CAN PATIENTS DETECT PERI-IMPLANT MUCOSAL INFLAMMATION? RESULTS FROM A MULTICENTRE RANDOMIZED TRIAL

By

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ABSTRACT

Background: Tooth loss in the maxillary anterior region is known to have the greatest impact on facial aesthetics and is a major cause of concern for patients. Replacement with dental implants may achieve favourable results due to their predictability and viability over other treatment options. In recent decades, the goals of oral implantology have switched from achieving osseointegration-based implant stability and survival to achieving the best aesthetic outcomes. With this recent shift, patient satisfaction with treatment has become as important as clinical success outcomes. Whereas many studies have been conducted to determine survival rates, complications and other clinician reported outcomes of implant, limited data exist on patient perceptions and satisfaction with their anterior implant therapy.

Objective: The objective of this study was to compare patient reported outcomes (PROs) of peri-implant soft tissue aesthetic changes around single-tooth implants in the anterior maxillary region with three different implant-abutment interface designs.

Methods: This multicentre randomized clinical trial recruited 141 participants who required one or more single tooth replacements in the maxillary anterior region. They were randomized to one of three different types of implant-abutment interface designs [Conical (CI), Flat-to-Flat (FI), and Platform Switched (PS)]. Implants and provisional crowns with prefabricated titanium abutments were placed 5 months following extraction and/or ridge augmentation. Permanent ceramic crowns with zirconia abutments were placed after 12 weeks. To assess PROs, patient appearance questionnaires were completed at appointments following provisional crown placement to the 3-year follow-up.

Results: Participants' ratings of tooth appearance with CI, FI, and PS implants at the 3-year follow-up were significantly different ($p=0.049$; Kruskal-Wallis test). PS was rated better than FI ($p=0.047$) at 1 year for appearance of soft-tissue and satisfaction with mucosal colour. There

were no differences in ratings of self-consciousness, smile avoidance and pain/discomfort while eating hard foods.

Conclusions: Although participants tended to rate the health of the mucosa around platform switch implants as slightly better than around the other two tested systems, the differences were minimal and inconsistent. Because these findings do not coincide with clinical outcomes from the same patients, they indicate that patients are unable to detect mucosal inflammation around their implants. Therefore, these results support the importance of routine follow-up examinations by dentists; thus, patients should not delay these visits, even if their mucosa appears to them to be healthy.

RÉSUMÉ

Contexte : La perte de dents dans la région antérieure du maxillaire est connue pour avoir le plus grand impact sur l'esthétique du visage et constitue une cause majeure de préoccupation pour les patients. Le remplacement par des implants dentaires peut donner des résultats favorables en raison de leur prévisibilité et de leur viabilité par rapport aux autres options de traitement. Au cours des dernières décennies, les objectifs de l'implantologie orale sont passés de l'obtention de la stabilité et de la survie des implants par ostéo-intégration à l'obtention des meilleurs résultats esthétiques. Avec cette évolution récente, la satisfaction des patients à l'égard du traitement est devenue aussi importante que les résultats cliniques. Alors que de nombreuses études ont été menées pour déterminer les taux de survie, les complications et autres résultats cliniques des implants, il existe peu de données sur la perception et la satisfaction des patients concernant leur traitement implantaire antérieur.

Objectif : L'objectif de cette étude était de comparer les résultats rapportés par les patients (PRO) des changements esthétiques des tissus mous péri-implantaires autour des implants à dent unique dans la région maxillaire antérieure avec trois conceptions différentes d'interface implant-pilier.

Méthodes : Cet essai clinique multicentrique randomisé a recruté 141 participants qui avaient besoin d'un ou plusieurs remplacements de dents uniques dans la région antérieure du maxillaire. Ils ont été répartis au hasard dans l'un des trois différents types d'interface implant-pilier [conique (CI), plat à plat (FI) et plateforme commutée (PS)]. Les implants et les couronnes provisoires avec des piliers en titane préfabriqués ont été placés 5 mois après l'extraction et/ou l'augmentation de la crête. Des couronnes permanentes en céramique avec des piliers en zircone ont été placées après 12 semaines. Pour évaluer les PRO, des

questionnaires sur l'apparence du patient ont été remplis lors des rendez-vous suivant la pose de la couronne provisoire jusqu'au suivi de 3 ans.

Résultats : Les évaluations des participants sur l'apparence des dents avec les implants CI, FI et PS lors du suivi à 3 ans étaient significativement différentes (p=0,049 ; test de Kruskal-Wallis). PS a été mieux noté que FI (p=0,047) à 1 an pour l'apparence des tissus mous et la satisfaction de la couleur de la muqueuse. Il n'y avait pas de différence dans les évaluations de la gêne, de l'évitement du sourire et de la douleur/inconfort lors de la consommation d'aliments durs.

Conclusions : Bien que les participants aient eu tendance à évaluer la santé de la muqueuse autour des implants Platform Switch comme légèrement meilleure qu'autour des deux autres systèmes testés, les différences étaient minimes et inconsistantes. Comme ces résultats ne coïncident pas avec les résultats cliniques des mêmes patients, ils indiquent que les patients sont incapables de détecter une inflammation de la muqueuse autour de leurs implants. Par conséquent, ces résultats soutiennent l'importance des examens de suivi de routine par les dentistes ; les patients ne devraient donc pas retarder ces visites, même si leur muqueuse leur semble saine.

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CONTRIBUTION OF AUTHORS

Shwetha Sherigar: Master's candidate- Prepared search strategies for literature review, performed data analyses and interpreted the findings; she also wrote the manuscript and thesis.

Dr. Raphael F de Souza: Associate professor, Faculty of Dental Medicine and Oral Health Sciences, McGill University, Quebec, Canada, performed the data analyses and interpretation, as well as edited the thesis and manuscript**.**

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Contribution of Authors to the Manuscript

Manuscript - Can patients detect peri-implant mucosal inflammation? Results from a multicentre randomized trial.

Dr. Shwetha Sherigar performed data analysis, interpreted the findings and drafted the manuscript. Prof. Feine participated in designing the study as one of the co-investigators for the primary and secondary outcomes, developed/validated the patient appearance questionnaire, and edited the thesis and manuscript. Drs. Cooper, Stanford, Barwacz, McGuire, and Abi-Nader designed and participated in carrying out the full study, gathered data at their individual sites, and published manuscripts on other aspects of this study. Dr. de Souza supervised the data analysis and interpretation, edited the manuscript. All authors read, commented on, and approved the final manuscript.

LIST OF ABBREVIATIONS

CI – Conical Implant

FI – Flat-to-flat Implant

PS – Platform-Switched Implant

FDI – FDI World Dental Federation

OHRQoL- Oral Health-Related Quality of Life

RPDs - Removable Partial Dentures

FDPs - Fixed Dental Prostheses

PROs- Patient Reported Outcomes

WHO – World Health Organization

TDI – Traumatic Dental Injury

TDIs -Traumatic Dental Injuries

GBD – Global Burden of Disease

CDC – Center for Disease Control and Prevention

QoL – Quality of Life

IAJ – Implant-Abutment Junction

BTT – Buccal Bone Thickness

ARP – Alveolar Ridge Preservation

IAI – Implant-Abutment Interface

PT – Periotest

RFA – Resonance Frequency Analysis

VAS – Visual Analog Scale

PROMs – Patient-reported Outcome Measures

ITI – International Team for Implantology

NIHR - National Institute for Health Research

BOP – Bleeding on Probing

1. INTRODUCTION

Oral health is a key indicator of overall health, well-being and quality of life.[1] In 2016 FDI stated that "Oral Health is multifaceted and includes the ability to speak, smile, smell, taste, touch, chew, swallow, convey a range of emotions through facial expressions with confidence and without pain, discomfort, and disease of the craniofacial complex."[2] The main challenges to oral health include dental trauma and diseases like dental caries, periodontal disease, oral cancer, and cleft lip/palate. Tooth loss due to trauma, dental caries, periodontal disease or congenitally missing teeth is often a cause of major concern for most patients [3] and is responsible for causing 7.6 million disability-adjusted-life-years.[4] With improvements in dental care access, the prevalence of tooth loss has decreased in recent years, although the rate of anterior tooth loss in adults in Western countries is still 25%.[5] With anterior tooth loss, patients have reported that the loss of aesthetics has the greatest impact on their lives, followed by loss of function and phonetics. Tooth loss also has a negative influence on the psychological, social, financial and general health on the people suffering from it.[6] Therefore, it has a direct impact on the oral health-related quality of life (OHRQoL).[7] A recent study shows that tooth loss can negatively influence cognitive function and that in several patients with Alzheimer's disease show a greater loss of teeth and complete edentulism.[8]

Treatment options for anterior tooth loss include removable partial dentures (RPDs), fixed dental prostheses (FDPs) or implant-supported fixed dental prostheses. When compared with RPDs and FDPs, implant treatment with fixed dental prostheses is considered to be the most viable treatment option with high survival rates.[9, 10] Over the past two decades, implant success rates were measured by criteria like implant stability, osseointegration and survival, along with preservation of the hard and soft tissues around the implant.[11] However, there has been a gradual shift in success criteria as more importance has now been given to maximizing

implant success based on patient-reported outcomes (PROs), rather than determining success using only clinical and/or laboratory assessments, especially in the aesthetic zone.[12] [13]

In the anterior zone, the peri-implant soft tissue should preferably blend in with the mucosa around the adjacent teeth and the implant crown should be in proportion to the surrounding dentition to achieve maximum aesthetic results.[14] Marginal bone loss and inflammation of the peri-implant mucosa is one of the major complications over the long term with 9.7% of implant supported single crowns presenting with soft-tissue complications over a period of 5 years.[15, 16]

In implant systems, the stability of the mucosal tissue relies on the connection between the implant body and the abutment, which is called the "implant-abutment interface". Many systematic reviews have shown that different implant-abutment designs are associated with a decrease in peri-implant marginal bone loss. [13, 17] Any implant design that allows micromotion and microbial leakage will lead to accumulation of bacteria, followed by inflammation and crestal bone loss.[18, 19]

Investigations have suggested that implants with connections that allow micromotion (e.g., flat-to-flat interface design) will be associated with more crestal bone loss. [20] Other studies have shown that there is less bone loss with conical implant connections due to absence of reactive bone loss [21] and less microleakage. [22] Occlusal overloads applied on the implant-supported prosthesis may cause peri-implantitis and stress on the marginal bone. Hence, the selection of the implant-abutment interface plays a vital role in maximizing mucosal health and aesthetic outcomes.[23] Current studies suggest placing an abutment one size smaller than the implant platform – this is known as platform switching (PS). This approach has been reported to reduce crestal resorption, thereby diminishing any potential inflammatory impact.[24, 25] Because of the importance of aesthetics in anterior tooth replacement, it is important to understand patients'

perceptions of their mucosal health surrounding different types of implant abutment-interface designs. [26]

Patient reported outcomes (PROs) are defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else." [27] PROs provide information about the patient's perception of a treatment; furthermore, as with all interventions that have an impact on an individual's life, it is vital to know how that intervention affects his/her satisfaction and quality of life. When measuring and evaluating treatment outcomes, it is increasingly acknowledged that the implications on Oral Health Related Quality of Life (OHRQoL) should be considered. Literature also suggests that clinical measures only are not adequate to describe treatment outcomes and that patients with chronic diseases have a profound ability to perceive and accurately rate treatment outcomes on their quality of life. [28]

If peri-implant soft tissue responses to different implant designs vary, then clinical and patient assessment of these responses may also vary. Many studies have been conducted to measure the clinical success rate following implant placement in the anterior region regarding clinical outcomes, such as peri-implant bone tissue responses, complications, and implant survival.[10, 11, 29-32] However, no study has of yet determined whether patients can detect signs of mucosal inflammation around their implants with three implant abutment interface designs.

Therefore, our group has compared different designs of implants placed in the upper anterior and premolar region. The primary outcome of the main study involved clinical assessment of peri-implant mucosa in three implant abutment interface designs.[33-40] This study addresses the secondary outcome of patient perceptions of mucosal inflammation (redness, bleeding, and pain) and appearance with these three implant designs.

2. LITERATURE REVIEW

The general health status of a person is closely associated with oral health and has been a subject of interest for research. The World Health Organization (WHO) defines oral health as "a state of being free from mouth and facial pain, oral and throat cancer, oral infections and sores, periodontal (gum) disease, tooth decay, tooth loss and other diseases and disorders that limit an individual's capacity in biting, chewing, smiling, speaking and psychosocial well-being". [1] According to many studies, tooth loss at any stage increases the risk of negative health outcomes. In fact, studies have indicated that tooth loss is a marker for ischaemic heart disease, stroke, diabetes, and cancer. [41-43]

2.1 Tooth loss in the anterior maxillary region - Causes

Teeth can be lost in the anterior region due to a variety of reasons, including orofacial trauma, caries, and periodontal disease.

