-which occurs when the software uses a computer algorithm to fill the interproximal inaccurate or uncaptured data-the process of printing, which can produce its own errors (Alrasheed et al., 2022; Morton et al., 2017).

Additional research is needed to evaluate the accuracy of dental case study models obtained using various scanners (intraoral and laboratory), printers, and production parameters, with measurements made using dedicated applications.

Conclusions

Within the limitations of the current study, it can be concluded that the precision of digital measurements of teeth widths, using DentalCAD 3.0 Galway (exocad GmbH, Darmstadt, Germany) on digital models, was comparable to direct measurements with a portable digital caliper Gedore No. 711 (GEDORE Austria GmbH, Österreich, Austria) on physical dental models.

Digital measurements of mesiodistal teeth width showed higher values compared with manual ones; therefore, the difference between the average values recorded had no clinical significance.

For orthodontic teaching purposes, dental study models manufactured by direct light processing (DLP) and traditional pouring are both acceptable.

1.1.4. Othognatic surgery- Managing Predicted Post-Orthognathic Surgical Defects Using Combined Digital Software: A Case Report

Aim of the study

This paper aims to present a fully digitized workflow using a combination of three digital software to correct the discontinuities in the mandible body obtained by an upward sliding genioplasty.

Case Report

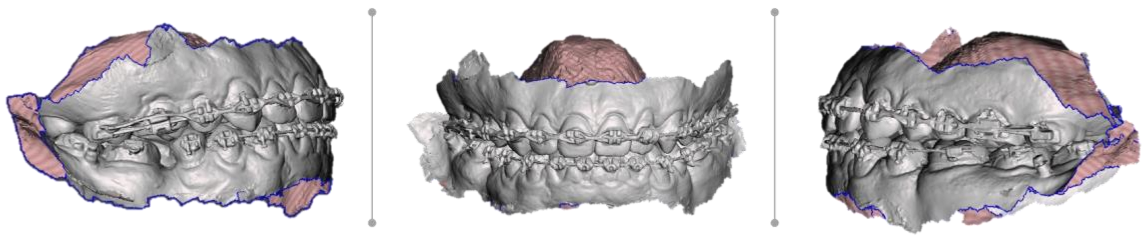
A 28-year-old man with long face syndrome, under orthodontic treatment for 2 years, was referred to our dental office for orthognathic surgery (OS) intervention. He had no systemic diseases or family history of significant issues.

His main complaints were excessive tooth exposure, a gummy smile, and a long and retruded chin.

Before OS, a clinical examination, CBCT, and intraoral scans of the dental arches and occlusion were performed.

The CBCT images were acquired using a DentriMax CBCT (DentriMax, HDX Will, Seoul, South Korea) with the following parameters 90 kV, X-ray tube current = 10 mA, Field of view (FOV) 18/16.5, focal spot = 0.5 mm, Voxel size = 0.10. the CBCT scans were acquired in the natural head position (NHP) in an upright position. The condyles were sited in centric relation (CR), and the preoperative occlusion in CR was fixed with a wax-byte at the preoperative CBCT scanning; however, without the wax-byte at the postoperative CBCT scanning acquisition. The CBCT data were exported in the digital imaging and communications in medicine (DICOM) format.

Intraoral scans were performed with Medit i700 (MEDIT corp. 8, Seoul, Republic of Korea), with the following parameters: 3D motion video technology/ 3D full-color streaming capture, scanning frame up 70 FPS, tip size 22.2X15.9 mm, 45-degree mirror angle, scan at 15/13 mm, and recorded images were saved as standard tessellation (.STL) files (Figure 17a-c).



(**a**) (**b**) (**c**)

Figure 17. Pre-surgical paraclinical intraoral scans: (**a**) right lateral view; (**b**) frontal view; and (**c**) left lateral view.

The clinical examination was confirmed by the cephalometric analysis of a skeletal class III patient (Table VII and Table VIII).

Table VII. Soft tissue cephalometric analysis (STCA)- projections using NemoFab (Nemotec, Madrid, Spain).

STCA Projections					
Cephalometric variables		**Normal range**	**Patient**	**Retruded**	**Protruded**
High midface Projection	Glabella	–9.5 to 4.5	–11	✓	-
	Orbital rims	–21 to –15	–22.9	✓	-
	Cheekbones	–27 to –17	–43.3	✓	-
	Subpupil	–18 to –12	–28.5	✓	-
Maxillary Projection					
	Nasal base	–14 to –10	–15.6	✓	-
	Nasal Tip	13.2 to 18.2	24.1	-	✓Large
Soft tissue Projection	Upper lip angle	2.11° to 6°	3.3	✓Upright lip	-
	Nasolabial angle	114.4° to 98.4°	85.2	-	✓Acute
	Upper lip to Nasal Tip	114.4° to 98.4°	22.2	✓	-
	Upper lip thickness	11.9 to 14.7	8.6	✓Thin	-
Hard tissue support	Mx 11 angle	60.8° to 54.8°	62.5	✓Upright	-

Mandibular Projection					
Soft tissue Projection	Pogonion	–5.2 to –1.2	–9.7	✓	-
Hard tissue support	Md 11 angulation	67° to 61°	67.5	✓Upright	-
A-P dentoskeletal					
Intra–jaw relationship	Facial angle	167 to 173	163.2	✓Convex	-
Maxillary	Mx 11 inclination	60.8 to 54.8	62.5	✓Upright	-
Mandibular	Md 11 angulation	67° to 61°	67.5	✓Upright	-

Note: Mx 11 -The maxillary central incisor; Md 11-The mandibular central incisor.

Table VIII. Soft tissue cephalometric analysis (STCA)- heights (NemoFab, Nemotec, Madrid, Spain).

STCA Heights					
Cephalometric variables		**Normal range**	**Patient**	**Short**	**Long**
Soft tissue	Interlabial gap (ULB to LLT)	1.1 to 3.3	–4	✓ Deficient	-
	Lower lip height (LLT to Me')	46.5 to 51.3	54.5	-	✓
Maxillary vertical balance	Mx 11 exposure-relaxed (Mx11-ULB)	2.5 to 4.5	7	-	✓ Excessive
Mandibular vertical balance	Lower lip height (LLT to Me')	46.5 to 51.3	54.5	-	✓

Note: Mx 11 -The maxillary central incisor.

In Figure 18, an overview of the proposed framework is illustrated.

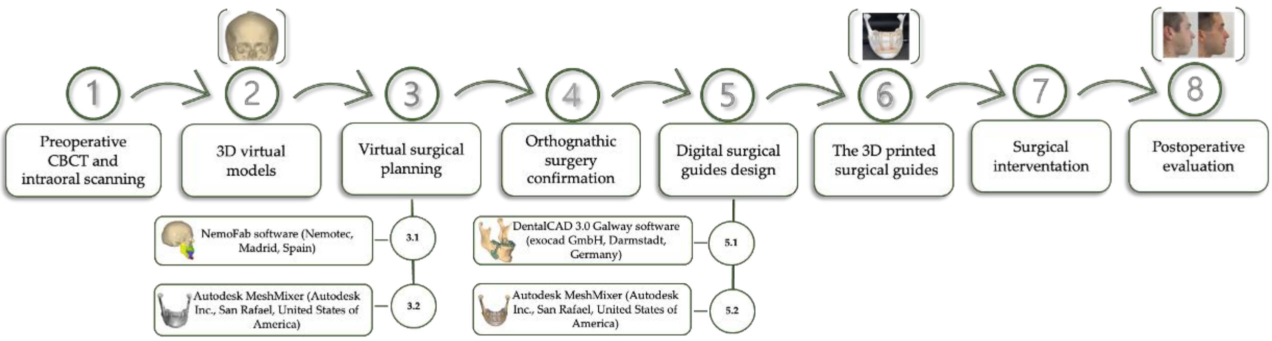
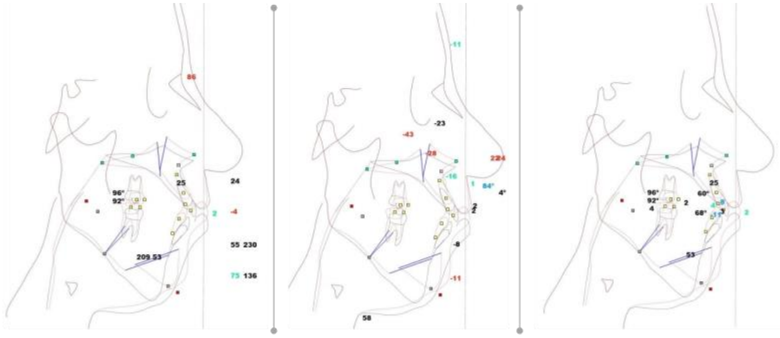


Figure 18. The orthognathic surgery workflow.

Consent was obtained after the patient was informed of the diagnosis, the prognosis with and without therapy, the specific treatment steps, and the benefits of the procedures, including specific risks and possible adverse effects.

Virtual Surgical Plan

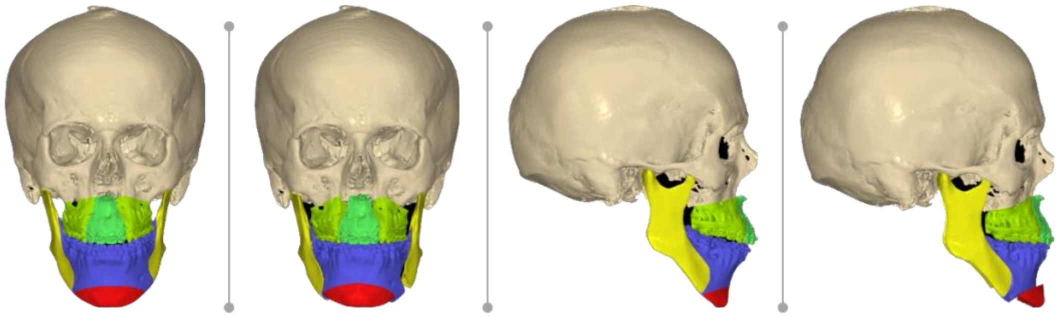
All obtained data were first imported into NemoFab surgical planning software (Nemotec, Madrid, Spain) before being analyzed (Figure 19a-c).



(a) **(b)** **(c)**

Figure 19. Cephalometric analyses using NemoFab (Nemotec, Madrid, Spain): (a) Dentoskeletal factors; (b) Projections; (c) Heights.

We first opted for an upward sliding genioplasty rather than a reduction in the anterior mandible because the latter would not achieve the proper advancement needed, the mandible angle degree would not be decreased, and would not preserve bony contact (Figure 20a-d).



(**a**) (**b**) (**c**) (**d**)

Figure 20. Pre-surgical computer-assisted virtual simulation using NemoFab (Nemotec, Madrid, Spain): (**a**) frontal view of patient skull; (**b**) frontal view of planned final reposition; (c) lateral view of patient skull; and (**d**) lateral view of planned final reposition.

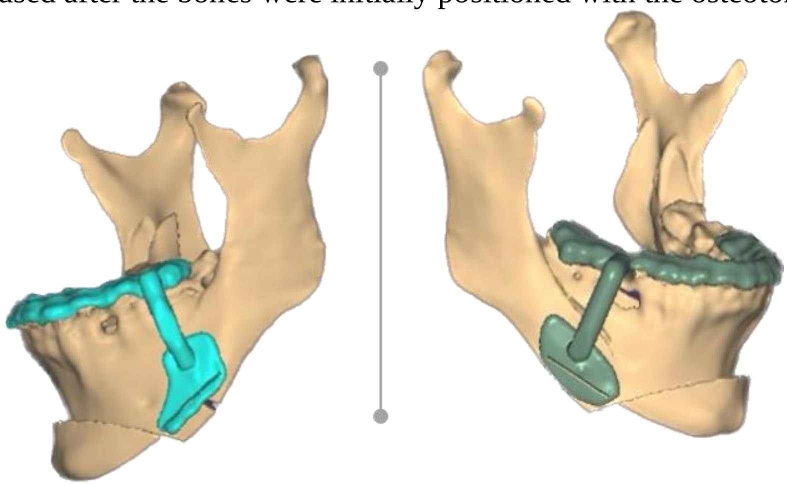
By selecting this solution, the anterior mandible height and the proper position of the Pogonion (Pg) to the TVL were both resolved, but this resulted in a 7.5 mm step between the posterior wing of the chin and the body of the mandible, which was detrimental to a continuous base of the mandible.

Since the NemoFab surgical planning software did not allow us to design a new set of osteotomies, it was necessary to export the .STL files of the mandible in its final position (both condylar bearing fragments, body of mandible, and upward sliding genioplasty) into software capable of performing Boolean operations (the union). For this purpose, Autodesk MeshMixer (Autodesk Inc., San Rafael, CA, USA) was used (Figure 21).

Figure 21. The combination of all the mandible fragments into a single .STL file using Autodesk MeshMixer (Autodesk Inc., San Rafael, CA, USA).

Digital Surgical Guides Design

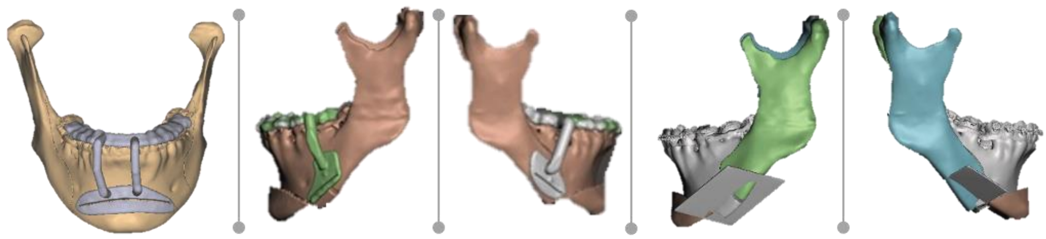
Following this step, a single unified .STL file was exported into DentalCAD 3.0 Galway software (exocad GmbH, Darmstadt, Germany) to create three digital surgical guides: one mental and two laterals (Figure 22a,b). Although NemoFab included a guided designing option, it could only be used after the bones were initially positioned with the osteotomy design.



(**a**) (**b**)

Figure 22. Virtual images of the designed guides using DentalCAD 3.0 Galway (exocad GmbH, Darmstadt, Germany): (**a**) left lateral view; and (**b**) right lateral view.

Since DentalCAD 3.0 Galway (exocad GmbH, Darmstadt, Germany) was also deficient in Boolean operations, the .STL files of the guides and the mandible with the fragments in their final positions were then exported to Meshmixer (Autodesk Inc., San Rafael, CA, USA) to complete the final process (Figure 23a-e).



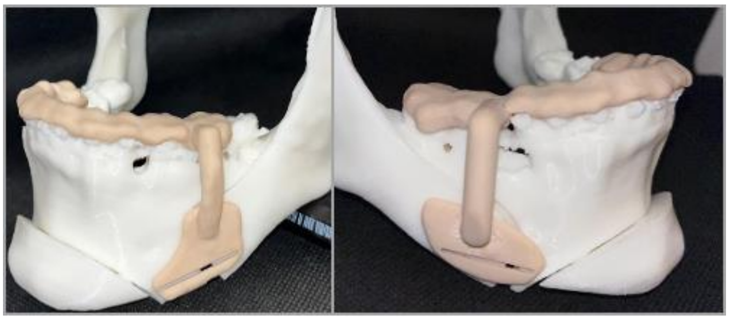
(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 23. Virtual images of the designed guides and the reduction plane using MeshMixer (Autodesk Inc., San Rafael, CA, USA): (**a**) frontal view of anterior guide; (**b**) left lateral view of lateral reduction guide; (**c**) right lateral view of lateral reduction guide; (**d**) left lateral view of reduction plane; and (**e**) right lateral view of reduction plane.

In our case, five digital guides were created: an intermediate splint, a palatal splint, lateral reduction guides left and right, and an anterior guide (mental guide).

Digital Guides Fabrication

The surgical guides were fabricated from acrylic resin (Phrozen Water-Washable Dental Model 3D Printer Resin, Phrozen Technology, Hsinchu, Taiwan) using an ASIGA 3D MAX UV printer (ASIGA, Alexandria, NSW, Australia) before they were then sterilized for surgery (Figure 24a-c).



(**a**) (**b**)

(**c**)

Figure 24. Three-dimensional printed digital guides and splints: (**a**) left lateral view of lateral reduction guide; (**b**) right lateral view of lateral reduction guide; and (**c**) frontal view of mental guide and the intermediate and palatal splints.

Sterilizing by immersion for 25 minutes in peracetic acid (Gigasept PAA, Schülke & Mayr GmbH, Norderstedt, Germany) was performed prior to surgery.

Surgical Intervention

Blood tests were in the normal range.

The patient had surgery while under general anesthesia and nasotracheal intubation. In order to reduce bleeding and facilitate tissue dissection, a vasoconstrictor solution (6 vials of 1.7ml of articaine, 1 vial of epinephrine, 1 vial of tranexamic acid, and 100 ml of saline) was used locally.

Bilateral sagittal split osteotomy (BSSO) was performed using an intermediate splint. The fragments were fixed with single 4-hole straight plates (I plate, Medicon eG, Tuttlingen, Germany), bilaterally 2/6 mm monocortical screws (Medicon eG, Tuttlingen, Germany), and two bicortical screws (2/13 mm, Medicon eG, Tuttlingen, Germany) inserted on either side of the osteotomy.

Mental osteotomy followed, upward sliding it into the new position to correct the anterior mandible height and securing the new position by using a prebent rectangular 5 holes plate and monocortical screws (2/6 mm, Medicon eG, Tuttlingen, Germany), which led to a 7 mm advancement.

The prior designed reduction guides were placed in the designated position using the same access for BSSO with a slight anterior reflection of the periosteum until and beneath the mental foramen. To facilitate the placement of the guide and to retain visual control of the osteotomy, mental and BSSO accesses were united by a tunneling reflection of the periosteum beneath the mental nerve (Figure 25a,b). Mandible osteotomy was performed using a piezoelectric instrument (Woodpecker Ultrasurgery, Guilin Woodpecker Medical Instrument Co., LTD., Guilin, China) with a properly angled tip (US1L-Left Angle 90 degrees Micro-Saw 0.5 mm, Guilin Woodpecker Medical Instrument Co., LTD., Guilin, China).

(**a**) (**b**)

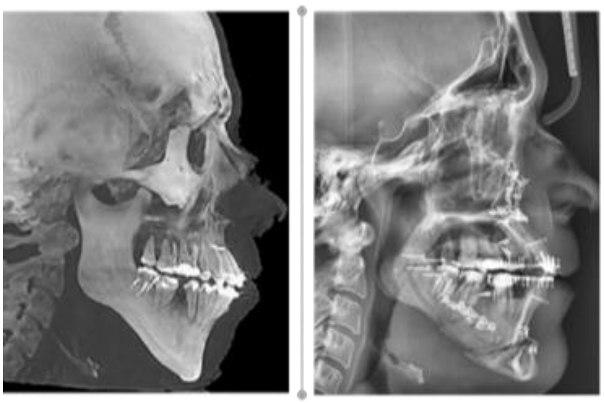
Figure 25. Resulted bone fragments from mandible body marginal base reduction: (**a**) right lateral view; and (**b**) left lateral view.

Maxillary excess was treated with a multisegmental Le Fort I osteotomy, which involved septoplasty and inferior turbinate reduction, followed by a 5 mm clinical vertical repositioning to return the maxilla to its correct occlusal position. There was no final splint used. For the fixation, two double plates were applied, each with seven monocortical 2/5 mm screws (Medicon eG, Tuttlingen, Germany). Again, osteotomy gaps were filled using a ground homologous bone graft collected from the impaction sites.

From the first week after orthognathic surgery, there was an aesthetic significant improvement in facial appearance (Figure 26a-d and Figure 27a,b).

(**a**) (**b**) (**c**) (**d**)

Figure 26. The extraoral images of patient profile: (**a**,**c**) preoperative; and (**b**,**d**) 7 days postoperative.



(**a**) (**b**)

Figure 27. The profile teleradiography images: (**a**) preoperative; and (**b**) 3 weeks postoperative.

Postoperative treatment included 7 days of intravenous antibiotic therapy and regular pain medications. An ice pack was used intermittently in the first 72 hours following the intervention.

During the first three days post-surgery, the surgeon cleaned the patient and instructed him on how to maintain proper oral hygiene using a soft toothbrush and rinsing with a chlorhexidine solution for ten days. The patient was advised to follow a liquid diet for a month and was given elastic therapy for 40 days, after which he started post-surgical orthodontic treatment.

Cephalometric Planes

Using the true vertical line in a natural head position state as a landmark for facial aesthetics, the modified parameters are described in Table IX.

Table IX. Measured parameters before and after surgery (NemoFab, Nemotec, Madrid, Spain).

Parameters	Preoperative	3 weeks Postoperative
Upper incisor (UI) exposure	7 mm	2 mm
Upper incisor to the soft tissue plane (UI-STP)	–6 mm	–8.5 mm
Maxillary occlusal plane	103 degrees	94 degrees
Mandibular occlusal plane	99 degrees	92 degrees
Articulare -Gonion -Menton (Ar-Go-Me)	136.49 degrees	128.7 degrees
The width of the mandible (Go-Go)	90.5 mm	96.2 mm

The mandibular angle degree significantly decreased from 136.49° to 128.7°. The width of the mandible (Go-Go) increased from 90.5 mm (pre-surgery) to 96.2 mm (post-surgerysurgery).

Discussion

Long faces with maxillary or/and mandibular hyperplasia with or without asymmetry require a special interdisciplinary approach. Digital planning becomes increasingly important in these situations. The confection and use of different splints and surgical guides ensure the high predictability of surgical outcomes.

Occlusion or oral function correction is the most frequent reason for orthognathic surgery, followed by improvements to aesthetic and psychosocial functions. From the patient's point of view, facial appearance is one of the primary motives for accepting surgical interventions (Mugnier et al., 2020). A descriptive quasi-experimental study conducted by Rezaei et al. (2019) on 112 Persian adult patients with class III skeletal malocclusion before and after OS revealed that surgery interventions enhanced the individuals' quality of life, as well as their contentment, self-confidence, and oral function. The current case report supports such findings since the patient was satisfied with the aesthetic and functional outcomes.

The treatment plan varied from one team to another, with OS indicated either before or after orthodontic treatment. In the recent literature, the term" surgery first" is described with potential benefits in shortening treatment time and improving facial aesthetics from begging (Naini, Gill, 2019; Dall'Magro et al., 2021). OS was proposed after the patient had undergone orthodontic therapy for two years.

This therapeutic approach consisted of two stages. The first stage involved an orthodontic strategy comprising decompensation and alignment. The maxillary arch was maintained and unchanged while correcting the mandibular Spee and Wilson curves. The second stage involved a surgical strategy, which encompassed maxillo-mandibular repositioning in all three spatial axes, along with the counterclockwise (CCW) rotation of the occlusal plane, in this case, of a hyper-divergent mandibular pattern. Our decision was influenced by the desire to establish an aesthetic profile connected to TVL and NHP aesthetic planes.

The current VSP software exhibits constrained versatility and limited applicability when used for the analysis of osteotomies executed in orthognathic surgery (Holte et al., 2021). In our case, NemoFab (Nemotec, Madrid, Spain) did not allow us to perform osteotomies after virtual surgical planning.

Bone reduction in this region was indicated as a viable treatment for the bottom border of the mandible's aesthetic imbalance; in order to make the process more precise, we chose the digital method. NemoFab surgical planning software (Nemotec, Madrid, Spain) predicted that a major step would be present after upward sliding genioplasty.

The patient had undergone BSSO in addition to Le Fort 1 osteotomy and genioplasty followed by mandible base recontouring ostectomy. Stable fixation was used for each osteotomy.

Hernández-Alfaro stated that the surgical management of Long Face Syndrome could involve the following methods, either alone or in combination: maxillary impaction, vertical chin reduction, and the counterclockwise rotation of the occlusal plane (Hernández-Alfaro, 2016). In some circumstances, another procedure, guided mandible base ostectomy, could be added to achieve a straight line and a continuous mandible base.

By impacting the anterior part of the maxilla by 5 mm, the position of the chin was moved 3 mm superior, and the mandible was advanced by 1 mm. The same findings were reported by Jayakumar et al. in a study on 45 patients with vertical maxillary excess. The authors observed that a superior maxillary impaction of 1 mm generated a chin movement of 0.6 mm vertically and 0.2 mm sagittally (Jayakumar et al., 2020).

The 9-degree flattening of the occlusal plane translated into an advancement of 8 mm and an improvement of 4 mm, and the upward sliding genioplasty resulted in an advancement of 7 mm and an improvement of 5 mm.

The potential for recognizing consequences, including mental nerve injury and step deformity, is mentioned in the specialized literature (Zide et al., 1999; 2007).

The usage of only two dedicated software programs could be considered a limitation of the current case report. In light of this constraint, a comparative analysis of clinical case resolutions using commercially available software is required.

Conclusions

Rehabilitation standards in dentistry have evolved and improved as a result of new multidisciplinary concepts and more complex perspectives on additional interventions that may help patients to restore function, health, and aesthetics.

The outcomes of combining these software results proved satisfactory for both the medical team and the patient. The use of cutting guides reduced the duration of the surgery and increased the precision of mandible base ostectomy, resulting in a continuous and improved mandible base ostectomy.

In our case, current orthognathic surgery planning software was unable to perform all the necessary operations autonomously; thus, future updates should make single software applications possible, reducing the amount of time required for learning the software and the amount of money required for multiple licenses.

1.2. FINITE ELEMENT ANALYSIS (FEA) A MODERN METHOD FOR SIMULATING THE BEHAVIOUR OF DENTAL APPLIANCES

1.2.1. State of art

The laws of physics can be applied to almost every natural phenomenon. These laws can be mathematically defined through algebraic, differential, or integral equations that relate different measurable quantities.

In the last decade, Finite Element Analysis (FEA) and Finite Element Method (FEM) have gained widespread recognition as an excellent, non-invasive method for researching biomechanics and the influence that mechanical forces have on biological systems.

FEA is a computer-based numerical method that enables the investigation of structures by dividing them into small elements connected at nodes. Each element's mechanical behavior is expressed as a function of the displacement of the nodes, which can then be analyzed to evaluate stress and strain in the entire structure.

This analysis has been applied in various fields, including dentistry, since its development by mathematician Richard Courant in the 1940s. In 1956, Turner et al. made an attempt to define numeric analyses more broadly for aeronautical engineering, while the term "Finite Element" was coined by Ioannis Argyris and R.W. Clough in 1960. FEA's application in dentistry was first reported in 1976, when Weinstein et al. used it to assess the effect of occlusal loads on implants and adjacent bone (Bandela, Kanaparthi, 2020). Since then, the use of FEA has undergone rapid and sophisticated development, spanning from micro-computer to large-scale structural systems (Geng et al., 2001; Mohammed, Desai, 2014).

In the process of conducting a Finite Element Analysis (FEA), there are a number of actions that must be followed. The initial action is to determine what the problem is named, and it is not required but recommended. Next, it is decided which type of investigation will be done (structural, chemical, thermal, electric, etc.). The model is then created in 1D, 2D, or 3D space using the appropriate units of measurement. The type of element is defined as either 1D, 2D, or 3D. The mesh is then applied to the model, which involves dividing the analysis continuum into discrete parts or finite elements. Material properties, such as Young's modulus, Poisson's ratio, density, and thermal conductivity, are assigned to the model. In a stress analysis, loads are applied on the mathematical model. These loads can be a point load, a pressure, or a movement. Lastly, border conditions are added to the model to avoid infinite acceleration in the computer's virtual environment, and they can be placed on nodes, key points, areas, or lines in all or specific directions.

The solution action in the FEA process consists of three main parts: pre-solver, mathematical engine, and post-solver. The pre-solver reads the model created by the pre-processor and creates the mathematical representation of the model. The solver then processes the results, while the post-solver calculates the relevant data for each node in the component or continuum, such as strains and stresses. During post-processing, the results are analyzed and presented in different formats, such as contour plots, tables, or animations. Additionally, post-processors can calculate stress and strains in any of the x, y, or z directions, or in a direction at an angle to the coordinate axes. They can also determine principal stresses and strains, or yield stresses and strains based on the main theories of failure.

The advantages of the FEM include its non-invasive nature, ability to easily interpret results in physical and mathematical terms, and capability to handle non-homogeneous structures by assigning different properties to different elements. The method allows for properties to be varied within an element based on the applied polynomial and can minimize the need for laboratory testing, though not completely replace it. It can be applied to linear and non-linear, solid and fluid structural interactions, and can break down complex problems into smaller ones. FEM can accurately model biological circumstances pre-, intra-, and post-operatively without affecting material qualities. It replaces stereo lithographic models for pre-surgical planning, offers static and dynamic analysis, is faster with complicated structures, and requires less equipment. Due of its systematic generality, FEM can solve many issues (Bandela, Kanaparthi, 2021; Naoum et al., Lu et al., 2019).

The periodontal ligament (PDL) is a specialized tissue with the primary function to support the tooth, being crucial in designing 3D tooth models. Various studies have investigated its biomechanics and stress distribution. To ensure accurate stress and strain values, it is important not to ignore the PDL. Authors recommended simulating the tooth model as a contact model at the tooth root and alveolar process interface, reinforcing the use of PDL to increase accuracy and contribute to smooth interface stress distributions (Tuna et al. 2014).

Finite element analysis (FEA) has proved to be a reliable and valid tool in evaluating applied orthodontic forces. Researchers have utilized FEA to study various aspects of orthodontics, including the interaction between tooth mobility and periodontal ligament, the effect of compensating curves on tooth movement, and orthodontic tooth movement (OTM).

In 1995, Tanne et al. conducted a study using 3D FE analysis to determine the location of the center of resistance (CRe) of the nasomaxillary complex. The researchers applied 9.8 N of force at five different levels, in different directions, and found that the CRe of the complex is located on the postero-superior ridge of the pterygomaxillary fissure, registered on the median sagittal plane.

Many other researchers have also developed FE models to explore the relationship between tooth mobility and periodontal ligament. In 2001, one study was conducted to validate an FE model and discovered that the periodontal ligament (PDL) is the primary mediator for orthodontic tooth movement. However, the material properties of PDL are challenging to quantify (Piccioni et al., 2013).

The popularity of lingual orthodontic technique has grown due to its aesthetic appeal to adults. Sung et al. (2003) conducted a study to evaluate the impact of compensating curves on canine retraction in lingual and labial orthodontic techniques. Their results showed that the pattern of tooth movement differed between the two techniques, and the anti-rotation and anti-tip action of the compensating curve on the canine retraction was greater in the labial archwire. Cattaneo et al. (2009) investigated OTM and supporting structure modelling and remodelling owing to periodontium stress/strain distribution changes. They pointed out that classical OTM theories did not consider the complex mechanical properties of the PDL, morphology of alveolar structures, and magnitude of the applied force. The authors also highlighted that FEA should be patient-specific and not based on general models.

In restorative dentistry, biomechanical studies are indispensable for comprehending the mechanical properties of materials and dental tissues (Borcic, Braut, 2012; Piccioni et al., 2013). Various studies have been conducted to investigate the stress and failure of restorative materials such as resin-based, glass ionomer cement (GIC), and composite.

According to Goel et al. (1991), the enamel in the cervical region may be more prone to cracking because of weaker mechanical interlocking between enamel and dentin. In a study by Ausiello et al. (2002, 2004), the impact of variations in the elastic modulus of resin-cement on stress transmission during vertical occlusal loading was investigated, and it was found that indirect composite resin-inlays dissipated stress better compared to glass ceramic inlays.

Several studies have reported findings related to FE modeling of dental structures and restorations. The authors developed a quick method for generating FE models and observed that restorations with loss of tooth structure exhibit a progressive decrease in cuspal stiffness (Magne et al., 2006). Another study reported that restorative materials with an elastic modulus around 1 GPa minimize mechanical failure under realistic loading conditions (Mohammed, Desai, 2014). A different study suggested that higher modulus of elasticity in occlusal restorations of resin composite reduces the likelihood of marginal deterioration (Asmussen et al. 2008). An investigation found that increased adhesive layer thickness does not compromise the strength of clear fill SE Bond (Coelho et al. 2008).

Finally, Magne and Oganesyan (2009) measured cuspal flexure in intact and restored maxillary premolars and found that ceramic inlays had a greater cusp-stabilizing effect than composite ones. These studies highlight the importance of understanding the biomechanical principles involved in restorative dentistry and the need to consider material properties and stress concentration when designing dental restorations.

In 2011, authors compared an inlay-supported all-ceramic bridge to a traditional full crown supported all-ceramic bridge and found that peak stresses in the inlay bridge were approximately 20% higher than in the full crown supported bridge. To prevent excessive forces that can lead to fracture, the authors recommended using an optimal inlay preparation form and an optimized bridge design that broadens the gingival embrasure to distribute mastication forces more evenly (Thompson et al., 2011).

Preserving the root canal anatomy and achieving a good apical seal and foramen as small as possible while avoiding deviation from the original canal curvature are the main objectives of endodontic instrumentation (San Chong, 2016). However, during the process of canal shaping, excessive pressure can be exerted against the dentinal walls, resulting in inappropriate canal preparation or the formation of microcracks, which can ultimately lead to tooth loss.

Nitinol (NiTi) is a commonly used shape-memory alloy for forming the root canal during instrumentation. The material and technique used during instrumentation must be carefully followed to avoid instrument breakage inside the canal. Finite Element Analysis (FEA) helps to predict treatment outcomes (Carpegna et al., 2020).

Research studies have shown that torsional failure due to excessive apical force during instrumentation is the most frequent cause of NiTi rotary endodontic file failure (Sattapan et al., 2000). Stress variations generated by vertical and lateral condensation on mandibular first molar mesio-buccal root canal have been found to cause vertical root fracture due to over-force and improper operation (Mohammed, Desai, 2014). ProTaper is stiffer than ProFile, and the distribution of stresses is uniform in the ProTaper model. According to Subramaniam et al. (2007), ProFile possesses greater flexibility than ProTaper. Additionally, Kim et al. (2008) found that ProTaper had the highest pull in the apical direction and the greatest reaction torque from the root canal wall, whereas ProFile exhibited the least amount. As per Lee et al. (2011), instruments with higher stiffness display a greater concentration of stress and a lower number of rotations before failure in cyclic fatigue fracture tests.

To avoid instrument breakage and ensure successful treatment outcomes, careful consideration of the materials used, and techniques employed during canal preparation is necessary. Researchers have shown that stresses generated during canal preparation can cause vertical root fractures and instrument failure.

The post and core system are the most commonly used method to restore structurally weakened teeth. The two types of post and core system are custom cast metal posts and cores and a two-component design comprising a prefabricated post and other core materials subsequently adapted.

The distribution of stress in a post is influenced by both the design of the post and the elastic modulus of the post material. It is important to carefully consider these factors in order to optimize stress distribution and minimize the risk of failure. Studies show that when the elastic modulus of the post material is higher than that of dentin, it can cause dangerous, non-homogenous stress in root dentin. To ensure proper stress distribution, it is important for clinicians to select post materials that have similar stiffness to dentin.

Glass fiber dowels have been shown to generate less stress compared to metal, carbon, and ceramic posts. According to Zhou et al. (2009), trapezium and cone fiber post designs are optimal for crown and root portion restoration. For luting the post and core to the remaining tooth structure, various classes of cements (zinc-phosphate, glass ionomer, resin-modified glass ionomer, resin cement) are used. However, differences in the elastic modulus of these cements, post materials, and dentin can lead to stress concentration during function, as reported by Piccioni et al. (2013).

Several studies highlighted the relevance of the ferrule effect and recommended the use of adhesive resin-fiber posts and composite cores as the optimal luting technique for improving tooth fracture resistance and biomechanical performance. The authors suggested the application of 3D finite element analysis to identify areas of stress concentration. Furthermore, their study showed that smaller diameter posts with an elastic modulus similar to dentin resulted in better stress distribution (Al-Omiri et al., 2010, 2011).

Accurately simulating structures is crucial to achieve successful FEA, considering material properties of the implant and bone, surface characteristics and design of the implant and its components, loading method, support conditions, and the biomechanical behavior of the implant-bone interface. Advanced imaging techniques can successfully simulate the responses of living tissues to applied load, overcoming the primary difficulty of simulating living tissues.

Stress patterns in implant components and surrounding bone are well studied, with von Mises stress being the most frequently used scalar-valued stress invariant to evaluate yielding and failure behavior of dental materials. The highest and lowest principal stresses are also applied to assess mechanical stress on bone, implant, and bone-implant interface. Different implant shapes and designs produce various stress patterns, with cylindrical implants being more desirable for stress distribution than conical implants (Mohammed, Desai, 2014; Mailath et al., 1989). To achieve favorable stress distributions in implants, larger diameters are recommended. Implant materials with a lowest modulus of elasticity of 110,000 N/mm2 are also preferred (Mailath et al., 1989).

FEA has led to significant improvements in implant design and implant insertion techniques. Clinicians can use FEA to better understand the process of bone remodeling and improve surgical techniques. The use of soft-liner materials and implant thread-form configurations can affect compressive stress intensities in the bone, but not von Mises stress distribution in the supporting bone. Studies suggest that square thread shapes with a small radius are more effective in stress distribution than other dental implants (Chun et al., 2002). Additionally, masticatory force around the implant neck decreases with increased implant diameter, reducing the risk of bone resorption (Himmlová et al., 2004).

According to Ding et al. (2009), increasing the implant diameter reduces masticatory force around the implant neck and helps clinicians understand bone remodeling. Other authors examined the impact of various implant thread designs on stress distribution and found that while implant thread forms have no effect on von Mises stress distribution, they produce dissimilar compressive stress intensities in the bone (Piccioni et al., 2013). Dos Santos et al. (2011) evaluated the impact of healing cap height and soft-liner materials on peri-implant bone stress distribution during mastication and found that non-submerged implants with soft liner materials had better results. Finally, Demenko et al. (2011) emphasized the importance of selecting the appropriate implant size to determine load bearing capacity and avoid peri-implantitis, a common cause of mandibular implant supported overdenture failure.

A recent systematic review of literature on stress distribution in dental implants and abutments composed of carbon fiber-reinforced polyetheretherketone (PEEK) composites identified that unfilled PEEK showed low values of elastic modulus and strength that negatively impacted stress distribution towards bone tissue. The incorporation of 30% carbon fibers improved the elastic modulus and strength of PEEK-matrix composites, but some studies did not find significant differences in stress magnitude when compared to unfilled PEEK (Souza et al., 2021).

Diken Turksayar and Donmez (2023) conducted a study to investigate the stress generated on peripheral bone, implant, and prosthetic components using PEEK and polyetherketoneketone (PEKK) hybrid abutments under two loading situations. They used nonlinear 3D finite element analysis to evaluate stress distribution and found that PEEK and PEKK abutments caused greater stress on the implant and standard titanium abutment compared to peripheral bone. Oblique forces generated more stress than horizontal forces, and PEEK hybrid abutments caused excessive stress accumulation on the titanium base abutment under immediate loading.

Orthognathic surgery is a surgical procedure that corrects jaw and facial conditions related to structural abnormalities, growth modifications, temporomandibular joints (TMJ) disorders, sleep apnea, malocclusion, and other orthodontic problems.

Bridging elements are a key determinant of successful outcomes in corrective mandibular surgery, such as bilateral sagittal split osteotomy (BSSO), and FEA is an important tool in selecting appropriate bridging elements. In 2011, authors compared three types of fixations during bilateral sagittal split osteotomy (BSSO) using a 3D FE model and concluded that the most stable bridging after BSSO can be obtained with bicortical screw fixation (Stróżyk et al., 2011).

Surgically assisted palatal expansion (SARPE) is another orthognathic surgical procedure performed frequently in patients with a narrower maxilla. FEA has shown that steps in the zygomaticomaxillary buttress and the pterygomaxillary disjunction are important in decreasing the harmful dissipation of tensions during SARPE (De Assis et al., 2014).

In another research non-linear 3D finite element analysis (FEA) was applied to simulate pterygomaxillary dysjunction during Le Fort I osteotomy (LFI) and predict changes in the fracture pattern that could occur with extension of the cutting line. The study showed that this technique can be a useful tool for predicting the outcomes of LFI-non COSep (Fujii et al., 2017).

