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New Techniques, Materials and Technologies in Dentistry

Edited by
Ricardo Castro Alves, José João Mendes and Ana Cristina Mano Azul

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Editorial

Special Issue on New Techniques, Materials and Technologies in Dentistry

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1. Introduction

Dentistry has seen significant technical and technological advances in recent years. These achievements have made it possible to increase the accuracy of diagnoses and treatment plans, improve the predictability and durability of certain treatments, make procedures safer and faster and improve patient experience and acceptance, among other benefits.

The speed at which these advances are developing justifies the publication of this Special Issue helping clinicians to stay up to date on the latest breakthroughs in this field. This Special Issue covers practically all areas of dentistry: implantology, periodontology, operative dentistry, pediatric dentistry, orthodontics, endodontics and oral rehabilitation. Of the 29 papers submitted to this Special Issue, 21 were accepted. In this Editorial, we highlight some of the main conclusions and impacts of these studies.

2. New Techniques, Materials and Technologies in Dentistry

All patients are different, so the "one size fits all" approach to prevention, diagnosis and treatment is evolving into a more personalized concept of medicine. Better knowledge of patients' genetic profile can help guide clinical decisions. An example of this is peri-implantitis, a growing problem that requires better approaches in terms of prevention and treatment. Cardoso et al. [1] carried out a systematic review via a meta-analysis with the aim of evaluating the association between IL-1A, IL-1B and IL-1RN polymorphisms and peri-implantitis. The results showed that patients who have the polymorphic allele at position +3954 of the IL-1B gene have on average almost twice the risk of developing peri-implantitis.

In the area of disease diagnosis, the use of biomarkers can enable timely diagnosis and better monitoring of disease progression and response to treatment. In an innovative study, Salim et al. [2] evaluated salivary interleukin-6, interleukin-1β and C-reactive protein as a diagnostic tool for plaque-induced gingivitis in children. Based on the results, the authors suggest that salivary IL-1β and CRP can be used as potential diagnostic tools to differentiate between moderate and severe plaque-induced gingivitis.

In another field, Raducanu et al. [3] tested the potential use of salivary nitric oxide as a biomarker of bone response following the application of different types of orthodontic appliances. The results showed that metal brackets lead to a significant temporary increase in oral oxidative stress as an adaptive reaction to the presence of foreign bodies in the oral cavity.

Conventional prevention and treatment strategies of caries, periodontal and peri-implant diseases present some limitations, making it necessary to search for alternatives or adjuvants. Probiotics may play an important role in this context. Saiz et al. [4] carried out a systematic review on the use of probiotics in the prevention and treatment of oral diseases, supporting the existing evidence in this regard. In relation to novel therapeutic approaches, the effect of passive ultrasonic irrigation on the elimination of organic remnant tissue from infected, narrow and curved mandibular root canals during their instrumentation was

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evaluated in an in vitro study by Alcota et al. [5]. The results suggest that clinicians should incorporate passive ultrasonic irrigation in their regular therapeutic strategy.

Several articles focused on the use of digital technologies in dentistry. This area has seen extremely rapid development in recent years, with a strong impact on clinical practice. For instance, digital technologies bring several advantages, such as reducing errors and complications, faster treatments and faster patient recovery. Wachol et al. [6] evaluated the advantages of dynamic navigation in prosthetic implant treatment in terms of clinical results and salivary pro-inflammatory biomarkers. Dynamic navigation and the application of the flapless technique reduced surgical trauma, leading to a reduced risk of infection, reduced patient discomfort and faster recovery. Implant stability is critical in implant therapy, and there are several devices on the market that allow it to be assessed through resonance frequency analysis and the implant stability coefficient to be calculated. However, there are few studies that have compared the reliability and agreement of different devices. In an in vitro study, Blazquez-Hinarejos et al. [7] compared inter- and intra-rater reliability and the agreement level among three of these devices. Rebelo et al [8] carried out a systematic review on the use of bisphosphonates and implant failure, also identifying other factors such as smoking, poor hygiene, diabetes and hypertension, which increase the risk of failure.

In prosthetic procedures, digital techniques have assumed an increasingly relevant role. Intraoral scanners have gained great clinical acceptance and undergone constant improvements in recent years. Despite this, there are still some relevant issues that need to be investigated. Lee et al. [9] presented a strategy with which operators could acquire more accurate digital impressions in single implant cases in terms of the orientation of the scan body and the scanning method. Until now, stereophotogrammetry has scarcely been investigated in cases of tilted implants. Thome et al. [10] evaluated, in an in vitro study, the accuracy of implant-level intraoral scanning and photogrammetry impression techniques in a complete arch with angled and parallel implants. The alteration of the occlusal vertical dimension for prosthetic restoration using a target-tracking system was evaluated by Lee et al. [11]. This new technique seeks to overcome some of the limitations of conventional methods using mechanical articulators. Also, in oral rehabilitation, concerning removable prosthesis, Lee et al. [12] proposed a digital workflow to fabricate complete dentures for edentulous patients using a reversing and superimposing technique. This four-step, completely digital workflow eliminates the need for conventional impressions and reduces patient discomfort and the number of visits.

