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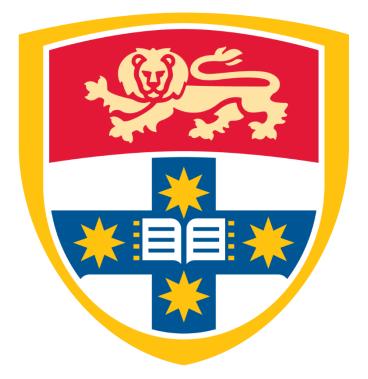
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A COMPARATIVE HISTOMORPHOLOGICAL AND MICRO CT STUDY OF THE PRIMARY STABILITY AND THE OSSEOINTEGRATION OF THE SYDNEY MINI-SCREW: AN ANIMAL STUDY USING NEW ZEALAND RABBITS

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A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Clinical Dentistry (Orthodontics)

September 2014

Dedication

This thesis is dedicated to my parents Constantino Bacopulos and Chrisula Marangu, for their so valued sacrifices so my brothers and I can experience happiness through the achievement of our goals. Their genuine enthusiasm in supporting my extended academic journey was the motor to every accomplished aspiration.

To my brothers Giorgo and Ermis for all the fantastic feelings they bring to my life.

To my partner Jose Antar, who stood by my side offering endless support, love and encouragement at all times.

To Gisela Contasti and Astrid Contasti for accepting my energy and converting it into this learning experience. For showing me the road and helping me get started on the path to this degree.

To Genesis Andreina Manzo from whom I always heard special words of motivation and encouragement since the first instance I decided to endeavour my postgraduate dream. You might not be with us anymore, but nothing will erase the beautiful memories. I miss you my dear friend.

You all made my hours fly away in the most grateful manner. I could not have asked for a superior assembly of souls watching my steps.

Anastacia Bacopulos Marangu

Declaration

CANDIDATE CERTIFICATION

This is to certify that the candidate carried out the work in this thesis in the Orthodontic Department, University of Sydney, and this work has not been submitted to any other University or Institution for a higher degree.

Anastacia Bacopulos Marangu

Acknowledgements

It is a pleasure to convey my immense appreciation towards those who assisted with the completion of this thesis project.

Professor M. Ali Darendeliler, Head of Department of Orthodontics, University of Sydney for his assistance and guidance through this project.

Dr. Oyku Dalci, Senior Lecturer, University of Sydney for being a great teacher and mentor, investing long hours in reviewing the content of the thesis.

Dr, Alexandra Papadopoulou, Senior Lecturer, University of Sydney, for conveying her positive spirit and unceasing enthusiasm in guiding me through the final preparation towards submission.

To Ali Fathi, Bioengineering and Tissue engineering Laboratory, School of Chemical and Bimolecular Engineering, University of Sydney, who has always been a constant source of guidance, knowledge and inspiration from the very beginning.

To Maria Missikos and her team within the laboratory of the Orthodontic Department, University of Sydney, for the way they reached out to hold my hand at unexpected moments and for always being available to help.

To Mr. Mathew Foley, from the Australian Centre for Microscopy & Microanalysis Research Facility at the University of Sydney for his for his skilled technical guidance and help with the micro CT analysis.

Trevor Shearing, Senior Technical Officer and Dr Shao Cong Dai, Rheology Group, School of Aerospace, Mechanical and Mechatronic Engineering, for allowing me to use their scale and lab to run pilot experiments prior to beginning the animal project. Associate Professor Colin Dunstan, in Biomedical Engineering, School of Aerospace, Mechanical and Mechatronic Engineering at the University of Sydney, for dedicating a valued amount of his personal time to discuss my project, preparation of the histology samples and expert technical assistance.

To Ashley Wu, Bachelor of Biomedical Engineering, School of Aerospace, Mechanical and Mechatronic Engineering at the University of Sydney, and current visiting student within the Faculty of Dentistry, for devoting an appreciated amount of his time to discuss and contribute in this project.

Elizabeth Mazzei, clinic manager and Rebecca Chan, Administrative Officer, Department of Orthodontics, Faculty of Dentistry for their support and ordering of most of the materials required for this project.

Sabrina Michael for her appreciated contribution in providing advice for the thesis, for keeping me smiling at all times and for listening my endless adventures throughout this research season.

To Claudia Cespedes for her friendship and encouragement despite of all the occurring difficulties.

The postgraduate students and tutors, for their continuous patience and encouragement. All the team within the Department of Orthodontics for encouraging me to try harder, and who have provided me with an amazing learning and welcomed me into a profession that will be eternally rewarding.

Dr Kit Chan, for her support in allowing me to present the content and progress of this investigation for the first time in the 49th Begg conference.

I would like to thank you deeply. My sincere appreciation goes to all those involved in providing me with this tremendous opportunity. This experience has led me to continue my strong passion within the field.

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ABBREVIATIONS

SAS	Skeletal anchorage systems
TADs	Temporary anchorage devices
MS	Miniscrew
MSs	Miniscrews
SMS	The Sydney Mini Screw
BGS	Bone graft substitutes
iBGS	Injectable bone graft substitute
μCT	Micro CT
CaPO ₄	Calcium phosphate
CaSO ₄	Calcium sulphate
CaSO ₄ /CaPO ₄	Calcium sulphate/calcium phosphate
CaSO ₄ /CaPO ₄ CaSO ₄ -DCPD	Calcium sulphate/calcium phosphate Dicalcium phosphate dihydrate
CaSO ₄ -DCPD	Dicalcium phosphate dihydrate
CaSO ₄ -DCPD CAD	Dicalcium phosphate dihydrate Computed aided design
CaSO ₄ -DCPD CAD CPC	Dicalcium phosphate dihydrate Computed aided design Calcium phosphate cement
CaSO ₄ -DCPD CAD CPC iCPC	Dicalcium phosphate dihydrate Computed aided design Calcium phosphate cement Injectable calcium phosphate cement
CaSO ₄ -DCPD CAD CPC iCPC FE	Dicalcium phosphate dihydrate Computed aided design Calcium phosphate cement Injectable calcium phosphate cement Finite element
CaSO ₄ -DCPD CAD CPC iCPC FE FEA	Dicalcium phosphate dihydrate Computed aided design Calcium phosphate cement Injectable calcium phosphate cement Finite element Finite element analysis

1 INTRODUCTION

Temporary anchorage devices (TADs) involve an array of benefits which have led to a rapid rise of miniscrews (MSs) popularity for orthodontic clinical applications. Innovative data presented by Gainsforth and Higley in 1945¹ suggested the idea of using basal bone as anchorage. Creekmore and Eklund published a case report demonstrating the usefulness of metal implants in orthodontics, increasing interest lead to the constant improvement in the field.² Roberts *et al.*³ investigated the potential of endosseous implants as means of rigid skeletal anchorage for orthopaedic and orthodontic use. Furthermore, human studies found minimal need for patient compliance by using rigid osseointegrated implants in the retromolar and palatal areas.^{4, 5} However, their application was limited due to their large size and the need for osseointegration prior to force application. To overcome this, MSs were introduced as an alternative to osteointegrated implants for skeletal anchorage.^{6, 7} Ever since, significant findings have contributed to advocate titanium MSs within the orthodontic armamentarium.

Anchorage, known as "the resistance to unwanted tooth movement", is commonly used for orthodontic treatment to control the mechanics implemented in the correction of skeletal or dental malocclusions. The application of orthodontic and orthopedic mechanotherapy and its reactive forces may need to be controlled by the resistance provided by anchorage systems.⁸ As a result, successful orthodontic treatments require a balance of force systems based on Newton's third law of motion, which states that for every action there is an equal and opposite reaction.⁹

Amongst TADs, MSs and surgical miniplates fixed to bone are the two major choices used by clinicians as orthodontic anchorage.¹⁰ Occasionally higher forces are needed in order to achieve orthopaedic results.¹¹ The use of surgical plates often entail a more invasive approach¹² adding considerable risk and cost to the overall treatment. An alternative to this could be the use of MS via improved primary and secondary stability which are vital in order to reduce failure rates and maximize efficacy. Failure rates of miniscrew (MS) are high,¹³⁻¹⁸ and success rates depend on multiple factors such as:

operator's experience, MS design and features, method of placement, site of placement, and patient care.^{17-19,13, 14, 20} Even though osseointegration is not expected or required for the achievement of miniscrew anchorage, the quantity and quality of the bone are key factors strictly related to the miniscrew's failure or success.²¹

To overcome some of the limitations of MS, interest has arised in reinforcing the patient's bone characteristics in such a way that optimal orthodontic mechanics could satisfy both the patient and the clinician.

Injectable calcium phosphate bone graft substitutes (BGS) have been used in conjunction with skeletal anchorage devices promoting a local osteoinductive and osteoconductive behaviour with promising results in aiding MSs retention.^{22,23} The bone-iCPC-titanium surface has displayed close contact; an ideal trait for increasing primary stability.

The aim of this study was to evaluate the feasibility of using an injectable bone graft substitute (iBGS) in conjunction with a modified novel hollow MS design to enhance primary stability of MS in an animal model.

2 REVIEW OF THE LITERATURE

2.1 ANCHORAGE

2.1.1 HISTORIC BACKGROUND AND DEFINITION

Anchorage is a significant consideration for orthodontic intervention, and often a critical component in treatment planning within all techniques and philosophies pursued by clinicians. It was defined by Louis Ottofy in 1923 as "the base against which orthodontic force or reaction of orthodontic force is applied".²⁴ The application of orthodontic or orthopedic mechanotherapy and its reactive forces are controlled by the resistance given through anchorage systems.^{8, 25} The key role of bone, as an anatomical structure, is fundamental to overcome the issues of anchorage as a biological problem that arises with the application of orthodontic forces.^{25, 26}

Limitations in providing orthodontic treatment due to inadequate anchorage was reported by Wright in 1938²⁶, as well as Gainsforth and Higley in 1945¹. They stressed that to preserve anchorage is amongst one of the most difficult problems in orthodontic mechanics.

2.1.2 CLASSIFICATION OF ANCHORAGE

Special consideration is given to anchorage during treatment planning to evaluate and control the reciprocal effects of tooth movement where required. For this, different strategies of anchorage control are considered in all three planes of space. Anchorage can be obtained from intraoral, extraoral, tooth dependant and non-tooth dependant sources.

The categorization of anchorage has been modified over time by different authors with the intent of involving all possible aspects interacting among tooth movement, growth, muscle function and soft tissue changes which could all modify the effect of orthodontic treatment aims.

Louis Ottofy $(1923)^{24}$ categorized anchorage into simple, stationary, reciprocal, intraoral, inter-maxillary or extra-oral. This has been adjusted with several variations.

Two general types of intra-oral anchorage were described by Wright (1938):²⁶

- Simple anchorage "defined as that form of anchorage where the attachment is such that upon the application of force the tooth is permitted to tip". In this scenario, the force is distributed among a larger tooth or group of teeth with the aim of controlling the movement of a smaller tooth.
- Stationary anchorage "defined as that form of anchorage where the attachment is rigid and causes the tooth to move bodily, if it moves at all". This is the situation where the use of light forces tip a segment of teeth with a simultaneous restriction of bodily movement of the teeth subjected to the reactionary force.

Moyers $(1973)^{27}$ further expanded the classification of anchorage according to²⁵:

- The site.
 - \checkmark Intra-oral involves musculature, teeth, alveolar bone or basal bone
 - ✓ Extra-oral− involves the cranium (occipital or parietal anchorage), cervical anchorage (cervical or neck region), or facial bones (mandibular symphysis and forehead).
- The manner of force application as simple, stationary or reciprocal.
- The jaws involved as inter-maxillary or intra-maxillary.
- The number of anchorage units as single or primary, compound, multiple or reinforced.

Burstone (1982)²⁸ added a space closure classification into 3 anchorage groups:

- Group A space closure mainly by anterior retraction.
- Group B space closure by at least half of the space being used for retraction.
- Group C space closure mostly by protraction of posterior teeth.

Burstone's influence on segmented mechanics supported the following strategies in extreme situations comprised in groups A or C to minimize unwanted tooth movements:²⁸

- Separate canine retraction (severe crowding).
- En masse space closure (adequate arch length).
- Springs with differential residual moments with a distally off-centered loop for protraction of posterior teeth by controlled tipping with nonexistent or minimal labial movement of the anterior teeth.
- Symmetrically placed attraction springs in combination with Class II or Class III elastics; otherwise protraction headgear to encourage mesialization of the posterior units.

Melsen and Verna $(2000)^{29}$ presented a rational approach to orthodontic anchorage which involved the use of metallic implants:

- Intraoral Anchorage
 - Intramaxillary
 - Dental,
 - Extradental (mucosa of the palate, wires, or metallic implants).
 - Intermaxillary
 - The occlusion itself,
 - Class II and Class III elastics,
 - Bite jumping devices, and other appliances capable of transferring forces from one arch to the other.
- Extraoral anchorage
 - Head, neck, head and neck, or the chin.

Proffit (2007)³⁰ defined a number of anchorage situations:²⁵

- Reciprocal tooth movement mutual forces upon teeth and arch sections are the same.
- Reinforced anchorage addition of resistance units, for example teeth or extraoral structures that reduce the pressure on the anchor units by distributing the reaction force over a larger area.
- Stationary anchorage minimizes the displacement of anchor teeth by affecting them bodily if they happen to move at the same time that the group of movement teeth tip.
- Differential effect of very large forces obtained with additional movement of the arch fragment with the larger periodontal ligament (PDL) area.
- Cortical anchorage given by the density of this layer of bone which is more resistant to resorption compared with medullary bone and hence slowing tooth movement as the roots contact cortical plates.
- Skeletal (absolute) anchorage provides no tooth movement except for that desired.

Schopf and Bowman (2008)³¹ highlights the following three types of anchorage:²⁵

- Intra-arch anchorage this method is achieved between teeth within the same dental arch.
- Inter-arch anchorage efficacy of mechanics obtained from teeth of the opposite dental arch.
- Anchorage support that is independent from teeth techniques which involve extra-oral structures or devices based on the skeletal support or that given by muscles.

Flaws in earlier anchorage classifications failed to include the transverse and vertical dimensions. Knowing that orthodontic treatment has a natural extrusive effect, it is important to control the vertical since the early stages of treatment. Additionally, orthodontic mechanics should always mind the transverse and should also be aimed in maintaining torque, arch coordination and arch width to avoid interferences within posterior and anterior relationships.

2.1.3 ADVANCES IN ORTHODONTIC ANCHORAGE

Traditionally, extraoral anchorage was often the gold standard to reinforce intraoral anchorage. It consisted of headgear and facial masks which transferred anchorage from cranial or facial structures to the teeth. This concept has been documented as early as 1866 by Norman William Kingsley and was adopted by Angle in 1888.³² Extraoral anchorage has been found successful if worn for 12-14 hours per day.^{33, 34} However, disadvantages such as trauma³⁵ and compliance has encouraged the use of alternative skeletal anchorage methods to provide an intraoral approach to anchorage control, tooth movement, orthopaedic changes and control of cants of the occlusal plane.

In 1945, Gainsforth used implants in basal bone as orthodontic anchorage to improve treatment outcomes. Even though all the implants were lost within 16-31 days, a new concept was introduced which led further research to be conducted.¹

In 1952, the concept of osseointegration was first introduced to the field by the orthopaedic surgeon Dr. Per-Ingvar Brånemark and co-workers. This was an accidental discovery while conducting a bone-healing experiment which demonstrated the potential for direct and functional bone integration via the use of a titanium implant surface. It was initially applied as part of an animal study, and by 1965 it was used in conjunction with prosthetic appliances to restore intraoral function leading to an incredible advance in the dental field.³⁶⁻⁴⁰ Since then, many orthodontists showed interest in using a variety of implant materials as skeletal anchorage.

The clinical use of implants as an orthodontic anchorage unit has been investigated widely during the past 69 years. The first published clinical case report involving the successful use of a miniscrew type anchorage was demonstrated by Creekmore and Eklund (1983). Simultaneous research was conducted by Turley *et al.* (1980 - 1988) and Roberts *et al.* (1984 – 1994) amongst others.^{3, 4, 41-44} They developed implant systems for orthodontic use based on the primary principles of Wehrbein and Glatzmaier, *et al.*⁴⁵⁻⁵⁰ Nowadays, the appliance is available as temporary devices which allow clinicians to gain outstanding control of force direction while applying tooth mechanics in a more

effective and efficient way compared with conventional orthodontics. Additionally, new technologies and advances in implant tools, techniques and systems were achieved and continue to be a research interest all over the world.^{22, 51-55} The miniscrew use in orthodontics aims for absolute anchorage, which by definition implies no tooth movement (zero anchorage loss) as a result of reactional forces.^{8, 10, 56}

2.2 SKELETAL ORTHODONTIC ANCHORAGE

Skeletal anchorage systems (SAS) are an effective orthodontic source to enhance stability during orthodontic loading for the treatment of diverse malocclusions.^{9, 12, 57-67} It can be achieved via the use of osseointegrated dental implants alone, or combined with surgical fixation wires, miniplates, onplants and non-osseointegrated miniscrews.³¹

Three main areas of clinical application for skeletal anchorage in orthodontics have been described:⁶⁸

- Skeletal orthodontic-prosthetic anchorage, where prosthetic implants are placed during orthodontic treatment to serve in direct anchorage for tooth movement and later used as abutments to attach the fixed prosthetic replacement. Not indicated in growing patients.
- Skeletal orthodontic anchorage, where direct or indirect skeletal anchorage is needed to replace conventional anchorage or eliminate the need of compliance. It provides controlled tooth movement in all three dimensions, especially in the interdisciplinary patient that most often will present high anchorage requirements.⁶⁹ Furthermore, as an alternative camouflage treatment to selected invasive orthognathic surgery procedures in the adult patient.^{70, 71}
- Skeletal anchorage for orthopedic procedures, where higher forces are applied to the devices placed in the bony facial structures in order to modify the existent skeletal discrepancy^{11, 62} with potential optimized control on relapse tendency and undesired dental compensations.^{55, 72} This includes implant supported palatal expanders,⁷³ miniplates,^{11, 55, 74} and distractors.^{75, 76}

It is beyond the scope of this review to further discuss alternative SAS to TADs, specifically miniscrews.

2.2.1 TEMPORARY ANCHORAGE DEVICES – TADS

2.2.1.1 Definition

A TAD is defined as "devices that are temporarily fixed to bone for the purpose of enhancing orthodontic anchorage by supporting the teeth of the reactive unit or by obviating the need for the reactive unit altogether and which is subsequently removed after use".⁷⁷

There is substantial variation of terminology, and the acronym given to MSs is thought to lack appropriate descriptive value as it could include other sources of temporary anchorage, namely headgears, lip bumpers, lingual arches, among other orthodontic appliances.⁷⁸ The term miniscrew (MS) describes its size, shape and osseointegration and will therefore be used in this review.

The continuous development and improvements on dental implants, orthognathic fixation procedures and conventional orthodontic anchorage systems, resulted in the creation of MS implants as a provisional method which allows clinicians to overcome the limitations of using teeth as anchorage. The use of miniscrews for orthopaedic treatment of skeletal malocclusions can offer patients an alternative to surgical procedures which they commonly refuse. For instance, a mandibular retrognathic, high angle, growing patient can benefit from substantial orthopaedic correction by selectively intruding the posterior teeth. This allows for mandibular autorotation and improved chin projection, decrease of the mandibular plane angle, improvement of the facial convexity and decrease of the lower facial height.⁶² Considering the variability in miniscrews success rates, current research is focused on preparing long-term data to support and improve its stability,²⁵ yet this approach continues to be a useful addition to the orthodontic armamentarium.⁷⁹

Presently, several classifications of TADs have been reported. It involves different features and designs which are often adjusted to each particular treatment requirement. Miniscrews have been included in different categories within the various classifications.^{4, 80-83}

2.2.1.2 Classification of TADs

Cope (2005) described MS as biocompatible fixation screws able to provide mechanical retention. The author classified TADs in two different categories according to their nature:^{10, 25}

A. Biocompatible TADs

- Osseointegration
 - ✓ Dental implant
 - Palatal implant
 - Retromolar implant
 - ✓ Palatal Onplant
- Mechanical Retention
 - ✓ Fixation Screws
 - Fixation screws with Plates
 - Miniscrew implants
 - ✓ Fixation Wires
- B. Biological TADs
 - Osseointegration
 - ✓ Ankylosed Teeth
 - Mechanical
 - ✓ Dilacerated Teeth

Brite Melsen (2005) described MS as surgical devices that allow immediate loading for three dimensional control. The author described two categories of SAS according to their origin:^{25, 69, 84}

- As developed from dental implants The intraosseous part is surface-treated to enhance the osseointegration. Predrilling procedure combined with a period of time for healing is required prior to loading. This category includes the following devices:
 - Palatal implants
 - Onplants
 - Retromolar implants
 - Orthodontic implants
- As developed from surgical screws The intraosseous surface is smooth with a surgical screw attached and allows immediate loading. This category includes the following devices:
 - Miniplates with various transmucosal extensions (one-point contact)
 - Single screws or mini implants (one-point contact)
 - Aarhus mini-implant (three-dimensional control)

Labanauskaite, *et al.* (2005) described MS as cylindrical, osseointegrated or nonosseointegrated devices used for orthodontic purposes. The author classified the TADs according to shape and size, bone-to-implant contact (BIC), and application:^{25, 85}

- ✤ According to the shape and size
 - Conical (cylindrical)
 - ✓ Miniscrew implants
 - ✓ Palatal implants
 - ✓ Prosthodontic implants
 - Miniplates implants
 - Disc implants (onplants)

- ✤ According to the implant bone contact
 - Osseointegrated
 - Nonosseointegrated
- ✤ According to the application
 - Used only for orthodontic purposes (orthodontic implants)
 - Used for prosthodontic and orthodontics purposes (prosthodontic implants)

2.2.1.3 Miniscrews versus Miniplates

Jenner and Fitzpatrick introduced orthodontic anchorage through bone plates in 1985.⁸⁶ The authors used a 4 unit plate as anchorage in the ascending ramus to move a first molar distally for space creation to correct premolar crowding.⁸⁶ Acceptance of miniplates, which are thought to be the second most used TAD in the field of orthodontics⁷⁷ has increased in the last couple of decades, and it is attributed to the extensive research published by Sugawara's group.^{12, 74, 87-89} Its popularity relies on improved SAS because of their biocompatibility, ability to load immediately and rigidity to resist orthopedic and orthodontic mechanics.⁹⁰ This is possible given its fixation with more than one screw, which eventually provides higher stability than single miniscrews.^{63, 65, 77, 91}

While some clinicians claim benefits such as decreased risk of sinus perforation or damaging nerves and tooth roots given to the small size of the MS fixing the titanium anchor plate to the bone,⁹² others find it invasive and not practical. This is due to the need of specific location placement which involves a larger bony area compared to miniscrews.⁷⁷ Additionally, a flap operation is necessary to engage the miniplate with the cortical bone. This is associated to greater discomfort and pain on placement and removal, and mild to moderate swelling¹³ with possible risk of infection ^{20, 90, 93} compared to the use of miniscrews alone. However, being anchored to the bone by several miniscrews, greater stability and success rates are attributed to miniplates.¹²

Sugawara *et al.* (2007) found minimal loosening, fracture, and mucosal overgrowth complications linked to the application of miniplates.⁹³

At present, clinicians can rely in osseous anchorage for more predictable biomechanics that will allow treatment of the following aspects of a malocclusion excluding the need of a surgical approach:^{31, 56, 62, 94-97}

- Class I and II dentoalveolar protrusion,
- Class III dentoalveolar protrusion,
- Class II mandibular retrognathism.
- Anterior deep or open bite,
- Occlusal plane cant,
- Dental midline asymmetry,
- Impacted teeth extrusion,
- Tooth or group of teeth movement (intrusion, extrusion, uprighting, distalization, mesialization, space closure or opening)

Currently, most scientific data supports the use of MS and miniplates among the principal treatment modality for managing such orthodontic conditions.^{12, 20, 65, 74, 81, 87-89, 98,98} The literature shows that to achieve the above mentioned treatments, MS are generally preferred over miniplates. Despite the advantages provided by the miniplates, the need of a surgical procedure to fix the plates with miniscrews can be more expensive, time consuming and invasive compared to miniscrews alone.^{99, 100} An alternative to miniplates is required.