A study conducted by Knoops et al. (2019) compared the accuracy of soft tissue prediction in patients with LFI using various computer programmes, such as Dolphin, ProPlan CMF, and Probabilistic Finite Element Method (PFEM). They found that PFEM can provide accurate soft tissue prediction due to its ability to define patient or population-specific material properties, while ProPlan does not allow for adjustment of soft tissue parameters. As an outcome, PFEM can be a useful tool in preoperative patient communication.

The application of FEA had demonstrated its efficacy as a valuable instrument in reconstructive and oncosurgeries, particularly in cases where substantial resection is deemed necessary and mandibular reconstruction is imperative.

In their research, Moiduddin et al. (2017) explored two different methods, mirroring and anatomical, for designing and analyzing customized porous mandibular reconstruction plates. Their findings suggested that the mirror design technique is preferable as it enhances the stability and flexibility of mandibular reconstruction during chewing.

Hu et al. (2019) conducted research to analyze the mechanical properties of 3D-printed anisotropic scaffolds as bone analogs using fused deposition modeling (FDM). Their study involved designing and producing a customized graft with a porous scaffold structure based on CBCT images of a 50-year-old edentulous patient. The optimized graft, which was tailored to the patient's needs, exhibited superior mechanical properties. This underscores the benefits of utilizing numerical simulations and 3D printing technology in creating artificial porous grafts.

However, finite element analysis does not provide a formula or solution for a class of problems. The understanding of biomechanical properties and their relationship to different situations exhibits variability across individuals. Thus, it is important to consider the limitations of FEA before making any decisions in experimental or clinical dentistry. FEA experiments are repeatable and modifiable, but clinical evaluation should accompany FEA research due to its limitations.

My research interests were focused on the fields of prosthodontics and orthodontics. Within the domain of prosthodontics, I have been studying the biomechanical behavior of inlay-retained dental bridges and single pontic dental bridges made from titanium-based alloys using 3D modeling and FEA. In the field of orthodontics, I have been exploring the use of FEA to model and simulate orthodontic tooth movement, with a focus on understanding the role of the periodontal ligament in this process.

	The following are the most significant personal scientific contributions in this field
Published articles in ISI journals	1*. Luchian I, Martu MA, **Tatarciuc M,** Scutariu MM, Ioanid N, Pasarin L, Kappenberg-Nitescu DC, Sioustis IA, Solomon SM. Using FEM to Assess the Effect of Orthodontic Forces on Affected Periodontium, Appl Sci-Basel, **2021**, 11(16): art. no 7183. IF=2.838 2*. **Tatarciuc M**, Maftei GA, Vitalariu A, Luchian I, Martu I, Diaconu-Popa D. Inlay-Retained Dental Bridges-A Finite Element Analysis, Appl Sci-Basel, **2021**, 11(9): art. no 3770. IF=2.838 3*. **Tatarciuc M**, Vitalariu A, Luca O, Aungurencei A, Aungurencei O, Fratila D, Popa DD. The Influence of Food Consistency on the Abutment Teeth in Fixed Prostheses A FEA study, Rev Chim, **2018**, 69(2): 407-409. IF=1.605 4. Popa DD, Vitalariu A, **Tatarciuc M**, Munteanu F. Effect of Silver Nanoparticles Incorporation in Dental Resins on Stress Distribution Finite element analysis, Rev Chim, **2016**, 67(8): 1571-1574. IF=1.232
Published articles in BDI journals	1. Luchian I, Tanculescu O, Rudnic I, **Tatarciuc M**, Martu S. The analyze by finite element of strains in periodontal ligament and alveolar bone during orthodontic tooth movement, Rom J Oral Rehabil, **2012**, 4(1): 35-39 (Index Copernicus)

**Publications described in detail in the next subchapters*

1.2.2. Fixed prosthesis - Inlay-retained dental bridges-a finite element analysis

Aim of the study

The present study aims to analyze stress levels at a three-element dental bridge, with inlays used as retainers to evaluate tension levels on abutment teeth and analyze the maximum tensions applied to abutment teeth and the dental prosthesis, considering the dynamic action of masticatory forces.

For this purpose, we used finite element analysis, a method that provides an image of the distribution of forces, both at the artificial substitute and the biological support level.

Materials and Methods

The finite element method attempts to approximate a solution to a problem by admitting that the domain is divided into subdomains or finite elements, with simple geometric shapes and the function of an unknown state variable that is defined around each element.

The operation of choosing the number and type of finite elements, corroborated with the division of the domain into several finite elements, is called discretization. When preparing the analysis model, one must take into account that the shape and dimensions of the design influence the accuracy and time of analysis; in this sense, for a given problem, there are several variants of analysis models.

Description of the geometric model and finite element modeling was first performed, a stage that includes modeling of material characteristics, choosing the finite elements and introducing properties, generating the finite element structure, introduction of limit conditions and forces. Analysis and solution of the finite element model involved setting the solving parameters and then visualizing the states and variations of the parameters. Images of molars, canines, premolars and incisors were taken as a reference; their dimensions were made on a scale, according to the dimensions of the molars on computed tomography (CT) images. Based on the mandibular model, the absence of tooth 3.5 was simulated. To simplify the finite element analysis, only the dental elements 3.3, 3.4, 3.6 and 3.7 were preserved from the assembly.

For the application of optimal forces to simulate physiological masticatory load, the main muscles of the mastication process, the masseter muscles and lateral and medial pterygoid muscles were taken into account (figure 28).

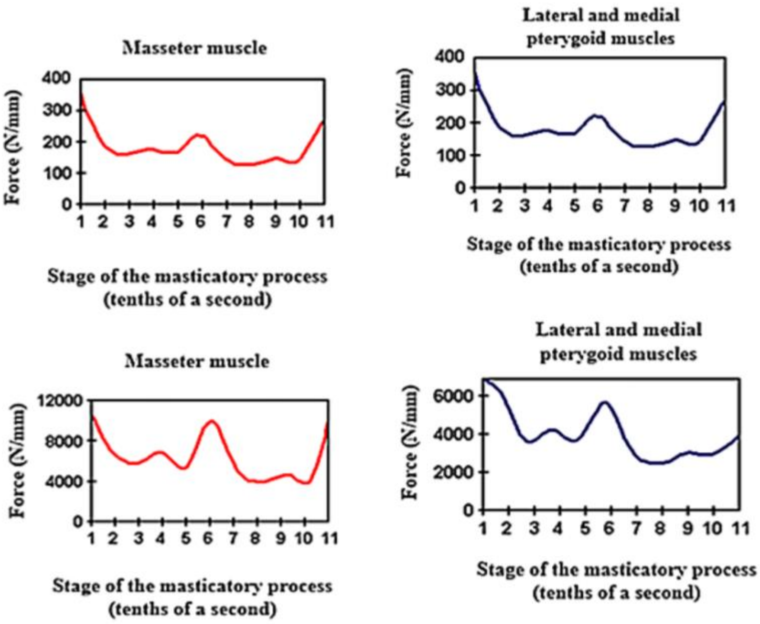


Figure 28. Variation of forces and moments developed by the masseter pterygoid muscles during the masticatory process (a mastication cycle).

The average values of masticatory forces vary from individual to individual and are also influenced by food consistency. In this study, we applied an average force value of 220 N in the premolar area and 400 N in the molar area, introduced in the Autodesk Simulation Mechanical 2014 program (2014, San Rafael, California, US). The model was subjected to loading with a vertical force, applied, in turn, on the occlusal surfaces of each element of the dental bridge: both retainers and pontic. The modeling of an inlay-retained dental bridge was performed, with retainers on teeth 3.4 and 3.6 and pontic on 3.5 (figure 29). The material used for the bridge was a titanium alloy (Ti6A14V) (Dentaurum, Germany).

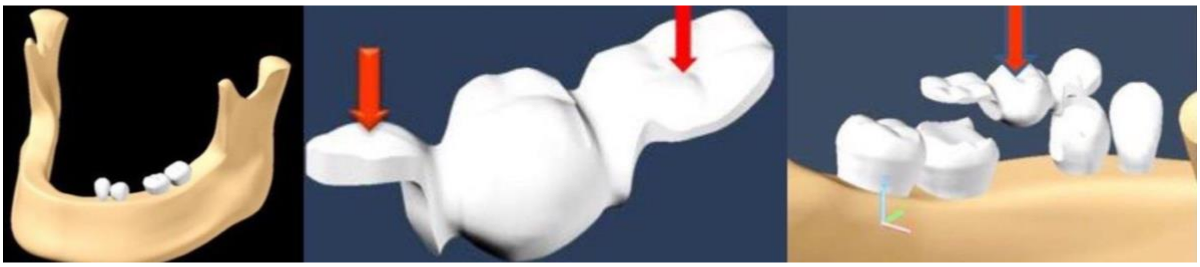


Figure 29. The models of the mandible and the bridge.

The force was applied first in the contact area of the occlusal surface of the inlay at the level of 3.4, then at the occlusal face of 3.6 and then on 3.5, occlusal surface, simulating the pressure induced by the food fragment during the masticatory act.

FEM analysis consists of a mesh realization by splitting a solid volume into finite elements of parallelepiped or tetrahedron shape. Each element behaves individually, with the same characteristics as the base material. Depending on the pressure applied to every element, a specific load or temperature will be exerted and transmitted to the adjacent elements through nodes. For an enhanced accuracy of results, a condition was imposed for the mesh realization: the length between two nodes must always be the same. The model was exported to Autodesk Simulation Mechanical 2014 with a file ending in*.*Sat. These files are opened one by one in Autodesk Simulation Mechanical 2014. After determining the type of analysis (static stress), the mesh command was given.

Depending on the objectives of the analysis, the used material properties were: modulus of elasticity, Poisson's ratio and density. The values for these parameters were taken from the literature (Smielak et al., 2016) (table X).

Table X. Material characteristics for each element of the structure subjected to finite element analysis.

Element	Modulus of Elasticity (MPa)	Poisson's Ratio	Density(kg/m3)
Bone	13,800	0.30	1450
Dentine	18,600	0.31	1900
Ti6A14V alloy	110,000	0.40	4381

We analyzed the tensions induced as a result of the application of these forces, on each element of the bridge, in the contact areas located between retainers and pontic and also on abutment teeth.

For the area where the bridge is in contact with the food fragment, during mastication, it is considered that there is no degree of freedom, and restrictions will be placed for all six movements. In Autodesk Simulation Mechanical 2014, these types of supports are represented by triangles.

Results

Once all the input data of the models were established, the analyze command was given. The results of the finite element analysis follow, according to the determination of loads applied to each area of the dental bridge. First, the distribution of deviatoric stresses (von Mises tensions) at the pontic level was analyzed when the reaction force,which opposes the muscular force, is located in the area of the missing premolar, 3.5 (figure 30).

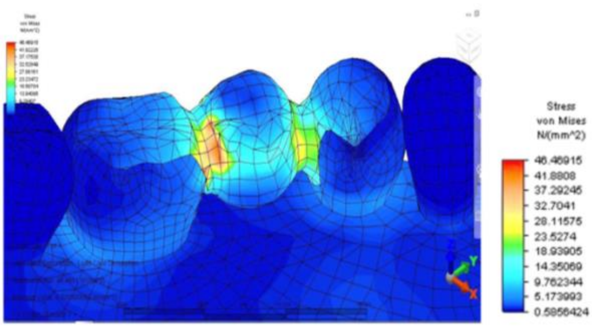


Figure 30. Tensions distribution at the bridge level, when the reaction force is placed in the 3.5 area.

From the model, we observed a higher tension on the prosthetic construction at the margin between the bridge and abutments. This phenomenon is related to the difference between the higher modulus of elasticity of the bridge alloy and the modulus of elasticity of abutment teeth. Furthermore, higher tensions develop at the junction between the bridge elements, and the maximum value is 46,469 MPa, between molar 3.6 and premolar 3.5. This high value of stress is explained by the smaller surface of the junction area.

When analyzing stress values on abutment teeth, respectively molar 3.6 and premolar 3.4, they have a maximum value in the cervical area of the junction between teeth and bridge: the value of 14.456 MPa is equally distributed on the two abutment teeth (figures 31 and 32).

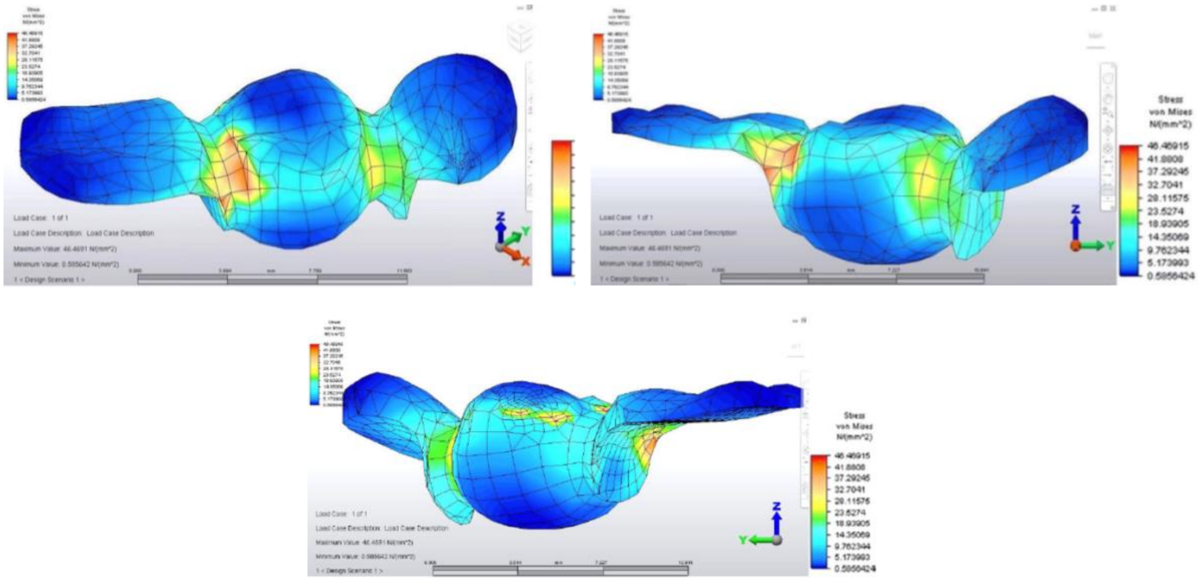


Figure 31. Tension distribution at the bridge level in three directions: axonometric, right and left, when the force is placed in the 3.5 area.

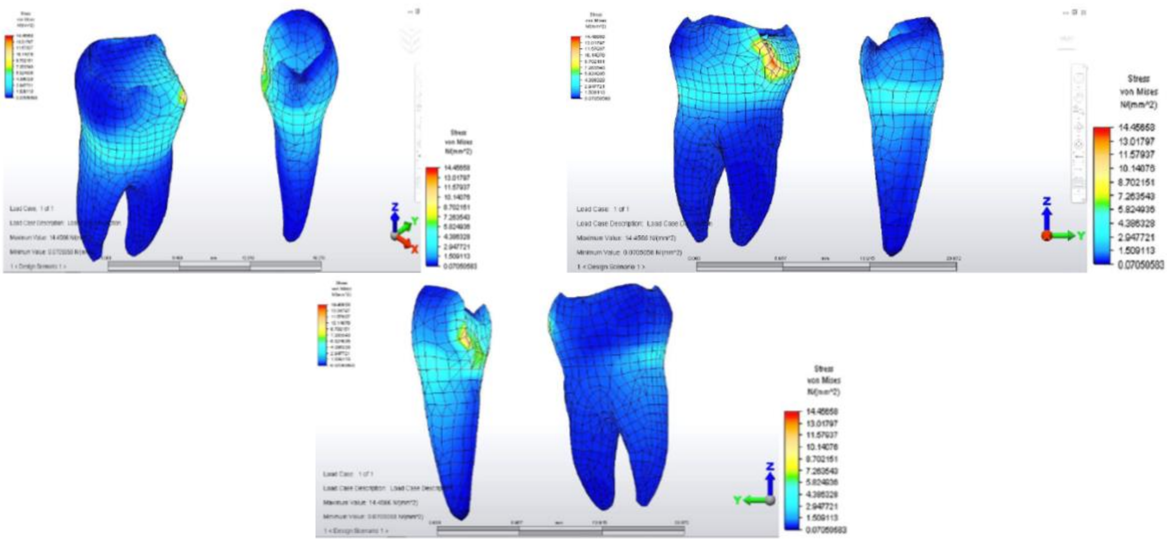


Figure 32. Tension distribution at the abutments level in three directions: axonometric, right and left when the force is placed in the 3.5 area.

Distribution of tensions at bridge level was then observed in the situation where the reaction force, which opposes the muscular force, is placed in the area of molar 3.6 (figure 33).

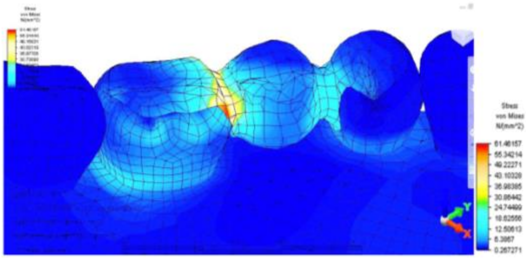


Figure 33. Tension distribution at the bridge level when the reaction force is placed in the 3.6 area.

The distribution of stresses at the level of the dental crown revealed that there is increased stress at the junction area between the pontic and the retainer, on molar 3.6; its value of 61.461 MPa, being 1.5 times higher than in the previous case. Abutment teeth are subjected to a maximum tension of 15.054 MPa, the higher value being encountered in molar 3.6, both in the contact area with the bridge and in the area of contact with the mandibular bone, toward molar 3.7 (figures 34 and 35).

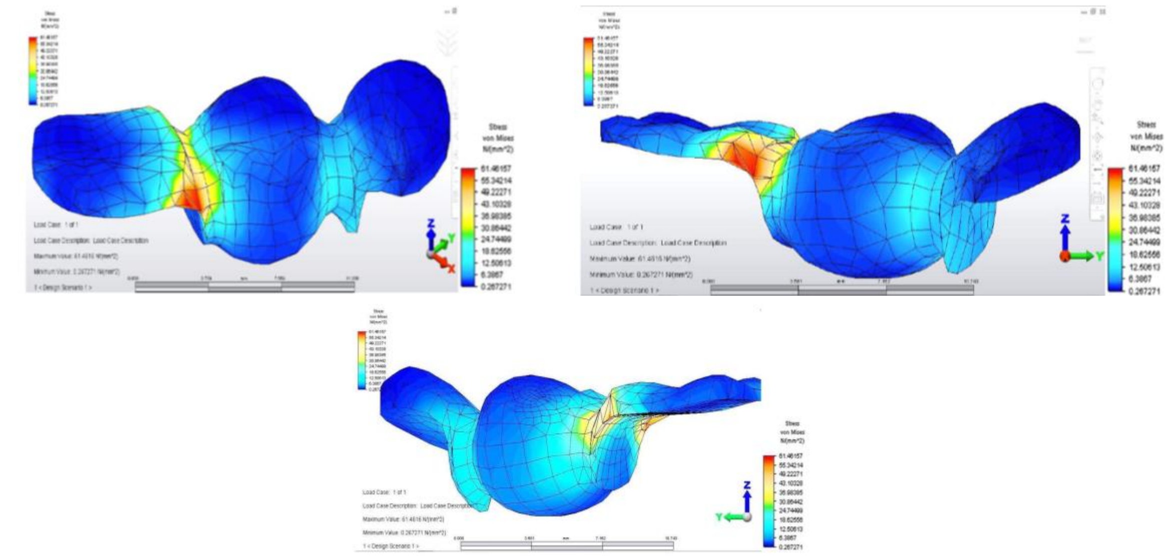


Figure 34. Tension distribution at the bridge level in three directions: axonometric, right and left, when the force is placed in the 3.6 area.

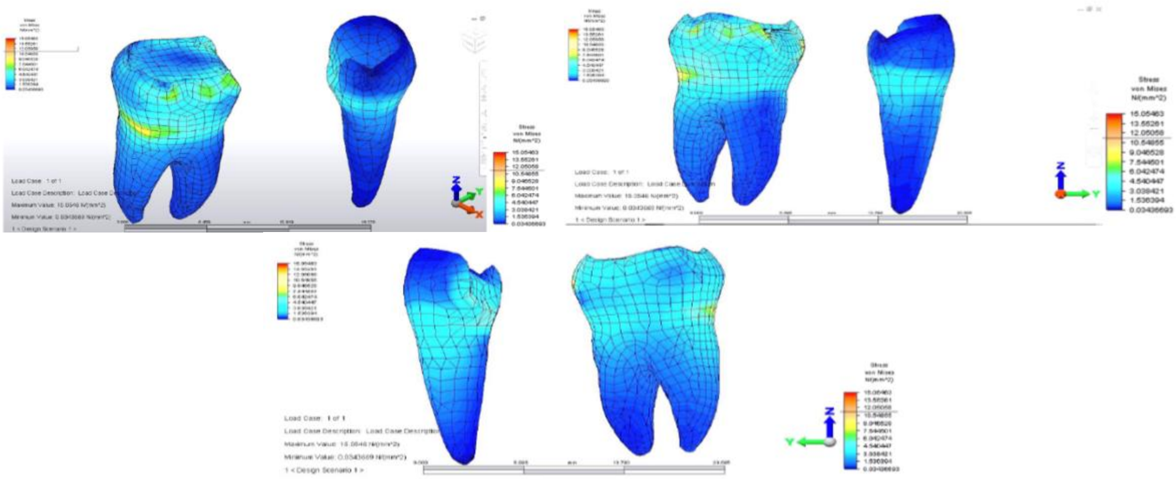


Figure 35. Tension distribution at abutments level in three directions: axonometric, right and left when the force is placed in the 3.6 area.

Regarding analyzing tensions in the mandible-abutments-dental bridge complex, when the reaction force acts on premolar 3.4, a tension jump is observed between the dental bridge and the teeth. This inequality is more evident at the junction between premolar 3.5 and the inlay applied on the occlusal surface of premolar 3.4. As a resuult of the reaction force exerted on tooth 3.4, the mandibular bone also supports a significantly higher tension (figure 36).

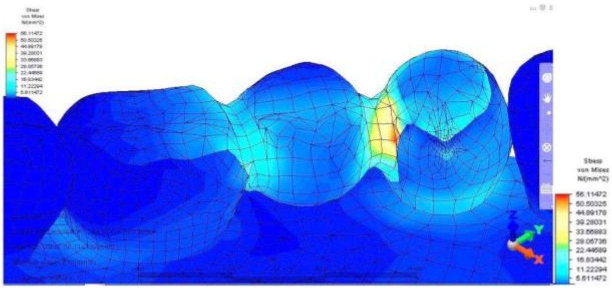


Figure 36. Tension distribution at the bridge when the reaction force is placed in the 3.4 area.

The dental bridge has an asymmetric stress distribution due to the reaction force, which has a maximum value of 56.114 MPa. However, the value is lower when the load is applied on the molar but higher when the force acts on the pontic. This is due to the greater distance of the premolar from the rotation center and also as a result of the direct action of the reaction force on premolar 3.4.

The pressure on abutments is also unevenly distributed. Stress distribution has a maximum value (12.553 MPa) on the premolar on which the reaction force acts. In addition, as in the case of applying for support on the molar, a higher value of tension is observed in the upper area of the root of premolar 3.4, towards the canine.

Both in this situation and in the previous case, the direct action of the reaction force on abutments also determines a tilt of the supporting teeth (figures 37 and 38).

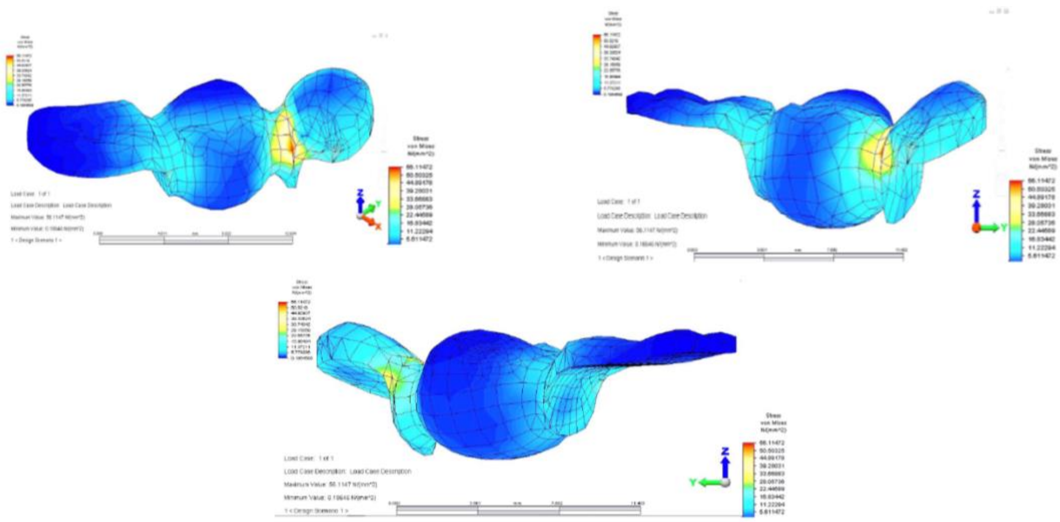


Figure 37. Tension distribution at the bridge level in three directions: axonometric, right and left, when the force is placed in the 3.4 area.

If the load is applied to premolar 3.4, the mandibular bone has slightly higher tension values in the loading area. If the load is applied on molar 3.6, a jump in tension values is observed between the dental bridge and abutment tooth (figure 38).

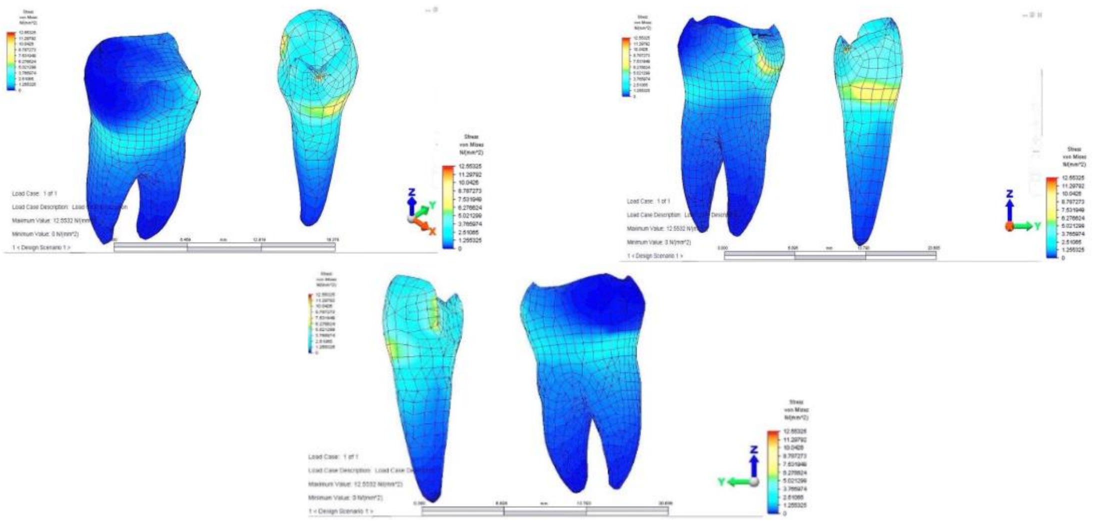


Figure 38. Tension distribution at abutments level in three directions: axonometric, right and left when the force is placed in the 3.4 area.

Discussion

The finite element analysis, being a purely mathematical method, has a series of disadvantages because it imposes certain simplifications, which lead to a certain degree of approximation of results. This type of study does not take into account several im-portant parameters that may influence clinical longevity of fixed prosthetic rehabilitation: anisotropy and heterogeneity of alveolar bone, periodontal structures, the viscoelastic response of periodontal structures to functional stresses, coefficients of thermal expansion of analyzed structures, the fatigue effect manifested by prosthetic restoration materials, the complexity of masticatory forces regarding their application point, intensity, summation of action forces with neighboring forces (Ferreira et al., 2011). In addition, the physiological mobility of supporting teeth and particularities of the mandibular bone were not taken into account- density, height, profile (Ferreira et al., 2011).

Several authors reported that single implants with fixed prosthetic rehabilitation are the gold standard in the case of mono-edentulism in terms of success rate, patients' reported outcomes and marginal bone loss (Sanz-Sánchez et al., 2018; Cosola et al., 2020).

In our study, the models were subjected to loading with a constant vertical force applied to different points on the occlusal surface of the bridge. However, in a real-life situation, masticatory forces are variable according to an individual's food consistency and muscle activity.

Despite these limitations, finite element analysis provides valuable information and insight into the area of biomechanical research and offers clinical studies a base for devel-opment (Kareem et al., 2013; Al-Quran et al., 2011).

For this study, we chose to model an inlay retained dental bridge due to this being a model less studied in the literature. Furthermore, clinicians are reluctant to use this type of restoration because of a higher clinical failure percentage as a result of being a more technique-sensitive prosthetic solution. On the other hand, it is an important addition to the therapeutic options employed in clinical practice due to the fact that it can be used as a provisional prosthetic rehabilitation method during the 4-months period for bone healing and osteointegration of a dental implant (Cao et al., 2021). For this type of prosthesis, the most frequent failure causes are marginal leakage and debonding of restorations when compared to conventional fixed dental prostheses and single crowns supported by implant (Chen et al., 2017). Conversely, regarding advantages, it is a more conservative approach, as it can be applied to patients with contraindications of implant placement, and if executed properly, has a high success rate (Bömicke et al., 2020).

In our study, when first developing the analysis, we evaluated the distribution of deviatoric stresses (von Mises tensions) at the pontic level, when the reaction force, opposing the muscular force, is located in the missing premolar 3.5 area. This phenomenon occurs due to the difference between the higher modulus of elasticity of the bridge alloy and the modulus of elasticity of abutment teeth. According to Hooke's law, at the same specific deformation, located at the tooth-restoration interface and at different modulus of elasticity, higher stresses result in the prosthetic restoration. We noticed higher tensions developing at the bridge elements junction, the highest value being between teeth 3.6 and 3.5. This high value of stress is explained by the smaller surface of the junction area, which in turn could constitute a potential fracture point. This result is in concordance with other studies in the literature (Thompson et al., 2011).

Moreover, when evaluating the mandible-abutments-dental bridge as a whole, with the application of a reaction force on premolar 3.4, a tension jump is observed between the teeth and the dental bridge. This disparity is more obvious at the premolar 3.5 and the inlay applied on the occlusal surface of the junction with 3.4. The force is further transmitted to the mandibular bone due to increased stress, which upholds a considerably higher tension.

Results similar to ours were obtained in a study that analyzed three interim restorative materials by the FEM method regarding stress resistance. The authors found that the biggest tensile stress magnitude, regardless of the restorative material, was in the region of the prosthetic connector, and the highest stress peak was observed in resin composite, followed by polyetheretherketone and acrylic resin (Campaner et al., 2021).

The asymmetric stress distribution of the dental bridge is due to the placement of the reaction force. Thus, when the load is applied to the molar, the value is lower. However, it is higher when the force is placed directly on the pontic. This situation can be explained because the premolar is further from the rotation center and the reaction force, which acts directly on tooth 3.4. Moreover, the abutments have an uneven stress distribution, the value being elevated on the premolar on which the reaction force acts, and an augmented value of tension is noticed in 3.4, towards the coronal area of the root, near the canine. In both analyzed scenarios, there is a tilt of the supporting teeth caused by the direct action of the reaction force on abutments.

A study by Bömicke evaluated the load-bearing capacity, load at initial damage and the failure pattern of posterior resin-bonded fixed dental prostheses to replace a maxillary first molar fabricated from veneered cobalt-chromium, veneered zirconia and monolithic zirconia. Of all tested models, veneered resin-bonded fixed prostheses were more prone to cracking of the veneer component (Bömicke et al., 2018). Other authors observed similar results, who compared fracture resistance of veneered zirconia and metal-ceramic inlay-retained fixed dental prostheses and pinpointed the veneer as being the weakest component (Mohsen, 2010; Kilicarslan et al., 2004).

Another study, which used the finite element method aimed at testing materials to restore a missing mandibular first molar, found no difference between a posterior inlay-retained full zirconia fixed dental prosthesis and a chromium cobalt substructure, porcelain coating, and adhesive resin as wings. The authors applied a load of 400 N and observed a slight advantage regarding stress-bearing for zirconia, however, not significantly when compared to the chromium cobalt substructure and porcelain coating (Yossef et al., 2018).

A study that analyzed tensile stress between restoration-cement, cement and cement-cavity observed that the tensile stress was directly proportional to the restorative materials elastic modulus. Thus, a more rigid cement material increases tensile zones in the layer but decreases the stress between prosthesis and cement. The highest stress concentration between restoration and cement was observed in the molar cavity when compared to the premolar (Tribst et al, 2019).

Other factors that could further influence fracture resistance are the design of the preparation, framework design, and surface treatments of fixed dental prosthesis (Bakitian et al., 2020; Malysa et al., 2021; Ciocan-Pendefunda et al., 2020). A study demonstrated that the highest fracture resistance values were observed in the case of the butterfly wings design followed by inlay and box designs (Samhan, Zaghloul, 2021). Furthermore, the additional surface treatment by sandblasting and tribochemical silica coating of zirconia surfaces displayed the highest mean fracture resistance values when compared to Er, Cr: YSGG laser (Samhan, Zaghloul, 2021; Alpízar et al., 2020).

Bone density and width of maxillary bones in the edentate area have an important impact on the choice of the future prosthetic appliance, which can be applied. Thus instruments, which analyze these parameters are of utmost relevance, especially when considering implant placement. Furthermore, a mechanical risk evaluation before plac-ing inlay-retained dental bridges or before placing other therapeutic options, especially implant treatment using endoral radiographs, ortopanoramics and cone-beam computer tomography and other paraclinical examinations, should be an obligatory step in treatment planning (Cosola et al., 2021; Kullman et al., 2007).

The most fragile part of the bridge is represented by the junction between the bridge body and aggregation elements; the smaller the section of this area, the more prone it will be to fracture (Lakshmi et al., 2015; Kale et al., 2020). Our study confirmed these results; furthermore, we also emphasized the distribution of forces on the bridge elements and on abutments, highlighting the areas of maximum load, as clinical maneuvers, such as periodontal instrumentation, can further weaken the resistance of abutment teeth (Solomon et al., 2016).

Knowing the vulnerable areas, clinicians wil1 have useful information for designing such a dental bridge and will have the opportunity to increase stability and retention.

The results of our study show that the inlay-retained dental bridge represents an optimal therapeutic solution, in terms of the resistance of abutments, with the added benefit of an important economy of dental tissues.

Conclusions

The finite element analysis demonstrates that stress determined by the loading force is not able to cause damage to the prosthetic device or to abutment teeth. However, special attention must be paid to its design, especially in the connection area between the bridge elements, because connectors and retainers represent the weakest parts.

Within the limits of this preliminary study, the inlay-retained dental bridge for single-tooth replacement is a viable alternative, not only from a clinical point of view as the integrity of dental tissues are preserved to a very large extent but also from a biomechanical point of view. Thus, it can be considered an optimal economical solution for treating class III Kennedy edentation in young patients or as a provisional pre-implant rehabilitation.

1.2.3. Fixed prosthesis- The influence of food consistency on the abutment teeth in fixed prostheses a FEA study

Aim of the study

The modeling was done starting from the hypothesis that the dental elements are deformable structures under the action of various variable demands such as intensity, application point (Gao et al., 2006; Molin et al., 2007).

Material and method

A FE model representing a single tooth gap in the lateral left mandible, represented by the second premolar was created. The first premolar and first molar served as abutment teeth. The missing premolar was replaced by one unit pontic. The 3D images of the bridge with full crowns as retainers were obtained using a contact scanner and computer aided design (CAD) system (figures 39, 40).

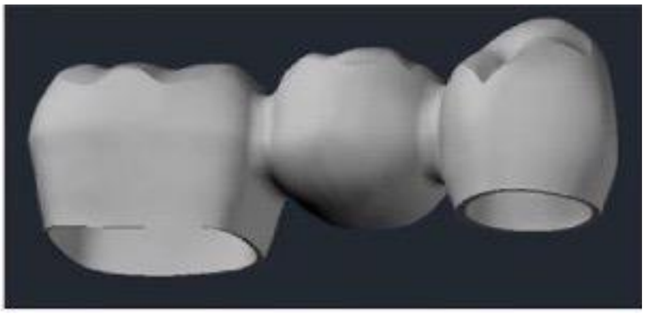


Figure 39. Model of the dental bridge

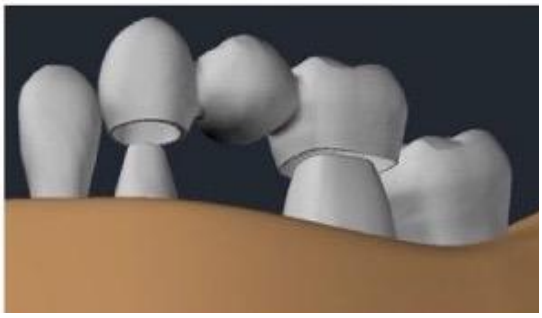


Figure 40. Model of the bridge with full crowns on the abutments

Mesh Generation

Meshing is a process that discretifies a certain solid volume in finite elements of the parallelepiped or tetrahedron type. Each element behaves as an entity with the same characteristics as the base material. After the type of finite element was chosen the discretization can be done manually or through a program (Pesqueira et al., 2014; Vitalariu et al., 2007). In our study the Autodesk Simulation Mechanical 2014 was used to perform the model. Load application considered the maximum force developed by the masseter and pterygoid muscles. The action of the forces developed by the manducatory muscles during mastication produces reaction forces in the temporomandibular joint and on the contact area between occlusal surfaces and the food. Depending on the loading on an element, it will support a certain stress and transmit it to the neighboring elements through the nodes. Although, the muscle activity and craniofacial morphology affect the occlusal load in actual clinical situation, it is difficult to simulate individual muscle forces to FEA modeling. So, usually vertical or oblique load on the teeth is used as an input load in FEA (Liu et al., 2014; O'Mahony et al., 2001).

The model is exported to Autodesk and after determining the type of static stress, the mesh command is given. Absolute mesh size and absolute mesh dimension are set to l mm for the purpose of an accurate analysis. In order to get accurate results with the finite element analysis, the loads should be similar to the physiological ones. Stress levels were calculated according to the Von Mises criteria for each node. The geometry of the healthy standard tooth as abutment has been taken from literature. The prepared surfaces of the abutments were: 14.015 mm^2 for premolar and 17.56 mm^2 for the molar. The analyzed model is presented in figures 41 and 42.

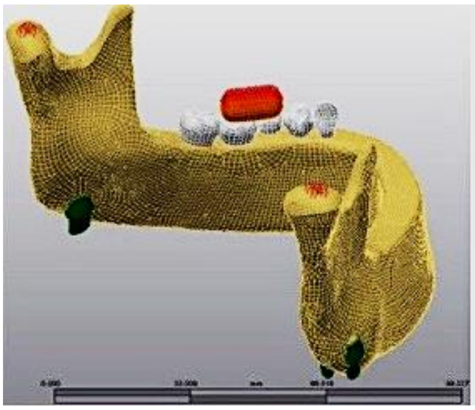


Figure 41. Model of the mandible with the bolus applied on the bridge

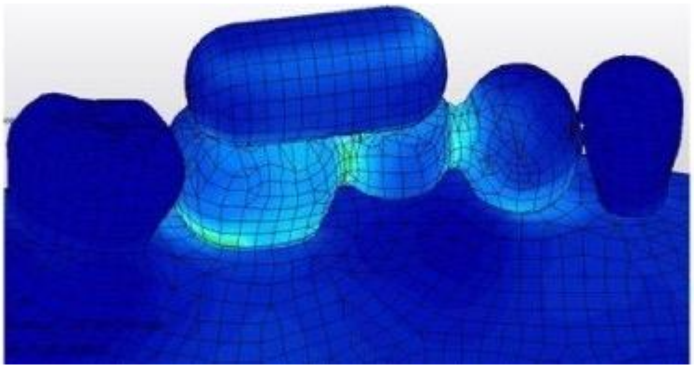


Figure 42. Model of the mandible with the bolus applied on the pontic and abutment 3.6

A more realistic modeling situation is the one in which a deformable food fragment is applied on the bridge, thus lowering the direct loading exerted on the dental bridge and, implicitly, on the abutment teeth (Finkelstein, Ambrosius, 2015). We surveyed the stress induced by different food consistency with elasticity modulus between 0 MPa and 20000 MPa. Every finite element was ascribed with the biomechanical caracteristics of the component represented by the group (Modulus of elasticity, Poisson's ratio). The differences in elastic modulus are believed to affect the clinical performance of the bridge. All the materials were assumed to be isotropic, homogeneous, and linear elastic. For the bridge we choosed a Ti alloy due to its high biocompatibility and biomechanical behaviour (Diaconu-Popa et al., 2017). The properties of materials used into the simulation were adopted from those available in the literature (table XI) (Eick et al., 2007).