2.1.1 Trauma

A traumatic dental injury (TDI) is a forceful impact that can harm the teeth along with the surrounding hard and soft tissue structures. It is not classified as an oral disease but is a result of multiple inevitable hazard factors that are incidental and unforeseen. The most common reasons for TDI are attributed to falls, followed by sporting accidents, traffic injuries, and acts of violence. [44, 45]

Dental injuries not only affect a person physically, but also psychologically and economically, with associated costs estimated to be US $2-$5 million/1 million people per year. [46]

Despite accounting for only 1% of the total body surface area, the oral cavity undergoes 5% of all bodily injuries. TDIs affect 1-3% of the total population with a prevalence rate of 18% in the permanent dentition. [46, 47] According to a review published in 2016 by Lam et al., the yearly incidence rate of dental trauma could reach 4.5% (1-44 new cases per 1000 persons/year)

of the total world population.[44] However, estimates by Petti et al, indicate that the incidence rate of world traumatic dental injuries in 2018 was 2.82% (95 CI, 2.28%-3.42%) per 100 person-years. [48]

Maxillary central and lateral incisors are the teeth most involved in TDIs for both the permanent and primary dentitions. It is also reported that certain individuals are more at risk to sustain TDIs, and TDIs are also corelated to socioeconomic status, lifestyle, and behaviour patterns. [47, 49] Studies have shown that gender is a known risk factor for TDIs, with males being twice as prone to these as females. However, this disparity has been decreasing over time, as females are increasingly exposed to the same risk factors as males. [44, 45, 47, 49]

Certain age groups are more vulnerable to TDIs, even if no one is ever completely at zero risk.[44] Oral injuries are extremely common in young children and account for 17% of all body injuries in preschool children.[44-48, 50] Prevalence rates can reach at least one-third of preschool children, one-fourth of adolescents and one-third of adults with permanent teeth. [44, 47] Regarding the dentition type, the global prevalence rate of TDIs in the permanent dentition is 15.2% (95 CI, 13.0%-17.4%), and 22.7% (95 CI, 17.3%-28.7%) in the primary dentition. [48] Results from a study by Glendor et al. and Petti et al. showed that 18.4% of the population in USA aged 6-20 years has suffered from at least one TDI.[47, 48] One in five children in the UK have suffered from TDIs to their anterior permanent teeth.[48]

TDIs could be classified as a public health problem for four main reasons: (1) They occur frequently and comprise 5% of all bodily injuries; (2) They have a tendency to occur at a young age during growth and development; (3) Treating TDIs can have huge financial implications; and (4) Most TDIs are irreversible, and treatment is likely to continue over the course of a person's lifetime.[47]

2.1.2 Oral Disease

Untreated oral diseases (i.e., dental caries and periodontal disease) are present in 15-20% of adults and are also a major cause of tooth loss.[51] Oral diseases affect approximately 3.5 billion people globally, according to the Global Burden of Disease (GBD) Study 2019, with dental decay being the most frequent cause of tooth loss.[52, 53]

Dental caries is the term for decay of tooth structure caused by acid-forming bacteria. Untreated dental caries affect the permanent dentition of more than 2.4 billion people worldwide, as well as the deciduous dentition of about 520 million children.[1],[54] With a growing population attributed to longevity, the burden of caries has shifted from children to adults.[51],[54] According to the Centers for Disease Control and Prevention (CDC), in 2019 the prevalence of dental caries amongst American children aged 6-11 years was 17%, and in adolescents aged 12-19 years, 57% experienced caries in the permanent dentition. Regarding adults, the prevalence of caries reached 90% in ages 20-64 years and 96% in ages 65 or more years. [55] The number of cases of dental caries in permanent teeth has increased by 46.1% from 1990 to 2019, the reason for which was attributed to population growth.[56]

Periodontal disease is a bacterial infection that causes inflammation of the hard and soft tissues surrounding the teeth. Approximately 14% of the global adult population (over one billion cases worldwide) is believed to be affected by severe periodontal diseases.[1] The global prevalence and incidence rates have remained the same from 1990 to 2010, with the prevalence at 11.2% and incidence rate of 696 cases per 1000 000 person-years in 1990 to a prevalence of 10.8% and an incidence rate of 701 cases per 100 000 person-years in 2010. These diseases cause an increased economic burden, with the direct cost being estimated at US $356.80 billion worldwide. [54]

2.2 *Epidemiology of Tooth Loss*

2.2.1 Age: Adolescents, Adults and Older Adults

The influence of age on tooth loss deserves specific comments. For instance, a longitudinal analysis showed that the risk for tooth loss increases with age, with participants aged 55 years and above having more tooth loss than their younger counterparts. There was steep rise in tooth loss for adults around the age of 70 years. The risk was also higher for an individual who had a previous record of tooth loss.[41],[57] Although there has been a decrease in the prevalence of tooth loss globally, the incidence rate has not reduced for all age groups. The age-standardized prevalence of tooth loss in 2017 was 3.3% with 267 million prevalent cases.[58]

2.2.2 Geographic location

Bernabe et al. reported no between-gender difference for the global burden of oral diseases.[58] According to the GBD study (2010), dental caries in permanent teeth is the highest-ranking oral disease worldwide, with a prevalence of 35% of the global population. It is followed by severe periodontal disease with a prevalence of 11% and severe tooth loss with a prevalence of 2% of the population.[53, 59] According to a study by Kassebaum et al. (2014), the prevalence of severe tooth loss decreased from 4.4% to 2.4% on the global scale. The incidence rate of tooth loss showed a significant decrease by 45%- from 374 cases per 100,000 person-years to 205 cases per 100,000 person-years from 1990-2010. [60] In 2017, 267 million people globally still suffered from tooth loss.[58]

Tooth loss is also affected by geographic differences. The prevalence of tooth loss varied from country to country. The age-standardized prevalence was significantly higher in New Zealand, Turkey, Brazil, Iran, and Mexico than in Japan, Sweden, China, Sri Lanka and globally. The data analysed by Kassebaum et al. (2014) revealed an improvement in global oral health status in both developing and developed countries across the 21 GBD world regions. However, the

prevalence and incidence rates have not shown much improvement across South-Asia, Central Sub-Saharan Africa, Eastern Europe, and Southern Latin America.[60]

In Canada, oral diseases affected over 95% of adults in 2009. Approximately, $12.8 billion was spent for dental care. Around 20% of Canadians suffered from dental caries, while another 20% suffered from periodontal disease. [61, 62] Canadians have experienced significant decreases in levels of dental caries over the past 40 years. The percentage of adults with no natural teeth has decreased from 23.6% to 6.4%.[55] We were unable to find any published data on tooth loss in Canada, other than that of complete tooth loss.

2.2.3 Impact

Tooth loss is considered to be an indicator of oral health and function. Tooth loss has not only a negative functional impact, but that negative impact is also psychological, social, and financial. Unlike posterior tooth loss, loss of an anterior tooth has direct bearing on aesthetics, along with physical and psychosocial function. Functional impact includes impaired mastication and speech, with possible consequences like perceived chewing difficulties, weight loss, nutritional deficits, and poorer social life. This can have a negative effect on a person's emotions and confidence levels. [6, 63] In Canada, approximately 40 million hours per year were lost due to dental issues and their treatment. This represents nearly 3.5 hours per person lost either from school, work, or other activities. This loss was greater in people with higher incomes, with an estimate of over $230 million in losses. [55, 61]

Studies have confirmed that tooth loss has a direct impact on quality of life (QoL). [28, 64] Oral health related quality of life (OHRQoL), i.e. the component of health-related QoL that concerns how oral diseases and dental interventions affect patients,[65] is severely affected by a missing anterior tooth.[28] Measuring the impact of oral diseases and the effect of their treatment on OHRQoL has gained popularity over time, in both research and clinical practice. As described

previously, tooth loss causes impairment of function, aesthetics, and chewing, thus resulting in a reduced OHRQoL.

2.3 Restoration options for tooth loss

2.3.1 Removable Partial Dentures (RPDs)

RPDs are fabricated to replace missing teeth and are made to be inserted and removed by the patient, thus improving the mastication and phonetics along with enhancing the aesthetics of the facial appearance. They also help to prevent residual ridge loss and unwanted drifting of teeth. The most common reasons for choosing an RPD over other restorative options includes financial constraints, a long edentulous span contraindicating a fixed prosthesis, or to facilitate access to oral hygiene. [66-68] RPDs are also considered to the least invasive option for tooth restoration and is a less time-consuming procedure.[69]

Although RPDs are considered as an affordable option to replace a lost tooth, studies have shown that patients are not completely satisfied with them. The success rate of an RPD greatly depends on the patient's individuality and attitude.[70] The following disadvantages are associated with removable partial denture users:

I. Increased risk of dental caries and periodontal changes over fully dentate individuals. [67, 69, 71]

II. Mobility and loss of abutment teeth have been reported with long term use of RPDs due to gingivitis, periodontitis, and stress on teeth, primarily associated with attachment clasps. [67, 69, 71, 72]

III. Poor acceptance rate by patients due to insufficient aesthetics, comfort, and retention.[66, 67, 69, 73-75]

IV. Avoidance of certain food types due to eating difficulties, as occlusal stability can be an issue. [67, 73-75]

V. Discomfort and pain at times due to the denture plate impinging on the soft tissues. [67, 73]

VI. Failure to comply with proper denture cleaning routine, as patients find it tedious and messy. [66, 69, 72]

2.3.2 *Conventional fixed dental prosthesis (FDPs)*

FDPs, or tooth-supported bridges, are considered to be a better treatment option over RPDs for most cases of anterior tooth loss. FPDs help to maintain periodontal health and help the patient to have a better OHRQoL.[76, 77] Fixed prostheses are also considered a better option from an aesthetic point of view. Patient satisfaction rates with FDPs in the maxillary anterior aesthetic zone tend to improve after treatment with RPDs.[78]

A 5-year survival rate study by Le et al. did not reveal major differences in the survival rate of tooth supported FDP (93.5%) and implant supported FDPs (100%). [79] Failure of the veneer material, fracture of framework and caries were the most common reason for the failure of tooth supported FDPs. [80, 81] Another complication that arose was loss of retention or crown loosening, i.e., failures associated with the luting agent and/or geometry of prepared teeth. Also associated with FDPs were sensitivity and loss of tooth vitality in abutment teeth leading to endodontic problems, fracture of abutment teeth, and secondary caries.[81-84]

2.3.3 Implants

Contemporary implant treatment follows the principles of osseointegration and has been a restorative option for almost 50 years. Professor PI Branemark was the first to introduce osseointegrated implants in 1971; these are now widely considered to be the first choice of treatment due to their being minimally invasive for aesthetic regions like the anterior maxilla.[15, 85] Studies indicate that fixed implant supported prostheses have higher success and satisfaction rates than RPDs and FDPs.[73] Dental implants are screw-shaped devices placed directly into the alveolar bone; thus, the integrity and vitality of the adjacent teeth are not

harmed. The rate of marginal bone loss (a critical factor for long-term esthetics) was also low, with a mean of 0.56 mm after 1 year.[31] [85] Stein-Lausnitz et al. (2019) reported a 5-year implant survival rate of 94.8% and a 10-year rate of 89.8%. Those findings disagreed with previous studies by Pjetturrson et al. (2012) in which they reported a 5-year implant survival rate of 95.6% and a 10-year rate of 93.1%.[10, 76] However, another systematic review and meta-analysis by Howe et al. (2019) reported a 10-year implant survival rate to be 96.4% (95% CI 95.2%-97.5%). [30]

As potential disadvantages, there is a possibility of implant-specific technical and biological complications. Peri-implantitis and peri-mucositis are the most common biological complications associated with implant placement. A review by Lee et al. reported a prevalence rate of 9.3% for implant-based peri-implantitis and 19.8% for subject-based peri-implantitis. Implant-based peri-implantitis was calculated by dividing the number of implants affected by peri-implantitis by the total number of all implants whereas subject-based peri-implantitis prevalence was calculated by dividing the number of subjects having peri-implantitis affected implant/implants by the number of all subjects. The prevalence of implant-based peri-mucositis was 29.5% and for subject-based was 46.8%. [86] For technical complications, reports suggest a 7% complication rate with implants and 11% for the superstructures, the most common complications being screw loosening, crown loosening, and chipping of the crown material.[32, 85] Studies published by Vogel et al. and Losenicka et al. showed that single crown implant treatment is more cost-effective than a three-unit FDP. Despite a higher initial cost, dental implants are considered cost-effective over the long term. Patient satisfaction, acceptance, and willingness to pay were also reported to be higher.[87, 88]

Despite the limitations, implant treatment in the anterior maxillary region is considered a good treatment option with high success and survival rates. Patients tend to rate the aesthetics of implant-supported FDPs higher than tooth-supported FDPs.[89]

2.4 Treatment planning aspects of implants

2.4.1 Treatment planning

To achieve successful outcomes from implant treatment, it is important to consistently meet patient expectations; hence, meticulous attention to details must be noted and addressed during treatment planning. Proper patient selection depends on several factors related to clinical and medical health status. It is imperative to obtain a thorough health history for patients, as there are a few absolute and relative contraindications for implant placement, including local and systemic factors. Some medical conditions, including active treatment for malignancy and intravenous bisphosphonates, are absolute contraindications.[90] Other factors may also impact implant survival and patient suitability for surgical implant placement.[91] A history of periodontitis as a cause for tooth loss is of great concern, given the increased risk for peri-implantitis. Studies have shown that use of alcohol and tobacco products affect osseointegration and increases the risk of implant failure.[92, 93] Several systemic conditions like diabetes, heart disease, and osteoporosis can also create complications for the implant surgery, thus leading to a stricter treatment protocol.[92-94]

Radiographic examination (and further imaging methods in selected cases) should be considered after a thorough clinical examination of the local implant site. It is important to thoroughly evaluate the implant site for its bony architecture, soft tissue anatomy and health of the site.[91] For anterior maxillary sites with high visibility, there is very little leeway for aesthetic compromise. The clinician must harmoniously integrate the restoration into the existing anterior teeth, thus ensuring an optimal esthetic outcome.[95] A diagnostic wax-up is recommended for the anterior region to provide information of pre- and post-treatment soft tissue architecture and crown ratios.[96]

In the anterior maxillary zone, the aesthetic success of an implant treatment is as important as the implant survival rate. Multiple factors contribute to this success rate. They include the

condition of the hard (bone) and soft tissues (peri-implant mucosa), implant loading time, and type of implant, as well as provisional and final restorations. It also includes aesthetic perception, techniques for tissue augmentation, and the aesthetics of final implant-supported restorations.