Another current trend in dentistry is the use of minimally invasive techniques. Manaia et al. [13] presented a case series of patients with pre-eruptive enamel defects in esthetically compromised tooth regions, which were treated with the microabrasion technique. This technique does not require local anesthesia, is less destructive than restorative interventions and allows good esthetic outcomes with no significant postoperative sensitivity. Distinguishing composite remnants from tooth structure after trauma splint removal can be challenging. Magni et al. [14] compared the fluorescence-aided identification technique with conventional light illumination in terms of accuracy and time required for the detection of composite remnants after trauma splint removal.

In terms of new surgical techniques, [15] evaluated the clinical results of the double lateral sliding bridge flap technique with connective tissue graft in the treatment of isolated and multiple gingival recessions. Treating gingival recessions in the mandibular anterior region is a challenge due to anatomical constraints. This study adds more evidence regarding a technique that is still little addressed in the literature.

Five studies in the field of dental materials were published in this Special Issue. The effect of feldspathic thickness on the fluorescence of a variety of resin cements and flowable composites was evaluated in an in vitro study by Pereira et al. [16]. Color changes in temporary acetal resins manufactured by a fully computerized design and fabrication process were evaluated in vivo by Gómez-Polo et al. [17], with clinically relevant results.

Choudhry et al. [18] tested the antifungal efficacy of sodium perborate and microwave irradiation for the surface disinfection of polymethyl methacrylate polymer, providing a new perspective on the best disinfection strategy for this material.

Also, building a bridge with the digital area, Anes et al. [19] evaluated the retentive forces from removable partial denture clasps manufactured using the digital method. The objective of this study was to evaluate retentive forces and the change in clasps with digitally manufactured different designs over time.

Regarding biomaterials used in bone regeneration and an intersection with the field of new therapeutic approaches, Cenicante et al. [20] carried out a literature review on the use of autogenous dentin in alveolar preservation procedures. In this article, the authors summarize new evidence on the use of autogenous teeth as a biomaterial in ARP, different protocols and future directions.

In terms of translational science, the effect of non-thermal atmospheric pressure plasma on the differentiation potential of human deciduous dental pulp fibroblast-like cells was evaluated by Okuno et al. [21], revealing a potential tool to expand the population of various adult stem cells in vitro for medical applications.

These investigations are united by the common final objective of improving diagnosis accuracy and providing more predictable and long-lasting treatments for patients and with better acceptance. For clinicians, some of these innovative techniques and materials will also make work simpler, faster and more effective.

3. Future Perspectives

Some important topics could not be covered in this Special Issue, and others will require further investigation. Technical and technological advances in dentistry will continue to grow at an incredible speed.

Although this Special Issue is now closed, the success it achieved led us to launch a second edition of "New Techniques, Materials and Technologies in Dentistry". Submissions are now open, so we invite everyone to participate and share their research work.

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Systematic Review

Association between IL-1A, IL-1B and IL-1RN Polymorphisms and Peri-Implantitis: A Systematic Review and Meta-Analysis

José Maria Cardoso [1,2,*,†], Sofia Duarte [2,†], Ana Clara Ribeiro [1,3], Paulo Mascarenhas [1,3], Susana Noronha [4] and Ricardo Castro Alves [1,2]

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Featured Application: Feature Application: The evaluation of genetic polymorphisms may have great clinical relevance since they can be measured before the onset of the disease and may be of great benefit for treatment planning and prognosis at an early stage.

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Abstract: Recent studies report that individuals with polymorphisms in the genes that encode for interleukin (IL)-1α and IL-1β (IL-1A and IL1B, respectively) and for IL-1 receptor antagonist (IL-1RN) may be more susceptible in developing peri-implantitis. Therefore, the current systematic review evaluates what is reported about the role of genetics, more specifically of single nucleotide polymorphisms (SNP) on IL-1 and variable number of tandem repeats (VNTR) on IL-1RN, in the development of peri-implantitis. This systematic review was carried out by screening PubMed, B-on, Cochrane and Scopus databases, for articles English, Spanish, and Portuguese, with no limit regarding the publication year. Eight articles were selected for systematic review and four for meta-analytic syntheses. Our results show that although there is a lack of consensus in the literature, there seems to be an association between IL-1A, IL-1B, and IL-1RN polymorphisms with peri-implantitis. The results of the meta-analysis showed that patients who have the polymorphic allele at position +3954 of the IL-1B gene have on average almost twice the risk of developing peri-implantitis (*odds ratio* = 1.986, 95% confidence interval).