Clinical indications involving miniscrew implants have been presented by numerous authors^{47, 95-97, 101} who agree on a generalized success with minimum patient compliance and more importantly, with reduced side effects such as root resorption.

The results of clinical research on miniscrews failure are still controversial within the existing literature.¹⁸ Clinicians continue to experience miniscrew loosening during treatment with a high percentage being surgery related (technique sensitive).¹⁰² To

improve miniscrews success, primary focus is given to its initial stability which is essential for maximized treatment outcomes.

Overall, TADs significantly expand the scope of biomechanical therapy and often enhance clinical outcomes.^{4, 63, 81-83, 85} Particular focus is given to MS in order to overcome current failures.¹⁰²

2.2.2 BENEFITS AND COMPLICATIONS OF MINISCREW IMPLANTS

2.2.2.1 Benefits of Miniscrews

Miniscrews offer numerous advantages. It involves a low cost due to its simple and minimally invasive surgical procedure for insertion and removal. It can eliminate the need of unnecessary braces in arches comprising well-aligned dentitions, thus also offering a treatment option for those patients with high aesthetics requirements.

When appropriately used, rapid healing and integration of the MS with the surrounding tissues, allow for immediate loading where required.^{10, 58, 59} This is particularly important if it can allow a decrease in treatment time and an improved quality of treatment. Moreover, MSs show stable and biocompatible integration to cortical and trabecular bones when individual circumstances and specific insertion areas are carefully evaluated.^{59, 61} Furthermore, the use f MSs restore functional requirements of the dentition at the same time as contributing with aesthetic expectations by restricting the appliances to the arch or segment involved.¹⁰³ If these benefits can decrease the treatment time and the costs involved, then an increased predictability of the treatment outcome is possible.^{10, 59, 103}

2.2.2.2 Complications of miniscrews

Careful planning is essential and a multifactorial approach must be considered in order to maximize the success of the MS device. Common clinical problems have been reported over time, and the general agreement relies on lasting stability after the fourth

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month ¹⁰⁴ when inflammation around the implant is controlled accordingly.¹⁰⁵ Topouzelis (2012) ¹⁰⁶, is in agreement with most of the failures taking place within the first months of MS loading, and showed that an additional reduction of success by 47% was accounted for every month of loading.

This treatment modality will suit most of the patients. Those with unhealthy surrounding soft tissues and poor bone density are at risk and prone to failure of the MS implant.¹⁰⁷ Special attention in the presence of varying oral anatomies within patients is required in order to identify narrow interradicular space, extended maxillary sinus, areas with severe alveolar bone loss, or dilacerated roots⁶³ which can easily generate complications that involve intraoperative or postoperative consideration.¹⁰⁸

Having most failures occurring during the initial stages of placement, the surgical procedure, operators experience and primary stability are important factors to consider. Miniscrew insertion requires training and accurate techniques to provide safety to the anatomical structures near the site of placement. The clinician may require preparation of the site with precise orthodontic mechanics to align and create sufficient space for a safe MS insertion.^{81, 103, 109}

Patient education is essential and a strict protocol including precise instructions should be reinforced regarding care and oral hygiene. Regardless of being a compliance-free anchorage system, inflammation can compromise the stability of the MS. This is supported by Park (2003) who compared inflammation resistance relative to the anatomy of the mucosa. The author showed higher success rates associated to implants placed in the thicker masticatory mucosa in the palate compared to the thin oral mucosa in the buccal segments.¹¹⁰ A comparable scenario is appreciated when implants are located close to muscle attachments such as the frenum tissue exposing the device to mobility and failure of the miniscrews. A common recommendation suggests the MS to be placed 1 mm below the mucogingival junction zone within attached gingiva in order to better control inflammation. The attached gingiva or palatal masticatory mucosa will resist and sometimes minimize inflammation, nevertheless, it represents an anatomically narrower interradicular space for MS placement.¹⁰⁵ This is particularly important to minimize damage of anatomical structures.

Swelling is not common unless minor flap surgery is required. Additional complications include discomfort on chewing and speech difficulty with occasional postoperative pain.²⁰

Irritation to the tongue and cheek is a cause of complain as sharp edges cause soft tissue trauma. It is recommended to cover those surfaces with composite or a light curing periodontal pack. Kuroda *et al.* (2007), treated 75 subjects and showed postoperative pain in 95 % of patients treated with titanium MS measuring 2.0 in diameter, and a 100 % in those with two or three MS of 2.3 mm in diameter combined with miniplates. The author reported a reduction in pain complaint within two weeks after surgery; however, following 2 weeks, 10 % of the sample experienced tenderness. Different discomfort rates were evident among the different groups after one hour of surgery being lower on those subjects who had been treated with smaller diameter miniscrews of 1.3 mm.²⁰

The location of miniscrews is considered with caution to avoid root damage. The site varies among patients, where root and periodontal structures damage may occur due to proximity of the adjacent roots during the miniscrew insertion or even during tooth movement. As a consequence, thermal sensitivity and tenderness on percussion or mastication could be considered a warning sign of potential invasion of the adjacent anatomical structures, mainly the periodontal ligament.^{20, 103} Miniscrews placed within the periodontal ligament space tend to become loose, suggesting the selection of a miniscrew diameter that will perform safely within the given bone width.^{79, 111} The data available looking into the amount of bone between the roots at the level of the attached gingiva close to the mucogingival junction recommends the use of MS diameter below 1.6 mm¹¹²⁻¹¹⁴. Individual variations may demand lower diameters which can range from 1.2 to 1.5 mm^{105, 112, 115}, preference is to the later given that smaller diameters such as 1.2 mm may not withstand torsional forces that could lead to fracture on placement.^{56, 116}

Fabbroni *et al.* (2004) prospectively evaluated a large sample of 232 MS and showed that 15.9% had minor root contacts, while only 11.2% had major root contacts where more than 50% of the screw diameter engaged the surface of the root. The authors concluded that complications such as loss of vitality can occur, however, the incidence is considered to be very low.¹¹⁷

According to the animal study conducted by Asscherickx *et al.* (2005), the periodontal damage caused by root contact with a miniscrew may be repaired within 6 weeks following removal.¹¹⁸ Nevertheless bigger diameter MSs could lead to irreversible damage. To avoid this, some authors suggest MS placement with a 30-40 or 10-20 degree angle to the long axis of the posterior maxillary and mandibular teeth respectively. A greater angle of 90 degree is suggested when placement involves the retromolar area or distobuccal bone surrounding the mandibular second molars. This is intended to increase bone contact but mainly to avoid root damage without reducing the length of the device.^{105, 119} Perpendicular placement to the alveolar bone surface is also suggested by the author in order to reduce accidental proximity to the roots.⁹⁶

Little evidence is available involving intentional root damage in humans due to obvious ethical limitations. Yet, two studies have been reported in the literature, one with low¹⁴³ and the other with moderate¹⁴² methological quality. In the event of outer root surface injury, the available human studies suggest uneventful repair and healing within a few weeks after removal of the MS.^{120, 121} On the other hand, perforation injury involving the pulp tissue has been reported to cause loss of vitality and potential destruction of the surrounding periodontal tissue. This is usually treated by a combination of endodontic therapy and surgical perforation repair; the evidence in this aspect is weak mainly relying in case reports.^{122, 123}

Reports on MS migration under orthodontic loading¹²⁴ has been found in both an animal and human model. The clinical value of this data highlights the potential damage to anatomical structures.^{15, 125} Comparable displacement of two types of MSs under orthodontic forces was found by Wang and Liou (2008)¹²⁵ who reported no compromise in the stability found by the lack of measurable mobility or loosening of the MS.

A COMPARATIVE HISTOMORPHOLOGICAL AND MICRO CT STUDY OF THE PRIMARY STABILITY AND THE OSSEOINTEGRATION OF THE SYDNEY MINI-SCREW; AN ANIMAL STUDY USING NEW ZEALAND RABBITS

Therapeutic limits are determined by the patient's health conditions such as systemic, metabolic and hematologic conditions. Bone metabolism, regeneration potential, and coagulation are generally affected by such diseases and the medications involved in treating. Medically compromised patients with conditions such as osteoporosis, uncontrolled diabetes, or pre-existing blood conditions require adequate screening of the relevant medical history. Those conditions associated to bone disease are often associated to bone fracture when bone formation and osteoid volume are reduced.

Osteoporosis may increase the risk of premature loss of the MS due to compromised bone strength.¹²⁶ On the other hand, a recent animal study conducted by Park *et al.* (2014) concludes that the primary stability of orthodontic MS was not affected in the diabetes type 1 sample independent from the method of placement used. From their findings, the diabetic group showed significant difference in the bone marrow structure as higher trabecular separation was appreciated compared to the controls. The authors assumed that better stability may be achieved if MS are placed in areas of thicker cortical bone.¹²⁷

Emphasis has also been made on the importance of bone quality; however the evidence to support the relationship between bone density and primary stability is not strong. There is lack of well-designed clinical trials. Still, current studies suggest that primary stability can be improved if implant dimensions and insertion technique are adjusted to compensate for little bone density.^{128, 129}

Particular attention should be given to patients with active infection diseases, allergies or under medication treatment, since specific precautions need to be considered towards each individual patient care.¹³⁰ Factors such as uncontrolled periodontal disease, parafunctional habits, smoking, and the use of biphosphonates must be investigated carefully prior to commencement of orthodontic treatment.

2.3 BONE

Bone quality is assessed by some authors in relation to the equivalent of bone mineral density¹³¹, and according to cortical bone thickness by others.¹³² However, both characteristics are equally important in terms of MS primary stability. The bone consists of cells and extracellular substance with 35% of organic materials and water, and 65 % of inorganic matrix. The later is found in the form of apatite crystals as calcium, sodium, potassium, magnesium citrate and phosphorus.¹³³ Its architecture contains a combination of cortical and cancellous bone. The cortical bone has a higher density due to the displacement of the water by the mineral component.¹³⁴

Bone quality is fundamental in achieving primary stability.¹³⁵ An improved bone-toimplant contact is provided by the denser constitution of the cortical bone layer.¹³⁶ However, progressive injury to the periodontal tissues and cortical bone has shown high risk of MS failure.^{137, 138}

Lee (2005) reviewed the literature and stated that finite element analysis studies point towards masticatory forces being primarily distributed within the crestal bone level.¹³⁹

Placement technique and initial mechanical integration is shown to be largely obtained from the cortical plate thickness. Moreover, design MS features such as length and outer diameter could can influence insertion torque.^{140, 141}

Huja *et al.* studied the effects of cortical bone thickness on pull-out strength in the jaws of dogs whom bone composition closely resembles that of humans.¹⁴² A weak but significant correlation between the maximum force at pull-out strength and the thickness of the cortical bone was shown. Their results highlight the tendency of higher success rates in the anterior segment of the upper jaw and posterior segment of the mandible due to a thicker and more dense cortical bone.²¹

Farnsworth *et al.* emphasized the difference in thickness within the upper and lower jaw in correlation to age and gender. Their data points towards significantly greater thickness values in adult patients when compared to adolescents.¹⁴³

2.4 TOOTH MOVEMENT FORCE VALUES

The forces applied during treatment vary depending on the expected tooth movement and weather orthodontic or orthopaedic modalities are applied. The treatment of dentofacial discrepancies with traditional orthopaedic techniques require tooth borne appliances and sometimes extra-oral devices, such as headgears and chin-cups. The limitations to these techniques require a surgical approach. Some of these invasive procedures that are often rejected by the patients can be replaced by using skeletal anchorage. To date, limitations exist on the timing and amount of loading that SAS, specifically MSs, can sustain without compromising primary stability.

Kokich (1985)¹⁴⁴, showed the potential of skeletal anchorage by using ankylosed maxillary canines for maxillary protraction of a hypoplastic upper jaw. Increasing interest has arise in the proposed concept to confer such advantage to skeletal anchorage via the use of MSs.^{145, 146} Different lengths and widths have been tested in the mid-sagittal area of the palate as an insertion site for maxillary anchorage where MSs tend to perform better to those placed in the buccal areas.^{98 5, 80}

When MSs are used for skeletal modifications, greater forces are recommended.¹⁴⁷ The magnitude of orthopaedic forces are in the range of 200-500 grams, while 100-200 grams will suffice if tooth movement is required.¹⁴⁸ These values do not apply to all patients the same due to individual variations. For instance, a different value will be transmitted to the structures of a patient with a healthy periodontum compared to that in individuals with generalized bone loss.

Nowadays, most of the publications on orthopedic treatment utilizes miniplates as skeletal anchorage given the restriction in loads often found in conventional orthodontic MSs.^{11, 149, 150}

2.5 PRIMARY STABILITY

Miniscrews success is greatly determined by primary stability given that early loading is often required.¹⁵¹ Primary stability is believed to be a combination of lack of MS mobility at placement, and its appropriate mechanical integration with the surrounding tissues.^{58, 141} Continuous and early orthodontic force are thought to enhance osseous integration through bone formation and additional periimplant remodelling.^{13, 152, 153} As a result, secondary stability is achieved over time.¹⁴¹

To measure primary stability, qualitative and quantitative methods have been proposed. Quantitative non-destructive intraoral testing methods are the choice of preference. Resonance frequency analysis (RFA),¹⁵⁴⁻¹⁵⁶ Periotest technique,¹⁵⁷ and insertion torque measurements^{158, 159} are available. Histologic and micro-CT evaluations allow for both methods to be conducted by either measuring bone to implant contact, bone volume, or by describing the bone to implant integration.¹⁶⁰ Further methods for determining MS stability involve the measurement of removal torque,^{161, 162} pull-out strength,¹⁶³ and radiological examination.¹⁶⁴

Periotest value (PTV) can be used to measure MS mobility at placement, and it is considered an appropriate index of primary stability.¹⁶⁵ A recent study combined the use of cone beam computed tomography (CBCT) and PTV. The authors confirmed the tendency of greater mobility in mandibular rather than maxillary MS in the absence of root contact.¹⁶⁴

Roberts (1988, 1989) showed the human mechanism and timing of nonvital osseous interface healing which requires between 13 and 18 weeks; yet, a lack of osseous healing response is expected when immediate forces are applied.^{166, 167}

Particular focus is stressed on the insertion technique and mechanical integration between the MS device and the bony tissue. Motoyoshi's group showed that primary stability is largely obtained from the cortical plate.^{168, 169} However, there is lack of well

designed studies in the literature looking at the relationship between the primary stability of the MS and cortical bone thickness.

Ten features related to bone physiology were listed by Frost in 2003.¹⁷⁰ He proposed that strain absorbed by the bone subjected to loading promotes the activation of a cellular phenomenon that results in consequent modelling. A repetitive exposure to bone strains can either result in microdamage or fracture. The former can be perceived and repaired by osseous mechanisms, while the later tends to be a result of accumulative high strains which eventually surpasses the repair capabilities. Varying behaviours are often encountered among patients, especially in the existence of a medical conditions affecting the bone.¹⁷⁰

Miyawaki *et al.* (2003) did a retrospective evaluation of 51 patients treated with skeletal anchorage involving surgical plates and MSs which were placed at the buccal posterior region of the upper and lower jaws. The authors found a significant association between bone quality and the primary stability of MSs, and consider it as a critical factor. They concluded that MS diameters less than 1 mm, periimplantitis and thin cortical bone associated to hyperdivergent patients were associated with MS mobility.¹³

Chen *et al.* (2008) conducted a retrospective study to assess the stability of surgical plates and MSs used for orthodontic anchorage and found that inflammation of periimplant tissues, and early loading of MS within 21 days of placement might compromise the functionality of MSs. The authors believe it is a technique sensitive procedure which requires sufficient training in order to reduce failure. ⁸¹

Complications related with initial MS stability at placement can involve risk factors and anatomical limitations related to interradicular spaces and cortical bone thickness.^{16, 61}

Kuroda *et al.* evaluated the proximity between roots and MS devices using 2dimensional dental radiographs. They found that root proximity was a major risk leading to failure; this tendency was more obvious in the mandible.¹⁷¹ However, it is not a common clinical difficulty. In a survey of orthodontists' attitudes and experiences regarding MS, root damage was the least frequent biological complication with less than 10%.¹⁷² Ideally, root contact should be avoided and the use of 3-dimensional imaging such as CBCT is recommended for undistorted and accurate view of the anatomical structures which maximize the quality in diagnosis and evaluation of MS placement.^{164, 173, 174} Most of the latest 3-dimensional softwares allow the use of the data provided by a conventional diagnostic CBCT for the creation of surgical guides for MS placement.¹⁷⁵ This will hopefully reduce the chances of sinus perforation and root proximity which eventually can compromise the MS stability.¹⁷⁶

Duaibis *et al.* (2012) evaluated the stability of MS using Finite element analysis (FEA) on a bone block model and looked at the effect of several factors on the stress in bone surrounding and within the MS devices. They showed that factors such as MS diameter, head length, thread size, and elastic modulus of cancellous bone influenced the stresses within the cortical layer, while cortical bone thickness, thread shape and pitch aspects did not seem to affect MS stability.^{177, 178}

The effect of a controlled maximum insertion torque on the success rate of MSs has been recently reported. Some studies have found an association between insertion torque values and MS stability.^{158, 179} Failure rates were significantly higher when more than 10 Ncm of torque were tested. Furthermore, ischemia and necrosis are potential complications in those areas exposed to high levels of stress.¹⁷⁹⁻¹⁸² The results from the human sample studied by Motoyoshi's group suggests insertion torques between the range of 5-10 Ncm.^{158, 179} McManus *et al.* conducted an experimental study that showed greater resistance to movement on MSs placed at higher maximum torque compared to those placed at lower maximum torque. However, the authors suggest the use of a torque measurement tool to aim for at least 5Ncm insertion torque in order to allow for greater primary stability. Preferably with an incorporated sound alert feature to notify when torque reaches 5Ncm. They advocate that a lower insertion torque is an indication for MS repositioning or replacement with a larger diameter device.¹⁸⁰

Even though high insertion torques are shown to deliver greater primary stability, excessive values are not favourable.¹⁸⁰ The insertion site and bone quality determine the

need of a pilot hole in order to reduce the insertion torque while improving secondary stability.¹⁴⁰ Miniscrews have shown to be successful in the maxilla by both self-drilling and self-tapping techniques. ^{183, 184}However, in the presence of thicker cortical bone, such as that in the mandible, requires pre-drilling. Where cortical bone thickness exceeds, 1.3mm initial pre-drilling is recommended prior to MS insertion to avoid overtorquing and risking the creation of microfractures surrounding the MS.¹⁸⁵ The correct size for pilot holes to enhance primary stability have been reported to be in the range of 69-80% of the MS diameter to be used.^{165, 186}

Implant design factors such as length and outer diameter of the MS implant determine insertion torque.^{140, 141} Wilmes *et al.* (2008) evaluated the impact on implant design of orthodontic MS by looking at the discrepancy on insertion torque and initial stability among six different MS systems with varying dimensions. They found a positive correlation between insertion torques and primary stability determined by MS thread design and diameter according to the site of placement.¹⁸⁷

Numerous MS designs have been recently developed to enhance primary stability. A recent publication found in the literature for this purpose was initially described by Hong et al. (2011) who simulated cortical and trabecular bone in a lab setting to test maximum insertion torque, maximum removal torque, and displacement of 5 different implant designs. Among their sample, the authors described a wide but short hollowcentered MS designed to mainly engage cortical bone and allow bone formation within its internal chamber to compensate for its reduced length. Their results showed improved primary stability in those MS with tapered shape and double threaded configuration. Most importantly, the new hollow design showed improved stability and reduced risk features among all the other commercial designs. Considering their high values upon insertion torque, further refinements were required.¹⁸⁸ A later study used a commercially available MS placed in humans as a control. These values were compared to an in-vitro sample of the original hollow MS design and to a modified shorter and narrower hollow MS design. Their results showed enhanced stability with better torque levels and lateral displacement values for the modified hollow MS.¹⁸⁹ Their latest publication was an animal study testing a conventional type versus the modified hollow

MS type on the maxilla and mandible of 12 beagle dogs. The histomorphometric and histologic analysis showed higher success rates in the mandible compared to the maxilla. The results of this animal study showed improved bone-to-implant contact and bone volume around the hollow MS placed in the maxilla, with stability of those placed in the mandible. The authors recommend the selection of MS use according to the bone quality and implantation site.⁵¹

Primary stability can be affected by both bone quality (mineral density) and quantity (thickness). Shah *et al.* (2011) conducted an experimental study to simultaneously evaluate the effects of cortical bone thickness, cortical bone density, MS length, and MS outer diameter by measuring insertion torque and pullout strength in an experimental model. They found that the MS design factors such as length and diameter, and the host factors such as increase in cortical bone thickness and density influence primary stability. ^{190,163}

Bioactive coating has been tested to increase implant fixation and long term survival within the orthopaedic field. Reigstad *et al.* $(2011)^{191}$ used a rabbit model to show the effectiveness of calcium phosphate and hydroxyapatite coated implants to enhance the primary stability and survival of implants. The authors found a different pattern among their sample where the calcium phosphate group exhibited a slower but higher fixation compared to those with hydroxyapatite coating.