2.4.2 Factors influencing aesthetics during the implant treatment process

2.4.2.1 Bone

The long-term aesthetics with implants in the anterior maxillary region is strongly influenced by the thickness of the buccal bone. When the initial bone volume is insufficient, a portion of the buccal bone could gradually diminish due to over-loading resorption over time, and this increases the risk of soft tissue recession. Hence, the buccal bone morphology around an implant is a primary factor in reducing peri-implant resorption. [97]

In general, buccal bone thickness (BBT) is thinner in the anterior maxillary region than in the posterior region. It is also directly affected by the extraction technique, which affects remodelling of the buccal bone. Alveolar ridge preservation (ARP) after tooth extraction or contour augmentation at the time of early implant placement can mitigate the resorption process. [98] Implant survival and success rates are also proportional to the quality of the available bone at the implant site. [99, 100] According to a report by Oliveira et al., the most frequent bone quality in the anterior maxillary region was Lekholm and Zarb type III (73.3%; thin cortical bone surrounding a dense medullary bone), followed by type II bone quality (20%; cortical bone with marrow cavity) and type IV bone quality (6.7%; very thin cortex and low-density trabeculae). [101] The bone around the implant structure must withstand occlusal stress and strain since implants placed in bone with poor quality might fail more easily.[102]

The direct anchorage of implants to bone also may raise some biomechanical issues. In natural teeth, the periodontal ligament allows the tooth to move and distributes occlusal forces, thus

minimizing stress accumulation. However, dental implants are fixed in bone and, thus, forces are transmitted directly to the bone. This leads to a potential concentration of stress that, in turn, may foster bone resorption. Hence, dental implant type and design must be selected according to the bone quality and quantity for optimal stress distribution and bone preservation.[103, 104]

Alveolar ridge resorption results in reduction of the height and width of the bone, which may cause major functional and aesthetic challenges. Besides choosing different implant types, better clinical outcomes may be attained by bone augmentation procedures. Implants placed in augmented alveolar ridges have a high success rate, similar to that of an implant placed in non-deficient native bone.[105] Guided tissue regeneration along with collagen tissue matrix derivate can provide excellent results, especially in the aesthetic zone.[106] Grafting is usually important for deficient bone structure, with autogenous grafts being considered as the most effective and reliable graft type. Autogenous bone grafts are notoriously osteogenic and osteoconductive. Alternatives include allografts (or synthetic bone grafts), which have shown little to no difference than autogenous grafts, although the latter might aid in the healing process.[107]

2.4.2.2 Peri-implant mucosa

The peri-implant soft tissue anatomy depends on multiple factors for adequate esthetics. Important anatomic factors include the presence of keratinized mucosa and gingival biotype, as well as connective tissue attachment to adjacent teeth and their gingival margins. This can be assessed through radiographs and periodontal probing.[91, 108] A thin biotype and lack of keratinized mucosa are known risk factor for poor aesthetics with dental implants. Both increase the risk of exposure of the implant, which directly affects the aesthetics. [91]

An aesthetic implant restoration should appear to emerge from the surrounding tissue like a natural tooth. The interface between the restoration and the soft tissue also must look natural.

The emergence profile of the implant restoration should always match the emergence profile of the contralateral tooth, providing a natural-looking appearance.

The provision of a natural look for peri-implant mucosa stresses on the combination of adequate surgical and prosthetic planning for operatory procedures. The clinician must be able to visualize each stage prior to treatment as this will facilitate the adaptation of the consecutive stages.[109, 110] It is important to understand the different zones (subgingival contour) of emergence profile (esthetic zone, bounded zone and crestal zone) and their relation to implant design and position, as well as thickness of the soft tissue. Emergence profile design helps provide a favourable biological response to dental implants.[111] An optimal emergence profile supports the soft tissue surrounding the implant restoration and prevents food from being trapped. [79]

It is no understatement to say that that esthetics with implants in the anterior region is strongly dependent on the architecture of the peri-implant mucosa. This leads to the recommendation to analyze the patient's smile based not only on the teeth or white component (tooth position, shape, and angulation of the crown in the arch), but also on the pink component (peri-implant mucosa and its relationship with the gingival margins of the neighboring teeth). The embrasure spaces around the teeth comprise a third and final component to analyze; this is called 'black esthetics'.[91]

Different types of dental implants have been designed to promote adequate peri-implant architecture and thus optimal esthetics, as detailed subsequently.

2.5 Types of dental implants

2.5.1 Endosteal implants

An endosteal implant is an alloplastic material surgically inserted into the residual bone ridge to serve primarily as a prosthodontic foundation. They are the most common and safest type of

implant used when compared to subperiosteal and zygomatic implants. The two main primary categories of endosteal implants are plate-form implants and root-form implants.[112] Plate-form implants have a flat and narrow buccolingual/labiolingual dimension and uses the horizontal dimension of the bone. Root-form implants are placed in the vertical column of bone.

Almost all implants used nowadays for small prosthetic reconstructions fall into the root-form category. They are made of biocompatible materials and can be smooth or threaded, perforated, solid or vented; they can also be coated or textured. Root-form implants can be further described by surface characteristics, interface designs, means of insertion, and surgical requirements. They have also been further categorized into 3 types based on the implant design:

a. Cylinder root-form implant – They are tapped or pushed into a prepared bone site and rely on microscopic retention and/or bonding to the bone.
b. Screw root-form implant – They are threaded into a bone site and have macroscopic retentive elements. Today, this is the most used shape of a single-rooted tooth design.
c. Combination root-form implant – It has the features of both the cylinder and screw root form implant.[113]

Unless clearly stated, any discussion in the following sections will refer to the screw root-form implants.

2.5.2 Implant design

Implants are broadly classified further into macro or micro design. Macro design includes the thread design and body shape. Micro design consists of implant material and surface morphology.[102, 103, 114] Dental implants are designed to attain primary mechanical stability in the bone and to stimulate a strong bone-implant interface over time through osseointegration

(i.e., secondary stability). The implant design affects the long-term biomechanical properties at the interface and is responsible for the success or failure of the implant. [112] Design should also maximize favourable stress distribution and to minimize undesirable stresses/strain as bone tissue heals. An ideal design will distribute stress evenly throughout the surrounding bone and encourage bone development and aid in implant stability. [112, 114] Despite the high success rates of osseointegrated implants, mechanical and biological problems such as loosening of abutment screws, micro gaps and bacterial microleakage are still possible. [11, 32]

2.5.2.1 Thread design

Thread shapes in dental implants are employed to achieve maximal preliminary contact with bone and improve the initial stability after loading. It also aids in force transmission and absorption of interfacial stress. The four kinds of threads are V-form, buttress, reverse buttress, and square. Maximum stress has been observed at the cortical bone, compared to the cancellous bone.[102, 103] Through finite element analysis, a minimum Von Mises stress concentration was observed for tapered implant bodies with a reverse buttress thread design under an axial load of 100N, which signifies bone preservation.[102]

2.5.2.2 Screw connection

Implant-abutment connections can be broadly divided into 2 types, i.e., external connection and internal connection, depending on whether the geometric characteristic is present above or below the coronal surface of the implant. This geometry affects the interaction between the implant and bone, distribution of occlusal forces through bone itself and stability of the implant. The external hexagon connection is designed to provide a rotational torque-transferring mechanism for the implant. However, it allows the formation of a micro-gap in the implant-abutment interface which will ultimately cause peri-implant mucosal inflammation and affect

implant stability.[115] The internal hexagonal connection was developed to increase the implant-abutment contact and promote a more uniform force dissipation. Thus, internal connections demonstrate maintenance of the crestal bone level.[116]

As suggested above, crestal bone resorption is strongly linked to the type of implant-abutment connection. The crestal bone surrounding the implant undergoes continuous remodelling after implant and prothesis placement. With external connection implants, vertical crestal bone loss can reach 1.5-2 mm below the implant-abutment junction (IAJ) after one year of loading. This can be aggravated by occlusal overload and peri-implantitis,[117] as well as by the presence of a micro gap and microleakage between implant and the abutment. That microbial leakage is known as microleakage of the implant-abutment interface (IAI), a term coined in the 1990s, and is attributed to a micro-gap or micromotion.[118] The bacterial leakage allows bacterial colonization of the implant sulcus, causing inflammation close to the crestal bone with subsequent bone loss. [117, 119] In an effort to prevent or reduce marginal bone loss, modifications have been made to the implant-abutment connections.[119] However, only the platform-switching concept and conical connection will be elaborated on further in this review. According to Lazzara et al., platform switching is a method used to preserve crestal bone present on top of wide-diameter implants and alters the initial point from which crestal bone remodelling begins.[120] The platform switching concept is based on using an abutment of a smaller diameter than the implant neck. This connection shifts the implant-abutment junction's perimeter inward, closer to the central axis/center of the implant. This potentially enhances the force distribution and places the implant-abutment gap away from the peri-implant bone.[117, 120, 121] There is minimal marginal resorption (less than 0.8mm) after 8 months follow-up; moreover, platform switching results in highly satisfactory aesthetic results in the anterior zone. [117, 122]

The inward shift of the implant-abutment gap can physically reduce the impact of the inflammatory cell infiltrate in the peri-implant tissues.[121] This inward shift of the implant-abutment gap helps to bring microleakage (and thus, the presence of bacteria) more internally and, therefore, away from the bone crest, limiting bone resorption.[117, 123] According to a study by Enkling et al., with platform switching, the micro-gap is located more distant to the first point of bone-implant contact and creates a circular horizontal step, which might be seen as an extension of the biological width.[124] Platform switching increases the exposed horizontal area of the implant surface and allows more space for the connective component (epithelial attachment) of biologic width to be attached. [125] The formation of a more stable connective sleeve with platform switching also helps to form a mucosal seal. [117]

Multiple studies have reported on the biomechanical advantages of using platform switched implants over conventional implants. For platform-switched connections, stress tends to concentrate at the center of the implant, whereas conventional implants concentrate stress at the lateral surface and implant neck areas. In other words, stress concentration shifts itself away from the bone-implant interface towards the long axis of the implant. Moreover, shear forces on the cortical bone are lower with platform-switching than conventional implants. [117, 126]

Due to reduced microleakage, a conical connection is considered superior to a non-conical connection. It also results in reduced loading of the implant-abutment interface due to stress transfer along the two conical constructions.[127] A study by Fugl et al. reported mean bone gain after the expected initial loss of 0.11 ± 1.05 mm between 6 and 12 months with a tapered conical connection. They also reported improvement in soft tissue outcomes, along with high patient satisfaction of the esthetics. Conical connections show rapid stabilization of bone remodelling and papilla regeneration following tissue healing. [128]

The most frequently used type of conical connection is the Morse taper. It was developed by Stephen Morse for engineering applications in 1864 and adapted to health devices over time.