Keywords: genetics; peri-implantitis; interleukin-1; interleukin-1 receptor antagonist; interleukin-1 genotype; genetic polymorphisms; peri-implant disease

1. Introduction

Dental implants are now considered as an effective and predictable treatment modality for the functional and aesthetic rehabilitation of either partially or completely edentulous patients [1,2]. This rehabilitation method has a success rate of more than 90% for implants in function for more than five years [3]. However, despite the high success rates associated with implant rehabilitation, biological complications may arise in the peri-implant soft tissues, such as peri-implantitis, which can compromise the permanence of the implant [4]. Peri-implantitis is a plaque-associated pathological condition occurring in tissues around dental implants, characterized by inflammation in the peri-implant mucosa and progressive loss of supporting bone [5,6]. This definition is in accordance with the more recent classification of periodontal and peri-implant diseases (American Academy of Periodontology—AAP and European Federation of Periodontology—EFP 2018) [6].

According with the Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions, there is strong evidence from animal and human experimental studies that plaque is the etiological factor for peri-implant mucositis, which is assumed to precede peri-implantitis [6]. Data indicate that patients diagnosed with peri-implant mucositis may develop peri-implantitis, especially in the absence of regular maintenance care. However, the features or conditions characterizing the progression from peri-implant mucositis to peri-implantitis in susceptible patients have not been identified [6].

With a growing number of dental implants inserted, the potential number of sites for implant-associated diseases increases [7]. But the actual value of the incidence/prevalence of this disease is uncertain since the method of classifying peri-implantitis has varied between authors over the years and, in addition, few studies follow up and evaluate the sample for several years [8]. The characteristics of the populations included also vary between studies, which may influence the results [8]. In a systematic review carried out by Atieh et al., the prevalence of peri-implantitis obtained per patient was 18.8% while the prevalence per implant was 9.6% [9]. Lee et al. conducted a systematic review and meta-analysis, that included forty-seven articles, and concluded that the mean prevalence of peri-implantitis, at implant and subject level was 9.25% and 19.83%, respectively [10].

There are some similar features in the sequence of immunopathological events in peri-implant and periodontal infections [11]. Both are initiated primarily by Gram-negative anaerobic bacteria, while the inflammatory process goes faster and deeper around implants than around natural teeth and thus is a more significant problem for patients with dental implants [12]. However, Becker et al. in a study in which the transcriptome profiling using mRNA from patients suffering from either peri-implantitis or periodontitis was compared, the authors observed that these two pathologies react in a different way [13]. These differences may be explained by the anatomy, which is very different comparing the scar tissue in peri-implantitis with the specialized fibers inserting the surface of the teeth. In peri-implantitis tissue, transcripts associated to innate immune responses, and defense responses were dominating, while in periodontitis tissues, bacterial response systems prevailed [13].

Research evidence indicates that implant complications tend to be clustered in a subset of individuals rather than being randomly distributed in the population implying that patient's host response might play a role for the implant success [14,15].

Interleukin-1 (IL-1) is the pivotal mediator of the immune-inflammatory response that acts both in response to bacterial infection and in bone metabolism [16]. IL-1 family has at least 11 cytokines; clustered on the long arm of chromosome 2q, and the three most studied members are IL-1A, IL-1B, and IL-1RN genes, which encode the agonistic proteins IL-1α and IL-1β, and IL-1 receptor antagonist (IL-1Ra), respectively [17]. The effect of IL-1 is determined by the balance between IL-1α, IL-1β, and IL-1Ra through competitive binding of IL-1Ra to the IL-1 receptor to block the activity of IL-1α or IL-1β. IL1 is strongly induced by lipopolysaccharides from the cell walls of Gram-negative bacteria and acts either directly or indirectly to initiate and amplify inflammatory responses through inducing expression of a substrate of effectors including cytokines/chemokines and matrix metalloproteinases [18].

The variations of IL-1 gene cluster, including IL-1A and IL-1B genes, and the variations of IL-1 RN are the most commonly studied functional polymorphisms for peri-implantitis.