The importance of primary stability relies on the fact that most MS loss occurs within the early stages after insertion.¹³ It is therefore suggested to continue thorough investigations that could lead to the formula for ultimate MS stability.¹⁰ To date, no publications combining the added benefits of a hollow MS with BGSs are available within the orthodontic literature.

2.6 FAILURE RATES

The first publication on failure rate of MSs studied in a human sample is attributed to Miyawaki *et al.* who evaluated the influence of four sources of skeletal anchorage and the factors associated with their stability in the posterior region.¹³ Miniplates and 3 types of MS were used and 11 variables were evaluated in a small sample of 41 patients. From their results they concluded that MS diameter of 1.0 mm or smaller, the presence of peri-implant tissue inflammation, and hyperdivergent patterns were associated with MS mobility when placed in the buccal posterior area.¹³

Clinically, the function of MS is aimed to achieve absolute anchorage. Important clinical variables widely described in the literature include minimal mobility of the MS implant¹⁶⁰ and inflammation of the surrounding soft tissue^{13, 81, 105} as crucial conditions that may well interfere with the success and treatment of specific malocclusions dependant of absolute anchorage. ^{81, 105, 187}

Miniscrew reports on failure rates are as high as 51^{192} -100%^{13, 193}; however, broad definitions for success criteria including either satisfactory orthodontic movement¹³⁻¹⁵ or lack of mobility and peri-implantitis following MS placement¹⁶⁻¹⁸ have been considered. This could explain the differences in success rates reported by different investigators. The success rates of MSs are multifactorial. It includes operator's experience, MS design and features, method of placement, site of placement, and patient care. ^{17-19,13, 14, 20} Immediate and delayed failure rates of MSs have been reported to be in the range of 7 % to 50 %.

The literature variation on failure rates may be related to the study period on assessment. Park and Kim (1999) achieved 18 % of titanium MS failure following a five month observation period.¹¹⁹ A larger evaluation was examined by Park (2003) where 7 % failure rate was shown after 15.8 months follow up of 180 MSs.¹¹⁰ The same year, Miyawaki (2003) evaluated three types of MSs of 1.0 mm, 1.5 mm, and 2.3 mm over a period of 12 months and demonstrated 100 %, 16.1 %, and 15 % failure rates, respectively.¹³ Three years later, Park (2006) studied four types of MSs loaded for 15

months in eighty seven consecutive patients and expressed 8.3 % failure within his sample; the author reported that less success was found in the right side of implantation and in the lower jaw as well.¹⁰⁵

Literature reviews on failure rates show superior success in palatal MS in comparison to maxillary and mandibular MS.

- Schätzle *et al.* (2009) reported 10.5% for palatal, and 16.4% for buccal MSs.⁹⁸
- Rodriguez *et al.* (2014) reported 6.2% failure in the palate compared to 12.2% in the other locations.

Several studies have associated failure with the different factors listed below:

- Unsatisfactory primary stability,^{59, 108, 172, 187}
- Thick soft tissue^{104, 135, 194}
- Peri-implantitis^{13, 81, 179}
- Miniscrew migration¹⁵
- Interference with tooth movement¹⁷²
- Excessive loading^{7, 194}
- Fracture⁶⁹
- Progressive damage of the cortical bone during insertion^{105, 135, 187}
- Unexpected force of the MS head during mastication⁷
- Reduced or excessive bone remodelling around the MS¹⁹⁵
- Root surface contact and proximity^{7, 135, 171, 172}
- General and local bone turnover around the MS¹⁹⁶

The reported percentage of failure rates are multifactorial and are affected by both the sample size, and the various parameters evaluated in each particular study.^{187, 197} A moderate relationship between MS type and failure has been found.^{116, 198} In some cases, it has been demonstrated that mobile MSs perform satisfactory in providing anchorage control.¹⁰⁸ Yet, failure rates and primary stability need to be improved to overcome the loss of the devices during orthodontic treatment.

2.7 DESIGN FEATURES

The overall design of The Sydney Miniscrew (Patent number: PCT2009014) was based upon the clinically proven Aarhus anchorage system (Medident, Hellerup, Denmark) and presented as part of a Master of Philosophy Thesis in 2011. The Aarhus MS design has been adjusted to suit an array of biomechanics that allow replacement of conventional anchorage and it is based on previous and continuous studies by Melsen and co-workers to offer an improved MS system. The authors claim superior clinical solutions for the application of diverse force systems that could only be achieved with MS skeletal anchorage: ^{196, 199}

- Intrusion and distal movement of upper anterior teeth,
- Intrusion of overerupted molars and distalization of premolars including:
 - o highly atrophic bone in adult patients
 - o insufficient dental tissue for the establishment of conventional anchorage
- Mesialization of molars into premolar agenesis spaces, anterior modelling of the lower jaw and space closure where reactive forces are anticipated to cause adverse effects.

Several MS are commercially available with certain variations in their design, dimensions and composition all of which seem to affect properties or performance of the temporary skeletal anchorage appliance for orthodontic application.

2.8 BONE GRAFT SUBSTITUTES

The biochemical structure of BGS is similar to the inorganic content of bone extra cellular matrix (ECM). ^{200,201} The iBGS, therefore, have brought significant benefits in orthopaedics, e.g. augmentation of osteoporotic fractures^{202, 203} for certain indications in spine injuries,²⁰⁴⁻²⁰⁶ and dentistry and maxillofacial surgeries.²⁰⁷ The iBGS usually consist of a solid powder (mainly calcium and phosphate) and a fluid component, e.g.

sodium chloride. Upon mixing, a paste is formed which can be delivered to different sites through a relatively thick gauge needle (18 G or thicker). The paste is then cured within few minutes *in situ* through a slightly exothermic or isothermal reaction.^{205, 208} The main types of BGS are calcium phosphate apatite, calcium phosphate brushite and calcium sulphate contained compounds. The mechanical properties and the degradation mechanism of these three types of BGS and their clinical applications are summarised in Table 1.

Compound	Mechanical Properties	• Degradation Rate/ • Ref Mechanism
• CSC	Compression Modulus:10 to 15 MPa	Resorb by desolation in body fluid in 3-6 months, 205, 2 211
• BCPC	 Tension mod: .6±0.4 GPa Compression mod:7.9 ±0.3 GPa 	 Macrophage or • ²¹²⁻²¹⁴ Osteoblast medicated process in 6 months
• ACPC	 Tension mod: 12.3±0.8 GPa Compression mod: 13.5±0.8 GPa 	 Osteoclast mediated process, Might be not fully resorbable

Table 1: General properties of apatite and brushite calcium phosphate and calcium sulphate cements.

CSC: Calcium Sulphate Cemenet; BCPC: Brushite Calcium Phosphate Cement;

ACPC: Apatite Calcium Phosphate Cement

Bone graft substitutes are used for numerous bone related clinical applications, e.g. dental, maxillofacial and load-bearing bone repair, due to their osteoconductive and high mechanical properties. In general, calcium sulphate cements exhibit low mechanical strength in compression (~0.015 GPa), and thus have been commonly used for less load bearing applications, such as dental and maxillofacial bone regeneration. ^{210, 220, 221} The augmentation of screws in less load bearing applications, such as arm long bone and wrist, brushite cements are used, ^{222,223} whereas for highly load bearing applications, such as calcaneal fractures, apatite bone cements are more favourable due to their high mechanical strength.²²⁴⁻²²⁶ In addition, combinations of calcium phosphate and calcium sulphate have been also used to alter the biomechanical properties of the resulting BGS and its bio-absorption rate.

2.8.1 CALCIUM SULPHATE CEMENTS

Calcium sulphate cements are osteoconductive, self-setting, and brittle biomaterials that can be found in three forms: anhydrites, dihydrate and hemihydrate.²²⁷ Gypsum is a dehydrate calcium sulphate cement, which is commonly used for different clinical applications. Upon heating at 110 °C, gypsum loses its water content in a process known as calcination. The resulting product is hemihydrate calcium sulphate (also known as plaster of Paris).²²⁸ By mixing hemihydrate calcium sulphate with water, dihydrate cement is formed through a mild exothermic reaction.²²⁹ The calcium sulphate cements promotes the mineralisation of the bone and thus stimulates bone growth. The degradation products of these cements are all biocompatible and thus this bone graft materials are well tolerated *in vivo* and non-immunogenic.^{223, 230} The calcium sulphate cements degrade rapidly in less than 6 months after in vivo implantation.²³¹ The compression modulus of dihydrate calcium sulphate cements is in the range of 10 to 15 MPa,²⁰⁵ which is far less than of the cortical bone (~175 MPa) and in the same range for cancellous bone (~ 15 MPa).²¹³ Calcium sulphate BGS are mostly used for non-loadbearing applications, such as sinus augmentations, due to their moderate mechanical strength.^{209, 211} Osteoset[®], Surgiplaster[®], MIGX3[®] are the three main calcium sulphate based biomaterials that are commercially available. 209, 211, 220, 221

2.8.1.1 Dental Application

In variety of dental applications, such as the treatment of infrabony periodontal defects and post extraction maxillary buccal dehiscence, BGS are used to promote the bone formation at regions with inferior bone density. In comparison between different types of BGS, calcium sulphate cements are more commonly used for dental applications as (a) the implants are not under compression stress in these applications and thus the lack of mechanical strength in calcium sulphate cements does not induce technical problem, and (b) implants with fast bio-absorption rate (in the range of three to six months) are more favourable to avoid interference with natural wound healing and bone remodelling process. ^{221,232}

Tooth extraction leads to alveolar bone resorption and ultimately reduction in ridge volume. Therefore, an implant is required following extraction in order to minimise the ridge volume reduction. SurgiplasterTM, as a medical grade calcium sulphate cement has been used as a graft material for extraction sockets for this purpose.²²¹ The implanted calcium sulphate cements were bio-absorbed in three months and trabecular bone was formed within this period.²²¹ In addition, other studies reported the regenerative effect of calcium sulphates for treatment of post-extraction maxillary buccal dehiscence. The ridge volume was preserved by using this method after the tooth extraction where the BGS prevented the bio-absorption of the alveolar bone.²³² Calcium sulphate cements have been used in other dental applications, such as treatment of infrabony periodontal defects. Peltier in 1959 tested Sterile plaster of Paris pellets (calcium sulphate hemihydrate) as implants in a preliminary clinical study for treatment of periodontal lesions in 35 patients.²³³ No inflammation, minimal foreign body reaction, no rejection of the implant and infection was noted in the patients. In addition, in 79% of defects treated with these calcium sulphate cements demonstrated regeneration of osseous tissues.²³³ These results were in agreement with other studies, testing the efficacy of calcium sulphate cements for osseous regeneration.²³⁴ This is relevant in situations such as an upper tooth loss which may lead to gradual degradation of the maxillary bone and lowering of the sinus.

The maxillary bone remodelling process following extraction leads to the formation of a void at the sinus site and thus decreases the density of the bone at the region. During the dental implantation, if the dental implant is placed at this region with an inadequate bone depth and density, there is high risk of mobility leading to displacement and eventually failure due to inadequate stability (primary and secondary) at the implantation site.²³⁵ In such situations, calcium sulphate BGS are injected in the extraction site previously occupied by teeth and bone. The injection of the BGS promotes the formation of new bone in the sinus area to increase the height and volume

of the maxillary bone and thus enhance the stability of the dental implant post-surgery. ²²⁰

A clinical and radiographic evaluation showed that it is feasible to use SurgiPlasterTM calcium sulphate BGS in maxillary sinus augmentations to regenerated new tissues that are quantitatively and qualitatively suitable for implant placement. ²²⁰ The overall success rate for the 130 placed implants at 12 months post implantation was high (98.5 %). Histological analysis indicated type II or III bone in all specimens. ^{220, 236} Another clinical study conducted by Guarnieri *et al.*(2006) evaluated the efficacy of SurgiPlasterTM granules for sinus augmentation with radiographic and histological techniques. The biomaterial was endoscopically added to the maxillary defect. The authors showed that the application of the chosen calcium sulphate BGS promotes adequate bone volume before implant placement.²²¹ All these clinical studies confirmed the potential of commercially available calcium sulphate cements for dental applications.

2.8.1.2 Maxillofacial Application

Calcium sulphate BGS are used for the treatment of facial bone defects. Patients with maxillofacial defects have asymmetries expressed as a discrepancy between the right and left side of their facial structure both in size and shape. The treatment of these defects involves distraction osteogenesis to lengthen the jaw bone by fracturing the bone into two segments and gradually moving them apart to promote the formation of new bone in the gap.^{221,237}

To promote the regeneration of bone, BGS are press-fit into the pre-generated bone gap. For instance, pellets of calcium sulphate Osteoset® cement, are used to fill the gap in the osteotomy region with the intention to promote bone formation.²¹¹ Kim *et al.* (2006) prepared an injectable form of Osteoset by grinding pellets into small particles. The particles were mixed with carboxymethylcellulose to form the injectable paste which was injected through a very thick needle (e.g. 14G needle) to the distraction osteogenesis site (intentionally generated bone gaps) with craniofacial microsomia.²¹¹ It was concluded that the application of this injectable calcium sulphate shortens the

treatment process and promotes bone regeneration. The clinical study showed that the addition of Osteoset significantly (p<0.05) increased the bone regeneration rate at the osteotomy site. ²¹¹ Therefore, the application of calcium sulphate has a superior effect on early consolidation in distraction osteogenesis.

2.8.2 CALCIUM PHOSPHATE CEMENTS

This type of BGS is highly osteoconductive and osteogenic. ^{203, 222, 223, 238, 239} The paste of calcium phosphate BGS solidifies *in vivo* through a dissolution-precipitation reaction which relies on the solubility of the reactants *in situ*. Calcium phosphate BGS undergo a cell mediated bio-absorption process, either with osteoclast or macrophages. This degradation behaviour is highly favourable for *in vivo* bone regeneration.²⁴⁰

Generally, by controlling the pH in the equilibrium calcium and phosphate solution, two types of calcium phosphate cements, e.g. apatite ($Ca_5(PO_4)3OH$) and brushite (4CaHPO₄. 2H₂O) cements, can be produced. ^{205, 241}

Apatite BGS is formed when in the equilibrium calcium phosphate solution pH is near 4 or higher.^{242, 243} Apatite cements are intensively studied for load bearing applications due to their high compression strength.²¹⁴ The compression modulus of apatite calcium phosphate BGS is 13.5 ± 0.8 GPa and its tensile modulus is 13.5 ± 0.8 GPa.²¹³ The bio-absorption of these BGS is osteoclast mediated. However, in some studies, incomplete bio-absorption associated to these BGS is being reported which may eventually lead to clinical complications.²⁴⁴⁻²⁴⁶ Beside this unfavourable bio-absorption behaviour, the apatite bone cements have been widely used for different clinical applications, such as implant screw augmentation, bone filler in open surgeries, and bone void filler in non-surgical approaches due to their osteogenic properties and high mechanical strength.²²⁴⁻²²⁶

Brushite BGS (4CaHPO₄. $2H_2O$) is formed when the pH of the calcium phosphate equilibrium solution is less than 4 as the dicalcium phosphate dehydrates is more likely

to form in acidic solutions. ²⁴² The compression modulus of brushite calcium phosphate cement is 7.9 ± 0.3 GPa, which is nearly two fold weaker than the apatite calcium phosphate cements.²¹³ The bio-absorption rate of brushite BGS is also faster compared with apatite BGS. ²¹³ In addition, the degree of osteoconductivity and the ostegenicity of the brushite cements are lower than apatite BGS.²²³ ChronOs inject [®] is a brushite calcium phosphate BGS and Norian SRS[®], Bonesource[®], and HydroSet[®] are apatite calcium phosphate BGS that are commercially available. These BGS are widely used for different clinical applications such as the treatment of craniofacial malformation and load bearing bone regeneration.

2.8.2.1 Craniofacial and Skull

Calcium phosphate BGS can be used for the treatment of craniofacial bone defects and abnormalities. Constantz *et al.* (1995) treated 5 patients with different craniofacial malformations (frontal, cranial irregularities and temporal hollowing) with Norian SRS. This injectable CPC is composed of monocalcium phosphate, monohydrate α -tricalcium phosphate and calcium carbonate, mixed with sodium phosphate solution. This biomaterial remains injectable up to five minutes after mixing and reaches its maximum compression strength (nearly 55 MPa²²⁶) after 24 hours of setting.²⁴⁴ The authors reported a wound dehiscence with subsequent infection of the material in 1 patient where Norian SRS was employed for treatment of a craniofacial malformation. They concluded that this biomaterial may offer an option for the treatment of paediatric patients with diverse craniofacial malformation but at the same time there is the chance of infection upon the application of this biomaterial.²⁴⁴

More recently, Da Costa *et al.* (2014) used a commercially available injectable hydroxyapatite for surgical repair of the skull and calvarial bone in 26 patients. The results of this study showed that the thickness of the calvarial bone was increased 0.67 mm (p<0.05).²⁴⁷ An uncontrollable and incomplete bio-absorption behaviour of the apatite BGS, regardless of their application, remain a challenge for their clinical use.

2.8.2.2 Augmentation of Calcaneal Fractures

Injection of calcium phosphate BGS under subtalar joints can provide augmented support for calcaneal fractures in a non-surgical treatment approach. The rationale for using iBGS in this type of fracture is to fill the space in the fractured bone with a material with high compression strength. In a clinical study, 36 patients with calcaneal fractures were treated with CPC injection. The last patient allowed for full weight bearing after three weeks with no radiological evidence on loss of reduction in the fractured bone.²⁴⁸ In another clinical study with 15 patients, 9 patients were allowed for full weight bearing after three weeks and 6 patients after 6 weeks. The different full weight bearing periods suggested that a randomised study is of need to clinically confirm the beneficial effect of iCPC for the treatment of calcaneal fractures.²³⁹

2.8.2.3 Enchondroma and Juvenile Bone Cyst Treatment in Kids

Norian SRS[®] CPC have been used in an attempt to treat patients with enchondroma, which is a non-cancerous cartilage tumor in bone. Welkerling *et al.* started a prospective single cohort study which included 20 patients with an enchondroma, but the study was stopped after four treatments due to very poor initial clinical outcomes. The tested patients had pain for up to nine months after operation, with pain level of 6, 7, and 8 (in a scale from 1-10; ten was the maximum) and were not able to work for six months; all these patients had limited movement for three months. The authors concluded that soft tissue reaction was induced by application of Norian SRS which leads to very high level of pain in the patients.²²⁶

The application of iBGS to fill bone voids, for example in juvenile bone cyst, has been beneficial. Juvenile bone cyst is benign, fluid containing bone cavities, lined with a membrane consisting of thin vascularised connective tissue with scattered osteoclast-like cells. Two treatment techniques were used, e.g. invasive Depo-Medrol and less invasive injection of chronOs Inject. The bone cysts in the tested patients were filled with the iBGS. The outcome of this treatment method indicated 100% successful

outcome (no need for additional surgery), which was significantly better than of the control group with only 50% success rate.²⁴⁹

2.8.2.4 Screw Augmentation

Augmentation around pedicle screws in osteoporotic spine is crucial. Calcium phosphate BGS are used for this application due to their high compression strength. By using these BGS, the risk of the screw loosening in low density vertebrae is diminished and consequently, the holding power of the screws has been improved.^{206, 218} Similarly, in application of sliding screws in trochanteric hip fractures, augmentation with CPC displayed a greater stiffness, stability and strength compared with negative control group (screws with no fixation). The patients had less pain and the quality of life variable was more favourable in augmented fractures with BGS.^{216, 217}

2.8.2.5 Vertebral Body

Injectable biomaterials with very high compressions strength are required for surgeries in vertebral body due to high degree of compression stresses at this part of the musculoskeletal system. In fracture vertebral body, injection of polymethylmethacrylate cement resulted in considerable pain relief. ^{205, 250-252} However, major questions around the efficacy of this technique have been raised due to the non-biodegradable nature of polymethylmethacrylate cements and their exothermic setting reaction in body.²⁵³ For this reason, CPC have been alternatively suggested.²⁰⁵ For instance, Calcibon®, commercially available iCPC, has been used for treatment of osteoporosis vertebral fractures. The authors observed a marked symptom reduction in 89% of patients.²⁵⁴ However, leakage of the injected biomaterial to the vertebral bodies was reported in 92% of the cases. This could be due to the protracted and uncontrollable curing process of BGS as one of the most important associated drawbacks to this type of biomaterials.²⁵⁴

2.8.2.6 Metaphysal Space Filling

Fractures of tibial plateau often resulted in the depression of the articular fragment, the formation of metaphyseal space and thus instability in the knee joint. The resulting void is commonly filled with autologous or allogenic BGS through an open surgery. However, lack of mechanical stability and low rate of integration with the host tissue in these bone grafts, leads to clinical complications and unfavourable outcomes.²⁵⁵⁻²⁵⁸ Injection of the CPC with high mechanical strength and reshapable properties has been suggested to provide strength to the fractures and faster weight bearing capacity to the patients.²¹⁵ In a clinical study on 120 patients with tibial plateau fractures, the effect of filling the bone void with either autogenous BGS or enthothermic CPC was tested. The authors concluded that the application of autogenous bone grafts must be discouraged in favour of calcium phosphate cements as fewer complications and better stability of the articular fragments were noticed in patients treated with CPC.²¹⁹ For some clinical applications, in conjunction with internal fixation devices, such as screws and plates, CSCs are also used.

