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Examination of the biomechanical properties of the All-on-Four™ treatment concept

Ph.D. Thesis

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I. PUBLICATIONS

1. Publications related to the subject of the thesis

I. **<u>Szabó ÁL</u>**, Nagy ÁL, Lászlófy C, Gajdács M, Bencsik P, Kárpáti K, Baráth ZL: Distally Tilted Implants According to the All-on-Four® Treatment Concept for the Rehabilitation of Complete Edentulism: A 3.5-Year Retrospective Radiographic Study of Clinical Outcomes and Marginal Bone Level Changes. *Dent J* 2022; 10(5): e82.
IF_{2022}: 2.6, SJR ranking: Q2, Citations: 6 (Independent citations: 5)

II. **<u>Szabó ÁL</u>**, Matusovits D, Sylteen H, Lakatos ÉI, Baráth ZL: Biomechanical Effects of Different Load Cases with an Implant-Supported Full Bridge on Four Implants in an Edentulous Mandible: A Three-Dimensional Finite Element Analysis (3D-FEA). *Dent J* 2023; 11(11): e261.
IF_{2022}: 2.6, SJR ranking: Q2, Citations: - (Independent citations: -)

<u>ΣIF: 5.2</u>

2. Publications not related to the subject of the thesis

I. Körtvélyessy G, **<u>Szabó ÁL</u>**, Pelsőczi-Kovács I, Tarjányi T, Tóth Z, Kárpáti K, Matusovits D, Hangyási BD, Baráth Z: Different Conical Angle Connection of Implant and Abutment Behavior: A Static and Dynamic Load Test and Finite Element Analysis Study. *Materials* 2023; 16(5): e1988.
IF_{2022}: 3.4, SJR ranking: Q2, Citations: 1 (Independent citations: 1)

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<u>ΣIF for all publications: 8.6</u>

II. INTRODUCTION

Edentulism is a definite condition, which most commonly occurs as a consequence of untreated caries of the permanent teeth and its complications, severe periodontal disease or traumatic injuries, can lead to the extraction of affected teeth. Endosseous, osseointegrated implant-supported, fixed full-arch restorations are widely recognized as a safe and effective treatment alternative for the oral rehabilitation of edentulous patients. The characteristics of load transmission and stress distribution in the bone and around the implants are important determinants of implant health and survival. Previously, conventional (delayed, two-stage) loading protocols were carried out, where patients received their restorations after a healing period of 2–3 months; however, recently, immediate loading (one-stage) protocols have been extensively investigated for their clinical applicability and comparability. However, due to the anatomical constraints of the edentulous jaw (especially in the case of the mandible), or if the quality and the amount of residual alveolar bone is limited, implant-supported prosthetic treatment is impossible without complex surgical interventions preceding implant placement (i.e. alveolar crest augmentation, bone grafting, nerve transposition, soft tissue management), which carry considerable risks, and correspond to higher costs and longer recovery time intervals. The use of tilted implants in the jaw is another recognized alternative to avoid bone grafting procedures, as there is no significant clinical difference in success rates compared to axially placed implants, and their acceptability by patients is also higher. The "All-on-Four" (Ao4) treatment concept—devised by Maló et al. (Nobel Biocare, Göteborg, Sweden) in 2003 – has also been described as a viable method that allows clinicians to overcome the anatomical limitations of the mandibular bone. This strategy for oral rehabilitation involves the placement of four implants in the interforaminal area of the mandible and the premaxillary region – two axial implants, which are positioned in the anterior alveolar region, while the other two implants are tilted (15–45°) in the posterior region—to support immediately loaded, one-piece full-arch fixed restorations. Considerable gaps still exist in the knowledge regarding the biomechanical stresses observed in the peri-implant bone, implants, and prostheses during the treatment of edentulous jaws using the Ao4 concept. The long-term success and predictability of implant-supported restorations largely depend on the distribution of these forces and the rate of load transfer at the bone-implant interface, as they may affect both primary (critical in immediate loading) and secondary stability (affecting bone remodeling processes). With the use of a lower number of (tilted) implants, one of the disadvantages of the Ao4 concept is that the higher stress and strain around the implant and in the bone may exceed the load bearing capacity of the bone (i.e., overload), resulting in microdamage accumulation and marginal bone resorption. Clinicians should be aware of the various stresses arising in the jawbone from masticatory forces and implants during treatment planning, to ensure the best possible distribution of stress following prosthetic treatment. The use of finite element analyses (FEA) to generate three-dimensional (3D) qualitative and quantitative biomechanical data in the field of medicine and dentistry have received substantial attention, and has become a widely accepted, non-invasive research method to estimate specific biomechanical parameters and behaviors in complex biological systems, such as the edentulous mandible, the peri-implant bone or the restorations.