The unique feature of the Morse taper implant-abutment connection is the internal joint design between two conical structures.[129] The integrity between the abutment and implant is ensured even with the smallest micromovements detected at a narrow (2° to 4°, depending on the materials) inclination angle of implant crown. This significantly helps reduce loosening of the implant crown.[127] The internal Morse-taper implant abutment interface decreases the microgap size and places it away from the marginal bone.[127] Lower levels of bacteria accumulation and penetration occurs due to the higher contact area between implant and biconical abutment surface. This reduces biofilm accumulation, peri-implantitis and crestal bone loss.[129] When compared to external and internal connection implants, Morse taper connection implants show lower levels of microleakage, which is inversely proportional to the used torque.[129-131] It also eliminates the need of additional screw retained connections that are necessary with other implant-abutment designs.[129, 132]

Multiple studies evaluating different implant designs showed that internal conical connection implants were more effective in reducing stress at the bone-implant level.[133, 134] Pellizzer et al. evaluated the stress distribution with different implant systems through photoelasticity. Morse taper implants showed a favourable stress distribution and presented the lowest stress concentration at the cervical third, whereas external hexagon implants showed the highest stress concentration. This reduction in stress is important for reduced marginal bone loss by minimizing the chances of saucerization.[133] The threaded v-format shape of Morse taper implants transmits the axial loads through a combined force of compression, tension, and shear. Hence, the tensional stress is better distributed.[113]

However, even Morse taper implant systems cannot completely prevent microbial leakage and bacterial accumulation. In a study that evaluated bacterial leakage along two different conical implant-abutment connections (Bicon/tapped-in vs Ankylos/screwed-in) found no difference

in bacterial growth inside both assemblies 48 hours following incubation; furthermore the level of bacterial leakage was low at the micro gap region.[135]

2.5.3 Surface treatments

Contemporary implants usually undergo some surface treatment to enhance the osseointegration process, including topographic modifications and coatings with different materials. The microtopography of the implant surface can be modified by acid-etching, sandblasting, anodization, and different coating procedures. This increases the roughness of the surface that can influence osseointegration by improving cell adhesion.[136] The surface changes in topography alter the growth, metabolism and migration of cytokine and osteogenic cells.[137] Implants with acid-etched surfaces can achieve significantly greater bone-implant contact, especially in poor bone quality sites. Sandblasted implant surfaces have been found to increase peri-implant bone formation by increasing osteoblastic activity.[138, 139]

2.6 Biomechanical considerations

2.6.1 Osseointegration

The concept of osteointegration was introduced by the Swedish orthopaedic surgeon, PI Branemark, in 1969. He defined it as "a direct connection between living bone and a load-carrying endosseous implant at the light microscopic level." He discovered that bone formation occurs around titanium, and a successful union of the bone with titanium is possible without rejection. [140] The introduction of the concept of osseointegration for dental implant treatment was a major discovery for oral restorations. The mechanical contact of an implant with the surrounding bone determines the primary stability. The degree of new bone formation at the implant-bone junction determines the secondary stability of a dental implant. Bone density, implant material, surgical technique, and implant shape all affect primary stability which, in

turn, determines the secondary stability. Around 60%-70% of the implant surface is covered by bone at the end of the remodelling phase and is used to measure the degree of osseointegration.[137, 138, 141]

Traditionally, measurements of primary stability were tensional tests and removal torque tests, both of which are highly invasive and not clinically applicable. The newer non-invasive techniques are reverse torque analysis, Periotest (PT), and resonance frequency analysis (RFA). It is important to measure primary stability of the implant to determine when to load the implant.[141] Immediate implant placement, as opposed to the 2 stage conventional surgical approach, is now recommended; this reduces the healing time period, lowers alveolar bone resorption and helps to achieve optimal aesthetic results.[142] [143, 144]

Immediate provisionalization involves the prosthesis being attached to the implants on the same day that the implants are placed, as opposed to conventional loading in which the prosthesis is attached in a second procedure after a healing period of 3-6 months.[145] Studies on immediate placement and provisionalisation of single-tooth implants revealed high survival rates of implants and implant crowns with a treatment survival rate of 98%. Furthermore, there was a mean peri-implant marginal bone gain of 0.5mm.[144, 146] However, a review by Block et al. showed no difference in crestal bone response to immediate or delayed implant loading.[147]

The preferred insertion torque also determines implant stability, with minimum torque values of 32, 35 or 40 Ncm being recommended for immediate loading. [138] According to Neugebauer et al., insertion torque above 50 Ncm is considered high and should not be exceeded, whereas a torque of 35 Ncm is considered optimum for immediate loading. As compared to unloaded implants, immediately loaded implants showed a higher level of bone formation and remodelling after 4 months of observation. [148]

2.6.2 Occlusal forces

One of the main factors contributing to dental implant failure is implant overloading. The risk for overload varies widely amongst different individuals due to broad variations in bite forces. Occlusal forces are of high load magnitude and can range from 100 to 2400 N for people with natural dentition. The force exerted in the molar region is higher than that in the incisor region. When masticatory force is applied to a prosthesis, the crown is affected before the bone-implant interface. Factors like magnitude of occlusal force, type of prosthesis, implant-prosthesis connection and surrounding bone influence the loading forces on implants. Most of the stress is found at the crestal region, as opposed to the apical part.[149]

The maximum occlusal force for a complete denture wearer ranges from 5 -50 lb. People with implant-supported fixed prostheses can increase their maximum bite force by 85% within 2 months of implant treatment; it may further increase by more than 300% after 3 years. As a result, an implant prosthesis wearer may exhibit a force similar to a person with a tooth supported fixed restoration.[150]

Forces can be categorised as compressive, tensile and shear. Compressive forces are best accommodated by implant-supported prostheses. Anterior implants are more at risk for complications, as the bone and screws are weaker under tensile forces. Tensile forces tend to pull the implant body apart. The implant body has a high tendency to slide if shear force is applied and is considered to be the most unfavourable force, as it can cause damage to implants and the surrounding bone. [113, 149]

2.7 Patient reported outcomes (PROs)

2.7.1 Definition

Traditionally, the successful outcome of dental implant treatment has been determined based on clinical parameters, such as implant survival, complications, and bone loss. In addition, economic success has been determined by the cost-effectiveness of the implants and prostheses. [30, 151-154] However, patient-reported evaluations of implant treatment are another major determinant of treatment success.[155] There has been a recent shift amongst practitioners and researchers to incorporate patient perceptions and preferences into the decision-making process. Patient perception of a treatment in the medical or dental field is now considered as the centre point of a healthcare system. This indicates a paradigm shift from physician-centred care to patient-centred care. It enables the patients to provide effective feedback on the quality and impact of the treatment provided.[156]

The tools used to measure and assess PROs are known as patient-reported outcome measures (PROMs) and are used to understand how aspects of an individual's health and disease has an impact on treatment and QoL. [157] At the 8th European Federation of Periodontology Consensus Conference, PROMs for implant dentistry were proposed with the goal of focussing on patients' viewpoints and evaluating OHRQoL.[158]

In oral health, PROMs are mostly quantified by self-completed questionnaires with different types of questions and different scoring systems like Visual Analog Scale (VAS), Likert, etc. [158] [159]. Assessment can also be qualitative in the form of interviews. The main goal of PROs is to complement clinician reported treatment outcomes in oral health research. [160]

PROM questionnaires can be categorized as generic or specific to a condition. The generic ones can be utilized to measure health concepts that are of importance to a wide range of patient groups and general populations; they can be used to make comparisons across different health conditions, as well as with healthy population. However, these generic instruments might

include questions/items that are of no relevance to many patients or group of patients. Disease-specific questionnaires are designed to measure only certain elements of health relevant to a particular group; thus, they cannot be used to make comparisons across other health conditions. Outcome measures can be derived depending on the development and scoring manner. They can be unidimensional (targeting one characteristic to yield a single overall score) or multidimensional (targeting a group of characteristics to provide a profile of scores).[158, 159]

2.7.2 Importance of PROs

PROs are considered as endpoints that add value to the interpretation of a clinical trial or study. They are developed in co-ordination with clinicians, patients, and health experts to ensure that they are relevant to patients and clinically important. These measurement tools provide unique and significant information on the impact of a medical/dental condition and its treatment from a patient's point of view. The use of PROMs in clinical trials has increased from 14% to 27% from 2004-2007 to 2007-2013. This has been attributed to the fact that the patient's experience can enrich the understanding of certain domains that are difficult to observe (e.g., pain).[161] They enable understanding the relative standards of a dental treatment along with associated experiences, which paves the way for holistic approaches to care.

Fleming et al. studied the importance of PROs in dental research through a literature review. They showed that, out of 220 RCTs, quality of life and functional measures were rarely considered as primary outcomes. Forty-four percent (44%) of the studies focused on clinician-based reports, 34% were patient-centred and 22% focussed on both aspects. This highlights the emphasis previously placed on technical and clinician-centered outcomes. There is a growing acceptance that research outcomes should be significant and beneficial to the patients.[162] Traditionally, survival outcomes of different diseases demonstrated the benefits of treatment. This is likely valid for acute disease. However, with PROs, the patient's perspective provides

a more extensive and multidisciplinary assessment of the benefits of the treatment and care, particularly for prosthetic approaches.

PROMs as measuring tools should be both reliable and valid. The questionnaires can include tools that measure health related QoL, health and functional status, personal experience of treatment and care, disease, and symptom burden. Therefore, PROMs are distinctive indicators of the impact of a disease on patients and can be utilized to empower patients and determine the efficacy of treatment. It also helps create a rapport between patients, clinicians, and health providers. [163-165] Feine et al recommended that PROMs data collection should be gathered at baseline and at designated post-treatment points. The choice of PROMS should be selected according to a validated study questionnaire as they differ according to which and how an aspect of the oral health experience will be measured. It is also important to assess patient perception of QoL and satisfaction at baseline.[166, 167] Patients have certain expectations for their treatment outcomes, and it is important to understand and measure their expectations prior to treatment to achieve successful PROs.[167]

2.7.2.1 Quality of life (QoL)

With the change of the definition of health by WHO, the concept of health related QoL was introduced. This reflects the subjective perception of health and includes everything that contributes to and affects a person's general well-being. With treatment outcomes targeting a multidimensional approach, QoL has gained importance in recent decades. PROs help determine QoL especially in patients with chronic diseases. QoL plays an important role is such cases in which survival from the disease is not the ultimate goal. It is affected by three major dimensions- physical, mental, and social well-being and, thus, has a broad scope. [168]

QOL that focuses on oral health is known as oral health related quality of life (OHRQoL) in which functional, social, and psychological impacts on oral health and disease are measured. It was introduced in 1994 by Slade and Spencer[169] and is now constructed into 4 dimensions:

oral function, orofacial pain, orofacial appearance and psychological impact. One or more of these four OHRQoL dimensions can effectively reflect the impact that any oral disease has on a patient.[170, 171] OHRQoL is directly related to the number of missing teeth, as tooth loss has a negative impact on a patient's life. A systematic review to assess OHRQoL with implant supported prostheses showed that OHRQoL improved significantly following implant treatment in patients with missing anterior teeth.[172-174]

2.7.2.2 Patient satisfaction and aesthetics

According to the ITI consensus report on patient-reported outcome measures associated with dental implants, general aesthetics (100-mm VAS: 90 mm) and mucosal aesthetics (VAS: 87 mm) of implant supported FDPs were highly rated by patients. It was also found that high patient satisfaction with aesthetics can be achieved for implant-supported FDPs.[166] Satisfaction with implant treatment has been reported in multiple studies, and more than 90% of patients are highly satisfied over a 10-year time frame. However, according to some literature, patients might have unrealistic expectations of implant treatment that may affect their satisfaction with the final treatment outcomes. This could be attributed to lack of reliable information and perceived novelty of implant treatment, along with the high cost of this therapy. [167] Patient satisfaction is an important aspect of patient reported outcome, as it allows a direct assessment of patients' views of different aspects of the given treatment. [170]

Patient expectations for anterior aesthetic restorations are high and, therefore, clinically challenging. More than functionality, aesthetics determines the success of an anterior tooth treatment.[175] Arunyanak et al. carried out a review, and they found that patient satisfaction ratings were significantly higher than ratings of their clinicians. Most of the studies in this review used VAS response outcomes with a range of measurement from 0-mm (indicating extreme dissatisfaction) to 100-mm (indicating complete satisfaction). [176]

2.7.3 Scope for future improvements

With PROs gaining importance in determining the success rate of a treatment, there are some challenges that must be addressed for future optimization. Mercieca-Bebber et al. reviewed 75 trial protocols for PRO specific content submitted to the United Kingdom's National Institute for Health Research (NIHR) Health Technology Assessment program in 2012-2013; they found that routine inclusion of PRO information in trial protocols was around 33%, and more than half (61%) of the included PRO items were incomplete.[177] Thus, trial protocols were often incomplete without clearly defined endpoints. It is also important to provide clear and extensive PRO study content as this ensures whether the chosen PRO measures, and time points for measurements are appropriate and provide valid and meaningful data. It is imperative to include a PRO measure early on during the study design phase. Individual questions within PRO measures should be appropriate to the study question, and it is imperative to consider how all the items combine into one summary scale. PRO measures should also be gauged for their reliability and validity.[159, 161] There is a need to develop a concise and pragmatic index to assess the aesthetic outcomes for single-tooth implant restorations in the aesthetic zone.[176]

3. OBJECTIVE

The main objective of this study was to assess the secondary outcome of patient perceptions of mucosal inflammation (redness, bleeding, and pain) and appearance with three different designs of implants placed in the upper anterior and premolar region.

The primary objective of the main study was the clinical assessment of peri-implant mucosa in these three implant abutment interface designs and the results have already been published. [33-35, 37-40]

4. METHODS AND RESULTS:

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Can patients detect peri-implant mucosal inflammation? Results from a multicentre randomized trial.

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ABSTRACT

Purpose: The objective of this study was to compare patient reported outcomes (PROs) of peri-implant soft tissue inflammation and aesthetics around single-tooth implants in the anterior maxillary region with three different implant-abutment interface designs.

Methods: Participants were randomized to one of three different types of implant-abutment interface designs [Conical (CI), flat-to-flat (FI), and Platform Switched (PS)]. Implants and provisional crowns with prefabricated titanium abutments were placed 5 months following extraction and/or ridge augmentation. Permanent ceramic crowns with zirconia abutments were placed after 12 weeks. To assess PROs, patient appearance questionnaires were completed from provisional crown placement to the 3-year follow-up.

Results: Tooth appearance at the 3-year follow-up revealed a difference amongst CI, FI and PS implants ($p=0.049$; Kruskal-Wallis test). PS was rated better than FI ($p=0.047$) at 1 year for appearance of soft-tissue and satisfaction with colour. There were no differences for self-consciousness, smile and pain/discomfort while eating/hard food items.

