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Interfacce in implantologia

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LEGENDS

A- Research Project: Overview and Aims of the Work

A- Progetto di Ricerca: Visione Generale, Scopi del Lavoro

B- The Bone/Implant Interface. A Novel Implant Surface and its Effects on Osseointegration

C- The Implant/Abutment Interface. Role of The Implant/Abutment Connection in the Incidence of Complications Affecting Fixed Implant-Supported Restorations

D- The Restoration/Mucosa Interface. The Aesthetic Outcomes of Implant Treatment

E- Concluding Remarks

Research Project: Overview and Aims of the Work

Dental implants are a safe and effective solution for the prosthetic rehabilitation of partially and totally edentulous patients, as has been clearly demonstrated by several clinical articles with follow-up up > 20 years [1]. The high percentage of long-term survival (> 95% at 10 years) that characterizes dental implants has made them an essential tool in modern dentistry [2], and today, implants are commonly used to support various types of prosthetic rehabilitation, such as fixed prostheses (single crowns, fixed partial dentures, fixed full arches) and removable dentures (various types of overdentures with different attachment systems) [3-5].

If we analyse an implant-fixed prosthetic restoration, it is possible to identify three critical levels or interfaces:

1. Bone/implant interface
2. Implant/abutment interface
3. Restoration/mucosa interface

The strengthening of each of these three interfaces is of fundamental importance in the ability to ensure the survival, biological integration, functional stability and aesthetic success of a prosthetic implant-supported restoration.

Bone/implant interface

Dental implants are titanium screws, of macroscopically cylindrical or conical shape, characterized by the presence of more or less accentuated threads that are adapted to guide their placement into a suitably prepared surgical site. When an implant is first placed into the bone, it is mechanically stabilized in an underprepared site, thus obtaining adequate primary stability; this initial mechanical stabilization, however, tends to be lost in the following months due to remodelling, and should be replaced by

a valid secondary or biological stabilization due to deposition of new bone on the implant surface (osseointegration). The original protocol provided by Branemark was based on a submerged healing period (4-6 months) before the functionalization and prosthetic loading, in order to ensure undisturbed and safe osseointegration [6]. The first dental implants were characterized by the presence of a smooth implant surface (machined surface), which required longer healing times [6]. Today, however, dental implants are characterized by micro- and nano-rough surfaces, the result of specific surface treatments. Such surface treatments are performed to increase the area of the implant surface that is available for bone integration [7,8]. The presence of implant surfaces with characteristics of micro- and nano-roughness can stimulate the apposition of new bone onto the fixture, strengthening and accelerating the bone healing process and the integration of the implant into the bone (osseointegration) [7,8]. Such support for the bone healing process is a necessity, as modern implantology is increasingly using early or immediate loading protocols in order to meet the aesthetic and functional needs of patients. The clinician is forced to anticipate the functionalization of the implant in difficult situations, such as when the bone quality is poor, as it is in the posterior areas of the jaw, or when the amount of bone is reduced, or it is necessary to regenerate bone, or in extraction sockets. In this context, considering the progressive transformation of the clinical paradigms of osseointegration, the study of phenomena at the bone/ implant interface is key. Several years ago, Albrektsson [9] emphasized the importance of the implant surface for obtaining adequate osseointegration, along with aspects related to the material used (titanium), the implant design (macrostructure), the host response, the surgical technique and the conditions and loading times. The old histological definition of osseointegration as a "direct connection between bone and implant, without interposition of fibrous tissue" is no longer adequate. Osseointegration is now defined as a "process to obtain and maintain, in the bone, a clinically asymptomatic rigid fixation of an alloplastic material subjected to functional load" [10]. This definition is certainly more clinical and closer to reality, since a direct connection

between bone and implant practically never reaches 100% of the implant surface, but rather 60-70%. Thus, the osseointegration phenomenon can be defined spatially discontinuous [11]. The new definition also clarifies how osseointegration represents a dynamic and evolving phenomenon that is directly influenced by the implant surface and the occlusal loading [11]. The aims of modern implantology are basically two-fold: on the one hand, to maximize the integration between bone and implant (reaching a direct connection on 100% of the implant surface), and on the other hand, to reduce the healing time in order to proceed as soon as possible with the loading and functionalization of the fixture [11]. The study of surface dynamics is a key to obtaining these results, and the creation of new surfaces, designed to promote osseointegration, is now of great importance.

Implant/abutment interface

An endosteal implant is connected to a prosthetic abutment, stabilized by means of a connecting screw. To date, different types of connections between implant and abutment exist, and these can be classified generally as internal and external connections. In external connections, an external hexagon is present over the implant shoulder, with an anti-rotational function. The prosthetic abutment is placed on the edge of the fixture and stabilized by means of a screw. In recent years, external connections have been progressively replaced by internal connections, since the latter have proven able to more effectively stabilize the system [12-14]. In internal connections, the collar of the walls of the fixture are flared towards the interior and end, and there is a hexagon with anti-rotational purpose; once again, a connecting screw stabilizes the fixture. In certain circumstances, the classic shape of the anti-rotational hexagon may be replaced by innovative designs (multilobes, etc.). A particular type of internal connection is given by the conical connection, in which the abutment, the profile of which is tapered, is inserted into an appropriate housing physically created within the fixture, thereby creating a conical coupling with the fixture itself

[15]. This type of connection between implant and abutment seems able to ensure greater mechanical stability compared to all other screw-type connections [15]. A further development in this type of connection is the locking taper connection between implant and abutment (Morse taper) [16]. In the locking taper connection, the connecting screw is removed and the connection between implant and abutment is made through a Morse taper (<1.5 °); a "cold welding" is obtained for large contact and frictional resistance between the surfaces of the implant and abutment. Several recent studies have shown that the locking taper connection is able to ensure greater mechanical stability than all other types of connections [16-18]. The functional stability of the connection is of fundamental importance in an implant prosthesis because an effective solidification between the abutment and implant can reduce the incidence of prosthetic problems and ensure the health of the hard and soft tissues around the fixture over time. The rehabilitation of patients with implant-supported fixed restorations (single crowns, fixed partial dentures and fixed full arches) is nowadays a treatment characterized by high survival and success rates [1,2]. Nevertheless, prosthetic complications still occur with fixed implant-supported restorations [19,20]. These complications are commonly divided into mechanical and technical complications [20]. Mechanical complications are those that affect pre-fabricated elements such as the implant-abutment connection; among these are the loosening or fracture of the connecting screw or fracture of the prosthetic abutment [20]. Technical complications are complications that affect the restoration itself, such as fracture/chipping of the ceramic or loss of retention of the restoration or debonding [20]. Looking at some of the more recent systematic reviews of the scientific literature that have used meta-analysis to collect clinical studies on fixed prostheses supported by implants with follow-up from 5 to 10 years, it emerges that the incidence of prosthetic problems, particularly of mechanical nature, is still quite high [21-24]. In fact, the cumulative incidence of loosening of the screw connection at 5 years is around 8%, almost regardless of the type of prosthetic restoration; this percentage may even double in 10 years [21-24]. In addition, complications of increased

severity may occur, such as fracture of the screw between the implant and the abutment, especially in more complex restorations (for example, fixed full arches). While the cumulative incidence of fracture of the connecting screw in full arch at 5 years stands at around 10%, it may also double in 10 years [21-24]. These data are particularly important because they emerge from the critical analysis of the most important scientific works from around the world, led by renowned clinical researchers and performed under ideal conditions, i.e. using the best knowledge applied to the best materials. Such reviews are therefore able to accurately describe the current situation of the 'state of the art' in implant-prostheses. However, they may also underestimate the extent of the problems occurring with less experienced clinicians who use in their practices materials or implant systems of lower quality. Both minor (unscrewing of the connection) and major (fracture of the connecting screw, fracture of the prosthetic abutment) complications occurring at the implant-abutment connection certainly represent an annoyance and a waste of time, both for the professional and for the patient [25]. In fact, even the repeated unscrewing a connecting screw in a single crown, though classified as minor complication, can be a problem if the clinician has opted for a cemented prosthetic restoration; it may not be easy, in fact, to remove the crown and to screw in the abutment again [25]. Such recurring problems may also be a source of patient dissatisfaction, which can undermine the perception of the quality of treatment received. Fracture of the connection screw in a prosthetic abutment, finally, represents a major complication, and forces the clinician to undertake complicated interventions while burdened with the risk of harming the inner portion of the implant and therefore the stability of the future prosthetic restoration [25]. Because of the persistence of such mechanical problems in clinical practice, the scientific literature must take care to study abutment-implant connections. Studies on the complications occurring at the implant-abutment interface are currently receiving great interest, and are critical in modern implantology, as the functional stability and reliability of the connection between the implant and abutment determines the success of the implant-supported restoration in the long term.

Restoration/mucosa interface

The final prosthetic restoration is screwed or cemented onto the transmucosal abutment. The relationship between the prosthetic restoration and the peri-implant tissues is key in order to achieve an aesthetically successful restoration over time. An incongruous prosthetic restoration can render oral hygiene difficult or impossible, and can therefore cause inflammation of the peri-implant tissues, putting the survival of the implant at risk. At the same time, a prosthetic restoration characterized by non-adequate emergency profiles can lead to the aesthetic failure of an implant-supported rehabilitation. In recent years, the practice of positioning dental implants into fresh extraction sockets (immediate post-extraction implants) is spreading [26]. This technique certainly has its advantages, such as a reduced number of surgical procedures and shortened rehabilitation time, with a psychological benefit to the patient; however, it requires more experience due to the difficulty of obtaining adequate implant stabilization in a socket of larger size. Recently, some authors have suggested that placement of immediate post-extraction implants may be particularly suitable in areas of high aesthetic impact; in fact, they suggested that this procedure could in some way reduce the amount of the bone resorption that normally affects the vestibular bone of the anterior maxilla after tooth loss [27,28]. It is well known, in fact, that the loss of a dental element causes a certain amount of bone resorption, particularly affecting the thin and delicate vestibular bone of the anterior maxilla. This phenomenon is physiological, as it is connected to the loss of vascular supply from the periodontal ligament; however, the results of this physiological resorption present a serious issue to the clinician, particularly in the rehabilitation of areas of high aesthetic impact (such as the anterior maxilla). Unfortunately, several important works have failed to demonstrate that the placement of immediate post-extraction implants can effectively reduce the bone resorption affecting the vestibular bone of the anterior maxilla, determined by the loss of teeth [29,30]. Nevertheless, the placement of immediate post-

extraction implants is now increasingly common in the high aesthetic impact regions for its ability to reduce rehabilitation time and to provide patients with an aesthetically integrated prosthetic restoration in the same surgical session (post-extraction immediate implants with immediate loading). This approach certainly poses a challenge, and requires investigation using the most modern aesthetic analysis tools. The results obtainable with the immediate post-extraction technique in high aesthetic impact areas should be compared to those obtainable with conventional techniques in order to clearly identify which technique can guarantee superior aesthetic integration. This issue is highly debated in the literature, as the analysis of the restoration/mucosa interface is crucial for the achievement and maintenance of the aesthetic success of an implant-supported rehabilitation in the long term.

Aims of the Research

The purpose of this research is to analyse the three different interfaces present in implant-supported fixed dental restorations in order to identify the key elements needed to achieve and maintain the biological integration, functional stability and aesthetic success over time.

Bone/implant interface

The study of the bone/implant interface is of fundamental importance in order to ensure the survival and the biological integration of the implant-supported restoration over time. The aim of this research project is to evaluate the biological response to a new nanostructured implant surface compared to the classically smooth (machined) surface, through a histologic and histomorphometric human study. A comparative, histological and histomorphometric human study is the best tool for assessing the effective capacity of the new implant surface to support and stimulate the bone healing process and osseointegration in vivo.

Implant/abutment interface

The implant/abutment interface is of great importance in being able to guarantee the prosthetic success of an implant-supported restoration over time. A mechanically stable implant/abutment connection reduces the incidence of prosthetic problems (both mechanical and technical), and ensures appropriate functional stability, with benefits for peri-implant tissues (soft and hard tissues) over time. The aim of this research project is to assess whether a locking-taper (Morse taper) implant/abutment connection can reduce the incidence of prosthetic complications (mechanical and technical) affecting implant-supported restorations in the long term.

Restoration/mucosa interface

Aesthetic success has become an important parameter in implant-supported restorations. The interaction of the implant restoration with the soft tissue determines the aesthetic success or failure of a rehabilitation, particularly in areas of high aesthetic impact such as the anterior maxilla. Therefore, analysis of the restoration/mucosa interface represents a key element. The aim of this research is to identify which rehabilitation protocols achieve a superior aesthetic result in modern implantology. This will be done through a clinical trial that compares the aesthetic results of post-extraction implants versus implants placed in fully healed sites, in the anterior maxilla.

Keywords

Dental implants; Bone/implant interface; Implant/abutment interface; Restoration/mucosa interface; Biological integration; Functional stability; Aesthetic success.

Gli impianti dentali rappresentano uno strumento sicuro ed efficace per la riabilitazione protesica di pazienti parzialmente o totalmente edentuli, come inequivocabilmente dimostrato da numerosi lavori in letteratura con follow-up fino a 20 anni [1]. Le elevate percentuali di sopravvivenza a lungo termine (>95% a 10 anni) che li caratterizzano hanno reso gli impianti dentali uno strumento imprescindibile nella moderna odontoiatria [2], ed oggi gli impianti vengono utilizzati come pilastri per poter sostenere varie tipologie di riabilitazione protesiche, quali protesi fisse (corone singole, protesi fisse parziali, arcate fisse complete) e protesi rimovibili (varie tipologie di overdenture con differenti sistemi di attacco) [3–5].

Analizzando un restauro implanto-protesico fisso, è possibile individuare tre diversi livelli critici o interfacce:

1. interfaccia osso/impianto;
2. interfaccia moncone/impianto;
3. interfaccia restauro/mucosa.

Il potenziamento di ciascuna di queste tre interfacce è di fondamentale importanza per potere garantire sopravvivenza, integrazione biologica, stabilità funzionale e successo estetico di un restauro protesico a supporto implantare.

Interfaccia osso/impianto

Gli impianti dentali sono viti endossee in titanio, macroscopicamente di forma cilindrica o conica, caratterizzate dalla presenza di spire più o meno accentuate, atte a guidarne il posizionamento nel sito chirurgico opportunamente preparato. Quando un impianto viene posizionato nell'osso, esso viene stabilizzato meccanicamente in un sito operatorio sottopreparato, ottenendo così una adeguata stabilità primaria; questa

iniziale stabilizzazione meccanica tende però ad essere perduta a causa di fenomeni di rimodellamento, nei mesi successivi all'inserimento, e deve essere sostituita da una valida stabilizzazione secondaria o biologica, dovuta all'apposizione di nuovo osso sulla superficie implantare (osteointegrazione). L'originale protocollo di Branemark prevedeva per gli impianti un periodo di guarigione sommersa (4-6 mesi) prima della funzionalizzazione e del carico protesico, in modo da poter garantire una indisturbata e sicura osteointegrazione [6]. D'altra parte, i primi impianti dentali erano caratterizzati dalla presenza di una superficie implantare liscia (machined), che richiedeva tempi di guarigione più lunghi [6]. Oggi, gli impianti dentali sono caratterizzati da superfici micro- e nanorugose, risultato di specifici trattamenti superficiali. Tali trattamenti superficiali hanno lo scopo di aumentare l'area della superficie implantare disponibile per l'integrazione ossea [7,8]. La presenza di superfici implantari con caratteristiche di micro- e nanorugosità è in grado di stimolare l'apposizione di nuovo osso sulla fixture, potenziando ed accelerando i processi di guarigione ossea, che esitano nell'integrazione dell'impianto nell'osso (osteointegrazione) [7,8]. Il potenziamento e l'accelerazione dei processi di guarigione ossea rappresentano una necessità: la moderna implantologia prevede infatti sempre più spesso il ricorso a protocolli di carico anticipato o immediato, per poter soddisfare le esigenze estetiche e funzionali dei pazienti. Il clinico si trova quindi a dover anticipare la funzionalizzazione dell'impianto in contesti difficili, in cui la qualità dell'osso è per natura scarsa, come nei settori posteriori delle ossa mascellari, o in cui la quantità ossea è ridotta, laddove è necessario ricorrere a chirurgia ossea rigenerativa, o in alveoli post-estrattivi. In questo contesto, e di fronte alla progressiva trasformazione dei paradigmi clinici dell'implantologia osteointegrata, lo studio dei fenomeni all'interfaccia osso/impianto assume un'importanza strategica. Già Albrektsson [9] sottolineava l'importanza della superficie implantare per l'ottenimento di un'adeguata osteointegrazione, insieme ad aspetti riguardanti il materiale (titanio), il design dell'impianto (macrostruttura), la risposta dell'ospite, la tecnica chirurgica e le condizioni e i tempi del carico. La vecchia definizione

istologica che descriveva l'osteointegrazione come "diretta connessione tra osso e impianto, senza interposizione di tessuto fibroso" non è più in grado di renderne la portata. L'osteointegrazione è oggi definita come un "processo che consenta di ottenere e mantenere, nell'osso, una fissazione rigida e clinicamente asintomatica di un materiale alloplastico sottoposto a carico funzionale" [10]. Questa definizione è certamente più clinica e vicina alla realtà, dal momento che la diretta connessione tra osso e impianto non è praticamente mai raggiunta sul 100% della superficie implantare, ma piuttosto sul 60-70%, cosicché il fenomeno dell'osteointegrazione può definirsi spazialmente discontinuo [11]. Inoltre, essa chiarisce come l'osteointegrazione rappresenti un fenomeno dinamico ed evolutivo, direttamente influenzato dalla superficie dell'impianto e dal carico occlusale [11]. L'obiettivo della moderna implantologia è sostanzialmente duplice: da un lato si desidera massimizzare l'integrazione tra osso e impianto (raggiungendo una diretta connessione sul 100% della superficie implantare), dall'altro si intende ridurre i tempi di guarigione ossea, per poter procedere quanto prima al carico e alla funzionalizzazione dell'impianto [11]. Lo studio delle dinamiche superficiali rappresenta un momento chiave per l'ottenimento di questi risultati, e la creazione di nuove superfici, disegnate per promuovere l'integrazione biologica e la neoformazione ossea, è oggi argomento di grande importanza e attualità.