III. AIMS OF THE STUDY

The Ao4 prosthetic concept has received substantial attention from dentists for the oral rehabilitation of edentulous patients, due to the advantageous, short-term clinical outcomes associated with this treatment protocol; furthermore, implant placement with Ao4 is followed by immediate loading, which is in line with the preferences of the patients. On the other hand, there are substantial gaps in the literature, associated with numerous practical aspects of the Ao4 concept. For example, there are limited number of mid- to long-term retrospective or prospective studies determining the success rate, survival and peri-implant bone-level changes of the implant placement according to the Ao4 concept. Furthermore, there is currently no established consensus of the type of loading to be favored, partly due to the limited knowledge of the biomechanical stress observed in the peri-implant bone, implants, and prostheses following treatment of the jawbone. Therefore, our present study aims: *i)* to assess the clinical success rate and the marginal bone loss (MBL) levels following the implantation of distally tilted implants according to the Ao4 prosthetic concept, in a retrospective, single-center experience, measured by radiological findings; and *ii)* to investigate the biomechanical behavior of an edentulous mandible with an implant-supported full bridge on four implants (aiming to model the Ao4 prosthetic concept) under simulated masticatory forces, in the context of different loading schemes and material properties, in a patient-specific finite element model, using 3D-FEA.

The specific goals of the study were the following:

1. Determination of **implant survival rates (%)** of distally tilted **Ao4 implants at baseline** (T_0; at the 3-month appointment), and after **18 months** (T_1; 1.5 years post-restoration), **30 months** (T_2; 2.5 years post-restoration), and **42 months** (T_3; 3.5 years post-restoration) of follow-up, in a retrospective fashion;
2. Determination of **MBL levels** around **maxillary and mandibular Ao4 implants at baseline** (T_0; at the 3-month appointment), and after **18 months** (T_1; 1.5 years post-restoration), **30 months** (T_2; 2.5 years post-restoration), and **42 months** (T_3; 3.5 years post-restoration) of follow-up, in a retrospective fashion;
3. Determination of **MBL levels** around **tilted (posterior) and axial (anterior) Ao4 implants at baseline** (T_0; at the 3-month appointment), and after **18 months** (T_1; 1.5 years post-restoration), **30 months** (T_2; 2.5 years post-restoration), and **42 months** (T_3; 3.5 years post-restoration) of follow-up, in a retrospective fashion;
4. Determination of **MBL levels** around the **mesio-approximal (MA) and disto-approximal (DA) aspects of Ao4 implants at baseline** (T_0; at the 3-month appointment), and after **18 months** (T_1; 1.5 years post-restoration), **30 months** (T_2; 2.5 years post-restoration), and **42 months** (T_3; 3.5 years post-restoration) of follow-up, in a retrospective fashion;
5. Determination of **maximum principal stress [P_{max}], minimum principal stress [P_{min}] and equivalent stress [P_{eqv}]** values in **the cortical and trabecular bone**, corresponding to four sets of **masticatory load cases (LC1-LC4)**, in a patient-specific finite element model of an edentulous mandible;
6. Determination of **maximum principal stress [P_{max}], minimum principal stress [P_{min}] and equivalent stress [P_{eqv}]** values in **the cortical and trabecular bone**, corresponding to different **implant-denture material configurations (S1 and S2)**, in a patient-specific finite element model of an edentulous mandible.

IV. MATERIALS AND METHODS

1. Clinical study

A single-center, institution-based retrospective study was carried out at the Faculty of Dentistry, University of Szeged, between 2017.01.01. and 2022.01.01., corresponding to patients – deemed eligible based on the inclusion and exclusion criteria – undergoing an implant surgical procedure with an immediately-loaded, four-implant-supported fixed prosthetic concept, following the Ao4 protocol. The study employed a convenience sampling approach at the study center, and has aimed to evaluate radiographic data (peri-implant bone-level changes) longitudinally from included patients.