Conclusions: Participants rated the platform switch and conical implants as more aesthetic than the flat-to-flat system. However, self-reported peri-implant inflammation ratings were inconsistent and similar for the three groups. Results indicate that patients are unable to detect mucosal inflammation and should receive routine follow-up visits, even if their mucosa appears healthy to them.

Keywords: implant-abutment interface, esthetics, patient-reported outcomes, peri-implant mucosa

I. INTRODUCTION

Tooth loss due to trauma, dental caries or congenitally missing teeth is often a major concern for most patients [1] and is responsible for causing 7.6 million disability-adjusted-life-years [2]. Even with improvements in dental care access and a decreased prevalence of tooth loss in recent years, the rate of anterior tooth loss in adults in Western countries is still 25% [3]. With anterior tooth loss, patients have reported that the loss of aesthetics has the greatest impact on their lives, followed by loss of function and phonetics, which has a direct impact on the oral health-related quality of life (OHRQoL) [4].

Treatment options for anterior tooth loss include removable partial dentures (RPDs), fixed dental prostheses (FDPs) or implant-supported fixed dental prostheses. When compared with RPDs and FDPs, implant treatment with fixed dental prostheses is considered to be the most viable treatment option with high survival rates [5, 6]. Success criteria for implants are based on implant stability and osseointegration, along with preservation of the hard and soft tissues around the implant. Over recent decades, more importance has been given to maximizing implant success based on patient-reported outcomes (PROs), rather than determining success using only clinical and/or laboratory assessments, especially in the aesthetic zone [7] [8].

In implant systems, the stability of the mucosal tissue relies on the connection between the implant body and the abutment, which is called the "implant-abutment interface". Many systematic reviews have shown that different implant-abutment designs are associated with a decrease in peri-implant marginal bone loss [8, 9]. Any implant design that allows micromotion and microbial leakage will lead to accumulation of bacteria, followed by inflammation and crestal bone loss [10, 11].

Investigations have suggested that implants with connections that allow micromotion (e.g., flat-to-flat interface design) will be associated with more crestal bone loss [12]. Other studies have

shown that there is less bone loss with conical implant connections due to absence of reactive bone loss [13] and less microleakage [14]. Current studies suggest that placing an abutment one size smaller than the implant platform; this is known as platform switching (PS). This approach has been reported to reduce crestal resorption, thereby diminishing any potential inflammatory impact [15, 16]. Because of the importance of aesthetics in anterior tooth replacement, it is important to understand patients' perceptions of their mucosal health surrounding different types of implant abutment-interface designs [17].

Patient reported outcomes (PROs) are defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else" [18]. PROs provide information about the patient's perception of a treatment; furthermore, as with all interventions that have an impact on an individual's life, it is vital to know how that intervention affects his/her satisfaction and quality of life. When measuring and evaluating treatment outcomes, it is increasingly acknowledged that the implications on oral health-related quality of life should be considered. Literature also suggests that clinical measures only are not adequate to describe treatment outcomes and that patients with chronic diseases have a profound ability to perceive and accurately rate their quality of life [19].

If peri-implant soft tissue responses to different implant designs vary, then clinical and patient appreciation of the aesthetic outcomes may also vary. Many studies have been conducted to measure the clinical success rate following implant placement in the anterior region regarding clinical outcomes, such as peri-implant bone tissue response, complications, and implant survival. However, there is a scarcity of studies in which the PROs for the health and aesthetics of the soft tissue architecture are measured. Therefore, in this study we assessed patient perceptions of their mucosa surrounding three different designs of implants placed in the upper anterior and premolar region.

II. METHODS

This clinical study was designed as an open, randomized, multi-centre, superiority study with three centres in the USA - Chapel Hill, Iowa, Houston, as well as one in Montreal, Canada. This report describes the analysis of a secondary outcome (patient perceptions of gingival health), whereas the primary outcome was to compare clinically measured buccal soft tissue changes (at the mid-buccal gingival zenith) around 3 different implant designs. Our group has previously published findings from the primary and other secondary analyses, in which soft tissue responses, bone tissue responses, implant stability and implant success were assessed (Appendix Table 1;[7, 17, 20-24]. The clinical study protocol, participant information and informed consent were approved by the four Institutional Review Boards (IRB) overseeing each centre before participants were enrolled. The study was registered on 12 January 2009 at ClinicalTrials.gov (trial ID: NCT00820235). All participants signed an informed consent form as a requirement for inclusion in this RCT.

Adults requiring one or more single tooth replacements in the anterior maxillary region between the upper left and right first premolars were recruited. During visit 1, potential participants were screened and enrolled in one of the four study centres if they fulfilled the inclusion and exclusion criteria (Appendix Table 2).

1. Clinical Procedures

Each alveolar ridge was assessed for implant placement and extraction sites; deficient alveolar ridges were augmented using recombinant human bone morphogenetic protein 2 (rhBMP2, Infuse, Medtronic) with or without mineralized bone allograft as indicated by the clinical situation and at the clinician's discretion. These procedures were performed to ensure an ideal ridge form with a minimum width of 5.5 mm for implant placement and to control any variables for the extraction site. After 5 months of healing, the participants were randomized to receive

any one of the three implants with the following implant-abutment interfaces: conical interface [CI], OsseoSpeed, Dentsply Implants; flat-to-flat interface [FI], NobelSpeedy Replace, Nobel Biocare; or platform switch interface [PS], NanoTite Certain Prevail, Biomet 3i).

During visit 2, all implants were placed using a flapless/tissue punch technique to ensure minimal mucosal damage. The implant abutment interface was placed 3mm apical to the gingival zenith. Primary implant stability was determined by the lack of lateral or axial implant movement when torqued according to the manufacturer's suggestions. The implants were immediately provisionalized utilizing Titanium abutments (CI = Direct Abutment, Dentsply Implants; FI = Snappy Abutment, Nobel Biocare; PS = GingiHue Abutment, Biomet 3i).

Provisional crowns were fabricated using bis-acryl composite resin made from a putty matrix and were relined and refined to fit the prefabricated abutment margins. Provisional crowns were either cement or screw retained and were free of any centric or eccentric occlusal contacts. Participants were clinically evaluated at 1 (visit 3) and 4 weeks (visit 4) post implant placement. Eight weeks after implant placement and healing (visit 5), provisional restorations were removed, and implant stability was assessed by the absence of pain or mobility when connecting the implant-level impression coping to the implant. A final elastomeric impression and shade selection was performed and sent to a central dental laboratory for the fabrication of computer-aided design/computer-assisted manufacture of (CAD/CAM) zirconia abutments (Atlantis, Dentsply Implants) and a lithium disilicate crowns (IPS e-max, Ivoclar Vivadent). The final crowns were cemented four weeks later (visit 6) using Rely X resin cement (3M ESPE). Clinical, radiographic and photographic evaluations were performed on the restorations at 6-months, 12-months, 36-months, 48-months and 60-months (Fig. 1).

2. Patient-Reported Outcomes (VAS)

At 1 (visit 4), 3 (visit 6), 6 (visit 7), 12 (visit 8), 24 (visit 9) and 36 (visit 10) months following implant placement, patient-reported outcome (PRO) data were gathered. (Fig.2) Visit 4 and 6

represent provisional crowns and visit 7, 8, 9 and 10 represent permanent crowns. The patients were blinded to the type of implant used.

PRO data collection at these specified visits involved a satisfaction questionnaire on mucosal appearance (Fig.3). This self-completed questionnaire includes nine questions concerning aesthetics, comfort, function, and psychosocial impact. A reliability assessment of the questionnaire was carried out at McGill University prior to the start of the study. Each of the nine questions were answered on 100 mm Visual Analog Scales (VAS), with most anchor words representing *never* (0) and *always* (100%; Fig 3). Participants were guided on how to respond to these scales through verbal instructions and a practice questionnaire exercise at the first session.

3. Randomization

Participant allocation to different groups followed a list of computer-generated random codes (simple randomization, rate: 1:1:1), stratified by study center. The sponsor generated the codes, which were stored in sealed opaque envelopes. Each envelope was assigned to a single participant and was opened immediately before implant placement (visit 2).

4. Sample size

The sample size calculation was based on the primary outcome of the RCT (i.e., soft tissue changes for mid-buccal gingival zeniths), as described previously. Calculations for the primary outcome considered a minimally important difference of 0.5 mm to be detected between groups and a standard deviation of 0.7 mm. This led to the recruitment of 48 participants per group in all study centres. With a drop-out rate of 15% (n=41/group), this trial would detect a 0.5-mm difference with a power close to 90% and significance level = 5% [7, 17, 20-24]. The current number of participants (at least 43 per group) for this secondary outcome enables the detection of a between-group difference of 10 mm on the 100 mm VAS, with a standard deviation of 16 mm, a significance (alpha) of 0.05 and power of 80%.

5. Statistical Analysis

Descriptive data for the ten satisfaction questions are reported separately as means (values in mm) and standard deviations (±SD). Groups were compared within each time point by the Kruskal-Wallis test, with the level of significance (α) set at 5%. In case of significant differences, post-hoc comparisons were performed by applying the Mann-Whitney test corrected by the Bonferroni method. Analyses were performed with SPSS (IBM Corp., Armonk, NY, USA) and Excel (Microsoft, Redmond, WA, USA).

III. RESULTS

1. Study Participants

One hundred seventy-one participants in the four centres were recruited during visit 1. Of these, 30 participants were excluded before randomization. One hundred fifty-six implants (CI=53, FI=53, PS=50) were placed. Per protocol, only one implant per participant was to be randomized and hence, 141 participants were randomized into one of the three different types of implant-abutment interface designs; 1. ***Group A***- OsseoSpeed (Conical interface design) n=48; 2**. Group B**- Nobel Speedy Replace (flat-to-flat interface design) n=49; and 3**. Group C**- NanoTite Certain Prevail (flat platform switch design) n=44.

2. Demographic and Clinical Study Outcomes

The mean age and ± SD of the 141 participants were 45 ± 16 years (range: 18 to 81 years), with no significant between-group differences. There were 61 (43%) males and 80 (57%) females; fewer males than females were randomly allocated to the FI group. The mean calculated body mass index was 27 ± 6 (range: 17-54), with all three groups having a similar mean average (Table 1).

Three participants presented with a history of periodontitis (all randomized to the FI group; Table 2). Study participants had 68 extraction sites and 73 healed ridges. All but two of 68 extraction sites were subjected to site preservation. Forty-two of the 73 healed ridges were developed using augmentation procedures (Table 2). Before implant placement, 26/104 participants were treated with rh-BMP-2 adsorbed to the absorbable collagen sponge and 68/104 participants were treated with rhBMP-2 adsorbed to the collagen sponge with a mineralized bone allograft. Ten others were treated with the bone filler only. A membrane or autogenous soft tissue graft was used in 28 (26%) and 8 (7%) participants, respectively. Soft tissue augmentation procedures were performed for 17% (CI), 22% (FI) and 25% (PS) site [7, 17, 20-24].

3. ***Discontinuations***

Subjects could be discontinued from the study at any time. Reasons for discontinuing a subject were: (i) Voluntary discontinuation by the subject at any time in the study; (ii) Incorrect enrollment- the subject did not meet the inclusion/exclusion criteria for the study; (iii) Severe non-compliance to the protocol as judged by the investigator; (iv) The participant lost to follow-up; (v) The participant lost the study implant(s).

4. ***Patient Reported Outcomes (PROs)***

The results from the patient satisfaction questionnaire are provided in Table 3. In general, participants were very satisfied with received treatment throughout the 3 years with the three tested implant systems. In most instances, there were no significant differences found in ratings when all factors in the questionnaire were compared for the three implant groups.

With permanent restorations, there were no significant differences in patient ratings of mucosal inflammation and bleeding. However, with provisional restorations, significantly less patient-perceived bleeding was detected by participants in Group C (3mm ± 5mm) than by those in

Group B (11mm ± 13mm), and Group A (8mm ± 13mm) at visit 6 (provisional restoration; Kruskal-Wallis test, p=0.005). Furthermore, Group C (PS) rated the level of soreness around their new tooth significantly lower (7mm ± 15mm) than those in Group B (FI) (19mm ± 25mm; p=0.001) for visit 4; no significant differences were detected between Group C and Group A.

With the permanent restorations, significant differences for tooth appearance were detected between the groups at visit 10 (3rd year; p=0.049, Kruskal-Wallis). However, the mean rating and standard deviation for Group C (95mm ± 6mm;) is different than Group B (86mm ± 17mm; p=0.025) but not different from Group A (93mm ± 8mm; p=0.749). At visit 8 (1 year), participants rated the appearance of soft tissue and their satisfaction with the colour of the mucosa around the implant; Group C (93mm ± 9mm) rated this better than Group B (82mm ±23mm; p=0.047). However, there were no significant between-group differences observed on the follow-up visits 9 (2nd year) and 10 (3rd year).

There were no statistically significant differences observed for questions 2, 6, 7, 8 and 9 that measured the impact of the implant on self-consciousness, smile, pain/discomfort while eating or drinking or with hard food items.