Table XI. Material properties used in this study

Element	Elasticity modulus [Mpa]	Poisson modulus	Density [kg/m^3]
Bone	13800	0.30	1450
Dentin	17600	0.25	1900
Ti6A14V	110000	0.40	4381.7

Oral rehabilitation is inherently difficult, due to the functional and parafunctional forces within the mouth that result in extremely complex structural responses by the oral tissue. The applied forces for this simulation were F = 400-800N (on the molar), F = 220-450N (on the premolar). The force value was increased every 100 MPa for each determination and the maximum value in abutments was recorded.

Loading conditions were vertical and distributed on a15 degrees to the vertical and concentrated. The principal stresses were calculated and compared for the retainers (first molar and first premolar) and pontic (second premolar).

Result and discussions

The results obtained from a FEA on the restored system contain information about the stress distribution of each component of the restoration, instead of only a single value of failure load typical of in vitro results. A correct interpretation of FEA results should be based on the stresses and strength of each component of the system.

For the analyzed items (dental abutments, dental bridge) a similar stress distribution is observed. The values for von Misses stresses were 54,33 MPa into the bridge and 15.798 MPa in the supporting teeth (figures 43, 44).

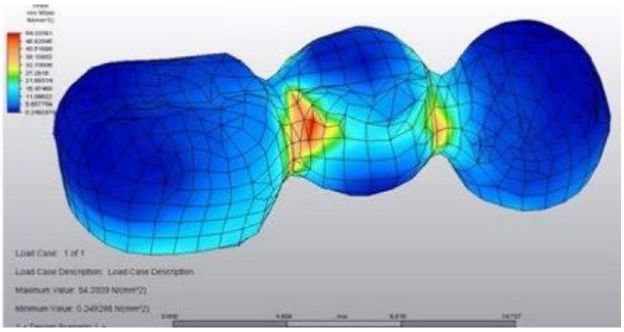


Figure 43. The von Misses Stress distribution and values registered on the bridge.

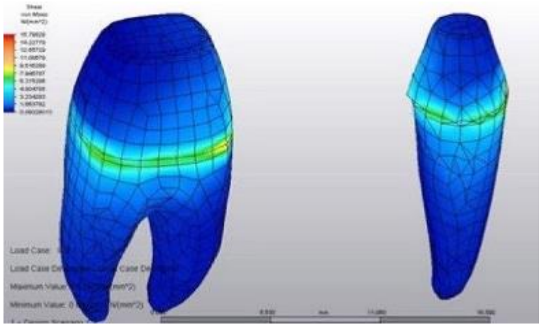


Figure 44. The von Misses Stress distribution and values registered into the abutments.

Upon to the analysis of the forces acting on the bridge, we noticed certain stress concentrators,especially between the pontic and the abutment 3.4 when the food fragment was located on the occlusal surface of the mesial abutment, and on the distal surface of the abutment 3.6 when the food fragment was placed on the occlusal surface of the distal abutment, indicating the highest stress area, therefore the highest breaking risk.

Evolution of the highest tensions into the abutments for variable modulus elasticity of the foodis presented in figure 45. No significant stress was registered until 200 MPa modulus of elasticity, when the fist stress value recorded was 8,5 MPa. The maximum von Misses stress value on abutments was 18 MPa, for a modulus of elasticity of the food fragment of 60000 MPa.

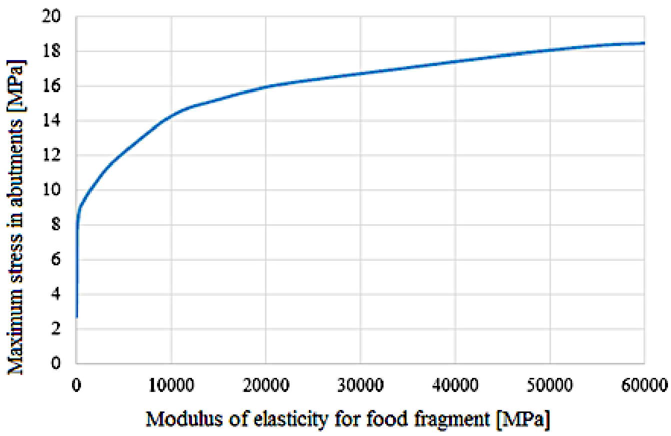


Figure 45. The von Misses stress/food elasticity modulus diagram

Conclussions

From a stress standpoint, the distribution on the abutments has the maximum values on the cervical area and on the bridge the stress is increasing distal between the retainer and the pontic related to the modulus of elasticity of the food fragments. The clinical longevity of the supporting teeth depends therefore also on the alimentary behaviour of the patient. The Finite Element Analysis method has advantages over methods that use real patterns. Analyzes are repeatable, there are no ethical considerations, and working hypotheses can be changed or modified sequentially.

1.2.4. Orthodontics- Using FEM to assess the effect of orthodontic forces on affected periodontium

Aim of the study

The objectives were to monitor the maximum equivalent stresses in the whole tooth-periodontal ligament-alveolar bone complex with various degrees of periodontal damage, to evaluate the maximum stresses that occur in the direction of force application and to assess quantitatively and comparatively the dental displacements produced in different clinical scenarios reproduced through mathematical modeling. Further, we determined whether, due to the morphological features of the frontal teeth, they may behave differently under stresses with forces of equal magnitudes in the same context of periodontal damage.

Materials and Methods

The current research using finite elements involved the realization of three-dimensional models that included the creation of a lower frontal group consisting of four incisors with and without periodontal damage. The dimensions of the teeth, thickness of the periodontal ligament, and specific morphological elements were taken from the literature (Bhalajhi, 2009).

The anatomical features were reproduced in the mathematical simulation using a real-scale Nissin didactic model with periodontal damage (Nissin Dental Products® Inc., Kyoto, Japan). During modeling, the following considerations were taken into accouint: the geometry and morphology of teeth; periodontal structures and dental arches; the physical properties of teeth, periodontal ligament, and alveolar bone; and the magnitude and direction of the force used to simulate orthodontic stress on patients with periodontal damage compared to patients with unaffected periodontium. The application point of the force was set on the center of the facial surface of each tooth. All forces with different magnitudes were applied to each individual tooth.

During the construction of the tooth-periodontal ligament-alveolar bone model we considered from the beginning that the three component elements of the complex have linear elasticity and isotropic properties of the same quality (Hohmann et al., 2011). The definition of the properties and the design of the dental mathematical model was done using the computer-assisted design (CAD) program Catia V5R19 (Dassault Systèmes®, Velizy-Villacoublay France), based on the dimensions and morphology elements taken from the (Bhalajhi, 2009). Table XII summarizes the tooth dimensions that were used.

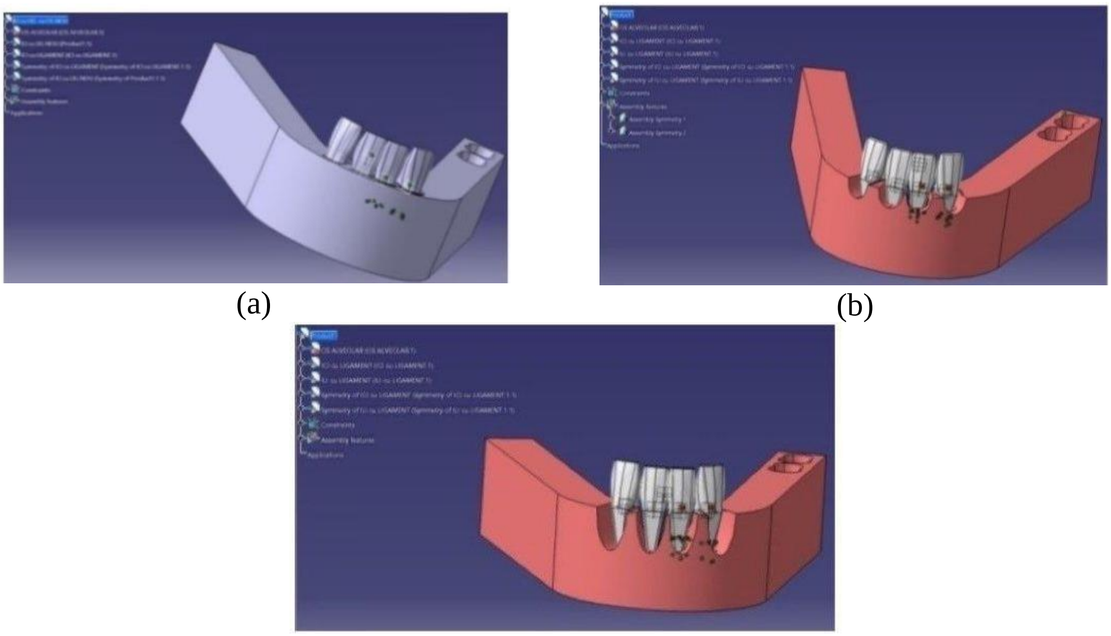
Table XII. Tooth dimensions (Bhalajhi, 2009).

	Lower Central Incisor (LCI)	**Lower Lateral Incisor (LLI)**
Crown length	9 mm	9.5 mm
Root length	12.5 mm	14 mm
Total length	21.5 mm	23.5 mm
M-D crown diameter	5 mm	5.5 mm
M-D crown diameter at cervical level	3.5 mm	4 mm
F-O crown diameter	6 mm	6.5 mm
F-O crown diameter at cervical level	5.3 mm	5.8 mm

M-D = mesio-distal; F-O = facial-oral; LCI = lower central incisor; LLI = lower lateral incisor.

Analysis Model

The stages of preparing the analysis model follow. We first define the analysis model, which involves identifying the shape and geometric dimensions of the structures to be modeled (in our particular case teeth and periodontal structures), constraints induced by the connections with adjacent elements, external loads, and material characteristics. In the next step, we describe the analysis model; the geometric shape and the dimensions of the analysis model are identical to those of the 3D structure of the assembly to be analyzed, associating the limit conditions (primary stability of monoradicular teeth) and loading the model with forces of various magnitudes and directions (Hohmann et al., 2011). In figure 46a-c, we depict the modeling of the mandibular anterior arch under three scenarios: no periodontal damage and 33% and 66% bone loss.



(a) (b) (c)

Figure 46. (a) Mandibular model with no periodontal damage, (b) mandibular model with 33% periodontal damage, and (c) 66% periodontal damage.

Finally, the characteristics of the material were established using data from the literature (table XIII) (Caballero et al., 2015; Kurgan et al., 2014; Xia et al., 2013).

Table XIII. Material characteristics.

Material	Young's Modulus	Poisson's Coefficient	References
Tooth	20 GPa	0.30	Caballero et al. 2015
Cortical bone	13.7 GPa	0.30	Kurgan et al. 2014
Spongy bone	345 MPa	0.30	Caballero et al. 2015
Periodontal ligament	0.71 MPa	0.40	Xia et al. 2013

Using the mathematical model of the mandibular structure and the anterior teeth, we recorded the maximum equivalent stresses (σ ech) that occurred at the level of the whole complex, the stresses in the direction of force application (σ c), and the displacements (f) consequential to the applied forces.

Statistical Analyses

Statistical analyses were performed with SPSS 24.0 for Windows (IBM Corporation, North Castle Drive, Armonk, NY, USA). Between-treatment comparisons were analyzed with the nonparametric multivariate Kruskal-Wallis test, and correlations were calculated with Spearman's rank-order test. Graphs were generated using STATA 16.1 (StataCorp LLC., College Station, TX, USA). A p-value less than 0.05 was considered statistically significant.

Results

The results obtained in the previously described clinical scenarios and translated into a mathematical model are summarized in the tables below for the lower central incisor (table XIV) and for the lower lateral incisor (Table XV).

Representative iconographic elements in various scenarios of force application and lingualization of the lower central incisor (LCI) using a 1 and 3 N force are shown in figures 47-49 and figures 50-52, respectively. Figures 53-55 depict representative icono-graphic elementsfor lingualization of the lower lateral incisor (LLI) using a 1 N force and figures 56 and 57 depict application of a 3 N force.

In the case of no HBL (figure 47), the 1 N force is evenly distributed along the central region of the root of the LCI, both on the buccal and on the lingual areas. This area becomes narrower in the 33% bone loss simulation, particularly close to the center of rotation of the tooth (figure 48), and finally as bone loss reaches 66% the tooth inclines lingually and the area of maximum tension is in the vestibular apical third (figure 49).

When a force of greater magnitude is applied, 3 N, we observed that in case of a healthy periodontium the tissues are able to absorb and compensate for the increased strain, and the areas of maximum stress remain the same as in the case of a 1 N force. However, lingualization of the LCI occurs even at a moderate periodontal bone loss of 33%; in this case the tissues are no longer able to compensate, and the areas of maximum stress are mainly concentrated on the buccal apical third of the root and to a lesser degree in the lingual area (figures 50 and 51). In figure 52, we observe a severe lingualization of the LCI, the stress being concentrated only in the apical vestibular area. The LLI has similar patterns of stress distribution and movement to the LCI and, as the periodontal tissue loss aggravates, so does the lingualization of the teeth.

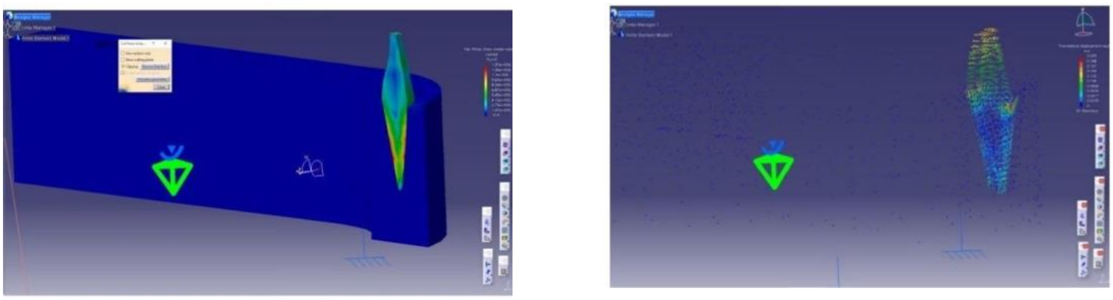
Table XIV. Simulation of lingualization in the lower central incisor according to the applied force and extent of periodontal damage.

Applied Force	**Extent of Periodontal Damage (HBL)**		
	No HBL	33% HBL	66% HBL
	σ ech = 0.0271 MPa	σ ech = 0.73 MPa	σ ech = 2.1 MPa
0.25N	σc = 0.0272 MPa	σc = 0.751 MPa	σc = 2.16MPa
	f = 0.00468 mm	f = 0.124 mm	f = 1.12 mm
	σ ech = 1.37 MPa	σ ech = 2.92 MPa	σech = 8.43 MPa
1N	σc = 1.38 MPa	σc = 2.98 MPa	σc = 8.67 MPa
	f = 0.208 mm	f = 0.497 mm	f = 4.48 mm
	σ ech = 4.12 MPa	σ ech = 8.74 MPa	σ ech = 25.3 MPa
3N	σc = 4.15 MPa	σc = 8.91 MPa	σc = 26 MPa
	f = 0.626 mm	fc1.49 mm	f = 13.4 mm
	σ ech = 6.86 MPa	σ ech = 14.6 MPa	σ ech = 42.2 MPa
5N	σc = 6.94 MPa	σc = 14.9 MPa	σc = 43.3 MPa

	f = 1.04 mm	f = 2.49 mm	f = 22.4 mm

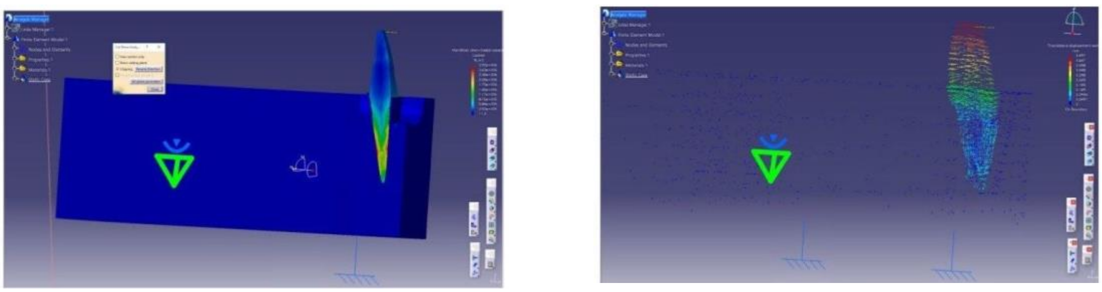
Table XV. Simulation of lingualization in the LLI.

Applied Force	**Extent of Periodontal Damage (HBL)**		
	No HBL	33% HBL	66% HBL
	σ ech = 1.03 MPa	σ ech = 1.4 MPa	σech = 7.67 MPa
0.25N	σc = 0.455 MPa	σc = 0.697 MPa	σc = 3.79 MPa
	f = 0.065 mm	f = 0.198 mm	f = 2.35 mm
	σ ech = 4.16 MPa	σ ech = 5.59 MPa	σ ech = 30.7 MPa
1N	σc = 1.86 MPa	σc = 2.79 MPa	σc = 15.2 MPa
	f = 0.26 mm	f = 0.794 mm	f = 9.41 mm
	σ ech = 12.3 MPa	σ ech = 16.8 MPa	σ ech = 92.1 MPa
3N	σc = 5.39 MPa	σc = 8.37 MPa	σc = 45.5 MPa
	f = 0.782 mm	f = 2.38 mm	f = 28.3 mm
	σ ech = 20.5 MPa	σ ech = 28 MPa	σ ech = 154 MPa
5N	σc = 8.92 MPa	σc = 14MPa	σc = 75.9 MPa
	f = 1.3 mm	f = 3.97 mm	f = 47.1 mm



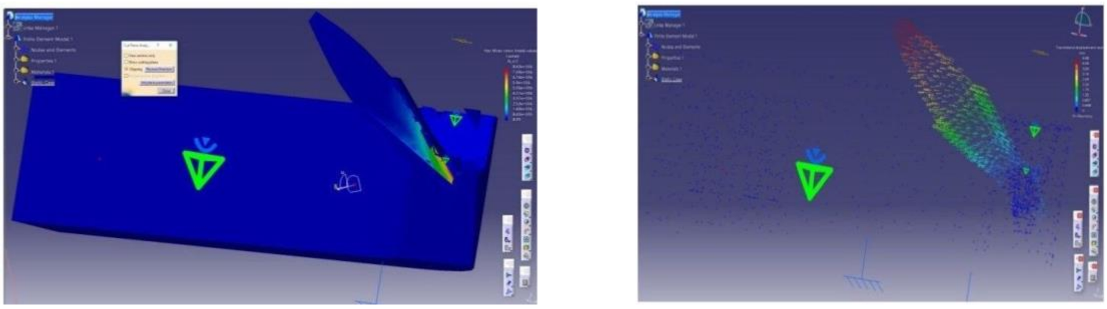
(a) (b)

Figure 47. Lingualization of the LCI using a 1 N force:(a) von Mises tensions, no HBL; (b) tooth movement obtained, no HBL.



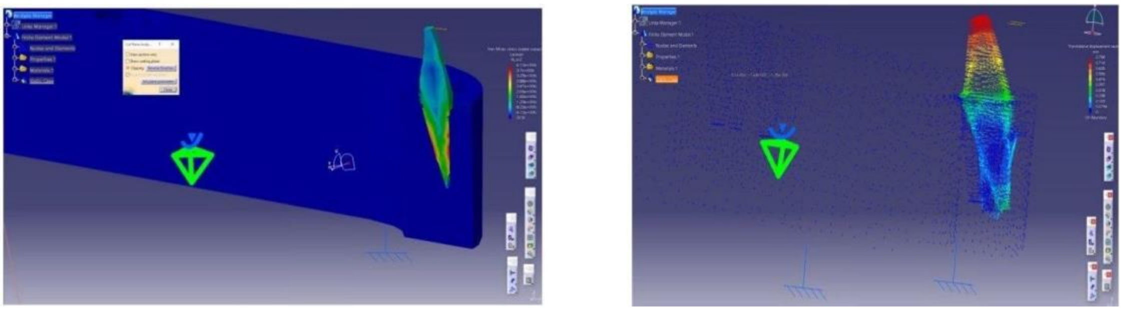
(a) (b)

Figure 48. Lingualization of the LCI using a 1 N force:(a) von Mises tensions, 33% HBL;(b) tooth movement, 33% HBL.



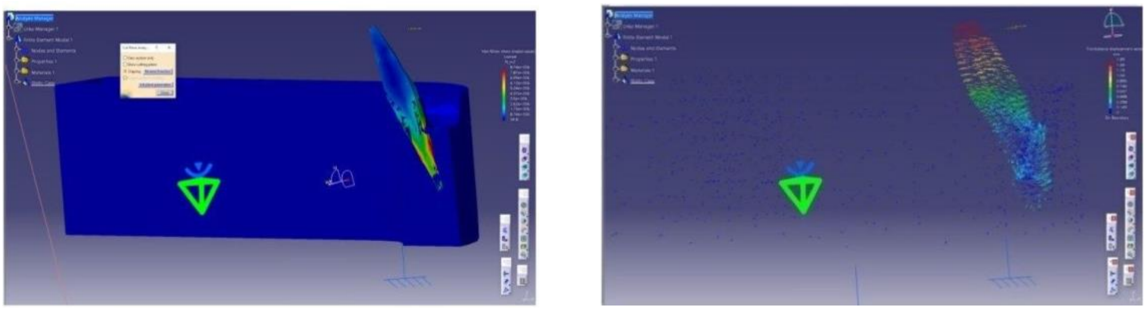
(a) (b)

Figure 49. Lingualization of the LCI using a 1 N force: (a) von Mises tensions,66% HBL;(b) tooth movement, 66% HBL.



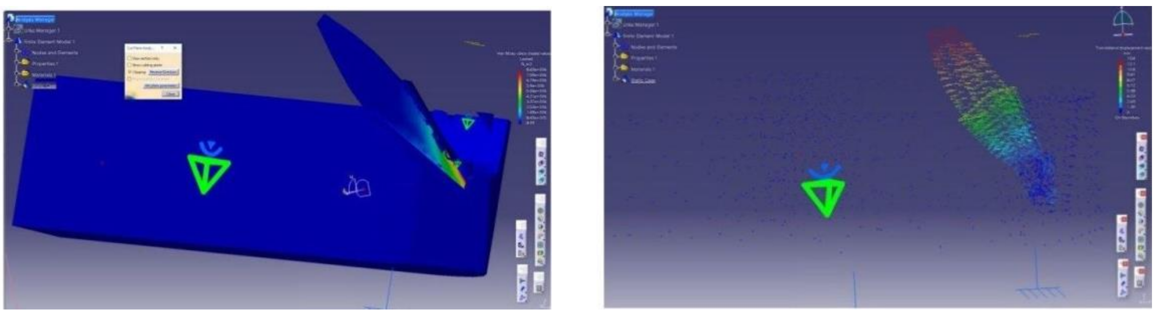
(a) (b)

Figure 50. Lingualization of the LCI using a 3 N force: (a) von Mises tensions, no HBL;(b) tooth movement, no HBL.



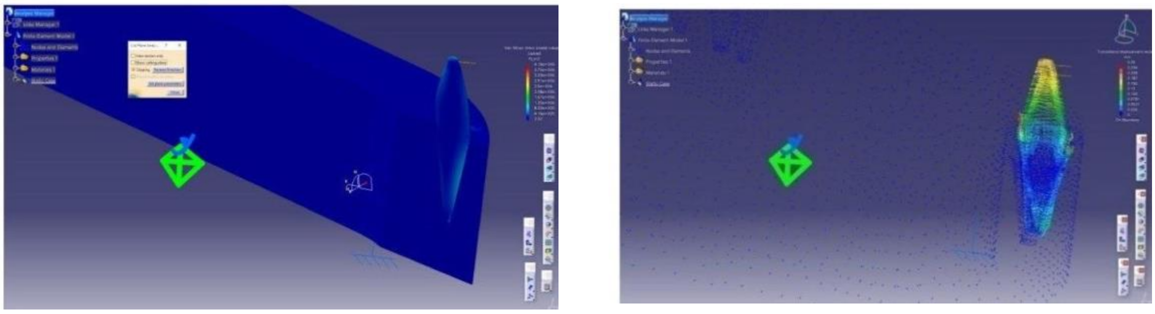
(a) (b)

Figure 51. Lingualization of the lower LCI using a 3 N force: (a) von Mises tensions, 33% HBL; (b) tooth movement, 33% HBL.



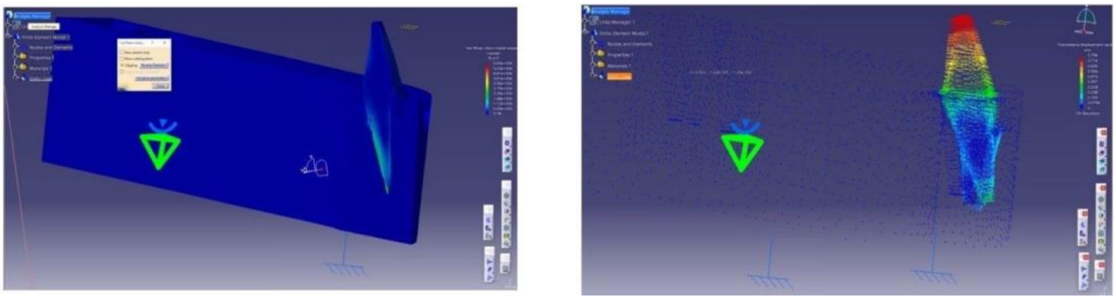
(a) (b)

Figure 52. Lingualization of the LCI using a 3 N force: (a) von Mises tensions, 66% HBL; (b) tooth movement,66% HBL.



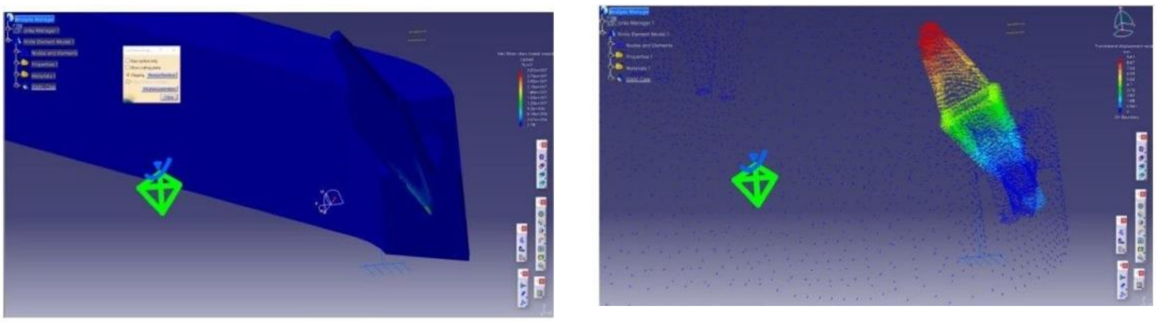
(a) (b)

Figure 53. Lingualization of the LLI using a 1 N force:(a) von Mises tensions, no HBL; (b) tooth movement obtained, no HBL.



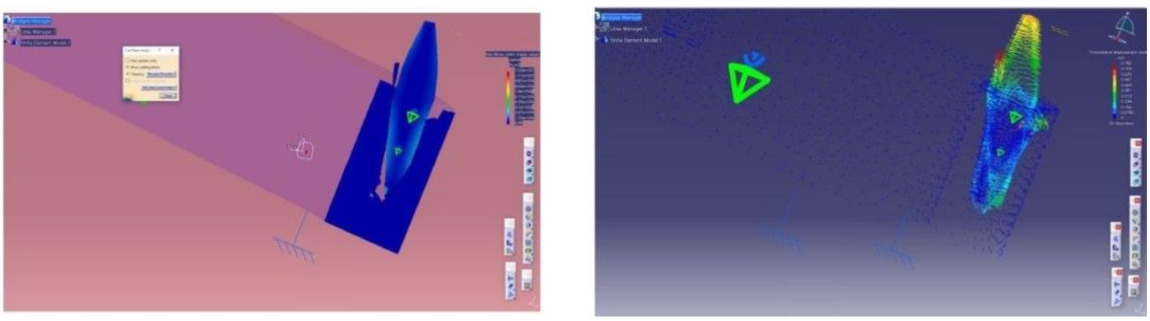
(a) (b)

Figure 54. Lingualization of the LLI using a 1 N force: (a) von Mises tensions, 33% HBL; (b) tooth movement, 33% HBL.



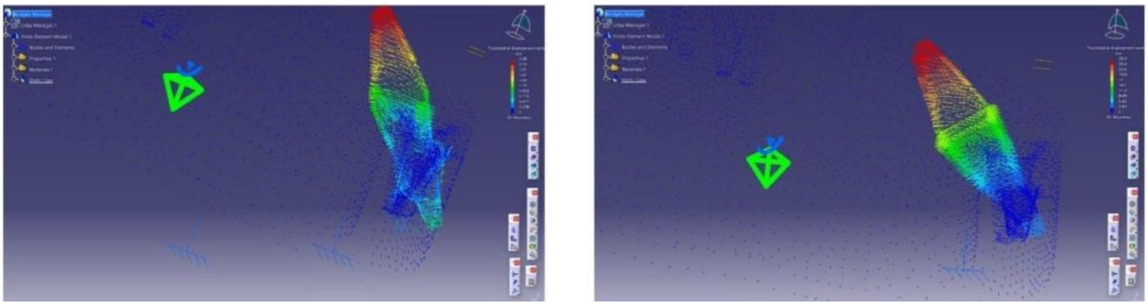
(a) (b)

Figure 55. Lingualization of the LLI using a 1 N force: (a) von Mises tensions, 66% HBL; (b) tooth movement, 66% HBL.



(a) (b)

Figure 56. Lingualization of the LLI using a 3 N force: (a) von Mises tensions, no HBL; (b) tooth movement obtained, no HBL.



(a) (b)

Figure 57. Lingualization of the LLI using a 3 N force: (a) tooth movement, 33% HBL; (b) tooth movement, 66% HBL.

Lower Central Incisor (LCI)

Predictive Factors in the Modification of the Equivalent Tension Values in the Tooth-Periodontal Ligament-Alveolar Bone Complex (σ ech)

The σ ech values show linear growth, based on the force applied in the case of healthy periodontium and when the damage is up to 33%. In the case of 66% periodontal damage, the growth is exponential. The values of o ech differ significantly depending on the applied force (H = 10.665, p = 0.009,95% CI). Using multivariate analysis, we subsequently analyzed the importance of the parameters that influence o ech tension values, the independent variables included were the applied force and the extent of the periodontium damage. The analysis of the results of the multiple correlation in the case of lower central incisor lingualization highlights that both the applied force and the degree of damage have a major effect on σ ech (βf = 0.65, p = 0.003, βAf.P = 0.56, p = 0.008) (table XVI).

Table XVI. Results of the multivariate analysis-partial correlation coefficient σ ech, σ c, and f.

	Correlation Coefficient (Beta)	**Std. Err.** (Beta)	**B**	**Std. Err. B**	**t**	**p** 95% CI
Partial correlation σ ech vs.						
Intercept			-837.143	249.0675	-3.36111	0.008
Applied force	0.659321	0.166887	4.260	1.0783	3.95071	0.003
Periodontal damage	0.560924	0.166887	8.207	2.4416	3.36111	0.008
Partial correlation σ c vs.						
Intercept			-862.383	256.3378	-3.36424	0.008
Applied force	0.656882	0.167272	4.358	1.1098	3.92702	0.003
Periodontal damage	0.562749	0.167272	8.454	2.5129	3.36427	0.008
Partial correlation f vs.						
Intercept			0.656882	0.167272	4.358	1.1098
Applied force	0.485140	0.208293	1.730	0.7429	2.32912	0.044
Periodontal damage	0.611691	0.208293	4.940	1.6822	2.93669	0.016

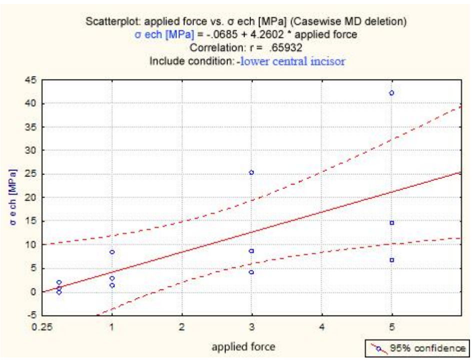
CI, confidence interval; Std. Err., standard error.

Predictive Factors in the Modification of the Tension Values in the Direction of an Applied Perpendicular Force to the Tooth's Vestibular Surface (σ c)

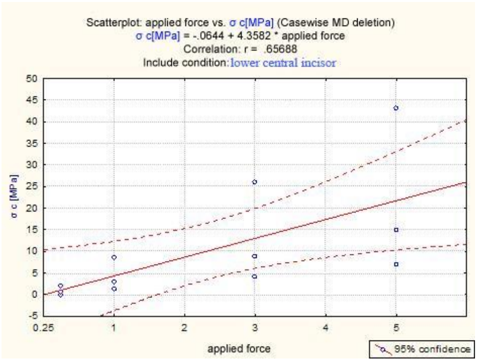
Using multivariate analysis, we determined the influence of σ c tension values with applied force and the extent of the periodontium damage as independent variables. As such, the applied force had a significant impact on the value of σ c for the lower central incisors (βf = 0.65, p = 0.003), with periodontal damage having a significant influence (βAfP = 0.56, p = 0.000.008) (table V). Correlation analysis showed that the applied force had a major impact on f (βf = 0.48, 0.044), as did the presence of periodontal disease f (βf = 0.48, p = 0.044 (βAf.P = 0.61, p = 0.016) (table VI).

Correlation of o ech, σ c, and f Based on the Value of the Applied Force

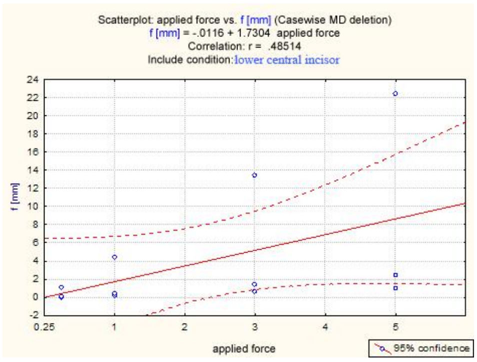
Figure 58 a-c shows that the equivalent tension in the tooth-periodontal ligament-alveolar bone complex (σ ech-r = 0.65) was most affected by the magnitude of the applied force; close behind was tension value in the direction in which the force is applied (σ c - r = 0.65). The recorded displacement values (f-r = 0.48) were not affected significantly by the magnitude of applied force.



(**a**)



(**b**)



(**c**)

Figure 58. Regression line of the correlation (**a**) σ ech, (**b**) σ c, and (**c**) f vs. applied force.

Lower Lateral Incisor (LLI)

Equivalent Tension in the Tooth-Periodontal Ligament-Alveolar Bone Complex (σ ech)

For both lower central and lateral incisors, the o ech values showed linear growth, depending on the force applied when the periodontium was healthy or affected 33%. If the periodontium was affected 66%, the increase of σ ech showed exponential evolution. Correlation analysis showed that both the magnitude of the applied force (βf = 0.56, p = 0.018) and the extent to which the periodontium is affected (βAfP = 0.57, p = 0.017) have a significant impact on the values of σ ech for lower lateral incisors (table XVII).

Tension Registered in the Direction of the Applied Force-Perpendicular to the Tooth's Vestibular Surface [σc]

The multivariate analysis identified the predictive factors in the changes of the *σc* tension values on the direction of application of a force perpendicular to the vestibular surface of the tooth. Correlation analysis showed that both the magnitude of the applied force and the extent to which the periodontium is affected have a significant impact on the values of σ ech and σ c (βf = 0.56, p = 0.018, βAfP = 0.57, p = .017 and βf = 0.55, p = 0.019, βAfP = 0.58, p = 0.016, respectively) (table XVII).

The multivariate analysis revealed the predictive factors in changes of values of displacement as a result of applying a lingualization force. The applied force does not have a significant impact on displacement f (βf = 0.46, p = 0.058), but that the extent βf = 0.46, p = 0.05 of periodontal damage significantly influenced displacement f (βAf.P = 0.61, p = 0.017) (table XVII).

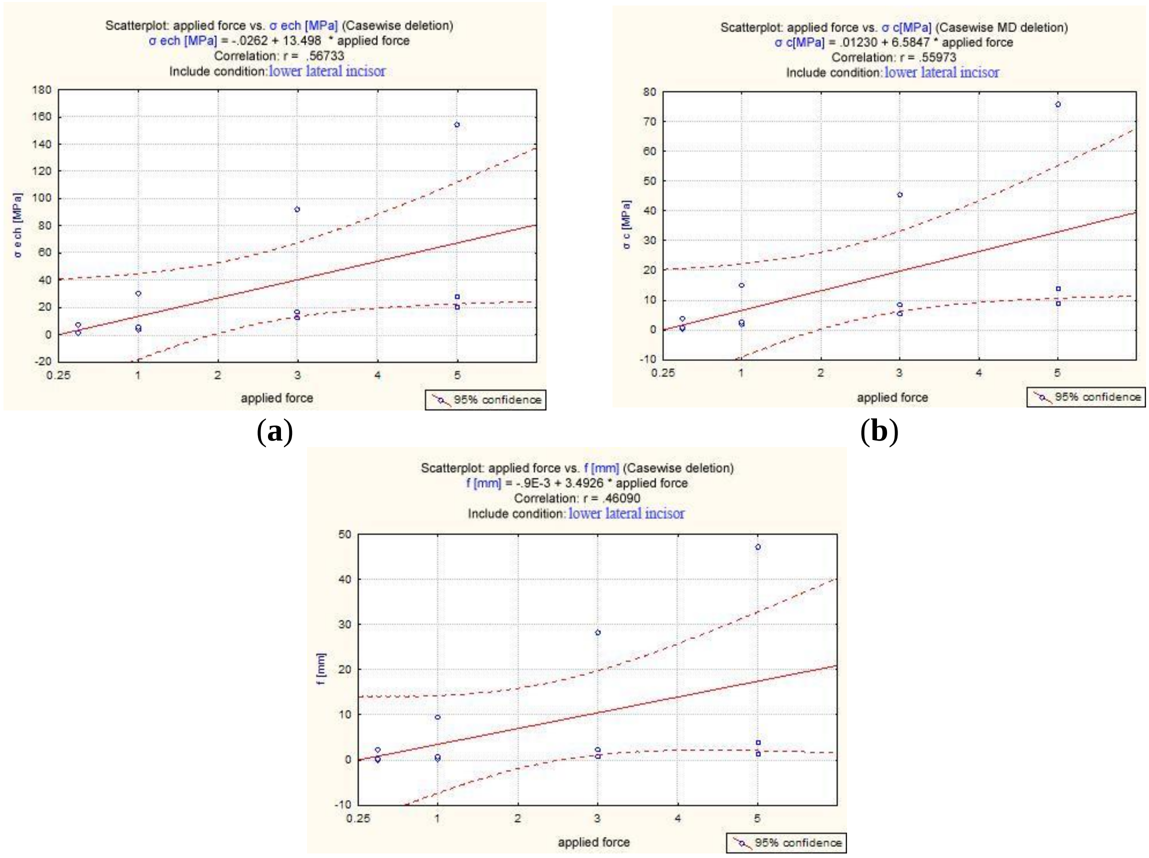
Table XVII. Results of the multivariate analysis-partial correlation coefficient σ ech, σ c, and f.