Before the initiation of the study, the following inclusion criteria were set for eligibility: *(i)* patients aged 18 years or older; *(ii)* patients in an overall good health condition, able to undergo surgical intervention; *(iii)* patients in need for a complete rehabilitation of the edentulous maxilla or mandible, and the possibility of placing a minimum of 4 implants (at least 10 mm long); and *(iv)* sufficient bone height in the sites intended for the placement of implants (min. 6 mm, evaluated by preoperative CT scans analysis). Furthermore, the following exclusion criteria were set: *(i)* presence of an acute infection at the planned implant sites; *(ii)* known coagulopathies or other hematologic diseases; *(iii)* recent occurrence of a severe cardiovascular or cerebrovascular event; *(iv)* diseases affecting the immune system; *(v)* uncontrolled diabetes mellitus (DM); *(vi)* pregnancy or lactation; *(vii)* metabolic illnesses affecting the bones, bisphosphonate therapy; *(viii)* heavy smoking (>10 packs/day); *(ix)* systemic chemotherapy or irradiation of the head and neck region within the last 12 months; *(x)* presence of parafunctional habits, such as severe bruxism or clenching (assessed and identified by clinicians, based on clinical signs and symptoms); and *(xi)* inadequate oral hygiene level (full-mouth plaque and bleeding scores over 20%), or poor perceived motivation on the part of the patient to maintain good oral hygiene throughout the study.

All relevant operative interventions were performed by the same surgeon with more than twenty years of experience associated with immediate loading procedures. Quantitative and qualitative assessment of the jaw bone was performed by means of preoperative radiographs, visual inspection, and tactile evaluation during drilling; while appraisal of bone quality was carried out using the CBCT scans. Each individual received *(i)* 2 distally tilted implants in the posterior region and, after that, *(ii)* 2 anterior implants in the maxilla or the mandible. In the maxilla, tilted implants were positioned just anterior to the maxillary sinus, while in the mandible they were positioned anterior to the mental foramen. The placement of implants was according to the Ao4 treatment concept, using the Ao4 surgical guide (Nobel Biocare; Kloten, Switzerland); comprehensive details regarding the procedure have been described elsewhere. Regarding bone regeneration, universal clinical protocols for immediate implant placement were used. Localized bone grafting was performed to cover exposed threads and/or other osseous defects associated with extraction sockets, as needed with demineralized allografts. For the fabrication of the master cast to create the patients' provisional restoration, open-tray multi-unit impression copings were placed on the multi-unit abutments to make an impression using precision impression material (Flexitime, Heraeus Kulzer, Hanau, Germany). Following the operative procedure, patients were instructed to abstain from brushing in the first 7 days post-op, and to rinse using warm water. For 24 h post-op, instructions and recommendations were given for a soft diet (cold or at room temperature), to be followed by a semi-solid diet for the following three months. Patients were supplied with antibiotics (amoxicillin 500 mg t.i.d. or clindamycin 300 mg t.i.d. for seven days) and analgesics (non-steroid anti-inflammatory drugs) to control post-operative pain and inflammation as per standard guidelines and protocols in oral surgery. To confirm implant positions, and the positions of the prosthetic components, a CBCT scan was taken immediately postoperatively.

Prior to the surgical intervention, a heat-cured acrylic resin (Ivocap High Impact acrylic, Ivoclar Vivadent; Amherst, NY, USA) was prefabricated, which was amended to the master model directly after the surgery. Fabrication was carried out using cold curing material (Probase, Ivoclar Vivadent; Amherst, NY, USA). Following 3–4 h after the completion of the operation, the provisional all-acrylic prosthesis was seated. Routine follow-ups were scheduled for the patients after surgery at 7, 14, and 28 days and 3 months after surgery, and on a yearly basis thereafter. Following the 3-month appointment, fabrication of the definitive prosthesis was initiated, consisting of a milled Ti frame with a wrap-around heat-cured acrylic resin (Nobel Procera Implant Bridge Ti framework veneered with composite). The antagonist denture was a fixed denture/implant supported restoration in all cases. A long-cone paralleling method was applied to obtain matched and calibrated orthopantomogram (OPT; panoramic X-ray) images at the 3-month appointment and at the subsequent appointments continuously. The 3-month radiographs after the time of placement of the definitive prosthesis were utilized as a baseline (T_0) to assess the bone levels longitudinally. At the respective follow-ups, the implants were assessed for signs of peri-implantitis, plaque, and bleeding on probing (BOP), based on routine clinical guidelines.