Interfaccia moncone/impianto

All'impianto endosseo viene collegato un moncone protesico, stabilizzato tramite una vite di connessione. Ad oggi, esistono diverse tipologie di accoppiamento o solidarizzazione tra moncone ed impianto, che si distinguono fondamentalmente in connessioni esterne ed interne. Nelle connessioni esterne, a livello del colletto dell'impianto è presente un esagono esterno con funzione anti-rotazionale, e la base del moncone protesico, di forma cilindrica, poggia sul bordo della fixture. Negli ultimi anni, le connessioni esterne sono state progressivamente sostituite da connessioni interne, poiché quest'ultime si sono dimostrate in grado di

stabilizzare più efficacemente il moncone sull'impianto [12–14]. Nelle connessioni interne, le pareti del colletto della fixture sono svasate verso l'interno e terminano con un esagono a scopo anti-rotazionale. In talune circostanze, la forma classica dell'esagono anti-rotazionale può essere sostituita da disegni innovativi (multilobature, ecc). Una particolare tipologia di connessione interna è data dalla connessione conica, nella quale l'abutment, il cui profilo è rastremato, si innesta fisicamente in un apposito alloggiamento creato all'interno della fixture, creando così un accoppiamento conico ed un tutt'uno con la fixture stessa [15]. Tale tipologia di solidarizzazione tra moncone ed impianto ha dimostrato di poter garantire maggiore stabilità rispetto a tutte le altre connessioni avvitate [15]. Un ulteriore sviluppo di tale tipologia di connessione è dato dalla connessione conometrica tra moncone ed impianto (Morse taper) [16]. Nella connessione conometrica, la vite di connessione è eliminata e la solidarizzazione tra moncone ed impianto avviene grazie ad accoppiamento tramite cono Morse (<1.5°): ciò in virtù della "saldatura a freddo" ottenuta per ampio contatto e resistenza frizionale tra le superfici dell'impianto e del moncone in esso attivato. Numerosi studi hanno recentemente evidenziato come la connessione conometrica sia in grado di garantire maggiore stabilità rispetto alle altre tipologie di connessione [16–18]. La stabilità funzionale della connessione riveste una importanza fondamentale in implanto-protesi, perché una efficace solidarizzazione tra moncone ed impianto può ridurre l'incidenza di problematiche protesiche a carico del restauro, e garantire la salute dei tessuti per-implantari (tessuti duri e molli) nel corso del tempo. La riabilitazione di pazienti con protesi fissa supportata da impianti (corone singole, protesi fisse parziali e arcate fisse complete) è oggi una modalità terapeutica caratterizzata da alte percentuali di successo, e per questo sempre più richiesta [1,2]. Nonostante ciò, a carico dei restauri fissi supportati da impianti possono verificarsi complicanze protesiche [19,20]. Queste complicanze vengono comunemente suddivise in complicanze di natura meccanica o tecnica [20]. Le complicanze meccaniche derivano da problematiche a carico di elementi pre-fabbricati, ovvero della connessione moncone/impianto: tra

queste ricordiamo lo svitamento o la frattura della vite di connessione o la frattura del moncone protesico [20]. Le complicanze tecniche dipendono invece da problematiche a carico del manufatto protesico, e tra queste ricordiamo la frattura della ceramica e la perdita di ritenzione del restauro o decementazione [20]. Dall'analisi di alcune delle più recenti revisioni sistematiche della letteratura scientifica con meta-analisi, che raccolgono studi clinici su protesi fisse supportate da impianti con follow-up da 5 a 10 anni, emerge come l'incidenza di problematiche protesiche, in particolare di natura meccanica, sia piuttosto alta [21–24]. Infatti, l'incidenza cumulativa dello svitamento della vite di connessione tra moncone ed impianto a 5 anni si attesta intorno all'8%, quasi indipendentemente dalla tipologia di restauro protesico; questa percentuale può addirittura raddoppiare a 10 anni, sino ad arrivare al 16% [21–24]. Inoltre, sono riportate complicanze di maggiore gravità, come la frattura della vite di connessione tra moncone ed impianto, in particolar modo a carico di restauri più complessi (come le arcate fisse impianto-supportate): l'incidenza cumulativa della frattura della vite di connessione a 5 anni in arcate complete si attesta intorno al 10%, e può raddoppiare a 10 anni [21–24]. Questi dati sono particolarmente indicativi perché emergono dall'analisi critica dei più importanti lavori scientifici al mondo, condotti da ricercatori clinici affermati e realizzati in condizioni ideali, impiegando cioè le migliori conoscenze applicate ai migliori materiali; sono pertanto in grado di descrivere con precisione la situazione attuale dello "stato dell'arte" in implanto-protesi, ma potrebbero sottostimare l'entità dei problemi per come essi si presentano al professionista meno esperto, o che impieghi nella propria pratica clinica materiali o sistematiche implantari di qualità inferiore. Le problematiche a carico della connessione moncone/impianto, siano esse minori (svitamento della vite di connessione) o maggiori (frattura della vite di connessione, frattura del moncone protesico) rappresentano certamente un fastidio ed una perdita di tempo, sia per il professionista che per il paziente [25]. Infatti, anche il ripetuto svitamento di una vite di connessione su una corona singola, benchè classificabile come complicanza minore, può rappresentare un problema laddove il clinico abbia optato per un restauro

protesico cementato: potrebbe non essere semplice liberare il moncone protesico dal restauro per provvedere al riavvitamento del moncone [25]. Il ripetersi di tale evenienza può inoltre rappresentare un motivo di insoddisfazione del paziente, in grado di minare la percezione dello stesso nei confronti della qualità del trattamento ricevuto. La frattura della vite di connessione o del moncone protesico, infine, rappresentano complicanze maggiori, e costringono il clinico a complicati interventi di rimozione, gravati dal rischio della compromissione della porzione interna dell'impianto, e quindi della stabilità del restauro protesico futuro [25]. A causa del persistere di tali problematiche meccaniche nella pratica clinica, la letteratura scientifica deve occuparsi di studiare le connessioni moncone/impianto. Lo studio delle problematiche all'interfaccia moncone/impianto raccoglie oggi un crescente interesse, ed è centrale nella moderna implantologia: dalla stabilità funzionale e dalla affidabilità della connessione tra moncone ed impianto dipende infatti il successo della riabilitazione protesica nel lungo periodo.

Interfaccia restauro/mucosa

Sul moncone transmucoso viene avvitato o cementato il restauro protesico definitivo. Il rapporto tra il restauro protesico ed i tessuti peri-implantari è determinante al fine del raggiungimento del successo estetico del restauro nel tempo. Un restauro protesico incongruo può rendere difficoltose o impossibili le manovre domiciliari per il mantenimento igienico, e può causare infiammazione dei tessuti peri-implantari mettendo a rischio la sopravvivenza stessa dell'impianto. Al tempo stesso, un restauro protesico caratterizzato da profili di emergenza non congrui può determinare l'insuccesso estetico di una riabilitazione a supporto implantare. Negli ultimi anni, si è diffusa la tecnica di posizionamento degli impianti dentali negli alveoli post-estrattivi (impianti post-estrattivi immediati). Un impianto post-estrattivo immediato è un impianto che viene posizionato immediatamente dopo l'estrazione di un elemento dentale compromesso, direttamente nell'alveolo chirurgico [26]. Questa tecnica presenta certamente dei

vantaggi, come la riduzione del numero degli interventi chirurgici e l'accorciamento dei tempi della riabilitazione, con beneficio psicologico per il paziente; tuttavia, essa richiede maggiore esperienza, per via della difficoltà nell'ottenere una adeguata stabilizzazione dell'impianto in un alveolo di dimensioni generalmente maggiori. Nel recente passato, alcuni autori hanno sostenuto come gli impianti post-estrattivi potessero essere particolarmente indicati nelle aree ad alto impatto estetico: secondo questa teoria, infatti, l'inserimento degli impianti negli alveoli chirurgici può in qualche modo ridurre l'entità dei fenomeni di riassorbimento osseo innescati dalla perdita degli elementi dentari a carico dell'osso vestibolare [27,28]. E' noto infatti come a seguito della perdita di un elemento dentale, si inneschi un meccanismo fisiologico di riassorbimento osseo, soprattutto a carico della teca ossea vestibolare. Tale fenomeno è da ritenersi fisiologico, essendo connesso alla riduzione dell'apporto vascolare a carico della teca ossea vestibolare, dovuto alla perdita del legamento parodontale e del suo contributo vascolare; tuttavia, gli esiti di tale riassorbimento fisiologico rappresentano per il clinico un grave problema, laddove lo stesso sia impegnato nella riabilitazione implanto-protesica di aree ad elevato impatto estetico (come la regione anteriore della maxilla). Purtroppo, alcuni importanti lavori sembrano avere smentito la teoria secondo la quale il posizionamento di impianti post-estrattivi possa ridurre il riassorbimento osseo a carico della teca vestibolare nella maxilla anteriore, innescato dalla perdita degli elementi dentali [29,30]. Nonostante ciò, il ricorso al posizionamento di impianti post-estrattivi immediati è oggi sempre più frequente a carico delle regioni ad elevato impatto estetico, per la possibilità di ridurre i tempi della riabilitazione e di fornire ai pazienti un restauro protesico esteticamente integrato nella stessa seduta chirurgica (impianti post-estrattivi immediati a carico immediato). Tale approccio pone certamente una sfida, e richiede di essere investigato attraverso i più moderni strumenti di analisi estetica. I risultati ottenibili in aree ad elevato impatto estetico con tecnica post-estrattiva immediata a carico immediato devono poter essere comparati a quelli ottenibili con tecniche convenzionali, per potere stabilire senza tema di smentita quale sia

l'approccio in grado di garantire una migliore integrazione estetica. Tale argomento risulta essere estremamente dibattuto nella letteratura, e senza dubbio l'analisi delle dinamiche a carico dell'interfaccia restauro/mucosa è di fondamentale importanza per il conseguimento ed il mantenimento del successo estetico di una riabilitazione a supporto implantare.

Obiettivi della ricerca

Lo scopo della presente ricerca è di analizzare le tre diverse interfacce presenti nei restauri implanto-protesici fissi, allo scopo di individuare gli elementi chiave atti a raggiungere e mantenere nel tempo l'integrazione biologica, la stabilità funzionale ed il successo estetico.

Interfaccia osso/impianto

Lo studio dell'interfaccia osso/impianto è di fondamentale importanza per poter garantire la sopravvivenza e l'integrazione biologica del restauro implanto-protesico nel tempo.

Scopo del presente progetto di ricerca è valutare la risposta biologica ad una nuova superficie implantare nanostrutturata, comparata ad una classica superfice liscia (machined), attraverso uno studio istologico ed istomorfometrico su uomo. Tale studio comparativo, istologico ed istomorfometrico su uomo rappresenta infatti il miglior strumento per valutare l'effettiva capacità della nuova superficie implantare di sostenere e stimolare i processi di guarigione ossea e l'osteointegrazione in vivo.

Interfaccia moncone/impianto

Lo stabilità dell'interfaccia moncone/impianto è di grande importanza per poter garantire ad un restauro protesico a supporto implantare il successo nel tempo. Una connessione moncone/impianto stabile riduce l'incidenza di

problematiche protesiche (meccaniche e tecniche) a carico del restauro, e garantisce una adeguata stabilità funzionale, con beneficio per i tessuti peri-implantari (duri e molli) nel tempo.

Scopo del presente Progetto di Ricerca è valutare se una connessione moncone/impianto di tipo conometrico (Morse taper) possa effettivamente ridurre l'incidenza di complicanze protesiche (meccaniche e tecniche) nel lungo periodo.

Interfaccia restauro/mucosa

Il successo estetico è divenuto un parametro di fondamentale importanza nelle riabilitazioni protesiche a supporto implantare. L'interazione del restauro implantare con i tessuti molli determina il successo o l'insuccesso di una riabilitazione, e l'analisi dell'interfaccia restauro/mucosa rappresenta perciò un elemento chiave.

Scopo del presente Progetto di Ricerca è individuare quali protocolli riabilitativi possano determinare un miglior risultato estetico nella moderna implantologia; ciò attraverso uno studio clinico che confronti il risultato estetico di impianti post-estrattivi a carico immediato versus impianti convenzionali posizionati in siti completamente guariti, nella maxilla anteriore.

Parole chiave

Impianti dentali; Interfaccia osso/impianto; Interfaccia moncone/impianto; Interfaccia restauro/mucosa; Integrazione biologica; Stabilità funzionale; Successo estetico

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A- First Part: The Bone/Implant Interface. A Novel Implant Surface and its Effects on Osseointegration

Early Bone Formation Around Immediately Loaded Implants with Nanostructured Calcium-Incorporated and Machined Surface: a Randomized, Controlled Histologic and Histomorphometric Study in the Human Posterior Maxilla

The present study has been submitted for publication, as a part of my PhD research project, to Clinical Oral Investigation: Mangano FG, Iezzi G, Shibli JA, Trabach Pires J, Luongo G, Piattelli A, Mangano C. Early Bone Formation Around Immediately Loaded Implants with Nanostructured Calcium-Incorporated and Machined Surface: a Randomized, Controlled Histologic and Histomorphometric Study in the Human Posterior Maxilla. Clinical Oral Investigation, submitted for publication

Abstract

Objective: The aim of the present randomized, controlled histologic/histomorphometric study was to compare the early bone formation around immediately loaded implants with nanostructured calcium-incorporated (NCI) and machined (MA) surface, placed in the human posterior maxilla.

Materials and methods: Fifteen fully edentulous patients (6 males; 9 females; mean age 57.9 ± 6.7) were selected for this study. Each patient was installed with two temporary transmucosal implants, with different surfaces: 1 NCI (test) and 1 MA (control) implant. All temporary implants were placed in the posterior maxilla, according to a split-mouth design, to

help to support an interim complete maxillary denture. After 8 weeks, all temporary transmucosal implants were retrieved for histologic/histomorphometric evaluation. The bone-to-implant contact (BIC%) and the bone density (BD%) were calculated. The Wilcoxon matched-pairs signed-rank test was used to evaluate differences (BIC%, BD%) between the surfaces. The level of significance was set at 0.05.

Results: In the MA implants, the histomorphometric evaluation revealed a mean (± SD) BIC% and BD% of 21.2 (± 4.9) and 29.8 (± 7.8), respectively. In the NCI implants, the histomorphometric analysis revealed a mean (± SD) BIC% and BD% of 39.7 (± 8.7) and 34.6 (± 7.2), respectively. A statistically significant difference was found between the two surfaces with regard to BIC% ($p<0.001$), while no significant difference was found with regard to BD% ($p=0.09$).

Conclusions: The NCI surface seems to increase the peri-implant endosseous healing properties in the native bone of the posterior maxilla, under immediate loading conditions, when compared with the MA surface.

Keywords

Immediate loading; Early bone formation; Implant surface; Human histology.

Introduction

In recent years, immediate loading protocols have become extremely popular in modern oral implantology: in fact, they meet the needs of patients, who ask for a reduction in the number of operating sessions, and therefore of time/costs of surgical and prosthetic therapy [1–3]. Immediate loading eliminates the need for second-stage surgery and is highly appreciated because it offers immediate comfort, avoiding the inconvenience, discomfort and embarrassment of temporary removable prostheses during the healing phase [4–6].

In order to load implants immediately, particularly in regions with poor bone quality (such as the posterior maxilla), some authors have recommended to use implants with surfaces that are able to stimulate new bone apposition, and can increase the values of the connection between the bone and the implant, reducing the healing time [7–9]. The objective of modern oral implantology is twofold: on the one hand, it aims to obtain satisfactory long-term bone-implant integration (achieving a direct bone-to-implant connection on most of the implant surface) [7,8]; on the other hand, it aims to reduce the healing time, in order to proceed as soon as possible with load and functionalization of the implant [2,3,7,9].

The study of the implant-surface interface is key, and the introduction of surfaces with specific microtopographical features (sandblasted, acid etched, sandblasted/acid-etched surfaces) designed to stimulate the apposition of new bone tissue has already allowed clinicians to obtain excellent results [10,11].

More recently, the focus has shifted to the nanotopography of the implant surfaces [12,13]. In fact, the nanotopography of moderately rough implant surfaces seems to promote osteogenesis, increase the ratio of bone-to-implant contact, and increase the mechanical strength of the bone to the implant at the interface [13,14].

Since titanium and its alloys exhibit bone-bonding bioactivity when a certain kind of thin ceramic layer is grown on their surface via simple chemical and heat treatments [13], various nanostructured, calcium-incorporated implant surfaces have been introduced [7,14]. Among these, there are surfaces treated with discrete crystal deposition of calcium phosphates [15,16], surfaces obtained through ion-beam assisted deposition of calcium ions [17–19], and surfaces enriched with calcium ions through hydrothermal methods [20].

Human histological studies are certainly the best way to study the bone healing on the implant surfaces [21,22]. Although several studies have shown that the clinical use of implants with nanostructured calcium-incorporated surfaces can ensure high survival and rates success, at least in the short term [23–26], little is known about the early bone response to nanostructured, calcium-incorporated implants in humans. In fact, only a few histologic and histomorphometric studies have addressed this topic [27–29]. Most of these studies were based on few samples, retrieved from the posterior maxilla of different subjects after an unloaded healing period [27–29]; to our knowledge, no human histological and histomorphometric studies on immediately loaded nanostructured calcium-incorporated implants are currently available in the literature.

Hence, the aim of the present randomized controlled histologic and histomorphometric study was to compare the early peri-implant endosseous healing properties of immediately loaded nanostructured, calcium-incorporated (NCI) implants and machined (MA) implants, placed in the native bone of the posterior maxilla.

Materials and methods

Study design

The present study was designed as a randomized controlled histologic/histomorphometric investigation reporting on immediately loaded

temporary transmucosal implants that were placed in the human posterior maxilla and retrieved after a period of 8 weeks. In particular, the study aimed to compare the early bone response to immediately loaded implants with a nanostructured calcium-incorporated (NCI) surface and machined (MA) surface, placed in the human posterior maxilla. During a normal surgical procedure for the placement of conventional implants, each enrolled patient also received 2 temporary transmucosal implants (n=1 NCI implant: test; and n=1 MA implant: control), which were inserted in the posterior maxilla, according to a split-mouth design. The temporary transmucosal implants were placed with the aim to support an interim complete maxillary denture, until healing of the conventional implants. After 8 weeks, during the 2-stage surgery to uncover the conventional implants, all temporary transmucosal implants were retrieved for histologic/ histomorphometric evaluation.

Patient selection

A total of 15 fully edentulous patients (6 males; 9 females; aged between 48– 69 years, mean age 57.9 ± 6.7, median 57, CI 95%: 54.6– 61.2) referred for oral rehabilitation with dental implants to the Oral Implantology Clinic, Dental Research Division, Guarulhos University, SP, Brazil, were consequently enrolled in the present study. Inclusion criteria were good systemic and oral health, and sufficient native bone to place implants of a 3.25 mm diameter and 8 mm length. Exclusion criteria were pregnancy, nursing, smoking, and any systemic condition that could affect bone healing. All participants received detailed explanations about the nature of the study and signed a written informed consent form. The Institutional Clinical Research Ethics Committee of Guarulhos University (CEP #201/03) approved the protocol of the present study, which was conducted according to the principles outlined in the World Medical Association's Declaration of Helsinki on experimentation involving human subjects (2008).

Experimental temporary transmucosal implants

The experimental, specially designed temporary transmucosal implants used in the present study were made of titanium grade 4. All implants were one-piece, macroscopically identical (3.25 mm diameter x 8 mm length), but different in the surface treatment. In fact, test implants (Anyridge®, Megagen Implant Co., Gyeongbuk, South Korea) had a novel calcium incorporated (NCI) titanium implant surface (Xpeed®), while the control implants had a conventional machined (MA) surface. The test implant surface was obtained by modifying an original surface produced by grit-blasting with particles of resorbable calcium phosphate (resorbable blast media, RBM), which was enriched with the calcium using hydrothermal method. In brief, RBM implants were immersed in a mixed solution of 0.2 M sodium hydroxide (NaOH) and 2 mM calcium oxide (CaO) dissolved in deionized water using a teflon-lined hydrothermal reactor system at 180 °C for 24 hrs under a water pressure of 1 MPa[2]. With this procedure, a nanolayer of Ca^{2+} ions was incorporated onto the RBM surface, giving a $CaTiO_3$ nanostructure. The NCI implant surface was investigated with scanning electron microscopy (SEM) *(**Figure 1**)*.

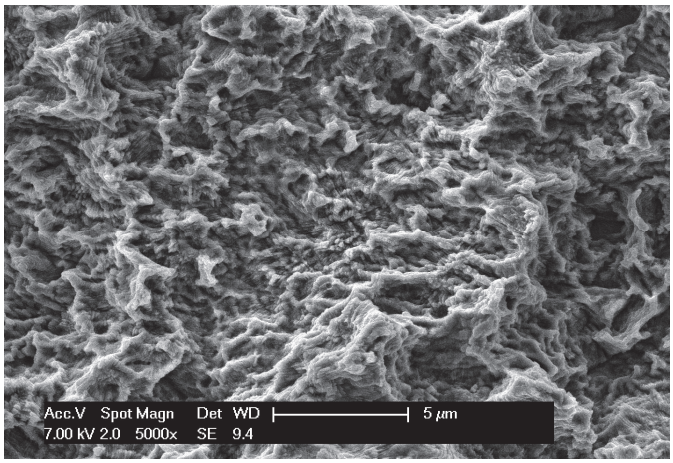

Fig. 1. Nanostructured calcium-incorporated (NCI) implant (test). Scanning electron microscopy evaluation revealed a mean Ra of 1.6 (± 0.2) µm, a mean Rq of 2.1 (± 0.3) µm, and a mean Rt of 15.7 (± 0.2) µm, respectively. Magnification 5000X.

The following standard roughness parameters were measured: Ra (the arithmetic mean of the absolute height of all points), Rq (the square root of the sum of the squared mean difference of all points) and Rt (the difference between the highest and lowest points). The SEM evaluation of NCI surface implants revealed a mean Ra of 1.6 (± 0.2) μm, a mean Rq of 2.1 (± 0.3) μm, and a mean Rt of 15.7 (± 0.2) μm, respectively.

Surgical protocol

Thirty experimental transmucosal temporary implants (n=15 test implants and n=15 control implants) were inserted in this study. All implants were placed under aseptic conditions. After local anesthesia, a crestal incision connected with two releasing vertical incisions was made. Mucoperiosteal flaps were raised and conventional implants were inserted, in accordance with the surgical and prosthetic plan prepared for each patient. After placement of the conventional implants, two experimental transmucosal temporary implants (n=1 test implant and n=1 control implant) were inserted in each patient, according to a split-mouth design. The transitional implants were inserted in the posterior region of the maxilla, among the conventional placed implants. The assignment of test and control implants (right posterior maxilla or left posterior maxilla) was random, as determined by a coin toss. The temporary implant sites were prepared according to the manufacturer's recommendations, under profuse irrigation with sterile saline. The stability of all implants was checked using a dedicated instrument (Osstell Mentor®, Osstell, Goteborg, Sweden): if an implant showed insufficient primary stability (implant stability quotient- ISQ <35), it was removed and a backup surgical site had to be prepared. The flaps were then sutured, to allow the emergency of the solid abutment of one-piece implants through the mucosa: these implants helped to support the interim maxillary denture during the entire healing period. Immediately after implant surgery, the interim maxillary denture was seated in the patient's

mouth and relined intraorally with soft resin. Interim maxillary denture stability, retention, and occlusion were immediately checked. Patients were instructed not to remove the denture for 24 hours to minimize swelling. Clindamycin 300 mg (ClindaminC®, Teuto, Anapolis, Goias, Brazil) was administered three times a day for a week, in order to avoid post-surgical infection. Post-operative pain was controlled with 600 mg ibuprofen (Actron®, Bayer Scherig Pharma, Berlin, Germany) every 12 h for 2 days. To enable subjects to control post-operative dental biofilm, 0.12% chlorhexidine rinses (Chlorexidine®; OralB, Boston, MA, USA) were prescribed, twice a day for 14 day. The sutures were removed after 10 days.