5. *Adverse events*

Forty-eight CI, 49 FI and 44 PS implants were placed in 141 participants at the start of the study. At the 1-year evaluation, 48 CI, 40 FI and 38 PS were present, which reflected the failure of 8 FI implants and 6 PS implants. Six FI implants and 5 PS implants were lost due to failure to osseointegrate and 2 FI and 1 PS were lost at the time of permanent crown placement. At the 3-year evaluation, 3 CI, 6 FI and 6 PS implants were lost to follow-up. Hence, 45 CI, 34 FI and 32 PS implants were present at the end of this study.

Other than failed implants (n= 0, 8 and 6 for groups A, B, and C respectively) and lost to follow-up (10.63% of cases), as detailed by Cooper et al, [7, 17, 20-24] this trial found no major adversity linked to any of the tested implant systems.

IV. DISCUSSION

This multi-centre RCT investigated self-perceived mucosal health after treatment with three different implant-abutment interface designs (namely CI, FI, and PS), as well as the implant mucosal aesthetics. Overall results indicate a similar performance with the three systems, at least from the patient perspective. The observations in this study were made from the time point of provisional crown delivery to the 3-year follow-up.

To our knowledge, this is the first study in which patients were asked to report on their mucosal health around their implants using three different implant-abutment interface designs. Evidence is needed to convince patients that clinical recommendations for routine follow-up examinations are scientifically based and that these additional dental visits are necessary. The fact that the study's clinical outcomes revealed differences and the PRO ratings did not, indicates that only a clinical examination will detect peri-implant mucosal inflammatory conditions. Thus, implant patients cannot wait until they notice inflammation or bleeding before seeing their providers. Our results offer the necessary scientific evidence that dentists need to reinforce their recommendation that implant patients must attend routine examinations following implant placement.

For most questions, there are few and inconsistent differences observed amongst the three implant groups. For mucosal inflammation and bleeding with the permanent restorations, there were no significant differences in patient ratings amongst the different implant designs. However, clinical assessments of mucosal inflammation within this study demonstrated that

the conical interface design demonstrated a relative absence of marginal loss following implant placement through the 5-year clinical follow up period [7, 17, 20-24]. During the 3-year follow up of the clinical study, pocket probing depth was the least for conical interface implant design and 80% of CI showed stable peri-implant mucosal zenith position as compared to FI (61%) and PS (84%) [24]. This finding is important because it provides clear evidence that patients are unable to detect inflammation around their implants. Thus, our findings highlight the need for clinicians to stress that their patients return for routine examinations to ensure the long-term health and retention of their implants.

In this study, during visit 6, participants perceived bleeding of the gingiva around the new tooth to be more frequent with flat-to-flat connections than conical and platform-switched interfaces. These differences appeared only when the patients were wearing provisional crowns and were not observed with the permanent crowns. That bleeding might be attributed to normal mucosal inflammation following a surgical procedure and prosthetic rehabilitation. Studies have found that the gingival papilla had a general tendency to slowly increase in height. This progressive increase in aesthetics and changes in soft tissue shape is attributed to gradual papillae formation and healing process of the mucosa over a period [25, 26]. The clinical results of this study showed no significant differences over the same given time frame for bleeding on probing (BOP). Differences with the provisional crowns became insignificant once the final restorations were placed; in agreement with the clinical data, this implies that soft tissue inflammation tends to be similar with the three tested implant systems. [7, 17, 20-24]

This study outcome corelates with findings from other studies which showed that most variation in soft tissue health occur during the first three to six months following the implant surgery [27, 28]. PES score for mesial and distal papilla shows a significant increase after 6-8 months of follow up, suggesting the regeneration of papilla and reconstruction of periodontal attachment, leading to soft tissue stability [27].

At visit 4 (post-operative stage), more reports of sore gums around the new tooth were associated with flat-to-flat connections as compared to platform-switched and conical connections. Soreness of the mucosa at this stage can be attributed to healing characteristics, for example the emergence profile can induce a different positioning of soft tissues. This could also be linked to peri-implantitis on the long-term, which may result in pain accompanied by inflammation and bone loss [29]. The soreness could also be attributed to recession around the adjacent natural teeth that causes saucerization which leads to resorption of the surrounding bone. This happens when there is an extremely short or narrow space between the implant and tooth (less than 1.5mm). This recession might cause the tooth surfaces to be exposed to hot or cold, resulting in soreness.

While there were significant differences over the 3-year follow-up period, the individual ratings were all relatively high. For tooth appearance, Group C (PS) demonstrated significantly better results when compared to Group B (FI) but was not rated differently than Group A (CI) at most timepoints. The few differences observed are minimal and possibly of little clinical relevance. These differences may be explained by the direct influence of implant-abutment interfaces on bony changes, which affect the soft tissues and have a direct bearing on aesthetics [30]. Multiple studies have found that platform switch implant-abutment systems experience significantly less marginal bone loss and are thus considered better than flat-to-flat systems in terms of peri-implant esthetics [9, 31]. Platform switching is suggested to shift the inflammatory response in an inward direction towards the axis and away from the crestal bone. This reduction in the inflammatory response influences the hard and soft tissue stability [15, 32].

However, the clinical results from this RCT revealed that there is a relative absence of marginal bone loss with conical implant-abutment interface designs than with flat-to-flat and platform-switch interface designs [17, 24]. In a recent comparative analysis study of flat-to-flat and

conical implant abutment connections revealed significantly less marginal bone loss with conical connections after 1 year of loading [33]. An ITI consensus report suggests that the implant neck design has no effect on patient's ratings of mucosal esthetics. This statement was supported by 1 RCT, 3 prospective cohort studies and 1 cross-sectional studies [34]. Another study demonstrated that marginal bone loss and soft tissue recession is not dependent on implant neck design but is determined by different biological and biomechanical factors [35]. As the current literature provides insufficient evidence, further studies are warranted.

At the one-year visit only, statistics for patient satisfaction ratings on the appearance of the soft tissue and colour of the gingiva suggest that participants found platform switched connections better than flat-to-flat connections. Studies evaluating the microleakage and biologic seal of the different implant abutment interfaces have demonstrated that a 100% success rate is unrealistic. However, previous clinical studies have shown that the performance of conical connection systems is superior to platform switched and flat-to-flat connections. [8-11] This may be attributed to the fact that micro gaps and bacterial microleakage are comparatively few due to better sealing ability with conical connections [36-39]

RCTs comparing platform switched connections with conventionally restored platform-matching dental implants have shown significantly less marginal bone loss and limited bone resorption [40]. A decrease in papilla height at the contact point between the tooth surfaces leads to gap formation in the interproximal gingival joint. This affects the aesthetics by creating a black triangle that may be noticeable to the patient [41]. Less marginal bone loss leads to preservation of crestal bone which directly impacts the papilla height. Also, the difference observed by patients for the soft tissue appearance was only noted during the first-year visit. During the 3-year outcome visit, no implant-abutment interface connection yielded superior outcomes for aesthetics when evaluated by patients; their scores were consistent with the clinical findings of this study from Pink Aesthetic Scores (PES). This could be attributed to the

extended time required for peri-implant mucosal healing [26]. Other studies demonstrate a statistically significant improvement in the PES from initial placement and after 1 year. It shows a perfect mucosal aesthetics after 12 months and suggests that the PES and the White Esthetic Index (WES) results stabilize with time due to soft tissue healing and adaptation [25] [42].

Amongst the potential limitations of this study, one could mention the sample size as not having been planned based on patient-reported outcomes. However, our study had sufficient participants to detect differences in patient satisfaction on a 100-mm VAS, as observed in other trials.[43] Dental care providers/operators could not be blinded, which was another limitation of our study design. This was compensated for by focusing on blinding the participant and, for this specific report, by collecting data of participant perspectives.

Regarding the generalisability of this trial, data were gathered from four North American centers. Thus, the results should be generalizable, at least for North America. However, these findings may be applicable only for a patient needing a single implant-supported crown in the esthetic region. In addition, it may be that specific patient groups (e.g., those with major esthetic challenges due to high demand/expectations or poor mucosal phenotype) may perceive greater/other differences between the tested implant systems.

Our study used a rigorous multi-site randomized controlled trial design with an appropriate sample size and patient reported outcomes enhanced by clinical outcomes from the same RCT [7, 17, 20-24].

V. CONCLUSION

In general, all three tested implant systems result in high patient satisfaction in terms of esthetics and self-perceived health of the peri-implant mucosa. The fact that patients cannot perceive mucosal inflammation supports the need for professional assistance to detect peri-implant pathology. Thus, these results support the fact that routine follow-up examinations by dentists are necessary, even if the mucosa appears to them to be healthy.

VI. ACKNOWLEDGEMENTS

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VIII. CONFLICT OF INTEREST

The authors have no known financial or personal conflict of interest that could have influenced the work reported in this paper.

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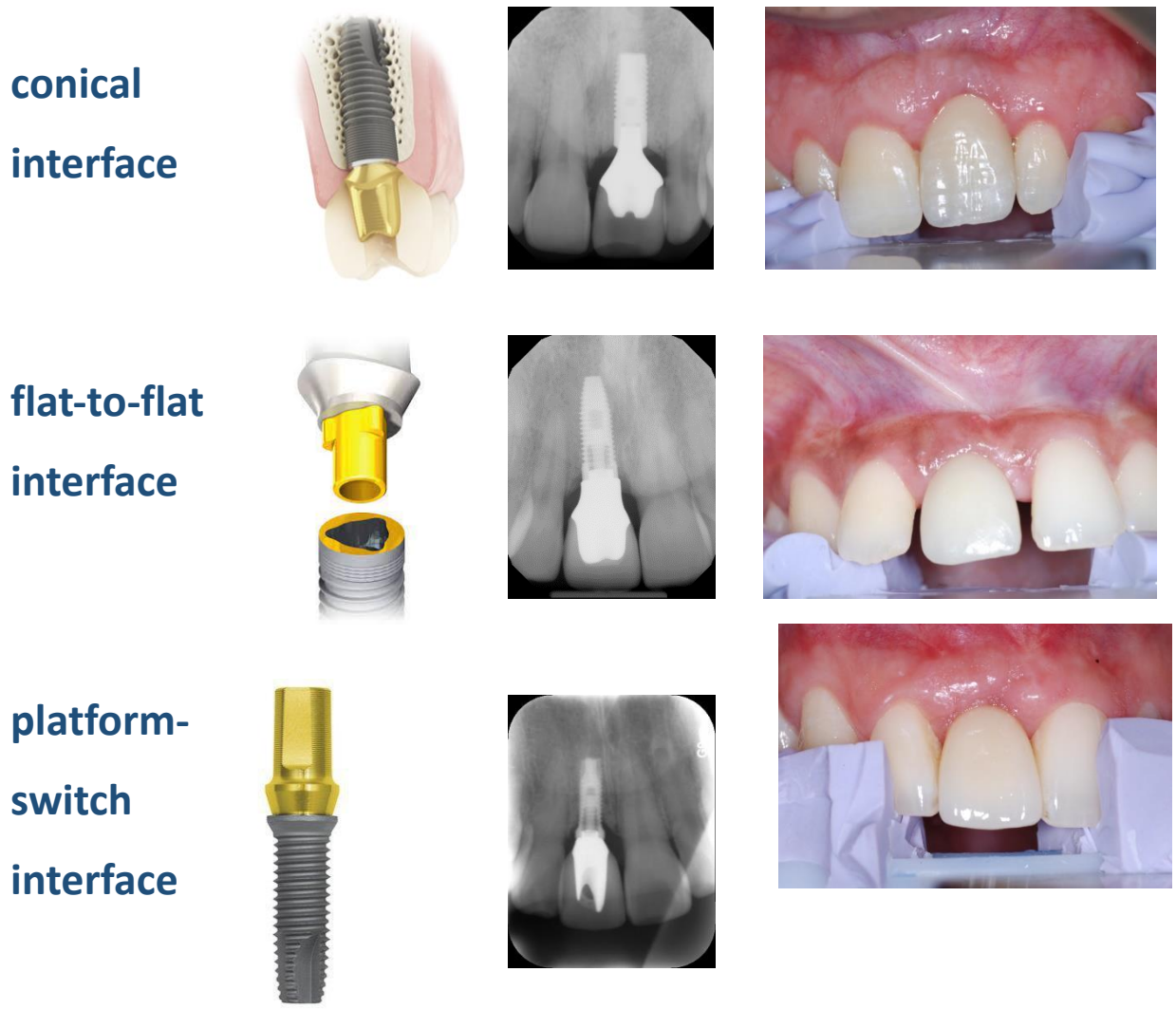
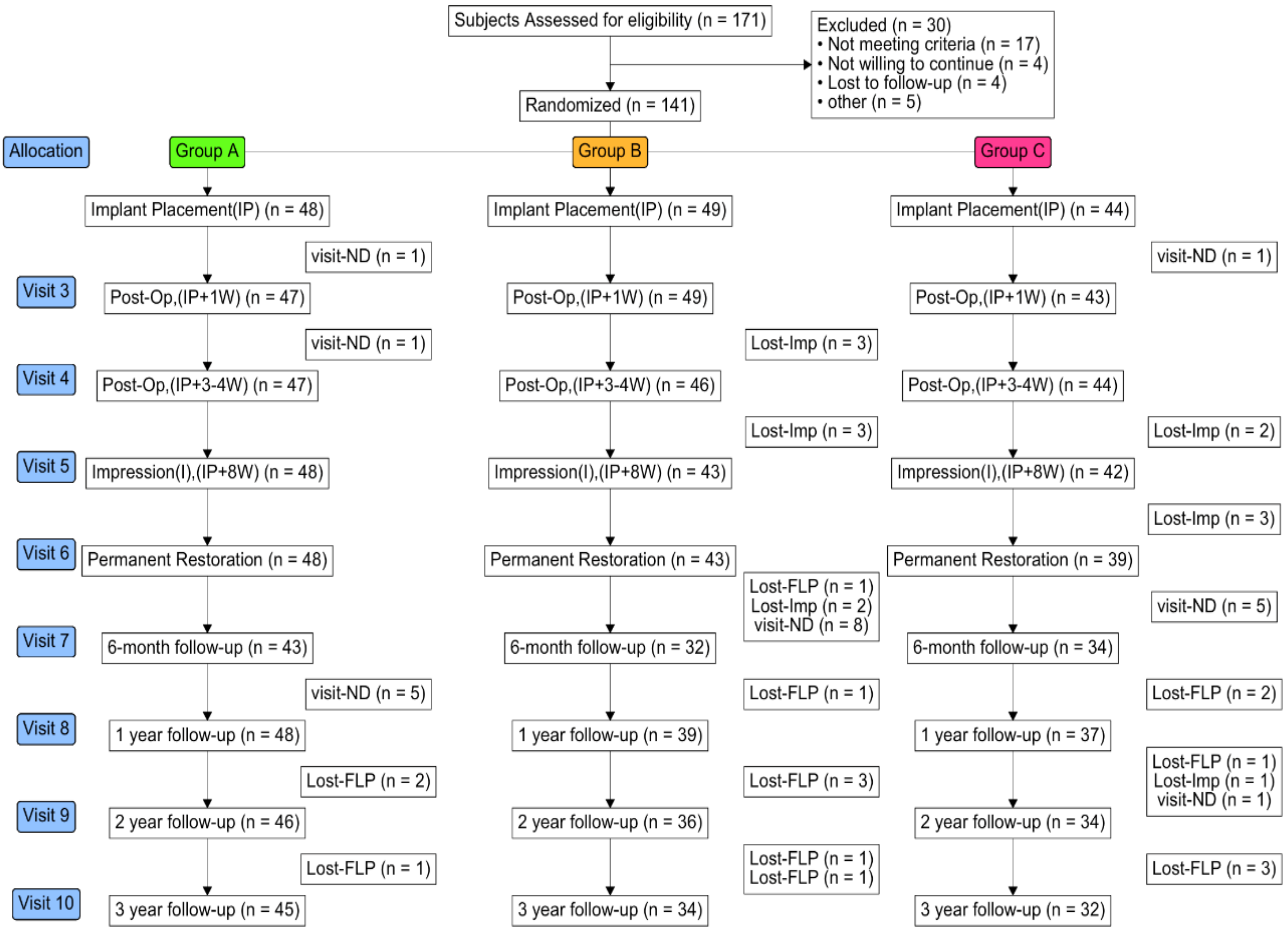
Figure 1: Clinical and radiographic images on 3-year follow-up.