Many studies have investigated different single nucleotide polymorphisms (SNPs) in the IL-1 genes as a risk factor for peri-implantitis. Among them, the IL-1A −889 C/T (rs1800587) and IL-1B +3954 C/T (rs1143634) have been mostly investigated [19]. The IL-1B-511 (rs16944) is also studied in some studies. These polymorphisms are characterized by the substitution of cytosine with thymine in the DNA sequence, which has been demonstrated to be associated with directly changed levels of gene expression and secreted cytokines, respectively [20]. In the IL-1RN gene, there is a genetic polymorphism located in intron 2 which is composed of a variable number of tandem repeats (VNTR) of 86 base pairs length. Several studies have analyzed the relationship between these polymorphisms and peri-implantitis. However, studies have yielded conflicting results on this issue [21–26].

A clarification of the genetic basis associated with peri-implant pathology could be used to predict peri-implantitis occurrence and to improve treatment and monitoring of patients with dental implants [21].

Most of these studies had a relatively small sample size and thus had insufficient statistical power to detect the genetic associations. Some of them do not refer to confounding variables such as periodontal condition, ethnicity and smoking habits. Furthermore, many studies, including published systematic reviews, assess the relationship of these polymorphisms with the peri-implant disease, pooling in the same group patients with bone loss, implant loss, and peri-implantitis [27–29]. However, peri-implant tissue health can exist around implants with variable levels of bone support [6]. In addition, an implant can fail without having an associated chronic inflammatory reaction as occurs in peri-implantitis.

Therefore, we performed a systematic review and meta-analysis, quantitatively synthesizing previous studies, to evaluate the association of common functional polymorphisms in the IL1 and IL-1RN genes with susceptibility to peri-implantitis.

2. Materials and Methods

2.1. Study Design

The guidelines of PRISMA were followed while reporting this systematic review and meta-analysis.

The research question used for this systematic review was: "What is the importance of the interleukin-1 genotype (IL-1A −889 (rs1800587), IL-1B −511 (rs16944), and IL-1B +3954 (rs1143634)) and the IL-1 receptor antagonist genotype (IL-1 RN (rs2234663)) in the development of peri-implantitis, in adults, smokers or not, after at least one year of the implant in function?". In addition, the PECO nomenclature was also used:

P (Population)—Adult patients
E (Exposure)—Genotype including selected polymorphisms of interleukin-1 and its antagonist
C (Control)—Genotype not including selected polymorphisms of interleukin-1 and its antagonist
O (Outcomes/Outcome)—Development of peri-implantitis

A search protocol was specified in advance and registered at PROSPERO (International Prospective Register of Systematic Reviews ID 322662).

2.2. Search Strategy

Two authors (J.M.C.) (S.D.) extracted the specific studies from the databases, and the same authors removed duplicates and irrelevant studies. Discrepancies, if occurred, were resolved by a third researcher (P.M.).

Systematic searches were performed on the PubMed, B-on, Cochrane and Scopus literature databases for studies published until January 2022.

The MESH terms and other keywords were used in combination, and Boolean operators such as AND and/or OR and/or NOT were added to obtain more relevant studies regarding the topic in question [30].

We used a specific search strategy with the following focused key terms:

("dental implants" or "oral implants") and ("polymorphism" or "interleukins" or "interleukin-1"); ("peri-implantitis") and ("interleukin-1" or "interleukins") and ("gene polymorphism" OR "genotype") not animal.

2.3. Inclusion and Exclusion Criteria

The inclusion criteria were: (1) Human case-control studies; (2) peri-implantitis as the outcome of interest in functional implants with at least one year follow up; (3) studies reporting IL-1A −889, IL-1B −511, IL-1B +3954 and IL-1RN (VNTR), and composite genotype of IL-1A −889/IL-1B +3954 polymorphisms; (4) articles written in English, Spanish or Portuguese.

The exclusion criteria were: (1) Studies that included patients with uncontrolled systemic diseases; (2) studies in which patients with peri-implantitis were included in a general category disease group of peri-implant diseases or other conditions (presence of suppuration, development of fistula, radiographic bone loss or implant loss).

The author (S.D.) screened all the titles and abstracts based on the eligibility criteria and included/excluded studies for full-text review. Another author (J.M.C.) rechecked relevant articles. Discrepancies, if occurred, were resolved by a third researcher (P.M.).

2.4. Data Extraction

One author (S.D.) independently extracted the information or data from each study and another author (J.M.C.) rechecked them.

2.5. Risk of Bias Assessment

Two authors (S.D. and P.M.) evaluated the quality of included articles using the Joanna Brigs Institute (JBI) checklist [31]. This tool evaluates "cross-sectional analytical" studies regarding eight domains. These domains evaluate if the criteria in the sample were clearly defined, if the study subjects and the setting were described in detail, if the confounding factors were identified and strategies to deal with, and if the outcomes were measured in a valid and reliable way.