Specimen retrieval and histologic/histomorphometric analysis

The interim prosthesis remained connected to the temporary implants for a period of 8 weeks. After this period, during the 2-stage surgery to uncover the conventional implants, all clinically stable experimental fixtures (one test and one control implant) and the surrounding tissues were retrieved from each patient, using a 4.5-millimeter-wide trephine bur. Clinically mobile temporary implants were not considered for the histologic/histomorphometric evaluation. The specimens were fixed by immediate immersion at 10% buffered formalin and processed (Precise 1 Automated System®, Assing, Rome, Italy) to obtain thin ground sections, as previously described. The specimens were dehydrated in an ascending series of alcohol rinses and embedded in glycolmethacrylate resin (Technovit 7200 VLC®, Kulzer, Wehrheim, Germany). After polymerization, the specimens were sectioned longitudinally along the major axis of the implants with a high-precision diamond disc at about 150 μm and ground down to about 30 μm. Two slides were obtained for each implant. The slides were stained with basic fuchsin and toluidine blue. The specimens were analyzed under a transmitted light microscope (Laborlux S®, Leitz, Wetzlar, Germany) that was connected to a high-resolution video camera (3CCD-

JVC KY-F55B®, JVC, Yokohama, Japan) and interfaced to a monitor and a personal computer (Intel Pentium III 1200 MMX®, Intel, Santa Clara, CA, USA). This optical system was associated with a digitizing pad (D-Pad®, Matrix Vision GmbH, Oppenweiler, Germany) and controlled by a software package with image capturing capabilities (Image-Pro Plus® 4.5, Media Cybernetics, Immagini & Computer Snc, Milan, Italy). For the histomorphometric evaluation, the bone-to-implant contact (BIC%), defined as the amount of mineralized bone in direct contact with the implant surface, was measured around all implant surfaces. Finally, the bone density (BD%) in a 500µm-wide zone lateral to the implant surface was measured bilaterally, as previously reported.

Statistical analysis

All collected data were inserted in a sheet for statistical analysis (Excel 2003®, Microsoft, Redmond, WA, USA). Mean, standard deviation, median and confidence intervals (CI 95%) of histomorphometric values (BIC%, BD%) were calculated for each implant and then for each group of implants (test vs control implants). Comparisons of the differences in bone-implant percentage values in both groups were carried out using the non-parametric Wilcoxon-test, for paired samples. The level of significance was set at 0.05. Results were presented as mean ± standard deviation (SD), and differences at $p < 0.05$ were considered statistically significant. All computations were carried out with a statistical analysis software (SPSS 17.0®, SPSS Inc, Chicago, IL, USA).

Results

Clinical observations

Two months after placement, a total of 30 temporary transmucosal implants (n= 15 test implants and n=15 control implants) were evaluated and

retrieved. Five implants (two test implants and three control implants) in three different patients were clinically unstable, and showed no osseointegration, although they did not show any sign of infection. All implants retrieved from these three patients were excluded from the study, and were not histologically/histomorphometrically evaluated. The remaining 24 implants were clinically stable at the time of retrieval, and were therefore histologically/ histomorphometrically evaluated.

Histologic/ histomorphometric evaluation

In the ground sections from the NCI implants (test), at low-power magnification, it was possible to see newly formed bone around the implant surface. In a few samples, the implants were almost completely surrounded by newly formed bone (***Figure 2***), while in others mature bone was evident far from the implant surface and bone neoformation between the pre-existing bone and the implant surface (***Figure 3***). In the coronal portion only newly formed bone with a trabecular structure and strongly stained with acid fuchsin and a few areas of osteoid matrix could be observed. In some specimens new bone on the surface, even in areas far from the pre-existing bone, was present (***Figure 4***). In some areas of the middle and apical portions of the implants, the native bone was evident far from the surface and newly formed bone was present on the surface. Wide osteocyte lacunae could be observed and they often were in close vicinity to the implant surface (***Figure 5***).

In the MA implants (control), at low-power magnification, compact bone with small marrow spaces was present around all the fixtures, but not in contact with their surface. Only in the apical portion of the threads was it possible to see pre-existing bone in contact with the surface, whilst newly formed bone was evident only in the apical portion of the implants (***Figure 6***).

In the NCI implants (test), the histomorphometric analysis revealed mean (± SD) BIC% and BD% of 39.7 (± 8.7) and 34.6 (± 7.2), respectively. The BIC% ranged from 24.6 to 60.9; the median was 39.1; and the confidence interval (95%) was 34.8– 44.7. The BD% ranged from 19.0 to 45.0; the median was 33.4; and the confidence interval (95%) was 30.5– 38.7.

In the MA implants (control), the histomorphometric evaluation revealed mean (± SD) BIC% and BD% of 21.2 (± 4.9) and 29.8 (± 7.8), respectively. The BIC% ranged from 12.5 to 34.5; the median was 21.0; and the confidence interval (95%) was 18.4– 24.0. The BD% ranged from 19.2 to 44.0; the median was 29.1; and the confidence interval (95%) was 25.4– 34.3.

A significant difference was found between the two implant surfaces with regard to BIC% ($p<0.001$). Although BD% was higher in the test group than in the control group, this difference was not statistically significant ($p=0.09$). The histomorphometry was summarized in ***Figures 7, 8***.

Fig 2. Nanostructured calcium-incorporated (NCI) implant (test). Newly formed trabecular bone surrounded the whole implant perimeter. Acid fuchsin and toluidine blue, magnification 12X.

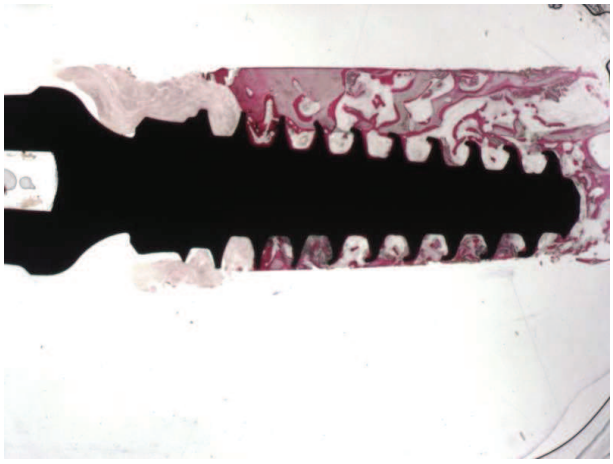

Fig 3. Nanostructured calcium-incorporated (NCI) implant (test). Pre-existing bone far from the implant surface and newly formed bone close to it were evident. Acid fuchsin and toluidine blue, magnification 12X.

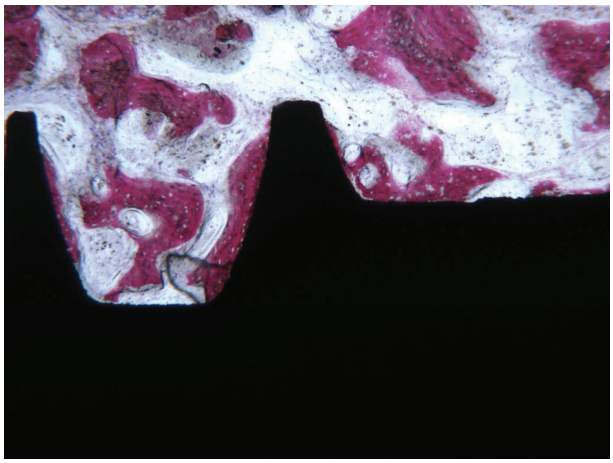

Fig 4. Nanostructured calcium-incorporated (NCI) implant (test). Newly formed trabecular bone around and in contact with the coronal portion of the implant. Acid fuchsin and toluidine blue, magnification 40X.

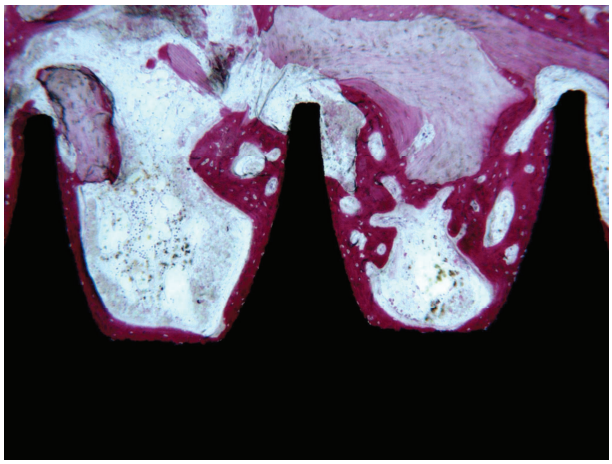

Fig 5. Nanostructured calcium-incorporated (NCI) implant (test). The implant thread was lined by newly formed bone and an intense osteoblastic activity was still evident. Acid fuchsin and toluidine blue, magnification 40X.

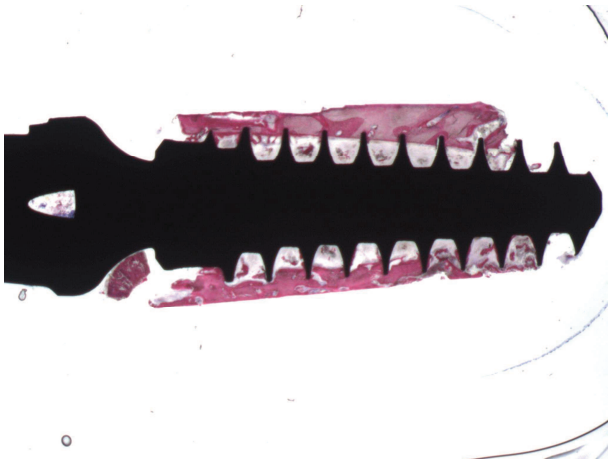

Fig 6. Machined implant (control). Compact bone with small marrow spaces was present around the implant but not in contact with its surface. Acid fuchsin and toluidine blue, magnification 12X.

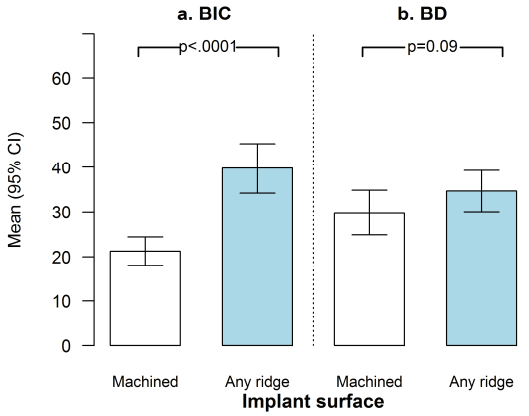

Fig 7. Histomorphometric results with MA and NCI implants: bone-to-implant contact (BIC%) and bone density (BD%). In the MA implants, the histomorphometric evaluation revealed mean (± SD) BIC% and BD% of 21.2 (± 4.9) and 29.8 (± 7.8), respectively. In the NCI implants, the histomorphometric analysis revealed mean (± SD) BIC% and BD% of 39.7 (± 8.7) and 34.6 (± 7.2), respectively.

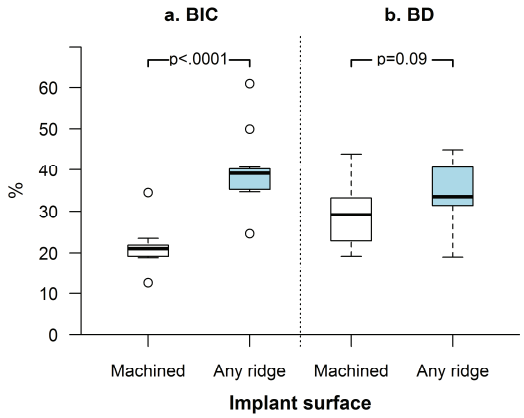

Fig 8. Histomorphometric results with MA and NCI implants: bone-to-implant contact (BIC%) and bone density (BD%). A statistically significant difference was found between the two surfaces with regard to BIC% (p<0.001), while no significant difference was found with regard to BD% (p=0.09).

Discussion

At present, histologic/histomorphometric assessment is the most accurate method to investigate the bone healing processes and morphological characteristics of the bone–implant interface [21,22].

Unfortunately, only a few studies in the present literature have dealt with histologic/ histomorphometric evaluation of human-retrieved NCI implants [27–30]: this is because of ethical issues related to implant retrieval from human subjects.

In a human histologic and histomorphometric study, Goenè and coll. [27] inserted 9 pairs of small experimental implants (9 dual acid-etched conditioned with discrete crystal deposition of nanometer-scale crystals of calcium phosphate as the test, and 9 conventional dual acid-etched as the control) in the native bone of posterior maxilla. The implants were retrieved with trephine drills after 4 or 8 weeks of unloaded healing, for the purpose of assessing the rate and extent of new bone development through histologic analysis [27]. The mean bone-to-implant contact value for the test implants was significantly increased over that of the control implants at both time intervals [27]. The authors concluded that the addition of a nanometer-scale calcium phosphate treatment to a dual acid-etched implant surface increased the extent of bone apposition after 4 and 8 weeks of healing [27].

Similar results were obtained by Orsini and coll. [28], who evaluated the bone response to the same nanostructured implant surface, obtained through discrete deposition of nanometer-sized calcium phosphate particles on a dual acid-etched surface. One experimental mini-implant with a novel nanostructured calcium-phosphate added surface (test) and one dual acid-etched surface mini-implant (control) were placed in the posterior maxilla of 15 patients. After 2 months, the mean BIC% was 32.2 (± 18.5) and 19.0 (± 14.2) for test and control implants, respectively: this difference was statistically significant [28]. In the test specimens, new bone was tightly contacting the implant surface, with better adaptation to the threads. These

results were confirmed by the 3D reconstruction of sections obtained using confocal laser scanning microscopy (CLSM), that showed the intimacy of the contact between the bone and test surface through the entire thickness of the specimens [28]. The authors concluded that the use of implants with novel nanostructured calcium-phosphate surface may be indicated in areas of poor bone quality [28].

Finally, Tellemann and coll. [29] inserted two experimental mini-implants (one dual acid-etched implant as the control, and one dual acid-etched implant conditioned with discrete deposition of nanometer-sized calcium phosphate particles as the test) to fixate an iliac crest bone graft to the maxilla of 15 patients. A part of each mini-implant was in contact with the grafted bone and a part extended into the native maxillary bone [29]. After an undisturbed healing period of 3 months, the specimens were harvested for the histological evaluation [29]. At the end of the study, the discrete deposition of nanometer-size crystal of calcium-phosphate increased the peri-implant endosseous healing properties in the native bone of the maxilla compared with the conventional dual acid-etched surface, with a statistically higher BIC%; however, no significant difference in new bone apposition was reported in the bone graft area [29].

Shibli and coll. [30] evaluated the influence of two different implant surfaces (a bioceramic molecular impregnated surface as the test, versus a dual acid-etched surface as the control) on the bone-to-implant contact (BIC%) and bone osteocyte density in the human posterior maxilla after 2 months of unloaded healing. Ten patients received two implants (one of each surface) during conventional implant surgery in the posterior maxilla [30]. After an undisturbed healing period of 2 months, the implants and the surrounding tissue were removed for histologic/histomorphometric analysis [30]. Histometric evaluation showed significantly higher BIC% for the test compared to the control surface. These data suggested that the bioceramic molecular impregnated surface-treated implants positively modulated bone healing at early implantation times compared to the dual acid-etched surface [30].

Although all the aforementioned human studies suggest that treatment with nanometer-sized calcium phosphate particles can promote osseointegration, supporting new bone formation on the implant surface [27–30], still there are no histologic/histomorphometric studies on the immediate loading of NCI implants in humans.

Therefore, the aim of our present randomized, controlled histologic/histomorphometric study was to evaluate the early bone formation around immediately loaded NCI implants placed in the human posterior maxilla, and to compare these results with those obtained with macroscopically identical implants with a MA surface. Fifteen fully edentulous patients were installed with two temporary transmucosal implants with different surfaces: 1 NCI (test) and 1 MA (control) implant. All temporary implants were placed in the posterior maxilla, according to a split-mouth design, and were subjected to immediate loading conditions, since they helped to support an interim complete maxillary denture. After 8 weeks, all temporary transmucosal implants were retrieved for histologic/histomorphometric evaluation. In the MA implants, the histomorphometric evaluation revealed mean (± SD) BIC% and BD% of 21.2 (± 4.9) and 29.8 (± 7.8), respectively. In the NCI implants, the histomorphometric analysis revealed mean (± SD) BIC% and BD% of 39.7 (± 8.7) and 34.6 (± 7.2), respectively. A statistically significant difference was found between the two surfaces with regard to BIC% ($p<0.001$), while no significant difference was found with regard to BD% ($p=0.09$). Hence, the results of our study seem to confirm that the deposition of calcium-phosphate nanoparticles on the implant surface can actually stimulate bone healing in the short-term, even under critical conditions, such as immediate loading in the posterior maxilla [22]. This can represent an important advantage today, in a context in which immediate loading is increasingly demanded by patients and practiced by clinicians [31,32], as it may contribute to the survival and success of dental implants in the long term [22]. In our present study, in particular, a blasted titanium surface was thermally modified to form a nanostructured calcium-incorporated (NCI) surface [20]. This procedure has the potential to increase the

osteoconductivity of endosseous implants at the cellular level. In fact, calcium titanate ($CaTiO_3$) has been shown to promote osteoblast adhesion and proliferation; moreover, increased calcium composition in the outer oxide layer increased protein adsorption onto the titanium surface by ionic bonding at a physiological pH, which subsequently affected cell adhesion [11,12,20]. This finally results in a biochemical bone bonding of NCI implants in vivo, as previously reported [12,20] and confirmed here. Recently, several clinical studies have reported excellent survival and success rates for implants with a surface enriched with calcium ions through hydrothermal methods, in different clinical contexts [5,25,26,33,34].

Our present study has limits, such as the limited number of implants placed and retrieved. In addition, only patients in whom both implants were clinically stable were considered for the histologic/ histomorphometric evaluation. In fact, five implants (two test and three control implants) in three different patients were clinically unstable, and showed no osseointegration: these patients were therefore excluded from the study, and their implants were not considered for the histologic/ histomorphometric evaluation. For all these reasons, more randomized controlled clinical studies are needed to confirm the evidence emerging from our present histologic/histomorphometric work.

Conclusions

Within the limits of these histologic/histomorphometric data, immediately loaded NCI temporary implants in human posterior maxilla presented statistically significantly higher BIC% compared to MA implants. However, these data must be considered with caution because of the study design and methodology (only stable implants were evaluated). Therefore, additional controlled randomized clinical studies are needed to draw more specific conclusions about the early bone response to NCI implants, when subjected to immediate loading.

Acknowledgments

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C. The implant/Abutment Interface. Role of The Implant/Abutment Connection in the Incidence of Complications Affecting Fixed Implant-Supported Restorations

Survival and Complication Rates of Fixed Restorations Supported by Locking-Taper Implants: a Prospective Study with 1- to 10- Years of Follow-up

The present study has been submitted for publication, as a part of my PhD research project, accepted and published in its current form by the Journal of Prosthodontics: Mangano F, Macchi A, Caprioglio A, Sammons RL, Piattelli A, Mangano C. Survival and complication rates of fixed restorations supported by locking-taper implants: a prospective study with 1- to 10-years of follow-up. J Prosthodont 2014; 23 (6): 434-444. Permission has been obtained to publish the present work here.

Abstract

Purpose: The aim of this 10-year follow-up study was to evaluate the implant survival and complication rates of fixed restorations supported by locking-taper implants.

Materials and methods: Over a 10-year period (January 2002- December 2011) all patients referred to a single private dental practice for treatment with fixed restorations (single crowns, SCS; fixed partial prostheses, FPPs; fixed full arches, FFAs) supported by dental implants were considered for inclusion in this study. At each annual follow-up session, clinical, radiographic and prosthetic parameters were assessed. The surviving implant-supported restorations were defined as “complication free” in the absence of any biological or prosthetic (mechanical or technical)

complication. The cumulative implant survival and the “complication-free” survival of fixed implant-supported restorations were assessed using the Kaplan-Meier survival estimator. The Log-rank test was applied to evaluate correlations between the study variables.