2.8.3 OVERVIEW

Different paste compositions of materials ²⁵⁹⁻²⁶⁵ have been reported in the use of injectable synthetic bone graft substitutes. Similar to bone, these pastes contain an inorganic component of mineralized tissues, hence their excellent biocompatibility and osteoconductivity. Orthopedic²⁶⁶⁻²⁷¹ and dental^{269, 272-275} applications of bone augmentations for have been reported. Some studies looking at the use of bone cements and screw fixation²⁷⁶ within the orthopedic²⁷⁷ and very few within the dental²² field have been published. Indeed, no scientific evaluation of published studies on the combining the use of iBGSs and MS implants for orthodontic applications appears registered up to date.

Rheological properties such as low and stable viscosity is essential to ensure that the pressure required during injection is reasonable.²⁷⁸

Several studies have grouped the desirable properties of an ideal BGS as follow:^{262, 279, 280}

- High radiopacity
- Around 6–10 min working time and 15 min setting time
- Easiness of preparation and handling
- Neither too high nor too low biodegradability
- Very easy injectability into the collapsed vertebral body
- Exceptional osteoconductivity
- No toxicity
- Excellent osteoinductivity
- Excellent biocompatibility
- Excellent bioactivity
- Low-cost
- Non exothermic
- Adequate mechanical properties
- Appropriate cohesion
- Low viscosity
- Microporosity (mean pore diameter < 10 lm), which enables circulation of body fluid
- Macroporosity (mean pore diameter >100 lm), which creates an ideal scaffold for blood-cell colonization

An ideal BGS comprises biological properties that promote adequate healing following implantation. Complications such as inflammatory responses or extreme cytotoxicity or immunogenicity may interfere with tissue regeneration.²⁸¹ A minimum of 50 μ m²⁸² pores configuration is preferred to optimize cell and blood vessel invasion into the BGS, which will eventually contribute with the bio-absorption and replacement of the graft material into new mature bone.^{283, 284}

It is well known that calcium phosphate and calcium sulphate BGS perform better in non-load-bearing applications.^{265, 285} Mechanical properties, however, may vary quite extensively upon implantation.²⁸⁶ Tensile strength,²¹³ compressive strength, shear

component,²¹³ fatigue properties, and fracture mechanics^{287, 288} will be temporary and further determined by the site of implantation once replaced by the local bone tissue containing it. Identical bony tissue and the same or even improved structural characteristics can be obtained in areas where BGS provide good initial stability maintained throughout the first stages of healing.²⁸⁹

Sanzana *et al's* (2008) used a rabbit model to compare the diverse composition, microstructure and solubility of CPC and phosphate glasses which are both biocompatible and biodegradable materials. They found that a higher degradation rate was encouraged by faster bio-absorption, lower crystallinity, and higher porosity. Rapid loss of compressive strength was associated to higher porosity and larger pore size.²⁶³

BGS comprise diverse mechanisms of action which encourage different growth tissue formation, vascularization, and degradation depending on their composition. The importance of degradation rates rely on the need of a favorable environment for tissue regeneration in the site of BGS implantation which also determines its load-bearing capabilities.^{262, 290, 291}

Calcium sulphate has high regenerative properties and resorbs more rapidly than the calcium phosphate.²⁹² The combination of both BGS maintain their different resorption rates allowing appropriate angiogenesis into the calcium phosphate scaffold.²⁹¹ Thomas and Puleo (2009) reviewed the available literature which support completely biodegradation of calcium sulphate exclusive of inflammation signs in human bodies.²⁹² It is known that the stimulation and guide to bone creation is encouraged by the binding and further bio-absorption of CaPO4 particles.²⁹³ This consist of a process of osteoblastic differentiation stimulated by an increase of calcium ions that are released during degradation of the CaPO4 particles.²⁹²

Radiographic evaluation of the mechanical integration and consequent degradation follow-up will only be possible if using BGS containing a radiological contrast. Strategies to add these radiolucent products is not recommended.²⁶⁵

2.9 REFERENCES

- 1. Gainsforth BL, Higley LB. A study of orthodontic anchorage possibilities in basal bone. American Journal of Orthodontics and Oral Surgery 1945;31(8):406-17.
- 2. Creekmore TD EM. The possibility of skeletal ahncorage. Journal of Clinical Orthodontics 1983;17(4):266-9.
- 3. Roberts WE, Smith RK, Zilberman Y, Mozsary PG, Smith RS. Osseous adaptation to continuous loading of rigid endosseous implants. American Journal of Orthodontics 1984;86(2):95-111.
- 4. Roberts WE, Marshall KJ, Mozsary PG. Rigid endosseous implant utilized as anchorage to protract molars and close an atrophic extraction site. The Angle orthodontist 1990;60(2):135-52.
- 5. Wehrbein H, Merz BR, Diedrich P, Glatzmaier J. The use of palatal implants for orthodontic anchorage. Design and clinical application of the orthosystem. Clinical Oral Implants Research 1996;7(4):410-16.
- 6. Costa A RM, Melsen B. Miniscrews as orthodontic anchorage: A preliminary report. International journal of adult orthodontic and orthognathic surgery 1998;13:201-9.
- 7. Liou EJW, Pai BCJ, Lin JCY. Do miniscrews remain stationary under orthodontic forces? American Journal of Orthodontics and Dentofacial Orthopedics 2004;126(1):42-47.
- 8. Daskalogiannakis J, editor. Glossary of orthodontic terms: Quintessence Publishing Co, Leipzig; 2000.
- 9. Rossouw P, Buschang P. Temporary orthodontic anchorage devices for improving occlusion. Orthodontics & Craniofacial Research 2009;12(3):195-205.
- 10. Cope JB. Temporary Anchorage Devices in Orthodontics: A Paradigm Shift. Seminars in Orthodontics 2005:3-9.
- 11. De Clerck, E.E.B, Swennen GRJ. Success rate of miniplate anchorage for bone anchored maxillary protraction. The Angle Orthodontist 2011; 81(6): 1010-1013.
- 12. Sugawara J, Nishimura M. Minibone plates: The skeletal anchorage system. Seminars in Orthodontics 2005;11(1):47-56.
- 13. Miyawaki S, Koyama I, Inoue M, Mishima K, Sugahara T, Takano-Yamamoto T. Factors associated with the stability of titanium screws placed in the posterior region for orthodontic anchorage. American Journal of Orthodontics and Dentofacial Orthopedics 2003;124(4):373-78.
- 14. Moon C-H, Lee D-G, Lee H-S, Im J-S, Baek S-H. Factors associated with the success rate of orthodontic miniscrews placed in the upper and lower posterior buccal region. The Angle orthodontist 2008;78(1):101-06.
- 15. Liou EJW PB, Lin JCY. Do miniscrews remain stationary under orhtodontic forces? Am J Orthod Dentofacial Orthop 2004;126:42-7.
- 16. Cheng S-J, Tseng IY, Lee J-J, Kok S-H. A prospective study of the risk factors associated with failure of mini-implants used for orthodontic anchorage. International Journal of Oral & Maxillofacial Implants 2004;19(1):100-6.
- 17. Papageorgiou SN, Zogakis IP, Papadopoulos MA. Failure rates and associated risk factors of orthodontic miniscrew implants: a meta-analysis. American Journal of Orthodontics and Dentofacial Orthopedics 2012;142(5):577-95. e7.

- 18. Viwattanatipa N, Thanakitcharu S, Uttraravichien A, Pitiphat W. Survival analyses of surgical miniscrews as orthodontic anchorage. American journal of orthodontics and dentofacial orthopedics 2009;136(1):29-36.
- 19. Tseng YC, Hsieh CH, Chen CH, Shen YS, Huang IY, Chen CM. The application of mini-implants for orthodontic anchorage. International journal of oral and maxillofacial surgery 2006;35(8):704-07.
- 20. Kuroda S, Sugawara Y, Deguchi T, Kyung H-M, Takano-Yamamoto T. Clinical use of miniscrew implants as orthodontic anchorage: success rates and postoperative discomfort. American Journal of Orthodontics & Dentofacial Orthopedics 2007;131(1):9-15.
- 21. Huja SS, Litsky AS, Beck FM, Johnson KA, Larsen PE. Pull-out strength of monocortical screws placed in the maxillae and mandibles of dogs. American Journal of Orthodontics and Dentofacial Orthopedics 2005;127(3):307-13.
- 22. Arisan V, Anil A, Wolke JG, Özer K. The effect of injectable calcium phosphate cement on bone anchorage of titanium implants: an experimental feasibility study in dogs. International Journal of Oral and Maxillofacial Surgery 2010;39(5):463-68.
- 23. Albrektsson T, Johansson C. Osteoinduction, osteoconduction and osseointegration. Eur Spine J 2001;10:S96-S101.
- 24. Ottofy L. Standard Dental Dictionary. Chicago: Laird and Lee, Inc.; 1923.
- 25. Bacopulos Marangu A. "The feasibility of an injectable bone graft substitute to enhance the primary stability of a novel miniscrew The Sydney Mini-screw for orthodontic applications" [Sydney: The University of Sydney; 2011.
- 26. Wright CF. A consideration of the Anchorage Problem. Midwest Component of the Edward H. Angle Society of Ortodontia. Chicago; 1938. p. 152-59.
- 27. Moyers R. Handbook of Orthodontics for the Student and General Practitioner Chicago: Year Book Medical Publishers Inc; 1973.
- 28. Burstone CJ. The segmented arch approach to space closure. American Journal of Orthodontics 1982;82(5):361-78.
- 29. Melsen B, Verna C. A rational approach to orthodontic anchorage. Progress in Orthodontics 2000;1(1):10-22.
- 30. Proffit WR. The Biologic Basis of Orthodontic Therapy. in Contemporary Orthodontics. Fourth Edition ed. St Louis: Mosby/Elsevier; 2007. p. 751.
- 31. Peter Schopf BL, S. Jay Bowman. The Problem of Anchorage. Mini-implants in orthodontics: innovative anchorage concepts. Berlin: Quintessence; 2008. p. 5-10.
- 32. Angle EH. Treatment of malocclusion of the teeth and fractures of the maxillae: Angle's system: White Dental Manufacturing Company; 1900.
- 33. Poulton DR. Changes In Class II Malocclusions With And Without Occipital Headgear Therapy*. The Angle orthodontist 1959;29(4):234-50.
- 34. Ricketts RM. The influence of orthodontic treatment on facial growth and development. The Angle Orthodontist 1960;30(3):103-33.
- 35. Samuels RH, Jones ML. Orthodontic facebow injuries and safety equipment. The European Journal of Orthodontics 1994;16(5):385-94.
- 36. Tolman DE, Desjardins RP. Extraoral Application of Osseointegrated Implants. J Oral Maxillofac Surg 1991;49:33-45.

- 37. Brånemark P-I, Breine U, Adell R, Hansson BO, Lindstrom J, Ohlsson A. Irmaosseous anchorage of dental prostheses. I. Experimental studies Stand J Plast Reconstr Surg 1969;3:81.
- 38. Adell R, Lekholm U, Rockier B, Brånemark P-I. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. Int J Oral Surg 1981;10:387.
- 39. Brånemark P-I. Osseointegration and its experimental background. J Prosthet Dent 1983;50:399.
- 40. Adell R. Clinical results of osseointegrated implants supporting fixed prostheses in edentulous jaws. J Prosthet Dent 1983;50:251.
- 41. Creekmore T, Eklund M. The possibility of skeletal anchorage. J Clin Orthod 1983;17(4):266-9.
- 42. Turley PK, Kean C, Schur J, Stefanac J, Gray J, Hennes J, et al. Orthodontic Force Application to Titanium Endosseous Implants. The Angle orthodontist 1988;58(2):151-62.
- 43. Turley PK, Shapiro PA, Moffett BC. The loading of bioglass-coated aluminium oxide implants to produce sutural expansion of the maxillary complex in the pigtail monkey (Macaca nemestrina). Archives of Oral Biology 1980;25(7):459-69.
- 44. Roberts W, Nelson C, Goodacre C. Rigid implant anchorage to close a mandibular first molar extraction site. J Clin Orthod 1994;28(12):693-704.
- 45. Glatzmaier J, Wehrbein H, Diedrich P. [The development of a resorbable implant system for orthodontic anchorage. The BIOS implant system. Bioresorbable implant anchor for orthodontic systems]". Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 1995;56(3):175-81.
- 46. Glatzmaier J, Wehrbein H, Diedrich P. Biodegradable implants for orthodontic anchorage. A preliminary biomechanical study. The European Journal of Orthodontics 1996;18(1):465-69.
- 47. Wehrbein H, Glatzmaier J, Mundwiller U, Diedrich P. The Orthosystem--a new implant system for orthodontic anchorage in the palate. Journal of Orofacial Orthopedics 1996;57(3):142-53.
- 48. Wehrbein H, Glatzmaier J, Yildirim M. Orthodontic anchorage capacity of short titanium screw implants in the maxilla. An experimental study in the dog. Clinical Oral Implants Research 1997;8(2):131-41.
- 49. Wehrbein H, Merz B, Hammerle C, Lang N. Bone-to-implant contact of orthodontic implants in humans subjected to horizontal loading. Clinical Oral Implants Research 1998;9(5):348-53.
- 50. Vande Vannet B, Sabzevar MM, Wehrbein H, Asscherickx K. Osseointegration of miniscrews: a histomorphometric evaluation. The European Journal of Orthodontics 2007;29(5):437-42.
- 51. Youn J-W, Cha J-Y, Yu H-S, Hwang C-J. Biologic evaluation of a hollow-type miniscrew implant: An experimental study in beagles. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(5):626-37.
- 52. Yu J-H, Lin Y-S, Chang W-J, Chang Y-Z, Lin C-L. Mechanical Effects of Micro-thread Orthodontic Mini-screw Design on Artificial Cortical Bone. Journal of Medical and Biological Engineering 2014;34(1):49-55.
- 53. Brown RN, Sexton BE, Gabriel Chu T-M, Katona TR, Stewart KT, Kyung H-M, et al. Comparison of stainless steel and titanium alloy orthodontic miniscrew

implants: A mechanical and histologic analysis. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(4):496-504.

- 54. Cuairán C, Campbell PM, Kontogiorgos E, Taylor RW, Melo AC, Buschang PH. Local application of zoledronate enhances miniscrew implant stability in dogs. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(6):737-49.
- 55. Wilmes B, Nienkemper M, Drescher D. Application and effectiveness of a miniimplant-and tooth-borne rapid palatal expansion device: the hybrid hyrax. World J Orthod 2010;11(4):323-30.
- 56. Papadopoulos MA, Tarawneh F. The use of miniscrew implants for temporary skeletal anchorage in orthodontics: A comprehensive review. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 2007;103(5):e6-e15.
- 57. Kanomi R. Mini-implant for orthodontic anchorage. J Clin Orthod 1997;31(11):763-7.
- 58. Costa A, Raffaini M, Melsen B. Miniscrews as orthodontic anchorage: A preliminary report. Int J Adult Orthodon Orthognath Surg. 1998 13(3):201-09.
- 59. B. Melsen AC. Immediate loading of implants used for orthodontic anchorage. Orthodontics & Craniofacial Research 2000;3(1):23-28.
- 60. Park Y. Intrusion of posterior teeth using mini-screw implants. American Journal of Orthodontics and Dentofacial Orthopedics 2003;123(6):690-94.
- 61. Park J, Cho HJ. Three-dimensional evaluation of interradicular spaces and cortical bone thickness for the placement and initial stability of microimplants in adults. American Journal of Orthodontics and Dentofacial Orthopedics 2009;136(3):314.e1-14.e12.
- 62. Buschang PH, Carrillo R, Rossouw PE. Orthopedic Correction of Growing Hyperdivergent, Retrognathic Patients With Miniscrew Implants. Journal of Oral and Maxillofacial Surgery 2011;69(3):754-62.
- 63. Chung K-R, Kim S-H, Kang Y-G, Nelson G. Orthodontic miniplate with tube as an efficient tool for borderline cases. American Journal of Orthodontics & Dentofacial Orthopedics 2011;139(4):551-62.
- 64. Lee J, Park H-S, Kyung H. Micro-implant anchorage for lingual treatment of skeletal Class II malocclusion. J Clin Orthod 2001;35(10):643-7;quiz 20.
- 65. Leung MT-C, Lee TC-K, Rabie ABM, Wong RW-K. Use of miniscrews and miniplates in orthodontics. Journal of Oral & Maxillofacial Surgery 2008;66(7):1461-6.
- 66. Kuroda S, Katayama A, Takano-Yamamoto T. Severe Anterior Open-Bite Case Treated Using Titanium Screw Anchorage. The Angle orthodontist 2004;74(4):558-67.
- 67. Lee J, Park H-S, Kyung H. Micro-implant anchorage for lingual treatment of a skeletal Class II malocclusion Journal of Clinical Orthodontics 2001;35(10):643-7.
- 68. Wehrbein H, Göllner P. Skeletal anchorage in orthodontics–basics and clinical application. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2007;68(6):443-61.
- 69. Melsen B. Mini-Implants: Where Are We? Journal of Clinical Orthodontics 2005;39(9):539-47; quiz 31-2.

- 70. Baik HS. Limitations in orthopedic and camouflage treatment for Class III malocclusion. Paper presented at, 2007.
- 71. Yamada K, Kuroda S, Deguchi T, Takano-Yamamoto T, Yamashiro T. Distal movement of maxillary molars using miniscrew anchorage in the buccal interradicular region. The Angle Orthodontist 2009;79(1):78-84.
- 72. Chamberland S, Proffit WR. Closer Look at the Stability of Surgically Assisted Rapid Palatal Expansion. Journal of Oral and Maxillofacial Surgery 2008;66(9):1895-900.
- 73. Harzer W, Schneider M, Gedrange T, Tausche E. Direct bone placement of the Hyrax fixation screw for surgically assisted rapid palatal expansion (SARPE). Journal of Oral and Maxillofacial Surgery 2006;64(8):1313-17.
- 74. Umemori M, Sugawara J, Mitani H, Nagasaka H, Kawamura H. Skeletal anchorage system for open bite correction. Am J Orthod Dentofacial Orthop. 1999;115:166-74.
- 75. Gerlach KL, Zahl C. Transversal palatal expansion using a palatal distractor. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2003;64(6):443-49.
- 76. Saltaji H, Major MP, Altalibi M, Youssef M, Flores-Mir C. Long-term skeletal stability after maxillary advancement with distraction osteogenesis in cleft lip and palate patients: A systematic review. The Angle orthodontist 2012;82(6):1115-22.
- 77. Cope JB, Owens SE. Historical Development and Evolution of Temporary Anchorage Devices. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 3-20.
- 78. Buschang PH, Kim KB. Considerations for Optimizing the Use of Miniscrew Implants in Orthodontic Practice. Temporary Skeletal Anchorage Devices: Springer; 2014. p. 1-27.
- 79. Lin J, Liou E, Yeh CL, Evans CA. A comparative evaluation of current orthodontic miniscrew systems. World Journal of Orthodontics 2007;8(2):136.
- 80. Block MS, Hoffman DR. A new device for absolute anchorage for orthodontics. American Journal of Orthodontics and Dentofacial Orthopedics 1995;107(3):251-58.
- 81. Chen Y-J, Chang H-H, Lin H-Y, Lai EH-H, Hung H-C, Yao C-CJ. Stability of miniplates and miniscrews used for orthodontic anchorage: experience with 492 temporary anchorage devices. Clinical Oral Implants Research 2008;19(11):1188-96.
- 82. Wehrbein H, Feifel H, Diedrich P. Palatal implant anchorage reinforcement of posterior teeth: A prospective study. American Journal of Orthodontics and Dentofacial Orthopedics 1999;116(6):678-86.
- 83. Takaki T, Tamura N, Yamamoto M, Takano N, Shibahara T, Yasumura T, et al. Clinical study of temporary anchorage devices for orthodontic treatment-stability of micro/mini-screws and mini-plates: experience with 455 cases. Bulletin of Tokyo Dental College 2010;51(3):151-63.
- 84. Melsen B, Godtfredsen LM. Factors in the Decision to Use Skeletal Anchorage. Temporary Anchorage Devices in Orthodontics: Mosby; 2009. p. 73-89.
- 85. Labanauskaite B, Jankauskas G, Vasiliauskas A, Haffar N. Implants for orthodontic anchorage.Meta-analysis. Stomatologija, Baltic Dental and Maxillofacial Journal 2005;7:128-32.