2.6. Statistical Analysis

Statistical analysis was performed using the Open Meta [Analyst] for Windows 8 (built 04/06/2015) software, from Center for Evidence Synthesis in Health (Brown University, Providence, RI, USA), which allowed us to obtain all meta-analysis and meta-regression plots, which are described later [32]. Allele frequencies against peri-implantitis incidence were converted in odds ratios effect size and associated 95% confidence intervals in a binomial model framework. Model parameters were estimated applying the restricted maximum likelihood method.

Heterogeneity was assessed using the I^2 index and it was considered high if it was above 50%. A high I^2 value means that the authors of the different articles analyzed are not in consensus. To counteract this value, covariates can be added [33].

We used 95% confidence intervals and considered the *p*-value test results lower than 0.05 to correspond to a statically significant result.

A subgroup analysis was done in relation of the odds ratio (OR) of the ethnicity in the difference in the frequency of the mutated allele between the disease and control group.

Meta-regressions were carried out for longitude and latitude of the sample's provenance, the mean age, the percentage of males and females, the representative ratio of the mutated allele, sample size and year of publication.

3. Results

3.1. Study Selection

Initially, 324 articles were obtained from all databases. After excluding the duplicates, 218 articles remained, of which the titles and abstracts were read. Since 199 were not included in the theme of this systematic review, they were excluded, leaving only 19. These were read in full and, as eleven articles did not meet the inclusion and exclusion criteria, only eight articles remained, which were included in this systematic review [21–26,34,35]. However, only four of these articles contained eligible quantitative data, and were included in the meta-analysis [21,23,24,26].

A PRISMA flowchart was carried out to systematize the selected information throughout the different research phases (Figure 1).

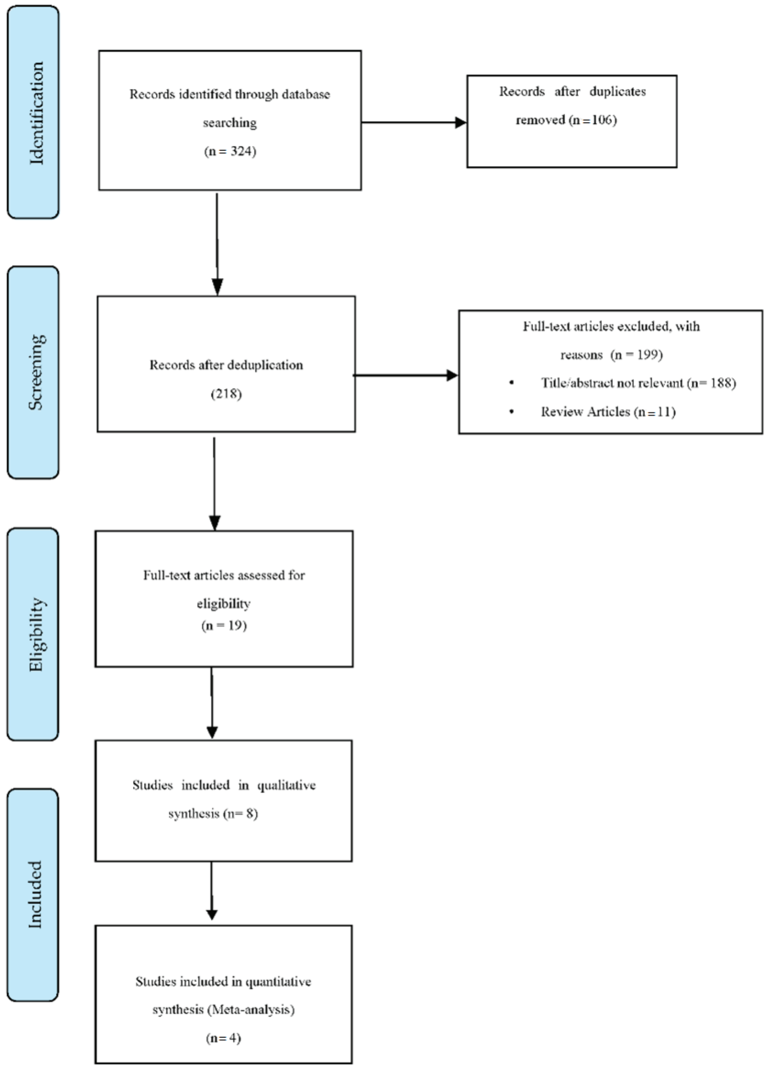

Figure 1. Flow chart of the study selection.

3.2. *Results of the Bias Risk Assessment*

In order to know the risk of bias in the articles, by completing the JBI checklist, a Traffic Plot-type graph was obtained (Figure A1), where it is possible to clearly observe the risk of bias for each article selected for this systematic review. None of the articles had three or more high risk judgments and they were all included in the review.