	Correlation Coefficient (Beta)	**Std. Err.** (Beta)	**B**	**Std. Err. B**	**t**	**p** 95% CI
Partial correlation σ ech vs.						
Intercept			-3142.65	1085.324	-2.89558	0.017
Applied force	0.567328	0.197499	13.50	4.699	2.87256	0.018
Periodontal damage	0.571916	0.197499	30.81	10.640	2.89580	0.017
Partial correlation σ c vs.						
Intercept			-1577.99	535.3633	-2.94752	0.016
Applied force	0.559729	0.197028	6.58	2.3178	2.84086	0.019
Periodontal damage	0.580795	0.197028	15.47	5.2482	2.94778	0.016
Partial correlation f vs.						
Intercept			-1080.60	371.9040	-2.90559	0.017
Applied force	0.460901	0.212483	3.49	1.6101	2.16912	0.058
Periodontal damage	0.617439	0.212483	10.59	3.6458	2.90583	0.017

CI, confidence interval; Std. Err., standard error.

Correlation Analysis of σ ech, σ c, and f Based on the Value of Applied Force

None of the analyzed parameters was significantly influenced by the magnitude of the applied force, values of the tension recorded in the direction of force application (σc-r = 0.55, p = 0.058),values of equivalent tension at the level of the tooth-periodontal ligament-alveolar bone complex (σ ech-r = 0.56, p = 0.054), or values of the recorded displacement(f-r = 0.46, p = 0.132) (figure 59a-c).



(**a**) (**b**) (**c**)

Figure 59. Regression line of the correlation (**a**) σ ech, (**b**) σ c, and (**c**) f vs. applied force.

The values of σ ech presented a uniform increase for no periodontal damage group and for the 33% HBL. However, for the 66% periodontal damage group, σ ech shows an exponential increase. The values of o c showed the same tendency, but for the 66% periodontal damage group, the increase was significantly higher compared with the other two groups. Displacement parameter (f) had increased absolute values that were dependent not only on the magnitude of the applied force but also on the degree of HBL.

Discussion

Currently, there is no consensus as to what the optimal force for orthodontic tooth movement should be; however, most agree that it is up to 1 N (Theodorou et al., 2019; Flores-Mir et al., 2020). Although this may be true theoretically, in practice it is difficult to control and assess the precise force applied to every tooth. As the force magnitude increases, so do the potential unwanted side effects such as undesired tooth movements, external apical root resorption, hyalinization, and patient discomfort (Theodorou et al., 2019; Romanyk et al., 2020; Cuoghi et al., 2019).

Due to the inconsistencies in the literature and because of the theoretical nature of the study,we considered various force magnitudes in our simulation, up to 5 N, to illustrate the effect on periodontal tissues of different force magnitudes on various scenarios of bone loss.In the case of 1 N force,we noted that when the profound periodontium tissues are intact, the forces are evenly distributed along the central region of the root of the central lower incisor, both on the buccal and lingual areas. As the periodontal tissues start to break down, the stress concentrates to a narrower area, mostly around the tooth's center of rotation. Finally, as the bone loss reaches 66% the crown of the tooth is lingualized, while the rootis buccally inclined. The area of maximum tensionis in the vestibular apical third. Even though in all three scenarios the force magnitude was the same (1 N), the biomechanical behavior of the tooth was different due to the contrasting periodontal status: intact, moderate, and severe periodontal breakdown. Our results were similar to those found in the literature that considered orthodontic tooth movement on an intact desmodontium and observed that the stresses were concentrated in the apical root area in the case of the application of a purely intrusive, extrusive, or rotational force (Rudolph et al., 2001; Gupta et al., 2020; Vikram et al., 2012; Li et al., 2019). For the tipping movement, the main stress area was situated at the alveolar crest while for bodily movement, it was throughout the desmodontium (Rudolph et al., 2001). In contrast, others have argued that the morphology of the alveolar bone dictated the stress-strain observations and due to the nonlinear behavior of the desmodontium different areas of compression and tension cannot be detected; thus, light continuous forces are recognized as intermittent by the periodontal ligament (Cattaneo et al., 2009).

In the case of an affected desmodontium, one study reports result similar to ours in the case of applying a 1 N force on an incisor and showed that as the severity of the bone loss upsurges the amount of tooth movement increased to a maximum of 2.60 mm (Zargham et al., 2016).

The lateral lower incisor has similar patterns of stress distribution and movement to the central incisor; as bone loss aggravates, so does the lingualization of the teeth. If the periodontal tissue is intact, it is able to absorb and compensate for the heightened forces to a certain degree, even those exceeding the accepted physiological values for orthodontic tooth movement. However, in the case of a reduced periodontium lingualization is observed, in this case the tissues are no longer able to compensate, and the areas of maximum stress are unevenly distributed. Toms et al. considered both linear and nonlinear models of the periodontal ligament of a mandibular premolar and after applying extrusive and tipping forces examined the minimum and maximum principal stresses and von Mises stresses in the desmodontium. When the periodontium was given nonlinear mechanical properties, the stresses were substantially different from the uniform thickness model; in the apical and cervical area the stresses were significantly increased when compared to the linear model (Toms, Eberhardt, 2003). Considering the fact that in our study the periodontium was linear, a nonlinear analysis might yield even more dramatic results in the case of reduced bone level.

Optimal orthodontic movement should be calibrated to the degree of periodontal disease progression. Strain of anterior teeth is reported to be concentrated in the cervical region at the top of the alveolar crest, and it increases even more as the bone level decreases. Moreover, this strain increases even more in subjects with excessively inclined anterior teeth. This is a common side effect that is usually addressed during orthodontic therapy of periodontally compromised patients. To avoid the deformation of the alveolar ridge crest in these cases, Ma and Li (2021) recommend displacements of less than 0.18 mm for normal alveolar bone, 0.15 mm for 1/3 resorption, and 0.10 mm for 1/3-1/2 resorption.

The values of displacement resulting from the application of force maintain a significant linear increase in our study, coupled with the increase in the magnitude of the applied force, with no significant differences for no periodontal disease and 33% bone loss. However, in the 66% bone loss, the values of f are significantly greater, both compared to the intact periodontium and to the 33% group, depending on the magnitude of the applied force. One study that analyzed the biomechanical properties of desmodontium to assess intrusion through orthodontic force of 0.5, 1, and 3 N found that the location and the applied force levels were statistically significant in theireffects on the modulus; the apical part also had greater stiffness. In this study, however, the authors proposed a heterogenous periodontium in which the modulus varied in relation to location (Uhlir et al., 2017).

The maximum equivalent tension in the tooth-periodontal ligament-alveolar bone complex (σ ech) is most affected by the magnitude of the applied force; close behind is tension in the direction of the force (σ c), but the displacement values (f) were not affected significantly by the magnitude of the applied force.

Another significant aspect that must be taken into account is orthodontic appliance placement (Mascarenhas et al., 2015). Research has pointed out that increasing the length of the brackets' hook can reduce the stress on the periodontal ligament. Thus, a 7 mm-long hook delivered 22 kPa, while a bracket withouit a hook, 80 kPa. Moreover, by the apical angulation of the applied force from 0° to 30° there was a diminution on the effect of the periodontium stress profile (Ammar et al., 2011). A more streamlined tooth movement can be obtained, with less stress along on the desmodontium, by simply increasing the length of the bracket hook due to the application of the force closer to the center of resistance.

In the lower incisor model, the maximum equivalent tensions and tensions in the direction of the applied force show linear growth when the periodontium is healthy or affected 33%; however, if the periodontium is affected 66%, the increase shows an exponential progression, with significant higher values than those encountered in cases in which the periodontium was unaffected or affected to a lesser degree. Multivariate analysis yielded the predictive factors in the changes of the o ech and o c values in the tooth-periodontal ligament-alveolar bone complex. The magnitude of the applied force and the extent to which the periodontium is affected have major impact in the case of lower incisors. However, in the case of displacement as a result of applying a lingualization force, correlation analysis showed that only the extent of periodontal damage significantly influences displacement, but the applied force does not. We also showed that none of the analyzed parameters was significantly influenced by the magnitude of the applied force, values of the tension recorded in the direction of force application, values of equivalent tension at the level of the tooth-periodontal ligament-alveolar bone complex, or values of the recorded displacement.

A similar study to ours in design that analyzed a lower premolar model assessed the compressive stress quantitatively and qualitatively in periodontium for a model of gradual periodontal breakdown (0-8 mm) under orthodontic movements. The authors carried out correlations between bone resorption level, type of applied forces (intrusion, extrusion, rotation, tipping, and translation), and decrease of force magnitude. They found that the highest apical and cervical stress was caused by translation and rotation, whereas intrusion determined the lowest cervical stress to be higher than apical stress. For in-intact periodontium, only intrusion and extrusion exhibited compressive stresses lower than maximum hydrostatic pressure (MHP) and maximum tolerable stress (MTS). In reduced periodontium, however, compressive stress (except for intrusion) exceeded these two parameters; thus, in the case of periodontal breakdown, lighter forces of 0.2 N are considered safer, and anything exceeding 0.6-1.2 N may compromise the desmodontium by producing stresses surpassing both maximum tolerable stress and hydrostatic pressure. The authors did not observe a correlation between the applied force, compressive stress increase, and periodontal breakdown, applicable to all five movements (Moga et al., 2021). These results are confirmed by our studies as we could not find a correlation between these parameters.

Lingualization in the lower frontal group is more important once the loss of attach-ment increases, both in terms of tensions in the system and in terms of the displacement per se, and, from a clinical point of view, in terms of unwanted side-effects. One of the possible deleterious effects is orthodontically induced inflammatory root resorption. When analyzing linear to nonlinear models, a study that considered pure intrusion, buccal tipping, and their combination, applied with either a light (0.25 N) or a heavy (2.25 N) force, found notable differences in stress distribution patterns and magnitude. None of the light-force models reached the critical compressive hydrostatic stress when a nonlinear periodontal ligament was considered, whereas all the heavy-force models reached it. Moreover, the authors observed that the areas of critical compressive hydrostatic stress corresponded to those with resorption craters in clinical studies (Roscoe et al., 2021).

Another potentially hazardous effect may occur, especially in the case of the LLI, because of the inherent root morphological characteristics and differences. Due to the anatomical features and location in the mandibular bone, the LLI is less protected when compared to the LCI. Our study emphasizes an increased risk of deleterious side-effects when applying a lingualization force to the LLI, with a potential emergence of the "wedge effect". This effect entails applying a higher amount of force on a significantly reduced surface, and it may be extremely damaging for the supporting periodontal tissues. When taking into account an affected periodontium, the periodontal prognosis may be extremely different between the two lower incisors; thus, clinicians should be aware of these important differences and apply a lighter force on the LLI.

The point of force application is also important. For example, the results obtained by Lombardo et al. (2012) showed that when the vertical force was applied on the lingual surface, a larger displacement was observed, and the type of the movement obtained was tipping. In addition, the authors stated that applying an intrusive lingual force to the lower incisor determines bodily movement and the same intrusive labial force determines labial tipping. These observations also agree with another study that compared labial orthodontics to lingual orthodontics in terms of force magnitude. The differences in biomechanics of tipping were evaluated for a 50 g force applied on the labial and the lingual side, and the main stress patterns in the periodontal ligament for orthodontic tooth movement were recorded. The same force on the labial side caused approximately 0.0252 N/mm^{2}2 maximum principal stress and on the lingual side it resulted in 0.0375 N/mm^2 maximum principal stress; thus, tipping for a lingually applied force requires about 1/3 less force when compared to a labial one (Mascarenhas et al., 2015).

This study has several limitations. First, in order to simplify the analysis, we assumed that the tooth-periodontium-alveolar bone complex has linear elasticity and isotropic properties of the same quality; however, this is only an approximation of reality. Second, we only discussed the effect of a lingualization force on the lower incisors; however, other teeth might behave differently when submitted to orthodontic forces, especially multirooted teeth. We did, however, focus on these teeth due to the reduced bone thickness at this level in a majority of cases and the increased likelihood of further periodontal tissue breakdown during orthodontic treatment.

Conclusions

The lingualization of the lower anterior teeth is an essential stage during the interdis-ciplinary therapeutic approachof the adult periodontal patient. Our results showed that none of the analyzed parameters were significantly influenced by the magnitude of the applied force: σ ech, σ c, or f. Thus, lingualization can be considered as a reliable option during complex periodontal treatment. Anatomical particularities should also be consid-ered since they may contribute to increase in periodontal risk in case of lingualization of the LLI compared to that of the LCI, with a potential emergence of the "wedge effect". Thus, differences in anatomical features of the roots are important because they may influence the absorption of force by the supporting periodontium. Although orthodontic forces applied on anterior teeth with affected periodontium are very difficult to quantify in a clinical setting,we recommend that they should be light, efficient, and not exceed 1 N, in order to minimize periodontal hazards.

Future studies are necessary, in order to investigate and validate our results; therefore, we consider that a correct and uniform protocol of orthodontic management in periodontal cases may significantly contribute to an increased rate of success with minimal associated risks.

CHAPTER 2

RESEARCH ON CONTEMPORARY COMPOSITE RESINS

2.1. State of art

Conservative dentistry uses composite resins to limit the negative aspects of acrylic resins, which replaced silicate cements as the sole aesthetic material in the 1940s. Buonocore employed orthophosphoric acid in 1955 to increase enamel-acrylic resin bonding. Since acrylic resin monomers only created linear chain polymers, Bowen developed the bisphenol A-glycol dimethacrylate (Bis-GMA) monomer in 1962 to enhance their physical qualities (Bowen, 1963). Early chemically cured composites paired the base paste with the catalyst, causing proportion, mixing, and colour stability issues (Kinomoto et al., 1999). Electromagnetic radiation polymerized composite materials in 1970, eliminating mixing and related drawbacks. After shallow polymerisation and iatrogenic side effects, UV light (365 nm) was replaced with visible light (427-491 nm), which is now in use and being developed (Hofmann et al., 2002).

Dental composites consist of an organic matrix or organic phase, an inorganic matrix, also known as filler or dispersion phase, and an organosilane or coupling agent to connect the filler to the organic resin. This agent is a molecule containing silane groups at one end (ion bond to $SiO2$) and methacrylate groups at the other (covalent bond with resin) (Goldstein, 2002).

The composite resins' organic matrix primarily comprises mono-, di-, or tri-functional monomers. The initiation system for free radical polymerization in photocurable composite resins involves the use of camphoroquinone in combination with a tertiary aliphatic amine reducing agent. In chemically-curable composite resins, benzoyl peroxide is used alongside n,n-dihydroxyethyl-p-toluidine. Additionally, an acceleration system is employed (Hervás-García et al, 2016).

Bis-GMA remains the predominant monomer utilised in the production of contemporary composites, either as an independent component or in combination with urethane dimethacrylate. It represents approximately 20% (v/v) of typical composite resin formulations. In general, it is widely acknowledged that a decrease in the mean molecular weight of a monomer or combination of monomers results in an increase in the percentage of shrinkage. The high viscosity of this resin necessitates its dilution with low-viscosity monomers, which are known as viscosity controllers, to facilitate both the manufacturing process and clinical handling. Examples of such monomers include bisphenol A dimethacrylate (Bis-DMA), ethylene glycol dimethacrylate (EGDMA), triethylene glycol dimethacrylate (TEGDMA), methyl methacrylate (MMA), and urethane dimethacrylate (UDMA) (Holter et al, 1997; Culbertson et al., 1997; Hervás-García et al., 2016; Suryawanshi, Behera, 2022).

The inorganic filler governs the physical and mechanical characteristics of the composite. The mechanical properties of a restoration material are significantly determined by the nature, origin and quantity of the filler. Filler particles are introduced into the organic phase with the purpose of enhancing the physical and mechanical characteristics of the organic matrix. Therefore, the primary objective is to incorporate the maximum possible amount of filler. The incorporation of filler into the material leads to a reduction in the thermal expansion coefficient and overall curing shrinkage, while also providing radio-opacity. In a previous studie, Labella et al. (1999) reported that the inclusion of filler improves improves the handling of the material and enhances the aesthetic outcomes.

The chemical composition, morphology, and dimensions of the filler particles employed exhibit significant variability. Silicon dioxide is the primary substance utilised as a filler, while boron silicates and lithium aluminium silicates are frequently utilised as well. Numerous composites exhibit partial substitution of quartz with radio-opaque heavy metal particles like barium, strontium, zinc, aluminium, or zirconium. Currently, there is an ongoing search for materials, such as calcium metaphosphate, that possess lower hardness compared to glass materials. This is due to the fact that such materials result in reduced wear on the opposing tooth (Xu, 1999).

The nanotechnology has facilitated the creation of a novel composite resin distinguished by its inclusion of 25 nm nanoparticles size and 75 nm nanoaggregates size. These nanoaggregates consist of zirconium/silica or nanosilica particles.

The incorporation of smaller particle size in composite resins has yielded favourable outcomes such as enhanced surface texture and diminished biodegradation over an extended period. The advancement of technology has facilitated the development of mechanically effective resins that are appropriate for employment in the anterior and posterior regions. Furthermore, the smaller particle size reduces curing shrinkage, cusp wall deflection, and the presence of microfissures. Nevertheless, smaller particles do not exhibit light reflection, thereby requiring an association of larger particles having an average diameter within the visible light spectrum to augment their optical efficacy and serve as a substrate (Geraldi et al, 2003; Meyer et al., 2003).

The Lutz and Phillips classified composite resins into three groups: macro, micro filler composites and hybrid composites (comprising fillers of varying sizes) (Lutz, Phillips, 1983).

The composition of dental composite cements as luting materials, is the same as those of other dental composites, consisting of a resin matrix, filler and coupling agent. Composite cements include smaller-sized particles for a thinner film and a higher amount of resin to enhance flow.

One significant advantage of composite cements is their ability to bond dental restorations to tooth structures, making them a preferred choice as luting materials for ceramic restorations. Additionally, composite cements are useful in cases where there is inadequate retention of dental preparations, such as crown preparations that have a small height or excessively tapered form.

Fibre-reinforced composites (FRCs) are composed by three distinct constituents: the organic matrix, the fibres filler, and the interphase that exists between them (Amiri et al., 2021). The classification of fibre-reinforced composites can be established into two distinct types, continuous (unidirectional and bidirectional) and discontinuous (aligned and randomly orientated). Continuous fibre reinforcement composites are those with long fibre reinforcements, while discontinuous fibre reinforcement composites are those with short fibre reinforcements (Rajak et al., 2019).

The effectiveness and mechanical characteristics of FRCs are influenced by numerous factors. These include the type of fibre employed, like carbon, aramid, glass, or polyethylene; the amount of fibres used; the fibre arrangement, such as unidirectional, bidirectional, or randomly oriented; the fibre placement; the adhesion between the fibre and resin matrix; the properties of both the fibre and resin matrix; the quality of the fibre saturation; and the water absorption of the FRC matrix (Rajak et al., 2019; Amiri et al., 2021).

When referring of dental applications, these materials are typically exposed to flexural or bending stresses (for the posterior areas). Although clinical performance ultimately determines the success of a material, flexure remains the most reported mechanical property. Test results pertaining to flexure are valuable in the development and selection of new materials for clinical applications, as evidenced by numerous studies (Ilie et al, 2017; Amiri et al., 2021)

Short fiber fillers are minimised by up to 70% the polymerization shrinkage and increases composites' physical properties, such as modulus and flexural strength (Bocalon et al., 2016). Glass fibre is the most frequently utilised short fibre (Kruzic et al., 2018; Soares et al., 2017). According to Garoushi et al. (2007) research, a short glass fiber reinforced restorative composite resin with semi-inter penetrating polymer network matrix increases mechanical properties along the convex surface. This suggests that glass fibre reinforced composites perform well in high-stress environments (Suryawanshi, Behera, 2022.

With the improvements in the mechanical properties of PFCs, these materials are used for anterior and posterior dental restorations, direct onlay restorations, repairing fractured porcelain veneers, reinforcing removable acrylic resin prosthesis, creating periodontal splints, producing retainers and space maintainers for orthodontic purposes, and utilising root canal posts in restorative dentistry (Garoushi et al., 2013; Zhang M, Matinlinna, 2012; Rajak et al., 2019, Suryawanshi, Behera, 2022).

Periodontitis is a persistent inflammatory disease that results from bacterial plaque. The primary symptoms are gingival bleeding, clinical attachment loss (CAL), alveolar bone loss, the absence of increasing periodontal pocket depth, and loss of periodontal tissue support (Papapanou et al., 2018). Pathological tooth mobility may develop as a consequence of extensive alveolar bone loss, acute periodontal inflammation, traumatic occlusion, and an apical shift of the rotational centre of the tooth. According to research, periodontal splinting is recommended as a therapy to stabilize mobile teeth and improve their long-term prognosis (Watkins, Hemmings, 2000; Sonnenschein et al., 2021; Graetz et al., 2019). When dealing with periodontal disease, excessive occlusal forces can worsen pre-existing lesions if they exceed the resistance threshold of a compromised epithelial attachment (Sonnenschein et al., 2017; Durrani et al., 2019; Zhang et al., 2023). The anterior mandible region is particularly susceptible to periodontal disease and occlusal trauma, as the bone size is smaller, resulting in larger deformations, despite lower occlusal forces (Sonnenschein et al., 2021, 2022). Selecting the appropriate periodontal splint type requires consideration of the mechanical interaction between the materials used and the dento-periodontal substrate (Zhang et al., 2023). However, there is limited literature on how bone resorption and periodontal immobilization impact the biomechanical response of the bone-tooth-periodontium complex. As a result, choosing the type of immobilization and its material remains challenging for practitioners.

My research focused on exploring the use of composite resins in two specific areas of dentistry. Firstly, their application as splinting materials in periodontology, and secondly, their use as direct inlays and luting elements in restorative dentistry.

	The following are the most significant personal scientific contributions in this field
Published articles in ISI journals	1*. Goriuc A, Jitareanu A, Martu I, Dascalu CG, Kappenberg-Nitescu DC, Solomon SM, Martu A, Foia L, Tapu I, Istrate B, **Tatarciuc M**, Luchian I. Experimental EDX analysis of different periodontal splinting systems, Exp Ther Med, **2021**, 22(6): art. no 1384. IF=2.751 2*. Luchian I, Nanu S, Martu I, Martu MA, Nichitean G, Kappennerg-Nitescu DC, Gurau G, Stefanescu V, Pasarin L, **Tatarciuc M,** Solomon SM. The Influence of the Composite Resin Material on the Clinical Working Time in Fiberglass Reinforced Periodontal Splints, Mater Plast, **2020**, 57(1): 316-320. IF=0.593 3*. Diaconu D, **Tatarciuc M**, Vitalariu A, Stamatin O, Foia L, Checherita LE. Research on the Influence of the Resin Cements Micro-leakage to the Resistance of the Composite Inlays, Mater Plast, **2014**, 51(3): 271-274. IF=0.824
Published articles in BDI journals	1. Luchian I, Nanu S, Martu I, Teodorescu C, Pasarin L, Solomon S, Martu MA, **Tatarciuc M**, Martu S. The influence of highly viscous

	flowable composite resins on the survival rate of periodontal splints, Rom J Oral Rehabil, **2018**, 10(2): 63-69 (ESCI-WSCC) 2. **Tatarciuc M**, Zamfirache IC, Craciun ME, Dunca S, Surdu S, Rosu CM, Stefan M. Study regarding the adherence of oral microbiota on composite material, An Stiint Univ Alexandru Ioan Cuza Iasi, Genet Biol Mol, **2008**, 9(4): 61-67 (B+)

**Publications described in detail in the next subchapters*

2.2. Experimental EDX analysis of different periodontal splinting systems

Aim of the study

The aim of the present study was to evaluate comparatively, by means of energy dispersive electron spectrometry (EDX), the chemical composition in the case of in vitro samples that structurally reproduce direct periodontal immobilization systems using fiberglass strips and fluid composite resins.

Materials and methods

Materials

In order to achieve the proposed aim, 54 samples of teeth were selected with the following dimensions: 15 mm in length, 4 mm in width and 2.5 mm in thickness, using a heat-resistant silicone conformer.

For the construction of the immobilization systems, the same fiberglass tape, Interlig® (Angelus®, Brazil) and three different fluid composites were used: G-aenial Flo X® (GC Corporation®, Japan), GrandioSO Heavy Flow® (Voco®, Germany) and Clearfil Majesty ES Flow® (Kuraray Noritake Dental®, Japan). The number of samples produced and later subject to elemental investigation was equal, namely 18 for each composite resin. The photopolymerization of the samples was carried out using a Celalux 2® type lamp (Voco).

Subsequently, all 54 periodontal splint samples were grouped, and their microstructure was analyzed using a Quanta 200 3D scanning electron microscope (FEI, The Netherlands) in the laboratory of the Faculty of Mechanics from the 'Gheorghe Asachi' Technical University of Iasi, Romania.

EDX spectrometer

The EDX spectrometer is an instrument that determines quantitatively the elements in a sample by irradiating it with X-rays and then analyzing the re-emitted X-rays. It represents a standard method to identify and quantify element compositions of very small samples of material (even a few cubic micrometers). The EDX elemental analysis was performed for each type of composite separately, G-aenial Flo X (GC Corp.), GrandioSO Heavy Flow (Voco) and Clearfil Majesty ES Flow (Kuraray), in three different areas of each sample.

The data were automatically corrected for atomic number, absorption and fluorescent excitation effects using the ZAF correction method for each investigated element. Following the investigations, we analyzed, for each element, both the mass percentage (wt%) and the atomic percentage (at%).

Statistical analysis

The statistical analysis was performed using SPSS 25.0 (IBM Corp.) The Kolmogorov-Smirnov test was used to test the distribution of the numerical variables. The average value, the standard error and the standard deviation of the numerical variables were calculated. The Kruskal-Wallis and Mann-Whitney non-parametric tests were used to compare the variables with non-normal distributions. $P<0.05$ was considered to indicate statistically significant results.

Results

Carbon (C) content

The values found for carbon were significantly different between the three types of materials, in the case of both measurements, both globally and comparatively between materials two by two. For example, for wt% determinations, the highest C content was recorded for G-aenial Flo X (21.7644±1.32468) and the lowest for GrandioSO Heavy Flow (5.9611±0.87104); the C content for Clearfil Majesty ES being intermediate (12.9989±3.44164). However, the differences between the three materials were statistically significant in all combinations. A similar behavior was observed in the case of at% determinations (figure 60).

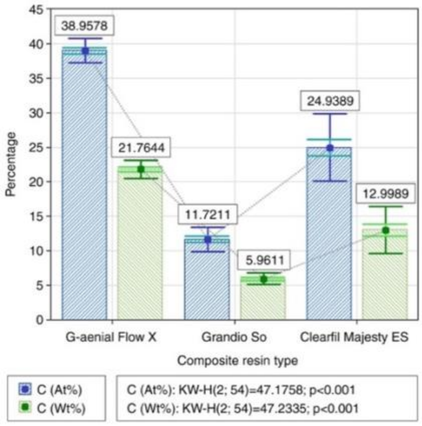


Figure 60. Statistical analysis of the mass (Wt%) and atomic percentage (At%) of the carbon (C) content for the three types of materials.

Oxygen (O) content

The O content was also significantly different between the three types of materials, in both measurements, both globally and comparatively between materials two by two. In the case of the wt% measurement, the highest O content was observed for GrandioSO Heavy Flow (33.878±1.74974), followed by Clearfil Majesty ES (30.1978±2.91155), and lastly by G-aenial Flo X (28.5767±2.05314). The observed differences were considered statistically significant (Table XVIII). The same results were observed in the case of at% measurements (figure 61).

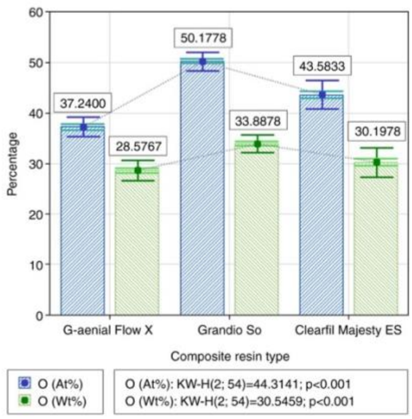


Figure 61. Statistical analysis of the mass (Wt%) and atomic percentage (At%) of the oxygen (O) content for the three types of materials.

Table XVIII. Statistical analysis of the mass (wt%) and atomic percentage (at%) for all analyzed elements in the three types of materials.

		Mann-Whitney test (2 samples) P-value		
Mass and atomic percentage of the elements	**Kruskal-Wallis test (3 samples) P-value**	**G-aenial Flo X vs. Grandio SO Heavy Flow**	**G-aenial Flo X vs. Clearfil Majesty ES**	**Grandio SO Heavy Flow vs.Clearfil Majesty ES**
C(wt%)	<0.001[b]	<0.001[b]	<0.001[b]	<0.001[b]
C(at%)	<0.001[b]	<0.001[b]	<0.001[b]	<0.001[b]
O(wt%)	<0.001[b]	<0.001[b]	0.037[a]	<0.001[b]
O(at%)	<0.001[b]	<0.001[b]	<0.001[b]	<0.001[b]
Al(wt%)	<0.001[b]	<0.104	<0.001[b]	0.027[a]
Al(at%)	<0.001[b]	<0.001[b]	<0.001[b]	0.293
Si(wt%)	<0.001[b]	<0.001[b]	<0.001[b]	<0.001[b]
Si(at%)	<0.001[b]	<0.001[b]	<0.001[b]	<0.001[b]
Ba(wt%)	<0.001[b]	<0.001[b]	0.864	<0.001[b]
Ba(at%)	0.211	0.719	0.293	0.068

[a]Statistically significant, P<0.05;
[b]highly statistically significant, P<0.001. C, carbon; O, oxygen; Al, aluminum; Si, silicium; Ba, barium.

Cobalt (Co) content

The average Co content was observed only for the Clearfil Majesty ES material, being 1.4167±0.33941 in the case of the wt% measurement and 0.5356±0.15523 in the case of the at% measurement, respectively (figure 62).

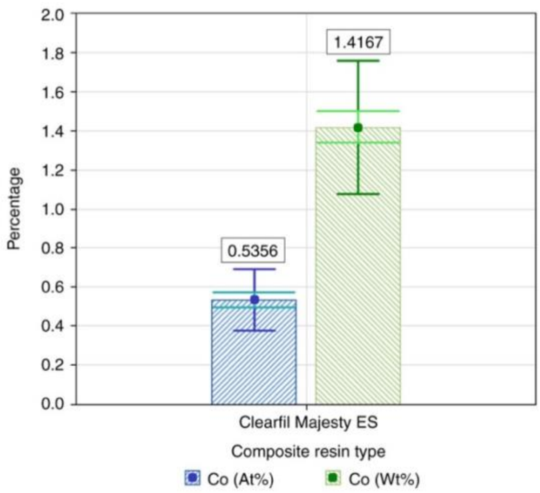


Figure 62. Statistical analysis of the mass (Wt%) and atomic percentage (At%) of the cobalt (Co) content for the three types of materials.

Aluminum (Al) content

The Al content was also significantly different between the three types of materials, in both measurements, but only globally. In the case of the wt% measurement, the highest Al content was observed for Clearfil Majesty ES (6.3511±1.04642), followed by Grandio So (5.5056±0.83701) and lastly, by G-aenial Flo X (5.0978±0.26932). The Al content of Clearfil Majesty ES was statistically significantly higher than that of the other two materials tested;

however, the differences between the latter two (G-aenial Flo X and Grandio So) were small and had no statistical significance (figure 63). A similar behavior was observed in the case of at% measurements, except that in this case the difference between Clearfil Majesty ES and Grandio So was smaller, not statistically significant, while other differences between varying combinations of materials were important and statistically significant (Table XVIII).

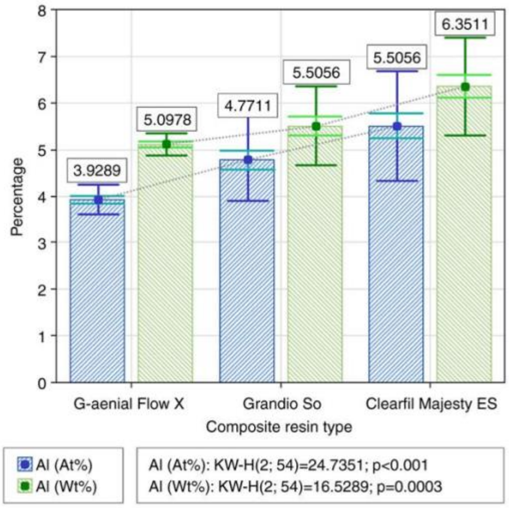


Figure 63. Statistical analysis of the mass (Wt%) and atomic percentage (At%) of the aluminum (Al) content for the three types of materials.

Silicium (Si) content

The Si content was also significantly different between the three types of materials, in the case of both measurements, both globally and comparatively between materials, two by two. In the case of the wt% measurement, the highest Si content was observed again for GrandioSo Heavy flow (35.6133±1.23026), followed by Clearfil Majesty ES (26.4044±1.93859) and lastly, by G-aenial Flo X (22.1044±0.64334), the observed differences being large enough to be statistically significant. The same phenomenon was observed in the case of at% measurements (figure 64).

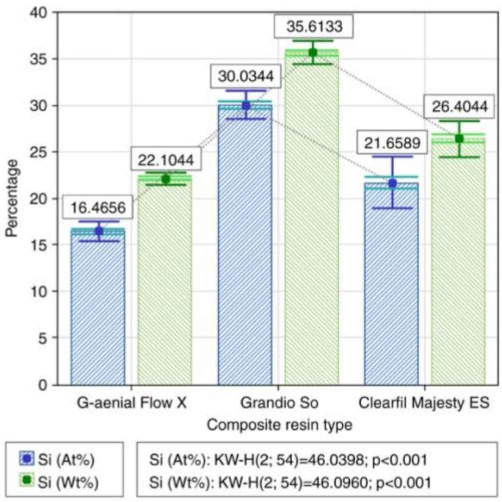


Figure 64. Statistical analysis of the mass (Wt%) and atomic percentage (At%) of the silicone (Si) content for the three types of materials.

Barium (Ba) content

The Ba content was significantly different between the three types of materials, but only globally and only in the case of the wt% measurement. In the case of the wt% measurement, the highest Ba content was observed for Clearfil Majesty ES (22.6356±3.09334), followed by G-aenial Flo X (22.4600±2.11290) at a very small difference and without statistical significance and, at a difference that was higher and with low statistical significance, by Grandio So (19.0311±0.92871) (Table XVIII). The order of the three materials was the same in the case of at% measurements in terms of Ba content, only in this case the recorded values were close to each other, without statistically significant differences between the analyzed materials (figure 65).

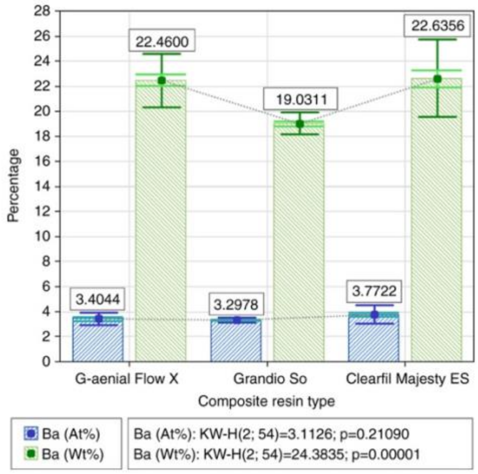


Figure 65. Statistical analysis of the mass (Wt%) and atomic percentage (At%) of the barium (Ba) content for the three types of materials.

Discussion

The composition of composite resins is complex and from the perspective of energy dispersive electron spectrometry (EDX) analysis, general information was obtained regarding the structural elements of resins (Vilchis et al., 2008). Elements such as C, O, Al, Si and Ba were identified as common elements among the resins tested in the present study. The only difference in terms of the component elements was found in the case of the fluid composite Clearfil Majesty ES flow, which, apart from the elements mentioned, also presented Co in its structure.

Clearfil Majesty ES flow is a light-curable, radio-opaque composite resin containing nanoparticles and a high refraction matrix (Scougall-Vilchis et al., 2009). It has a light diffusion property very similar to the structure of natural teeth, which makes it versatile for almost any situation in which a composite must be used. The high refraction matrix also offers another key benefit: a very small change in transparency after photopolymerization/light curing (Karadas, 2016).

GrandioSO Heavy Flow is a nanohybrid composite with high viscosity which, due to its high filling rate, has exceptional physical properties including stability, compressive strength, adaptability, and flexural strength. It is capable of withstanding abrasion, shrinkage, wear and polishing, thus giving the dentist many solutions to the challenges posed by practice. With an initial shrinkage of less than 3% and flexural strength above 400 MPa, GrandioSO Heavy Flow creates varied opportunities for use compared to other flow composites. Compared to the other composites used in the present study, G-aenial Flo X is a composite with high strength and radio-opacity, specially designed for optimal handling in microcavities and cracks.

There are two basic properties by which fibers can increase the effectiveness of a composite resin. Fibers act as a stress-bearing component. This enhances the otherwise brittle effect of the composite matrix. Secondly, fibers have a fracture-arresting property or a crack deflection mechanism, which in turn increases the strength of the material. It is important for the clinician to manufacture a system able to withstand all failure mechanisms in the most favorable manner possible. All these mechanisms depend on the direction in which the stress is applied to the device (Özcan, Kumbuloglu, 2017).

Fiberglass-reinforced composite resins are a type of material that combine a polymeric matrix and reinforcing fibers. When pressure is applied to the material, the intervening fibers are the composite fibers, which lend the material strength and hardness. The reinforced fibers can be unidirectional continuous (rovings), bidirectional continuous (weaves), randomly oriented continuous (matte) or they can be discontinuous and randomly oriented (Vallittu, 2018).

Currently, many materials are used for a dental immobilization system, including metal wires or fiber-reinforced composites. In the medical field, composite materials are used more often because they are chemically stable and do not induce negative effects, as the human body tolerates them easily. The most widely used materials today for making fiber-reinforced composite resin systems are glass and polyethylene fibers. The fibers have been developed in order to be able to strengthen the dental composite resins, thus forming strong, but thin structures (Bechir et al., 2016). Based on the results of their study, Juloski et al concluded that the reinforcement of fibers with fluid composite does not affect the shear strength of the enamel, and that the flexural strength of the fibers is significantly influenced by their composition and model (Juloski et al., 2013).

An important factor in the success of periodontal splinting is the biomechanical behavior of these systems on dental units. The type and material of the immobilization system also play an important role in the success of the treatment. There are differences between composites reinforced with polyethylene fibers and those made of metal wires. Thus, the stresses on the bone in the case of incisors were higher in the polyethylene fiber tapes compared to those containing metal wires, this being attributed to the more elastic behavior of the polyethylene fibers. When the force was applied to the canines, higher stresses were identified in the case of metal immobilization systems (Vieriu et al., 2020).

The capacity of the material used must be evaluated primarily according to the durability and efficiency it offers. These two characteristics are also influenced by the consistency of the composite material used. Other findings on the influence of composite resins on the success rate of periodontal immobilization have concluded that high viscosity flow composite resins showed the best treatment success rate (Luchian et al., 2018). Compared to these, solid composites showed an acceptable success rate, the failures being closely related to the consequences of difficult handling of this type of material on the lingual face of the teeth. At the opposite end, avoidance of classical flow composites in periodontal immobilization is recommended, since their mechanical strength is not sufficient for the stress to which they are subjected (Luchian et al., 2020).

The differences in the chemical composition of the investigated materials can influence their physiochemical properties, but also their biological and toxicological reliability. Local and systemic toxic effects of dental materials can appear if these materials are placed in the oral cavity for a long period of time (Shahi et al., 2019). The general opinion of the scientific community is that no material can be 100% safe biologically, and that most adverse effects of materials are mediated by substances released from the material during corrosion (Wataha, 2012).

In vitro studies performed on cultured mouse fibroblasts revealed changes in the growth and morphology of cells exposed to cobalt. Co exposure was found to be associated with the depression of the cell growth rate, concluding that increased concentrations of cobalt could affect the normal reconstructive activity of fibroblasts (Polyzois, 1994). However, significant health effects (neurological, cardiovascular and endocrine deficits) are unlikely to occur at blood Co concentrations under 300 µg/l in healthy individuals, and chronic exposure to acceptable doses is not expected to pose considerable health hazards (Leyssens et al., 2017).

Although a higher percentage of aluminum present in the material is associated with low material density, good malleability and good ductility, it is important to take into account the fact that aluminum is a toxic metal, and its release in high quantities can lead to unwanted adverse effects (pro-oxidant, inflammagen, immunogen), which is involved in human neurodegenerative diseases (Exley, 2013). However, Meryon and Jakeman investigated the release of aluminum from several materials and its in vitro toxicity towards culture cells, but the aluminum concentrations released in the medium did not exceed 15 ppm, while levels of 40 ppm were usually associated with toxic effects on fibroblasts and macrophages (Meryon, Jakeman, 1987).