- 86. Jenner J, Fitzpatrick B. Skeletal anchorage utilising bone plates. Aust Orthod J 1985;9:231-33.
- 87. Sugawara J, Baik UB, Umemori M, Takahashi I, Nagasaka H, Kawamura H, et al. Treatment and posttreatment dentoalveolar changes following intrusion of mandibular molars with application of a skeletal anchorage system (SAS) for open bite correction. Int J Adult Orthodon Orthognath Surg. 2002;17:243-53.
- 88. Sugawara J, Daimaruya T, Umemori M, Nagasaka H, Takahashi I, Kawamura H, et al. Distal movement of mandibular molars in adult patients with the skeletal anchorage system Am J Orthod Dentofacial Orthop. 2004;125:130-38.
- 89. White L, Sugawara J. Dr. Junji Sugawara on the skeletal anchorage system. J Clin Orthod 1999;33:689-96.
- 90. Chung K-R, Kim S-H, Kook Y-A. The C-Palatal Plate. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 431-38.
- 91. Ritto AK. Skeletal Anchorage: Different Approaches. Temporary Anchorage Devices in Orthodontics: Mosby; 2009. p. 238-59.
- 92. Chung K-R, Kim S-H, Kook Y-A. The C-Tube. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 439-48.
- 93. Sugawara J, Umemori M, Takahashi I, Nagasaka H, Kawamura H. The Skeletal Anchorage System. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 449-61.
- 94. Liou EJ-W, Lin JC-Y. Appliances, Mechanics, and Treatment Strategies Toward Orthognatic-Like Treatment Results. temporary anchorage devices in orthodontics: Mosby; 2009. p. 167-97.
- 95. Park H-S. Clinical Application of Microimplants. temporary anchorage devices in orthodontics: Mosby; 2009. p. 260-86.
- 96. Park H-S. Micro-implant anchorage for treatment of skeletal Class I bialveolar protrusion. Journal of clinical orthodontics 2001;35(7):417-22.
- 97. Fortini A, Cacciafesta V, Sfondrini MF, Cambi S, Lupoli M. Clinical Applications and Efficiency of Miniscrews for Extradental Anchorage. Orthodontics 2004;1(2):1-12.
- 98. Cornelis MA, Scheffler NR, Nyssen-Behets C, De Clerck HJ, Tulloch JFC. Patients' and orthodontists' perceptions of miniplates used for temporary skeletal anchorage: a prospective study. American Journal of Orthodontics & Dentofacial Orthopedics 2008;133(1):18-24.
- 99. Chen Y-J, Chang H-H, Huang C-Y, Hung H-C, Lai EH-H, Yao C-CJ. A retrospective analysis of the failure rate of three different orthodontic skeletal anchorage systems. Clinical Oral Implants Research 2007;18(6):768-75.
- 100. Ohnishi H, Yagi T, Yasuda Y, Takada K. A Mini-Implant for Orthodontic Anchorage in a Deep Overbite Case. The Angle orthodontist 2005;75(3):444-52.
- Rodriguez JC, Suarez F, Chan H-L, Padial-Molina M, Wang H-L. Implants for Orthodontic Anchorage: Success Rates and Reasons of Failures. Implant Dentistry 2014;23(2):155-61.
- 102. Maino B, Mura P, Bednar J. Miniscrew implants: The Spider Screw anchorage system. Seminars Orthod 2005;11(1):40-46.
- 103. Wiechmann D, Meyer U, Büchter A. Success rate of mini- and micro-implants used for orthodontic anchorage: a prospective clinical study. Clinical Oral Implants Research 2007;18(2):263-67.

- 104. Park H-S, Jeong S-H, Kwon O-W. Factors affecting the clinical success of screw implants used as orthodontic anchorage. American Journal of Orthodontics and Dentofacial Orthopedics 2006;130(1):18-25.
- 105. Topouzelis N, Tsaousoglou P. Clinical factors correlated with the success rate of miniscrews in orthodontic treatment. International Journal of Oral Science 2012.
- 106. Kravitz ND, Kusnoto B. Risks and complications of orthodontic miniscrews. American Journal of Orthodontics and Dentofacial Orthopedics 2007;131(4, Supplement 1):S43-S51.
- Fritz UB, Diedrich PR. Clinical Suitability of Titaniun Microscrews for Orthodontic Anchorage. Temporary Anchorage Devices in Orthodontics: Mosby; 2009. p. 287-94.
- 108. Lim H-J, Choi Y-J, Evans CA, Hwang H-S. Predictors of initial stability of orthodontic miniscrew implants. The European Journal of Orthodontics 2011.
- 109. Park HC. Clinical study on success rate of microscrew implants for orthodontic anchorage. Korean journal of orthodontics 2003;33:151-56.
- 110. Rygh P, Reitan K. Ultrastructural changes in the periodontal ligament incident to orthodontic tooth movement. Transactions. European Orthodontic Society 1972:393.
- 111. Poggio P IC, Velo S, Carano A. Safe zones: a guide for miniscrew positioning in the maxillary and mandibular arch. Angle Orthod 2006;76:191-7.
- 112. Costa A, Pasta G, Bergamaschi G. Intraoral hard and soft tissue depths for temporary anchorage devices. Seminars in Orthodontics 2005;11(1):10-15.
- 113. Schnelle MA, Beck FM, Jaynes RM, Huja SS. A radiographic evaluation of the availability of bone for placement of miniscrews. The Angle orthodontist 2004;74(6):832-37.
- 114. Ludwig B BSaBS. Mini-implants in orthoodntics: Innovative anchorage concepts. Berlin: Quintessence Publishing Co Ltd; 2007.
- 115. Dalstra M CP, Melsen B. Load transfer of miniscrews for orthodontic anchorage. Orthodontics 2004;1:53-62.
- 116. Fabbroni G, Aabed S, Mizen K, Starr DG. Transalveolar screws and the incidence of dental damage: a prospective study. International journal of oral and maxillofacial surgery 2004;33(5):442-46.
- 117. Asscherickx K VB, Wehrbein H, Sabzevar MM. Root repair after injury from mini-screw. Clinical Oral Implants Research 2005;16:575-8.
- 118. Park H-C. The skeletal cortical anchorage using titanium microscrew implants. Korean journal of orthodontics 1999;29(6):699-706.
- 119. Kadioglu O, Büyükyilmaz T, Zachrisson BU, Maino BG. Contact damage to root surfaces of premolars touching miniscrews during orthodontic treatment. American Journal of Orthodontics and Dentofacial Orthopedics 2008;134(3):353-60.
- 120. Maino BG, Weiland F, Attanasi A, Zachrisson BU, Buyukylmaz T. Root damage and repair after contact with miniscrews. Journal of Clinical Orthodontics 2007;41:762–66.
- 121. Hwang Y-C, Hwang H-S. Surgical repair of root perforation caused by an orthodontic miniscrew implant. American Journal of Orthodontics and Dentofacial Orthopedics 2011;139(3):407-11.
- 122. Bargholz C. Perforation repair with mineral trioxide aggregate: a modified matrix concept. International endodontic journal 2005;38(1):59-69.

- 123. Mortensen MG, Buschang PH, Oliver DR, Kyung HM, Behrents RG. Stability of immediately loaded 3-and 6-mm miniscrew implants in beagle dogs: a pilot study. American Journal of Orthodontics and Dentofacial Orthopedics 2009;136(2):251-59.
- 124. Wang Y-C, Liou EJW. Comparison of the loading behavior of self-drilling and predrilled miniscrews throughout orthodontic loading. American Journal of Orthodontics and Dentofacial Orthopedics 2008;133(1):38-43.
- 125. Genant HK, Cooper C, Poor G, Reid I, Ehrlich G, Kanis J, et al. Interim report and recommendations of the World Health Organization task-force for osteoporosis. Osteoporosis International 1999;10(4):259-64.
- 126. Park J-B, Kim E-Y, Paek J, Kook Y-A, Jeong D-M, Cho I-S, et al. Primary Stability of Self-Drilling and Self-Tapping Mini-Implant in Tibia of Diabetes-Induced Rabbits. International Journal of Dentistry 2014;2014.
- 127. Marquezan M, Mattos CT, Sant'Anna EF, de Souza MMG, Maia LC. Does cortical thickness influence the primary stability of miniscrews? A systematic review and meta-analysis. The Angle Orthodontist 2014; 84(6): 1093-1103.
- 128. Wilmes B, Rademacher C, Olthoff G, Drescher, D. Parameters affecting primary stability of orthodontic mini-implants. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2006;67(3):162-74.
- 129. Glasl B, Björn L, Lietz T, Bowman SJ, Baumgaertel S. Risks and prevention strategies. In: Baumgaertel S, Bowman SJ, editors. Mini-implants in orthodontics: innovative anchorage concepts. Berlin: Quintessence; 2008. p. 123-25.
- 130. Bergkvist G, Koh K-J, Sahlholm S, Klintström E, Lindh C. Bone density at implant sites and its relationship to assessment of bone quality and treatment outcome. The International journal of oral & maxillofacial implants 2009;25(2):321-28.
- 131. Gracco A, Lombardo L, Cozzani M, Siciliani G. Quantitative cone-beam computed tomography evaluation of palatal bone thickness for orthodontic miniscrew placement. American Journal of Orthodontics and Dentofacial Orthopedics 2008;134(3):361-69.
- 132. Ten Cate AR. Oral histology : development, structure, and function St. Louis : Mosby; 2007.
- 133. Gong JK, Arnold JS, Cohn SH. Composition of trabecular and cortical bone. The Anatomical Record 2005;149(3):325-31.
- 134. Melsen B, Graham J, Baccetti T, Koga M, Boyd R, Park J, et al. Factors contributing to the success or failure of skeletal anchorage devices: an informal JCO survey. Journal of Clinical Orthodontics 2010;44(12):714-8; quiz 43.
- 135. Lietz T. Mini-screws Aspects of Assessment and Selection Among Different Systems. In: Baumgaertel S, Bowman SJ, editors. Mini-implants in orthodontics: innovative anchorage concepts. Berlin: Quintessence; 2008. p. 188.
- 136. Zitzmann NU, Berglundh T, Ericsson I, Lindhe J. Spontaneous progression of experimentally induced periimplantitis. Journal of Clinical Periodontology 2004;31(10):845-49.
- 137. Ericsson I, Berglundh T, Marinello C, Liljenberg B, Lindhe J. Long-standing plaque and gingivitis at implants and teeth in the dog. Clinical Oral Implants Research 1992;3(3):99-103.

- 138. Lee J-H, Frias V, Lee K-W, Wright RF. Effect of implant size and shape on implant success rates: A literature review. The Journal of Prosthetic Dentistry 2005;94(4):377-81.
- 139. Wilmes B, Rademacher C, Olthoff G, Drescher D. Parameters Affecting Primary Stability of Orthodontic Mini-implants. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2006;67(3):162-74.
- 140. Huja SS. Mechanisms of Bone Adaptation to miniscrew Implants. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 537.
- 141. Aerssens J, Boonen S, Lowet G, Dequeker J. Interspecies Differences in Bone Composition, Density, and Quality: Potential Implications for in Vivo Bone Research. Endocrinology 1998;139(2):663-70.
- 142. Farnsworth D, Rossouw PE, Ceen RF, Buschang PH. Cortical bone thickness at common miniscrew implant placement sites. American Journal of Orthodontics & Dentofacial Orthopedics 2011;139(4):495-503.
- 143. Kokich VG, Shapiro PA, Oswald R, Koskinen-Moffett L, Clarren SK. Ankylosed teeth as abutments for maxillary protraction: a case report. American Journal of Orthodontics 1985;88(4):303-07.
- 144. Jamilian A, Haraji A, Showkatbakhsh R, Valaee N. The effects of miniscrew with Class III traction in growing patients with maxillary deficiency. International journal of orthodontics (Milwaukee, Wis.);22(2):25.
- 145. Wilmes B, Nienkemper M, Ludwig B, Kau C, Drescher D. Early class III treatment with a hybrid hyrax-mentoplate combination. Journal of clinical orthodontics 2011;45(1):15.
- 146. Schätzle M, Männchen R, Zwahlen M, Lang N. Survival and failure rates of orthodontic temporary anchorage devices: a systematic review. Clinical Oral Implants Research 2009;20(12):1351-9.
- 147. Shroff B, Yoon W, Lindauer S, Burstone C. Simultaneous intrusion and retraction using a three-piece base arch. The Angle Orthodontist 1997;67(6):455.
- 148. Bishara S. How orthodontic appliances work. Textbook of orthodontics. Philadelphia; 2001. p. 208-31.
- 149. Baccetti T, De Clerck H, Cevidanes L, Franchi L. Morphometric analysis of treatment effects of bone-anchored maxillary protraction in growing Class III patients. The European Journal of Orthodontics 2010:cjq170.
- 150. Şar Ç, Şahinoğlu Z, Özçırpıcı AA, Uçkan S. Dentofacial effects of skeletal anchored treatment modalities for the correction of maxillary retrognathia. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(1):41-54.
- 151. Melsen B, Costa A. Immediate loading of implants used for orthodontic anchorage. Clinical Orthodontics and Research 2000;3(1):23-28.
- 152. Fritz U, Diedrich P, Kinzinger G, Al-Said M. The Anchorage Quality of Miniimplants towards Translatory and Extrusive Forces. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2003;64(4):293-304.
- 153. Wehrbein H, Yildirim M, Diedrich P. Osteodynamics around orthodontically loaded short maxillary implants. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 1999;60(6):409-15.
- 154. Meredith N, Shagaldi F, Alleyne D, Sennerby L, Cawley P. The application of resonance frequency measurements to study the stability of titanium implants

during healing in the rabbit tibia. Clinical Oral Implants Research 1997;8(3):234-43.

- 155. Glauser R SL, Meredith N, Ree A, Lundgren A, Gottlow J, et al. . Resonance frequency analysis of implants subjected to immediate or early functional occlusal loading. Successful vs. failing implants. Clinical oral implant research 2004;15:428-34.
- 156. Katsavrias G. Reliability and validity of measuring implant stability with resonance frequency analysis [Saint Louis University; 2009.
- 157. Florvaag B, Kneuertz P, Lazar F, Koebke J, Zöller J, Braumann B, et al. Biomechanical Properties of Orthodontic Miniscrews. An In-vitro Study. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2010;71(1):53-67.
- 158. Motoyoshi M, Hirabayashi M, Uemura M, Shimizu N. Recommended placement torque when tightening an orthodontic mini-implant. Das empfohlenen Drehmoment beim Festziehen eines orthodontischen Mini-Implantats. Clinical Oral Implants Research 2006;17(1):109-14.
- 159. Friberg B, Sennerby L, Roos J, Lekholm U. Identification of bone quality in conjunction with insertion of titanium implants. A pilot study in jaw autopsy specimens. Clinical Oral Implants Research 1995;6(4):213-19.
- 160. Kim J-W, Ahn S-J, Chang Y-I. Histomorphometric and mechanical analyses of the drill-free screw as orthodontic anchorage. American Journal of Orthodontics and Dentofacial Orthopedics 2005;128(2):190-94.
- 161. Klokkevold PR, Johnson P, Dadgostari S, Davies JE, Caputo A, Nishimura RD. Early endosseous integration enhanced by dual acid etching of titanium: a torque removal study in the rabbit. Clinical Oral Implants Research 2001;12(4):350-57.
- 162. Favero LG, Pisoni A, Paganelli C. Removal torque of osseointegrated miniimplants: an in vivo evaluation. The European Journal of Orthodontics 2007;29(5):443.
- 163. Shah AH, Behrents RG, Kim KB, Kyung H-M, Buschang PH. Effects of screw and host factors on insertion torque and pullout strength. The Angle orthodontist 2011;82(4):603-10.
- 164. Shigeeda T. Root proximity and stability of orthodontic anchor screws. Journal of oral science 2014;56(1):59-65.
- 165. Uemura M, Motoyoshi M, Yano S, Sakaguchi M, Igarashi Y, Shimizu N. Orthodontic mini-implant stability and the ratio of pilot hole implant diameter. The European Journal of Orthodontics 2012;34(1):52-56.
- 166. Roberts W. Bone tissue interface. J Dent Educ 1988;52(12):804-09.
- 167. Roberts WE, Helm FR, Marshall KJ, Gongloff RK. Rigid endosseous implants for orthodontic and orthopedic anchorage. Angle Orthodontist 1989;59:247–56.
- 168. Ono A, Motoyoshi M, Shimizu N. Cortical bone thickness in the buccal posterior region for orthodontic mini-implants. International Journal of Oral & Maxillofacial Surgery 2008;37(4):334-40.
- 169. Motoyoshi M, Yoshida T, Ono A, Shimizu N. Effect of cortical bone thickness and implant placement torque on stability of orthodontic mini-implants. The International journal of oral & maxillofacial implants 2006;22(5):779-84.
- 170. Frost HM. A 2003 Update of Bone Physiology and Wolff's Law for Clinicians. The Angle orthodontist 2004;74(1):3-15.

- 171. Kuroda S, Yamada K, Deguchi T, Hashimoto T, Kyung H-M, Takano-Yamamotod T. Root proximity is a major factor for screw failure in orthodontic anchorage. Am J Orthod Dentofacial Orthop 2007;131(4 Supp 1):S68-S73.
- 172. Hyde JD, King GJ, Greenlee GM, Spiekerman C, Huang GJ. Survey of Orthodontists' Attitudes and Experiences Regarding Miniscrew Implants. Journal of clinical orthodontics: JCO 2010;44(8):481.
- 173. Mah JK, Huang JC, Choo H. Practical applications of cone-beam computed tomography in orthodontics. Journal of the American Dental Association (1939) 2010;141:7S-13S.
- 174. Watanabe H, Deguchi T, Hasegawa M, Ito M, Kim S, Takano-Yamamoto T. Orthodontic miniscrew failure rate and root proximity, insertion angle, bone contact length, and bone density. Orthodontics & Craniofacial Research 2013;16(1):44-55.
- 175. Kim S-H, Choi Y-S, Hwang E-H, Chung K-R, Kook Y-A, Nelson G. Surgical positioning of orthodontic mini-implants with guides fabricated on models replicated with cone-beam computed tomography. American Journal of Orthodontics and Dentofacial Orthopedics 2007;131(4):S82-S89.
- 176. Kim S-H, Kang S-M, Choi Y-S, Kook Y-A, Chung K-R, Huang JC. Cone-beam computed tomography evaluation of mini-implants after placement: is root proximity a major risk factor for failure? American Journal of Orthodontics and Dentofacial Orthopedics 2010;138(3):264-76.
- 177. Duaibis RB. Factors affecting the stability of miniscrew implants: A stepwise three dimensional finite element study [Chicago: University of Illinois. ; 2010.
- 178. Duaibis R, Kusnoto B, Natarajan R, Zhao L, Evans C. Factors affecting stresses in cortical bone around miniscrew implants. The Angle orthodontist 2012;82(5):875-80.
- 179. Motoyoshi M, Yoshida T, Ono A, Shimizu N. Effect of cortical bone thickness and implant placement torque on stability of orthodontic mini-implants. The International journal of oral & maxillofacial implants 2007;22(5):779.
- 180. McManus MM, Qian F, Grosland NM, Marshall SD, Southard TE. Effect of miniscrew placement torque on resistance to miniscrew movement under load. American Journal of Orthodontics and Dentofacial Orthopedics 2011;140(3):e93-e98.
- 181. Motoyoshi M, Hirabayashi M, Uemura M, Shimizu N. Recommended placement torque when tightening an orthodontic mini implant. Clinical Oral Implants Research 2006;17(1):109-14.
- 182. Meredith N. Assessment of implant stability as a prognostic determinant. The International journal of prosthodontics 1998;11(5):491.
- 183. Gupta N, Kotrashetti SM, Naik V. A Comparitive Clinical Study Between Self Tapping and Drill Free Screws as a Source of Rigid Orthodontic Anchorage. Journal of Maxillofacial and Oral Surgery 2012;11(1):29-33.
- 184. Son S, Motoyoshi M, Uchida Y, Shimizu N. Comparative study of the primary stability of self-drilling and self-tapping orthodontic miniscrews. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(4):480-85.
- 185. Tachibana R, Motoyoshi M, Shinohara A, Shigeeda T, Shimizu N. Safe placement techniques for self-drilling orthodontic mini-implants. International journal of oral and maxillofacial surgery 2012;41(11):1439-44.

- Heidemann W GK, Grobel KH, Kollner HG. Influence of different pilot sizes on torque measurements and pulllout analysis of osteosynthesis screws. Journal of Craniofacial Surgery 1998;26:50-55.
- 187. Wilmes B, Ottenstreuer S, Su Y-Y, Drescher D. Impact of Implant Design on Primary Stability of Orthodontic Mini-implants. Journal of Orofacial Orthopedics 2008;69(1):42-50.
- 188. Hong C, Lee H, Webster R, Kwak J, Wu BM, Moon W. Stability comparison between commercially available mini-implants and a novel design: Part 1. The Angle Orthodontist 2011.
- 189. Hong C, Truong P, Song HN, Wu BM, Moon W. Mechanical stability assessment of novel orthodontic mini-implant designs: part 2. The Angle Orthodontist *In Press*.
- 190. Shah AH. Effect of miniscrew characteristics and bone properties in insertion torque and pullout strength [Saint Louis: Saint Louis University 2011.
- 191. Reigstad O, Johansson CB, Stenport V, Wennerberg A, Reigstad A, Røkkum M. Different patterns of bone fixation with hydroxyapatite and resorbable CaP coatings in the rabbit tibia at 6, 12, and 52 weeks. journal of Biomedical Materials Research Part B: Applied Biomaterials; 2011.
- 192. Herman RJ, Currier GF, Miyake A. Mini-implant anchorage for maxillary canine retraction: a pilot study. American Journal of Orthodontics and Dentofacial Orthopedics 2006;130(2):228-35.
- 193. Reynders R, Ronchi L, Bipat S. Mini-implants in orthodontics: A systematic review of the literature. American Journal of Orthodontics and Dentofacial Orthopedics 2009;135(5):564.e1-64.e19.
- 194. Büchter A, Wiechmann D, Koerdt S, Wiesmann HP, Piffko J, Meyer U. Loadrelated implant reaction of mini-implants used for orthodontic anchorage. Clinical Oral Implants Research 2005;16(4):473-79.
- 195. Park HS, Lee K-J. Biomechanical Principles in Miniscrew-Driven Orthodontics. Temporary Anchorage Devices in Orthodontics: Mosby; 2009. p. 93-144.
- 196. MELSEN B, VERNA C, LUZI C. Mini-implants and their clinical applications: The Aarhus Experience; 2013. p. 104.
- 197. Baek S-H, Kim B-M, Kyung S-H, Lim JK, Kim YH. Success rate and risk factors associated with mini-implants reinstalled in the maxilla. The Angle orthodontist 2008;78(5):895-901.
- 198. Wu T-Y, Kuang S-H, Wu C-H. Factors associated with the stability of miniimplants for orthodontic anchorage: a study of 414 samples in Taiwan. Journal of Oral and Maxillofacial Surgery 2009;67(8):1595-99.
- 199. Melsen B, Verna C. Miniscrew implants: The Aarhus anchorage system. Seminars in Orthodontics 2005;11(1):24-31.
- 200. Ma PX. Biomimetic materials for tissue engineering. Advanced drug delivery reviews 2008;60(2):184-98.
- 201. Kim TG, Shin H, Lim DW. Biomimetic scaffolds for tissue engineering. Advanced Functional Materials 2012;22(12):2446-68.
- 202. Masala S, Nano G, Marcia S, Muto M, Fucci FPM, Simonetti G. Osteoporotic vertebral compression fractures augmentation by injectable partly resorbable ceramic bone substitute (Cerament[™]| SPINE SUPPORT): a prospective nonrandomized study. Neuroradiology 2012;54(6):589-96.