3.3. *Characteristics of the Studies*

The Table 1 provides the characteristics of eight articles [21–26,34,35] included in the systematic review. Four articles included individuals from Europe [21,25,34,35], two from Asia [24,26], one from North Africa [22] and one from South America [23]. Five studies reported IL-1A −889 polymorphism [21,22,24,25,34], two IL-1B −511 [21,23], seven IL-1B +3954 polymorphism [21–26,34], two IL-1RN (VNTR) polymorphism [21,35] and five composite genotype of IL-1A −889 and IL-1B +3954 polymorphisms [21,22,24,25,34].

demineralization of the enamel, they should hamper the organization of the extracellular matrix responsible for biofilm formation, limit the production of cytotoxic products by pathogenic bacteria, and beneficially alter the biochemical parameters that influence the dental plaque (e.g., salivary components, buffer capacity) (Figure 1) [9]. In addition, oral probiotics must be safe for the host [10,11].

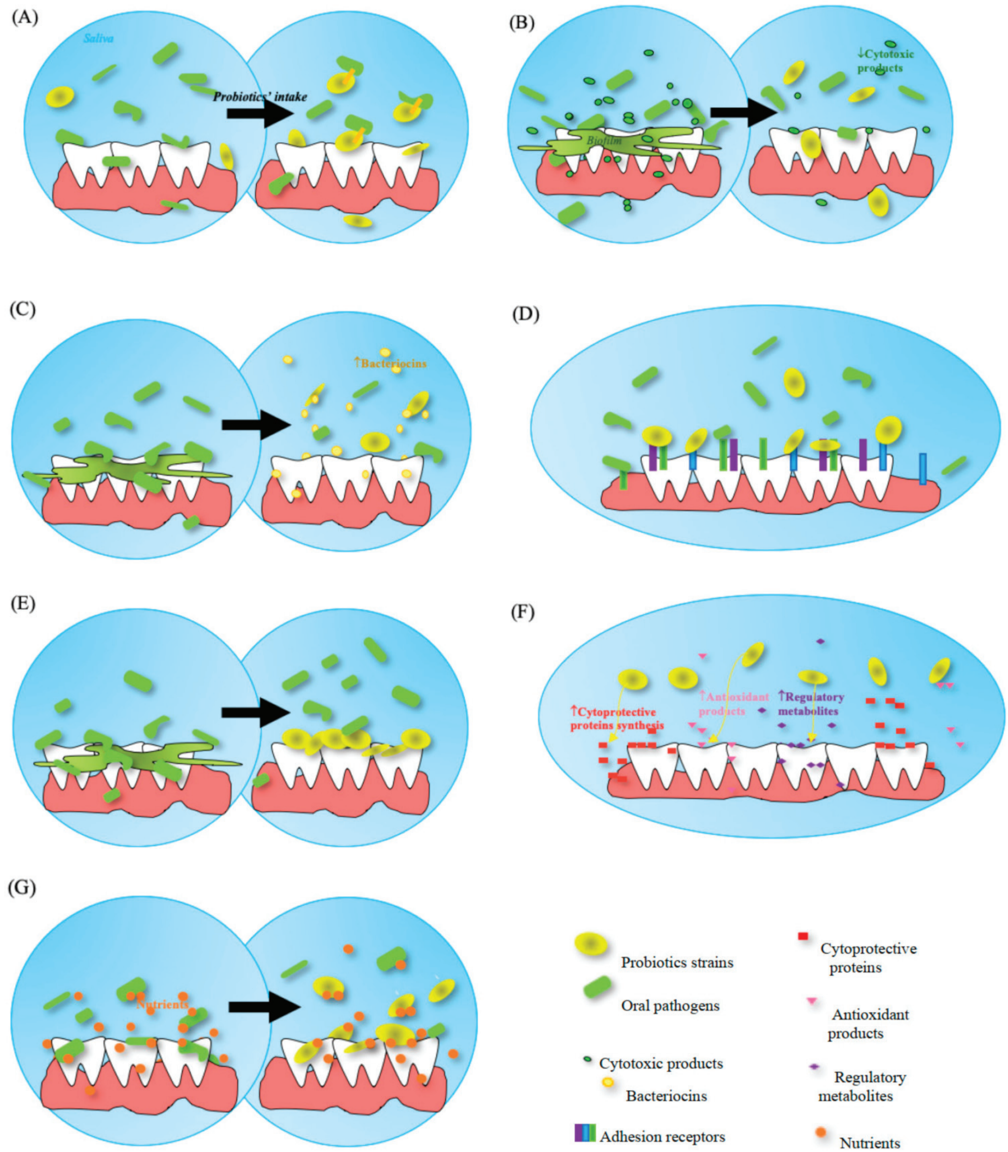

Figure 1. Potential mechanisms of action of probiotics in oral health and disease: (**A**) direct interaction with pathogens to prevent pathogen colonization; (**B**) antagonistic activity on pathogens cytotoxic metabolites, oral biofilm, and extracellular matrix; (**C**) synthesis of antibacterial agents (e.g., bacteriocins) against oral pathogens; (**D**) alter adhesion, aggregation, colonization, and proliferation of pathogens in oral tissues due to mechanisms of exclusion and competition; (**E**) coating oral tissues to protect oral surfaces from pathogens action; (**F**) maintain oral ecosystem balance by synthetizing cytoprotective proteins, antioxidant products, and regulatory metabolites on surface of oral cells; (**G**) competition for nutrients.