Peri-implant bone-level changes were measured by matched and calibrated OPT images taken at the 3-month appointment (i.e., baseline, T_0) and follow-ups after 18 months (T_1; 1.5 years post-restoration), 30 months (T_2; 2.5 years post-restoration), and 42 months (T_3; 3.5 years post-restoration); marginal bone level (the most coronal bone-to-implant contact) was assessed on the MA and DA aspects. An independent researcher—not affiliated with the primary center and investigators—evaluated the OPT images. Radiographs were digitized in a 640 (H) × 480 (V) pixel matrix image with an 8-bit depth. The density and contrast were then adjusted for optimal visualization of the marginal bone, and the digital images were saved as a .TIF extension image. The 2D images were then exported and analyzed using the CLINIVIEW image analysis software (MI Dental; Knowsley, Prescot, UK). Calibration for image analysis was performed on an individual implant-level (n = 288) to achieve the most accurate results possible, where the known size and specifications of the individual documented implants were used as the basis for calibration, to allow for the calculation of marginal bone level changes in the area. Assessment of bone levels were carried out and captured separately on the MA and DA sides of the implant. The change in marginal bone levels (expressed in mm) from the baseline (T_0) to the values recorded at the follow-ups T_1, T_2, and T_3 were calculated.

2. Finite element analysis (FEA)

To perform FEA in the context of our study, a patient-specific finite element model was constructed using pre- and post-implantation CT images of a 63-year-old male patient with adequate bone supply, who was eligible for treatment with an implant-supported full bridge on four implants. Implant placement occurred 6 months post-extraction. The patient's final prosthesis consisted of a milled cobalt−chromium (Co−Cr) alloy frame with a cold-curing pour-type acrylic denture base (Vertex Dental B.V., Soesterberg, The Netherlands) and Ivoclar Vivadent (Schaan, Liechtenstein) denture teeth. To ensure the most accurate bone modelling possible, finite element models of the trabecular and the compact bone were created by the segmentation of the CT images of the pre-implantation edentulous mandible. This prevented the adverse effect of X-ray image artifacts in the environment of metallic materials on the subsequent material properties. The geometry and precise location of the implants in the jawbone were obtained by processing the post-implantation CT images. The two datasets—obtained by separate segmentations—were fused to create the final model including the trabecular bone, compact bone, and implants. CT images (in .dicom format) were imported into the 3D Slicer Computer Aided Design (CAD) software, where the mandibular model was created. The 3D geometry of the cylindrical implants was constructed using the same patient's CT images, who received four implants in both the maxilla and the mandible, according to the SmartGuide® protocol (iRES®, Mendrisio, Switzerland). The resulting CAD models were recorded in ".step" and ".iges" formats, which could be imported into the ANSYS SpaceClaim software (ANSYS 19.1, Canonsburg, PA, USA) to create the solid body mesh of the implants and mandible components. SOLID187 (a 10-node, higher order 3D element with quadratic displacement behavior, ideal for modeling irregular meshes) and CONTA174 (an 8-node 3D element used to model contact and sliding between surfaces) elements were used to generate the mesh of the mandible and the implants using ANSYS SpaceClaim. After checking for vertical alignment with the implants, the denture was integrated into the implant mesh, creating a single facet interpenetrating the mandible, which was then subtracted from the model of the cortical and trabecular bone.

The peri-implant bone in the model was made up of cortical and trabecular bones, with a transition region that extends past the implant's outermost edge. The interface between the bone and the implant was set as bonded; osseointegration was assumed to be 100%. The material properties, which define the physical properties of the modelled structures, were entered into the software. The physical features of the peri-implant bone were modelled to reflect the features of type II bone, according to the Lekholm and Zarb classification. All parts in the model were accepted as homogeneous, isotropic, and linear elastic. Two sets of simulations were performed: *i)* in the first set of simulations (denoted as S1), the denture body and the implant bodies were assigned the same material (Ti, i.e., TiAl6V4), and *ii)* in the second set of simulations (denoted as S2), different material properties were assigned to the implant bodies (TiAl6V4) and the denture bodies (a Co-Cr alloy in 70–30% ratio). The effects of different occlusion settings – i.e., the appropriate location of the masticatory force – were assessed. For the sake of comparability, the vertical components of the masticatory forces were included in the calculations; these were set at 300 N to be exerted on the denture in four different simulated load cases (LC1-LC4). Stress outputs for the mandible from the ANSYS Workbench were taken as maximum principal stress (or first principal stress/tensile stress, [P_{max}]), minimum principal stress (or third principal stress/compressive stress, [P_{min}] and equivalent stress (or von Mises stress, [P_{eqv}]).