Based on various property measurements, silica-filled cured composites showed highly desirable comprehensive performances including dielectric, breakdown, mechanical, thermal and mass stability properties. Thus, low permittivity, low dielectric loss, high electric breakdown strength, high ageing breakdown strength, high shock strength, high thermal conductivity and low weight loss percentage were obtained in micro-silica loaded composites, leading to their promising application in electrical insulation cases. The large band gap and relatively high deformation ability of silica particles could contribute to favorable breakdown and mechanical properties of composites. Silica-filled cured composites exhibited a breakdown strength of ca. 48 MV m-1 and shock strength of ca. 9950 J m-2. This study may open the door towards the large-scale manufacture of high-performance epoxy composite potting-adhesives (Hu, 2020).

To enhance the penetration of dental adhesives, the enhancement of hydrophilicity and homogeneity of adhesive formula is the most commonly used strategy.

Silica fillers are hydrophilic, so there is a restriction in their affinity to hydrophobic resins. Through surface treatment with silane-coupling agents, the mixing of hydrophilic silica filler and the interaction between filler and organic components could be improved. Kim et al (2020) hypothesized that an increased hydrophilicity of the fillers can increase the even dispersion within the adhesive layer under moist conditions, thus increasing the bond strength.

Carefully modified handling property is helpful in producing a uniform adhesive layer at a feasible thickness, thus leading to a satisfactory bonding performance. In addition to texture, viscosity is an important parameter in evaluating the handling properties of dental adhesives (Wang et al., 2017).

Bonding performance is one of the most important aspects for the evaluation of dental adhesives. High-bond strength of the adhesion joint is always an aim in the development of dental adhesives.

In the current study, the highest amount of Si was identified in the samples produced using GrandioSO Heavy flow, which suggests a higher biomechanical strength of this product by comparison with the other samples included in the study. The presence of cobalt was identified only in the samples of Clearfil Majesty ES Flow and from the point of view of our results is irrelevant to the oral toxicity. The issue of metal ions release over time in the oral medium must be taken into account and evaluated frequently. The acid environment in the mouth leads to erosion, and cobalt release from dental materials has been associated with allergic reactions (Kostić et al., 2017; Bationo et al., 2019).

Conclusion

The statistically significantly higher amount of aluminum was determined in the samples made using the Clearfil Majesty ES composite resin, which can thus be associated with low material density, good malleability and good ductility.

The high amount of carbon identified in the samples that involved the use of G-aenial Flo X may indicate a slightly higher abrasive potential of the material in the clinical context.

Although the materials included in the present study can be successfully used for periodontal splinting, their behavior towards the adjacent tissues should also be evaluated. For this reason, the future research direction could assess the cytotoxicity of these materials and potentially establish a link between the presence of certain chemical elements, material strength and biocompatibility.

Thus, further studies are necessary and must be focused on the biological compatibility of the composite resins used for periodontal splinting in order to minimize the toxicological hazards at the level of oral tissues.

2.3. The influence of the composite resin material on the clinical working time in fiberglass reinforced periodontal splints

Aim of the study

Our study aims the analysis of the adhesive and biomechanical behaviour of 3 types of current composite biomaterials, used in the periodontics immobilisation technique, structural of each category having a defining role in carrying out the immobilisation especially upon the dental and periodontal stability of the support.

In equal degree, we propose the correlation of the structural aspects and of the behaviour of this bioadhesive behaviour, with an especially important parameter, with a profound impact in improving the dental medical practice, namely the working time.

Materials and methods

We included in our study 30 patients that had indication for periodontal splinting at the level of the 5th sextant. We randomly divided the 30 patients into three groups named A, B and C. For the entire study group, we used the same fiberglass (Interlig Angelus) and the same bonding agent. Patients included in group A were treated using Grandioso Heavy flow composite (Voco) while patients included in group B were treated using Gaenial flow universal composite (GC). For the patients included in group C we used Gaenial Posterior composite (GC). Clinical working time is a very important parameter in modern dentistry. The manoeuvres carried out must take as little time as possible, must have increased effectiveness and be durable in time. Of course, this aim is difficult to achieve, but by increasing the practitioner's experience and through the evolution of dental materials, the length of the work stages is reduced, and the ergonomic principles are respected. The working time was calculated using a stopwatch since the rubber dam was applied and until the clinician finished the procedure. All procedures were performed by the same clinician (figures 66-68).

Figure 66. Initial clinical aspect of the 5th sextant.

Figure 67. Lingual aspect of the 5th sextant after etching.

Figure 68. Final clinical aspect of a periodontal splint bonded with a highly viscous flow composite resin.

GrandioSO Heavy Flow is a highly viscous nano-hybrid restorative material. GrandioSO Heavy Flow has a much lower contraction during polymerisation (2.96%) compared to conventional flow materials and has high compression and bending strength (417 MPa, and 159 MPa, respectively), a very high elastic modulus for a flow material (11.85 GPa), a very tough surface (175 MHV), as well as low abrasion (40 µm, ACTA with 200 000 cycles). Studies have confirmed that G-aenial Universal Flo has a higher strength, a better resistance towards wearing and a polish retention that is higher than in other tested composites. Newly introduced, it offers higher strength, better aesthetics and manoeuvrability, and combined many of the advantages of fluid and non-fluid composites.

The innovative filling chemistry consists of 200 nm strontium particles that are silanated a new, proprietary technology, are very dispersed and have a low refraction index. G-aenial posterior is a radio-opaque hybrid composite restoration material with a combination of two types of pre-polymerised filling resins. The elastic modulus (Young's modulus) is one measure of a material's elasticity. A material with a high modulus is rigid, whereas a material with a low modulus is flexible. Ideally, a material should not have a very high elastic modulus, as fragile materials are less capable of buffering mastication pressure. G-aenial Posterior shows a similar flexibility to that of most tested composites. Flexible materials have an ability to buffer forces in the areas with high pressure and wear similar to the nano-hybrid composite materials.

Results and discussions

It can be noticed that the lowest values appear in the case of patients in group A, with an average of 6.74 minutes per procedure. These results are followed by the ones recorded in group B with an average value approximately one minute longer (7.82 minutes). The values of the clinical working time recorded in the patients from group C are almost double when compared to the ones from group A and B. The clinical working time at the level of group C reached an average of 14.6 minutes (Table XIX).

Table XIX. Results of the clinical working time

Patient	Time(min)		
	A (HEAVY FLOW)	B (FLOW)	C (SOLID)
1	6.80	7.30	12.40
2	6.70	8.20	13.20
3	7.20	9.10	14.50
4	8.00	10.10	15.20
5	6.40	9.40	12.40
6	6.20	9.30	13.40

7	6.10	9.20	15.40
8	6.50	8.70	16.20
9	6.70	8.80	16.80
10	6.80	8.90	17.30
Average work time	6.74	7.82	14.68
Standard deviation	0.5460	0.7512	1.7862
Minimum value	6.1	7.3	12.4
Maximum value	8	10.1	17.3

The shorter clinical working time is achieved due to the characteristics of materials, because flow composites are applied directly from the syringe and require a shorter trimming and polishing time, due to the fact that they have fewer irregularities after photo polymerisation (figure 69).

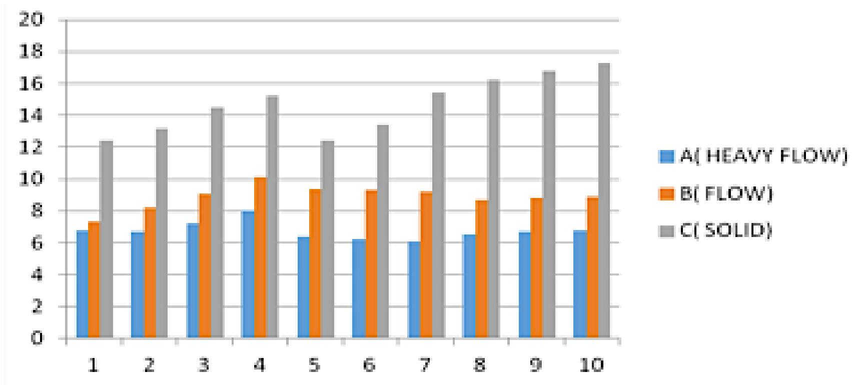


Figure 69. Comparative results in the three groups.

In the case of solid composites, the composite is applied on the splint using a spatula, fact that increases the working time, as it is difficult to appreciate the thickness with precision.

Sometimes, lengthy use of a certain type of material creates additional comfort for the practitioner and improved clinical working times. Therefore, the time values obtained may be influenced by the practitioner's experience in using that particular type of material.

Sfondrini et al. tested the flexural strengths differences between conventional and nanofilled fiber- reinforced composites (Sfondrini et al., 2013). Further clinical studies can be conducted in order to conclude if the use of conventional versus nanofilled fiber reinforced composites can influence the clinical working time (Tanculescu et al., 2017; Vieriu et al., 2015).

The importance of monitoring clinical working time has not been highlighted in many previous scientific studies. The main focus has been on the periodontal splinting' durability and efficiency over time, rather than on the time allotted to the actual operations (Scribante et al., 2018a, 2018b).

Modern dental medicine must also focus on the time allotted to certain procedures, the trend being towards optimising the time/quality ratio and increase the comfort of the patient.
Scribante et al. show as well that splints can be easily repaired, so in many cases it is not necessary to completely debond the framework with the substitution with a new one (Scribante et al., 2018b).
Khan et al. concluded in a systematic review that glass fiber reinforced composites have emerged as a major class of structural material and are either used or being considered as substitutes for traditional materials in dental applications (Tanculescu et al., 2017; Vieriu et al., 2015; Khan et al., 2015).

Other studies emphasized that the selection of the splint and of the type of fibreglass suitable for the procedure is made based on the advantages, disadvantages and individual clinical experience (Luchian et al., 2018). The same study pointed out that the ideal immobilisation system must be designed in such a way that will retain a minimal amount of bacterial plaque, will allow maintenance in the long term, will be able to fulfil the assigned function and will not interfere with occlusion or with phonetics (Luchian et al., 2018).

Conclusions

Our study indicated that the highly viscous flow composite resins offer the shortest clinical working time out of all tested materials.

Using this type of composite resins might be a reliable solution to reduce the clinical working time when applying fiberglass reinforced periodontal splints.

2.4. Study on the behaviour of the luting cement for aesthetic inlays

Aim of the study

In this study we aimed a comparative analysis of the behavior of the different luting materials in different conditions. As the composite fixing resins suffer most changes in the grip reaction, we focused our research on analyzing the stress generated by the polymerization contraction of these materials at the level.

Materials and methods

The study was performed on 60 premolars, extracted from periodontal or orthodontic reasons. The teeth were cleaned of any traces of periodontal tissue or tartar deposits, using a Gracey curette, washed with a 2% sodium hypochlorite solution, and then kept in distilled water for one week; at the coronary level, mesio-occlusal-distal cavities were performed, using diamond burs, under continuous cooling. The occlusal cavity was 3 mm depth at the isthmus level between the horizontal and vertical cavities, the proximal cavities were prepared with a mesio-distal dimension of 4 mm, and their cervical-occlusal diameter is also 3 mm. The lateral walls of the occlusal and proximal cavities have a 6º divergence towards the occlusal side, to allow the unforced insertion of the prosthetic piece; the cervical threshold was performed in a 90º angle. All the angles were rounded to avoid the occurrence of internal tensions in the restoration and its fracture.

The teeth were divided into two groups: a first one, consisting of 30 premolars, was restored with composite material, by indirect method, using SR Nexco resin (Ivoclar), a purely light-curing lab composite with micro-opal fillers, which allows achieving a lifelike shade, even if space is limited.

The other group was restored with ceramic inlays, made of IPS Empress system (Ivoclar), a leucite-based glassceramic extremely homogeneous, that scatters light naturally and provides a balanced chameleon effect. The inlays were fixed using as material for 30 restorations (15 ceramic and 15 composite resin), Variolink N (Ivoclar) light curing composite resin, a double-cure and light-curing luting composite for glass-ceramic, lithium disilicate glassceramic and composite resin restorations.

Another 30 inlays (15 ceramic and 15 composite resin) were fixed with Meron Plus material (Voco), a glass ionomer cement, improved with resins.

To simulate the oral environment, two limit solutions were chosen: ANFOR-type artificial saliva and an acid solution, represented by citric acid. The artificial saliva only partially reproduces the inorganic component, excluding the organic and microbial component and has in composition NaCl 0,7 g/L, KCl 1,2 g/L, Na2HPO4H2O 0.26 g/L, NaHCO3 1.5 g/L, KSCN 0.33 g/L, urea 1.35 g/L and a pH of 6,78. The citric acid, at 20% concentration, with a pH of 1.90, is an aggressive environment, which can be accidentally encountered in the oral environment.

Ten samples were kept as control, and 25 samples were fixed with Variolink N resin (12 from composite resin and 13 from ceramic), were introduced into artificial saliva, which is a relatively mild corrosion agent, in which the samples were kept at 37°C, for 70 hours.

The other 25 samples, fixed with Meron Plus material (12 from composite resin and 13 ceramic) were introduced into citric acid, where they were kept for 40 hours at 37°C. The teeth were sectioned in mesial-distal direction using diamond discs, at low speed, under cooling with water. The sections were examined using an optical microscope (Carl-Zeiss AxioImager. A2 with LED), coupled with a high-resolution digital camera at 50X magnification.

Results and discussions

The initial microscopic aspect at the level of the tooth-restoration interface proves a very good marginal adaptation and the absence of defects or discontinuities of the Meron Plus fixing material in both type of inlays (composite and ceramic) (figures 70 and 71).

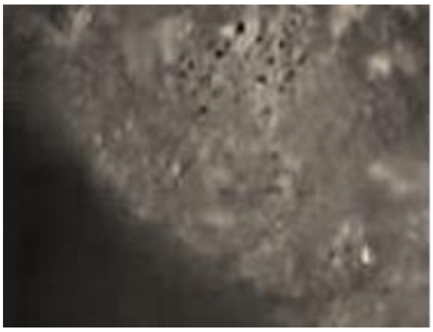


Figure 70. The composite inlays

Figure 71. The ceramic inlays

In case of inlays made of composite resin and ceramic fixed with Meron Plus, after 70 hours of immersion in AFNOR artificial saliva, a percolation space of approximately 0.005 mm appears at the level of the interface; in addition, there is a marked oscillation of level between the restoration surface and the cementing material. This fact indicates that after being maintained in the artificial saliva, the luting material will present irregularities and deep cracks. This may be due to the deterioration of the cement, the contraction of the grip or the absorption of water from the immersion environment.

There are no significant differences between the two types of restorations - composite and ceramic (figures 72 and 73).

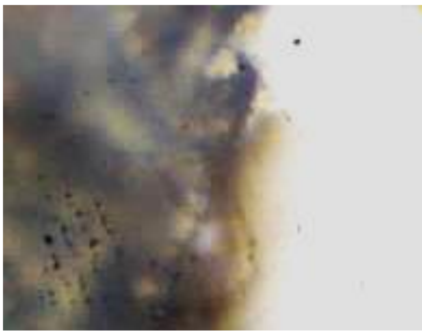


Figure 72. The aspect of interface at the level of the composite restoration fixed with Meron Plus after the immersion in artificial saliva

Figure 73. The aspect of interface at the level of the ceramic restoration fixed with Meron Plus after the immersion in artificial saliva

After the immersion for 40 hours in citric acid, the fixing material, both in the case of composite and ceramic inlays, will be completely destroyed, observing the occurrence of an irregular space at the dental-prosthetic joint level (figures 74 and 75).

Figure 74. The aspect of interface at the level of the composite restoration fixed with Meron Plus after the immersion in 20% acid citric

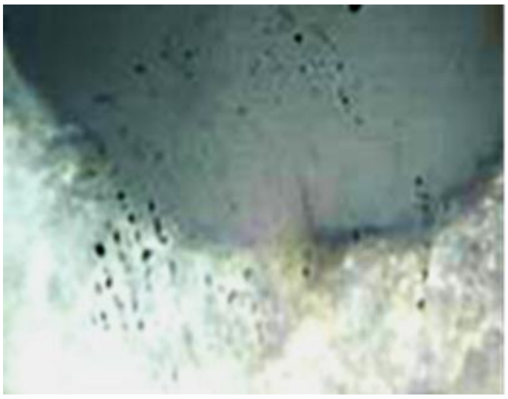


Figure 75. The aspect of interface at the level of the ceramic restoration fixed with Meron Plus after the immersion in 20% acid citric

The microscopic aspect of the interface in the case of inlays fixed with VariolinK N resin showed a very good marginal adaptation immediately after the fixing procedure, the connection surface having a continuous and homogeneous aspect, both in the case of composite and ceramics inlays. The absence of the percolation spaces proves a good adhesion between the luting material and inlay material, and no influence of the polymerization shrinkage on the dental-prosthetic joint. There is a very good grip between the ceramic inlay and the Cavitan material; it is possible to notice the continuity of the outlet throughout the contour and the absence of the percolation spaces (figures 76 and 77).

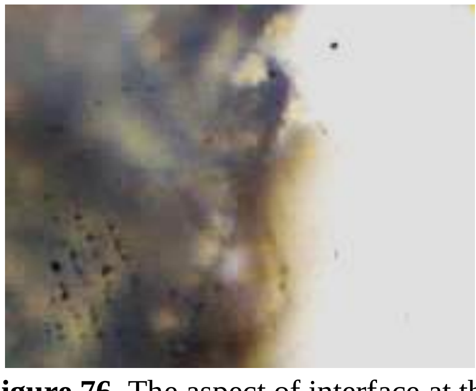


Figure 76. The aspect of interface at the level of the composite restoration fixed with Meron Plus after the immersion in artificial saliva

Figure 77. The aspect of interface at the level of the ceramic restoration fixed with Meron Plus after the immersion in artificial saliva

After the immersion of the samples in the artificial saliva for 70 hours, at the level of the interface between the composite and the luting material, small cracks (of the order of 0.005… 0.01 mm) are observed in the mass of the Variolink resin and loss of substance at the level of the restoration, which are, however, superficial and do not affect the quality of the dental-prosthetic joint (figure 78).

Figure 78. The interface between the composite restoration and the Variolik N resin after the immersion in artificial saliva

In case of ceramic inlays, after 70 hours in the artificial saliva at the level of the interface, imperfections and irregularities are observed, less obvious than in the case of the Meron Plus fixing material, but more obvious than in the previous situation, of the inlays from the light cured composite resin (figure 79).

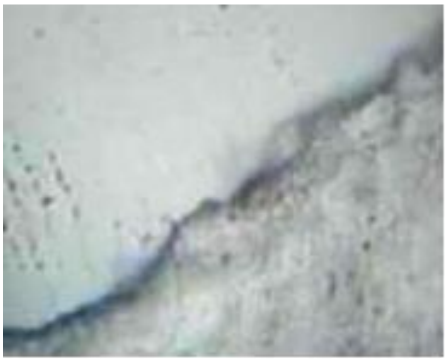


Figure 79. The interface between the ceramic restoration and the Variolik N resin after the immersion in artificial saliva

In citric acid, the attack of the cement is more pronounced (figures 80 and 81), in some areas the loss of the substance is deep, probably caused by the contraction of the cement under the action of the strong acid environment. There are no significant differences between the two types of inlay-composite and ceramic.

Figure 80. The interface between the composite restoration and the Variolik N resin after the immersion in citric acid

Figure 81. The interface between the ceramic restoration and the Variolik N resin after the immersion in citric acid

The clinical success of any fixed dental restoration is strongly related, among numerous other factors, to the fixing procedure. The deficiencies occurred during the inlay cementation lead to defects, either of depth or on surface, which often lead to clinical failure. Each of these luting materials has specific physical and chemical properties, without any of them proving to be perfect for any clinical situation (Morimoto et al., 2016; Soares et al., 2017; Odian, 1991).

Although the shape of the preparations and the restoration material are the factors of great importance for the longevity of the inlays, the fixing material acts as a barrier against marginal microbial infiltration, sealing the dental-prosthetic interface (Kim et al., 2015).

In the case of aesthetic inlays, self- or light cured composite resins are preferred for fixation, but the polymerization contraction of these resins is higher than other fixing materials.

This volumetric change generates a load of almost 130 kg/cm between the composite and the cavity walls. The tensions require the connection between the two contact surfaces, resulting in spaces that can allow the infiltration of the area. Also, the stress may exceed the tension strength of the enamel, resulting in cracks or fractures of the dental tissues at the level of the interface (Versluis, Tantbirojn, 2009; Pereira et al., 2018; Patrascu et al., 2018). The lower the volume of the polymer in the composite resin, the greater the volume change during the polymerization reaction. Therefore, it is recommended to use composite resins with a large number of particles and a high module of elasticity for fixing intra-tissue inlays (Taraboanta et al., 2018; Tatarciuc et al., 2018; Tanculescu et al., 2017; Bolat et al., 2019).

The self-cured cementing material undergoes more important changes, both in artificial saliva and in acid environment. The light cured cementation resin provides a smooth, continuous interface, without any irregularities, being more stable even after the immersion in the two studied environments.

Conclusions

The materials used for inlay restorations, the dimension of the dental-prosthetic space and the fixing material are factors of great importance, which influence the quality and the behavior of these devices on the long-term.

By analyzing the two cementing materials studied, we can conclude that the self-cured resin, even if it initially allows a good marginal adaptation, after the action of the artificial saliva and the citric acid, it presents important depreciation that will affect the longevity of the inlays. This behavior is explained by the fact that these materials undergo significant volumetric changes during the grip reaction.

The Variolink N light-cured resin ensures a better marginal closure, being even more stable in the acid environment; the connection proved to be stronger between the fixing material and the composite resin from which the restoration was performed.

This study shows that the restoration material does not influence the quality of the dental-prosthetic joint, only the fixing material contributing to the obtainment a good quality marginal closure.

CHAPTER 3

INTERDISCIPLINARY RESEARCH ON CONTEMPORARY TEHCNOLOGIES FOR DIAGNOSTIC AND TREATMENT

3.1. Diagnostic Biomarkers for Periodontal Diseases

3.1.1. State of art

Periodontal Diseases (PD) is a chronic disease that affects the supporting tissues of teeth and affects 7-11% of the adult population and leads to tooth loss and a negative impact on quality of life (Richards, 2013; Kassebaum et al., 2014, 2017). Recent research suggests that is linked to several chronic disorders such as cardiovascular disease (Sanz et al., 2020) type 2 diabetes mellitus, and Alzheimer's disease. The imbalanced interaction between the periodontal microbiome and the host's inflammatory response can explain the local tissue destruction in periodontitis, but it is unclear whether and how this relationship links periodontitis to extra-oral comorbidities. It is crucial to determine whether the association between periodontitis and associated comorbidities is correlative or orchestrated by causal mechanistic interactions, from both medical and therapeutic perspectives.

Saliva has been found to be a useful source of markers for periodontal disease. One of the most well-studied markers of inflammation is aspartate aminotransferase (AST), which rises in the blood plasma during inflammation, and it is associated with the severity and degree of extentation of periodontal inflammation (Chambers et al., 1991; Sanz et al., 2020). Proteinases, lactoferrin, and metalloproteinases are also important markers that increase in saliva during periodontal inflammation.

Many studies address to matrix metalloproteinases 8 (MMP8), 9 (MMP9) and 13 (MMP13) (Luchian et al., 2022).

Sexton et al. (2011) found that higher amounts of salivary MMP8 (or collagenase 2) are linked to increased bleeding when probing, clinical attachment level, and pocket depth. This suggests that salivary MMP8 could be utilised for monitoring the progress of periodontal disease (Sorsa et al., 2016, 2020). Other studies indicate MMP-8 as a highly significant indicator of tissue destruction, exhibiting sensitivity levels that vary from 65% to 87% and specificity from 48% to 87% (Ebersole et al., 2013, 2015).

Matrix metalloproteinase 9 (or gelatinase B) plays a significant role in the process of periodontal disease, such the loss of tissue and immune reactions. Matrix metalloproteinase 9 was found to be higher in the saliva of patients with clinical manifestations of the PD, and it was lower in the saliva of patients with clinically stable conditions (Kinney et al, 2011). Same results were obtained by Gursoy et al. (2013). Furthermore, it has been observed that MMP9 levels decrease after periodontal therapy (Meschiari et al., 2013).

MMP 9 was found to be linked to acute coronary syndrome (Lahdentausta et al, 2018), cancer, multiple sclerosis, and mental diseases like schizophrenia and bipolar mood disorder (Kinney et al, 2011; Schenkein, Loos, 2013).

In addition to MMP-9, MMP-13 (or collagenase 3) has been linked to periodontal tissue degradation and alveolar bone resorption. Depending on the specific tissue and microenvironment, the regulatory mechanisms of MMPs may vary. These MMPs may be activated independently or in conjunction with pathogens and host proteases during the progression of periodontal disease (Leppilahti et al., 2014).

Saliva also contains other markers such as chitinase and hexosaminidase, which replicate the activity of periodontal inflammation. The reduction of nitric oxide radical levels in the saliva among patients with periodontitis has been observed. These diatomic free radical plays a crucial role in the optimal functioning of neutrophils and macrophages (Ghallab, 2018).

The presence of specific and nonspecific proteins in saliva can provide valuable information about the state of oral and systemic health. Salivary biomarkers such as C-reactive protein (CRP), fibronectin, cystatins, neopterin, cytokines, and other protein markers can be used to detect and monitor inflammation and disease progression in the periodontium and other organ systems.

The biomarker C-reactive protein (CRP) is commonly utilised in the management of various diseases. There is a proposal to substitute plasma CRP (pCRP) with salivary CRP (sCRP). CRP levels in saliva increase during periodontitis and are indicative of local process risk for the formation or progression of cardiovascular disease. In a recent systematic review, the majority of the studies have indicated a correlation between the levels of sCRP and pCRP, suggesting that sCRP can serve as a reliable substitute for pCRP in the diagnosis and treatment of various medical diseases (Babaei et al., 2022).

Fibronectin levels decrease during periodontitis, while cystatins levels decrease in sulcular fluid and saliva (Murakami et al., 1998; Lie et al., 2001).

Neopterin levels increase during periodontal inflammation (Ozmeriç et al., 2002) and cytokines such as interleukin-1 beta, interleukin-6, and tumor necrosis factor-alpha are also elevated in individuals with periodontitis.

Gingival crevicular fluid (GCF) it was thought to be a transudate, but when it was stimulated, it turned into an inflamed exudate (Khurshid et al., 2018). Inflammatory agents, cytokines, leucocytes, enzymes, organic ions, tissue breakdown products, and proteins are some of the elements that can be found in GCF.

In periodontal research, different biological disease markers like interleukins (IL-1α-IL-1β), tumour necrosis factor alpha (TNF-α), and enzymes like acid phosphatase, alkaline phosphatase, matrix metalloproteinases, collagenases, and elastase are used to measure the periodontal disease progression (Oswal, Dwarakanath, 2010).

Macrophage inflammatory protein-1 alpha (MIP-1α) is a chemokine that plays a crucial role in the immune system's response to inflammation. According to Nisha et al., 2018, there is an elevation in the secretion of macrophages at the locations of periodontal inflammation and bone resorption. Elevated levels of this biomarker have the potential to unveil covert subclinical inflammation in periodontal sites that are clinically healthy (Miranda et al., 2020). Furthermore, it has the ability to differentiate periodontitis in patients with type II diabetes mellitus (T2DM) (Cafiero et al., 2021). The salivary level of MIP-1α can be impacted by non-surgical periodontal treatment (Grande et al., 2019). According to previous research, there seems to be a correlation between this particular factor and the process of periodontal bone remodelling. The sensitivity and specificity values for this association were reported to be 95% and 97% (Al-Sabbagh et al., 2012).

Interleukin-1beta (IL-1β) is a pro-inflammatory cytokine released by LPS-activated macrophages (Mø), lymphocytes, and fibroblasts. It stimulates the secretion of PGE2 by Mø and fibroblasts, leading to bone destruction and the release of MMPs by fibroblasts and Mø, causing connective tissue destruction. Variations in the IL-1β + 3954 gene have been associated with an increased risk of periodontitis in Koreans, as per a study controlling for confounding risk factors (Kim et al., 2020). Correlations have been observed between clinical parameters of periodontitis, such as gingival index (GI), probing depth (PD), and GCF flow, and tissue IL-1beta activity (Liu et al., 1996).

Interleukin-6 (IL-6) is another pro-inflammatory cytokine secreted by macrophages in response to specific bacteria and by osteoblasts to stimulate osteoclastic activity. Salivary levels of IL-6 have been found to be elevated in patients with chronic periodontitis compared to healthy individuals (Cafiero et al., 2021).

Hemoglobin (Hb) determination can be a simple screening method for periodontal status when a clinical examination is not possible. Nevertheless, the test lacks specificity and therefore cannot serve as an appropriate substitute for a periodontal clinical evaluation. Studies have detected the presence of Hb in GCF from periodontal disease sites, with invisible bleeding potentially occurring in a pocket with early periodontitis despite negative findings from bleeding on probing (BOP) inspection (Mäkinen et al., 1996; Hanioka et al., 2015). These findings suggest that the detection of Hb derived from microbleeding in gingival sulci may serve as an index for preclinical diagnosis (Ito et al., 2016, 2021).

The presence of salivary neuropeptides (vasoactive intestinal peptide and neuropeptide Y) was observed to be significantly higher among patients diagnosed with periodontal disease. Furthermore, such levels were found to be positively associated with BOP scores (Haririan et al., 2018).

In a review, Chen et al. (2019) associated oxidative stress-related biomarkers in saliva and GCF with chronic periodontitis. A notable reduction in the overall antioxidant capacity was observed, alongside a marked increase in the levels of malondialdehyde, nitric oxide, total oxidant status, and 8-hydroxy-deoxyguanosine in the saliva of individuals diagnosed with CP.

According to Al-Rawi et al. (2020), the microRNAs (MiRNA-146a and miRNA155) have been identified as accurate biomarkers for monitoring periodontal health status in both diabetic and non-diabetic patients. These biomarkers are consistent, non-invasive, and can be used for diagnostic and prognostic purposes in saliva samples.

A cross-sectional study was conducted to examine salivary biomarkers of oxidative stress and advanced glycation end products in patients with periodontitis, as well as in patients with type 2 diabetes who were periodontally healthy, and in corresponding controls who were systemically healthy. According to Altıngöz et al. (2020), the detection of salivary 8-hydroxy-2'-deoxyguanosine (8-OHdG) either alone or when combined with other markers has the potential to function as a non-invasive screening tool for periodontitis.

Soluble Neuropilin-1 (sNRP-1) has been found to have a positive correlation with periodontitis and may play a role in the pro-inflammatory mechanisms that are observed in the inflammation of clinical periodontal tissue (Prieto et al., 2021).

Several studies have investigated whether saliva and GCF biomarkers could be used to identify periodontal disease (Kinney et al., 2014; Ghallab, 2018; Grant et al., 2022).

Offenbacher et al. (2007) conducted a molecular epidemiological investigation wherein they observed that higher levels of GCF Interleukin-1β (IL-1β) and Interleukin-6 (IL-6) were present in individuals with deep pocket depths (PD) and more severe BOP.

The findings of a reent systematic review indicate that the individual biomarkers of MMP8 (all or active forms) and interleukin 6 demonstrated the most optimal diagnostic performance. According to Ebersole et al. (2015), the utilisation of combinations of biomarkers has been shown to exhibit enhanced sensitivity, specificity, and diagnostic precision in contrast to individual biomarkers. The utilisation of a non-targeted approach in quantitative proteomics enables the detection of multiple protein biomarkers. The technique has enabled the identification of biomarkers for periodontitis, as reported by Rizal et al. (2020) in a recently systematic review and emphasised the importance of further exploration of these preliminary findings.

My studies on this field were primarily organised upon the evaluation of periodontal inflammation during orthodontic and prothetic treatments, as well as doxicciclyne treatment for aggressive periodontitis. The focus of the research was on matrix metalloproteinases 8 and 9, interleukin-1beta (IL-1β), and tumour necrosis factor alpha (TNF-α).

	The following are the most significant personal scientific contributions in this field
Published articles in ISI journals	1*. Luchian I, Moscalu M, Goriuc A, Nucci L, **Tatarciuc M,** Martu I, Covasa M. Using Salivary MMP-9 to Successfully Quantify Periodontal Inflammation during Orthodontic Treatment, J Clin Med, **2021**, 10(3): art. no 379. IF=4.964 2*. Aungurencei A, Luchian I, Goriuc A, Constantinescu D, Martu I, Popa DD, Vitalariu A, Luchian D, Earar K, **Tatarciuc M.** Collagenase-2-(MMP-8) as a Poimt - of- care Biomerker in Periodontal Disease in Patients with or Without Fixed Prosthesis Therapeutic Response to Doxycycline, Rev Chim, **2019**, 70(11): 4068-4072. IF=1.755 3. Luchian I, Martu I, Ioanid N, Goriuc A, Vata I, Stefanache AM, Hurjui L, **Tatarciuc M,** Matei MN, Martu S. Salivary IL-1 beta: A Biochemical Marker that Predicts Periodontal Disease in Orthodontic Treatment, Rev Chim, **2016**, 67(12): 2479-2483. IF=1.232 4. Martu I, Luchian I, Goriuc A, **Tatarciuc M**, Ioanid N, Cioloca DP, Botnariu GE, Martu C. Comparative Analysis of Some Antioxidant Markers in Periodontal Disease, Rev Chim, **2016**, 67(7): 1378-1381. IF=1.232
Published articles in BDI journals	1. Martu I, Luchian I, Goriuc A, Budala D, Martu A, **Tatarciuc M**, Martu C, Jitareanu A. Salivary tumor necrosis factor-alpha (tnf-alpha)- a potential marker of periodontal destruction. evolution under doxycycline treatment, Rom J Med Dent Educ, **2020**, 9(6): 62-67 (DOAJ) 2. Martu I, Goriuc A, Luchian I, Cioloca Holban C, Surdu Macovei A, **Tatarciuc M**, Balan A, Martu S. The quantification of tnf-alpha as a marker in the assessment of the chronic and aggressive periodontal pathology, Rom J Oral Rehabil, **2014**, 6(4): 92-98 (ESCI-WSCC, DOAJ)

**Publications described in detail in the next subchapters*

3.1.2. Using salivary MMP-9 to successfully quantify periodontal inflammation during orthodontic treatment

Aim of the study

To determine whether MMP-9 levels can reliably predict the chronic inflammatory oral diseases, in this study, we examine the effects of periodontal treatment on salivary MMP-9 levels in patients with stabilized pre-existing periodontal history, where treatment is done either without or coupled with orthodontic treatment.

Materials and Methods

Subjects

The study was performed under the Institutional Review Board protocol no. 5329/2018 approved by the ethics committee of the Grigore T. Popa University of Medicine and Pharmacy, and signed informed consent was obtained from each participant in the study. The sample population included in the current research consists of consecutive patients that were selected in a 12-month interval. Sixty individuals of which 32 males and 28 females in good general health from 21 to 38-year-old were enrolled in the study. The following inclusion criteria were used: a minimum of 20 teeth in functional dentition, moderate or severe periodontitis and without periodontal treatment at the time of enrolment. Periodontal exam included the recording of periodontal pocket depths (PPD) from six sites of each tooth. The six probing sites were distributed as follows: three sites on the buccal surfaces (mesial, central, and distal) and three sites on the lingual surfaces of the teeth (mesial, central, and distal). Bleeding on probing was recorded and the sulcus bleeding index (SBI) was determined. A complete periodontal probing was performed using an electronic probe (PaOn®, Orange Dental, Biberach a. d. Riss, Baden-Würtemberg State, Germany), and data were transferred using additional software. The following exclusion criteria were applied: smoking, heavy drinkers, immunocompromised, use of anti-inflammatory drugs or other medication affecting the periodontium, use of antibiotics and steroids, and a history of systemic and infectious diseases.

The sixty patients included in the study were randomly divided in three groups as follows: group 1, a control group that included 16 (7 men, 9 women) subjects without periodontal disease and/or clinical gingival modifications; group 2, which included 22 subjects (10 men, 12 women) with periodontal disease (chronic periodontitis localized in minimum 3 teeth) who received periodontal treatment (PD); and group 3, which included 22 (11 men, 11 women) subjects with periodontal disease (chronic periodontitis localized in minimum 3 teeth), who received both periodontal and orthodontic treatment (POD). All individuals received periodontal examination and were diagnosed based on the clinical criteria established by the American Academy of Periodontology (Greenwell, 2001). All patients underwent treatment including oral hygiene instructions. Periodontal treatment was identical for both PD and POD groups and consisted of supra- and subgingival scaling and root planning over a maximum 4-week period. The subgingival scaling was performed using the same ultrasonic device (Acteon Satelec®, Mérignac, Gironde, France), and the same type of subgingival inserts while for root planning area specific curettes (Hu-Friedy®, Chicago, IL, USA) were used. Therapeutic treatments were performed every 8 weeks starting 10 days after study commencement. For orthodontic treatment, we used metallic fixed appliances that were bonded after the periodontal status stabilized. No dropouts occurred prior or during the treatment.

Saliva Sample Collection and Analysis

Saliva was collected at two time points from patients included in PD and POD groups as follows: for the PD group, one initial baseline collection and a second collection 6 months following completion of periodontal treatment; for the POD group, one initial baseline collection and a second collection 6 months after completion of periodontal treatment and stabilization of the orthodontic treatment. The timing for the second saliva collection in the POD group was delayed compared to the PD group to allow for an evaluation of the effects of the orthodontic treatment on the inflammatory markers level once the treatment has stabilized. One baseline saliva collection was performed in the control group at the beginning of the study. All samples were collected by one investigator to ensure consistency in the protocol. Saliva was collected without stimulating its secretion from the salivary glands (i.e., paraffin gum or citric acid) in order to avoid any interference of the stimulating agent on marker release. Collection was carried out using Eppendorf tubes placed on ice; particular attention was given to contamination with blood, since MMP is also present in blood and its levels were shown to be different (i.e., higher) in blood compared to those present in the salivary fluid. Samples suspected of blood contamination were discarded.

Samples were stored at 20ºC pending analysis. The levels of MMP-9 in collected saliva samples were measured via ELISA immunoassay following the manufacturer’s instructions (R&D Systems Inc., Minneapolis, MN, USA) (Marcaccini et al., 2010).

Statistical Analyses

Statistical analyses were performed using SPSS 24.0 forWindows (IBM Corporation, North Castle Drive, Armonk, NY, USA). The Kruskal–Wallis test was applied to determine the differences in MMP concentrations between groups of patients according to treatment and clinical parameters. The Newman–Keuls post hoc test was also applied for the pair analysis of two groups of patients. MMP-9 values were reported as mean values and standard deviation. The evolution of MMP-9 values was also presented in %, with the proportion being represented by the decrease of the MMP-9 value related to the value registered before the treatment. The univariate correlational analysis was performed based on the Spearman rank order correlations test. To better highlight the effect of the treatment and the degree of malocclusion, the graphs were generated using STATA 16.1 (StataCorp LLC., College Station, TX, USA). A p-value of less than 0.05 was considered statistically significant.

Results

Clinical Parameters

Analysis showed a significant difference before treatment between PD and control groups for PPD (4.18 ± 0.21 vs. 1.65 ± 0.14, $p < 0.0001$) and SBI (2.9 ± 0.11, vs. 0.31 ± 0.11, $p < 0.0001$) as well as between POD and control groups for the same parameters: PPD = 4.54 ± 0.17, $p < 0.0001$; SBI = 3.45 ± 0.12, $p < 0.001$. Periodontitis treatment significantly improved PPD (3.23 0.19, $p < 0.01$) and SBI (2.04 ± 0.12, $p < 0.01$) while periodontitis combined with orthodontic treatment had a greater effect compared to the control group and the PD group's treatment for both clinical parameters, i.e., PPD = 2.4 ± 0.1, SBI = 2.04 ± 0.12, $p<0.0001$ for both.