Results: In total, 1494 locking-taper implants (727 maxilla, 767 mandible) were placed in 642 patients (356 males, 286 females). Nineteen implants (12 maxilla, 7 mandible) failed. Implant failures were attributed to lack of osseointegration (14 implants), peri-implantitis (4 implants), mechanical overloading (1 implant). An overall 10-year cumulative implant survival rate of 98.7% (98.3% maxilla, 99.1% mandible) was found. The implant survival rates did not differ significantly with respect to implant location, position, bone type, implant length and diameter, type of restorations. Among the surviving implant-supported restorations (478 SCs, 242 FPPs, 19 FFAs), a few biological (11/739: 1.4%) and prosthetic (27/739: 3.6%) complications were reported. The incidence of mechanical complications was low (3/739: 0.4%), with 3 loosened abutments in 3 SCs (3/478: 0.6%), and no abutment fractures; technical complications were more frequent (24/739: 3.2%), with an incidence of decementation of 2.0% (SCs 2.0%, FPPs 1.6%, FFAs 5.2%) and ceramic/veneer chipping/fracture of 1.2% (SCs 0.0%, FPPs 2.8%, FFAs 10.5%). At the end of the study, a 10-year overall cumulative “complication-free” survival of restorations of 88.6% (SCS 91.7%, FPPs 83.1%, FFAs 73.8%) was reported. The complication rates differ significantly with respect to the type of restoration ($p<0.05$).

Conclusions: Fixed restorations on locking-taper implants seem to be a successful procedure for the rehabilitation of partially and completely edentulous arches.

Keywords

Implant survival, Mechanical complications, Technical complications, Morse taper connection implants.

Introduction

Implant treatment has proven to be a predictable modality for replacing missing or failing teeth with various types of fixed dental prostheses, and more than 30 years of evidence of the clinical use of endosseous implants has revealed satisfactory long-term results [1–3].

Although dental implants have become the state of the art method for tooth replacement, implant-supported restorations are still subject to biological and prosthetic complications [4,5]. Prosthetic complications arising in implant-supported fixed restorations range from mechanical complications, defined as failures or complications of pre-fabricated components (screw or abutment loosening, screw or abutment fracture) and technical complications, defined as superstructure-related failures or complications (ceramic or veneer fractures) [6,7].

A series of systematic reviews based on clinical studies have evaluated the survival and complication rates of fixed implant-supported reconstructions of different designs, and described a high incidence of mechanical complications after an observation period of at least 5 years, such as abutment screw fracture and loosening, with percentages between 1.3% and 9.3%, 5.3% and 10.4% respectively [4,6,8–11]. Screw loosening, in particular, appears to be a greater problem with single-tooth restorations replacing maxillary and mandibular molars, where the mechanical load is higher [12,13]. Clinical studies on single-unit restorations have reported abutment screw loosening percentages between 5% and 48% [12–17]. This may not lead to implant loss, but is significant in relation to the amount of repair and maintenance needed, time and cost, and may adversely affect the patient's satisfaction with the implant treatment [5,11,18].

As to the commonly observed mechanical failures, loosening and/or fracture of fixation screws or abutments have been related to the type of implant-abutment connection [18,19]. Currently, the most commonly used systems for securing the abutment to the implant involve screw-type connections [18,19], and two basic designs are available for clinical use:

butt-joint indexed external or internal connections. A butt joint only stabilizes the connection between the abutment and the implant fixture by the axial preload of the abutment screw. Occlusal force to the connection is concentrated at the abutment screw, thus the optimum preload is critical for joint stability [20,21]. In fact, stability of screw-type connections is challenged by forces exceeding that of the torqued implant-abutment system: if occlusal loads exceed the preload, the screw can loosen or break [20,21]. In addition, lower masticatory forces, applied repeatedly, although they do not necessarily surpass the failure threshold of the assembly, may potentially lead to gradual loosening of the implant-abutment connection, as a result of fatigue [20,21].

A suitable alternative to butt-joint connections may be the introduction of frictional systems such as conical connections [20], including pure interference-fit (locking-taper) connection implants [22–26]. In these screwless implant systems, the abutment is retained by means of friction force: the connection is based on the principle of ‘‘cold welding’’, as it relies on the large contact pressure and frictional resistance between the surfaces of the implant and the abutment [22,23].

The mechanical advantages of pure interference-fit connection over external and internal hexagonal design were reported in several in vitro studies [22–27], demonstrating that locking-taper implants can resist eccentric loading complexes and bending moments, ensuring an absolute mechanical stability at the implant-abutment connection. Previous clinical studies with locking-taper implants have confirmed a reduction of the incidence of prosthetic complications [18,28–30]; however, there are no studies dealing with the prosthetic complications encountered during the maintenance phase with these implants in the long-term. An accepted way of describing the susceptibility to complications is to report the “complication-free” survival rate [31]: this useful success index indicates that a restoration is free of both biological and prosthetic problems [31].

The aim of this prospective 10-year follow-up study was to assess the implant survival and “complication free” survival rate of fixed restorations

supported by locking-taper implants, with particular attention to the evaluation of the incidence of mechanical (abutment loosening, abutment fracture) and technical (loss of retention, fracture of porcelain) complications.

Materials and methods

Patient selection

Between January 2002 and December 2011, all patients referred to a single private dental practice (Gravedona, Como, Italy) for treatment with fixed rehabilitations supported by dental implants were considered for inclusion in the present study. All treatments were carried out by the same practitioner. Inclusion criteria were as follows: (1) age >18 years; (2) good systemic and oral health; (3) adequate bone height and width to place an implant of 3.3 mm in diameter and 8.0 mm in length; (4) at least 6 weeks of healing after tooth extraction; (5) dentition in the opposing jaw to obtain occlusal contacts. Exclusion criteria were: (1) poor oral hygiene; (2) active periodontal infections or other oral disorders; (3) insufficient bone quantity to place an implant of at least 3.3 mm in diameter and 8.0 mm length; (4) bone augmentation procedures with autogenous bone or bone substitutes; (5) uncontrolled diabetes mellitus; (6) coagulation disorders; (7) systemic immune disorders; (8) drug or alcohol abuse. Smoking and bruxism were recorded but were not considered as exclusion criteria for this study. Patients received detailed information about the study protocol and were required to sign an informed consent form. The requirements of the World Medical Association's Declaration of Helsinki on experimentation involving human subjects (2000) and those of the Local Ethics Committee were met.

Pre-surgical preparation

Before the implant installation, a complete oral examination regarding periodontal disease, caries and soft tissue disorders was carried out for each patient. Patients received appropriate treatments and oral hygiene instruction. Panoramic radiographs and in some cases computed tomography (CT) scans were obtained before implant placement. CT datasets were acquired and then transferred to implant navigation software, to perform a three- dimensional reconstruction of the maxillary bones. With this navigation software it was possible to correctly assess the width of each implant site, the thickness and the density of the cortical plates and the cancellous bone, as well as the ridge angulation. Pre-operative work-ups also included an assessment of the edentulous ridges using casts and diagnostic wax-up.

Surgical and restorative procedure

Sandblasted and acid-etched implants, made of grade-5 titanium (Leone Implant System®, Florence, Italy) were used [18,30]. This implant system uses a cone Morse taper-interference-fit locking taper combined with an internal hexagon (***Figure 1***). The Morse taper presents a taper angle of 1.5° [18,30]. The implant neck was positioned at the bone crest level. A two-stage technique was used to place the implants, which were left submerged for a period of 3-4 months as previously described. After the healing period, provisional restorations were provided consisting of single crowns (SCs), fixed partial prostheses (FPPs) and fixed full-arches (FFAs). The temporary restorations remained in situ for 3 months, and after this period definitive restorations were placed. All definitive restorations were ceramo-metallic, cemented with temporary zinc oxide- eugenol cement (Temp-Bond®, Kerr, Orange, CA, USA). All restorations were carefully evaluated for proper occlusion, and protrusion and laterotrusion were assessed on the articulator and intraorally.

Fig. 1. Schematic representation of the implant-abutment connection of the Exacone Implant System® (Leone, Florence, Italy). The implant-abutment connection features a self-locking Morse taper combined with an internal hexagon for the repositioning of the abutment. The Morse taper presents a taper angle of 1.5°.

Follow-up examinations

All patients were enrolled in an annual recall program. During each annual follow-up visit, the following clinical, radiographic and prosthetic parameters were assessed by a surgeon and a prosthodontist, who were not directly involved in the treatment of the patients:

(1) Clinical parameters. The following clinical parameters were investigated: (a) presence/absence of pain or sensitivity [32]; (b) presence/absence of suppuration or exudation [32]; (c) presence/absence of implant mobility, tested manually using the handles of two dental mirrors [32]; (d) periodontal probing depth (PPD) in mm, measured using a periodontal probe (PGF-GFSR®, Hu-Friedy, Chicago, IL, USA) on the same surfaces. For each implant, the PPD value was calculated based on the average of four measured values [32].

(2). Radiographic parameters. Intraoral periapical radiographs were taken for each implant, using a Rinn alignment system (Rinn®, Dentsply, Elgin, IL, USA) with a rigid film-object-X-ray source coupled to a beam-aiming

device in order to achieve reproducible exposure geometry [33]. Customized positioners, made of polyvinyl siloxane, were used for precise repositioning and stabilization of the radiographic template. Radiographs were taken at the baseline (immediately after implant insertion), and at each follow-up session [33]. Changes in peri-implant marginal bone level, as modifications in the distance from the implant shoulder to the first visible bone-to-implant contact (DIB), were measured on periapical radiographs which were taken immediately after installation and at each follow-up examination [33]. The DIB was measured in mm, at the mesial and distal implant side of each implant, with the aid of an ocular grid. In order to correct dimensional distortion, the apparent dimension of each implant was measured on the radiograph and then compared with the real implant length; mean values between the mesial and the distal measures were obtained for each implant [33].

(3) Prosthetic parameters. Static and dynamic occlusions were evaluated using standard occluding papers (Bausch articulating paper®, Bausch inc, Nashua, NH, USA). All prosthetic complications, including mechanical (abutment loosening, abutment fracture) and technical complications (decementation, ceramic/veneer chipping or fracture) were carefully registered, and if possible, managed during the follow-up visit; additional appointments were arranged if needed.

Outcome variables

The primary outcome variables were the implant survival and the “complication-free” survival rate of the implant-supported restoration. The evaluation of implant survival and the “complication-free” survival rate of the implant-supported restoration was performed according to the following clinical, radiographic, and prosthetic parameters:

(1) Implant survival. Implant losses were all categorised as failures. Failure to osseointegrate with implant mobility in the absence of clinical signs of

infection, persistent/recurrent peri-implant infections with pain/suppuration/bone loss, progressive marginal bone loss due to mechanical overload and implant body fracture were the conditions for which implant removal could be indicated. A distinction was made between “early” (before the abutment connection) or “late” (after the abutment connection) implant failures [32,33].

(2) “Complication free” survival rate of implant-supported restoration. The surviving implant-supported restorations were defined as “complication free” in the absence of any complication, during the entire follow-up period. Complications were divided into two types:

(a) Biological complications, including: (aa) disturbances in the function of the implant characterized by a biological process affecting the supporting tissues and structures, such as soft tissue inflammation (peri-implant mucositis with pain/swelling) or peri-implant infection with fistula formation, pain, suppuration or exudation (the threshold to define peri-implantitis was set at a probing pocket depth ≥6 mm with bleeding on probing/suppuration and a radiographic bone loss/distance between the implant shoulder and the first visible bone-to-implant contact (DIB)>2.5 mm); (aaa) bone loss, defined as a distance between the implant shoulder and the first visible bone-to-implant contact (DIB)> 1.5 mm after the first year of function, or exceeding 0.2 mm for each following year, without clinical signs of peri-implant infection [32,33].

(b) Prosthetic complications, including: (bb) mechanical complications, defined as failures or complications related to implant pre-fabricated components, such as abutment loosening or abutment fracture; (bbb) technical complications, defined as superstructure-related failures or complications, such as decementation or ceramic/veneer chipping or fractures.

Statistical analysis

Data collection and analyses were performed by two independent examiners (a surgeon and a prosthodontist) who were not directly involved in the study. Databases were created with Excel 2003 (Microsoft Excel®, Microsoft Corporation, Redmond, WA, USA) and used for the analysis. Descriptive statistics were used for patient demographics, distribution of implants, radiographic bone loss, biologic and prosthetic complications. Absolute and relative frequency distributions were calculated for qualitative variables, and means ± standard deviations (SD) were calculated for quantitative variables. The implant survival and the "complication-free" survival rate of implant-supported restorations were the principal outcomes of the study, and were analyzed as a function of time using the Kaplan-Meier survival estimator [34]. The cumulative implant survival rate was estimated by an implant-based analysis (at the implant level), while the cumulative "complication-free" survival rate of implant-supported restorations was estimated by a restoration-based analysis (at the restoration level). Variables including implant location (mandible or maxilla), implant position (incisors, cuspids, premolars or molars), bone type (type I, II, III or IV), implant length (8.0, 10.0, 12.0 or 14.0 mm), implant diameter (3.3, 4.1 or 4.8 mm) and the type of prosthetic restoration (SCs, FPPs, FFAs) were analyzed at the implant-level; the variable of prosthetic restoration (SCs, FPPs, FFAs) was analyzed at the restoration level too. Bone quality was ascertained clinically by tactile evaluation at the time of implant placement, during drilling, according to the clinician's judgment and by radiographic assessment. In particular, following the withdrawal of an osteotomy reamer, an assessment of the bone in the reamer flutes was conducted in terms of quality and appearance. Bone quality was classified as type I if the bone was compact, cortical and near bloodless. Type II bone was red and filled the flutes of the reamer. If no bone remained in the flutes, the bone quality was classified as type IV. If the findings were intermediate between those described for types II and IV, the bone was categorized as type III. In both the implant-based and the restoration-based analysis, the Log-rank Mantel-Cox test was used to compare the primary outcomes

within comparable subgroups. All computations were carried out with the statistical software package SPSS 17.0® (SPSS Inc., Chicago, IL, USA). The significance level was set at 0.05.

Results

Patient population and implant-supported rehabilitations

From January 2002 to December 2011, 664 patients (368 males and 296 females) were considered for inclusion in this prospective clinical study. With regard to the inclusion/exclusion criteria, 22 patients could not take part (9 for inadequate bone height and width, 13 for poor oral hygiene and active periodontal infections). In total, 642 patients (356 males and 286 females, aged 20 to 82 years) fulfilled the inclusion criteria, presenting no conditions listed in the exclusion criteria, and were subsequently enrolled in this study. Among these patients, 72 were smokers and 45 were bruxists. One-thousand, four-hundred and ninety-four implants were placed. Seven-hundred and twenty-seven implants (48.7%) were inserted in the maxilla, while 767 implants (51.3%) were inserted in the mandible. Two-hundred and twenty-eight (15.2%) implants were placed in the maxillary anterior region, while 499 implants (33.4%) were placed in the maxillary posterior region; 114 implants (7.6%) were placed in the mandibular anterior region and 653 implants (43.8%) in the mandibular posterior region. The distribution of the implants by position was in accordance with ***Figure 2***. The most frequently used implant diameter was 4.1 mm, with 820 implants (54.8%), followed by 4.8 mm, with 417 implants (28.0%), and 3.3 mm, with 257 implants (17.2%). Despite the implant diameter, the most frequently inserted implants were 12.0 mm long (767 implants, 51.3%), 10.0 mm long (356 implants, 23.9%) and 14.0 mm long (272 implants, 18.2%), while 8.0 mm implants (99 implants, 6.6%) were the least used. The most frequent indication was the treatment of partially edentulous patients (636 implants, 42.6%) while the least frequent was the restoration of fully edentulous

patients (376 implants, 25.1%); 482 implants (32.3%) were used to restore single tooth gaps.

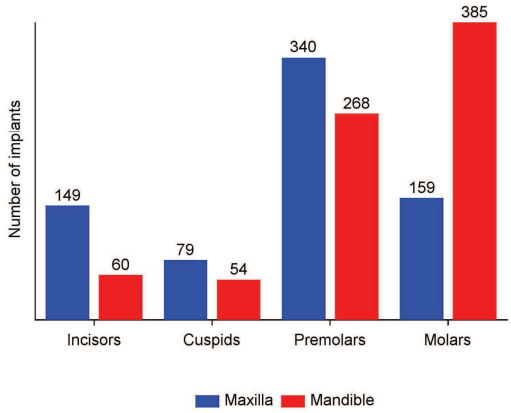


Fig. 2. Implant distribution by position.

Implant survival

Of the 642 patients who received implants during the period from 2002 to 2011, 18 patients were classified as dropouts, because they were lost to follow-up, as they did not attend the final examination. Among these, 4 patients had died, 5 patients missed the last scheduled appointment because of serious illness, while 4 patients were not available because they moved to other cities/countries; finally, 5 patients simply did not consult the clinic again for follow-up. At the end of analysis (December 2012), a total of 624 patients had completed the follow-up evaluation in full. Nineteen implants failed and had to be removed, in 18 different patients. At the end of the study, an overall cumulative implant survival rate of 98.7% was achieved at 10-year follow-up, with 1475 implants still in function. In the maxilla, the cumulative survival rate was 98.3%, with 12 implants failed and removed. In the mandible, the cumulative survival rate was 99.1%, with 7 implant failures. With regard to the position of the failed implants, 10 were molars (5 maxilla, 5 mandible), 8 were premolars (6 maxilla, 2 mandible), and 1 was a maxillary incisor. The majority of implants (16) were lost within

the healing period, before the connection of the prosthetic abutment. These implants were classified as “early failures” due to lack of osseointegration/implant mobility without any clinical sign of infection (14 implants), or recurrent/persistent peri-implantitis (2 implants) with pain and suppuration, before functional loading. Three implants failed and had to be removed after the abutment connection, and were classified as “late failures”. Two of these implants failed 2 years after placement, one because of progressive bone loss due to mechanical overloading, without clinical signs of peri-implant infection, and the other because of severe bone loss due to recurrent/persistent peri-implant infections. In addition, another implant failed 4 years after placement, because of recurrent/persistent peri-implant infections with pain, suppuration and severe bone loss. The details of the failed implants were recorded in ***Table. 1***. The evaluation of the potential influence of different implant-related variables on implant survival is shown in ***Table 2***. The implant survival rate did not differ significantly with respect to implant location, position, bone type, implant length, diameter and type of prosthetic restoration.

Complications

During the follow-up period, 3 of prostheses had to be removed due to late implant failures. These failures affected a single crown and 2 fixed partial prostheses; for this reason, these restorations had to be renewed. Among the surviving 739 implant-supported restorations (478 SCs, 242 FPPs, 19 FFAs), during the 10-year follow-up period, an overall incidence of biologic complications of 1.4% was reported. In fact, biological complications were recorded for 11 restorations (15 implants). Of these implants, 2 exhibited peri-implant mucositis, with clinical signs of soft tissue inflammation (redness, swelling and bleeding), while 7 restorations (10 implants) were associated with peri-implant infection with pain, probing pocket depth ≥6 mm with bleeding on probing/suppuration and severe bone loss (DIB > 2.5 mm). In all these cases, however, the anti-infection therapy was successful and the implants were maintained. Finally, 3 restorations (3 implants) were

associated with bone loss (DIB> 1.5 mm after the first year of function) without clinical signs of peri-implant infection. All other implants were clinically and radiographically successful, as they did not show any biological complication. They did not cause pain or exhibit clinical mobility, suppuration, or exudation, with a DIB <1.5 mm after the first year of function and not exceeding 0.2 mm for each following year. The radiographic evaluation of the implants revealed a mean DIB of 0.33 (± 0.23), 0.45 (± 0.26) and 0.78 (± 0.33) mm at the 1-, 5-, and 10-year follow-up session was evidenced, respectively. Minimal changes were seen in the bone level between the 1- and 10-year examinations (***Figures 3-4; Table 3***). Globally, there was a low incidence of mechanical complications related to pre-fabricated components (0.4%). Three prosthetic abutments became loose during the first year of loading, in three single crowns (SCs) located in the posterior area of the mandible. These abutments were re-inserted and no further loosening was observed in the period of the present study. The incidence of abutment loosening was 0.6% for SCs only. No mechanical complications were observed at the implant-abutment connection for FPPs and FFAs, and no abutment fractures were evidenced. These reported mechanical complications required only minor interventions (<10 minutes chair time), and no additional costs had to be charged to the patients. The overall incidence of technical complications was slightly higher (3.2%): in fact, 10 SCs, 11 FPPs and 3 FFAs had some technical complication. However, most of these were minor, such as decementation/loss of retention, with an overall incidence of 2.0% (SCs 2.0%, FPPs 1.6%, FFAs 5.2%) and no additional costs were charged since they required < 10 minutes chair time. Finally, the overall incidence of ceramic/veneer chipping/fracture of the laboratory-fabricated prostheses was 1.2%. Fracture of the porcelain occurred in 7 FPPs and in 2 FFAs, with an incidence of 2.8% and 10.5%, respectively. In these cases, major interventions (>60 minutes chair time) were needed, since new restorations were provided to the patients. For this reason, additional costs had to be charged. Additional costs included dental laboratory costs for new FPPs, FFAs and new porcelain on the frames. The biological and prosthetic

complications encountered in this study are summarized in ***Table 4***. At the end of the study, a 10-year overall cumulative "complication-free" survival of restorations of 88.6% (SCS 91.7%, FPPs 83.1%, FFAs 73.8%) was reported. The complication rates differed significantly with respect to the type of prosthetic restoration ($p<0.05$), as there were significantly less complications on SCs than on FPPs and FFAs (***Figures 5-6***).