- 203. Ryu K-S, Shim J-H, Heo H-Y, Park C-K. Therapeutic efficacy of injectable calcium phosphate cement in osteoporotic vertebral compression fractures: prospective nonrandomized controlled study at 6-month follow-up. World neurosurgery 2010;73(4):408-11.
- 204. Becker S, Franz K, Wilke I, Ogon M. Injectable bone cements in the treatment of spinal fractures, osteopromotive capacity and surgical considerations. Eur Cells Mater 2006;11(Suppl 1):1.
- 205. Larsson S, Hannink G. Injectable bone-graft substitutes: current products, their characteristics and indications, and new developments. Injury 2011;42:S30-S34.
- 206. Masaki T, Sasao Y, Miura T, Torii Y, Kojima A, Aoki H, et al. An experimental study on initial fixation strength in transpedicular screwing augmented with calcium phosphate cement. Spine 2009;34(20):E724-E28.
- 207. Wolff K-D, Swaid S, Nolte D, Böckmann RA, Hölzle F, Müller-Mai C. Degradable injectable bone cement in maxillofacial surgery: indications and clinical experience in 27 patients. Journal of Cranio-Maxillofacial Surgery 2004;32(2):71-79.
- 208. Ko C, Kohn D, Hollister S. Micromechanics of implant/tissue interfaces. The Journal of oral implantology 1991;18(3):220-30.
- 209. Cho BC, Park JW, Baik BS. Clinical application of injectable calcium sulfate on early bony consolidation in distraction osteogenesis for the treatment of craniofacial microsomia. Journal of Craniofacial Surgery 2002;13(3):465-75.
- 210. Guarnieri R, Aldini NN, Pecora G, Fini M, Giardino R. Medial-grade calcium sulfate hemihydrate (surgiplaster) in healing of a human extraction socket-histologic observation at 3 months: a case report. The International journal of oral & maxillofacial implants 2004;20(4):636-41.
- 211. Kim JY, Cho BC. Effect of calcium sulfate pellets on early bone mineralization in distraction osteogenesis for craniofacial microsomia in adults. Journal of Craniofacial Surgery 2007;18(6):1309-21.
- 212. Apelt D, Theiss F, El-Warrak A, Zlinszky K, Bettschart-Wolfisberger R, Bohner M, et al. In vivo behavior of three different injectable hydraulic calcium phosphate cements. Biomaterials 2004;25(7):1439-51.
- 213. Charrière E, Terrazzoni S, Pittet C, Mordasini P, Dutoit M, Lemaître J, et al. Mechanical characterization of brushite and hydroxyapatite cements. Biomaterials 2001;22(21):2937-45.
- 214. Ryf C, Goldhahn S, Radziejowski M, Blauth M, Hanson B. A new injectable brushite cement: first results in distal radius and proximal tibia fractures. European Journal of Trauma and Emergency Surgery 2009;35(4):389-96.
- 215. Keating J, Hajducka C, Harper J. Minimal internal fixation and calciumphosphate cement in the treatment of fractures of the tibial plateau A PILOT STUDY. Journal of Bone & Joint Surgery, British Volume 2003;85(1):68-73.
- 216. Mattsson P, Larsson S. Unstable trochanteric fractures augmented with calcium phosphate cement A prospective randomized study using radiostereometry to measure fracture stability. Scandinavian journal of surgery 2004;93(3):223-28.
- 217. Mattsson P, Alberts A, Dahlberg G, Sohlman M, Hyldahl H-C, Larsson S. Resorbable cement for the augmentation of internally-fixed unstable trochanteric fractures A PROSPECTIVE, RANDOMISED MULTICENTRE STUDY. Journal of Bone & Joint Surgery, British Volume 2005;87(9):1203-09.

- 218. Moore DC, Maitra RS, Farjo LA, Graziano GP, Goldstein SA. Restoration of pedicle screw fixation with an in situ setting calcium phosphate cement. Spine 1997;22(15):1696-705.
- 219. Russell TA, Leighton RK. Comparison of autogenous bone graft and endothermic calcium phosphate cement for defect augmentation in tibial plateau fracturesA multicenter, prospective, randomized study. The Journal of Bone & Joint Surgery 2008;90(10):2057-61.
- 220. De Leonardis D, Pecora GE. Prospective study on the augmentation of the maxillary sinus with calcium sulfate: histological results. Journal of Periodontology 2000;71(6):940-47.
- 221. Guarnieri R, Grassi R, Ripari M, Pecora G. Maxillary sinus augmentation using granular calcium sulfate (surgiplaster sinus): radiographic and histologic study at 2 years. International Journal of Periodontics and Restorative Dentistry 2006;26(1):79.
- 222. Schneider G, Blechschmidt K, Linde D, Litschko P, Körbs T, Beleites E. Bone regeneration with glass ceramic implants and calcium phosphate cements in a rabbit cranial defect model. Journal of Materials Science: Materials in Medicine 2010;21(10):2853-59.
- 223. Von Rechenberg B, Génot OR, Nuss K, Galuppo L, Fulmer M, Jacobson E, et al. Evaluation of four biodegradable, injectable bone cements in an experimental drill hole model in sheep. European Journal of Pharmaceutics and Biopharmaceutics 2013;85(1):130-38.
- 224. Gómez E, Martín M, Arias J, Carceller F. Clinical applications of Norian SRS (calcium phosphate cement) in craniofacial reconstruction in children: our experience at Hospital La Paz since 2001. Journal of Oral and Maxillofacial Surgery 2005;63(1):8-14.
- 225. Goodman SB, Bauer TW, Carter D, Casteleyn PP, Goldstein SA, Kyle RF, et al. Norian SRS cement augmentation in hip fracture treatment: laboratory and initial clinical results. Clinical orthopaedics and related research 1998;348:42-50.
- 226. Welkerling H, Raith J, Kastner N, Marschall C, Windhager R. Painful soft-tissue reaction to injectable Norian SRS calcium phosphate cement after curettage of enchondromas. Journal of Bone & Joint Surgery, British Volume 2003;85(2):238-39.
- 227. Thomas MV, Puleo DA, Al-Sabbagh M. Calcium sulfate: a review. Journal of long-term effects of medical implants 2005;15(6).
- 228. Su-Gwan K, Hak-Kyun K, Sung-Chul L. Combined implantation of particulate dentine, plaster of Paris, and a bone xenograft (Bio-Oss< sup>®</sup>) for bone regeneration in rats. Journal of Cranio-Maxillofacial Surgery 2001;29(5):282-88.
- 229. Kutkut A, Andreana S. Medical-grade calcium sulfate hemihydrate in clinical implant dentistry: a review. Journal of long-term effects of medical implants 2010;20(4).
- 230. Li Y, Rodrigues J, Tomas H. Injectable and biodegradable hydrogels: gelation, biodegradation and biomedical applications. Chemical Society Reviews 2012;41(6):2193-221.
- 231. Urban RM, Turner TM, Hall DJ, Infanger SI, Cheema N, Lim T-H, et al. Effects of altered crystalline structure and increased initial compressive strength of

calcium sulfate bone graft substitute pellets on new bone formation. Orthopedics 2004;27(1 Suppl):s113-8.

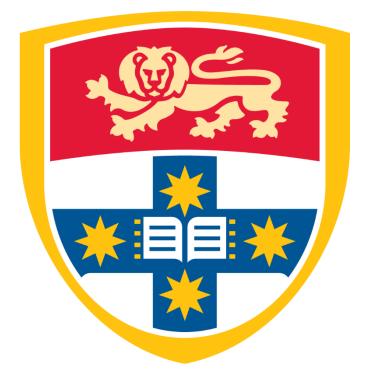
- 232. Sbordone L, Bortolaia C, Perrotti V, Pasquantonio G, Petrone G. Clinical and histologic analysis of calcium sulfate in treatment of a post-extraction defect: a case report. Implant Dentistry 2005;14(1):82-87.
- 233. Peltier LF, Bickel EY, Lillo R, Thein MS. The use of plaster of Paris to fill defects in bone. Annals of surgery 1957;146(1):61.
- 234. Juillet J. Use of plaster of Paris in implantology. Inf Dent 1976;58:51-3.
- 235. Johansson L-Å, Isaksson S, Lindh C, Becktor JP, Sennerby L. Maxillary sinus floor augmentation and simultaneous implant placement using locally harvested autogenous bone chips and bone debris: a prospective clinical study. Journal of Oral and Maxillofacial Surgery 2010;68(4):837-44.
- 236. De Leonardis D, Pecora GE. Augmentation of the maxillary sinus with calcium sulfate: one-year clinical report from a prospective longitudinal study. The International journal of oral & maxillofacial implants 1998;14(6):869-78.
- Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: Part

 The influence of stability of fixation and soft-tissue preservation. Clinical
 orthopaedics and related research 1989;238:249-81.
- 238. Sariibrahimoglu K, Wolke JG, Leeuwenburgh SC, Yubao L, Jansen JA. Injectable biphasic calcium phosphate cements as a potential bone substitute. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2014;102(3):415-22.
- 239. Yetkinler DN, Ladd AL, Poser RD, Constantz BR, Carter D. Biomechanical Evaluation of Fixation of Intra-Articular Fractures of the Distal Part of the Radius in Cadavera: Kirschner Wires Compared with Calcium-Phosphate Bone Cement*. The Journal of Bone & Joint Surgery 1999;81(3):391-9.
- 240. Larsson S. Calcium phosphates: what is the evidence? Journal of orthopaedic trauma 2010;24:S41-S45.
- 241. Gisep A, Wieling R, Bohner M, Matter S, Schneider E, Rahn B. Resorption patterns of calcium-phosphate cements in bone. Journal of Biomedical Materials Research Part A 2003;66(3):532-40.
- 242. Barralet JE, Grover LM, Gbureck U. Ionic modification of calcium phosphate cement viscosity. Part II: hypodermic injection and strength improvement of brushite cement. Biomaterials 2004;25(11):2197-203.
- 243. Xia Z, Grover LM, Huang Y, Adamopoulos IE, Gbureck U, Triffitt JT, et al. In vitro biodegradation of three brushite calcium phosphate cements by a macrophage cell-line. Biomaterials 2006;27(26):4557-65.
- 244. Constantz BR, Ison IC, Fulmer MT, Poser RD, Smith ST, VanWagoner M, et al. Skeletal repair by in situ formation of the mineral phase of bone. Science 1995;267(5205):1796-99.
- 245. Frakenburg EP, Goldstein SA, Bauer TW, Harris SA, Poser RD. Biomechanical and Histological Evaluation of a Calcium Phosphate Cement*. The Journal of Bone & Joint Surgery 1998;80(8):1112-24.
- 246. Khan SN, Tomin E, Lane JM. Clinical applications of bone graft substitutes. Orthopedic Clinics of North America 2000;31(3):389-98.
- 247. Da Costa G, Pare A, Goga D, Sury F, Laure B. [CT-scan evaluation of calvarial bone donor site reconstruction using calcium phosphate cement.]. Revue de stomatologie, de chirurgie maxillo-faciale et de chirurgie orale 2014.

- 248. Thordarson DB, Bollinger M. SRS cancellous bone cement augmentation of calcaneal fracture fixation. Foot & ankle international 2005;26(5):347-52.
- 249. Gal P, Ondrus S, Skvaril J, Straka M, Jochymek J, Planka L. [Synthetic biocompatible degradable material for juvenile bone cyst treatment]. Acta chirurgiae orthopaedicae et traumatologiae Cechoslovaca 2009;76(6):495-500.
- 250. Deramond H, Depriester C, Galibert P, Le Gars D. Percutaneous vertebroplasty with polymethylmethacrylate: technique, indications, and results. Radiologic clinics of north america 1998;36(3):533-46.
- 251. Doria C, Tranquilli Leali P. Percutaneous techniques in the treatment of osteoporotic, traumatic and neoplastic fractures of thoraco-lumbar spine: our institutional experience. Injury 2010;41(11):1136-39.
- 252. Klazen CA, Lohle PN, de Vries J, Jansen FH, Tielbeek AV, Blonk MC, et al. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. The Lancet 2010;376(9746):1085-92.
- 253. Stankewich C, Swiontkowski MF, Tencer AF, Yetkinler DN, Poser RD. Augmentation of femoral neck fracture fixation with an injectable calcium-phosphate bone mineral cement. Journal of Orthopaedic Research 1996;14(5):786-93.
- 254. Hillmeier J, Meeder PJ, Nöldge G, Kasperk C. Minimal invasive Reposition und innere Stabilisierung osteoporotischer Wirbelkörperfrakturen (Ballonikyphoplastie). Operative Orthopädie und Traumatologie 2003;15(4):343-62.
- 255. Betz RR. Limitations of autograft and allograft: new synthetic solutions. Orthopedics 2002;25(5 Suppl):s561-70.
- 256. Hornicek FJ, Gebhardt MC, Tomford WW, Sorger JI, Zavatta M, Menzner JP, et al. Factors affecting nonunion of the allograft-host junction. Clinical orthopaedics and related research 2001;382:87-98.
- 257. Mitchell N, Shepard N. The resurfacing of adult rabbit articular cartilage by multiple perforations through the subchondral bone. The Journal of Bone & Joint Surgery 1976;58(2):230-33.
- 258. Wozney JM, Rosen V, Celeste AJ, Mitsock LM, Whitters MJ, Kriz RW, et al. Novel regulators of bone formation: molecular clones and activities. Science 1988;242(4885):1528-34.
- 259. Hannink G, Wolke JGC, Schreurs BW, Buma P. In vivo behavior of a novel injectable calcium phosphate cement compared with two other commercially available calcium phosphate cements. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2008;85B(2):478-88.
- 260. Hayashi C, Kinoshita A, Oda S, Mizutani K, Shirakata Y, Ishikawa I. Injectable calcium phosphate bone cement provides favorable space and a scaffold for periodontal regeneration in dogs. J Periodontol 2006.
- 261. Horstmann WG, Verheyen CCPM, Leemans R. An injectable calcium phosphate cement as a bone-graft substitute in the treatment of displaced lateral tibial plateau fractures. Injury 2003;34(2):141-44.
- 262. Low KL, Tan SH, Sharif Zein SH, Roether JA, Mouriño V, Boccaccini AR. Calcium phosphate-based composites as injectable bone substitute materials J Biomed Mater Res B Appl Biomater 2010;94(1):273-86.

- 263. Sanzana ES, Navarro M, Macule F, Suso S, Planell JA, Ginebra MP. Of the in vivo behavior of calcium phosphate cements and glasses as bone substitutes. Acta Biomaterialia 2008;4(6):1924-33.
- 264. Kelly CW, Ross; Gitelis, Steven; Hartjen, Charles; Watson, J. Tracy; Kim, Poong Taek. The use of surgical grade calcium sulfate as a bone graft substitute: results of a multicenter trial. Clinical Orthopaedics & Related Research 2001;382:42-50.
- 265. Bohner M. Design of ceramic-based cements and putties for bone graft substitution. European Cells and Materials 2010;20:1-12.
- 266. Temenoff JS, Mikos AG. Injectable biodegradable materials for orthopedic tissue engineering. Biomaterials 2000;21(23):2405-12.
- 267. Yang H, Zou J. Filling materials used in kyphoplasty and vertebroplasty for vertebralcompression fracture: a literature review. Artificial Cells, Blood Substitutes, & Immobilization Biotechnology 2011;39(2):87-91.
- 268. Zhu X, Zhang Z, Mao H, Geng D, Zou J, Wang G, et al. A novel sheep vertebral bone defect model for injectable bioactive vertebral augmentation materials. Journal of Materials Science: Materials in Medicine 2011;22(1):159-64.
- 269. Komath M, Varma HK. Development of a fully injectable calcium phosphate cement for orthopedic and dental applications. Bulletin of Materials Science 2003;26(4):415-22.
- 270. Yu X-W, Xie X-H, Yu Z-F, Tang T-T. Augmentation of screw fixation with injectable calcium sulfate bone cement in ovariectomized rats. journal of Biomedical Materials Research Part B: Applied Biomaterials 2009;89B(1):34-44.
- 271. Panchbhavi VK, Vallurupalli S, Morris R, Patterson R. The Use of Calcium Sulfate and Calcium Phosphate Composite Graft to Augment Screw Purchase in Osteoporotic Ankles. Foot & ankle international 2008;29(6):593-600.
- 272. Bowen JA, Mellonig JT, Gray JL, HT. T. Comparison of decalcified freezedried bone allograft and porous particulate hydroxyapatite in human periodontal osseous defects. J Periodontol 1989;60(12):647-54.
- 273. El Deeb M, Holmes RE. Tissue response to facial contour augmentation with dense and porous hydroxylapatite in rhesus monkeys. Journal of Oral and Maxillofacial Surgery 1989;47(12):1282-89.
- 274. Rosen HM, McFarland MM. The Biologic Behavior of Hydroxyapatite Implanted into the Maxillofacial Skeleton. Plastic and Reconstructive Surgery 1990;85(5):718-23.
- 275. Mercier P. Failures in ridge reconstruction with hydroxyapatite: Analysis of cases and methods for surgical revision. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 1995;80(4):389-93.
- 276. Jansen J, Ooms E, Verdonschot N, Wolke J. Injectable calcium phosphate cement for bone repair and implant fixation. Orthopedic Clinics of North America 2005;36(1):89-95.
- 277. Leung KS, Siu WS, Li SF, Qin L, Cheung WH, Tam KF, et al. An in vitro optimized injectable calcium phosphate cement for augmenting screw fixation in osteopenic goats. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2006;78B(1):153-60.
- 278. Baroud G, Cayer E, Bohner M. Rheological characterization of concentrated aqueous [beta]-tricalcium phosphate suspensions: The effect of liquid-to-powder ratio, milling time, and additives. Acta Biomaterialia 2005;1(3):357-63.

- 279. Phillips F. Minimally invasive treatments of osteoporotic vertebral compression fractures. Spine 2003;28:S45–S53.
- 280. Heini P, Berlemann U. Bone substitutes in vertebroplasty. Eur Spine J 2001;10:S205–S13.
- 281. Thomson R, Wake M, Yaszemski M, Mikos A. Biodegradable polymer scaffolds to regenerate organs. Biopolymers II. In: Peppas N, Langer R, editors: Springer Berlin / Heidelberg; 1995. p. 245-74.
- 282. Lu JX, Flautre B, Anselme K, Hardouin P, Gallur A, Descamps M, et al. Role of interconnections in porous bioceramics on bone recolonization in vitro and in vivo. Journal of Materials Science: Materials in Medicine 1999;10(2):111-20.
- 283. Karageorgiou V, Kaplan D. Porosity of 3D biomaterial scaffolds and osteogenesis. Biomaterials 2005;26(27):5474-91.
- 284. von Doernberg M-C, von Rechenberg B, Bohner M, Grünenfelder S, van Lenthe GH, Müller R, et al. In vivo behavior of calcium phosphate scaffolds with four different pore sizes. Biomaterials 2006;27(30):5186-98.
- 285. Libicher M, Hillmeier J, Liegibel U, Sommer U, Pyerin W, Vetter M, et al. Osseous integration of calcium phosphate in osteoporotic vertebral fractures after kyphoplasty: initial results from a clinical and experimental pilot study. Osteoporosis International 2006;17(8):1208-15.
- 286. Ikenaga M, Hardouin P, Lemaître J, Andrianjatovo H, Flautre B. Biomechanical characterization of a biodegradable calcium phosphate hydraulic cement: A comparison with porous biphasic calcium phosphate ceramics. Journal of Biomedical Materials Research 1998;40(1):139-44.
- 287. Gisep A, Kugler S, Wahl D, Rahn B. Mechanical characterisation of a bone defect model filled with ceramic cements". Journal of materials science. Materials in medicine 2004;15(10):1065.
- 288. Morgan JP, Dauskardt RH. Notch strength insensitivity of self-setting hydroxyapatite bone cements. Journal of Materials Science: Materials in Medicine 2003;14(7):647-53.
- 289. Yaszemski MJ, Payne RG, Hayes WC, Langer R, Mikos AG. In vitro degradation of a poly(propylene fumarate)-based composite material. Biomaterials 1996;17(22):2127-30.
- 290. Thompson R, Wake M, Yaszemski M, Mikos A. Biodegradable Polymer scaffolds to regenerate organs Adv Polym Sci 1995;122:245-74.
- 291. Moseley J, Blum B. PRO-DENSE® Injectable regenerative graft: *in vitro* and *in vivo* observations, and a proposed mechanism of action 2008.
- 292. Thomas MV, Puleo DA. Calcium sulfate: Properties and clinical applications. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2009;88B(2):597-610.
- 293. Coetzee A. Regeneration of bone in the presence of calcium
- sulfate. Arch Otolaryngol 1980;106:405–09.