Group A= conical interface; Group B = flat-to-flat interface; Group C = platform-switch interface; visit-ND = visit not performed; Lost-FLP = lost to follow up; Lost-Imp = lost implant.

Figure 2: Participant flow diagram through the RCT.

APPEARANCE QUESTIONNAIRE

Subject number: | | | | | | | | | | | | | |

Site: | | | | | | | | | | | | | |

Date: | | | | / | | | / | | |
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Session: | | | | |

We would like to know how satisfied you are with your new implant tooth and the gums around it. Please read each of the following questions and draw a vertical line across the horizontal line, where you think your answer best fits.

1. Please indicate whether you like the way your new tooth looks.

I do not like it at all _____ I like it very much

2. Please describe the color of your gums around your new tooth.

Pink

White _____ Bright red

3. Do you like the color of your gums around your new tooth?

Do not like the color at all _____ Like the color very much

4. Do your gums around your new tooth bleed?

Always _____ Never

5. Do your gums around your new tooth hurt or or feel sore?

Always _____ Never

6. Do you feel self-conscious because of your new tooth?

Always _____ Never

7. Do you avoid speaking or smiling because of your new tooth? Always _____ Never _ 8. Do you feel any pain or discomfort in or near your new tooth when drinking or eating hot or cold foods? Always _____ Never _ 9. Do you feel any pain or discomfort in or near your new tooth when biting into hard foods, like apples or carrots? Always _____ Never _	

Figure 3: Patient Appearance Questionnaire

TABLES

Variable	CI	FI	PS	All
No. (%)	48 (34)	49 (35)	44 (31)	141 (100)
Mean ± SD age (range) (y)	43 ± 15 (18-70)	46 ± 17 (19-78)	46 ± 16 (18-81)	45 ± 16 (18-81)
Mean ± SD BMI (range)	28 ± 7 (19-54)	27 ± 6 (18-40)	26 ± 5 (17-44)	27 ± 6 (17-54)
Sex, No. (%)				
M	25 (52)	14 (29)	22 (50)	61 (43)
F	23 (48)	35 (71)	22 (50)	80 (57)
Smoking status, No. (%)				
Non-smoker	33 (69)	35 (71)	33 (75)	101 (72)
Ex smoker	15 (31)	14 (29)	11 (24)	40 (28)
Oral condition				
Abnormal jaw relations, No (%)				
With	1 (2)	0	2 (5)	3 (2)
Without	47 (98)	49 (100)	42 (95)	138 (98)
Periodontitis, No. (%)				
With	0	3 (6)	0	3 (2)
Without	48 (100)	46 (94)	44 (100)	138 (98)
Bruxism, No. (%)				
With	15 (31)	10 (20)	7 (16)	32 (23)
Without	33 (69)	39 (80)	37 (84)	109 (77)

CI= Conical interface; FI= flat-to-flat interface; PS= platform switch interface; BMI= Body Mass Index

Table 1: Study Population Demographics.

Variable	CI = 48		FI = 49		PS = 44		All	
Site History	**Ex**	**HR**	**Ex**	**HR**	**Ex**	**HR**	**Ex**	**HR**
No.	24	24	24	25	20	24	68	73
Site Preparation (yes/no)	24/0	14/10	23/1	12/13	19/1*	16/8	66/ 1+1*	42/31
Bone graft (yes/no)	24/0	14/0	23/0	11/1[†]	19/0	13/3^	66/0	38/4^
rhBMP-2 only	9	0	10	0	7	0	26	0
Rh-BMP-2 + other material	12	13	11	10	9	13	32	36
Other material only	3	1	2	1	3	0	8	2
Membrane (yes/no)	7/17	5/9	6/18	3/9	5/14	2/14	18/49	10/32
Auto soft tissue graft (yes/no)	2/22	0/14	1/23	1/11	1/18	3/13	4/63	4/38
Suture (yes/no)	22/2	14/0	22/2	12/0	19/0	16/0	63/4	42/0

CI= Conical interface; FI= flat-to-flat interface; PS= platform switch interface; Ex = extraction of tooth required; HR = healed ridge; rhBMP-2 = human recombinant bone morphogenetic protein; Aut = autogenous.

[†] *Only autogenous soft tissue graft*

* *Retained primary tooth extracted at time of implant placement.*

Table 2: Implant Site Preparation Variables.

Question (Q)	Group	V4 (PO)	V6 (PR)	V7 (6 m)	V8 (1 y)	V9 (2 y)	V10 (3 y)
Q1. Tooth appearance	A	77 (±25)	72 (±28)	93 (±10)	92 (±10)	93 (± 10)	93 (±8)^{A}
	B	74 (±28)	75 (±25)	93 (±14)	90 (±15)	91 (±15)	86 (±17)^{A}
	C	78 (±20)	77 (±24)	93 (±7)	94 (±7)	95 (±5)	95 (±6)^{A}
	Sig.	0.937	0.8582	0.6316	0.7759	0.8885	**0.0487***
Q2. Soft tissues, color	A	59 (±11)	56 (±10)	54 (±10)	57 (±13)	54 (±12)	56 (±10)
	B	58 (±12)	54 (±9)	53 (±7)	53 (±11)	54 (±14)	56 (±15)
	C	58 (±11)	57 (±13)	56 (±10)	58 (±13)	56 (±10)	55 (±13)
	Sig.	0.6861	0.3631	0.9134	0.8413	0.6636	0.8778
Q3. Soft tissue, satisfaction with color	A	84 (±18)	84 (±18)	91 (±12)	89 (±14)^{AB}	90 (±14)	89 (±18)
	B	80 (±18)	82 (±19)	91 (±13)	82 (±23)^{A}	87 (±20)	86 (±16)
	C	86 (±13)	83 (±17)	92 (±11)	93 (±9)^{B}	92 (±10)	91 (±13)
	Sig.	0.5135	0.7304	0.9308	**0.0472***	0.5211	0.4515
Q4. Soft tissue, bleeding	A	8 (±14)	8 (±13)^{AB}	5 (±7)	7 (±11)	7 (±10)	9 (±13)
	B	11 (±20)	11 (±13)^{A}	8 (±15)	12 (±21)	9 (±15)	15 (±19)
	C	4 (±8)	3 (±5)^{B}	5 (±12)	6 (±14)	6 (±11)	8 (±18)
	Sig.	0.0782	**0.0054***	0.7146	0.1414	0.4628	0.0997
Q5. Soft tissue, pain	A	10 (±16)^{AB}	8 (±14)	4 (±6)	8 (±15)	10 (±16)	15 (±26)
	B	19 (±25)^{A}	11 (±13)	8 (±15)	11 (±20)	8 (±10)	13 (±20)
	C	7 (±15)^{B}	7 (±11)	8 (±18)	4 (±5)	7 (±16)	10 (±17)
	Sig.	**0.0186***	0.2669	0.7096	0.6243	0.3285	0.8247
Q6. Self-consciousness	A	19 (±30)	16 (±26)	8 (±19)	5 (±12)	6 (±16)	6 (±16)
	B	20 (±27)	16 (±24)	13 (±28)	8 (±17)	6 (±13)	9 (±19)
	C	12 (±19)	13 (±22)	5 (±16)	6 (±16)	5 (±17)	2 (±3)
	Sig.	0.2641	0.5304	0.4926	0.8898	0.4006	0.1377
Q7. Avoid speaking/ smiling	A	8 (±17)	8 (±17)	2 (±4)	3 (±6)	3 (±5)	3 (±8)
	B	8 (±14)	11 (±20)	4 (±9)	3 (±5)	4 (±6)	4 (±8)
	C	6 (±13)	7 (±16)	2 (±4)	2 (±4)	2 (±3)	3 (±4)
	Sig.	0.3365	0.2097	0.8551	0.7356	0.0713	0.4449
Q8. General pain/discomfort, drinking or eating	A	8 (±15)	7 (±15)	6 (±10)	4 (±6)	4 (±7)	4 (±8)
	B	10 (±18)	7 (±10)	3 (±4)	6 (±9)	4 (±5)	6 (±10)
	C	7 (±15)	8 (±14)	4 (±7)	4 (±5)	7 (±12)	12 (±20)
	Sig.	0.5757	0.8053	0.974	0.4109	0.7183	0.1488
Q9. General pain/discomfort, biting hard foods	A	18 (±25)	9 (±13)	6 (±10)	6 (±12)	7 (±12)	5 (±6)
	B	11 (±20)	13 (±18)	3 (±5)	8 (±13)	5 (±9)	8 (±17)
	C	17 (±29)	8 (±11)	9 (±15)	9 (±18)	8 (±16)	14 (±23)
	Sig.	0.7647	0.6092	0.5577	0.5401	0.7415	0.3401

* Significant between-group difference (p-value ≤ 0.05).

Table 3: Mean (±SD) values and between-group significance levels (Kruskal-Wallis test) for answers to the patient-reported outcome questionnaire on 100-mm-VAS. In cases of significant p-values, different uppercase letters represent statistically significant differences by pairwise comparisons (Bonferroni-corrected Mann Whitney test).

APPENDIX TABLES

Primary objective	**Outcome measures**
1. Soft tissue response **– Buccal soft tissue changes from installation to 1 year follow-up**	*Changes in mid-buccal gingival zenith from implant installation*
Secondary objectives To evaluate and compare:	
1. Soft tissue response **– Buccal soft tissue changes from installation up to 5 years follow-up**	*Changes in mid-buccal gingival zenith from implant installation*
2. Soft tissue response – **Cytokines**	*Concentration of Cytokines measured in the Peri-implant Sulcular Fluid (PISF)*
3. Soft tissue response – **Peri-implant mucosa**	*Presence of Bleeding on Probing (BoP)* *Probing Pocket Depth (PPD)* *Presence of Plaque*
4. Soft tissue response – Pink **Esthetic Score (PES)**	*Pink Esthetic Score (PES) alterations*
5. Soft tissue response – **Papilla**	*Soft tissue changes (for the mesial and distal papilla, separately). Evaluated on clinical photos and measured clinically*
6. Soft/bone tissue response – **Alveolar ridge architecture alterations**	*Change in the alveolar ridge dimensions. Evaluated by optical scan of impressions/casts*
7. Bone tissue response – **Marginal Bone Level (MBL)**	*Marginal Bone Level (MBL) alterations (mesial and distal)*
8. **Implant stability**	*Evaluated by clinical examination* *Manual stability will be scored as "yes" or "no"*
9. **Implant success/survival**	*Success/survival as defined by Roos et al [44]*
10. **Patient reported outcomes – VAS**	*Responses on VAS questionnaire (esthetic focus)*

Appendix Table 1: Study objectives and outcomes of the multi-center RCT.