The clinical study and the FEA were conducted in accordance with the Declaration of Helsinki and national and institutional ethical standards. Ethical approval for the study protocols were obtained from the Human Institutional and Regional Biomedical Research Ethics Committee, University of Szeged (registration number: 158/2021-SZTE [5035]). All participants were informed of the nature and aims of the study and the data collected; and all participants of the study signed an informed consent form. Descriptive statistics (including means ± SEM (standard error of the mean), ranges and percentages) were performed using Microsoft Excel 365 (Microsoft Corp., Redmond, WA, USA). Statistical analyses were carried out by the SPSS v. 22.0 (IBM Corp., Endicott, NY, USA): the normality of variables was tested using the Shapiro–Wilk test; inferential statistics were performed using independent-sample t-test, one-way analysis of variance (ANOVA) with Tukey's *post hoc* test and Pearson's correlation (r) coefficient. p values < 0.05 were considered statistically significant. The results of FEA do not have variance, therefore there was no need to perform statistical analysis.

V. RESULTS

1. Clinical study

During the study period, $n = 36$ patients ($n = 24$ [66.7%] males and $n = 12$ [33.3%] females) with complete records of periapical radiographs underwent implant placement using the Ao4 concept at the Faculty of Dentistry, University of Szeged, and have been rehabilitated. The mean age of patients at the time of fixture installation was 58.75 ± 13.71 years (range: 19–90 years). In sum, $n = 144$ and $n = 144$ implants (Nobel Biocare) were placed in the maxilla and mandibles of patients, respectively, therefore the analysis of $n = 288$ individual implant data was carried out. During the 42-months study period, no implants have failed, resulting in 100% overall survival rate (100% for T_0, T_1, T_2 and T_3, respectively). No patients ($n = 0$) were lost to follow-up at either time points (i.e. at 3 months, at 18 months, at 30 months, and at 42 months post-restoration, respectively), all patients complied with the set timetables. The radiographic mean MBL at baseline (T_0) were 0.181 ± 0.011 mm (mean ± SEM; maxilla ($n = 144$): 0.178 ± 0.017 mm vs. mandible ($n = 144$): 0.184 ± 0.015 mm; $p > 0.05$); in the subsequent analyses, marginal bone level changes (ΔBL) at T_1, T_2, and T_3 follow-up times were compared to these initial values. The mean MBL rate after the 1.5-year follow-up was 0.558 ± 0.029 mm and 0.484 ± 0.024 mm, while by the 3.5-year mark, MBL rate was 0.770 ± 0.029 mm and 0.713 ± 0.026 mm regarding the implants placed in the maxilla and mandibular bone, respectively; bone-level changes were significant over time ($p = 0.035$ and $p = 0.033$, respectively), while the alterations observed around the maxilla and mandibular implants did not differ significantly ($p > 0.05$). Measured bone loss was significantly higher in posterior implants throughout the follow-up period (Table 1); in addition, bone-level changes were significant over time ($p = 0.041$ and $p = 0.039$). No significant differences were observed in the measured bone-level changes on the MA and DA aspects of the implants throughout the study period ($p > 0.05$ in all cases), while bone loss increased consistently during the follow-up periods in both the MA ($p = 0.029$) and DA ($p = 0.035$) aspects. During subgroup analysis, a tendency was shown for higher bone loss rates for both MA (T*1*: −0.586 ± 0.043, T*2*: −0.716 ± 0.046, and T*3*: −0.767 ± 0.042) and DA (T*1*: −0.545 ± 0.051, T*2*: −0.757 ± 0.063, and T*3*: −0.825 ± 0.060), however these differences were not statistically significant ($p > 0.05$).

Table 1. Marginal bone-level changes around axial and tilted implants during the 42-month study period

	Marginal bone level changes (ΔBL) (mm ± SEM)		
Follow-up	**Axial (anterior) (*n* = 144)**	**Tilted (posterior) (*n* = 144)**	***p*-value (between groups)****
T_1	-0.405 ± 0.021^a	-0.637 ± 0.027^a	***p = 0.008***
T_2	-0.592 ± 0.024^b	-0.676 ± 0.028^a	***p = 0.048***
T_3	-0.606 ± 0.022^b	-0.833 ± 0.029^b	***p = 0.002***
p*-value (between follow-ups)	***p = 0.041***	***p = 0.039***	

*based on ANOVA analysis, significant differences ($p < 0.05$) among groups (as demonstrated by post-hoc tests) are indicated by different superscript letters (*a* and *b*); **based on independent-sample t-test; p-values below 0.05 are shown in **boldface**