A COMPARATIVE HISTOMORPHOLOGICAL AND MICRO CT STUDY OF THE PRIMARY STABILITY AND THE OSSEOINTEGRATION OF THE SYDNEY MINI-SCREW: AN ANIMAL STUDY USING NEW ZEALAND RABBITS

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A condensed version of this manuscript will be submitted for the Dental Materials Journal

3 MANUSCRIPT

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3.1 ABSTRACT

Introduction: Failure rate of orthodontic miniscrews (MSs) is 7-50%. To address this problem and to promote primary stability of the miniscrew (MS), we recently designed and developed The Sydney Mini Screw (SMS, Patent number: PCT2009014) which can be used with substitutes injectable bone graft (iBGS). The aim of this study was to assess *in vivo* dispersion of bone graft substitutes (BGS) and the integration of the SMS to the cortical and trabecular bone using New Zealand femur and tibia rabbit model. Method: Twenty-four MSs were randomly placed in each proximal tibia and femur of 6 New Zealand rabbits with an open surgery process. Aarhus MS was used as a control and the effect of injection of BGS was studied by implanting SMS with and without BGS injection. The dispersion and integration of the MS were studied by using micro CT (μ CT) and histochemical analysis at two time points, 0 day and 8 weeks post-implantation. Results: BGS were successfully injected to the SMS and thereafter hardened *in situ* to fill the bone void. After 8 weeks, µCT results revealed that the iBGS were resorbed and bone tissue was formed around the MS and within its lateral exit holes. The osteointegration of the SMS samples showed similar histologic characteristics to that of Arhus controls, and initial drilling for injection of bone cements into SMS did not seem to affect adjacent bone quality. Conclusion: Results of this pilot animal study showed the high potential of SMS and the developed technique to promote the primary stability of MS.

Keywords: Primary stability; orthodontic miniscrew; injectable bone graft substitute.

3.2 INTRODUCTION

Ever since Creekmore and Eklund published a case report demonstrating the usefulness of metal implants in orthodontics, increasing interest has lead to constant improvement in the field.² Roberts *et al.*³ investigated the potential of endosseous implants as means of rigid skeletal anchorage for orthopaedic and orthodontic use. Furthermore, human studies found minimal need for patient compliance by using rigid osseointegrated implants in the retromolar and palatal areas.^{4, 5} Unfortunately, their application was limited due to their large size and the need for osseointegration prior to force application. To overcome this, miniscrews (MSs), smaller and temporary anchorage devices (TADs), were introduced as an alternative to osteointegrated implants for skeletal anchorage.^{6, 7} The initial stability of miniscrew (MS) is primarily derived from the mechanical interlocking of their threads with the cortical bone, yet being easily removed when needed. This phenomenon is described in the literature as primary stability, and it refers to the MS strength achieved at placement¹⁴⁰ and mainly affected by bone quality, MS design²⁹⁴ and surgery modality^{187, 295} which determine the mechanical engagement of the MS within the bone.²⁹⁶

The higher forces needed for successful¹¹ orthopaedic treatment require the use of surgical plates which often entail a more invasive¹² approach adding considerable risk and cost to the overall treatment. An alternative to this could be the use of MS via improved primary and secondary stability which are vital in order to reduce failure rates and maximize efficacy.

Failure rates of MS are reported to be as high as 51¹⁹²-100%^{13, 193}; however, definitions for success criteria are broad including either satisfactory orthodontic movement¹³⁻¹⁵ or lack of mobility and peri-implantitis following MS placement¹⁶⁻¹⁸. This could explain the differences in success rates reported by different investigators. The success rates of MS depend on multiple factors such as: operator's experience, MS design and features, method of placement, site of placement, and patient care. ^{17-19,13, 14, 20}

With the increasing popularity of arthroscopic and other minimally invasive procedures in orthopaedics, there has been great interest in fixation biomaterials that are injectable, such as Calcium phosphate cements (CPC). In the past 60 years, a large number of bone graft substitutes (BGS) have been introduced. The current generation of BGS, involve cell and gene activating materials, which encourage specific cellular responses at the molecular level. These BGS are resorbed by the body at the same time they stimulate tissue growth.²⁹⁷

CPC exhibits nontoxic, biocompatible, and bioactive properties. It integrates into bone by the same processes active in remodelling of healthy bone and this eliminates the need for its removal after healing. Previous reports have confirmed that injectable BGS have osteoconductive properties and give support to bone fragments as an osteosynthesis material.^{262, 291} More importantly, CPC has mechanical properties equal to or higher than bone.²⁹⁸ This attribute is considered an advantage when combined with other components that do not possess such characteristic – for instance, calcium sulphate. A combination of calcium sulphate and calcium phosphate involves joint benefits of both components with promising progression of bone formation and unique dissolution properties.²⁹¹ Evaluations of compression tests and module of cortical and trabecular bone determined in previous studies are valid to establish vital properties for a substitute material.²⁹⁸

In a recent study, injectable calcium phosphate cement (iCPC) when used as a bone graft material has shown promising results in aiding MS retention when injected in the implant beds pre-placement. The bone-iCPC-titanium surface has displayed close contact; an ideal trait for increasing primary stability.²² Therefore, the aim of this study was to evaluate the feasibility of using an injectable bone graft substitute (iBGS) in conjunction with a modified novel hollow MS design to enhance primary stability of MS in an animal model.

3.3 MATERIAL AND METHODS

3.3.1 THE SYDNEY MINISCREW DESIGN

The overall design of The Sydney Miniscrew (Patent number: PCT2009014) was based upon the clinically proven Aarhus anchorage system (Medident, Hellerup, Denmark) and presented as part of a Master of Philosophy Thesis in 2011²⁵. Further design modifications were implemented to the initial Sydney Mini Screw (SMS) (Error! Reference source not found.). Titanium cannulated cylinder MSs were manufactured by Russell Symes and Company Pty Ltd, Sydney, Australia. The total length of the SMS tested in this study is 8.3 mm, and it is tapered on its superior portion and cylindrical towards the extension of the body surface. The tapered soft tissue collar has 1.5 mm in height, with a maximum diameter of 4mm and a narrower portion of 3.2mm. The tapered neck is 1.5 mm in height, with a maximum diameter of 3.2 and a narrower portion of 1.6 mm. The outer thread diameter is 1.6mm. The central cannulated portion of the screw is 0.8 mm in diameter and extends from the open head to the lateral port holes. The cannula at the head is widened to 0.92 mm for a depth of 3.8 mm to accommodate the thickness of the syringe tip. The two lateral port holes (diameter: 0.60 mm) are found between the screw threads towards the bottom of the MS body (Figure 2).

3.3.2 MODELLING OF THE MINISCREW AND FINITE ELEMENT ANALYSIS (FEA)

A FEA of a 3-D computed aided design (CAD) model of the mini-screw and surrounding cortical bone to investigate various mechanical responses upon placement of the implant was conducted. A geometrically accurate 3-dimensional model of the mini-screw was generated with an integrated cortical bone block using a CAD program (Solidworks; Dassault Systemes Solidworks, Concord, Mass) to simulate the placement of the MS within the jawbone. This model was then imported into a finite element package (Ansys Workbench 14.5) where the material properties were assigned (Table 3).

When creating the mesh for the FEA, a Body Sizing Methods of 0.5 mm across the entire mini-screw was employed, and further refinement was employed to the element sizes in regions where we expected higher stresses (implant neck region and cortical bone threaded section), as shown in (Figure 3).

The outer faces of the bone block were then assigned as a fixed boundary to simplify the simulation. Following this, a clockwise moment of 10 N.cm was applied on the top face of the mini-screw to replicate the action of the implant placement.

3.3.3 INJECTABLE BONE GRAFT SUBSTITUTE

A sterile commercially available sample kit of a synthetic bone graft composite (PRO-DENSE® Extremity Mixing Pack, Wright Medical Technology, Inc. Arlington, TN) was used as a model powder. The calcium sulphate/phosphate (CaSO₄/CaPO₄) paste is composed of a CaSO₄/CaPO₄ mixture of powders incorporating a matrix of CaSO₄ and dicalcium phosphate dihydrate (CaSO₄-DCPD) with a distributed phase of β -tricalcium phosphate (β -TCP) granules.^{299, 300} The regenerative injectable graft was presented in two separate chambers containing 75 % CaSO₄ and 25 % CaPO₄ (brushite and granular TCP).²⁹¹ The liquid used was glycolic acid.

3.3.4 INJECTABLE BONE GRAFT PREPARATION

The iBGS preparation was adopted by selecting the ideal concentration for optimum injection using a 20 G needle as per results in a previous research.²⁵ The manufacturer concentration of the injectable regenerative graft was designed to go through needles larger than 20 G. For this reason, particle size was modified to less than 63 μ m. A fresh sample of each powder was manually ground under dry conditions using an agate mortar and pestle. The ground powder was sieved using a stainless steel frame and mesh of 63 μ m aperture (Endecotts LTD, London England) to exclude particles above the mesh pore diameter. The particle sizes less than 63 μ m were collected, while larger particles were further ground to a smaller diameter until they passed through the selected mesh sieve. The sieving method was completed using a laboratory vibrator

(**Talboys Advanced Model 1000 Mini s**haker, Troemner, U.S.A). The powders were individually stored in the amount of single injection, and in separate vials containing a ready-to-mix proportion²⁵ at the time of surgical procedure. These were sterilized by gamma irradiation to a minimum target dose of 25KGy and the actual result was 27.29KGy (Steritech Pty Ltd, NSW-Sydney, Australia).

3.3.5 IBGS MIXING AND DELIVERY

The composite graft at a composition of 2.5 g/mL was freshly prepared by the same operator under the same conditions and at room temperature immediately after placement of each SMS. It consisted of a powder element primarily of calcium sulphate hemihydrate with a moderate amount of calcium phosphate salts and a neutral aqueous diluents.³⁰¹ The iBGS powders were mixed with the liquid component in a silicone Dappen dish using a plastic spatula, resulting in a viscous and cohesive mixture. For each formulation, iBGS were prepared by mixing the cement powder and liquid for 30 seconds³⁰¹ by hand resulting in a workable paste that was transferred to a commercial disposable 1 cc syringe (BD Luer-LokTM Tip, Singapore) by means of a spatula.³⁰²

After loading the 1 cc syringe, a sterile 20 G blunt-type 10-mm-long needle was adjusted. It consisted of inner and outer diameters of 0.6 mm and 0.9 mm, respectively (BD PrecisionGlideTM Needle, Singapore). Handling time of 1.5 minutes was allowed to mix and load the iBGS in syringes. The injectability of the CaSO₄/CaPO₄ composite material was tested manually before each injection by means of a minimal volume of paste extrusion at the needle tip.

3.3.6 ANIMAL MODEL

Six male New Zealand White rabbits were included in the study (Ethics approval by Sydney West Area Health Service Animal Ethics Committee 5101.05.12). The rabbit's weights ranged between 3.5-4Kg and were 4 months old. They were provided by an approved animal supplier (S and J Hurrell, Pipers Farms, ABN: 26.979 678 721, Cowra-NSW, Australia) and completed an acclimatization period of 1 week prior to

commencement of the study. They were fed a standard diet and had full time access to water containers attached to the fence.

3.3.7 STUDY DESIGN

Twenty-four MSs were surgically placed under general anaesthesia in each proximal tibia and femur of 6 New Zealand rabbits (Figure 4). Rabbits were randomly divided equally into 2 groups according to the time period. Group (0W) was sacrificed the same day of surgery, while the other group (8W) was sacrificed after 8 weeks. For both time points, the number and type of MS inserted were as follows: 4 SMS with iBGS (SMS-BGS), 4 SMS without iBGS (SMS), and 4 Aarhus MSs (AC) (Figure 5). Aarhus implants were inserted to serve as control.

3.3.8 MINISCREW INSERTION - SURGICAL PROCEDURE

Table 4 shows the type of MS corresponding to each rabbit tibia and femur at the two different time points. The surgical procedure protocol was an adjustment from that provided by an earlier rabbit study within the same research group.³⁰³

On the day of surgery, rabbits were weighted prior to sedation and shaving. A state of sedation accompanied by a shorter period of analgesia and muscle relaxation was produced by means of a combination of 5mg/kg of xylazine hydrochloride (Ilium Xylazil®-20; Troy Laboratories Pty Ltd, NSW, Australia), and 35 mg/kg of ketamine hydrochloride HCL (Ketamav®-100; Mavlab Pty Ltd, QLD, Australia) intramuscular (IM) injection prior to general anaesthesia with 2-4% isoflurane (Aerrane®, Baxter Healthcare Pty Ltd, NSW, Australia) gas as an inhalant anaesthetic agent. A pre-surgical dose of IM opioid analgesic, 0.01 - 0.05mg/kg buprenorphine (Temgesic® Reckitt Benckiser; NSW, Australia) was used to relieve moderate to severe pain. In addition, a subcutaneous (S/C) injection of enrofloxacin (Ilium Enrotril® 50mg/ml, Troy Laboratories Pty Ltd, NSW, Australia) was supplied for antibiotic prophylaxis. Following this, the middle portion of their back legs was shaved to expose the lateral plateau of the tibia and medial aspect of the femoral condyle in order to

facilitate a more accurate surgical area at the time of the procedure. After this, an arterial catheter was clipped in one ear for continuous monitoring of vital signs and a mask was adjusted to enable general anaesthesia. Simultaneous oxygen administration was possible via the same mask. Additionally, rabbits were kept on a heat pad during the surgery. Anaesthetic documentation and vital signs monitoring was kept as a record throughout the course of the surgical procedure from beginning until recovery completion.

Prior to the surgical procedure, the skin at the surgical site was washed with a topical povidine-iodine (Betadine®, Purdue Products L.P., Connecticut, USA) antiseptic. The surgical site preparation for MS insertion required a full thickness surgical flap to expose the articular surface of the femoral and tibial condyles. In order to avoid important muscle or ligament attachments, the lateral plateau of the tibia and the medial aspect of the femur were chosen for MS placement. Special attention was given in preserving the integrity of the periosteum membrane during the entire procedure to be joined at the end of the procedure by the means of internal resorbable sutures. The MSs placement procedure was the same as that described by Melsen and Verna (2005)¹⁹⁹ who recommend manual insertion with a custom screwdriver (Aarhus anchorage system octagonal screwdriver, Medicon®, Germany). Furthermore, the authors comment on the possible need of preparation of a pilot hole which in this study has been modified in dimensions to suit the SMS design and also allow the delivery of iBGS.

In SMS with and without iBGS groups, the pilot hole was prepared using the same technique. This was done using a drill of 2.5 by 6.5 mm (Astratech 2.5 mm Twist Drill) with a low speed surgical motor (X-Cube V2.0 Surgical Implant motor, Saeshin, Korea) under constant saline solution irrigation. All MSs, including AC, were inserted by the same operator. The relevant SMS-iBGS implant beds required the injection of BGS explained in detail in the iBGS mixing and delivery section above (Figure 6).

Following 30 minutes after BGS injection, the 0W group was euthanized by means of injecting 1.5 cc of pentobarbitone sodium (Lethabarb®, Virbac Pty Ltd, NSW, Australia). In the 8W group, closure of the wound was done by suturing the periosteum

and skin using a combination of internal absorbable 3.0 braided coated vicryl polyglactin-910 (VICRYL® from Ethicon by DENTSPLY Pty Ltd, VIC, Australia) and external non-resorbable 3.0 monofilament (ETHILON® from Ethicon by DENTSPLY Pty Ltd, VIC, Australia) sutures respectively. Additionally, rabbits received antibiotics (enrofloxacin), analgesics (buprenorphine) and antinflamatories (5mg/mL meloxicam, Metacam®, Boehringer Ingelheim Vetmedica Inc., St. Joseph, USA) every 24 hours for 6 days. The rabbits were returned to a small collection cage where appropriate covering with towels was keeping them warm during recovery. Following complete recovery, each rabbit was transported to its habitual cage where post-operative care and medication was provided closely.

After 8 weeks of healing, the 8W rabbits were placed under general anaesthesia to expose the MSs and collect the bone section containing the MSs (Figure 7). This group was also sacrificed under the same protocol using sodium pentobarbital.

Bone sections were trimmed and stored accordingly in identified containers. The samples were fixed in 10% formalin for 48 hours followed by 3 consecutive rinses with saline and kept in a new container submerged in 70% ethanol. A total of 24 MSs were sent for microCT and histochemical analyses. The sample comprised 8 Aarhus positive controls, 8 SMS, and 8 SMS-iBGS.

Initial mechanical stability in this study is defined as the lack of mobility of the MS immediately after placement and its stability until the end of the eight week period. The stability of the MSs was assessed by visual and physical evaluation on collection of the bone blocks on the different time points. The latter was based in the method suggested by Woods et al.³⁰⁴ who used a periodontal scale³⁰⁵ to grade mobility from 0-3. In the 0W animals, the mobility testing was done prior to sacrifice, and in 8W animals following MS exposure and prior to sacrifice.

3.3.9 MICRO CT ANALYSIS

All twenty four implants were scanned for μ CT analysis. The samples were carefully arranged within a 50ml polypropylene centrifuge conical tube which allowed the use of a liquid medium to protect the sample from dehydration. The samples had an approximate size of 2 x 2 cm and were submerged in 70% ethanol separated by low-density polystyrene foam pieces. The samples were scanned using a MicroXCT-400 scanner (Carl Zeiss X-ray Microscopy, Pleasanton CA, USA) at room temperature with x-ray tube conditions set at 80 KeV, power of 5 W, current of 62 μ A, and pixel size of 27.5 μ m. The resultant two-dimensional (2D) projections were reconstructed to produce a series of axial cross sections that were then rendered as a three-dimensional (3D) video through the Avizo Fire software package (Visualisation Sciences Group, Burlington MA, USA). These videos also presented with an isotropic voxel dimension of 27.5 μ m3.

3.3.10 HISTOLOGY

After micro-CT, histologic examinations were performed to observe bone remodelling at the interface between the bone and the MS. All bone blocks were fixed in buffered 4% formaldehyde (pH 7), dehydrated in ethanol, embedded in methacrylate resin and 300 micron sectons were cut using an IsoMet® 5000 linear precision diamond saw (Buehler Ltd., Illinois, USA). All slices, except those containing iBGS, were polished using abrasive pads of decreasing grit size. iBGS in sections was found to be brittle and tended to fragment with polishing. Sections showing the most complete cross section of implant were stained with 2% toluidine blue for histological analysis. Subsequently, the samples were mounted on slides, viewed with a light microscope (Olympus® BX51, Tokyo, Japan) with a 1.25x objective, and images captured using DP Manager/ImageJ (Image Processing and Analysis in Java, 1.45s for Windows) software. The images were assessed qualitatively.

3.4 **RESULTS**

3.4.1 THE SYDNEY MINISCREW DESIGN

The design modification of the SMS allowed favourable delivery of the iBGS in the predrilled void without any complications (Figure 8). There was no statistically significant difference (p > 0.05) between the insertion time of SMS and Aarhus MS beside the fact that for the insertion of the SMS, the placement of a pilot hole at the bone site was required. The new design of the SMS enhanced the *in situ* adhesion of the periosteum to the MS, which was seen as a dense layer of tissue in the microCT images (Figure 9).

3.4.2 MODELLING OF FINITE ELEMENT ANALYSIS

From the finite element (FE) results, we can see that the maximum equivalent (Von Mises) stress occurs at the superficial edges of the neck region where there is immediate changes in implant diameter. This value was 146.58 MPa, shown by the red contours in Figure 10. It gradually decreased toward the mid-region of the neck (outer) where the stress almost halved (81.43 MPa), shown in (Figure 10 R) as the lighter green contours. The cortical bone was simulated, and the stresses resulting from initial screw placement was close to 0 (Figure 11). In addition, the maximum displacement observed at insertion was 0.0029 mm.

3.4.3 MINISCREW INSERTION

The pre-drilling method and MS insertion was successful for both SMS groups, with and without iBGS. The pilot hole preparation prior to the injection of the BGS formed a biological sealed area within the trabecular bone. The presence of this area decreases the infusion pressure of the BGS injection and thus prevents the structural displacement of the neighbouring bony tissue for iBGS housing. The pre-drilling also reduced the risk of structural displacement of the neighbouring bony tissue during the insertion of the SMS.

The working time between the method of placement and the site of insertion among the different groups, e.g. Aarhus, and SMS with and without BGS were relatively similar. However, due to the small sample size of the tests, further studies are of need to confirm this result. The SMS groups took an extra 10-15 seconds for predrilling with an additional 90 seconds on those that required iBGS. This comprised an average of 20 seconds to insert the control MS, 35 seconds for SMS, and 130 seconds for SMS with iBGS.

All 24 MSs showed initial mechanical stability at placement with no detectable mobility immediately after placement and remained stable until the end of the eight week period when investigated via the periodontal scale for tooth mobility method, showing a value of 0.

The rabbits maintained their well-being throughout the study period. All wounds healed favourably by secondary intention and with no scarring. Daily monitoring showed regular movement within the housing facility, as well as eating and drinking. No signs of discomfort were recorded.

3.4.4 MICRO CT AND HISTOLOGY ANALYSIS

The results in (Figure 12) confirm the successful insertion of all the MSs and the delivery of the iBGS to the site. All the MSs displayed integration at the cortical bone region. This result was further confirmed by the histological analyses. Osseointegration represents a process of new bone formation into the screw grooves, and thus cannot be assessed at 0W. At this time point, the control sample AC tended to show uniform integration with the trabecular bone across the body of the MS, while showing areas of incomplete coverage by bony tissue at the cortical layer. The SMS showed complete bone coverage of its threaded surface, suggesting that most of the bone-to-implant contact is at the wider section of the screw at implantation and during the initial healing

period. On the other hand, the integration with AC was uniform throughout the whole length of the MS. This is shown by a complete seal across the cortical bone region (Figure 12). However, we noticed some degree of structural damage and the presence of blood clotting (light purple donut shaped cells) at the bottom portion of the MS due to the pre-drilling process that is required for SMS insertion. The effect of the pre-drilling process in the μ CT analysis is evident by partial bony tissue coverage around its body.