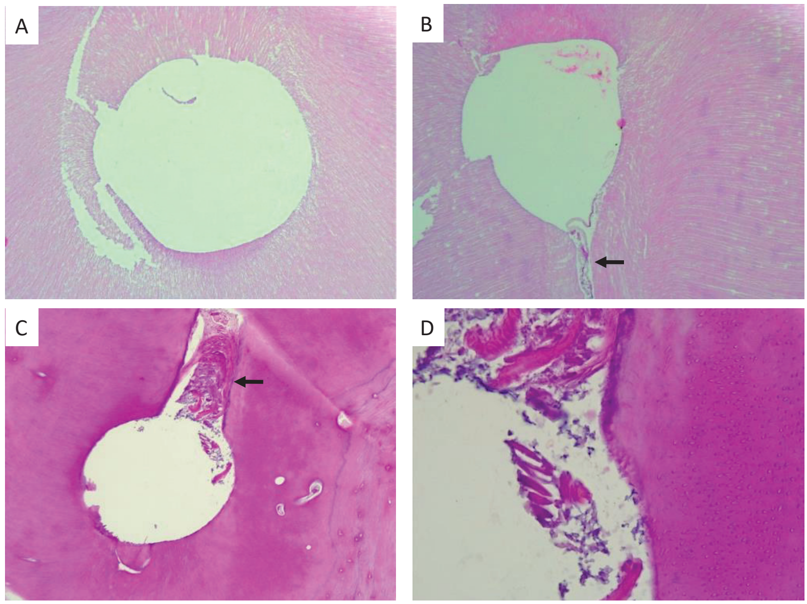

Figure 4. Representative images, at 2 mm from the apex, of roots canals prepared with different instrument diameters. (**A**): Root canal instrumented with #35 without PUI. Magnification 10×. (**B**): We can observe the remains of detritus in the isthmus after instrumentation (black arrow). Magnification 10×. (**C**): Root canal instrumented in a single pole with lime RaCe #25. We can observe the remains of detritus in the polar opposite (black arrow) Magnification 10×. (**D**): Approach of the previous case. Magnification 40×.

After applying a PCoA to the ordinal raw data obtained by the Langeland's ordinal scale for teeth cleanness, the effect of PUI explained 64.9% of the overall variance when compared with the control (conventional irrigation, CI). The percentage of PCo 1 expected by chance variance was below what was observed, implying a statistically significant difference between the PUI and CI samples (i.e., 52% vs. 64.9%, respectively, after a broken-stick model) (Figure 5). These results were corroborated by a one-way ANOSIM post-hoc test ($R = 0.3383$, p (same) = 0.0005, mean ranks = 95.7–134.8, using Manhattan similarity index after 9.999 permutations).

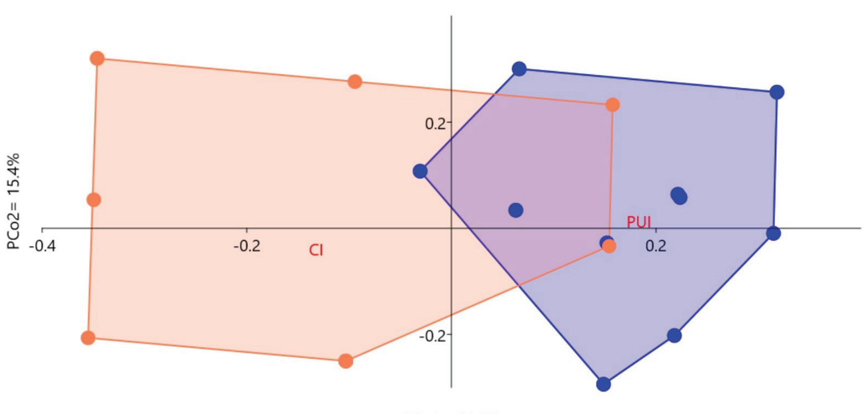

Figure 5. Principal Coordinate Analysis (PCoA) of the raw data. Visualization of the dissimilarities of the ordinal raw data