Table 1. Details of implant failures: FO= failure to osseointegrate/implant mobility without clinical signs of infection; PI= peri-implantitis; MO= mechanical overload.

Month	Reason	Location	Position	Bone	Length	Diameter
4	FO	maxilla	premolar	III	12	3.3
4	FO	maxilla	premolar	IV	14	3.3
3	FO	mandible	molar	III	14	4.1
4	FO	maxilla	premolar	III	12	4.1
4	FO	mandible	molar	III	12	4.1
3	FO	mandible	molar	III	12	4.1
4	FO	maxilla	molar	II	10	4.1
3	FO	mandible	molar	IV	10	4.1
4	FO	maxilla	molar	IV	14	4.1
4	PI	maxilla	premolar	IV	10	4.1
4	FO	maxilla	incisor	II	14	4.1
4	PI	maxilla	premolar	IV	12	4.1
3	FO	mandible	premolar	III	14	4.8
4	FO	maxilla	premolar	IV	10	4.8
4	FO	maxilla	molar	IV	12	4.8
4	FO	maxilla	molar	IV	8	4.8
24	MO	mandible	premolar	III	12	3.3
24	PI	mandible	molar	IV	12	4.1
48	PI	maxilla	molar	III	12	4.1

Table 2. Cumulative implant survival rate (CSR%).

	Implants	Failures	CSR (%)	P- value
Location				
Maxilla	727	12	98.3	0.206
Mandible	767	7	99.1	
Position				
Incisors	209	1	99.5	0.256
Cuspids	133	0	100	
Premolars	608	8	98.7	
Molars	544	10	98.1	
Bone type				
Type I	84	1	98.8	0.198
Type II	292	2	99.3	
Type III	727	7	99.0	
Type IV	391	9	97.7	
Length				
8.0 mm	99	1	99.0	0.825
10.0 mm	356	4	98.9	
12.0 mm	767	9	98.8	
14.0 mm	272	5	98.2	
Diameter				
3.3 mm	257	3	98.8	0.733
4.1 mm	820	12	98.5	
4.8 mm	417	4	99.0	
Restoration				
SCs	482	4	99.2	0.538
FPPs	636	10	98.4	
FFAs	376	5	98.6	

Table 3. Peri-implant bone loss (as distance between the implant shoulder and the first visible bone-to-implant contact, DIB, in mm)

Year	Mean	SD	Median	CI (95%)
1	0.33	0.23	0.3	0.32- 0.34
5	0.45	0.26	0.4	0.43- 0.47
10	0.78	0.33	0.7	0.72- 0.84

Table 4. Incidence of complications among the different implant-supported restorations.

	Single crowns (SCs)	Fixed partial prostheses (FPPS)	Fixed full arches (FFAs)	Overall
Biological Complications				
Soft tissue inflammation	0/478 (0.0%)	1/242 (0.4%)	0/19 (0.0%)	1/739 (0.1%)
Peri-implantitis	2/478 (0.4%)	4/242 (1.6%)	1/19 (5.2%)	7/739 (0.9%)
Peri-implant bone loss	0/478 (0.0%)	3/242 (1.2%)	0/19 (0.0%)	3/739 (0.4%)
Prosthetic complications				
Abutment loosening	3/478 (0.6%)	0/242 (0.0%)	0/19 (0.0%)	3/739 (0.4%)
Abutment fracture	0/478 (0.0%)	0/242 (0.0%)	0/19 (0.0%)	0/739 (0.0%)
Loss of retention	10/478 (2.0%)	4/242 (1.6%)	1/19 (5.2%)	15/739 (2.0%)
Ceramic chipping/ fracture	0/478 (0.0%)	7/242 (2.8%)	2/19 (10.5%)	9/739 (1.2%)
Total	15/478 (3.1%)	19/242 (7.8%)	4/19 (21.0%)	38/739 (5.1%)

Figure 3a. Maxillary second premolar, radiographic control of the implant after 1 year of function.

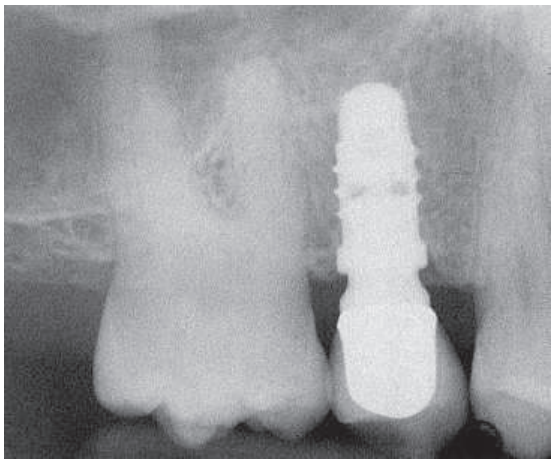


Figure 3b. Maxillary second premolar, radiographic control of the implant after 5 years of function.

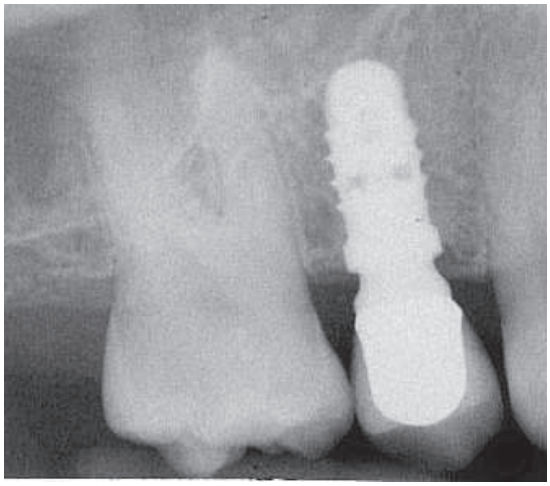


Figure 3c. Maxillary second premolar, radiographic control of the implant after 10 years of function.

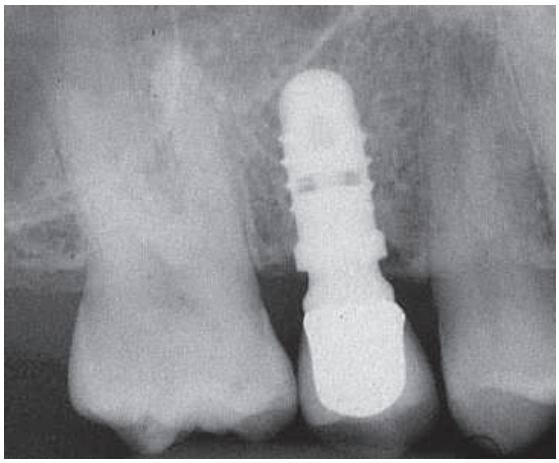


Figure 4a. Mandibular first molar, radiographic control of the implant after 1 year of function.

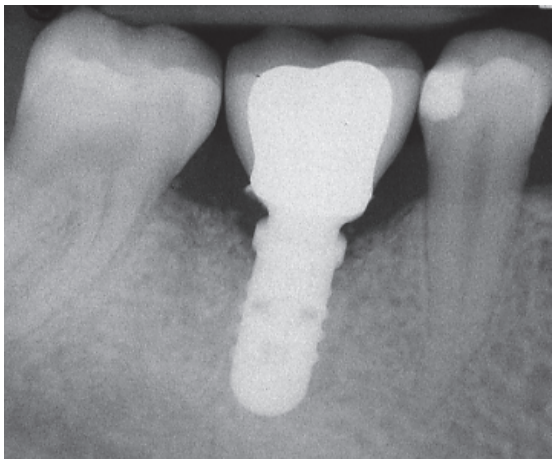


Fig. 4b. Mandibular first molar, radiographic control of the implant after 5 years of function.

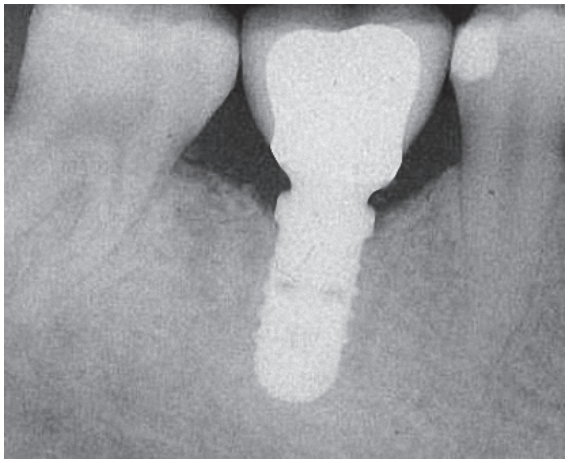


Figure 4c. Mandibular first molar, radiographic control of the implant after 10 years of function.

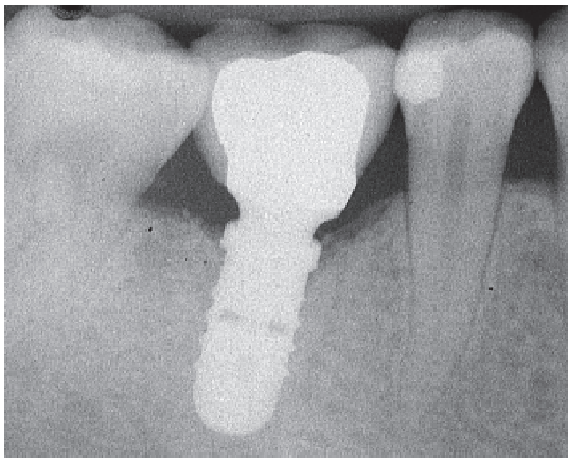


Figure 5. Overall cumulative "complication-free" survival of restorations.

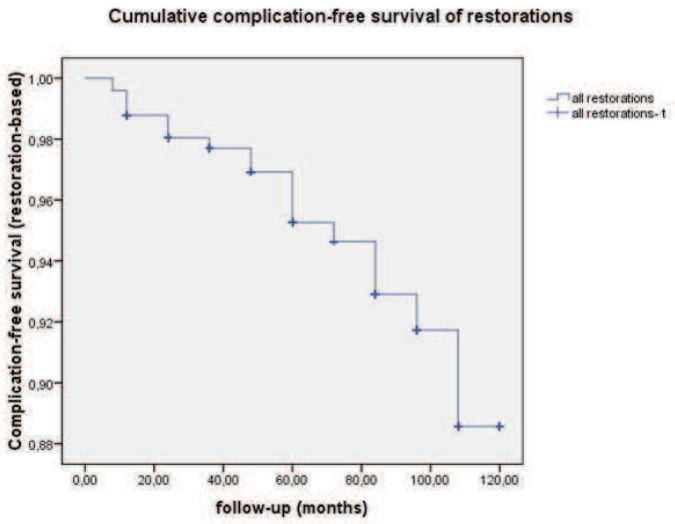
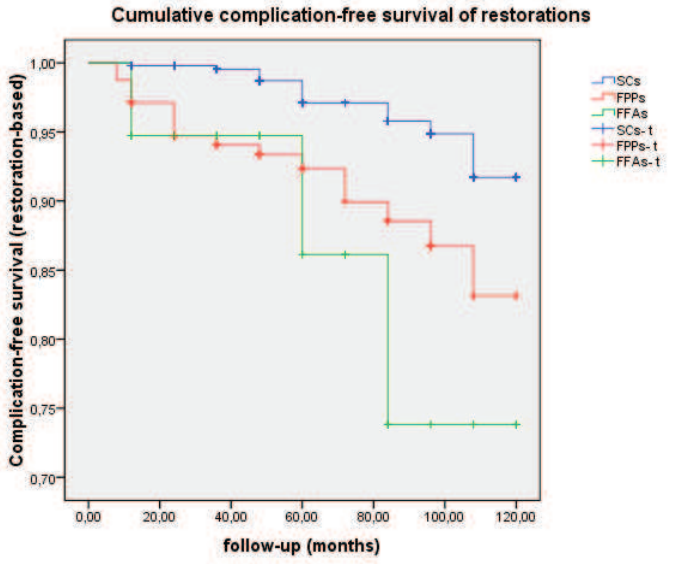


Figure 6. Cumulative "complication-free" survival of SCs, (FFPs and FFAs. The complication rates differ significantly with respect to the type of prosthetic restoration (p<0.05), as there were significantly less complications on SCs than on FPPs and FFAs.



Discussion

Despite good survival of implant-supported restorations, long-term clinical reports of dental implants have shown some biological and prosthetic complications; in particular, mechanical and technical complications have been frequently reported [5,6,21].

In a recent review of the 5-year prosthetic complication rates of fixed implant rehabilitations for fully edentuolous patients, Papaspyridakos et al. [8] reported a satisfactory implant survival rate, but a high disappointing incidence of veneering chipping/fracture (33.3%), occlusal screw loosening (22.9%) and abutment screw loosening (10.8%).

In other two reviews, it was demonstrated that after 5 years of service, the survival of implants ranged from 94.3% for cantilever FPPs [4] to 95.6% for conventional FPPs [9]; however, a high incidence of prosthetic complications, such as ceramic fracture and abutment screw loosening, has been reported [4,9].

Finally, a systematic review on single tooth implant restorations has reported a 5-year cumulative incidence of abutment screw loosening of 8.8% [11].

Butt-joints or slip-fit joints, indexed external or internal, are still the most widely used connection types in dental implants [19,20]. Although implants featuring an external hexagon are still widespread in the market, this connection is considered slightly unstable, as a result of horizontal and rotational misfits under loading [19–21]; in fact, it seems to be easily affected by mechanical complications, particularly in single-tooth restorations, with a high incidence of abutment screw loosening [12–117].

To fix some of the inherent problems associated with external-hex butt-joint connections, internal-hexagon connections have been introduced [19]. These have been claimed to be more mechanically stable, since the load is distributed deep within the implant, where engagement with a long internal wall shields the abutment screw [19–22]. However, instability at the

implant-abutment interface, whether caused by occlusal loads, inadequate screw preload, poor accuracy of thread coupling or large manufacturing tolerances, may lead to mechanical complications, such as screw loosening [22–26]. This can be a burden of maintenance and repair for both the patient and the practitioner, and a challenging complication [18,35]. In fact, in cement-retained, implant-supported restorations, the abutment screw comes loose from the implant body, whereas the crown usually remains cemented to the abutment. In such situations, crown removal without damage to the implant components is difficult [35].

Screw-retained, implant-supported restorations may facilitate the clinician's intervention in the case of abutment screw loosening; however, the presence of an occlusal access hole may disrupt the structural continuity of the porcelain, resulting in increased technical complication rates [7,36]. In a recent 15-year follow-up study comparing the complications of screw-retained and cement-retained implant-supported restorations, significantly higher ceramic fracture (38% vs. 4%) rates were found with screw-retained restorations [37]. These superstructure-related complications can lead to additional costs and time investment during the follow-up years [37,38].

At present, the patients' expectations related to the longevity of required reconstructions are high, due to the considerable costs involved for fixed dental prostheses on implants [5,9]. In addition, most of the patients are between 40-50 years old when provided with oral implants: with increasing life expectancy, it is likely that these patients will need their implant-supported restorations to function for decades [9,10]. Choosing from available options, the longevity and complication rates of restorations should be considered, in order to reduce the complexity of maintenance service to be expected. In this context, a fixture-abutment connection that offers some degree of biomechanical security is essential [39] and the stability of the implant-abutment connection becomes a key factor for the success of the restoration [19,20].

In an attempt to reduce the incidence of prosthetic complications, conical interface designs with friction fit joints have been developed [19,20,22–

27,40–42]. Unlike the external hexagon, the conical interface results in a relatively tight junction due to friction between implant and abutment [40–42]. Conical interfaces have been proposed to be more biomechanically stable than external or internal hexagonal implant-abutment connections [19,24–27,40–44], and more resistant to abutment movement and microgap enlargement under loading, as demonstrated in a recent systematic review of the literature [45].

Among conical interfaces, the self-locking (Morse taper) connection is defined as a tapered connection that has an angle < 1.5° [22]. In this pure locking-taper connection, implant-abutment mating occurs only by friction between the opposite surfaces, and a connecting screw, which represents the weakest point of many systems, is absent [18,22]. The major advantage of this type of connection is given by the mechanical stability: in fact, there are no micromovements at the interface between components, and many fewer clinical complications are associated with them [22].

In our present prospective study on locking-taper implants supporting fixed restorations, a satisfactory 10-year cumulative implant survival rate of 98.7% (98.3% maxilla, 99.1% mandible) was found. These results are similar to those reported in several other, long-term follow-up studies [1–3,5,8–12]. However, when compared to the evidence emerging from the current literature [4,6,8–11], the incidence of complications reported in our study was low (38/739: 5.1%), particularly with regard to prosthetic complications (27/739: 3.6%). Among the surviving implant-supported restorations (478 SCs, 242 FPPs, 19 FFAs), in fact, the incidence of mechanical complications (failures or complications of pre-fabricated components) was very low (0.4%), with only 3 loosened abutments in 3 SCs located in the posterior areas of jaws, over a 10-year period; in addition, no abutment fractures were noticed. These results are in accordance with previous clinical studies on locking-taper connection implants, where the incidence of mechanical complications was low [18,28–30]. Technical, suprastructure-related complications were more frequent (24/739: 3.2%), with an overall incidence of decementation of 2.0% (SCs

2.0%, FPPs 1.6%, FFAs 5.2%) and ceramic/veneer chipping/fracture of 1.2% (SCs 0.0%, FPPs 2.8%, FFAs 10.5%). However, the rate of technical complications reported in this study was lower than that reported in the current literature with butt-joint connection implant systems [4,8–11]. At the end of our present study, a 10-year overall cumulative “complication-free” survival of restorations of 88.6% (SCS 91.7%, FPPs 83.1%, FFAs 73.8%) was reported; the complication rates differed significantly with respect to the type of prosthetic restoration ($p<0.05$). This statistically significant difference may be related to the major incidence of technical complications among more complex prosthetic rehabilitations, such as FPPs and FFAs; however, it can also be interpreted as a result of the reduction of the mechanical complications (such as abutment loosening and fractures) that generally affect single-unit restorations, particularly in the posterior regions of both jaws.

When using the “complication-free” survival index, one has to keep in mind that ‘free of complication’ comprises both biological and prosthetic problems [31]. In our present study, among the surviving implant-supported restorations, only a few biological complications (11/739: 1.4%) were encountered during the 10-year follow-up period. Two implants showed clinical signs of peri-implant mucositis, 10 implants exhibited peri-implantitis with pain, probing pocket depth ≥6 mm, bleeding on probing/suppuration and severe bone loss (DIB > 2.5 mm), and 3 implants were associated with bone loss (DIB> 1.5 mm after the first year of function) without clinical signs of peri-implant infection.

It is noteworthy that all implants with screw-type connections show a microgap of variable dimensions (40-100 micrometers) at the implant-abutment interface [46–49]. Several in vitro studies have suggested that the presence of this microgap could result in microbiological colonization [46–49]. The colonization of bacteria inside the implant system and the penetration of bacteria or their products via the microgap may be a risk for soft tissue inflammation and bone loss [46–49]. Even though complete prevention of microbial penetration into the internal part of the implants has

not been demonstrated in vitro, the most favorable results have been reported when implants with a locking-taper connection have been utilized [48–50]. By reducing microgap dimensions (1-3 micrometers), in fact, the locking-taper implant-abutment connection may provide a hermetic seal against microbial penetration [48–50]. This may contribute to a minimal level of peri-implant soft tissues inflammation, and can guarantee long-term bone crest stability [50]. In our present study on locking-taper implants, a minimal marginal bone loss between implant installation and the 10 years' follow-up visit was reported, with a mean DIB of 0.33 (± 0.23), 0.45 (± 0.26) and 0.78 (± 0.33) mm at the 1-, 5- and 10-year follow-up session, respectively.