Inclusion Criteria
1. Provision of informed consent.
2. Aged 18 years or above at enrollment.
3. In need of one or more single implants replacing missing or non-restorable teeth in the maxilla within region 14 to 24.
The following were to be considered at inclusion but could not be fulfilled until the Visit 2 assessments:
4. Edentulous for at least 5 months at study site
5. A buccal-lingual bone width at study site of at least 5.5 mm
6. A mesial-distal bone level distance between adjacent teeth at study site of at least 5.5 mm
7. A keratinized mid-buccal mucosal height of at least 2 mm at study site
8. Teeth adjacent (mesial and distal) to study site must consist of two stable teeth on natural roots without signs of periodontal bone loss (>1 mm) and/or significant soft tissue loss
9. Teeth adjacent (mesial and distal) to study site must demonstrate a stable occlusal guidance that will allow non-functional disocclusion in all eccentric positions
10. An opposing dentition with teeth, implants or prosthetics
Exclusion Criteria
1. Insufficient interocclusal distance for implant placement and restoration at study site
2. Tooth adjacent (mesial and/or distal) to study site is ankylosed
3. More than 2 mm vertical bone loss at study site as measured from the mid-buccal crest of bone on the adjacent teeth
4. Site development (bone tissue) performed at less than 5 months before Visit 2 at study site
5. Untreated rampant caries and/or uncontrolled periodontal disease
6. Angle class II division 2 malocclusion
7. Use of tobacco within last 6 months
8. Uncontrolled diabetes (subjects' history does not reveal the absence of control of insulin-dependent/non-insulin dependent Diabetes Mellitus)
9. Current alcohol or drug abuse
10. Systemic or local disease or condition that would compromise post-operative healing and/or osseointegration
11. Use of any substance that will influence bone metabolism
12. Need for systemic corticosteroids or any other medication that would influence post-operative healing and/or osseointegration
13. History of radiation in the head and neck region
14. Known pregnancy, pregnancy tests will be performed as per local requirements.
15. Unable or unwilling to return for follow-up visits for a period of 3 years

16. Unlikely to be able to comply with study procedures according to Investigator's judgement
17. Involvement in the planning and conduct of the study (applies to both Sponsor staff and staff at the study centre).
18. Previous enrolment or randomization of treatment in the present study.

Appendix Table 2: Eligibility criteria of the multi-centre RCT.

5. DISCUSSION

In this multi-centre RCT, our group investigated self-perceived mucosal health and patient satisfaction with aesthetics following treatment with three different implant-abutment interface designs. Three significant findings were detected following the analysis of nine questions from the patient appearance questionnaire and considering the entire 3-year follow-up. Firstly, (i) participants observed slightly more peri-implant bleeding and soreness with flat-to-flat interface implants (FI) when wearing provisional crowns. Furthermore, (ii) they rated the platform switched (PS) implant-abutment interface more satisfactory regarding tooth appearance and the colour of the peri-implant mucosa after insertion of the permanent crowns. Finally, (iii) overall results indicate a similar performance with the three systems from the patient perspective.

To our knowledge, this is the first study in which patients were asked about their peri-implant mucosal health using three different implant-abutment interface designs. Evidence is needed to convince patients that clinical recommendations for routine follow-up examinations are scientifically based. The fact that the clinical outcomes in the same trial revealed differences, and the PRO ratings did not, indicates that only a clinical exam will detect most peri-implant mucosal inflammatory conditions. Thus, implant patients cannot wait until they notice inflammation or bleeding before seeing their providers. Our results offer the necessary scientific evidence that dentists need to reinforce their recommendation that implant patients must attend routine examinations after implant placement.

For most questions in our study, there are few and inconsistent between-group differences amongst the three implant groups. For mucosal inflammation and bleeding with the permanent restorations, there were no significant differences in patient ratings amongst the different implant designs. However, clinical assessments of mucosal inflammation within this study

demonstrated that the conical interface design demonstrated a significant absence of marginal loss following implant placement through the 5-year follow-up period. [12, 26, 34, 37-39, 178] During the 3-year follow-up, pocket probing depth was the least for the conical interface (CI) implant design, and 80% in the CI group had a more stable peri-implant mucosal zenith position than the FI (61%) and PS (84%). [178]

During visit 6, participants perceived mucosal bleeding around the new tooth to be more frequent with flat-to-flat connections compared to the others. These differences appeared only when the patients were wearing provisional crowns. That bleeding might be attributed to normal mucosal inflammation following a surgical procedure and prosthetic rehabilitation. Studies have found that the gingival papilla had a general tendency to slowly increase in height. This progressive increase in aesthetics and changes in soft tissue shape are attributed to gradual papillae formation and healing process of the mucosa over a period. [179, 180] The clinical results of this study showed no significant differences over the same given time frame for bleeding on probing (BOP). Differences with the provisional crowns became insignificant once the final restorations were placed. As with the clinical data, this implies that soft tissue inflammation tends to be similar with the three tested implant systems. [12, 26, 34, 37-39, 178]

This study outcome corelates with findings from other studies which showed that most variation in soft tissue health occur during the first three to six months following the implant surgery. [181, 182] PES score for mesial and distal papilla shows a significant increase after 6-8 months of follow-up, suggesting the regeneration of papilla and reconstruction of periodontal attachment, leading to soft tissue stability. [181] Studies show that the peri-implant soft tissue demonstrates greater stability with both conical and platform-switched interface designs after 12 months of follow-up. [183] This could be attributed to the fact that conical connections and platform switching resulted in statistically less marginal bone loss than the flat-to-flat interface and external-hexagonal connections. [25] Other studies have shown that a conical interface can

resist a larger axial occlusal load than a flat-to-flat interface before bone resorption is triggered. An implant design should be optimized such that the peak bone stress caused by the normal occlusal load maximizes the anchorage strength and minimizes bone resorption. [23, 184]

At visit 4 (post-operative stage), more reports of sore gums around the new tooth were associated with flat-to-flat connections than with the others. Soreness of the mucosa at this stage can be attributed to healing characteristics, for example the emergence profile can induce a different positioning of soft tissues. This could also be linked to peri-implantitis on the long-term, which may result in pain accompanied by inflammation and bone loss. [185] The soreness could also be attributed to recession around the adjacent natural teeth caused by saucerization/resorption of the surrounding bone. This happens when there is an extremely short or narrow space between the implant and tooth (less than 1.5mm). This recession might cause the neighboring tooth surfaces to be exposed to hot or cold, resulting in soreness.

Flat-to-flat interface designs are associated with increased micromotion and microleakage formation. [20, 186] Studies have demonstrated that micromotion and micro gap formation can result in severe peri-implant bone resorption. [118, 187] Another factor that could lead to soreness around the new tooth is the initial crestal bone loss after implant placement. Platform switching is known to preserve or prevent crestal bone loss by shifting the micro gap away from the bony crest. [117, 188-190] However, a few other studies have shown that platform switching does not reduce crestal bone loss over non-platform switched implants. [124, 191, 192] Another study demonstrated that marginal bone loss is less with internal implant connections than with external connections. [193] The results for marginal bone loss from our clinical study at 1 year demonstrate that CI demonstrated the least marginal bone loss -0.22 ± 0.28 mm (range, –1.1 to 0.2 mm), whereas FI and PS implants showed similar bone loss –1.20 ± 0.64 mm (range, –3.4 to –0.1 mm) and –1.32 ± 1.01 mm (range, –3.7 to 0.9 mm), respectively. [37]

While there were significant differences over the 3-year follow-up period, the individual ratings were all relatively high. At visit 10, for tooth appearance, Group C (PS) demonstrated significantly better results than Group B (FI) but was not rated differently than Group A (CI) at most timepoints. The few differences observed are minimal and probably of little clinical relevance. These differences may be explained by the direct influence of implant-abutment interfaces on bony changes, which affect the soft tissues and have a direct bearing on aesthetics [194]. Multiple studies have found that platform switch implant-abutment systems experience significantly less marginal bone loss and, thus, are considered superior to flat-to-flat systems in terms of peri-implant esthetics. [17, 193] Platform switching is suggested to shift the inflammatory response in an inward direction towards the axis and away from the crestal bone, thus influencing hard and soft tissue stability. [24, 120]

The clinical results from this RCT revealed a significant absence of marginal bone loss with conical implant-abutment interface designs, whereas mild resorption occurred with flat-to-flat and platform-switch interface designs. [26, 37, 178] Another recent comparative study of flat-to-flat and conical implant abutment connections revealed significantly less marginal bone loss with conical connections after 1 year of loading. [195] The discrepancy between clinical and patient-reported data is in line with an ITI consensus report that suggests that the implant neck design has no effect on patient ratings of mucosal esthetics. This statement was supported by 1 RCT, 3 prospective cohort studies, and 1 cross-sectional study. [166] Another study demonstrated that marginal bone loss and soft tissue recession is not dependent on implant neck design but is determined by different biological and biomechanical factors. [196] As the current literature provides insufficient evidence, further studies are warranted.

At the one-year visit (visit 8) only, statistics for patient satisfaction ratings on the appearance of the soft tissue and colour of the gingiva suggest that participants found platform switched connections better than flat-to-flat connections. Studies evaluating the microleakage and

biologic seal of the different implant abutment interfaces have demonstrated that a 100% success rate is unrealistic. However, previous clinical studies have shown that the performance of conical connection systems is superior to platform switched and flat-to-flat connections. [13, 17-19] This may be attributed to the fact that micro gaps and bacterial microleakage are comparatively less due to better sealing ability with conical connections. [22, 197-201] Studies have suggested that the implant connection design might influence bacterial activity differently under static and dynamic loading conditions. Internal conical implant connections showed positive results under static loading and also exhibited minimal microleakage under dynamic loading conditions than external hexagon implants. [22, 184]

RCTs in which platform switched connections with conventionally restored platform-matching dental implants were compared have shown significantly less marginal bone loss and limited bone resorption. [202] A decrease in papillary height at the contact point between the tooth surfaces leads to gap formation in the interproximal peri-implant mucosa. This affects the aesthetics by creating a black triangle that may be noticeable to the patient. [203] Less marginal bone loss leads to preservation of crestal bone which directly impacts the papilla height. Also, the difference observed by patients for soft tissue appearance was noted only during the first-year visit. During the 3-year outcome visit, no implant-abutment interface connection yielded superior outcomes for aesthetics when evaluated by patients; their scores were consistent with the clinical findings of this study from the Pink Aesthetic Scores (PES). This could be attributed to the extended time required for peri-implant mucosal healing. [180] Other studies demonstrate a statistically significant improvement in the PES from initial placement and after 1 year. It shows a perfect mucosal aesthetics after 12 months and suggests that the PES and the White Esthetic Index (WES) results stabilize with time due to soft tissue healing and adaptation. [179] [204]

Amongst the potential limitations of this study, one could suggest the sample size as not having been planned based on patient-reported outcomes. However, our study had sufficient participants to detect differences in patient satisfaction on a 100-mm VAS, as observed in other trials. [205] Dental care providers/operators could not be blinded, which was another limitation of our study design. This was compensated for by focusing on blinding the participant and, for this specific report, by collecting data participant perspective data.

Regarding the generalisability of this trial, data were gathered from four North American centers. Thus, the results should be generalizable, at least for North America. However, these findings may be applicable only for a patient needing a single implant-supported crown in the esthetic region. In addition, it may be that specific patient groups (e.g., those with major esthetic challenges due to high demand/expectations or poor mucosal phenotype) may perceive greater/other differences between the tested implant systems.

Our study used a rigorous multi-site randomized controlled trial design with an appropriate sample size and patient reported outcomes enhanced by clinical outcomes from the same RCT [12, 26, 34, 37-39, 178]. In general, all three tested implant systems result in high patient satisfaction in terms of esthetics and self-perceived health of the peri-implant mucosa. Participants tended to rate platform switch implants as slightly better than the other two tested systems, although the differences were minor and inconsistent. The results indicate that patients cannot detect mucosal inflammation; thus, clinical examinations are necessary for the detection of peri-implant changes.

6. CONCLUSION

Patients receiving implants in the esthetic areas are unable to detect peri-implant mucosal inflammation, regardless of the implant-abutment interface (i.e., conical, flat-to-flat, or platform-switched). The fact that the main study outcomes revealed a difference in clinically measured marginal bone loss levels and that the PRO ratings did not reflect this, indicates that only a clinical exam can detect peri-implant mucosal inflammatory conditions. Thus, it is advisable that implant patients do not wait until they notice inflammation or bleeding before seeing their providers, but rather follow clinicians' recommendations for routine appointments.

Our results have also shown that the three tested implant-abutment interfaces have good performance in terms of self-reported aesthetics. Between-treatment differences tend to favour the platform-switched connection in a few comparisons, but these have questionable clinical relevance.

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