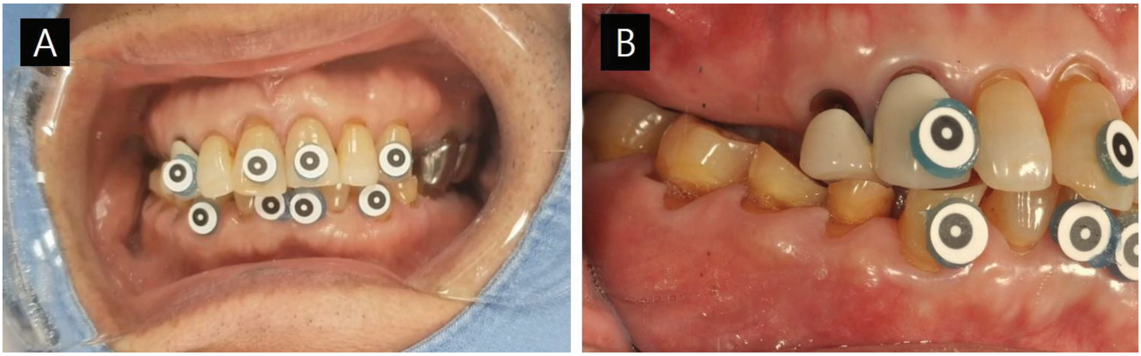

Figure 1. (**A**) Target tracking materials are attached to the labial surface of the upper and lower anterior teeth. (**B**) The restoration space is insufficient on the lateral side after losing the antagonist teeth.

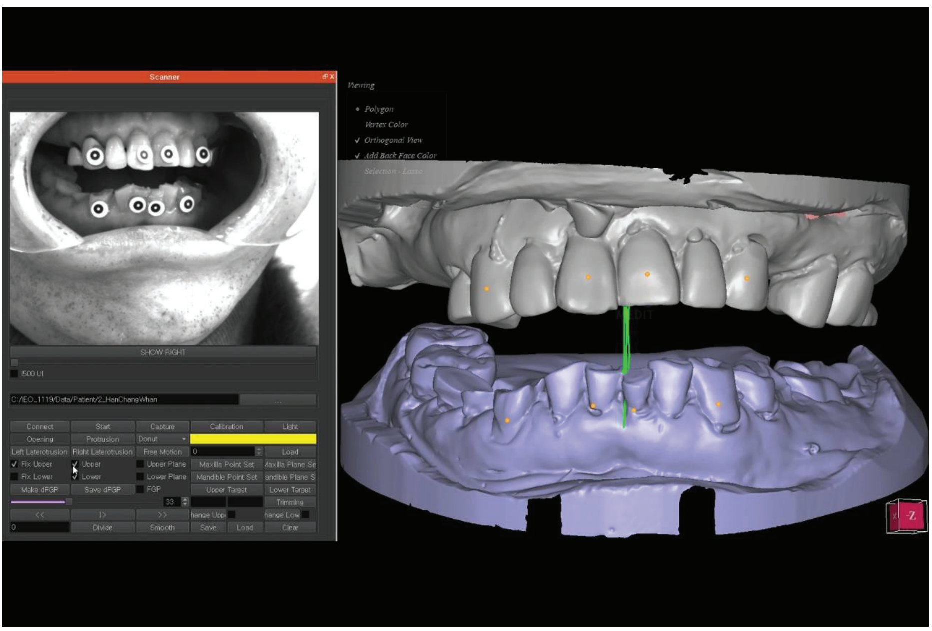

Figure 2. The mandibular movement is recorded in real time and replaced with data of the entire arch model.

The procedure of oral scanning after attaching the targets, target tracking of the anterior teeth using an optical scanner, and replacement of the entire arch data were performed in this case by aligning with referenced target stickers and the same position in the cast [11].

2.2. Confirmation of CR–MI Discrepancy

When the patient closes his mouth to the tooth contact position, it is possible to check whether a sliding motion occurs at the first contact position and the presence of CR–MI discrepancy can be checked (Figure 3A). If such a discrepancy is present, a horizontal trajectory (between two green dots) appears and its size can be measured by tracking software (Ezscan8; Medit Corporation, Seoul, Korea). Additionally, then it can be exported by specifying the positions of the maxilla and mandible in the centric relation position (Figure 3B). The centric relation recording followed the chin-point guidance method among