2. Finite element analysis (FEA)

During our analyses, stress results associated with the four sets of masticatory load cases (i.e. LC1–LC4), corresponding to different implant-denture material configurations (i.e. S1 and S2) were expressed in MPa, as the maximum principal stress (P_{max}; peak tension stress), minimum principal stress (P_{min}; peak compressive stress), and equivalent stress (P_{eqv}) values in the cortical and the trabecular bone. Results of the stress values in mandibular bone structure are shown in Table 2. Overall, based on the stress maps for principal stress distribution, the highest stress values were always seen at the implant—bone interface. Compressive stress values were 1.5–2.5-times higher and 1.1–1.4-times higher than tensile stress values in the cortical bone and trabecular bone, respectively. The highest maximum principal stress values were observed for the load case LC2, both regarding the cortical bone (S1 P_{max}: 89.57 MPa, S2 P_{max}: 102.98 MPa) and the trabecular bone (S1 P_{max}: 3.03 MPa, S2 P_{max}: 2.62 MPa). The highest tensile stress for LC2 was seen near the top of the third implant for the cortical bone, and near the top of the second implant for the trabecular bone. The highest minimum principal stress values for the cortical bone were seen in the S2 LC2 (P_{min}: −265.35 MPa) and S1 LC3 cases (P_{min}: −172.30 MPa), while in the case of the trabecular bone, these were seen in the case of LC4 (S1 P_{min}: −3.49 MPa, S2 P_{min}: −3.52 MPa), respectively, which were seen near the top of the second implant. Peak maximum principal stress values in the cortical bone were 15.87%, 14.97%, 11.50%, and 14.97% higher in the case of S2, for the LC1, LC2, LC3, and LC4 load cases, respectively. In light of this, peak minimum principal stress values in the cortical bone were 93.20%, 94.54%, 46.61%, and 87.96% higher in the case of S2, for the LC1, LC2, LC3, and LC4 load cases, respectively. Peak maximum principal stress values in the trabecular bone were 11.16%, 15.65%, 15.87%, and 15.87% higher in the case of S1, for the LC1, LC2, LC3, and LC4 load cases, respectively. On the other hand, differences in the peak minimum principal stress values in the trabecular bone were considerably smaller, i.e., 2.85%, 1.20%, 0.0%, and 0.86% higher in the case of S2, for the LC1, LC2, LC3, and LC4 load cases, respectively. Equivalent (von Mises) stress values were higher 47.19%, 68.12%, 61.58%, and 83.29% higher in the case of S2, for the LC1, LC2, LC3, and LC4 load cases, respectively (Table 2).

Table 2. Peak tension (P_{max}), compression (P_{min}) stress, and equivalent stress (P_{eqv}) values in the different parts of the mandibular bone structure [MPa].

		LC1		**LC2**		**LC3**		**LC4**	
		S1	**S2**	**S1**	**S2**	**S1**	**S2**	**S1**	**S2**
Cortical bone	P_{max} [MPa]	*76.39*	*88.51*	**89.57**	**102.98**	85.63	95.48	81.02	93.15
	P_{min} [MPa]	*−115.30*	*−222.76*	−136.4	**−265.35**	**−172.30**	−252.61	−125.20	−235.32
Trabecular bone	P_{max} [MPa]	*2.49*	*2.24*	**3.03**	**2.62**	2.95	2.52	2.92	2.59
	P_{min} [MPa]	*−2.81*	*−2.89*	−3.34	−3.38	−3.25	−3.25	**−3.49**	**−3.52**
P_{eqv} [MPa]		**166.40**	*244.92*	166.36	**279.69**	164.36	265.58	*142.27*	260.77

The values in *italics* represent the lowest, while values in **boldface** represent the highest tension stress (P_{max}), compression stress (P_{min}), and equivalent stress (P_{eqv}) values in each case; **LC1–LC4:** load case 1–4; **S1:** material assigned for denture body and implant bodies is TiAl6V4; **S2:** material assigned for implant bodies was TiAl6V4, while this was a Co-Cr alloy for the denture body; **MPa:** megapascal.