Effects of Periodontal and Combined Periodontal with Orthodontic Treatment on MMP-9 Levels

Patients with untreated periodontal disease had significantly higher levels of salivary MMP-9 compared to controls (control group: 155.6 ± 38.63 ng/mL; PD: 582.27 ± 48.2ng/mL; POD group: 602.55 ± 64.55 ng/mL; $p<0.0001$ for both, Figure 82). However, following intervention, periodontal treatment alone lowered MMP-9 significantly compared to the levels before treatment (17.3% reduction; $p = 0.0046$). A combination of periodontal with orthodontic treatment drastically decreased MMP-9 levels by 42.3% compared to pre-treatment levels ($p<0.0001$). Although MMP-9 levels dropped significantly after treatment in both PD and POD groups, there was a significant difference ($p = 0.00012$) in MMP-9 levels following each of the two treatments, with the treatment for the POD group having the most significant effect in lowering MMP-9 levels compared to the PD and control groups ($p = 0.0005$) (Figure 82).

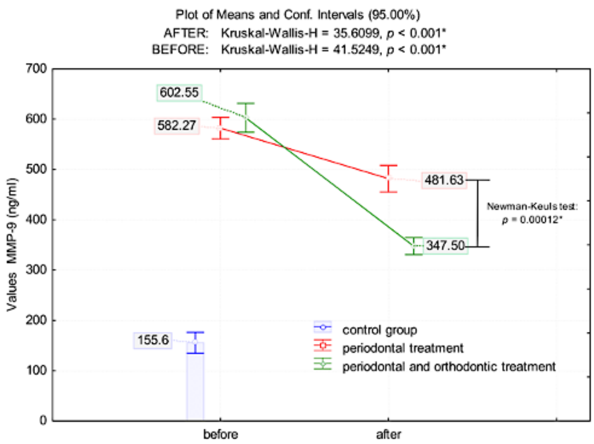


Figure 82. The means value of MMP-9 [ng/mL] in patients with periodontal disease prior and after periodontal treatment (PD) and periodontal and orthodontic treatment (POD) treatment;(*) indicates that marked effects are significant at p <0.05.

The Effect of Malocclusion on MMP-9 Levels

The degree of malocclusion significantly affected salivary MMP-9 levels. Because of this, prior to treatment, patients with periodontal disease had MMP-9 values that differed significantly depending on the angle class (PD group: p = 0.005; POD group: p = 0.003); this effect was more pronounced in patients with angle class II/1 and II/2 (Figure 83). Following the PD group's treatment, MMP-9 decreased significantly compared as a function of the angle class (p = 0.03). The treatment in the POD group significantly lowered MMP-9 levels compared to those of the PD and control groups (p<0.0001); however, there were no significant differences between the angle classes (p = 0.176) (Figure 83).

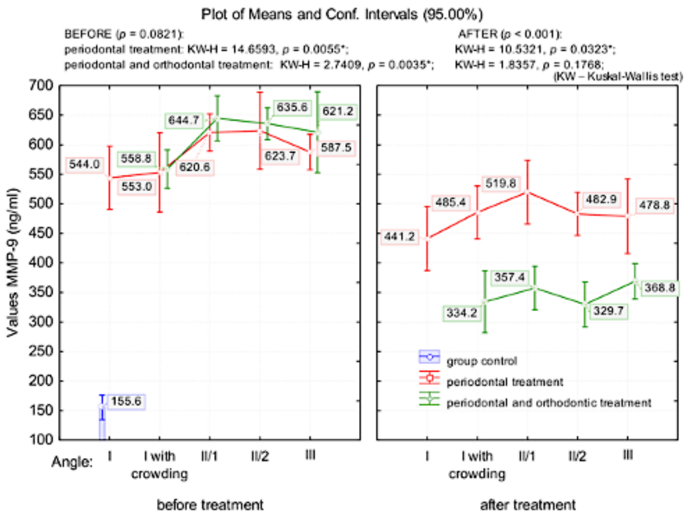


Figure 83. The means value of MMP-9 in patients with periodontal disease, in relation to angle class; (*) indicates that marked effects are significant at p <0.05.

Correlation Between Clinical Parameters and MMP-9 Levels

Before treatment, the Spearman rank analyses showed a significant positive association between the probing pocket depth (PPD) and MMP-9 levels in POD patients (r = 0.47, p = 0.03) with no difference in the PD group (r = 0.033, p = 0.88). Following intervention, MMP-9 levels were significantly correlated with PPD in the PD group (r = 0.33, p = 0.029) but not in the POD group (r = 0.678, p = 0.764). Similarly, there was a significant correlation between SBI and MMP-9 levels before treatment in the POD group (r = 0.47, p = 0.032) but not the PD group (r = 0.08, p = 0.71). After treatment in the PD group, MMP-9 levels in the PD group were significantly correlated with SBI (r = 0.46, p = 0.034) while the treatment in POD group abrogated the correlation between SBI and MMP-9.

Discussion

The results of this study show that both periodontal and the combination of peri-odontal and orthodontic treatments were effective in significantly lowering MMP-9 levels compared to patients who did not receive the treatment. However, it was the combination of periodontal with orthodontic treatment that had the greatest effect on MMP-9 levels compared to periodontal or control groups alone. Furthermore, while the treatment in both the PD and POD groups significantly improved clinical parameters, the POD group treatment had the greatest effect. This improvement of clinical parameters following inter-vention in the PD and POD groups was positively associated with MMP-9 levels. Finally, the degree of malocclusion significantly affected the effect of the treatment on MMP-9 levels with PD treatment having the most pronounced effect.

Periodontitis is one of the most prevalent inflammatory pathologies affecting nearly half of people over 30 years old (Papapanou, Susin, 2017). It is characterized by an immune inflammatory process ultimately leading to the destruction of periodontal attachment and supporting tissue and bone resorption. Several periodontal bacteria together with microbial proteases such as metalloproteases including host derived MMPs, all participate in the process leading to progression of periodontitis, tissue, and ligament degradation. Among them are *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Treponema denticola,* and *Tannerella forsythia*; together with the host's genetics and other environmental factors, these bacteria are active contributors in the infections and inflammatory processes that result in the production of metalloproteases, including host MMPs (Sorsa et al., 2006; Rathnayake et al., 2017; Cobzeanu et al., 2017). MMP-9 is among the best studied proteinases when it comes to its role in periodontitis and its activation in infections.

In the present study, salivary MMP-9 levels were associated significantly with periodontal and orthodontic treatment and differentiated from the control group. Therefore, MMP-9 can be used with high fidelity not only as a marker of periodontal inflammation but also as a tool for assessing the effectiveness of the nonsurgical periodontal and orthodontic therapy. The increased MMPs, whether in saliva or serum samples in periodontitis, were well documented. For example, salivary as well as circulating MMP-8 and MMP-9 levels were significantly elevated in periodontitis patients (Marcaccini et al., 2009) and reduced after periodontal treatment (Marcaccini et al., 2010; Correa et al., 2008; Figueredo et al., 2004).

The use of MMPs as salivary markers for local or systemic pathologies such as CVDs, diabetes, dyslipidemia has been of interest for sometimes, but not without challenges, given their vulnerability against local inhibitors in periodontitis condition that can limit their use in systemic diseases (Miller et al., 2010). In addition to the periodontitis group that was associated with increased MMP-9, patients who received both periodontal as well as orthodontic treatment displayed an augmentation in the inhibition of MMP-9 levels, compared with either treatment alone. To our knowledge, this is the first report demonstrating that combination of periodontal and orthodontic treatment is associated with a reduction in MMP-9 levels.

Previous work has shown increased salivary biomarkers in orthodontic treatment involving alignment with fixed appliances, which have been associated with tooth move-ment (Kapoor et al., 2014; Saloom et al., 2019). This is not surprising since there is increased osteoclast activity when or-thodontic forces are applied, and MMP-9 is expressed in osteoclasts where it controls proteolysis in bone resorption. Therefore, inflammatory markers such as MMP-9 are associated with osteoclasts activity, a phenomenon presents in response to orthodontic applied forces (Grant et al., 2013; Takahashi et al., 2006). In vitro studies showed an increase in MMP-9 following application of orthodontic forces, an effect that is dependent on the degree of tension and compres-sion (Kapoor et al., 2019). In our study, however, we measured MMP-9 levels after orthodontic treatment was completed and patients stabilized. This resulted in a further decrease in the MMP-9 levels in patients who received orthodontic treatment after periodontitis was improved or resolved. These results are also in line with findings demonstrating that MMP-9 levels decreased significantly in patients with periodontitis with orthodontic restorations (Kushlinskii et al., 2012) and that MMP-9 levels oscillated during application of orthodontic forces and decreased as early as 24h after appliance activation (Capelli et al., 2011).

Another important aspect of the study is highlighted by the findings that the MMP-9 values following the combined treatment dropped significantly more for all angle classes, with no significant differences between groups, whereas in the case of periodontal treatment MMP-9 values remain elevated in the patients who had angle classes II and III malocclusions. A comparative analysis of MMP-9 values in relation to the type of treatment and to the angle class shows that after combined periodontal and orthodontic treatment, the values of MMP-9 lowered significantly more, despite the fact that they were significantly higher before treatment.

Therefore, although at the start of the treatment patients with periodontal problems who were about to begin periodontal treatment combined with orthodontic treatment had higher values of MMP-9 (although not significant), these values dropped significantly more compared to those of patients who had only periodontal treatment. The persistence of high values of MMP-9 in patients who received only periodontal treatment, particularly in the case of those with angle classes II/2 and II/1 malocclusions, as well as those with angle class III malocclusions, is convincing and clearly demonstrates that orthodontic treatment combined with periodontal treatment significantly reduces inflammation in the affected periodontal tissues.

A complex analysis to assess changes in MMP-9 values in chronic inflammatory oral diseases could be performed using both MMP-9 levels and the type of treatment, in a clustered form. This method could lead to a significant increase in the prediction of the evolution of periodontal disease (Boiculese et al., 2009).

Existing literature shows that both the saliva tests and the tests performed on crevicular fluid provide valuable diagnosis information concerning the stage of the inflammation in periodontal disease. Several authors have shown that metalloproteinase-8 (MMP-8), an enzyme responsible for tissue destruction, was positively associated with periodontal disease (Herr et al., 2007; Kinane et al., 2003; Prescher et al., 2007). Because of this, an immunochromatography assay was developed and is commercially available for assessing MMP-8 in crevicular fluid. This test can be carried out in clinical practice and has the same accuracy as a laboratory test. This facilitates testing of this particular metalloproteinase and opens new perspectives in terms of the predictability of the chosen treatment plan (Sorsa et al., 2010). Currently, no similar test/assay exists for determining MMP-9 in saliva or in the crevicular fluid.

Conclusions

In conclusion, our results point to salivary MMP-9 as a strong candidate for quantifying inflammation in affected periodontal tissues during orthodontic treatment. It further indicates that MMP-9 can be used to accurately predict the level of inflammation associated with the type of malocclusion, which makes it a real and viable diagnosis instrument in monitoring the evolution of the periodontium during orthodontic treatment. Larger scale studies conducted on patients with various degrees of periodontitis and orthodontic treatments are needed to further establish the use of salivary MMP-9 as a predictor of inflammation following orthodontic treatment.

3.1.3. Collagenase-2-(MMP-8) as a Point-of-care Biomarker in Periodontal Disease in Patients with or Without Fixed Prosthesis Therapeutic Response to Doxycycline

Aim of the study

The study's purpouse was to determine and compare MMP-8 saliva concentrations in groups and subgroups of patients before and after Dox (Doxycycline) treatment.

Matherial and method

The study was conduced in Grigore. T. Popa University, the Periodontology Clinic. Patients' saliva samples were procesed into the Saint Spiridon Hospital Laboratory. The study included patients that adressed the Periodontology Clinic in the 2018-2019 period.

Three main groups were established. The first group included 12 patients with aggressive periodontitis (AgP) diagnosed according to clinical criteria: pocket depths over 4-5 mm, gingival bleeding on probing and radiological signs that proved osteolysis. In this group, 2 subgroups were established one of eight patients with fixed prosthesis, the second one of 4, without fp. Specific AgP exclusion criterias were: chronic periodontitis (CP) present and previous 6 months antiinflamatory treatment.

The second group included 18 patients with CP diagnosed according to clinical criteria: pocket depths over 6 mm, gingival inflamation, radiological proven horizontal osteolysis. In this group, 2 subgroups were established one for 10 patients with fixed prosthesis and another one for 8 patients without.

Specific group inclusion criteria: age over 35, more than 20 teeth present, no severe parodontitis episode present.

Specific group exclusion criteria: presence of severe periodontitis.

Third group included 10 patients with normal clinical peridontal status.

General inclusion criteria for the patients were: the signing of informed consent, chronic (CP) or AgP present according to criteria.

General exclusion criteria were smoking habit present, other chronic disease present, antibiotic treatment 3 months prior to the study, pregnancy, periodontal treatment 6 months prior to the study, allergies.

Fixed prosthesis patients were allready wearing their fp when entering the study, no fp was aplied as treatment during the study.

MMP-8 levels, for each patient, were evaluated using Elabscience provided ELISA testing kit before and after Dox treament.

Saliva was sampeled from all patients in Eppendorf tubes, centrifuged for 2 minutes at 1000 rpm, with the resulting supernatant being between 400 µl and 2000 µl. ELISA was performed using the supernatant to determine the concentration of MMP-8. Reactives used were adjusted to room temperature before use. Standard solution was achieved by adding 1 mL of reference standard sample diluent on the human liophilised standard MMP-8 left for 10 minutes incubation time at room temperature. Eight standards were prepared at halfed concentrations starting from 10 ng/mL, seventh dilution at 0,16 ng/mL and the eight being blank. In each ELISA plate well 100 microL from standard and probes were added. ELISA plate was than sealed and incubated at 37ºC for 90 minutes. 100 microL from biotinilated solution 0.01 dilution was added in each cell followed again by sealing and incubation for 60 minutes at 37 degrees. Bufer solution was than used for plate washing, 3 times at 1 minute interval. 100 mL of enzime Hrp (horseradish peroxidaze conjugate) in each ELISA plate well, followed by incubation at 37 degrees celsius for 30 minutes. Aspiration of each ELISA plate well with buffer solution, 5 times at 1 minute interval. 90 microL of substrate solution was than added in each ELISA plate well and than incubated for 15 miunutes at 37 degrees celsius. Coloration was observed. Color instensity dictated the necesity of increasing or decreasing the incubation time up till 30 minutes. 50 microL of Stopping solution was than added in each ELISA plate well. Absorbance was than read at 450 nm using a ELISA plate reader ELISA BIO-RAD and Magellan software was used for analysis.

After saliva prelevation, all patients had conventional periodontal therapy consisting in removal of dental plaque and calculus, followed by smothing and planing of exposed surface of the roots in teeth with deep periodontal pokets.

Doxycicline was administered oraly in subantibacterial concentrations of 20 mg twice daily for 7 days. No adverse effects were aknowledeged following antibiotic treatment.

Reevaluation of patient after Doxycycline included all examinations that were made at the begining of the study: periodontal status evaluation clinic and paraclinic. Saliva was resampeled and same assay protocol used for MMP-8 evaluation.

Results and discussions

All patients enroled completed the study. Patients were distributed into 3 main groups: AgP, CP and normal (control group). Each of the first two groups were split into with and without fp. All 4 subgroups thus obtained were further analysed before and after administration of Dox. Doxycycline was not administered to the control group.

Average, standard deviation and significance tests were performed on groups and subgroups. Intra subgroup variation was analysed between values of MMP-8 before and after Dox administration. Mean value of MMP-8 in control group was 0.257 ng/mL with standard deviation of 0.094 ng/mL and is the group that by far had the best concentration of values arround the average.

Highest average MMP-8 value has been acknowledged in the AgP without fixed prosthesis subgroup and before Dox treatment (mean value: 14.562 ng/mL, SD: 2.851 ng/mL) followed by the values, in the same subgroup after Dox treatment (mean value: 9.320 ng/mL, SD: 1.708 ng/mL). Lowest average MMP-8 was in the fixed prothesis CP subgroup after Dox treatment (mean value: 1.681 ng/mL, std: 0.904 ng/mL). The highest MMP-8 leve l variation was in the fixed prosthesis AgP subgroup, before and after Dox treatment with a drop of 40.8% from the initial MMP-8 level. The lowest variation between before and after Doxycycline treatment was in the non prothesis CP subgroup (a 14.1% drop in MMP-8 levels) (figures 84 and 85, table XX).

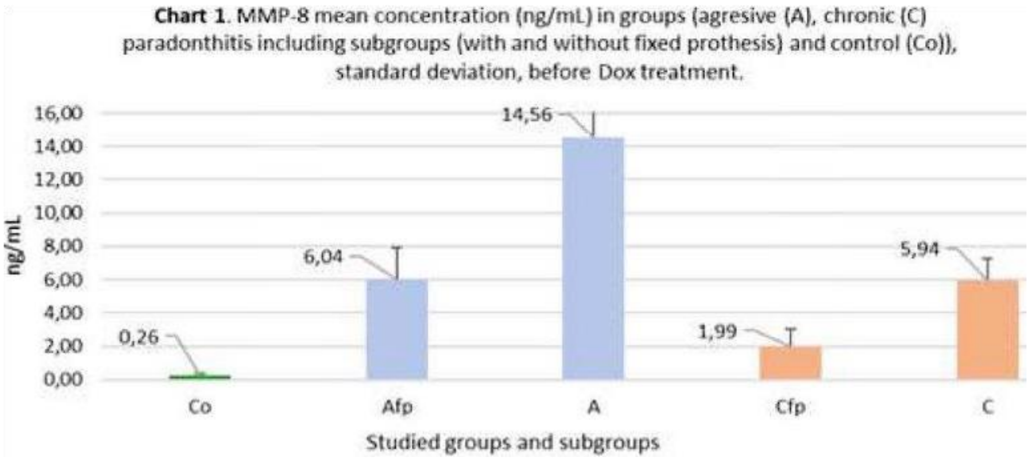


Figure 84. Co-control group; Afp-aggressive periodontitis (AgP) with fixed prothesis (fp) before doxycyclin treatment (Dox); A-AgP without fp before Dox; Cfp-chronic periodontitis (CP) with fp before Dox

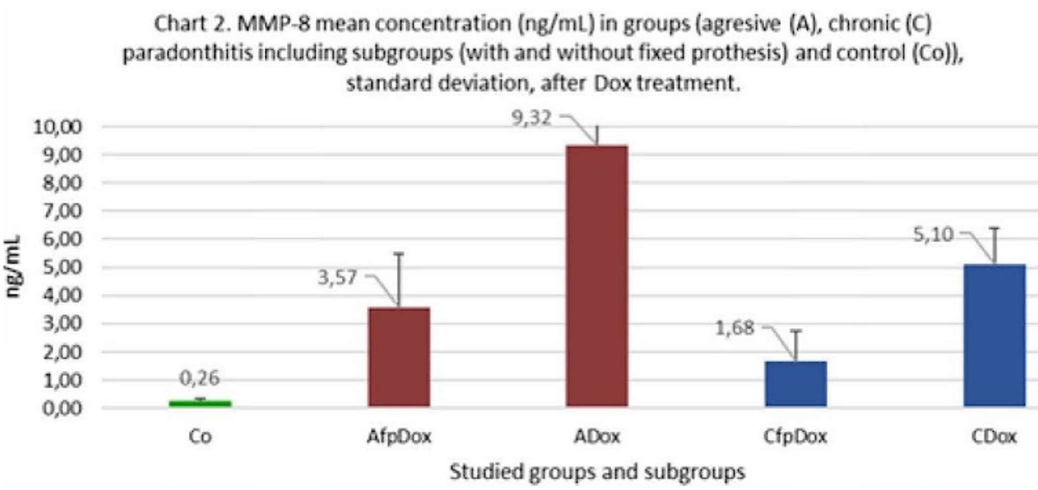


Figure 85. Co-control group; AfpDox-aggressive periodontitis (AgP) with fixed prothesis (fp) after doxycyclin treatment (Dox); ADox-AgP without fp after Dox; CfpDox-chronic periodontitis (CP) with fp after Dox; CDox-CP without fp after Dox

Table XX. MMP-8 levels in groups (aggressive-ap, chronic periodontitis-cp and control-c), subgropus (with fixed and without fixed prothesis), before and after doxycycline treatment and in group variation before and after Dox treatment

Groups and subgroups	Average (ng/mL)	Standard Deviation (ng/mL)	In Group MMP-8 level variation (the drop in value between before and after Dox treatment) in %
C	0,257	0.09	
Afp	6,039	1,919	40,8
AfpDox	3,570	1,162	
A	14,562	2,851	35,9
ADox	9,320	1,708	
Cfp	1,986	1,067	15,3
CfpDox	1,681	0,904	
C	5,938	1,297	14,16
CDox	5,097	1,113	

C-control group; Afp-aggressive periodontitis (AgP) with fixed prosthesis (fp) before doxycycline treatment (Dox); Afp Dox-AP with fp after Dox; A-AP without fp before Dox; ADx-AgP without fixed prosthesis after Dox; Cfp-chronic periodontitis (CP) with fp before Dox; CfpDox-CP with fp after Dox; C-CP without fp before Dox; CDx-CP without fp after Dox.

There was also significant MMP-8 level diference in the CP group between prosthetic and without prosthesis patients (mean value: 1.986 ng/ mL and 5.938 ng/mL respectevly). Because the MMP-8 assay was conducted on saliva instead of GCF the values (expresed in ng/mL) were lower than the average values in GCF in other published findings through a dilution mechanism most likley (Surlin et al., 2010; 2014).

When statistical analysis was made for AgP fp subgroup, a statistically significant difference was established between before and after Doxycycline treatment average MMP-8 values (6.04 ng/dL and 3.57ng/dL respectivley) and control group, $p<0.001$.

The same statistical analysis was made for AgP non fp subgroup, significant difference was established between before and after Dox treatment average MMP-8 values (14.56ng/dL and 6.039 ng/dL respectivly) and control group, $p<0.001$.

Statistical analysis on CP fixed prothesis subgroup did not establish significant diference between before and after Dox treatment average MMP-8 values (1,98 ng/dL and 1.68 ng/dL respectivley) ($p = 0.38$); same analysis made in CP non fixed prothesis subgroup also did not establish significant diference between before and after Doxycycline treatment average MMP-8 values (5.94 ng/dL and 5.09 ng/ dL respectively) ($p = 0.25$). This may be because CP as a hole has different lesions dominant trigerring pathways than MMP-8 mediated.

When statistical analysis was performed between fixed prothesis and non fixed prothesis patients it has been established that wearing fp significantly decreased mean MMP-8 values ($p<0.001$) both in AgP and CP groups before and after Dox treatment.

From the point of view of the doxycycline administration impact, only in AgP group Dox treatment significantly lowered the mean MMP-8 levels ($p<0.001$) while in CP group it didn't. Doxycycline treatment should be asociated with fixed prothesis treatment for maximum therapeutic effect.

Regarding host modulation therapies Doxycycline is one many posibilities, acting on one component of the inflammation cascade, on matrix metallooproteinases, however, another class of immunomodulatory drugs are DMARDS, which influence the release and action of certain biomolecules and cytokines such as IL 1, IL-6 Il 17, TNF alfa.

However, the detection of salivary MMP-8 can be considered a biomarker of periodontitis and could be used as a valuable indicator of health and pathologic process in patients with and without fixed prosthesis.

Conclusions

Salivary MMP-8 represents a reliable marker for AgP but not so reliable for CP. Doxycycline treatment administration is most effective in patients that have AgP and are also wearing fixed prothesis (dental bridges) and it is well proven through MMP-8 levels.

3.2 Modern dental therapeutic approaches

3.2.1. State of art

The advancements in computing technologies have facilitated the development of novel diagnostic tools, improved precision in therapeutic strategy, and provided alternative dental treatment options. The integration of advanced lasers and microscopes alongside innovative imaging methods, computer-aided design/computer-aided manufacture technology, and computer-aided implant surgery, has facilitated enhancements in routine dental practice.

The current periodontal therapies encompass a variety of surgical interventions, in conjunction with the utilisation of either natural or synthetic bone grafts, barrier membranes, and growth factors. The utilisation of these products in clinical settings has facilitated the development of innovative osseous tissues that exhibit comparable attributes to those of preexisting endogenous bone (Danesh-Sani et al., 2016). However, despite the implementation of these methods, the achievement of a consistent and favourable outcome in periodontal regeneration cannot always be guaranteed, and frequently culminates in epithelial lining healing as compared to the development of newly formed periodontal tissue.

Soft or cold lasers are compact, low-cost devices used primarily in applications, whereas hard lasers, such as carbon dioxide (CO2), neodymium yttrium aluminium garnet (Nd: YAG), and erbium doped yttrium aluminium garnet (Er: YAG), offer both hard tissue and soft tissue applications but have limitations due to their high costs and potential to induce thermal damage (Gross, 2007; Walsh, 2003).

Different types of lasers used in dentistry for various surgical and non-surgical procedures. CO2, Nd:YAG, Er:YAG, Er,Cr:YSGG, and diode lasers are among the lasers used for soft tissue surgery, dental hard tissue restoration, and periodontal therapy.

Each laser has specific properties, such as CO2 lasers with superior water selectivity, which may fast and effectively remove soft tissue and stop bleeding with minimum pen-etration (Sağlam et al., 2017). Erbium lasers have the highest water absorption and affinity for hydroxyapatite of any dental laser (Oliveira et al., 2012). Because of its excellent absorption by pigmented tissue, the Nd:YAG laser is a very effective surgical laser (Aoki et al., 2008).

Diode lasers are used for a variety of procedures, including aesthetic gingival re-contouring, soft tissue crown lengthening, soft tissue impacted tooth exposure, inflamed/hypertrophic tissue removal, frenectomies, and photostimulation of aphthous/herpetic lesions (Lesniewski et al., 2022).

Taking into account the classification of Placek and according to recent literature (Inchingolo et al., 2023), it seems that the laser surgery technique are superior in terms of haemostasis, surgical time, pain, edema, post-surgical inflammation, and healing time when compared with con-ventional surgery.

Dental implants' integration and their duration have been significantly enhanced by changing their surface with different coating materials (e.g., gold or silver nanoparticles) that allow for more rapid healing and adherence (Variola et al., 2011). However, there is a significant risk of infection of the tissues around the implant, a condition referred to as peri-implantitis.

The findings of the research undertaken on the use of laser therapy as an adjuvant in the treatment of peri-implant mucositis are contradictory (Lin et al, 2018; Aimetti et al., 2019; Mariani et al., 2020). Photodynamic antibacterial therapy (PDT) is apparent to be a safer option to antibiotics for treating periodontitis and peri-implantitis.

PDT has been found to be effective in treating aggressive periodontitis, especially in adolescents who are more susceptible to developing the disease. PDT using toluidine blue O (TBO) has been shown to inactivate various oral bacteria linked to periodontal disease such as *Porphyromonas gingivalis*, *Aggregatibacter actinomycetem-comitans*, *Fusobacterium nucleatum*, *Prevotella intermedia*, and *Streptococcus sanguis*. PDT has minimal cytotoxic impact on normal periodontal cells and has been found to be selective against periodontitis pathogenic bacteria while having no effect on resident oral bacterial growth. PDT has also been identified as a potential solution for treating denture stomatitis, a common condition that is difficult to treat with antifungal drugs due to resistance and recurrence. PDT works by exciting and oxidizing a photosensitizer dye with a certain wavelength of laser to generate singlet oxygen, which reduces the total number of bacteria.

Low-level light therapy (LLLT), also known as photobiomodulation therapy (PBMT), has gained attention in dentistry due to its potential to improve various oral conditions. PBMT has anti-inflammatory, antinociceptive, and antibacterial properties, and has been investigated for the management of oral mucositis, periodontal disease, temporomandibular disorder (TMD) pain, dental implant osseointegration, and orthodontic tooth movement in numerous studies.

A systematic review by Zadik et al. (2019) demonstrated that specific LLLT settings can be recommended for preventing oral mucositis in cancer patients. Injured nerves produce inflammatory mediators, but low-level laser treatment can decrease production while also promoting neuronal maturation and regeneration.

LLLT combined with non-surgical periodontal therapy was found to reduce inflammation, accelerate bone and gingival tissue regeneration, and reduce postoperative discomfort after periodontal surgery, according to Theodoro et al. (2002, 2021). Several studies have also shown that PBMT can effectively reduce pain and improve outcomes in patients with TMD and dental implant osseointegration.

LLLT has also been shown to effectively accelerate orthodontic tooth movement and decrease tooth sensitivity after dental bleaching, according to Zheng and Yang (2021).

Photodynamic inactivation (PDI) is a extensively studied in recent years light-based treatment that is used to eradicate bacteria and other microorganisms. For PDI to work, three conditions need to be met, which are the presence of oxygen, a photosensitizer that can transform light energy into harmful downstream products, and light of a specific wavelength that matches the absorption spectrum of the photosensitizer. Different photosensitizing dyes, such as methylene blue, Rose Bengal, hypericin, and xanthenes, are used in PDI, and each is paired with a specific wavelength that can generate sufficient amounts of reactive oxygen species (ROS) to destroy the target microorganism (Costa et al., 2008). In the 1920s, Schultz (1928) demonstrated the principle of photodynamic inactivation of microorganisms by using light waves and methylene blue to kill *Staphylococcus* bacteria. Despite these early findings, interest in the therapeutic use of PDI has emerged in the last 50 years due to technological advancements that have led to more efficient light sources and significant progress in research on the subject.

Chemotherapy side effects are a common challenge for both patients and healthcare providers to manage. Chemotherapy patients will experience different degree of local or systemic manifestation of the cytotoxic drugs' cases (Oun et al., 2018). Myelosuppression and the chain reaction it sets off, including neutropenia, leucopenia, thrombocytopenia, and even pancytopenia (Carey, 2003), are well-known to be among the most serious adverse effects. The resulting immunosuppression greatly raises the probability of infection problems, which may compromise the effectiveness of the chemotherapy and perhaps endanger the patient's life (Safdar et al., 2021). Mucositis, infections, bone degradation, dysgeusia, hyposialia, xerostomia, and an increased risk of bleeding are the end results inside the oral cavity (Daugėlaitė et al., 2019; Dreizen et al., 1977; An et al., 2023).

For the management and/or prevention of the oral side effects, there have not been any really evidence-based clinical practise recommendations available up to this point in time. Basic dental care, growth factors and cytokines, anti-inflammatory agents, anti-microbials, coating agents, anaesthetics, and analgesics, laser and other light treatments, cryotherapy, and natural and miscellaneous agents are different treatment methods (Lalla et al., 2014; Daugėlaitė et al., 2019).

My studies on this direction were primarily focused on the role that light plays in the treatment of periodontal diseases in patients who had been treated with dental implants and prosthetic restorations, as well as the effectiveness of oral rinse substances in chemotherapy patients.

	The following are the most significant personal scientific contributions in this field
Published articles in ISI journals	1*. Lazar L, Dako T, Muresan IE, Suciu M, Maftei GA, **Tatarciuc M**, Lazar AP. Is Laser Therapy an Adjuvant in the Treatment of Peri-Implant Mucositis? A Randomized Clinical Trial, Diagnostics, **2023**, 13(6): art. no 1192. IF=3.992 2. Luchian I, Budala DG, Baciu ER, Ursu RG, Diaconu-Popa D, Butnaru O, **Tatarciuc M**. The Involvement of Photobiology in Contemporary Dentistry-A Narrative Review, Int J Mol Sci, **2023**, 24(4): art. no 3985. IF=6.208 3*. Mocanu RC, Martu MA, Luchian I, Sufaru IG, Maftei GA, Ioanid N, Martu S, **Tatarciuc M**. Microbiologic Profiles of Patients with Dental Prosthetic Treatment and Periodontitis before and after Photoactivation Therapy-Randomized Clinical Trial, Microorganisms, **2021**, 9(4): art. no 713. IF=4.926 4*. Kappenberg-Nitescu DC, Luchian I, Martu I, Solomon SM, Martu S, Pasarin L, Martu A, Sioustis IA, Goriuc A, **Tatarciuc M**. Periodontal effects of two innovative oral rinsing substances in oncologic patients, Exp Ther Med, **2021**, 21(1): art. no 98. IF=2.751 5. Martu S, Amalinei C, **Tatarciuc M**, Rotaru M, Potarnichie O, Liliac L, Caruntu ID. Healing process and laser therapy in the superficial periodontium: a histological study, Rom J Morphol Embryol, **2012**, 53(1): 111-116. IF=0.62
Published articles in BDI journals	1. Luchian I, Martu S, **Tatarciuc M**, Martu I, Zetu I. Laser assisted versus conventional frenectomy in orthodontic patients, Rev Med Chir Soc Med Nat Iasi, **2015**, 119(1): 243-247 (Pubmed, ESCI-WSCC)

3.2.2. Is Laser Therapy an Adjuvant in the Treatment of Peri-Implant Mucositis? A Randomized Clinical Trial

Aim of the study

Regarding the use of laser therapy as an adjuvant in the treatment of peri-implant mucositis, the results of the studies conducted are controversial (Aimetti et al., 2019; Mariani et al., 2020; Lin et al., 2018; Tenore et al., 2020). That is the main reason why we aimed to evaluate the advantages and limitations of using laser therapy in the treatment of peri-implant mucositis in this study.

Materials and Methods

Study Design

This clinical study was conducted as a double-blind, randomized clinical trial.

Selection of Patients

Out of 76 adult patients with dental implant restorations who presented at the dental office in Targu Mures (Romania) for periodic check-ups, between 3 January 2021 and 22 December 2022, we selected 42 patients who met the following inclusion criteria:

- ✓ Presence of at least one implant on two different hemiarches;
- ✓ Implants must be pillars of fixed prosthetic works;
- ✓ Presence of bacterial plaque and signs of inflammation of the peri-implant gingival tissue.

The exclusion criteria were the following:

- ✓ Presence of radiographically detectable bone loss after the initial remodeling of the bone;
- ✓ Presence of systemic diseases with an impact on the periodontal tissues (diabetes, immunological diseases, acute articular rheumatism, tuberculosis, etc.);
- ✓ Pregnancy or breastfeeding;
- ✓ Non-surgical peri-implant treatment performed in the last 6 months;
- ✓ Antibiotic treatment in the last 6 months;

The use of non-steroidal anti-inflammatory drugs (figure 86).

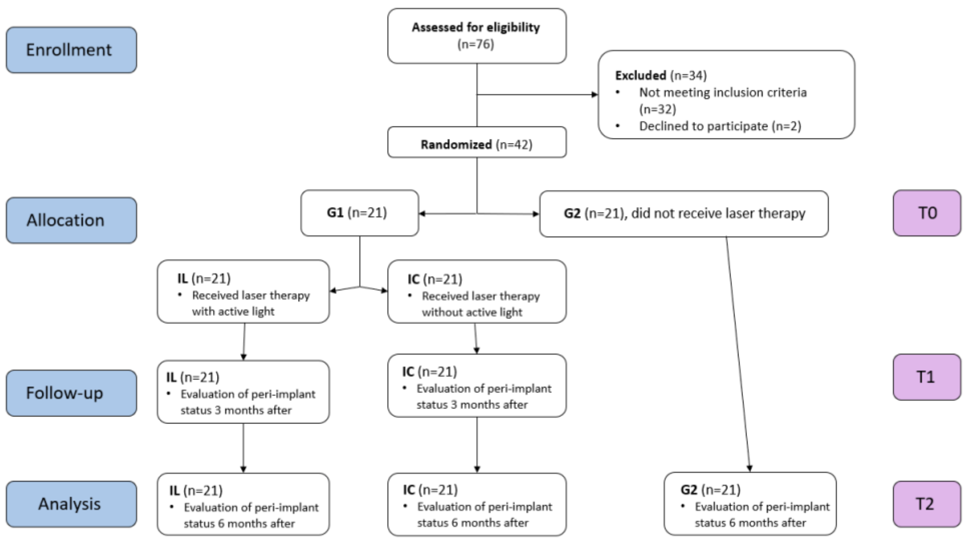


Figure 86. Flow diagram of the study.

The patients were informed about the procedure and about the fact that they could leave this study at any time and signed an informed consent. Sample size was determined using the power analysis calculation. A total of 17 patients per group were estimated to provide 90% power for the detection of 1.0 mm of difference in the probing pocket depth (PPD) between the two groups with a standard deviation of 0.8 mm, 0.05 type I error, and 0.1 type II error. Considering the potential withdrawal of patients, we sought to enroll at least 21 patients per group.

The Periodontal Protocol

The periodontal status was evaluated by a periodontologist other than the one who performed the laser therapy.

Patients who, at the check-ups, after the completion of the fixed prosthetic treatment with implant support, showed accumulation of bacterial plaque and signs of peri-implant gingival inflammation underwent a new periodontal examination. After the radiographic examination proved the absence of bone loss and after the initial physiological remodeling of the bone, the following indices were recorded in a periodontal record:

✓ Plaque index (PI): the presence (+) or absence (-) of bacterial plaque on the buccal, lingual, mesial, and distal surfaces following the application of a plaque disclosing solution. The PI value was calculated by dividing the sum of all surfaces presenting dental plaque by the total number of surfaces examined, multiplied by one hundred.

✓ Probing pocket depth (PPD): the distance from the gingival margin to the apical limit of the peri-implant gingival groove measured in 6 places (mesio-buccal/ centro-buccal/ disto-buccal/ mesio-oral/ centro-oral/ disto-oral) with a constant force.

✓ Bleeding on probing (BOP): by giving the following scores: 1, minimal punctate bleeding; 2, linear bleeding or in drops; 3, spontaneous or profuse bleeding, with or without suppuration (Dukka et al., 2021).

Patients were divided into two groups:

✓ Group 1: 21 patients who received instructions regarding dental plaque removal and underwent scaling around the implant surface using titanium curettes. Only one out of the two implants each patient had benefited from laser treatment. The peri-implant status was evaluated at the time of the initial examination (T0), three months after (T1), and 6 months after (T2).

✓ Group 2: 21 patients who received instructions regarding dental plaque removal and underwent scaling around the implant surface using titanium curettes. The peri-implant status was evaluated at the time of the initial examination (T0) and at 6 months (T2).

The Laser Protocol

Laser therapy was randomly performed for one of the implants (IL) for each patient in group 1. For the second implant, located on another hemiarch, the same protocol was followed but without active light (IC). The patients and the periodontologist who evaluated the periodontal status were informed that only one of the implants benefited from laser therapy without specifying which one. During the irradiation, both the patient and the doctor wore protective glasses. The peri-implant sites were irradiated at moments T0 and T1 by the same clinician for the same implant site.

Laser therapy was performed with a dental diode laser (Prime, Litemedics, SpA, Milano, Italy), with a power of 12 Watt, in pulsed system and operating wave of 980 nm, using the working mode “periodontology". A 320-micrometer optical fiber was inserted in the gingival sulcus and moved in a mesio-distal direction, both on the buccal surface and on the lingual surface, for 30 s.

Statistical Analysis

All data were collected in Microsoft Excel worksheets (Microsoft Corporation, Washington, DC, USA, 2018). Statistical analysis was performed with GraphPad Prism version 8.0.0 for Windows (GraphPad Software, San Diego, CA, USA). For each group of data, descriptive statistics such as mean, standard deviation, median, minimum, and maximum value were determined. Data normality was determined by the Kolmogorov-Smirnov test. The difference between the values of the clinical indices recorded at T0, T1, and T2 was determined using Fischer's and ANOVA tests. The significance level chosen was set at 0.05.

Results

Patients selected to participate in this study, based on the inclusion and exclusion criteria, were aged between 27 and 58 years. Group 1 consisted of 12 women with mean age of 43 years and 9 men with a mean age of 45 years. Group 2 included 11 women with an average age of 46 years and 10 men with an average age of 42 years. For each patient, the values of the main indicators of peri-implant health status were recorded: plaque index (PI), bleeding on probing (BOP), and probing pocket depth (PPD). The mean values recorded for PI, BOP, and PPD for each group are presented in Table XXI.

Table XXI. Mean values of PI, PPD, and BOP.

Index	Group	Moment T0	Moment T1	Moment T2
PI(%)	G1	41.07	19.46	5.31
	G2	42.85	-	17.85
PPD(mm)	G1 IL	3.28	2.80	2.33
	G1 IC	3.33	2.85	2.61
	G2	3.38	-	3.23
BOP(score)	G1 IL	2.14	0.52	0.33
	G1 IC	2.19	0.66	0.47
	G2	2.23	-	0.80

TO = initial examination, T1 = three months after, and T2 = six months after.