Conclusions

In the past, the main focus of clinical studies was the success of osseointegration and the survival of implants; the outcome of implant therapy was often presented without providing detailed information on the prosthetic rehabilitations, and it was commonly accepted that biological and prosthetic complications may occur with implant-supported fixed restorations. Managing these complications, however, can cause extra chair-side time, additional costs and patient dissatisfaction; for this reason, the number of mechanical and technical complications under loading should be minimized. In this scenario, the implant-abutment connection may well be regarded as a key factor in the long-term success. In the present prospective study on locking-taper connection implants, an overall cumulative implant survival and a cumulative "complication-free" survival of restorations of 98.7% (98.3% maxilla, 99.1% mandible) and 88.6% (SCS 91.7%, FPPs 83.1%, FFAs 73.8%) were reported, respectively, after 10 years of follow-up. A very low incidence of mechanical (3/739: 0.4%) and technical (24/739: 3.2%) complications was found. Within the limits of this study, the use of locking-taper implants seems to be a successful procedure for the rehabilitation of partially and completely edentulous arches, as the high mechanical stability of this connection seems to be able

to minimize the incidence of prosthetic complications in the long-term. Further long-term follow-up studies on locking-taper connection implants are needed to confirm these results.

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D- The Restoration/Mucosa Interface. The Aesthetic Outcomes of Implant Treatment

Aesthetic Outcome of Immediately Restored Single Implants Placed in Extraction Sockets and Healed Sites of the Anterior Maxilla: a Retrospective Study on 103 Patients with 3 Years of Follow-up

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Abstract

Objectives: The aim of this study was to compare the aesthetic outcome of single implants in extraction sockets and healed ridges of the anterior maxilla by means of the pink aesthetic score/ white aesthetic score (PES/WES) index.

Materials and methods: This retrospective study was based on data from 103 patients (43 males, 60 females) aged 24–65 years (mean age 41.4 ± 13.8 years) who had been successfully treated with a single implant in the anterior maxilla, in four different clinical centres. Forty-two patients (mean age 46.5 ± 15.1 years) were treated with a single implant in a fresh post-extraction socket (immediate implant treatment, IIT), while 61 patients (mean age 38.0 ± 11.8 years) were treated with a single implant in a healed

site (conventional implant treatment, CIT). Two independent calibrated examiners applied the PES/WES index to the 103 single-tooth restorations, respectively 3 months and 3 years after implant placement.

Results: A few biological (4.8%) and prosthetic (8.7%) complications were reported. Both IIT and CIT yielded satisfactory aesthetic outcomes. At the delivery of the final restoration, a PES/WES score of 16.6 ± 2.6 and 15.7 ± 3.0 was reported for IIT and CIT, respectively: this difference was not statistically significant. A higher decrease in the PES/WES score was observed with CIT over time. At 3 years, a PES/WES score of 16.4 ± 2.8 and 15.2 ± 3.3 was reported for IIT and CIT, respectively: this difference was statistically significant. IIT seemed to yield better aesthetic outcomes in young patients (≤30 years), with implants placed in central incisor/cuspid areas, in the presence of bone contouring.

Conclusions: Both immediate and conventional single-implant treatment in the anterior maxilla can yield satisfactory aesthetic outcomes, when performed by experienced clinicians in wellselected cases. Further studies are needed to confirm these results.

Keywords

Aesthetic outcome; Immediate implant treatment; Pink aesthetic score/white aesthetic score; Single implants.

Introduction

Single-tooth implants have become a routine and successful treatment procedure [1], as also demonstrated by several long-term follow-up studies [2–4].

However, since patients have high expectations in terms of aesthetic treatment outcome, rehabilitation of single-tooth gaps in the anterior maxilla by means of dental implants remains a therapeutic challenge for both surgeon and prosthodontist [5,6]. In fact, loss of teeth is usually associated with a reduction of hard and soft tissue volume [7–9], particularly in the anterior maxilla [10,11]. The progressive involution of the alveolar bone begins following tooth loss, and it can be accompanied by a marked reduction in both the quality and quantity of hard and soft tissues [7–9,12]. As demonstrated by several animal [13–16] and human studies [10,11,17,18], a reduction of the alveolar bone occurs after extraction of natural teeth, in the first 6 months to 2 years, with a marked decrease in facio-palatal width and height within the first year [8,12]. These physiological events can be detrimental to the definitive aesthetic results, and may render the predictability uncertain if reestablishing soft tissue aesthetics rather than a perfect natural situation is the aim [19,20].

Various indexes have been proposed to evaluate the aesthetic result of a single implant restoration [21–26]. Among these, the pink aesthetic/white aesthetic score (PES/WES) index has obtained considerable success [24]: its suitability for the objective outcome assessment of the aesthetic dimension of anterior single-tooth implants has been confirmed [27] and it has been used in several studies [5,19,28–35]. The PES/WES focuses on the soft tissue aspects of an anterior implant restoration and also on the visible part of the implant restoration [24]. It comprises 10 variables: mesial papilla; distal papilla; curvature of the facial mucosa; level of the facial mucosa; root convexity/soft tissue colour/texture at the facial aspect of the implant site; tooth form; volume; colour; surface texture; and translucency. A score of 2, 1 or 0 is assigned to all parameters. All parameters are

assessed by direct comparison with the natural, contralateral reference tooth, estimating the degree of match or mismatch [24].

Various modalities have been described for implant therapy in the anterior zone such as conventional implant treatment, CIT (4–6 months after tooth extraction), early (typically 4–8 weeks after extraction) and immediate implant treatment, IIT [20,36]. IIT is defined as the placement of a dental implant at the time of tooth extraction [20,36]. This procedure has several advantages as it reduces the number of dental appointments, the length of treatment and the number of surgeries, improving patient acceptance with the psychological benefit of simultaneously replacing a lost tooth with an implant [20,36,37].

However, as only a few studies on a limited number of patients have compared the aesthetic outcome of immediate vs. conventional single implants in the anterior maxilla [30,31,38,39], it remains unclear whether implant placement in healing sites yields superior aesthetic outcome when compared with healed sites.

Hence, the aim of the present retrospective 3-year follow-up study was to compare the aesthetic outcome of single implants in extraction sockets and healed ridges of the anterior maxilla by means of the PES/WES index.

Materials and methods

Patient selection

Patients enrolled in the present retrospective study were identified through the customized records of four different private dental centres. A complete review of the records was conducted, and patient-related information such as gender, age at surgery, reasons for loss or extraction of natural tooth were collected; in addition, implant-related information such as surgical protocol, date of installation, implant position (central incisor, lateral incisor,

cuspid, first premolar), use of bone contouring and/or connective tissue graft, date of prosthesis delivery (temporary and permanent) were available. Only patients treated with a single implant in fresh extraction sockets (immediate implant treatment, IIT) or healed sites (at least 4 months of healing after tooth extraction, i.e. conventional implant treatment, CIT) of the anterior maxilla (central and lateral incisors, cuspids, first premolars) between January 2009 and December 2011, with successful single-tooth restoration and complete 3-year follow-up were included in this study. Other inclusion criteria were: (1) good systemic and oral health; (2) age ≥ 18; (3) single-implant treatment in the anterior maxilla, in fresh extraction sockets or healed sites, alone or in conjunction with bone contouring (overbuilding the buccal aspect in combination with filling the gaps between the implant and the bone walls for extraction sockets; buccal bone grafting to reinforce/protect the buccal bone wall and interproximal grafting to cover exposed threads for healed sites) and/or connective tissue graft; (4) natural teeth present both mesial and distal to the implant and (5) dentition in the opposing jaw. Exclusion criteria were: (1) systemic diseases; (2) chronic periodontitis with advanced loss of support, defined by periodontal pocking depths (PPD) > 6 mm with clinical attachment loss (CAL) > 4 mm, radiographic evidence of bone loss and increased tooth mobility [40]; (3) other oral disorders (vesiculobullous or ulcerative diseases, red or white lesions, salivary gland diseases, connective tissue or lymphoid lesions, cysts of the oral region, benign or malignant tumours); (4) need for major bone augmentation procedures with autogenous bone or bone substitutes prior to implant insertion (although bone contouring was not an exclusion criterion); (5) presence of a thin gingival biotype (determined by the transparency of a periodontal probe through the gingival margin while probing the buccal sulcus of the upper central incisor) [41]; (6) smoking and (7) bruxism. Additional exclusion criteria for patients treated with immediate implants were: (8) loss or (9) damage of the buccal bone crest after extraction of the failing tooth. All patients had read and signed an informed consent before implant treatment. The study protocol was approved by the local Ethics Committee and was conducted in accordance

with the principles outlined in the Helsinki Declaration on clinical research involving human subjects of 1975, as revised in 2008.

Surgical and prosthetic procedure

A complete examination of the oral hard and soft tissues was carried out for each patient. Standardized periapical radiographs and panoramic radiographs formed the basis for the primary investigation. Where necessary, cone beam computed tomography (CBCT) scans were used as the final investigation. CBCT datasets were acquired and then transferred to specific implant navigation software, to perform a three-dimensional (3D) reconstruction of the maxillary bones. With this navigation software, it was possible to correctly assess bone quantity and quality; in particular, the width of each implant site, the thickness and the density of the cortical plates and the cancellous bone, as well as the ridge angulation were studied. Pre-operative work-up also included assessment of the edentulous ridge using casts and diagnostic wax-up. Screw-type, direct metal laser sintering implants (Tixos®; Leader Implants, Milan, Italy) were used in this study: these implants have a porous surface for bone ingrowth, with the potential to accelerate the bone healing processes [42,43]. The implants featured an internal hexagon connection. Immediate implants were placed immediately after tooth extraction, while conventional implants were installed at least 4 months after tooth removal. All procedures were performed under the same clinical protocol. In extraction sockets, after local anaesthesia obtained by infiltrating articaine 4% containing 1:100.000 adrenaline (Ubistesin®; 3M ESPE, St Paul, MN, USA), a mucoperiosteal flap was raised. Care was taken to perform an atraumatic extraction. The failing tooth was extracted following careful luxation of the root with a periotome, as atraumatically as possible, avoiding any lateral movement that might damage the buccal alveolar bone. Once the tooth was removed, the socket was debrided from any remains of granulation tissue by an excavator and irrigated with sterile saline. A periodontal probe (PCP-UNC 15®; Hu-Friedy Manufacturing, Chicago, IL, USA) was then used to scan

the internal surface of the alveolus for dehiscences and fenestrations, and to verify its integrity before implant placement. The presence of an intact buccal bone plate and a thick gingival biotype, as determined by De Rouck et al. [41] were considered fundamental pre-requisites for immediate implant treatment: if loss or damage of the buccal bone wall was present after extraction, the patient could not be included in the study. The preparation of implant sites was carried out with spiral drills of increasing diameter, under constant irrigation. With the aim of increasing primary stability, implants were placed in underprepared osteotomies and socket preparation was deepened beyond the alveolar apex, in order to engage the apical bone. Special attention was paid to ensure the correct three-dimensional position of the implant: the osteotomies were directed through the palatal aspect of the socket so that the implant was stabilized in the remaining alveolar bone without contacting the intact buccal plate. The implants were manually seated in the proper position, slightly subcrestally, using a hand ratchet, which gave a rough estimate of the maximum insertion torque obtained. For healed ridges, patients received an implant at least 4 months after the extraction of the failing tooth. After local anaesthesia, a mesiodistal crestal incision was made, and a full-thickness flap was reflected exposing the alveolar ridge. Osteotomies were initiated with a 2.0 mm diameter drill to the desired depth. Again, the preparation of implant sites was carried out with spiral drills of increasing diameter, as suggested by the implant manufacturer, under profuse saline irrigation. All implants were inserted at the bone crest level, and the implant stability was determined clinically as the absolute absence of axial or rotational movement by the removal of the implant driver without use of a stabilizing wrench. For both extraction sockets and healed sites, surgeons were free to perform bone contouring (overbuilding the buccal aspect in combination with filling the gaps between the implant and the socket walls for extraction sockets; buccal bone grafting to reinforce/ protect the buccal bone wall and interproximal grafting to cover exposed threads for healed sites) and/or connective tissue grafts, according to clinical indications. Bone contouring was performed using synthetic calcium phosphate granules (Biocer®;

Biocer Entwicklungs GmbH, Bayreuth, Germany), mixed with tetracycline powder, to obtain a local antibiotic effect; this mixture was moistened with physiological saline solution so that the composition could be moulded more easily to fill the defect. Where an increase of the width of keratinized gingival tissue was required, the surgeon was free to perform a connective tissue graft. The donor connective tissue graft was collected from the palate (size 8 x 8 x 1.5 mm); the graft was prepared, placed within the envelope flap and sutured in position. The flap was then replaced and secured in position by interrupted sutures, using the same suture size and material. After this, pre-fabricated temporary abutments were prepared with a high speed bur to the proper retentive and resistant form, and were hand tightened onto the implant with finger pressure. All patients received a provisional acrylic resin crown cemented with a temporary cement (Temp-Bond®; Kerr, Orange, CA, USA). The provisional crowns were delivered immediately after surgery if fabricated chairside with the help of singleshell crowns or clear vacuum-formed templates, and relined with light-curing flowable resin composite directly to the provisional abutment; they were delivered within 6 h if fabricated by the laboratory after taking an impression. All provisional crowns were carefully contoured and polished to provide correct emergence profiles (slightly flat or concave in interproximal and palatal sides, and slightly convex in the buccal aspect to support the soft tissues), adaptation to the gingival tissues, scalloped gingival architecture and appropriate support to the interdental papillae. The provisional restorations were taken out of any occlusal contacts both in centric occlusion and during excursive mandibular movements, as checked carefully with articulating papers (Bausch Articulating Papers®; Bausch, Nashua, NH, USA), and the patients were instructed to chew predominantly on the contralateral side and avoid hard food for a period of 2–3 weeks. Ice packs were provided postoperatively. All patients were prescribed oral antibiotics (Augmentin®; GlaxoSmithKline Beecham, Brentford, UK), 2 g per day for 6 days. Postoperative pain was controlled by administering 100 mg nimesulide (Aulin®; Roche Pharmaceutical, Basel, Switzerland), every 12 h for 2 days, and detailed instructions about oral hygiene were given,

including mouth rinses with 0.12% chlorhexidine (Chlorhexidine®; OralB, Boston, MA, USA) administered for 7 days. Suture removal was performed at 8–10 days. The temporary restorations remained in situ for 3 months, and after this period definitive restorations were placed. All single crowns were ceramometallic and were cemented with a temporary cement.

Clinical follow-up examination

The customized records of patients included a series of clinical and radiographic information about implants, peri-implant tissues and prostheses, collected during the entire 3-year follow-up period, including the occurrence of complications. Complications were divided into two types: (a) biological complications, including pain or swelling after surgery, soft tissue inflammation (peri-implant mucositis) and peri-implant infection (peri-implantitis) with fistula formation, pain, suppuration or exudation. The threshold for peri-implantitis was indicated by a probing pocket depth ≥6 mm and bleeding on probing or pus secretion; and (b) prosthetic complications (loosening or fracture of abutment, loss of retention, porcelain fracture). The prosthetic complications were divided into minor (no treatment needed or <20 min chair time, e.g. re-cementation) or major (>60 min chair time and additional laboratory costs, e.g. repositioning of a loosened abutment, removal of a fractured abutment or fabrication of new restorations) complications. Static and dynamic occlusions were evaluated using standard occluding papers. All prosthetic complications were carefully registered and managed if possible during the follow-up visits. Additional appointments were arranged if needed.

Aesthetic evaluation

The PES/WES score by Belser et al. [24] was used to objectively evaluate the aesthetic outcome of the peri-implant soft tissues and the implant crown, as previously described [29.30]. All implant crowns (central, lateral incisors, cuspids and first premolars) were photographed with a digital

camera (Nikon D100®; Nikon, Tokyo, Japan) and a 105 mm lens (AF micro Nikkor 105 mm 1:2.8 D®; Nikon) with a ring flash (Nikon Macro Speedlight SB-29S®; Nikon). For assessing anterior tooth replacements, the reference contralateral tooth had to be completely and symmetrically represented, in order to ensure comparability. For this purpose, the photographs were centred at the midline in order to facilitate the subsequent analysis, which was primarily based on symmetry. In addition, standardized clinical photographs were taken of each implant site, as tools for a more detailed evaluation. For the first premolars, the photographs could not be taken at the midline; accordingly, the approach was modified and a picture including the second premolar and the cuspid was taken, with these serving as references. All photographs were taken slightly superior to the occlusal plane, centred at the contact region. Photographs were then viewed on a 42-inch monitor screen (Samsung PPM- 42S3Q Flat Panel Plasma Monitor®; Samsung, Seoul, South Korea). Study casts, produced in type IV stone, were fabricated for each patient, to facilitate a direct and objective assessment related to the PES/WES index. The clinical photographs, taken 1 week after seating of the definitive restoration and 3 years after implant placement with the related study casts, were used to perform the aesthetic evaluation. The aesthetic evaluation was performed by two independent calibrated observers (a periodontist and a prosthodontist) who had not been involved in the treatment of the patients. To reduce bias and to achieve good reproducibility, each independent observer repeated the evaluation twice, on different days; in case of diverging scores, each observer carefully re-evaluated the photographs and the study casts prior to making his/her final decision. After this, there was a discussion between the two observers to arrive at the final decision. A score of 2, 1 or 0 was assigned to each PES/WES parameter. The highest possible combined PES/WES score was 20, which represented a close match of the peri-implant soft tissue conditions and the clinical single tooth crown compared to the respective features present at the contralateral natural tooth site. A PES/WES ≥ 12 was considered as the limit for an acceptable aesthetic outcome of implant treatment.

Statistical analysis

The collected data were manipulated using a spreadsheet programme (Microsoft Excel 2007®; Microsoft Corporation, Redmond, WA, USA). Descriptive statistics were obtained. Absolute and relative frequency distributions were calculated for qualitative variables; means, standard deviations (SDs), medians, ranges and confidence intervals (95% CI) were calculated for quantitative variables. In particular, the reasons for tooth loss in the overall study population and by implant type (immediate implants vs. conventional implants) were summarized, using relative frequencies; chi-square analysis was used to test the differences between the two groups. The main characteristics of the study population (patients' age and gender, position of the implants, presence of connective tissue graft and/or bone contouring) were summarized as mean (SD) or prevalence for continuous and discrete variables, in the overall sample and by implant group, respectively. Then, the t-test (for independent samples) or chi-square was used to test whether these features were equally distributed among the two groups (immediate implants vs. conventional implants). Since patients in the immediate implant group were on average 8 years older than in the conventional implant group, all the analyses were adjusted for age added as a linear covariate to the regression models. For each patient, the difference in the three scores (PES/WES, PES and WES) between the 3-year follow-up control and the delivery of the final restoration was computed, and the mean difference with 95% CI between the immediate and the conventional implants was estimated from a linear regression model. A 95% CI including the zero was suggestive of no change in the score during the follow-up period. From the same models, the hypothesis of no difference in the mean change between the two study groups (F-test) was also tested. Finally, as exploratory analyses, the mean difference with 95% CI in the PES/WES score between implant types according to patient's age, implant position, presence of connective tissue graft and bone contouring was estimated using linear regression models, both at the

delivery of final restoration and at the 3-year follow-up control. An interaction term was included into the models to test the hypothesis that the mean difference between immediate and conventional implants was independent of patients' characteristics (F-tests). The same analysis was repeated for the PES and WES sub-scales. All analyses were performed with a statistical software package (SAS release 9.4®; SAS Institute Inc., Cary, NC, USA). The level of significance was set at 0.05.