VI. DISCUSSION

1. Clinical study

The Ao4 treatment concept has been widely popularized in the recent years for the oral rehabilitation of an atrophic mandible, due to high level of functionality and patient satisfaction rates. The clear advantages of this technique include the small number of implants needed, less complex surgery, the use of longer, tilted distal implants (resulting in a shorter cantilever), and large inter-implant distances, leading to improved anchorage to the bone and higher primary stability. The aim of the retrospective clinical study was to provide additional evidence on the clinical outcomes associated with distally tilted implants according to the Ao4 therapeutic concept, and to assess the rates of marginal bone loss as a function of the elapsed time and patient characteristics using radiographic findings. Various procedures preceding implant placement (e.g., impression, drilling, and introduction of tools) may lead to inflammation and consequently, a baseline level of bone resorption will inevitably occur. Only around two-thirds of patients are completely complication-free following the restoration of the implant-supported fixed prostheses. The complications may include biological adverse events (e.g., peri-implantitis or loss of alveolar bone) and technical complications (screw loosening, retention loss, or fractures in the superstructures), that may lead to implant failure. The clinical utility of the Ao4 treatment concept has been demonstrated in numerous clinical studies, showing that this technique is distinguished by a predictable, positive prognosis and high patient satisfaction rates. The superiority of this concept is associated with the implementation of an atrophic maxilla or mandible, less complicated surgery and upkeep, and masticatory forces in the satisfactory range. The 3.5-years-long follow-up period involved thirty-six patients, with an overall implant survival rate of 100%, highlighting the clinical success of the Ao4 concept. Based on our MBL at baseline (T_0; ~0.18 mm) and at the three follow-up points (T1, T2, and T3), bone loss showed the kinetics characteristic for a saturation curve, i.e., showing relatively high ΔBL values at the first-follow-up, with bone-levels changes “flattening out” the curve. By the third follow-up, mean bone loss in our patients was around 0.7–0.8 mm in both the maxilla and mandible, with specific positions in the maxilla and the mandible disproportionally affected. Bone loss levels were significantly higher around tilted implants compared to axial implants at every time-point. Tilted or short implants provide viable alternatives to bone grafting; on the other hand, they may lead to increased stress on the surrounding bone due to bending. Overall, our study has concluded that the use of Ao4 prosthetic concept for total arch rehabilitation yields higher MBL in association with tilted implants and, in some cases, on the MA surfaces at vertically positioned implants after >40 months of function. The present study highlights some areas of concern during prosthetic rehabilitation with the Ao4 concept. The limitations of our study – including the retrospective, single-center study design, the relatively low number of subjects and the time of follow-up – should be taken into consideration when interpreting the results.

2. Finite element analysis (FEA)

Our 3D-FEA-based study aimed to evaluate the biomechanical effects of different occlusion/load cases and implant-denture material properties in an edentulous mandible (constructed using authentic CT scans of a patient) with an implant-supported full bridge on four implants, to model the biomechanical properties of the Ao4 concept. Due to the bone’s elastic material properties, tensile and compressive stress values were deemed appropriate to evaluate biomechanical properties in this study. Based on our analyses, the LC1 modeled was noted as the safest option, confirming our initial hypotheses. This load case was characterized by the most uniform stress distribution, and the lowest peak $\mathbf{P_{max}}$ and $\mathbf{P_{min}}$ values in the mandible body, throughout all simulations. On the other hand, LC2 – the load case where the force excluded the cantilevers of the denture extending behind the terminal implants – showed the highest peak $\mathbf{P_{max}}$ values in both cortical and trabecular bone for S1 and S2, respectively; therefore, it was the least desirable option in our analyses. As seen on the stress distribution maps, noted stress values were peak values denoted at a specific position; however, in reality, the maximum stress occurs as load transmitted at the bone–implant interface, not at a single point. The longevity of an implant may be ensured by keeping the stress of the bone in the physiological range, with the most even stress distribution possible. Overloading and subsequent bone resorption would occur if the tensile and compressive values exceed the physiological limits posed by the ultimate strength of the bone; stress values resulting from our FEA were below these physiological limits in all simulations and load cases. One of the main findings of the current study is the considerable effect that the load positions had on the distribution of the tested stress. It should also be noted that in our FEA model, peak stress values were measured near the implant−bone interface, which may be explained by the stress distribution characteristic of the cylindrical implants modeled in the present study. The framework applied (S1 and S2), had a relatively small effect regarding $\mathbf{P_{max}}$ values in the cortical bone (difference: 11.50–14.97%) and trabecular bone (difference: 11.16–15.87%); on the other hand, $\mathbf{P_{min}}$ values in the cortical bone (difference: 46.61–94.54%) and $\mathbf{P_{eqv}}$ values (difference: 47.19–83.29%) were considerably higher in the case of S2 (i.e., the simulated Ti and Co−Cr framework). To perform our analyses, some biologically complex objects (e.g., the anatomical complexity of the mandible, macrostructure, and microstructure of the implants, boundary conditions) and variable factors were considered constant out of necessity, e.g., all materials were considered homogeneous, isotropic, and linear elastic, a *Type II* bone was used for simulation, and osseointegration was assumed at 100%. The reliability of the 3D FEA stress analysis largely depends on the number and ratio of elements and nodes (including the use of higher order elements) in the model. In our case, the number of elements and nodes is in line with other studies already published to ensure maximum sensitivity of the model. Nevertheless, increasing their number would further enhance the reliability of the simulations. Mastication is a sophisticated and complex process, which makes its accurate estimation difficult for FEA studies: in this study, masticatory forces – which are multivectoral (vertical, horizontal, and oblique) under real circumstances – were modeled using a linear, continuous force exerted vertically on the simplified denture.