At the initial examination (moment T0), high PI values were recorded for most patients, with an average of 41.07% in the G1 group and 42.85% in the G2 group. In the G1 group at moment T0, 5 patients had PI values >50%, 12 recorded PI values of 30-50%, and 4 patients had PI between 10 and 30%. After a rigorous prophylactic cleaning session and patient instruction regarding dental plaque control, the PI values recorded at moments T1 and T2 were lower for all patients in the G1 group. Thus, at moment T1, no patient had a PI> 50%, and 3 had a PI value of 30-50%; for 17 patients, we recorded PI values of 10-30%, and 1 patient had a PI< 10% (figure 87).

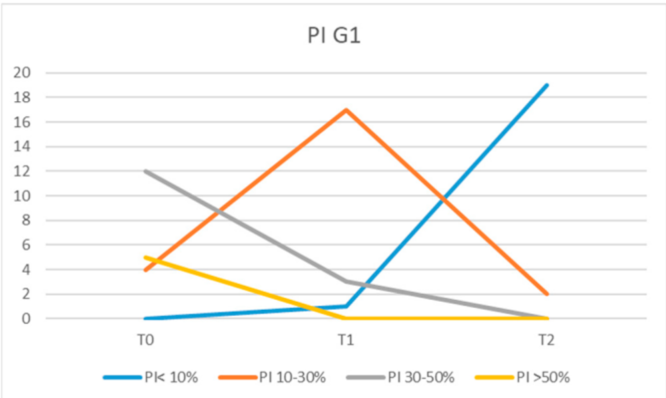


Figure 87. Values of PI in G1 at T0, T1, and T2.

The values recorded for PI in patients from group G2 at T2 moment, were low in most patients compared with the T0 moment. The values recorded at T2 were PI > 50% for three patients, PI = 30-50% for four, PI = 10-30% in eight of the patients, and PI < 10% in six of them (figure 88). However, three patients had PI values similar to those recorded at moment T0, and two patients showed higher PI values.

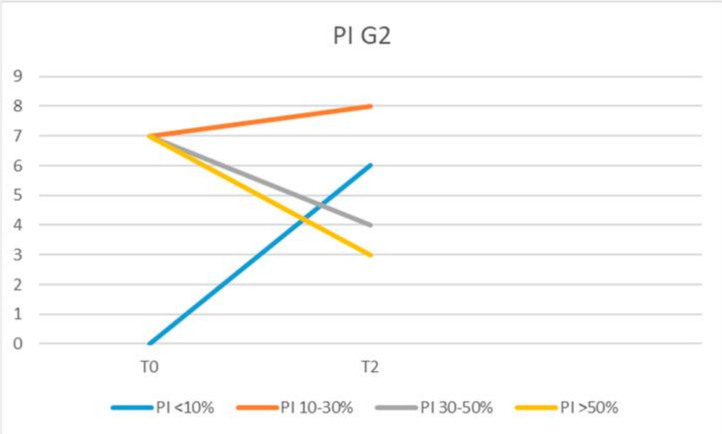
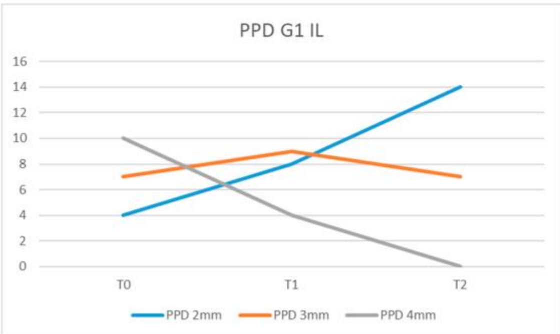


Figure 88. PI values in G2 at moments T0 and T2.

When comparing the average values of the plaque index between G1 and G2 at moment T2, a statistically significant reduction ($p = 0.0311$) was observed in patients from group G1.

The values recorded for PPD in the peri-implant sites in group G1 IL at moment T0 were 4 mm for 10 patients, 3 mm for 7 patients, and 2 mm for 4 of them. At moment T1, we recorded PPD = 4 mm in four patients, PPD = 3 mm in nine, and PPD = 2 mm in eight of the examined patients. At the 6-month examination (T2), the patients presented the following values:1 had PPD = 4 mm, 8 had PPD = 3 mm, and 12 of them had PPD = 2 mm (figure 89).



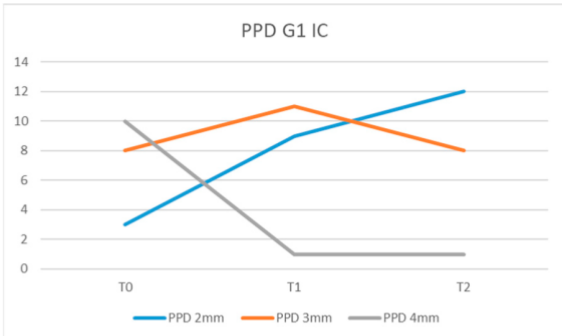


Figure 89. PPD values in G1 IL and G1 IC at moments T0, T1, and T2.

In G2, we recorded at the initial examination (T0) PPD = 4 mm in 10 of the examined patients, PPD = 3 mm in 9, and PPD = 2 mm in 2 of them (figure 90).

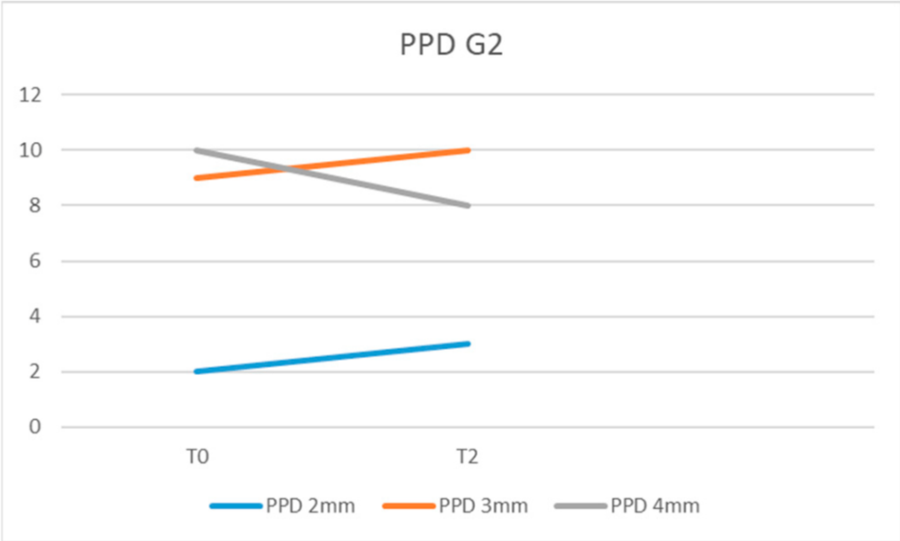


Figure 90. PPD values in G2 at moments T0 and T2.

The mean probing pocket depth (PPD) in the G1 IL group was 3.28 mm at T0, 2.80 mm at T1, and 2.33 mm at T2. For G1 IC, the values recorded for PPD were 3.33 mm (T0), 2.85 mm (T1), and 2.61 mm (T2). For G2, the average PPD values were 3.38 mm at T0 time and 3.23 mm at T2 time.

The difference between the mean values of PPD at T0, T1, and T2 between the G1 IL and IC groups was statistically insignificant (p = 0.48) as well as between G1 IL and G2 at the time of T2 (p = 0.4003). Comparing the mean values of PPD between G1 IL and G1 IC at T1 versus T0, no statistically significant difference was found (p = 0.48). Even when comparing the mean values of PPD for G1 IL and G1 IC, there was no statistically significant difference recorded at T2 compared with T1 (p = 0.194).

When recording the bleeding on probing (BOP), we found that all patients included in our study presented a higher score than one at moment T0.

In G1 IL, at moment T0, no patient had BOP = 0, 4 had BOP equal to 1, 10 had BOP = 2, and 7 had BOP = 3. At moment T1, 10 patients had BOP = 0 and 11 patients BOP = 1, and at time T2, 14 of them had BOP = 0, and 7 patients BOP = 1 (figure 91).

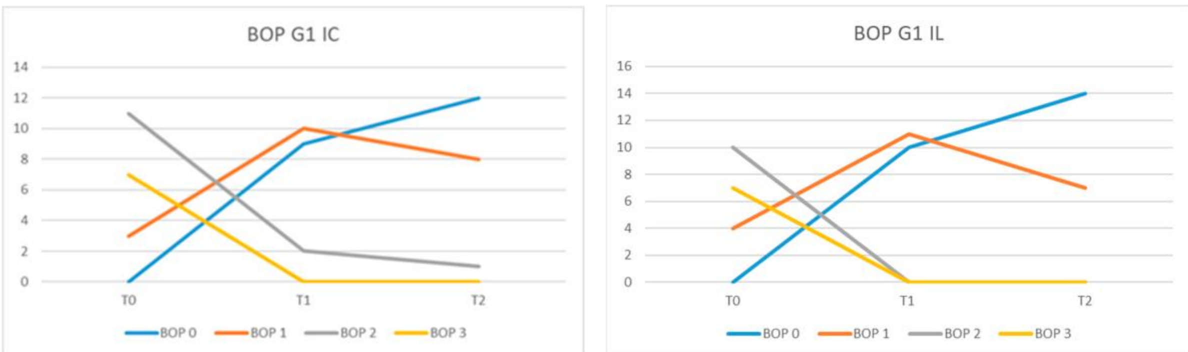


Figure 91. BOP values in group G1 Il and G1 IC at moments T0, T1, and T2.

In the G2 group at the initial examination (T0), 7 patients presented BOP = 3; 12 had BOP = 2; and, in 2 patients, we recorded BOP = 1. At the 6-month examination (T2), the recorded scores for BOP were 2 for 3 patients, 1 for 11 patients, and 0 for 7 of them (Figure 92).

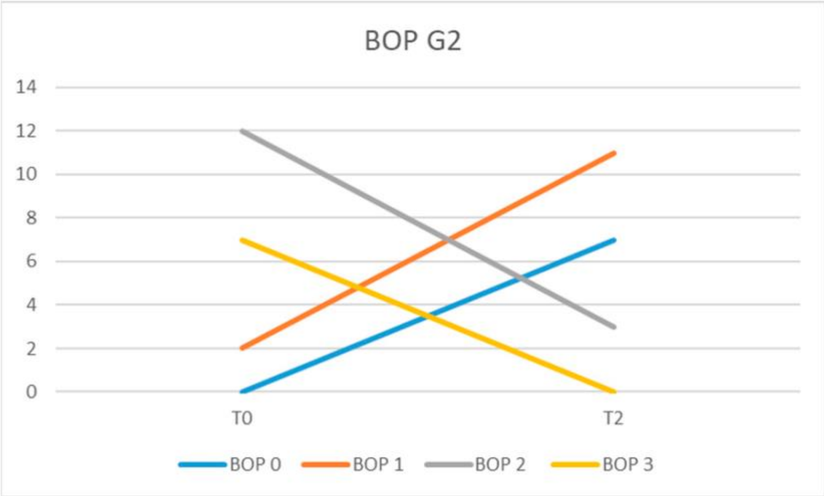


Figure 92. BOP values in group G at moments TO and T2.

The average values of BOP at time T0 were 2.14 for the patints of the G1 IL group, 2.19 for those in the G1 IC group, and 2.23 for patients from group G2. In the G1 IL group, the mean BOP values were 0.52 (T1) and 0.33 (T2), while in the G1 IC they were 0.66 (T1) and 0.47 (T2). In the G2 group at time T2, the mean BOP value was 0.80.

The difference between the mean BOP values at moments T0, T1, and T2 between the G1 IL and IC groups was statistically significant ($p = 0.0162$). When comparing mean BOP values in G1 IL versus G1 IC, a statistically significant reduction was observed ($p = 0.0182$) in T1 versus T0 and a highly significant difference between T2 and T1 ($p < 0.0001$). Comparing the mean BOP values between G2 and G1 IL, the difference was not statistically significant ($p = 0.0743$) nor between G2 and G1 IC (0.0584).

Discussion

Implant treatments are becoming more and more frequent and so are the potential negative effects that can come with implant-associated pathologies such as peri-implant mucositis and peri-implantitis. A recent review examined the potential risk factors for implant failure and treatments available and stated that pocket depth reduction can be achieved in the short-term with laser, and air powder abrasive could aid in cleaning a contaminated implant surface. The authors also stated that plaque control, surgical pocket elimination, and bone recontouring are other efficient treatments for peri-implantitis (Rokaya et al, 2020).

In our study, we tried to create patient groups that were as homogeneous as possible in terms of age and sex, so that these demographics did not influence the study results.

To establish the diagnosis of peri-implant mucositis, we examined the patients clinically (PI, PPD, and BOP) and radiographically. In G1, these assessments were made for two implants located at a certain distance from each other to ensure an objective assess-ment of the peri-implant status. If the patient presented several implants, the two implants that had the highest values of the recorded periodontal indices were included. In G2, the implants that recorded the most advanced signs of peri-implant mucositis were included. In group 1, laser therapy was randomly applied to one implant (IL), so that we could compare the values of the periodontal indices for IL with those obtained from the implant that did not receive active light (IC) in the same patient. Thus, the evaluation of the laser therapy was an objective one without oral hygiene habits, which differ from one patient to another, influencing the results.

We used PI, which assesses the plaque accumulation in the entire oral cavity as a percentage, to have an overview of the oral hygiene of each patient. The results of our study showed that there were patients who were not monitored at three months (T1) and had PI values comparable or even higher than those at the time of T0 during the 6-month examination (T2).

The findings that the mean values of PI for G2 at the time of T2 were not significantly lower than at TO and that, at G1, the differences between the PI values at these times were significant prove the importance of repeated controls at intervals of 3 months in patients with implant therapy. The frequency of intervals between training sessions and professional cleaning usually varies between 3 and 6 months, and their frequency should be based on the risk profile of each patient (Greenstein et al., 2022). Monje et al. (2017) observed that patients with a historyof periodontal disease are more compliant regarding oral hygiene measures and with periodic check-ups. Supportive therapy provides the clinician with the opportunity to monitor peri-implant status, and professional dental care improves peri-implant health and, hence, the success rate of dental implants. The patient's informed consent form should include the accordance of the patient to comply with personal and professional peri-implant supportive therapy. Rokn et al. (2017) observed that after 5 years of implant loading without following a regular maintenance schedule, one in five patients presents with peri-implantitis.

In this study we recorded no statistically significant change in PPD recording between G1IL, G1IC, and G2 at moment T2. However, we recorded reductions in PPD values for most patients, which explain the remission of inflammatory phenomena. Al Rifaiy et al. (2018) observed a statistically significant decrease ($p < 0.001$) in PPD in patients who benefited from laser therapy, both when comparing the values obtained at 12 weeks with the initial one and when comparing those recorded in patients who did not benefit from it. The same results of statistically significant reduction of PPD after using laser therapy were obtained by Lerario et al. (2016). The finding that 89% of the implant sites presented at initial levels of PPD higher than 4 mm may explain the difference to the results of our study, in which 71% of patients presented at an initial PPD = 4 mm and no value was higher than 4 mm.

For the BOP evaluation, we chose to use the variant of giving a score, proposed by American researchers (Dukka et al., 2021), because it allows the quantification of bleeding on probingat each individual implant site. The percentage evaluation in the entire oral cavity would not have allowed us to evaluate the results of the laser therapy at each implant's level. In our study, the finding that mean BOP values in G1 IL were significantly reduced at T2 compared with T0 and compared with G1 IC demonstrates that laser therapy can be an adjuvant in the treatment of peri-implant mucositis. Similar results were obtained by Al Rifaiy et al. (2018), who concluded that antimicrobial laser therapy, as an adjuvant in the treatment of peri-implant mucositis, is more effective than simple mechanical instrumentation. In a study conducted on 125 implants, the authors observed significantly reduced values of PPD and BOP, with values ≤ 5%, in patients treated with laser (Lerario et al., 2016). Repeated adjunctive application of laser therapy at 0, 7, and 14 days at peri-implant sites produced significant clinical improvements after an observation period of at least 2 years (Mettraux et al., 2016). The results of the study by Sánchez-Martos et al. (2020) showed that patients who received laser therapy as an adjunct to conventional treatment of mucositis had less bleeding at the 3-month reassessment than patients who received only conventional therapy ($p < 0.001$).

Starting from the observation that in patients who received adjuvant laser therapy, BOP was positive at 44 sites at T0 and t 6 sites at 3 months (T1), while for patients who received only mechanical treatment, BOP was positive at 52 sites at T0 and t 28 of places at 3 months (T1), Tenore et al. (2020) considered that laser therapy can be used as an adjunct to mechanical therapy method. Mariani et al. (2020) concluded that the additional use of laser showed small additional benefits in the treatment of peri-implant mucositis after a one-year observation period, which was not statistically significant.

On the other hand, the results of other clinical studies led the authors to the conclusion that the additional use of laser had no further positive influence on peri-implant healing compared with mechanical instrumentation as monotherapy (Aimetti et al., 2019; Arisan et al., 2015). Atieh et al. (2022) concluded that in the management of peri-implant mucositis, the combined use of diode laser and mechanical debridement provided no additional clinical advantage over mechanical debridement alone.

Adjunctive therapy such as laser or photodisinfection treatment could provide an auxiliary advantage in peri-implantitis, as was illustrated for periodontitis, especially in patients with other systemic pathologies, such as diabetes, myocardial infarction, or rheumatoid arthritis (Nicolae et al., 2016; Zhao et al., 2021; Dembowska et al., 2022; Martu et al., 2021).

Early diagnosis of peri-implant mucositis and the application of effective therapeutic methods are preventive measures in the occurrence of peri-implantitis (Jepsen et al., 2015).

The limitations of our study consist of the small group of patients evaluated and the evaluation of only clinical indexes; microbiological or biochemical data could have offered a more complete image of laser treatment efficacy. Another limitation is lack of comparison with other adjuvant methods in order to assess treatment superiority.

Given that the data regarding adjuvant laser treatment of peri-implant mucositis are sparse and controversial, future clinical trials are needed to evaluate the potential benefit of this approach.

Conclusions

The peri-implant health status is directly correlated with the maintenance of oral hygiene; therefore, the clinician must give importance to supportive therapy in order to increase the success rate of dental implants.

Laser therapy as an adjunct to conventional treatment of peri-implant mucositis led to a statistically significant reduction in probing bleeding at 3-month and 6-month re-evaluations. When PPD ≤ 4 mm, laser therapy leads to an evident reduction in probing depth but not enough to be statistically significant.

The conclusions of the present study should be considered preliminary and interpreted with caution. Further randomized clinical trials should be conducted to obtain solid conclusions.

3.2.3. Microbiologic profiles of patients with dental prosthetic treatment and periodontitis before and after photoactivation therapy-Randomized clinical trial

Aim of the study

To our knowledge, there are no data on the potential effects of photodynamic therapy on patients with fixed dental prosthesis and periodontal damage of different severity stages. We also did not identify research that reported the beneficial effects of photodynamic ther-apy in such patients to the so-called "gold standard" in periodontal antibacterial therapy: chlorhexidine. The null hypotheis in this case is that adjunctive photodynamic therapy offers no additional benefits to patients with periodontitis and fixed dental prosthesis when compared to scaling and root planning alone in terms of clinical and microbiological examination.

Therefore, we propose a study to evaluate the efficacy on clinical periodontal pa-rameters and periodontal pathogenic microorganisms of photoactivation therapy and irrigations with chlorhexidine 0.2% solution, which is supplementary to etiological peri-odontal treatment in patients with conventional fixed prosthetic treatment with periodontal tissue breakdown.

Materials and Methods

Trial Design

The present study was a randomized single-center clinical trial performed on a group of 169 patients with conventional fixed prosthetic treatments on natural teeth.

Study Group

The study was performed on subjects addressing The Dental Unit of The University of Medicine and Pharmacy "Grigore T. Popa" Iasi, Romania between 1 October 2017 and 1 October 2019. The inclusion criteria were systemically healthy patients over the age of 18 with a fixed dental prosthetic metal-ceramic bridge exclusively on natural teeth, which included at least 2 abutments and with periodontal disease, with at least 10 remaining teeth in the oral cavity. The exclusion criteria from the study were uncontrolled systemic medical conditions, diabetes or other metabolic disorders, autoimmune diseases, rheumatic diseases, smoking, use of systemic antibiotics and anti-inflammatory drugs or periodontal therapy in the last six months prior to the study.

Prior to the start of the study, all participants were informed about the study and signed a written agreement. The methodology of the study complied with the rules set out in the Helsinki Declaration. The study protocol was approved by the Ethics committee of The University of Medicine and Pharmacy “Grigore T. Popa" Iasi, nr. 19 July 2017.

Sample Size

Power analysis was performed to determine the minimum sample size for the study. Considering a type I error of 0.05 and 95% power, with a change of 1 mm in probing depth as the main clinical outcome of the study between the three study groups, based on a previous clinical study (Queiroz et al., 2015), the minimum sample size per group was 26 patients.

Periodontal Clinical Measurements

After the first session, subjects were randomly divided into three groups, using a computer-generated table: the group with conventional SRP and photoactivation therapy (PDT Group) (n=50), the group with SRP and chlorhexidine irrigation 0.2% (CHX Group) (n=67), and the group of subjects who followed only conventional mechanical therapy-SRP only (Control group) (n=52). Nine subjects required the discontinuation of chlorhexidine rinsing (4 of them reported dental and mucosal pigmentation, 4 reported taste disorders, and a patient reported burning sensation at the mucosal level after rinsing with CHX), thus leading to the exclusion from the study.

Patients underwent a complex periodontal clinical examination, determining the following periodontal parameters: probing depth (PD), loss of clinical periodontal attachment (CAL), probing bleeding index (BOP), and bacterial plaque index, with the determination of periodontal diagnosis (Armitage, 2004; Löe, 1967). For the diagnosis of periodontitis, we took into consideration the staging system according to the new classification of periodontal diseases (Severity stages 1-4) (Caton et al., 2018).

The periodontal probing was performed with a manual periodontal probe (CP-12, Hu-Friedy Mfg.Co., LLC, Chicago, IL, USA) by two calibrated periodontists. Probing depth, together with the loss of clinical periodontal attachment, was measured at six points per tooth: mesial-vestibular, central-vestibular, distal-vestibular, mesial-oral, central-oral, distal-oral. The probing depth, i.e., the distance from the gingival margin to the base of the periodontal sulcus/pocket, was measured using a graduated periodontal probe with a standardized tip diameter of approximately 0.5 mm. The applied probe force was standardized to 0.25 N. Bleeding on probing index (BOP) was assessed as present if bleeding was evident within 30 s of probing or absent, if no bleeding was observed; the plaque index was also calculated as a percentage, calculating the ratio between the number of dental surfaces that had bacterial plaque to the total number of surfaces examined. Periodontal parameters were evaluated at baseline, one month, and six months after the first session.

All examiners were experienced periodontists and were calibrated by the principal investigator (MD). Calibration was accepted if the measurements of the corresponding sites were equal to ≥90%. Examinations were performed blindly to the method of therapy used in the individual patient.

Therapeutic Interventions

All patients underwent conventional manual non-surgical scaling and root planing (SRP) treatment in the first session. In the photoactivation study group, after careful removal of the granulation tissue and mechanical debridement of the tooth surface, the treatment was performed using PDT laser (HELBO, Photodynamic Systems GmbH, Wels, Austria). The photosensitizer, phenothiazine chloride (HELBO, Bredent medical GmbH & Co. KG), was applied to the dental surface and photoactivated for 30 s/site, on a wavelength of 660 nm and irradiation of 100 mW (Rakašević et al., 2016). The photoactivation sessions were performed at baseline, at 7 and 14 days from baseline.

Patients with conventional prosthetic treatments in the group with CHX followed, in addition to conventional therapy in the first session, oral rinses at home with 0.2% chlorhexidine solution, twice a day, for 14 days. All patients were instructed to follow oral hygiene measures (dental brushing with manual toothbrush and cosmetic toothpaste), and for subjects in the PDT and control groups, it was recommended not to use mouthwash. Any side effects or side effects related to photoactivation, CHX irrigation, or even conventional mechanical therapy have been closely monitored.

All periodontal treatments were performed by periodontal specialists blinded to the purpose of the study.

Microbiological Examination

Bacterial plaque samples were taken at baseline, one month and six months after the first session; the deepest periodontal pocket was selected from each patient for sampling. At the selected site, each tooth was isolated with sterile cotton rolls, the supra-gingival plaque was carefully removed, and the site was gently dried with air spray. For the collection of crevicular fluid, a sterile paper cone, size 35 (Dentsply Maillefer, Ballaigues, Switzerland) was inserted into the site and held in place for 30 s; then, it was immediately transferred to a sterile Eppendorf tube with transport medium (Medizone, Dolj, Romania).

DNA Extraction

DNA extraction was performed with a commercial Wizard® Genomic Purification Kit (Promega, Madison, Wisconsin, USA) following the manufacturer's instructions. Simultaneously with the realization of the extraction protocol, control of contamination between samples was performed by processing a test sample represented by water with a degree of purity for molecular biology. The quantification and purity of the isolated DNA was determined by spectrophotometry using NanoPhotometer® (Implen Gmbh, München, Germany).

Quantification of Periodontopathogens

The sequence of primers and probes used for qPCR counting of the periodontids studied is shown in Table XXII.

Table XXII. Sequence of primers and probes.

Patogen	Primer 5'→3'	Probe 5'→3'	Gene
A.a	F:GCGAACGTTAGCGTTTTAC	ATTGCCCGCACCGAAACCCAAC	waaA
	R:GGCAAATAAACGTGGGTGAC	5'_Cy5→BHQ2_3'	
P.g	F: TGGTTTCATGCAGCTTCTT	GTACCTCATATCCCGAGGGGCTG	waaA
	R:TCGGCACCTTCGTAATTCTT	5'_HEX→BHQ1_3'	
T.d	F:CCTTGAACAAAAACCGGAA	GAGCTCTGAATAATTTTGATGCA	waaG

	R:GGGAAAAGCAGGAAGCATAA	5'_Cy5→BHQ2_3'	
T.f	F:CTCGCTCGGTGAGTTTGAA	CGATTCGCAAGCGTTATCCCGACT	waaA
	R: ATGGCGAAAAGAACGTCAAC	5'_HEX→BHQ1_3'	

A.a = Aggregatibacter actinomycetemcomitan; P.g = Porphyromonas gingivalis; T. d = Treponema denticola; T. f = Tannerella forsythia.

Periodontopagenic quantification was performed by real-time quantitative PCR, Taq-Man method, using the Mx3005P qPCR platform (Stratagene, La Jolla, CA, USA). The amplification was performed after the following thermal program: initial denaturation at 95°C for 10 min and 40 cycles of 95 °C-30 s, 60 °C-1 min. The qPCR reactions were performed in a total volume of 25 µL of which 2 µL of the DNA was isolated from the test sample, as well as 12.5 µL of GoTaq® qPCR Master Mix solution, and 0.4 µL ROX; the volume of primer, probe, and biopure water were optimized to determine the effective concentration. In the case of *A. actinomycetemcomitans*, the concentration of primers and probes was 100 nM and 200 nM, respectively, for *P. gingivalis* 300 nM and 200 nM, P. intermedia 100 nM and 100 nM, *T. denticola* 300 nM and 100 nM, and in the case of *T. forsythia*, 100nM and 100 nM.

Statistical Analysis

Clinical and microbiological measurements were expressed as percentages or median values (minimum, maximum). The Mann-Whitney U test was used for the statistical analysis of differences between the treatment modalities. Changes between the evaluation time-points were calculated using the Wilcoxon signed-rank test. The significance level was considered for p=0.05. All statistical and calibration calculations were performed using SPSS, Ver. 23 (SPSS Inc., Chicago, IL, USA).

Results

Table XXIII summarizes the demographic and general characteristics of the study groups at baseline.

Table XXIII. General characteristics of study subjects.

Group	Periodontitis Severity	Number of Subjects	Sites n(%)	Age (Years)	Gender	
				(Mean±SD)	Male	Female
PDT	S1	14	79(9.29%)	47.3±7.4	42.8	57.2
	S2	16	97(11.41%)	52.5±10.2	50.5	49.5
	S3	10	68(8.00%)	53.1±10.1	60.0	40
	S4	10	74(8.71%)	47.9±9.6	75.0	25
CHX	S1	18	75(8.82%)	45.3±7.9	66.7	33.3
	S2	10	67(7.88%)	47.5±7.6	60.0	40
	S3	16	71(8.35%)	57.2±11.9	62.5	37.5
	S4	14	63(7.41%)	50.3±12.4	71.4	28.6
Control	S1	8	51(6.00%)	46.9±8.8	50.0	50.0
	S2	14	74(8.71%)	52.1±10.8	42.8	57.2
	S3	16	77(9.07%)	50.8±11.4	50.0	50
	S4	14	54(6.35%)	49.2±8.6	57.1	42.9

PDT: SRP + photoactivation therapy group; CHX: SRP + chlorhexidine rinsing group; SD: standard deviation. S1: Periodontitis stage 1; S2: Periodontitis stage 2; S3: Periodontitis stage 3; S4: Periodontitis stage 4.

The analysis of the study was performed on the following groups:

- The group that underwent SRP therapy plus photoactivation therapy (PDT Group) (n=50 total patients; number of sites = 318) consisted of 14 patients with stage 1 periodontitis (S1) (number of sites = 79), 16 patients with stage 2 periodontitis (S2) (number of sites = 97), 10 patients with stage 3 periodontitis (S3) (number of sites =68), and 10 patients with stage 4 periodontitis (S4) (number of sites = 74).

- The group that underwent SRP therapy plus irrigation with chlorhexidine 0.2% (CHX Group) (n =58 total patients; number of sites = 276) consisted of 18 patients with stage 1 periodontitis (S1) (number of sites = 75), 10 patients with stage 2 periodontitis (S2) (number of sites = 67), 16 patients with stage 3 periodontitis (S3) (number of sites=71), and 14 patients with stage 4 periodontitis (S4) (number of sites=63).
- The group with SRP only therapy(Control Group) (n = 52 total patients; number of sites=256) consisted of 8 patients with periodontitis stage 1 (S1) (number of sites=51), 14 patients with periodontitis stage 2 (S2) (number of sites = 74), 16 patients with periodontitis stage 3 (S3) (number of sites = 77), and 14 patients with periodontitis stage 4 (S4) (number of sites =54) (Table XXIII).

Regarding the severity prevalence, 24.11% of the study sites presented superficial periodontal destruction (periodontitis stage 1), 28.00% moderate destruction (S2), 25.42% periodontitis stage 3, and 22.47% periodontitis stage 4.

Periodontal Clinical Parameters

Regarding periodontal parameters at baseline, all subjects with fixed prosthetic appliances on natural teeth and periodontitis showed plaque and bleeding on probing indices with a value close to 100%. Moreover, we did not notice differences in probing depth and loss of periodontal clinical attachment between the intervention groups by severity of periodontal lesions at baseline (Table XXIV).

Evaluation of plaque index and bleeding index one month after the first session revealed significant reductions for all three groups ($p < 0.001$), except for the bleeding index in patients in the control group with severe periodontitis (stages 3 and 4 of severity) (Table XXIV). At the 6-month evaluation, the plaque index was still significantly lower than baseline, but the bleeding index maintained a significant difference only for the PDT group (all stages of periodontitis severity) and for CHX group (stages 1 and 2 of severity); we observed a tendency for increased values for the other subjects (Table XXIV).

Following analysis of probing depth and loss of clinical attachment one month from baseline, we observed significant reductions in the PDT group (all stages), the CHX group (only subjects with superficial periodontitis, S1, and moderate, S2) and only for subjects with superficial periodontitis in the control group. Although lower than baseline, PD and CAL failed to reach a threshold of statistical significance in patients with severe periodontitis in the CHX group and moderate and severe periodontitis in the SRP only group (Table XXIV). Moreover, following comparisons between groups of values from one month, improvements in PD and CAL were more significant for the group that also underwent photoactivation therapy ($p <0.001$).

At the 6-month evaluation, we observed that significant decreases for probing depth and attachment loss were maintained only for the PDT and CHX subjects (stages 1 and 2 of periodontitis severity). Moreover, for the control group and CHX group (stages 3 and 4), the mean PD and CAL values were even higher than baseline, although without a significant difference (Table XXIV).

Table XXIV. Periodontal parameters on study groups and periodontitis severity at baseline, one month and six months evaluation.

Parameter	PDT				CHX				Control			
	S1	S2	S3	S4	S1	S2	S3	S4	S1	S2	S3	S4
Baseline evaluation												
PI (+)(%)	98.7	97.9	95.6	92.6	98.7	94.0	95.8	90.5	96.0	97.3	92.2	92.6
BOP (+)(%)	87.3	85.6	89.7	93.2	89.3	88.1	87.3	85.7	86.3	91.9	91.0	87.0
PD (Mean ±DS)	3.24± 0.42	4.40± 0.21	5.21± 1.93	7.20 ± 1.18	3.21± 0.74	4.20± 0.95	5.18± 1.27	7.50± 1.72	3.01± 0.79	4.10 ± 1.13	5.15 ± 1.87	6.90 ± 1.41
CAL (Mean± DS)	1.40 ± 0.32	3.50 ± 0.44	4.22 ± 0.42	5.68 ± 1.16	1.61 ± 0.28	3.23 ± 0.33	4.48 ± 0.99	5.90 ± 1.24	1.42 ± 0.78	3.19 ± 0.32	4.21 ± 1.31	5.41 ± 1.75
One month evaluation												
PI (+)(%)	5.1 *	6.2 *	3.0 *	8.1 *	1.3 *	7.5 *	11.2 *	12.7 *	4.0 *	8.1 *	7.8 *	7.4 *
BOP (+)(%)	2.5 *	2.1 *	1.5 *	4.1 *	4.0 *	3.0 *	5.7 *	9.5 *	13.7 *	12.2 *	31.6	42.2
PD (Mean± SD)	1.98 ± 0.31 *	2.21 ± 0.22 *	3.87 ± 0.41 *	5.42 ± 0.84 *	1.87 ± 0.63 *	3.12 ± 0.32 *	4.99 ± 0.55	6.62 ± 0.41	1.95 ± 0.1 *	3.72 ± 0.88	5.01 ± 1.16	6.39 ± 1.23
CAL (Mean± SD)	1.12 ± 0.42 *	1.81 ± 0.21 *	2.03 ± 0.35 *	4.32 ± 1.63 *	1.13 ± 0.17 *	2.67 ± 0.43 *	4.21 ± 1.17	5.22 ± 1.73	0.82 ± 0.24 *	2.93 ± 0.52	4.19 ± 1.16	5.40 ± 1.97
Six months evaluation												
PI (+)(%)	4.2 *	4.7 *	2.6 *	7.2 *	3.6 *	9.6 *	12.5 *	14.2 *	15.3 *	14.9 *	16.5 *	17.2 *
BOP (+)(%)	1.3 *	1.7 *	1.2 *	2.5 *	23.7 *	26.9 *	43.6	61.7	39.42	38.3	42.8	57.1
PD (Mean± SD)	1.61 ± 0.37 *	1.82 ± 1.41 *	3.34 ± 1.66 *	5.23 ± 1.92 *	2.02 ± 1.14 *	3.51 ± 1.42 *	5.29 ± 1.90	6.97 ± 2.46	3.05 ± 1.53	4.61 ± 2.07	5.56 ± 2.44	7.19 ± 2.88
CAL (Mean± SD)	0.95 ± 0.14 *	1.34 ± 0.27 *	1.88 ± 0.41 *	4.75 ± 2.63 *	1.27 ± 0.43 *	2.93 ± 0.63 *	4.65 ± 1.04	5.98 ± 1.48	1.24 ± 0.41	3.46 ± 0.73	4.91 ± 1.77	6.22 ± 2.24

PDT: SRP + photoactivation therapy group; CHX: SRP + chlorhexidine rinsing group; SD: standard deviation. S1: Periodontitis stage 1; S2: Periodontitis stage 2; S3: Periodontitis stage 3; S4: Periodontitis stage 4.
PI: Plaque index; BOP: Bleeding on probing index; PD: periodontal probing depth; CAL: clinical attachment loss; SD: standard deviation. * $p < 0.05$ was considered statistically significant.

Following analysis of bacterial load in patients with fixed prosthetic devices on nat-ural teeth, we did not notice significant differences between groups at baseline. At the one-month evaluation, we observed a significant reduction in all patients with super-ficial/moderate periodontitis who underwent PDT and CHX therapy (stages 1 and 2) (Tables XXV-XXVII), with supplementary improvements for patients who underwent photoactivation therapy. Patients with severe periodontitis (stages 3 and 4) who followed SRP+CHX rinsing, as well as those in the control group, although they showed lower values at the one-month evaluation, did not reach the threshold of statistical significance (Tables XXVI and XXVII).

Table XXV. Total bacterial load at baseline and at after treatment (one month and six months) in the PDT group.

Stage	Baseline	At one month	At 6 Months
S1	$5.4x10^{6}(2.6x10^{4}-8.3x10^{8})$	$1.6x10^{3}(9.5x10^{2}-8.9x10^{4})$*	$5.2x10^{3}(1.2x10^{2}-7.5x10^{5})$*
S2	$1.6x10^{7}(3.8x10^{6}-5.2x10^{9})$	$9.6x10^{3}(6.2x10^{2}-9.2x10^{4})$*	$1.7x10^{4}(9.1x10^{2}-9.6x10^{5})$*
S3	$3.2x10^{8}(6.8x10^{6}-9.8x10^{9})$	$6.9x10^{4}(1.4x10^{3}-8.1x10^{7})$*	$1.4x10^{5}(2.7x10^{3}-8.3x10^{7})$*
S4	$8.3x10^{8}(5.2x10^{6}-9.3x10^{9})$	$8.5x10^{4}(2.5x10^{3}-1.2x10^{7})$*	$1.8x10^{5}(5.5x10^{3}-5.3x10^{7})$*

PDT: SRP + photoactivation therapy group; S1: Periodontitis stage 1; S2: Periodontitis stage 2; S3: Periodontitis stage 3; S4: Periodontitis stage 4. Data are expressed as median (minimum-maximum). * $p < 0.05$; comparison between the evaluation at baseline and at one and 6 months in the same group.

Table XXVI. Total bacterial load at baseline and at after treatment (one month and six months) in CHX group.

Stage	Baseline	At one month	At 6 Months
S1	$5.6x10^{6}(6.2x10^{4}-7.5x10^{8})$	$8.4x10^{4}(5.5x10^{2}-2.1x10^{6})$*	$3.7x10^{5}(9.1x10^{2}-9.2x10^{6})$*°
S2	$1.9x10^{7}(4.6x10^{6}-9.2x10^{9})$	$0.5x10^{4}(7.8x10^{2}-6.3x10^{6})$*	$6.2x10^{5}(9.3x10^{2}-8.7x10^{6})$*°
S3	$3.6x10^{8}(6.5x10^{6}-9.1x10^{9})$	$9.1x10^{7}(2.9x10^{3}-0.1x10^{9})$°	$1.8x10^{8}(7.4x10^{5}-7.5x10^{9})$°
S4	$7.9x10^{8}(2.9x10^{6}-8.3x10^{9})$	$0.3x10^{8}(1.8x10^{5}-2.3x10^{9})$°	$6.2x10^{8}(5.9x10^{5}-8.4x10^{9})$°

CHX: SRP + chlorhexidine rinsing group. S1: Periodontitis stage 1; S2: Periodontitis stage 2; S3: Periodontitis stage 3; S4: Periodontitis stage 4. Data are expressed as median (minimum–maximum). * $p < 0.05$; comparison between the evaluation at baseline and at one and 6 months in the same group; °$p < 0.05$; comparison between groups at the same evaluation time.

Table XXVII. Total bacterial load at baseline and at after treatment (one month and six months) in control group (SRP only).