Results

This retrospective study was based on data from 103 patients (43 males and 60 females) aged between 24 and 65 years (mean age 41.4 ± 13.8 years; median 39 years; 95% CI: 38.8–44.0 years) who had been treated with a single implant in the aesthetic zone of the anterior maxilla (central and lateral incisors, cuspids, first premolars), between January 2009 and December 2011, in four different clinical centres. Among these, 42 patients (15 males, 27 females; mean age 46.5 ± 15.1 years) were treated with a single implant in a fresh post-extraction socket (immediate implant treatment, IIT), while 61 patients (28 males, 33 females; mean age 38.0 ± 11.8 years) were treated with a single implant in a healed site (with at least 4 months of undisturbed healing after tooth extraction: conventional implant treatment, CIT). The reasons for tooth loss within the two groups were reported in ***Table 1***. Root fracture was the most frequent reason for tooth loss in the IIT group (fractures were statistically higher in the immediate than in the conventional group, P = 0.007), while agenesis was the most common reason for missing teeth in the CIT group. The study groups were basically homogeneous by gender, implant position and presence of connective tissue graft and bone contouring (all P-values > 0.05); however, patients in the immediate implant group were on average 8.5 years older (46.5 vs. 38) than in the conventional implant group (P = 0.002) (***Table 2***). Only a few biological complications were reported. In fact, three patients experienced pain or swelling after surgery, and two other patients experienced an episode of soft tissue inflammation (peri-implant mucositis),

2- and 3-years after implant placement, respectively. However, these patients underwent professional oral hygiene treatment and they did not develop peri-implantitis. No peri-implant infections were reported. At the end of the study, an incidence of biological complications of 4.8% (5/103) was reported. Prosthetic complications were more frequent. Loss of retention was reported in five patients. These were considered minor complications (<20 min chair time treatment needed). No abutment fractures were reported, but two patients had their abutment loosened and re-inserted, and two other patients experienced porcelain chipping/fracture. These complications were considered major complications, as they required the removal of the damaged restorations and the fabrication of new restorations (>60 min chair time and additional laboratory costs). In total, over a 3-year period, prosthetic complications were reported in nine patients (9/103) for an overall incidence of prosthetic complications of 8.7%. At the delivery of final restorations, the mean PES/WES score was 16.1 ± 2.9 in the overall sample (n = 103). A satisfactory aesthetic outcome was found, with a PES/WES score of 16.6 ± 2.6 and 15.7 ± 3.0 reported for IIT (n = 42) and CIT (n = 61), respectively (***Figures 1–3***). On average, IIT scored 0.9 points higher than CIT; however, this difference was not statistically significant (age-adjusted P = 0.051). Similarly, the PES and the WES scores were also higher in the immediate group, although the difference between IIT and CIT was not statistically significant. At the 3-year follow-up, the mean PES/WES reduced to 15.7 in the overall sample (n = 103). In the IIT group, the mean change of –0.26 points was not significantly different from zero (95% CI: –0.68 to 0.15). Similar non-significant changes were observed for the PES and the WES scores. Conversely, a higher decrease in the PES/WES score was observed in the CIT group over time (–0.49 points; 95% CI: –0.83 to –0.15), mainly attributable to the PES score. As a consequence, a statistically significant difference was found in the PES/WES score between immediate and conventional implants, at the 3-year follow-up (P = 0.03). However, no statistically significant differences were found between the PES and the WES scores for IIT and CIT, 3 years after implant placement nor in the

mean change (95% CI) over the two evaluations. The mean values for the PES/ WES, PES and WES scores with immediate and conventional implants at the delivery of final restoration and at the 3-year follow-up control, as well as the mean change (95% CI) over the two evaluations were reported in ***Table 3***. Finally, ***Table 4*** reported the mean difference (95% CI) between the PES/WES scores of immediate and conventional implants (according to patient's age, implant position, presence of connective tissue graft and bone contouring) at the delivery of final restoration and at the 3-year follow-up control, respectively. At the delivery of final restoration, young age (≤30 years), implants placed in the central incisor/cuspid areas as well as the presence of bone contouring were associated with a significantly higher PES/ WES score for IIT than for CIT. The advantage of immediate over conventional implants varied according to implant position (P = 0.04) and bone contouring (P = 0.02). Similar findings were found at the end of the 3-year follow-up. In fact, as shown in ***Figures 4, 5***, the highest value of the PES/WES score in the immediate implant group was mainly attributable to the WES sub-score among the youngest and patients with bone contouring. Conversely, for implants located in the central incisors or cuspid areas, both the PES and the WES sub-scores were higher in the immediate than in the conventional implant groups.

Table 1. Reasons for tooth loss in the overall study population, and by implant type (immediate implant treatment, IIT vs conventional implant treatment, CIT).

	All patients (n = 103)	Patient groups		p[1]
		IIT (n = 42)	CIT (n = 61)	
Agenesis	21 (20.4%)	–	21 (34.4%)	–
Root fracture	38 (36.9%)	22 (52.4%)	16 (26.2%)	0.007
Caries	20 (19.4%)	11 (26.2%)	9 (14.8%)	0.2
Non-treatable endodontic lesions	16 (15.5%)	7 (16.6%)	9 (14.8%)	0.8
Root resorption	8 (7.8%)	2 (4.8%)	6 (9.8%)	0.5[a]

p[1]: chi-square test p-value for testing the null hypothesis of equal prevalence of tooth loss, by reason, between the two study groups.

a. Fisher exact test was used instead of the chi-square test (low number of expected counts)

Abbreviations: IIT = Immediate implant treatment; CIT = Conventional implant treatment.

Table 2. Characteristics of the overall study population, by implant type (immediate implant treatment, IIT vs conventional implant treatment, CIT).

	All patients (n = 103)	Patient groups		p[1]
		IIT (n = 42)	CIT (n = 61)	
Mean age, years (SD)	41.4 (13.8)	46.5 (15.1)	38.0 (11.8)	0.002
Gender (%)				
Males	43 (41.7%)	15 (35.7%)	28 (45.9%)	0.4
Females	60 (58.3%)	27 (64.3%)	33 (54.1%)	
Implant position (%)				
Central incisors	18 (17.5%)	11 (26.2%)	7 (11.5%)	0.1
Lateral incisors	41 (39.8%)	18 (42.9%)	23 (37.7%)	
Cuspids	16 (15.5%)	5 (11.9%)	11 (18.0%)	
First premolars	28 (27.2%)	8 (19.0%)	20 (32.8%)	
Connective tissue graft (%)				
Yes	29 (28.2%)	9 (21.4%)	20 (32.8%)	0.2
No	74 (71.8%)	33 (78.6%)	41 (67.2%)	
Bone contouring (%)				
Yes	58 (56.3%)	25 (59.5%)	33 (54.1%)	0.6
No	45 (43.7%)	17 (40.5%)	28 (45.9%)	

p[1]: p-value for testing the null hypothesis of no difference in main patients characteristics between the two study groups at the delivery of final restoration. Unless otherwise indicated, the statistical tests were: t-test for continuous and chi-square test for discrete variables, respectively.

Abbreviations: IIT = Immediate implant treatment; CIT = Conventional implant treatment.

Table 3. Mean PES/WES, PES and WES scores for immediate implant treatment (IIT) and conventional implant treatment (CIT), at the delivery of final restoration and at the 3-year follow-up control.

Score	Mean score (SD) at the delivery of final restoration			Mean score (SD) at the 3-year follow-up control			Mean change (95% CI) over the two evaluations		
	IIT (n = 42)	CIT (n = 61)	p[1]	IIT (n = 42)	CIT (n = 61)	p[1]	IIT (n = 42)	CIT (n = 61)	p[2]
PES/WES	16.6 (2.6)	15.7 (3.0)	0.051	16.4 (2.8)	15.2 (3.3)	0.03	-0.26 (-0.68; 0.15)	-0.49 (-0.83; -0.15)	0.4
PES	8.1 (1.5)	7.8 (1.8)	0.1	7.8 (1.8)	7.4 (1.8)	0.07	-0.24 (-0.54; 0.05)	-0.37 (-0.61; -0.13)	0.5
WES	8.6 (1.7)	7.9 (1.9)	0.1	8.6 (1.7)	7.8 (2.1)	0.08	-0.02 (-0.26; 0.24)	-0.12 (-0.32; 0.09)	0.5

1: p-value testing the hypothesis of no difference in the mean scores between the to implant groups, from linear regression models adjusting for age (F-test).
2: p-value testing the hypothesis of no difference in the mean change of the scores between the two implant groups, between the two observations, from linear regression models adjusting for age (F-test)
Abbreviations: SD = Standard Deviation; CI = Confidence Interval; IIT = Immediate implant treatment; CIT = Conventional implant treatment.

Table 4. Mean difference for the PES/WES scores between implant types (immediate implant treatment, IIT vs conventional implant treatment, CIT) according to patient's age, implant position, presence of connective tissue graft and bone contouring, at the delivery of final restoration and at the 3-year follow-up control.

	At the delivery of final restoration		At the 3-year follow-up control	
	Mean difference* (95% CI)	p[1]	Mean difference* (95% CI)	p[1]
All patients	0.92 (-0.22; 2.06)	–	1.19 (-0.05; 2.43)	–
Age groups				
≤ 30 years	3.38 (0.79; 5.98)	0.1	3.17 (0.32; 6.01)	0.2
31-40 years	1.48 (-0.73; 3.7)		2.08 (-0.34; 4.51)	
41-50 years	0.78 (-1.5; 3.05)		1.06 (-1.44; 3.55)	
≥ 51 years	-0.94 (-3.35; 1.48)		-0.88 (-3.52; 1.77)	
Implant position				
Central incisors	4.08 (1.47; 6.68)	0.04	3.17 (0.29; 6.05)	0.3
Lateral incisors	0.4 (-1.3; 2.09)		1.26 (-0.61; 3.13)	
Cuspids	2.95 (0.04; 5.85)		3.36 (0.15; 6.57)	
First premolars	-0.08 (-2.33; 2.18)		0.1 (-2.39; 2.59)	
Connective tissue graft				
Yes	1.77 (-0.53; 4.06)	0.4	2.22 (-0.28; 4.72)	0.4
No	0.73 (-0.61; 2.07)		0.86 (-0.59; 2.32)	
Bone contouring				
Yes	2.02 (0.53; 3.5)	0.02	2.04 (0.41; 3.67)	0.1
No	-0.6 (-2.32; 1.12)		0.01 (-1.89; 1.9)	

**Mean difference in the score between immediate implants and conventional implants. A positive difference indicates a higher mean score for the immediate group.*
1: p-value testing the null hypothesis of no difference in the mean score between the study groups, by patient's age, implant position, presence of connective tissue graft and bone contouring (F-test from linear regression models).

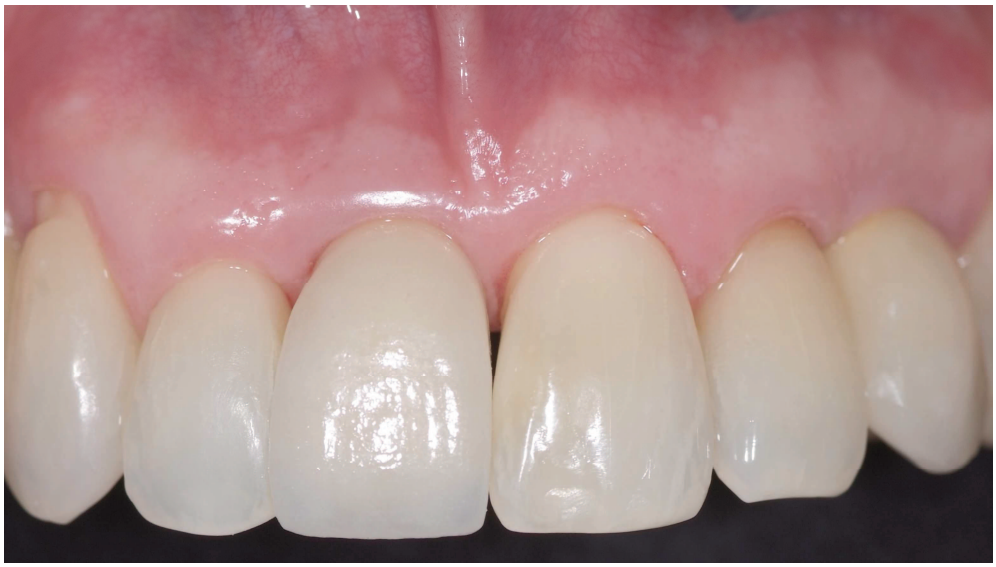

Figure 1a. Immediate implant treatment (IIT), right central incisor: the crown in situ at the delivery of the final restoration.

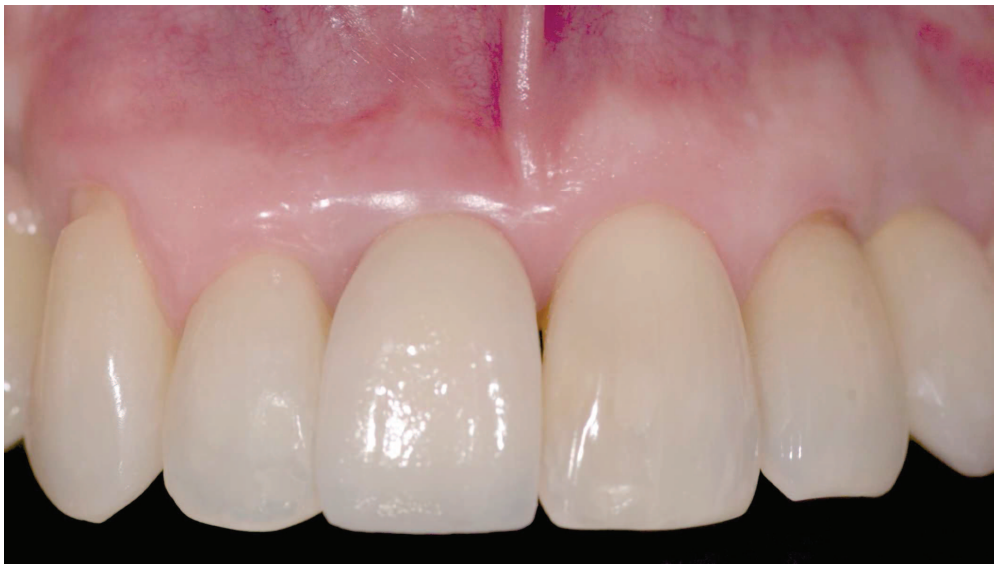

Figure 1b. Immediate implant treatment (IIT), right central incisor: the crown in situ after 3 years.

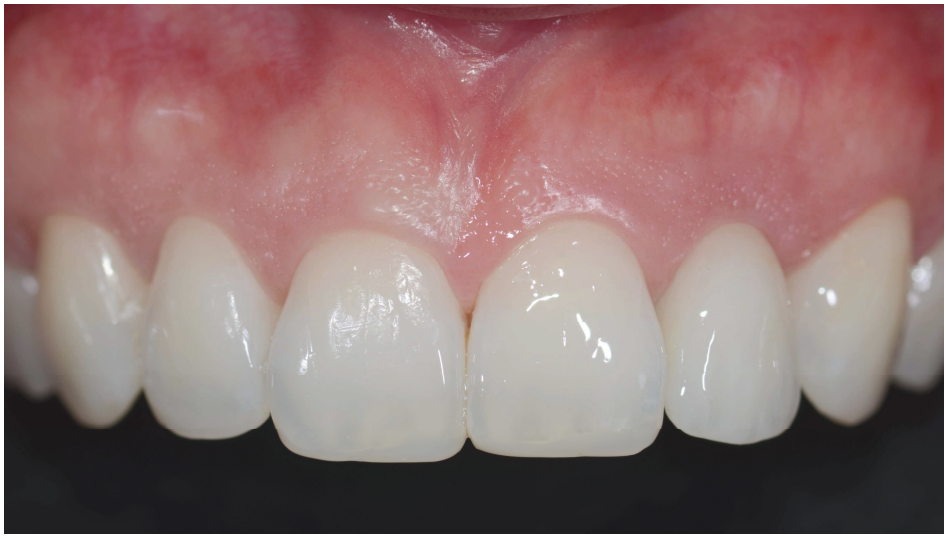

Figure 2a. Conventional implant treatment (CIT), left lateral incisor: the crown in situ at the delivery of the final restoration.

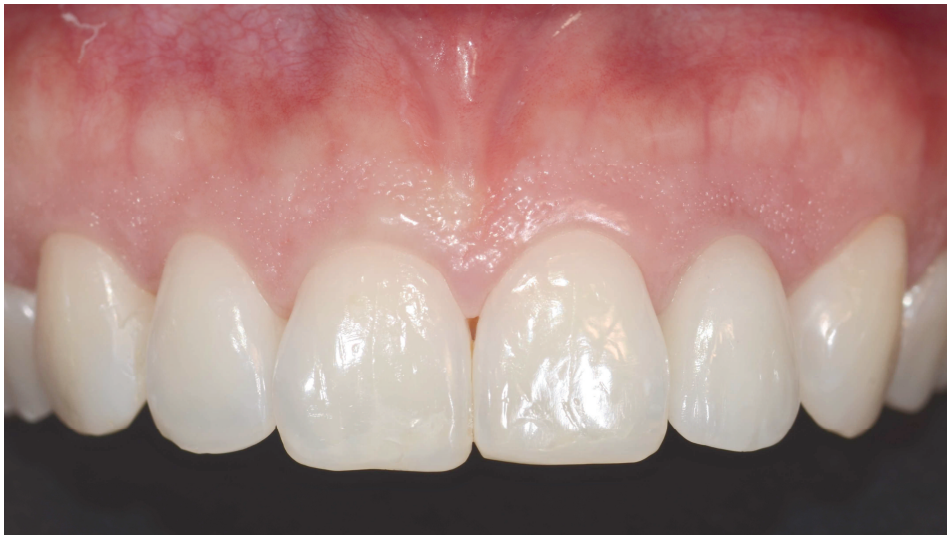

Figure 2b. Conventional implant treatment (CIT), left lateral incisor: the crown in situ after 3 years.

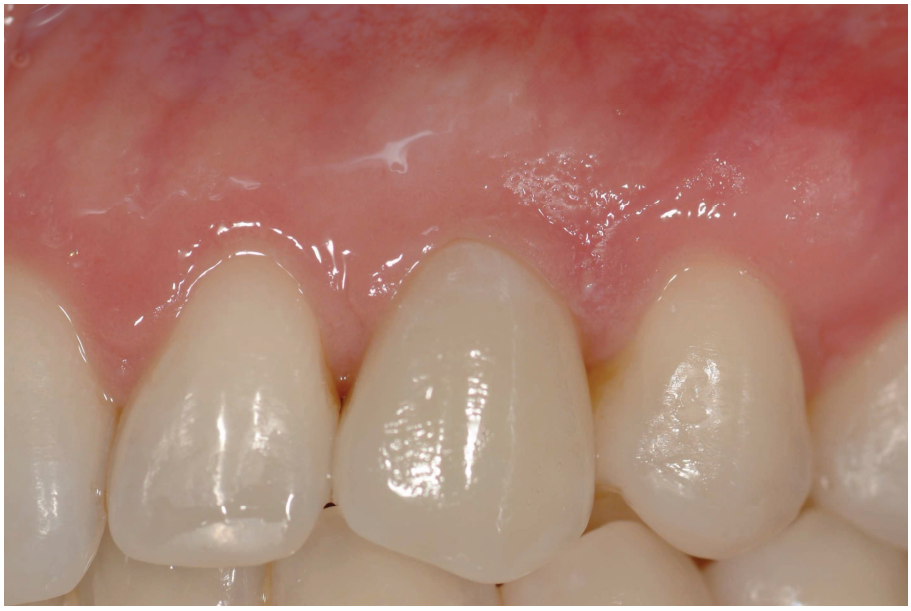

Figure 3a. Immediate implant treatment (IIT), left cuspid: the crown in situ at the delivery of the final restoration.

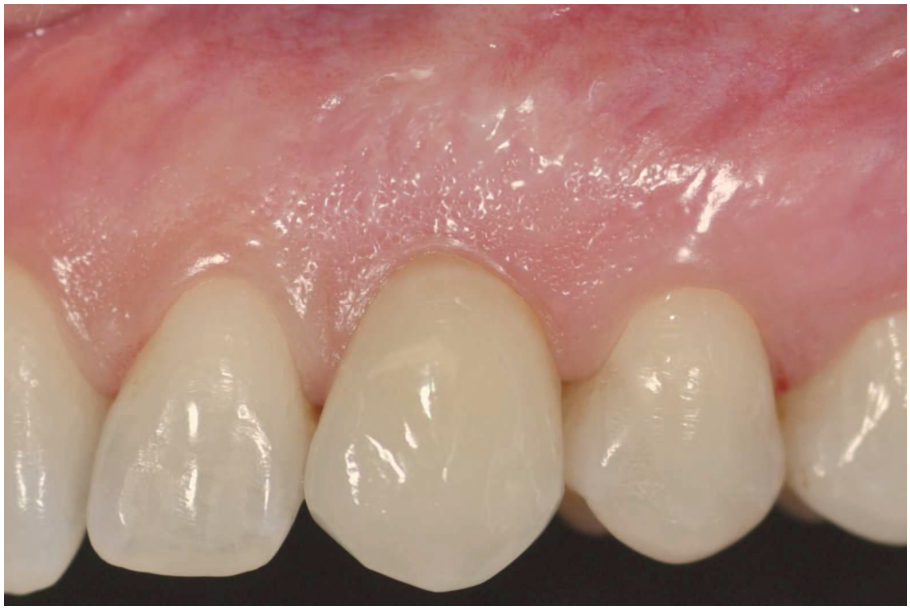

Figure 3b. Immediate implant treatment (IIT), left cuspid: the crown in situ after 3 years.