3. Summary

Overall, our research – both the retrospective clinical study and our FEA analyses – has shown the clinical utility and predictability of the Ao4 therapeutic concept, with highlighting some potential areas of interest for researchers and clinicians from the standpoint of prosthetic rehabilitation. To ensure the long-term maintenance and longevity of Ao4 concept – especially from the standpoint of the edentulous mandible, where the available bone supply, due to the post-extraction involutionary changes, is often limited – efforts to determine the stresses of the surrounding bone in the physiological range, with the most even stress distribution possible, have paramount importance. In our clinical study, we have shown the highest marginal bone loss levels around the DA aspects of tilted implants, and the MA aspects of axial implants, which corresponded to 0.7-0.8 mm of marginal bone loss – both in the maxilla and the mandible, after 3.5-years of follow-up; this rate of bone loss is comparable to the values found in the literature, corresponding to similar follow-up times. The results in the clinical study were further underlined in our FEA simulations: maximum stress values (tensile, compressive and equivalent, respectively) were observed at the implant-bone interface, most commonly localized near the top area of the second implant. Furthermore, according to our 3D-FEA models, highest peak tension stress (~ 100 MPa in the cortical bone, ~ 3 MPa in the trabecular bone) and highest peak compressive stress (~ -265 MPa in the cortical bone, ~ -3.5 MPa in the trabecular bone) values were all within the range that could be withstood by the jawbones (according to the physiological limits posed by the ultimate strength of the bone), without the fear of pathological complications. During treatment planning, care should be taken to reduce stress levels at the implant-bone interface in these highlighted areas of interest (e.g., by the appropriate choice of masticatory load distributions) to reduce marginal bone loss levels post-implant placement, and to ensure implant stability.

VII. NEW FINDINGS

a. During Ao4 treatment, rates of marginal bone loss around tilted (posterior) implants were consistently higher: significantly higher rates of marginal bone loss were observed around tilted (posterior) implants – compared to axial (anterior) implants – throughout all the follow-up measurements in the 3.5-year study period.
b. During Ao4 treatment, the rates of marginal bone loss around mesio-approximal (MA) and disto-approximal (DA) aspects of implants were similar: no significant differences were observed in marginal bone loss levels between the MA and DA aspects of implants, throughout all the follow-up measurements in the 3.5-year study period. Overall, highest marginal bone loss levels in our study were shown around the DA aspects of tilted implants, and the MA aspects of axial implants.
c. During 3D-FEA, the load case where linear masticatory forces covered the entire mesio−distal surface of the denture – including the cantilever – was the most advantageous: among our mandibular models, lowest maximum and minimum principal stress values, both in the cortical and trabecular bone, and the most uniform stress distribution was observed for load case 1 (LC1), where the masticatory force covers the entire surface of the denture, including the extension surface. In contrast, LC2 – where the linearly modelled masticatory forces excluded the cantilevers – was the least advantageous, with the highest observed maximum and minimum principal stress values.
d. During 3D-FEA, material properties of the implant and denture bodies has considerable effects on the stress values observed in the cortical bone: during the simulations (S2) where different material properties were assigned to implant bodies (TiAl6V4) and the denture bodies (Co-Cr), maximum principal stress values, minimum principal stress values and equivalent (von Mises) stress values were 11.50-15.87%, 46.61-94.54% and 47.19-83.29% higher, respectively (compared to S1, where implant and denture bodies were both TiAl6V4). In contrast, similar differences were not observed for the trabecular bone.

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