Stage	Baseline	At one month	At 6 Months
S1	$4.9x10^{6}(1.6x10^{4}-2.3x10^{8})$	$0.3x10^{6}(1.5x10^{4}-1.2x10^{8})$°	$5.1x10^{6}(5.5x10^{4}-4.7x10^{8})$°

S2	$1.7x10^7(7.1x10^6-8.1x10^8)$	$0.2x10^7(1.5x10^6-6.4x10^8)$°	$2.3x10^7(5.9x10^6-7.8x10^8)$°
S3	$3.1x10^8(6.3x10^6-8.8x10^9)$	$2.1x10^8(5.2x10^6-7.3x10^9)$°	$2.7x10^9(7.9x10^7-9.1x10^9)$†°
S4	$7.8x10^8(6.5x10^6-8.1x10^9)$	$6.6x10^8(4.2x10^6-5.3x10^9)$°	$8.7x10^9(8.8x10^8-9.8x10^9)$†°

S1: Periodontitis stage 1; S2: Periodontitis stage 2; S3: Periodontitis stage 3; S4: Periodontitis stage 4. Data are expressed as median (minimum-maximum). † $p < 0.05$; comparison between the evaluation at baseline and at one and 6 months in the same group with significant increase. ° $p < 0.05$; comparison between groups at the same evaluation time.

Although at the six-month evaluation we observed an upward trend, compared to the one-month evaluation, significant lower values when compared to baseline were maintained for the PDT subjects and CHX subjects (S1 and S2) (Tables XXV and XXVI). Moreover, subjects with periodontitis severity stages 3 and 4 who followed SRP only exhibited significant higher values than baseline (table XXVII).

In the study groups, *Aggregatibacter actinomycetemcomitans* was detected in subjects at baseline only in S2, S3, and S4 periodontal stages, the incidence being higher as the severity of periodontal disease increased. After one month, we observed a complete eradication for the pathogen in subjects with periodontitis stage 2 who followed PDT therapy, and the value was maintained after six months. CHX rinsing exerted a complete eradication for subjects with superficial periodontitis and significant lower incidence for subjects with periodontitis stage 2 and 3, but at 6 months, the incidence was close to baseline in subjects with periodontitis S2, S3, and S4 (tables XXVIII-XXX). PDT succeeded also in a significant reduction of *A. actinomycetemcomitans* in subjects with severe periodontitis, and, more importantly, the significant threshold of $p < 0.05$ was maintained also after 6 months. In the control group, a slight decrease was observed after one month only in patients with periodontitis stage 1 and 3 (table XXX).

Table XXVIII. Periodontal pathogens detection at baseline and after treatment (one month and six months) for the PDT group.

Pathogen	Stage	Baseline	At One Month	At 6 Months
Aggregatibacter actinomycetemcomitans	S1	0.0	0.0	0.0
	S2	2.1	0.0[a]	0.0[a]
	S3	30.9	1.4[b]	2.9[b]
	S4	33.8	2.7[b]	5.4[b]
Porphyromonas gingivalis	S1	6.3	0.0[b]	1.3[b]
	S2	14.4	0.0[b]	2.1[b]
	S3	63.2	4.4[b]	10.3[b]
	S4	83.8	6.7[b]	10.9[b]
Tannerella forsythia	S1	30.4	0.0[b]	2.5[b]
	S2	32.9	4.1[b]	6.2[b]
	S3	67.6	8.8[b]	10.3[b]
	S4	93.2	8.1[b]	12.2[b]
Treponema denticola	S1	22.8	2.5[b]	3.8[b]
	S2	29.9	2.1[b]	5.1[b]
	S3	57.4	5.8[b]	7.3[b]
	S4	66.2	8.1[b]	10.8[b]

PDT: photoactivation therapy group; S1: Periodontitis stage 1; S2: Periodontitis stage 2; S3: Periodontitis stage 3; S4: Periodontitis stage 4. Results are expressed as percentages. [a] $p <0.005$; [b] $p <0.001$; comparison between the evaluation at baseline and at one and 6 months in the same group.

Table XXIX. Periodontal pathogens detection at baseline and after treatment (one month and six months) for the CHX group.

Pathogen	Stage	Baseline	At One Month	At 6 Months
Aggregatibacter actinomycetemcomitans	S1	0.0	0.0	0.0
	S2	2.9	1.2	1.5
	S3	26.8	14.1[a]	23.9
	S4	30.1	19.1	22.2
Porphyromonas gingivalis	S1	9.3	4.0[c]	8.0
	S2	16.4	5.9[c]	13.4
	S3	63.4	30.9[c]	47.9
	S4	85.7	30.2[c]	71.8
Tannerella forsythia	S1	34.7	4.0[c]	14.7[b]
	S2	37.3	4.5[c]	32.8
	S3	57.7	32.4	47.9
	S4	85.7	69.8	73.0
Treponema denticola	S1	22.7	1.3[c]	21.6
	S2	32.8	4.5[c]	29.8
	S3	54.9	36.7	43.7
	S4	73.0	55.5	72.2

CHX: Chlorhexidine rinsing group; S1: Periodontitis stage 1; S2: Periodontitis stage 2; S3: Periodontitis stage 3; S4: Periodontitis stage 4. Results are expressed as percentages. [a] $p < 0.05$; [b] $p < 0.005$; [c] $p < 0.001$; comparison between the evaluation at baseline and at one and 6 months in the same group.

Porphyromonas gingivalis was detected in all groups, with higher prevalence for patients with severe periodontitis. Photoactivation therapy has resulted in the complete eradication in patients with stage 1 and 2 periodontitis after one month and significant decreases for subjects with severe periodontitis (S3, S4); the significant difference was observed also at the 6-month evaluation (table XXVIII). Irrigation with chlorhexidine 0.2% resulted in a significant reduction of *P gingivalis* in all the patients after one month, but after 6 months, the values increased again, with a tendency to return to baseline levels (Table XXIX). Conventional mechanical therapy resulted in a significant reduction in *P. gingivalis* only in patients with stage 1 and 2 periodontitis; however, at the 6-month evaluation, a trend of higher values for all stages of periodontitis severity was observed, similar to the CHX group (Table XXX).

Table XXX. Periodontal pathogens detection at baseline and after treatment (one month and six months) for the control group.

Pathogen	Stage	Baseline	At One Month	At 6 Months
Aggregatibacter actinomycetemcomitans	S1	0.0	0.0	0.0
	S2	4.1	2.7	2.7
	S3	28.6	22.1	24.7
	S4	35.2	29.6	31.5
Porphyromonas gingivalis	S1	9.8	3.9[b]	7.8
	S2	17.6	8.1[b]	13.5
	S3	62.3	45.5	51.9
	S4	81.4	66.7	74.1
Tannerella forsythia	S1	33.3	13.7[a]	27.4

	S2	39.2	27.0	29.7
	S3	76.6	57.1	67.3
	S4	90.7	77.8	85.9
Treponema denticola	S1	19.6	5.9[b]	17.7
	S2	28.4	14.9[a]	25.7
	S3	58.4	41.6	44.1
	S4	74.1	57.4	66.7

S1: Periodontitis stage 1; S2: Periodontitis stage 2; S3: Periodontitis stage 3; S4: Periodontitis stage 4. Results are expressed as percentages. [a] $p < 0.005$; [b] $p < 0.001$; comparison between the evaluation at baseline and at one and 6 months in the same group.

The complete eradication of *Tannerella forsythia* after one month was observed only in subjects with superficial periodontitis who underwent adjunctive photoactivation therapy. We observed significant results in decreased values in all the subjects with PDT after one month; after 6 months, the values slightly increased, but the difference maintained the statistical significance (table XXVIII). CHX rinsing generated similar results for patients with superficial periodontitis (S1) after one and six months, but even if the results were also significant for S2 patients at the first re-evaluation, after 6 months, the incidence increased, neutralizing the statistical significance; meanwhile, in patients with S3 and S4 periodontitis, even if CHX decreased the values, the difference was not significant (table XXIX). Patients who followed only scaling and root planing exhibited decreases in *T. forsythia* incidence, but the difference was significant only for S1 patients after one month; at the 6-month evaluation, the values increased, reaching the baseline incidence (table XXX).

Treponema denticola was also detected in all the study groups. After one month, the photoactivation therapy resulted in significant reductions of this microorganism for all subjects (table XXVIII). CHX irrigation therapy also exerted significant reductions in *T. denticola* for S1 and S2 subjects; however, the results were significantly more favorable for photoacti-vation therapy (table XXIX). Scaling and root planing resulted in significant reductions only in patients with superficial and moderate periodontitis (S1 and S2) (table XXX).

After 6 months, only PDT succeeded in maintaining the statistical significant decrease; in the CHX and control group, all the subjects experienced increased values of *T. denticola* incidence, with values close to baseline (tables XXVIII-XXX).

Discussion

Considering the fact that patients with fixed partial dentures have a worse periodontal status when compared to patients with natural dentition, periodontal maintenance and treatment must be carefully considered (Al-Sinaidi et al., 2014).

The present study proposed an investigation of the effects exerted on clinical and microbiological levels by photoactivation therapy as an additional periodontal therapeutic method in patients with prosthetic treatment on natural teeth, compared to additional irrigation with chlorhexidine 0.2% or single periodontal mechanical debridement. Although toluidine blue has generally been selected as a photosensitizer of choice in in vitro studies, methylene blue has been used primarily in clinical trials because clinical photodynamic therapy kits that include methylene blue are already commercially available (PeriowaveTM; Ondine Biopharma Corporation, Vancouver, Canada) (Helbo; Photodynamic Systems GmbH & Co. KG, Grieskirchen, Austria). Non-laser light sources, such as light-emitting diodes (LEDs), have been suggested as light activators in photodynamic therapy because LED devices are more compact and portable, and they cost much less than traditional lasers. In the present study, we used the laser as a light source (HELBO, Photodynamic Systems GmbH, Wels, Austria), with a wavelength of 660 nm and irradiation of 100mW, and the photosensitizer was represented by phenothiazine chloride (HELBO, Bredent medical GmbH & Co. KG). The photosensitizer is placed directly in the periodontal pocket, and the liquid agent can easily access the entire root before activating the laser light by placing the optical fiber directly in site.

A previous study (Andersen et al., 2007), compared the efficacy of antimicrobial photodynamic therapy with that of SRP for the non-surgical treatment of moderate to advanced periodontal disease. A total of 33 patients were assigned for single photodynamic therapy (methylene blue + 50 mW diode laser), single SRP, or SRP + photodynamic therapy. Clinical assessments of bleeding on probing, probing depth, and level of clinical attachment were performed. After three months, it was observed that a combination of SRP+photodynamic therapy led to significant improvements in the investigated parameters. Previous research evaluated the effect of adjunct antimicrobial photodynamic therapy (methylene blue + 100 mW diode laser) in chronic periodontitis using a split-mouth design. Twenty patients underwent an SRP procedure, and the arches were randomly assigned to an additional treatment with photodynamic therapy. After 3 months, complementary use of photodynamic therapy resulted in a significantly greater change in mean relative at-tachment level, probing depth, crevicular fluid flow, and bleeding on probing at sites that received photodynamic therapy compared to sites that followed only SRP (Braun et al., 2008).

On the other hand, other studies find no additional benefits to PDT as an adjunct to scaling and root planing regarding the reduction in pocket depth, bleeding on probing, clinical attachment depth, and eradication of bacteria when compared to conventional non-surgical treatment alone (Polansky et al., 2009; Ge et al., 2011), while others find some benefits regarding bacteria recurrence and bleeding on probing (Petelin et al., 2015). These differences may be explained by the number of PDT applications, as it is highly likely that only one application is not sufficient to induce a significant difference in the clinical or microbiological parameters.

Wavelengths of 632.8 nm (helium-neon laser) and 665 nm and 830 nm (diode laser) have been shown to have a high bactericidal effect on periodontal pathogenic microorganisms (Chan et al., 2003). In addition, the bactericidal effects of photodynamic therapy against the biofilm of the subgingival plaque, which included both Gram-positive and Gram-negative bacteria, were demonstrated; bacteria present in the deep layers of the biofilm were killed by the intense penetration of the photosensitizer into the biofilm (Soukos et al., 2005). In black pigment bacteria, such as *P. gingivalis* and *Prevotella spp*., endogenous porphyrins present on bacteria can also act as a photosensitizer. Moreover, it seems that antimicrobial photodynamic therapy not only kills bacteria, but it can also lead to a decrease in endotoxins; an in vitro study showed that lipopolysaccharides, following photodynamic therapy, did not stimulate the production of pro-inflammatory cytokines by mononuclear cells (Komerik et al., 2000); thus, photodynamic therapy can inactivate endotoxins by reducing their biological activity.

Yilmaz et al. (2002) conducted a study in which they randomly assigned a number of ten patients to follow SRP + photodynamic therapy (methylene blue + 30 mW diode laser), single SRP, single photodynamic therapy, or supra-gingival oral hygiene instructions. Methylene blue served as a photosensitizer and was used to rinse the mouth. SRP was performed on days 1 and 7, while the laser was repeatedly applied to each papillary region (not in periodontal pockets) on days 1, 2, 4, 7, 9, and 11. After 32 days of healing, clinically significant and microbiological improvements were observed only in groups with SRP + photodynamic therapy and SRP only. On the contrary, the improvements in patients undergoing only photodynamic treatment, as well as those receiving oral hygiene instructions, did not reach statistical significance. Regarding laser treatment, there were no complaints (such as discomfort, tenderness or pain) from subjects immediately after or 3 weeks after therapy, which were aspects that were observed in our study as well. The authors concluded that antimicrobial photodynamic therapy did not provide additional microbiological and clinical benefits compared to conventional mechanical debridement. The reduced efficacy of photodynamic therapy in this study may be the result of indirect application of photodynamic therapy to the external surface of the gingiva.

In our study, the photoactivation therapy with a photosensitizer was applied in the periodontal pocket, in three sessions, at an interval of one week apart, which resulted in significant improvements of clinical periodontal parameters in subjects with different severities of periodontal destruction. More interestingly, the improvements persisted even after 6 months since the first PDT session, which were beneficial results that were not observed in the chlorhexidine rinsing or SRP groups, especially in severe cases of periodontitis. On the other hand, regarding the bacterial plaque index, even if values at the one-month mark were significantly lower than baseline in the same study group, and the significance was maintained at 6 months, patients who rinsed with chlorhexidine and control subjects presented a tendency to increased plaque deposits and thus poor oral hygene, having higher overall scores, which were significant when compared to the photoactivation group. This particular aspect could partially explain the inter-group differences in terms of bacterial load and pathogen prevalence and the improved status for PDT treated subjects.

Moreover, regarding the microbiological profile, we demonstrated that PDT generated significant decreases in total bacterial load and specific periodontopathogenic bacteria, with a higher level of significance than additional chlorhexidine rinses or SRP alone. Importantly, the significant improvement was observed also after 6 months from baseline, proving the potential higher efficiency of this particular adjunctive method compared to CHX rinsing.

The re-contamination of previous negative sites from deep periodontal pockets could partially explain the higher incidence of periodontal pathogens at the six-month evaluation. Furthermore, even if the basic oral hygiene measures of toothbrushing were explained to patients and re-instated at each session and the technology of oral hygiene self-control devices is increasing in evolution, there is still no accurate method to assure that these practices were correctly followed; this particular aspect of patient motivation continues to represent a challenge in dental practice.

Chlorhexidine is a cationic polybiguanide (bisbiguanide). It is an antibacterial agent and is used as an antiseptic for other applications. Chlorhexidine is used in disinfectants, cosmetics, and pharmaceuticals. At physiological pH, the chlorhexidine salts dissociate and release the positively charged chlorhexidine cation. The bactericidal effect is the result of the binding of this cationic molecule to the walls of negatively charged bacterial cells. At low concentrations of chlorhexidine, a bacteriostatic effect results; at high concentrations, membrane disruption results in cell death (Bullock, Manias, 2014). For dental plaque and inflammation control, chlorhexidine is used for irrigation or inoral rinses in its digluconate form. Due to its very high therapeutic index, it is one of the most widely used antiseptics today. In the present study, additional rinses with chlorhexidine 0.2%, twice daily, for 14 days, generated satisfactory clinical and microbiological results, but in general, they were limited to patients with superficial and moderate forms of periodontitis; these aspects might suggest that CHX is ineffective in reaching deep periodontal pockets. Furthermore, it has been reported that antibiotics and antiseptics can lead to bacterial resistance and unwanted side effects (Baym et al., 2016), which are effects that are also found in the present study that led to the elimination of nine subjects from the study. These limitations have led to the search for new approaches that are effective and easy to apply in periodontal disease.

PDT efficacy has been reported to be greater in controlling or eliminating oral bacteria in the planktonic phase than in biofilms (Goulard et al., 2010). Probable reasons for the low effects of PDT in biotopes may be distinct and protected phenotypes, such as those of microorganisms in dental bacterial plaques that are able to adhere to teeth (Fontana et al., 2009). To this end, scaling, and root planing therapy for the disorganization of the bacterial biofilm remains an essential step, irreplaceable, in the periodontal treatment. Nevertheless, we cannot ignore the limitations of this procedure in deep periodontal pockets of severe periodontitis patients, where access might be impeded; in these particular situations, open flap debridement is generally recommended. However, the results of our study prove the efficiency of PDT therapy even in profound periodontal pockets, thus suggesting the possibility of reducing the need for surgical periodontal procedures.

Since antimicrobial photodynamic therapy can be applied topically, systemic administration of antibiotics can be avoided in the treatment of localized infections. In antimicrobial photodynamic therapy, a high concentration of the chemical agent at the infection site allows efficient elimination of bacteria, without generating side effects on the patient's tissues (Meimandi et al., 2017). Several photodynamic therapy sessions can improve healing results and its long-term effects. However, it has not been established how often photodynamic therapy should be applied to effectively eliminat bacteria, as well as to prevent the recolonization by bacteria of sites previously treated by non-surgical periodontal therapy. Another ad-junctive method that has been proposed recently in the literature is the administration of probiotics, either systemically or locally (Butera et al, 2021), and further studies should compare the two adjunctive methods for efficacy assessment.

As limitations of the study, we acknowledge the fact that the evaluations in the present study were performed one and six months after the first session; thus, supplementary research is needed to elucidate whether multiple sessions of antimicrobial photodynamic therapy can improve treatment outcomes in the long-term using more complex statis-tical tools such as correlation matrix analysis. Furthermore, all subjects in our study followed manual scaling and root planing; studies on motor-driven instruments and their antibacterial efficiency compared to PDT are also necessary. Regarding the microbiological determinations, in our study, we analyzed only four periodontopathogens: *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*; however, a more complete microbiological analysis is necessary for the bacterial profiling of these patients, before and after periodontal treatment.

Conclusions

Adjunctive photoactivation antimicrobial therapy resulted in significantly more important clinical and microbiological results, especially in cases of periodontitis with severe tissue loss, when compared to SRP alone or SRP plus chlorhexidine therapy, without any side effects. Oral rinses with chlorhexidine 0.2% generated favorable clinical and microbiological results, particularly in patients with conventional fixed prosthetic treatment with superficial and moderate periodontitis but also caused adverse reactions.

Antimicrobial photodynamic therapy is expected to solve the difficulties and problems of conventional antimicrobial therapy and can function as an adjunct to conventional mechanical treatments.

3.2.4. Periodontal effects of two innovative oral rinsing substances in oncologic patients

Aim of the study

The aim of the present study was to evaluate the effects of two antiseptic, antimicrobial and antifungal products on oral cavity and periodontal tissues in oncologic patients during chemotherapy.

Patients and methods

The study was conducted on 50 subjects with ages ranging between 48 and 60 years old, between November 2015 and October 2016 at the Oncology Clinic of" Victoria" Hospital in Iaşi, Romania. The present study was approved by the Ethics Committee of" Grigore T. Popa" University of Medicine and Pharmacy (Iasi, Romania). All patients included in the sample population signed an informed consent prior to being accepted to take part in this study. The total number of subjects included in the present study consisted of 22 females and 28 males, thus 44% were women and 56% were men, the distribution being similar regarding the sex (table XXXI). Most patients were from urban areas (90%) and only a small percentage were from rural areas (10%).

Table XXXI. Subject distribution in groups according to the oral antimicrobial, antiseptic and antifungal substance used.

Substance	Absolute frequency	Percentage frequency
Placebo (control)	12	24.0
Oral rinse	22	44.0
Oral coating	16	32.0
Total	50	100.0

Most patients were retired and only 20% were still working or unemployed. The chemotherapy administered to the patients was comprised of cisplatin, oxaliplatin and gemcitabine, the highest frequency of antineoplastic drugs being cisplatin (n=26,52%), followed by oxaliplatin (n=17,34%) and gemcitabine (n=7,14%) (figure 93).

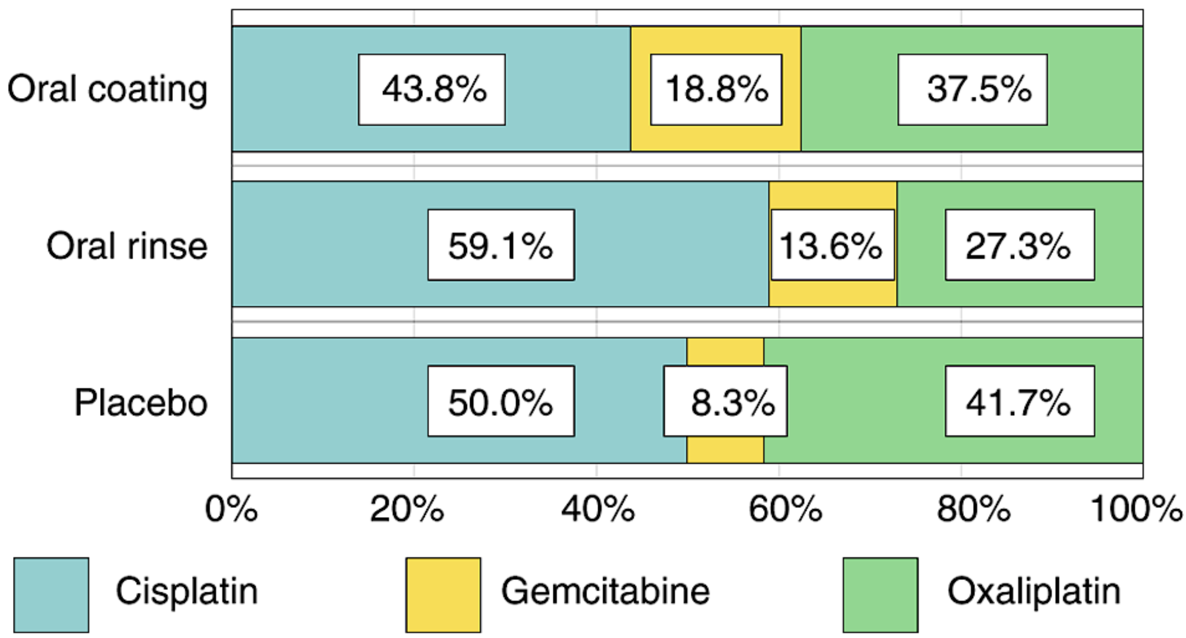


Figure 93. Distribution of the three groups depending on the chemotherapy agent.

The patients included in the present study suffered from systemic cancer, were undergoing chemotherapy and had a form of periodontal disease. In order to avoid compromising the relevance and validity of the results, the following exclusion criteria were considered: i) tobacco smokers; ii) patients with infectious and/or inflammatory disease that may have affected the periodontal status, with the exception of systemic cancer; iii) patients that had had periodontal treatment in the previous 6 months; iv) patients that had antibiotherapy or anti-inflammatory treatment in the previous 3 months, with the exception of chemotherapy; vi) patients that used antiseptic oral rinses or medical toothpaste.

All subjects were randomly split into three groups: i) controls, which included chemotherapy patients that did not use any active substance throughout the present study; ii) group A, which included chemotherapy patients that used oral rinses with cetrimide mouthwash three times a day; iii) group B, that included chemotherapy patients that used mouth coating with a pharmacy-made compound two times a day.

The clinical examination considered several elements: probing depth (PD), clinical attachment loss (CAL), dental mobility (M), plaque index and periodontal disease index (PDI). In addition, pathological probing depths higher than 3 mm on teeth with no gingival recessions were considered. The clinical examination took place at two time-points: T0, before beginning to use the active substances and T1, after 14 days of antiseptic, antimicrobial and antifungal substance usage.

The two substances evaluated in the present study were Citrolin oral rinse and an oral coating recipe developed at the pharmaceutical laboratory BabyFarm, Ltd. Citrolin is an oral rinsing solution that contains 25 mg cetrimide, 3 mg lidocaine and excipients per 100 ml of product and is administered in the form of oral rinses 15 ml per rinse, three times a day. The oral coating substance was developed in collaboration with BabyFarm, Ltd.laboratory and its composition contain neomycin, nystatin, metronidazole, sodium bicarbonate, vitamin A, xylene 2% and oleum helianthi.

The three groups were evaluated based on oral hygieneand periodontal status before the commencement of oral rinse use and oral coating and 14 days after use. None of the patients declared any side effects after using the two compounds included in the present study.

The statistical analysis of the data included in the present study consisted of descriptive statistics, one Sample t-test and a paired Sample t-test using the SPSS software version 21.0 (IBM Corporation). $P<0.05$ was considered to indicate a statistically significant difference.

Results

The paired Sample t-test revealed a high statistical significance of improvements for group A that used Citrolin oral rinse, the positive modification of all parameters being statistically significant ($p < 0.05$), with the exception of dental mobility, as revealed in Table XXXII.

Table XXXII. Statistical significance analysis for group A, between time-point T0 and T1.

	Group A, Citrolin oral rinse T0-T1		
Analyzed indices	**Mean difference**	**t**	**p-value**
Silness-Loe Plaque index	0.092	2.358	**0.028**
PDI	0.104	2.097	**0.048**
PBI	0.165	3.578	**0.002**
Mean dental mobility	-0.045	-1.821	0.083
Mean PD	0.145	4.661	**<0.001**
Mean CAL	0.161	3.409	**0.003**

Bold indicates statistical significance. PDI, periodontal disease index; PBI, papillary bleeding index; PD, probing depth; CAL, clinical attachment loss.

The results obtained for the controls revealed an increase in the values of all analyzed indices and periodontal disease progression. The modifications of values for these indices had statistical significance with the exception of the average tooth mobility value that had no statistical significance (p = 0.077) (Table XXXIII). Similarly, group B that used oral coating did not exhibit any improvement of the indices evaluated (data not shown).

Table XXXIII. Statistical significance analysis for controls between time-points T0 and T1.

	Placebo group T0-T1		
Quantified indices	**Mean difference**	**t**	**p-value**
Silness-Loe Plaque index	-0.164	-2.680	**0.021**
PDI	-0.472	-4.513	**0.001**
PBI	-0.301	-7.473	**<0.001**
Mean dental mobility	-0.080	-1.948	0.077
Mean PD	-0.479	-4.823	**0.001**
Mean CAL	-1.183	-3.467	**0.005**

Bold indicates statistical significance. PDI, periodontal disease index; PBI, papillary bleeding index; PD, probing depth; CAL, clinical attachment loss.

Moreover, CAL values were different for each of the three chemotherapy agents included in the study between T0 and T1. The average value of CAL was increased in patients treated with oxaliplatin (mean difference = -0.239) and cisplatin (mean difference = -0.19) (data not shown).

Discussion

The efficiency of antineoplastic treatment with platinum-based drugs (cisplatin, oxaliplatin) has been demonstrated multiple times in the past (Zhou et al., 2010; Park et al., 2013), although what does sometimes limit their dosage is their potential side effects. Patients treated with one of these chemotherapy agents may develop up to 40 specific adverse reactions. The most important and frequent effect is nephrotoxicity in the case of cisplatin administration and neurotoxicity in the case of oxaliplatin alongside the well-known myelosuppressive effects (Oun et al., 2018).

Ideally, periodontal disease should be assessed and treated before the beginning of chemotherapy, bearing in mind that a pre-chemotherapy evaluation and maintaining good oral hygiene has been demonstrated to be efficient in preventing oral and systemic complications during anti-neoplasic treatment (Chambers et al., 1995). Frequent erythematous lesions, ulcerations or candidiasis can occur in the oral cavity during chemotherapy (Napeñas et al., 2007). Moreover, modifications of periodontal parameters can be observed through an increase in the quantity of oral bacterial plaque, an exacerbation of gingival inflammatory signs and even modifications of the bacterial community composition at oral and periodontal levels (Jensen et al., 2008).

The use of antimicrobial and antiseptic substances is efficient in plaque reduction and improving periodontal parameters (DePaola et al., 1989). Cetrimide, the active substance in Citrolin, is an antiseptic with multiple quaternary ammonium salts that has a bactericidal effect on a wide spectrum of gram-positive and gram-negative bacteria (Engebretsen et al., 2015). Its action consists of affecting the permeability of the bacterial cellular membrane. It is used in a high number of pharmaceutical compounds with the role to decrease the level of gingival pain and increase oral hygiene (Elzanfaly et al., 2015). It is sometimes used in products that also contain chlorhexidine gluconate (Dostie et al., 2017); however, in the present study, cetrimide was the only active substance in the oral rinse to avoid errors in the results. The use of cetrimide can eliminate bacterial plaque to a great extent, some authors claiming that it has an even higher antimicrobial effect than that of chlorhexidine (Guerreiro-Tanomaru et al., 2014). The effects of cetrimide were also demonstrated to be efficient in preventing carious lesions; a concentration of 0.2% cetrimide used as oral rinse for a minute had the capacity to destroy *Streptococcus mutans* in a proportion of >99% (Ruiz-Linares et al., 2014).

Conversely, presently, there are available substances with topic application that contain either only metronidazole, or neomycin and prednisolone (Moisei et al., 2015). In the present study, we selected to introduce a new compound with topical administration that contained neomycin and metronidazole with the aim of evaluating its periodontal efficiency. This combination of drugs has been used in the past, but in association with general surgery of the digestive tract. The pre-operatory administration was revealed to be an efficient combination of antibiotics that leads to a significant reduction of post-operatory infections (Vallance et al., 1980; Espin-Basany et al., 2005).

The most important modifications of the Silness-Loe plaque index were observed in the subjects of group A that used oral rinses with cetrimide. The values of the plaque index were decreased after 14 days of using cetrimide and consequently improved the level oforal hygiene. Conversely, higher values in T1 compared to T0 in the control group (2.002 vs. 1.838) were obtained, thus manifesting an increase of 0.164 between the two evaluations. The values of the plaque index in group B were also increased after 14 days (T1 = 2.055 vs. T0 = 1.996) (data not shown).

Another fact for consideration is the medullar modifications that occur during chemotherapy that lead to thrombocytopenia, which can be translated into a pronounced tendency to gingival bleeding in the oral cavity, especially in the conditions of a pre-existing periodontal disease (Rapone et al., 2017). In the study, the PBI exhibited a decrease in value for group A after the 14 days of oral rinsing, signifying an improvement in the periodontal inflammatory status (T1 = 2.120 vs. T0 = 2.285; difference = 0.165). Then again, controls had higher values of the bleeding index in T1 (T1 = 2.338 vs. T0 = 2.037) and group B exhibited similar values at both evaluations (T1 = 2.206 vs. T0 = 2.238) (data not shown). These results reflect the modifications obtained for the level of oral hygiene, creating an association between the level of oral hygiene and level of bleeding at the periodontal level.

The average PD obtained in the present study revealed considerable differences between the controls and patients that used antimicrobial/ antiseptic/ antifungal substances. The highest improvements were observed in group A, which used cetrimide oral rinses. This may be explained by the fact that cetrimide has a higher salivary retention rate than chlorhexidine immediately after the rinse is performed but decreases more significantly at 4h than chlorhexidine (Bonesvoll, Gjermo, 1978), which is why the patients were recommended to perform the action of rinsing more often than they would otherwise in order to maintain an optimal concentration in the saliva and at the periodontal level.

Oral mucositis and periodontal disease progression are important modifiers for the level of quality of life of patients undergoing chemotherapy and negatively impact the affec-tive state of patients (Dodd et al., 2001), as we have shown in a previous study (Nitescu et al., 2017). The present study offers more options regarding the secondary means of oral hygiene that oncology patients can use in order to prevent the progression of periodontal disease and obtain an improved periodontal status during chemotherapy, thus improving their experience during chemotherapy and obtaining an improvement in their level of quality of life (Calenic et al., 2016; Boda, 2013; Neagu et al., 2011).

Conclusions

It can thus be concluded that cetrimide oral rinses were demonstrated to be the most efficient secondary means of oral hygiene assessed in the present study. Cetrimide oral rinse decreased the level of bacterial plaque and gingival bleeding, and it was efficient in preventing the progression of periodontal disease in patients undergoing chemotherapy.

The present results offer new perspectives regarding a reliable alternative to the contemporary-used secondary means of oral hygiene for oncologic patients undergoing chemotherapy. Thus, the periodontal status of these particular patients can be better controlled, and their quality of life can be significantly improved.

SECTION II

FUTURE PLANS OF DEVELOPMENT ON SCIENTIFIC AND ACADEMIC CAREER

Dental technologies have undergone a significant transformation based on computer sciences. Thus consisted in the development of novel materials and techniques used to create dental restorations like fillings, crowns, and bridges.

Dental prosthesis technology is a specialized field that requires a multidisciplinary approach. As dental materials continue to evolve, it is essential for dental professionals to be updated with the latest research and advancements in the domain. Pursuing an academic career in this scientific direction involves undertaking specialized educational activities and related scientific research to contribute to the field's growth and development.

To achieve this, I am considering a strategy that emphasizes a permanent connection between didactic and research activities. This will involve providing competitive educational and scientific programmes at both the national and European levels, ensuring that students and researchers are informed on recent advances in the domain.

II.1. FUTURE DIRECTIONS IN RESEARCH ACTIVITY

The experience of over 32 years in the area of Technology of Dental Prostheses as well as the activity carried out in the scientific research projects, as a member or project director, demonstrate my competence, competitiveness and ability to work and to form research teams.

The personal scientific research that I intend to develop after the habilitation to supervise doctoral students, will fall within the field of Dental prosthesis technology and will have the following future general directions:

D1. Experimental research in finite element analysis (FEA)

- Extension of directions already approached in the domain of finite element analysis of the biomechanical behavior of dental restorations;
- Realization of mathematical models to gain a more accurate simulation of movements, stress states and mechanical deformations in the specific conditions of the oral cavity;
- Simulation of fatigue in different situations such as biting, cleching, parafunction on teeth restored with different modern restorative materials, using various techniques;
- Simulation of the breaking mechanism of modern restorative materials at different stages of development, including generation, formation of microcracks, their development and formation of breaking surfaces, until final breakage;
- Modeling and analysis of the aging phenomenon of materials and the effects generated by this process on the biomechanical behavior of dental restorations;
- Evaluation of the influence of size, surface topography and angulation of the implant on the distribution of stresses at the level of bone tissue and in the vicinity under functional stress;
- Application of nonlinear finite element analysis in dental applications;
- Evaluation of reproducibility and validation of the finite element analysis model to ensure accuracy and consistency of the results obtained.

D2. Experimental research in substractive and additive manufacturings

- Diversification of experimental research by involving new gups of materials (nano ceramics, hybrid ceramics, zirconia, polyether ether ketone -PEEK, high-performance polymer reinforced with ceramic phases -BioHPPe) for the realization of fixed and removable prosthetic restorations;
- Study of influences exerted by AM processing technological parameters (scanning speed, laser power, exposure time, construction direction, etc.) on the mechanical properties of finished elements;
-Analysis of the influence of the thickness of the layers deposited by 3D printing on the process of initiation and development of microcracks in the breaking process;
-Comparative study on marginal adaptation of printed versus milled fixed prosthetic restorations;
- Development of CAD/CAM technologies used in digital dentistry, in order to achieve dental crowns and bridges (Trix CAD automatilly and Trixpress-CAM);
- Harnessing the potential of modernization and optimization of 3D printing technology in the production of prosthetic restorations from various materials (such as ceramic materials from the DeKema Trix range) and associated workflows;
- Implementation of LCM (lithography-based ceramic manufacturing, by Lithoz, Vienna, Austria) and DLP process for 3D printing of materials such as zirconia or ceramic-enriched diaacrylic composite resins;
-- Approaching digital technologies from the area of VAT polymerization: DLP, SLA, DUP (Direct UV printing).

II.2. FUTURE DIRECTIONS IN ACADEMIC CAREER

The development of academic activity will be oriented towards the following directions: educational, scientific research and community service.

The educational direction will aim to promote the Doctoral School for the acceptance to studies of the most valuable graduates, distinguished themselves during their academic studies. For this, the following steps will be required:

-continuous improvement of theoretical and experimental methods presented by the academic staff, in order to ensure qualitative progress of doctoral studies developed within the Faculty of Dental Medicine;

- prior theoretical preparation of interested students to accommodate the scientific level of the future topic of study;

-achievements of knowledges regarding working skills and ussing on the equipment necessary to carry out experimental determinations;

- orientation of the contents for the students' bachelor's and dissertation papers towards future scientific research topics that will be developed within future doctoral studies;

- training doctoral students for scientific research, documentation, systematization and synthesis of information;

- realization of scientific partnership contracts with universities and research institutes at national and international level, including the research topics of doctoral students;

- inclusion of doctoral students in these scientific research contracts, in the initiated National and International Programs, thus ensuring the increase of the performance level for the experimental research performed;

- initiation of doctoral students in dissemination activities of the results obtained by:

- participation with scientific papers in workshops, conferences and national or international congresses;

- publishing articles in congress proceedings, national and international journals indexed BDI and ISI, with impact factor.

- ensuring the necessary scientific research conditions for the development and fullfilment of activities within the Doctoral School.

The direction of future personal scientific research will have the following objectives:

- continuation of scientific activities on its own research directions:

- current trends in the development of CAD/CAM technologies specific to dental medicine;

- use of Finite Element Analysis to study the biomechanical behavior of dental prosthetic restorations (characterization of the state of internal stresses and mechanical deformations);

- studying the behavior during functions of the components of fixed and removable prosthetic restorations, made of different dental materials.

- participation as "Guest editor" in international specialized journals, with impact factor;

- participation, as reviewer at various International Scientific Journals;

-holding lectures and teaching activities as a "visiting professor" within the Faculties of Dental Medicine, in the country and abroad;

- extension of membership in national and international professional associations, specialized

- participation as a partner in the development of joint scientific research projects, within the National and International Programs;

- forming a scientific research team, with national and international participation, which, through dynamic management, could obtain funding for projects proposed in different National and European Programs.

The direction of doctoral activities for the benefit of the academic community will refer to:

- organizing extracurricular activities (student congresses) that allow identifying the most valuable students with aptitude for scientific research;

- development of topical scientific research topics in dental practice, through the implementation of which the inclusion on the labor market of the graduate of doctoral studies is ensured;

- involvement of doctoral students in the traineeship program through the Erasmus program

- diversification of international collaborations with prestigious universities and research institutes and joint participation in European Programs to ensure the mobility of doctoral students (Erasmus, Erasmus plus);

- participation in co-guardianship, coordination of scientific research activities, of specialists in the field, recognized nationally and internationally;

- organizing workshops, conferences, national and international congresses with specific topics of Dental Medicine in which all doctoral students within the faculty participate and support scientific papers.

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- organizing workshops, conferences, national and international congresses with specific topics of Dental Medicine in which all doctoral students within the faculty participate and support scientific papers.

The development of academic activity, on the three components presented (education, research and academic community) will occur gradually, accepting the terms long, medium and short.

Long-term perspectives will focus on the following important aspects:

- continuous diversification of collaboration relations with other teams of researchers from academia or national scientific research institutes;
- establishing complex scientific partnerships based on the development of common research themes in current and prospective fields of dental medicine;

The medium-term outlook will refer to:

- continuous development of scientific collaborations with all medical universities in the country (Bucharest, Cluj-Napoca, Constanta, Craiova, Timisoara, Targu Mures, Sibiu, Oradea) and abroad, on common topics of dental medicine;
- developing the applicative base of our faculty by purchasing new high-performance equipment that allows the implementation of modern technologies, based on computing;
- creating a team of young scientific researchers at faculty level, by selecting the best performing doctors of medical sciences who have completed doctoral theses and continue their studies within the post-doctoral training forms;

Short-term perspectives will involve:

- permanent encouragement of young graduates of university studies (bachelor and master) to complete their professional training within the Doctoral School;
- orientation of the research directions of young doctoral students towards the highly topical and prospective fields of dental medicine;
-ensuring conditions for graduates of the Doctoral School to continue their scientific career in major national or international centers of advanced scientific research.

My personal experience in the fields of education and scientific research will provide me with the main conditions for the successful fulfillment of the directions of development of the entire academic activity presented, as a contribution to the development of the Doctoral School within the University of Medicine and Pharmacy "Grigore T. Popa" Iasi.

SECTION III

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