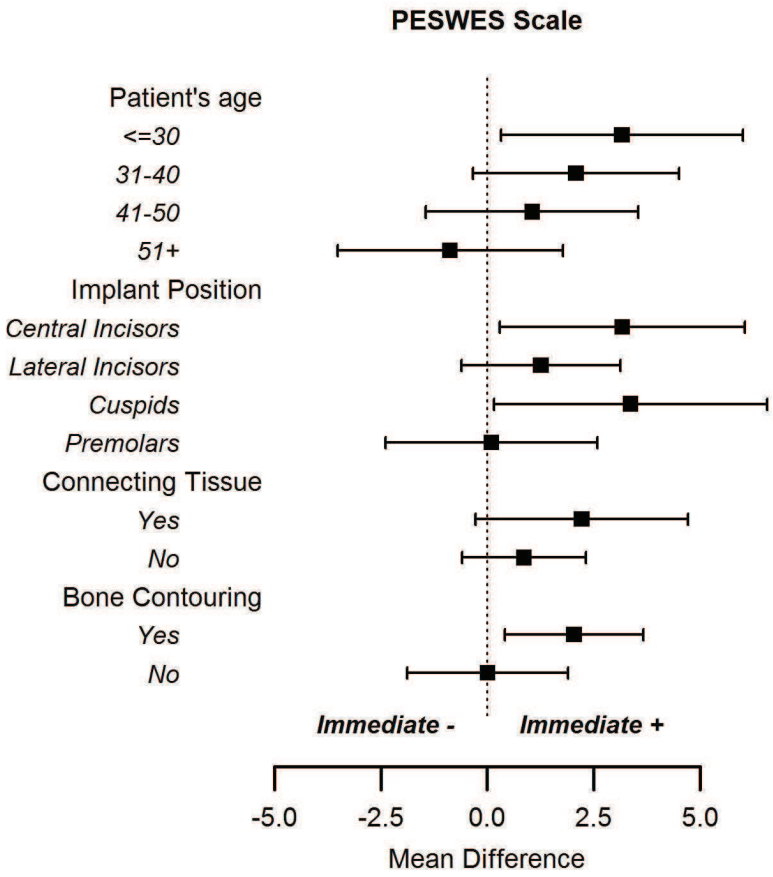

Figure 4. Mean difference for the PES/WES scores between implant types (immediate implant treatment, IIT vs conventional implant treatment, CIT) according to patient's age, implant position, presence of connective tissue graft and bone contouring, at the 3-year follow-up control.

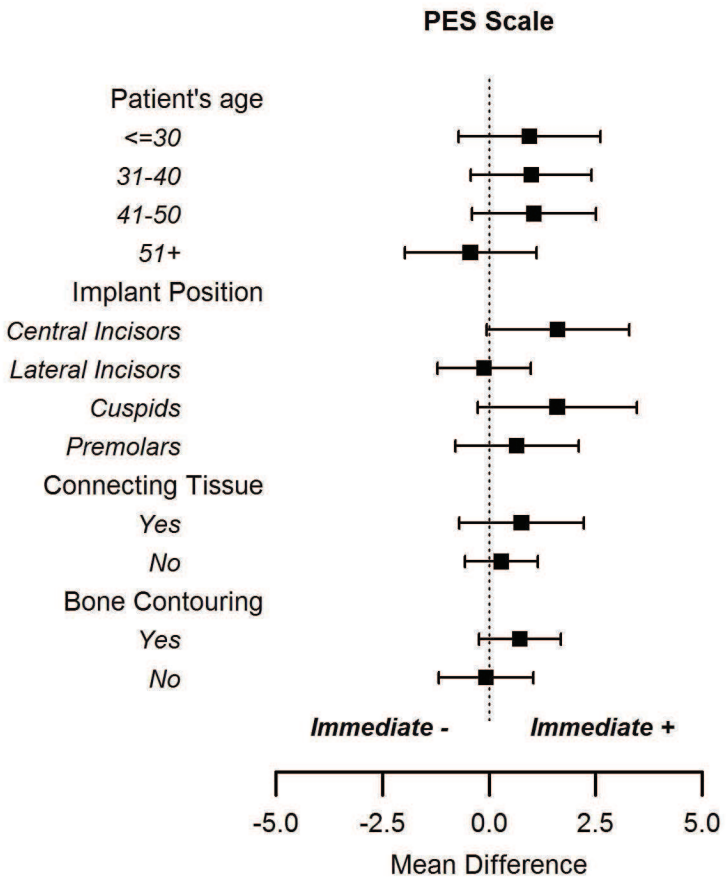

Figure 5a. Mean difference for the PES scores between implant types (immediate implant treatment, IIT vs conventional implant treatment, CIT) according to patient's age, implant position, presence of connective tissue graft and bone contouring, at the 3-year follow-up control.

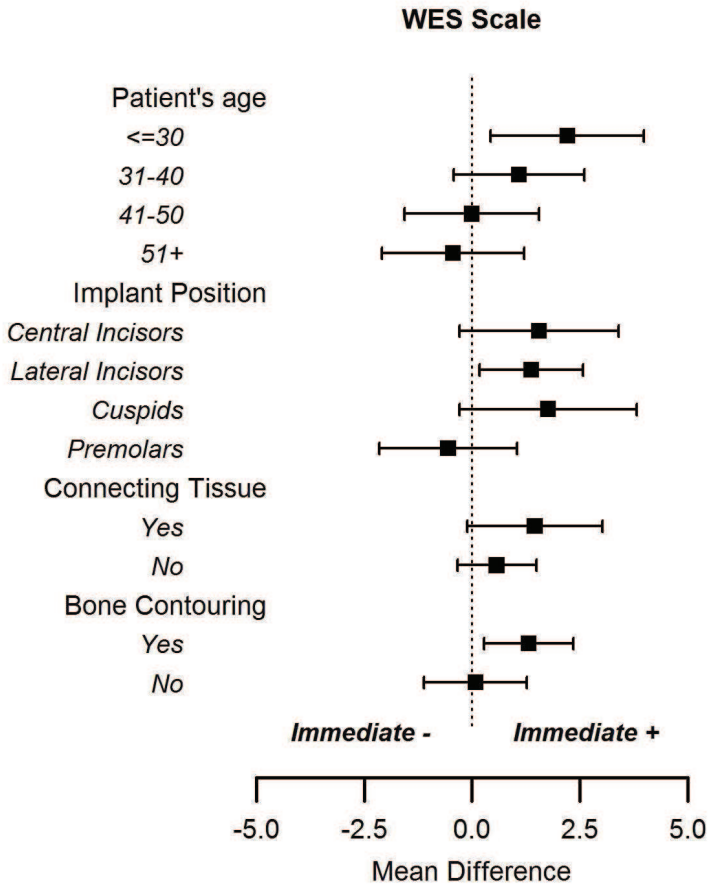

Figure 5b. Mean difference for the WES scores between implant types (immediate implant treatment, IIT vs conventional implant treatment, CIT) according to patient's age, implant position, presence of connective tissue graft and bone contouring, at the 3-year follow-up control.

Discussion

Nowadays, the aesthetic outcome has become the main focus of interest for the overall treatment success [38]. This is related to the fact that society is evolving, with more demanding patients expecting an aesthetic restoration that is indistinguishable from natural teeth and which is stable over time [38]. As a consequence, bone resorption affecting the buccal bone wall of the anterior maxilla after tooth extraction, correlated with the disruption of blood supply from the periodontal ligament and osteoclastic activity [13] can be a serious threat, as it can compromise the final aesthetic outcome of treatment. This should be considered before the planning of rehabilitation in the anterior segment of the maxilla [32].

At present, given the lack of long-term comparative studies with thorough aesthetic analyses, it remains unclear whether singleimplant placement in healing sites of the anterior maxilla yields superior aesthetic treatment outcome when compared with healed sites [30,31,38,39].

Raes et al. [38] compared the aesthetic outcome of immediate (16) vs. delayed (23) single implants in the anterior maxilla. No significant differences were found in the aesthetic result between immediate (PES: 10.33 ± 2.29, range 6–14) and delayed (PES: 10.35 ± 1.58, range 7–13) implants, respectively [38].

Similar results were reported by Cosyn et al. [31], who found no statistically significant differences between conventional (41) (PES: 10.07 ± 1.96, range 6–13) and immediate (26) single implants (PES: 10.88 ± 2.41, range 6–14) placed in the anterior maxilla.

In another recent study [30], 22 patients received an immediate implant, and 18 patients had conventional implant surgery. The mean follow-up was 31.09 months (SD 5.57; range 24–46) and 34.44 months (SD 7.10; range 24–48) for IIT and CIT, respectively. The mean PES/WES was 14.50 (SD 2.52; range 9–19) and 15.61 (SD 3.20; range 8– 20) for IIT and CIT,

respectively [30]. Immediate implants had a mean PES of 7.45 (SD 1.62; range 4–10) and a mean WES of 7.04 (SD 1.29; range 5–10). Conventional implants had a mean PES of 7.83 (SD 1.58; range 4–10) and a mean WES of 7.77 (SD 1.66; range 4–10). The two treatment procedures yielded comparable aesthetic outcomes [30].

These results were confirmed by Guarnieri et al. [39], who compared the aesthetic outcome of immediate (12) and delayed (13) singleimplant treatment in the anterior maxilla. After an average period of 3 years of function, no significant differences were found between IIT (PES: 11.06 ± 0.63; WES: 7.32 ± 0.71) and CIT (PES: 11.81 ± 0.55; WES: 7.53 ± 0.74) [39].

Within its limits (patients at high risk of aesthetic failure such as smokers, patients with thin gingival biotype and patients who underwent major bone augmentation procedures were not included), our present retrospective study, based on data from 103 patients who had been treated with an immediately restored single implant in post-extraction socket (IIT, 42 patients) or healed site (CIT, 61 patients) of the anterior maxilla, seems to confirm these results. In our study, the two groups (IIT and CIT) were basically homogeneous as they did not differ with respect to patients' gender, implant position, presence/absence of connective tissue graft or bone contouring (all P-values > 0.05); the only significant difference between the two groups was in patients' age (P = 0.002), since patients in the IIT group were on average 8.5 years older (46.5 vs. 38) than in the CIT group. This difference was determined by the presence of 21 young patients with agenesis of lateral incisors in the CIT group; accordingly, linear regression models to test the hypothesis of no difference in the mean scores between the two implant groups were adjusted for age. In this study, the aesthetic evaluation revealed satisfactory outcomes, with a PES/WES score of 16.6 ± 2.6 and 15.7 ± 3.0 for IIT (n = 42) and CIT (n = 61), respectively, at the delivery of the definitive restorations; PES/WES, PES and WES scores for IIT were slightly higher than those for CIT, although this difference was not statistically significant. However, as a higher

decrease in the PES/WES score was observed in the CIT group over time (–0.49 points; 95% CI: –0.83 to –0.15), mainly due to a reduction in the PES score (–0.37 points;95% CI: –0.61 to –0.13), a statistically significant difference was found in the PES/WES score between immediate and conventional implants at the 3-year follow-up (P = 0.03). This result can be difficult to interpret: it may be related to the fact that immediate implants had a higher score at delivery, or to the presence of a high number of patients with agenesis in the CIT group. Patients with missing lateral incisors are difficult to treat: they often need hard and soft tissue augmentation before or in conjuction with implant placement [28–30]. However, no statistically significant differences were found between the PES and the WES scores for IIT and CIT, 3 years after implant placement. Moreover, mean changes (95% CI) between IIT and CIT in the PES/ WES score over time were not statistically significant.

Presence of adequate bone volume (horizontal, vertical, contour), healthy and stable peri-implant soft tissues (form of the periodontium, biotype of the periodontium) as well as optimal three-dimensional implant position (mesio-distal, apico-coronal, buccolingual and angulation) and ideal prosthetic emergence profile are essential pre-requisites to achieve aesthetic success with immediate implant treatment [20,29,44,45].

The level of bone support and the soft tissue dimensions around the implant-supported single-tooth restoration are factors suggested to be important for the aesthetic outcome of implant therapy [20]. With immediate placement, the ideal extraction socket would present little or no bone loss. Atraumatic tooth extraction is therefore of key importance prior to immediate implant placement and the buccal plate has to be intact [46]. In our study, an important criterion for patient inclusion was the dimension of the available alveolar bone. Periodontally compromised patients were excluded from the study; in the immediate group, atraumatic extractions were performed, and the loss or damage of buccal bone wall was an exclusion criterion. In addition, patients with a thin-scalloped biotype were not included in our study: these patients, in fact, are characterized by a higher risk of soft tissue recession and underlying resorptive osseous

remodelling, exposing the metal margin of the implant, thus leading to unpredictable or unsatisfactory aesthetic outcomes [20]. Only patients with thick gingival biotype were included in the present study: these patients are better candidates for immediate implant placement because there is less chance that the tissues will recede post placement, thus resulting in stable aesthetics [20]. It has been suggested that immediate implants should be provided with bone walls about 1– 2 mm wide on buccal and lingual aspects to allow a stable bone height to be maintained [47,48]. Unfortunately, only a limited number of sites in the anterior maxilla display such a clinical situation; several studies suggested that in the majority of extraction sites in the anterior maxilla, thin (≤1 mm) buccal walls were present [49,50]. This, in turn, means that in most clinical situations encountered, augmentation procedures are needed to achieve adequate bony contours around the implant. Although the currently available evidence does not allow for any conclusive statements regarding the efficacy of a concomitant regenerative technique in preventing the amount of alveolar reduction after tooth extraction and immediate implant placement [51], grafting sockets with different materials have been proposed to counteract alveolar ridge reduction [52]. Clinical studies have been performed to evaluate the outcome of such surgical protocols, indicating that ridge contraction following tooth extraction could be diminished when combined with socket bone grafts [9,15] and/or the use of connective tissue grafts [53]. In our study, the hard tissue graft, a synthetic calcium phosphate bone substitute, was placed in the space between the implant surface and the inner surface of the buccal bone wall, whilst the soft tissue graft was adapted to the outer surface of the bone wall. Our results demonstrate that graft procedures may improve the final aesthetic outcome of implant treatment: in fact, the presence of bone contouring was associated with a significantly higher PES/WES score for IIT than for CIT. Moreover, in our study IIT yielded significantly superior aesthetic outcomes than CIT in younger patients (≤30 years), and with implants placed in the central incisor/cuspid areas. The first finding is not surprising, and it may be related to the better healing potential of the socket in the young patient:

bone repair is different between young and elderly patients [54]. The second finding may be related to the peculiar anatomy of the cuspid area, where the bone wall is generally thicker and well represented; however, it may also be determined by the limited number of patients treated with immediate implants in these areas, which represents a limit of our study.

Without any doubt, the position and the inclination of the implants play a pivotal role in achieving a predictable aesthetic outcome [20,45]. When an implant is placed in a fresh extraction socket, it is prudent to place it in the palatal portion of the socket, with its marginal border below the ridge of the fresh socket to compensate for the expected resorption [20,45]. In our study, care was taken to place the implant in an ideal 3D position in order to achieve a better aesthetic result.

Finally, it is essential to guarantee an adequate prosthetic emergence profile, to preserve as much of the circumferential bone height around the implant neck as possible [55]. In this study, all implants were immediately restored with provisional crowns. The provisional crowns, taken out of any occlusal contact, were carefully contoured to immediately provide correct emergence profiles, adaptation to the gingival tissues, and appropriate support to the interdental papillae, so that an aesthetically pleasing result could be obtained and maintained over the years [55].

Conclusions

This study has limits: in fact, all patients at high risk of aesthetic failure (smokers, patients with thin gingival biotype and patients who underwent major bone augmentation procedures) were excluded. However, among the enrolled, well-selected patients, both immediate and conventional singleimplant treatment in the anterior maxilla yielded satisfactory aesthetic outcomes. At the delivery of the final restoration, a PES/ WES score of 16.6 ± 2.6 and 15.7 ± 3.0 was reported for IIT (n = 42) and CIT (n = 61), respectively: this difference was not statistically significant. At the 3-year follow-up examination, a statistically significant difference (P = 0.03) was

reported between the two groups, with a PES/WES of 16.4 ± 2.8 and 15.2 ± 3.3 for IIT and CIT, respectively. This difference may be related to the presence of a high number of patients with agenesis in the CIT group: in fact, patients with missing lateral incisors are difficult to treat, and often require hard and soft tissue augmentation before or in conjuction with implant placement. However, no statistically significant differences were found between the PES and the WES scores for IIT and CIT, 3 years after implant placement nor in the mean change (95% CI) over the two evaluations. Finally, IIT seemed to yield better aesthetic outcomes than CIT in younger patients (≤30 years), with implants placed in the central incisor/ cuspid areas, as well as in the presence of bone contouring. Further long-term studies on a larger sample of patients are needed to confirm these results.

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E- CONCLUDING REMARKS

In the present research, we have investigated the three most important interfaces in implant dentistry, namely

1. the bone/implant interface;

2. the implant/abutment interface;

3. the restoration/mucosa interface.

This has been done in order to understand whether it is possible to enhance the biological integration, functional stability and aesthetic outcome of implant-supported restorations.

With regard to the bone/implant interface, our human histologic/histomorphometric evaluation has provided evidence that nanostructured calcium-incorporated (NCI) implants immediately loaded in the posterior maxilla achieve significantly higher bone-to-implant contact (BIC%) when compared to smooth-surface, machined (MA) implants. These findings are in accordance with the current literature reporting a better and faster biological integration with implants using micro- and nano-rough surfaces. It may therefore be important to use implants with micro- and nano-rough surfaces in difficult clinical contexts, such as in areas with poor bone quality (for example, the posterior maxilla), in order to improve the bone healing process and to facilitate osseointegration. Our data should, however, be interpreted with caution, due to the peculiar study methodology (only functionally stable implants were histologically/histomorphometrically evaluated) and the limited number of implants placed. Therefore, additional controlled randomized clinical studies are needed to draw more specific conclusions about the early bone response to NCI implants when subjected to immediate loading.

With regard to the implant/abutment interface, we have evaluated the clinical performance of locking-taper (Morse taper) connection implants in

the long term (10 years of follow-up) in order to investigate whether this new, screwless implant/abutment connection can effectively reduce the incidence of mechanical and/or technical complications in fixed implant-supported restorations. In the past, the main focus of clinical studies was the success of osseointegration and the survival of implants; the outcome of implant therapy was often presented without providing detailed information on the prosthetic rehabilitations, and it was commonly accepted that biological and prosthetic complications can occur with implant-supported fixed restorations. Managing these complications, however, requires extra chair-side time, additional costs and causes patient dissatisfaction. For this reason, the number of mechanical and technical complications that occur under loading should be minimized, and the implant/abutment connection is key to achieving this. In our present prospective study on locking-taper connection implants, we found an overall cumulative implant survival of 98.7% (98.3% maxilla, 99.1% mandible) and a cumulative "complication-free" survival of restorations of 88.6% (single crowns 91.7%, fixed partial prostheses 83.1%, fixed full arches 73.8%) after 10 years of follow-up. A very low incidence of mechanical (3/739: 0.4%) and technical (24/739: 3.2%) complications was found. This incidence of mechanical and technical complications implant/abutment connections was lower than that reported in the current literature. Therefore, in accordance with the evidence emerging from the literature, the use of locking-taper implants may help guarantee the mechanical stability of the implant/abutment connection in the long term. The use of locking-taper implants represents a successful procedure for the rehabilitation of partially and completely edentulous arches, as the high mechanical stability of this connection seems to minimize the incidence of prosthetic complications in the long term. Further long-term follow-up studies on locking-taper connection implants are needed to confirm these results. Nevertheless, the implant-abutment connection should be regarded as a key factor in the long-term success of fixed implant-supported restorations, and the locking-taper connection can certainly guarantee excellent functional stability of the assembly.

Finally, with regard to the restoration/mucosa interface, the aim of the present study was to compare the aesthetic outcome of single implants in post-extraction sockets (immediate implant treatment, IIT) and healed ridges (conventional implant treatment, CIT) of the human anterior maxilla, by means of the pink aesthetic score/ white aesthetic score (PES/WES) index. At the end of our study, both the immediate and conventional single implant treatments in the anterior maxilla yielded satisfactory aesthetic outcomes. At delivery of the final restoration, PES/ WES scores of 16.6 ± 2.6 and 15.7 ± 3.0 were reported for IIT (n = 42) and CIT (n = 61), respectively; there was no significant difference between treatments. At the 3-year follow-up examination, a statistically significant difference between the two groups (P = 0.03) was reported, with PES/WES scores of 16.4 ± 2.8 and 15.2 ± 3.3 for IIT and CIT, respectively. However, this difference may be related to the presence of a high number of patients with agenesis in the CIT group. In fact, patients with missing lateral incisors are difficult to treat, and often require hard and soft tissue augmentation before or in conjunction with implant placement. No statistically significant differences were found between the PES and the WES scores for IIT and CIT at 3 years after implant placement nor in the mean change (95% confidence interval) between the two evaluations. Finally, IIT seemed to yield better aesthetic outcomes than CIT in younger patients (≤30 years), with implants placed in the central incisor/cuspid areas, as well as in the presence of bone contouring. Our present study has limits, since all patients at high risk of aesthetic failure (smokers, patients with thin gingival biotype and patients who underwent major bone augmentation procedures) were excluded. Therefore, further long-term studies on a larger sample of patients (including patients with a high aesthetic risk profile) are needed to confirm our results. However, our study confirms that both treatment protocols (immediate implant treatment and conventional implant treatment) can guarantee satisfactory aesthetic results when performed by experienced clinicians on well-selected patients.