In SMS-iBGS group, the pre-drilled mini-gap was filled with the injectable graft, indicating the successful delivery of the cement to the site and fill of the pre-drilled zone. The 0W SMS-iBGS shares a very similar pattern to 0W of SMS alone. However, the iBGS appeared to generate a greater inflammatory response characterized by a higher amount of white cells (dark purple with big nucleolus).

AC showed uniform integration both, at 0W and 8W. The eight week SMS showed complete healing with organized and abundant bone integration at both the cortical and trabecular bone regions with significant bone-to-implant contact. The eight week SMS-iBGS displayed complete healing with no inflammation, absence of blood clotting, presence of osteoblast differentiation and ossification thus revealing normal trabecular and cortical bone structure. After 8 weeks, the residual iBGS was present encased in trabecular bone and within the marrow space. There was minimal iBGS left in the hollow chamber of the SMS as there was bone formation within the lateral port holes and the internal hollow chamber, in addition to the MS surface. Overall, a trend of mainly cortical bone engagement was observed among all the SMS and SMS-iBGS at 0W, while almost complete integration was seen at 8W with greater trabecular bone-to-implant contact.

3.5 DISCUSSION

Different MS designs had been introduced in the literature aiming to address the failure rates and increase the usage of MS to improve the efficacy of clinical orthodontics. Success rates have become promising focusing on the relationship between primary stability and bone properties, mainly cortical bone thickness; however, there is still lack of well designed clinical trials to support the existing literature.¹²⁸ There are no studies that had used iBGS as a biocompatible aid to enhance the primary stability of orthodontic MSs. This study was undertaken to investigate the integration and healing of the SMS with and without iBGS in the tibia and femur of New Zealand Rabbits.

There is difficulty in investigating the mechanical nature of a mini-screw using an experimental approach alone.³⁰⁶ Therefore, the finite element method was used to simulate the stress distribution and overall displacement within the MS.

Previous research has shown that mini-screws could tip forward by as much as 0.4mm at the screw head during orthodontic treatment in cases where no mobility was identified upon initial placement.¹⁵ The FEA showed that stress on the SMS was concentrated closer to the point of force application and gradually decreased toward the cortical bone region. The maximum displacement observed at insertion was negligible compared to the values observed by Liou *et. al.*¹⁵

The FEA was able to provide simulated mechanical outputs which are in agreement with the current understanding of MS biomechanics. The safety factor of the SMS indicated that this system would not fail due to tensile yielding upon initial placement. Overall, this FE study was able to provide simulated mechanical outputs which are in agreement with the current understanding of dental biomechanics, in a much more direct and manageable way. In this study, we did not model the cancellous bone environment around the bottom of the screw since literature indicates that it does not play a major role in the system's overall mechanical response.³⁰⁶

The recommended torque for orthodontic MS insertion is found to be between 5-10 Ncm.¹⁵⁸ Even though high insertion torques are shown to deliver greater primary stability, excessive values are not favourable.¹⁸⁰ The insertion site and bone quality determine the need of a pilot hole in order to reduce the insertion torque while improving secondary stability.¹⁴⁰ Miniscrews have shown to be successful in the maxilla by both self-drilling and self-tapping techniques.^{183, 184} However, in the presence of a thicker cortical bone such as that in the mandible, a minimum of 1.3mm pre-drilling is recommended in order to avoid over-torquing and decreasing the risks of microfractures within a higher cortical bone density surrounding the MSs.¹⁸⁵ The correct size for pilot holes to enhance primary stability have been reported to be in the range of 69-80% of the given MS diameter.^{165, 186} Given the dimensions of the SMS, and the need of a void for the iBGS housing, a greater pilot hole of 2.5 x 6.5 mm was required for the SMS. This is 65-85% of the diameter of the superior portion of the MS engaging the cortical bone.

Considering that self-tapping implants have been reported to have a reduced percentage of bone-to-implant contact,³⁰⁷ design modifications were implemented to the newly designed SMS. An increased surface area provided by a wider and tapered screw collar is aimed to increase contact with the cortical bone to enhance mechanical stability. Additionally, the tapered portion of the MS neck engages with the cortical bone at its threaded surface and this seemed to allow for increased integration. The reduced width of the MS body and its flat tip created the desired void for successful iBGS delivery (Figure 8). The mutual interaction of the mechanical lock of the MS provided by its threaded surface and the iBGS ^{22, 264, 308} is thought to assist in maximizing the thread engagement across the whole length of the MS.

Previous studies have measured the implant osseointegration potential using different methods to investigate bone to implant contact and bone volume. ^{22, 51, 309}

Given the small sample size and the variable sites of implantation among epiphysis, metaphysis and diaphysis which are all different in structure and function, diverse integration behaviour was found in this study and thus a qualitative approach was employed. In accordance with this study, an extensive variety in bone density across the different regions of the femur and tibia at various ages was described in an experimental study using dogs.³¹⁰ A better understanding of the biologic interaction between the unloaded hollow SMS and iBGS was possible by combining microcomputed tomography (μ CT) and histologic analysis.

Some degree of inflammatory response is of benefit to promote the *in vivo* bone regeneration and to enhance the healing process. The iBGS concentration fills the drilled void, and also distributes nicely within the trabecular architecture. The primary stability within different groups was investigated via the bone-to-implant contact, the uniform iBGS distribution and the bone formation within the pre-drilled void and around the MS bodies. The results elucidate the integration of the SMS surface with the host tissue, which is of a great importance for immediate stability of the MS at the insertion site. All MSs showed some degree of osseointegration with the bony tissue surrounding it. Uemura et al.¹⁶⁵ recently suggested that less bone support around the MS causes gaps in its interface, resulting in inadequate anchorage. On the other hand, MS resistance to orthodontic traction has been reported with as little as 5% of implant integration,³¹¹ and considered as reliable anchorage at a 25% integration index.³¹² A higher bone-to-implant contact of 75.5% has been reported in a human sample comprising palatal MS placement.³¹³ Furthermore, there is unclear evidence to reference the minimum bone-to-implant contact or integration necessary to avoid premature failure of the MS. This allows us to believe that clinically, a critical amount of MS stability is needed in order to achieve functional efficiency; however, it is not only dependant on osseous integration, but also on mechanical engagement.

This study showed the trend of significant bone-to-implant contact across the extension of the cortical bone for all SMS. In addition, the successful dispersion of the iBGS observed in the SMS-iBGS group (as observed histologically) at the trabecular layer may promote the bone regeneration process, and ultimately increase the primary stability. In the present study, 8 weeks after inserting the SMS and SMSC by drilling a pilot hole, bone proliferation was observed within the void. Therefore, it is thought that stability was reinforced possibly due to the modified SMS design which allowed cellular proliferation within the inside and surface of the screw. Uemura et al.⁴⁹ used pilot holes of varying diameters in the tibia of a rat model in which 1.2mm MSs were inserted and loaded over a 3 week period. The authors reported that hole diameter should range from 69-77% of the MS diameter. Furthermore, they showed that mobility measurements decreased gradually during the healing period imply that good prognosis is expected regarding MS stability.¹⁶⁵

Drilling a pilot hole prior to MS insertion is well supported in the literature in order to reduce failure.^{59, 185} A narrower pilot hole diameter is generally preferred.^{59, 160, 185, 314} The results in the present study suggest that pilot holes greater than the MS diameter can be used in combination with iBGS without compromising stability, in contrast to previous studies, reporting unsuccessful MS into the pre-drilled holes with the same diameter.³¹¹ It is interesting to observe that the histology data of SMS-iBGS at both 0W and 8W shows similar maximized thread engagement across the whole length of the MS by uniform dispersion of the IGBS and trabecular replacement respectively. This supports the use of iBGS which is well known for its capability during the initial healing period.^{48,49} By the end of 8W, eventhough difficulties were encountered with histologic analysis due to the brittleness of iBGS. The initial cortical bone engagement was maintained, demonstrating successful integration and biocompatibility.

Different healing periods have been suggested for improved stability when using MSs in an experimental model. This is related to the location of the MS, the insertion method used, animal age, and animal model.^{3, 50, 59, 315, 316} The interval of 6 weeks in a growing rabbit relates to about 3-4 months healing in humans due to the inherent slower remodelling rate.^{317, 318} The samples showed complete success in terms of lack of mobility and nearly absolute replacement of the iBGS, thus an 8-week healing period in growing rabbits is sufficient for the majority of the iBGS replacement to occur. It seems appropriate to assume that the proposed method has superior biocompatibility in the specific rabbit model. The question as to whether iBGS can be used to stimulate improved MS stability in humans is yet to be answered.

3.6 CONCLUSIONS

- A new SMS design in combination with iBGS was successfully tested on an animal model and showed its high potential to promote primary stability for orthodontic applications.
- Both SMS and SMS-iBGS showed biocompatible and uniform integration with the bone tissues and the graft substitute respectively. Minor inflammation was observed during healing, yet no complications related to its method of placement. Instead, it is associated to the pre-drilling of a pilot hole, which seems beneficial in triggering a biological response for an improved bony support around the MS.
- The pre-drilling method allowed the delivery of the iBGS and its extensive dispersion followed by almost complete replacement of bone around and within the MS with uneventful healing by the end of the study period.
- The CaSO4/CaPO₄ at a concentration of 2.5 g/ml seems to be the optimum concentration for adequate mechanical strength and subsequent trabecular bone formation/replacement. These characteristics are expected to protect the implant from disintegration or fracture under stresses within the bone structure.
- Further studies with larger sample size, quantitative assessment of osseointegration indices and longer observation periods are required in order to verify the results prior to clinical implementation of the method suggested.

3.7 ACKNOWLEDGEMENTS

The authors would like to thank Sydnovate and the Australian Society of Orthodontics Foundation for Research and Education (ASOFRE) for their kind financial support. Mary Hoang, and Chris Xu, for their kind assistance with the surgical procedures. Dr Ross Matthews and George Fior along with the friendly staff of the Department of Animal Care at Westmead Hospital for professional animal care. Ashley WU, for FE analysis and interpretation. Dr Alexandra Papadopoulou, for her valuable opinions.

3.8 REFERENCES

- 1. Gainsforth BL, Higley LB. A study of orthodontic anchorage possibilities in basal bone. American Journal of Orthodontics and Oral Surgery 1945;31(8):406-17.
- 2. Creekmore TD EM. The possibility of skeletal ahncorage. Journal of Clinical Orthodontics 1983;17(4):266-9.
- 3. Roberts WE, Smith RK, Zilberman Y, Mozsary PG, Smith RS. Osseous adaptation to continuous loading of rigid endosseous implants. American Journal of Orthodontics 1984;86(2):95-111.
- 4. Roberts WE, Marshall KJ, Mozsary PG. Rigid endosseous implant utilized as anchorage to protract molars and close an atrophic extraction site. The Angle orthodontist 1990;60(2):135-52.
- 5. Wehrbein H, Merz BR, Diedrich P, Glatzmaier J. The use of palatal implants for orthodontic anchorage. Design and clinical application of the orthosystem. Clinical Oral Implants Research 1996;7(4):410-16.
- 6. Costa A RM, Melsen B. Miniscrews as orthodontic anchorage: A preliminary report. International journal of adult orthodontic and orthognathic surgery 1998;13:201-9.
- 7. Liou EJW, Pai BCJ, Lin JCY. Do miniscrews remain stationary under orthodontic forces? American Journal of Orthodontics and Dentofacial Orthopedics 2004;126(1):42-47.
- 8. Daskalogiannakis J, editor. Glossary of orthodontic terms: Quintessence Publishing Co, Leipzig; 2000.
- 9. Rossouw P, Buschang P. Temporary orthodontic anchorage devices for improving occlusion. Orthodontics & Craniofacial Research 2009;12(3):195-205.
- 10. Cope JB. Temporary Anchorage Devices in Orthodontics: A Paradigm Shift. Seminars in Orthodontics 2005:3-9.
- 11. De Clerck, E.B. E, Gwen R.J. S. Success rate of miniplate anchorage for bone anchored maxillary protraction. The Angle Orthodontist 2011;81(6):1010-13.
- 12. Sugawara J, Nishimura M. Minibone plates: The skeletal anchorage system. Seminars in Orthodontics 2005;11(1):47-56.
- 13. Miyawaki S, Koyama I, Inoue M, Mishima K, Sugahara T, Takano-Yamamoto T. Factors associated with the stability of titanium screws placed in the posterior region for orthodontic anchorage. American Journal of Orthodontics and Dentofacial Orthopedics 2003;124(4):373-78.
- 14. Moon C-H, Lee D-G, Lee H-S, Im J-S, Baek S-H. Factors associated with the success rate of orthodontic miniscrews placed in the upper and lower posterior buccal region. The Angle orthodontist 2008;78(1):101-06.
- 15. Liou EJW PB, Lin JCY. Do miniscrews remain stationary under orhtodontic forces? Am J Orthod Dentofacial Orthop 2004;126:42-7.
- 16. Cheng S-J, Tseng IY, Lee J-J, Kok S-H. A prospective study of the risk factors associated with failure of mini-implants used for orthodontic anchorage. International Journal of Oral & Maxillofacial Implants 2004;19(1):100-6.
- 17. Papageorgiou SN, Zogakis IP, Papadopoulos MA. Failure rates and associated risk factors of orthodontic miniscrew implants: a meta-analysis. American Journal of Orthodontics and Dentofacial Orthopedics 2012;142(5):577-95. e7.

- 18. Viwattanatipa N, Thanakitcharu S, Uttraravichien A, Pitiphat W. Survival analyses of surgical miniscrews as orthodontic anchorage. American journal of orthodontics and dentofacial orthopedics 2009;136(1):29-36.
- 19. Tseng YC, Hsieh CH, Chen CH, Shen YS, Huang IY, Chen CM. The application of mini-implants for orthodontic anchorage. International journal of oral and maxillofacial surgery 2006;35(8):704-07.
- 20. Kuroda S, Sugawara Y, Deguchi T, Kyung H-M, Takano-Yamamoto T. Clinical use of miniscrew implants as orthodontic anchorage: success rates and postoperative discomfort. American Journal of Orthodontics & Dentofacial Orthopedics 2007;131(1):9-15.
- 21. Huja SS, Litsky AS, Beck FM, Johnson KA, Larsen PE. Pull-out strength of monocortical screws placed in the maxillae and mandibles of dogs. American Journal of Orthodontics and Dentofacial Orthopedics 2005;127(3):307-13.
- 22. Arisan V, Anil A, Wolke JG, Özer K. The effect of injectable calcium phosphate cement on bone anchorage of titanium implants: an experimental feasibility study in dogs. International Journal of Oral and Maxillofacial Surgery 2010;39(5):463-68.
- 23. Albrektsson T, Johansson C. Osteoinduction, osteoconduction and osseointegration. Eur Spine J 2001;10:S96-S101.
- 24. Ottofy L. Standard Dental Dictionary. Chicago: Laird and Lee, Inc.; 1923.
- 25. Bacopulos Marangu A. "The feasibility of an injectable bone graft substitute to enhance the primary stability of a novel miniscrew The Sydney Mini-screw for orthodontic applications" [Sydney: The University of Sydney; 2011.
- 26. Wright CF. A consideration of the Anchorage Problem. Midwest Component of the Edward H. Angle Society of Ortodontia. Chicago; 1938. p. 152-59.
- 27. Moyers R. Handbook of Orthodontics for the Student and General Practitioner Chicago: Year Book Medical Publishers Inc; 1973.
- 28. Burstone CJ. The segmented arch approach to space closure. American Journal of Orthodontics 1982;82(5):361-78.
- 29. Melsen B, Verna C. A rational approach to orthodontic anchorage. Progress in Orthodontics 2000;1(1):10-22.
- 30. Proffit WR. The Biologic Basis of Orthodontic Therapy. in Contemporary Orthodontics. Fourth Edition ed. St Louis: Mosby/Elsevier; 2007. p. 751.
- 31. Peter Schopf BL, S. Jay Bowman. The Problem of Anchorage. Mini-implants in orthodontics: innovative anchorage concepts. Berlin: Quintessence; 2008. p. 5-10.
- 32. Angle EH. Treatment of malocclusion of the teeth and fractures of the maxillae: Angle's system: White Dental Manufacturing Company; 1900.
- 33. Poulton DR. Changes In Class II Malocclusions With And Without Occipital Headgear Therapy*. The Angle orthodontist 1959;29(4):234-50.
- 34. Ricketts RM. The influence of orthodontic treatment on facial growth and development. The Angle Orthodontist 1960;30(3):103-33.
- 35. Samuels RH, Jones ML. Orthodontic facebow injuries and safety equipment. The European Journal of Orthodontics 1994;16(5):385-94.
- 36. Tolman DE, Desjardins RP. Extraoral Application of Osseointegrated Implants. J Oral Maxillofac Surg 1991;49:33-45.

- 37. Brånemark P-I, Breine U, Adell R, Hansson BO, Lindstrom J, Ohlsson A. Irmaosseous anchorage of dental prostheses. I. Experimental studies Stand J Plast Reconstr Surg 1969;3:81.
- 38. Adell R, Lekholm U, Rockier B, Brånemark P-I. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. Int J Oral Surg 1981;10:387.
- 39. Brånemark P-I. Osseointegration and its experimental background. J Prosthet Dent 1983;50:399.
- 40. Adell R. Clinical results of osseointegrated implants supporting fixed prostheses in edentulous jaws. J Prosthet Dent 1983;50:251.
- 41. Creekmore T, Eklund M. The possibility of skeletal anchorage. J Clin Orthod 1983;17(4):266-9.
- 42. Turley PK, Kean C, Schur J, Stefanac J, Gray J, Hennes J, et al. Orthodontic Force Application to Titanium Endosseous Implants. The Angle orthodontist 1988;58(2):151-62.
- 43. Turley PK, Shapiro PA, Moffett BC. The loading of bioglass-coated aluminium oxide implants to produce sutural expansion of the maxillary complex in the pigtail monkey (Macaca nemestrina). Archives of Oral Biology 1980;25(7):459-69.
- 44. Roberts W, Nelson C, Goodacre C. Rigid implant anchorage to close a mandibular first molar extraction site. J Clin Orthod 1994;28(12):693-704.
- 45. Glatzmaier J, Wehrbein H, Diedrich P. [The development of a resorbable implant system for orthodontic anchorage. The BIOS implant system. Bioresorbable implant anchor for orthodontic systems]". Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 1995;56(3):175-81.
- 46. Glatzmaier J, Wehrbein H, Diedrich P. Biodegradable implants for orthodontic anchorage. A preliminary biomechanical study. The European Journal of Orthodontics 1996;18(1):465-69.
- 47. Wehrbein H, Glatzmaier J, Mundwiller U, Diedrich P. The Orthosystem--a new implant system for orthodontic anchorage in the palate. Journal of Orofacial Orthopedics 1996;57(3):142-53.
- 48. Wehrbein H, Glatzmaier J, Yildirim M. Orthodontic anchorage capacity of short titanium screw implants in the maxilla. An experimental study in the dog. Clinical Oral Implants Research 1997;8(2):131-41.
- 49. Wehrbein H, Merz B, Hammerle C, Lang N. Bone-to-implant contact of orthodontic implants in humans subjected to horizontal loading. Clinical Oral Implants Research 1998;9(5):348-53.
- 50. Vande Vannet B, Sabzevar MM, Wehrbein H, Asscherickx K. Osseointegration of miniscrews: a histomorphometric evaluation. The European Journal of Orthodontics 2007;29(5):437-42.
- 51. Youn J-W, Cha J-Y, Yu H-S, Hwang C-J. Biologic evaluation of a hollow-type miniscrew implant: An experimental study in beagles. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(5):626-37.
- 52. Yu J-H, Lin Y-S, Chang W-J, Chang Y-Z, Lin C-L. Mechanical Effects of Micro-thread Orthodontic Mini-screw Design on Artificial Cortical Bone. Journal of Medical and Biological Engineering 2014;34(1):49-55.
- 53. Brown RN, Sexton BE, Gabriel Chu T-M, Katona TR, Stewart KT, Kyung H-M, et al. Comparison of stainless steel and titanium alloy orthodontic miniscrew

implants: A mechanical and histologic analysis. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(4):496-504.

- 54. Cuairán C, Campbell PM, Kontogiorgos E, Taylor RW, Melo AC, Buschang PH. Local application of zoledronate enhances miniscrew implant stability in dogs. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(6):737-49.
- 55. Wilmes B, Nienkemper M, Drescher D. Application and effectiveness of a miniimplant-and tooth-borne rapid palatal expansion device: the hybrid hyrax. World J Orthod 2010;11(4):323-30.
- 56. Papadopoulos MA, Tarawneh F. The use of miniscrew implants for temporary skeletal anchorage in orthodontics: A comprehensive review. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 2007;103(5):e6-e15.
- 57. Kanomi R. Mini-implant for orthodontic anchorage. J Clin Orthod 1997;31(11):763-7.
- 58. Costa A, Raffaini M, Melsen B. Miniscrews as orthodontic anchorage: A preliminary report. Int J Adult Orthodon Orthognath Surg. 1998 13(3):201-09.
- 59. B. Melsen AC. Immediate loading of implants used for orthodontic anchorage. Orthodontics & Craniofacial Research 2000;3(1):23-28.
- 60. Park Y. Intrusion of posterior teeth using mini-screw implants. American Journal of Orthodontics and Dentofacial Orthopedics 2003;123(6):690-94.
- 61. Park J, Cho HJ. Three-dimensional evaluation of interradicular spaces and cortical bone thickness for the placement and initial stability of microimplants in adults. American Journal of Orthodontics and Dentofacial Orthopedics 2009;136(3):314.e1-14.e12.
- 62. Buschang PH, Carrillo R, Rossouw PE. Orthopedic Correction of Growing Hyperdivergent, Retrognathic Patients With Miniscrew Implants. Journal of Oral and Maxillofacial Surgery 2011;69(3):754-62.
- 63. Chung K-R, Kim S-H, Kang Y-G, Nelson G. Orthodontic miniplate with tube as an efficient tool for borderline cases. American Journal of Orthodontics & Dentofacial Orthopedics 2011;139(4):551-62.
- 64. Lee J, Park H-S, Kyung H. Micro-implant anchorage for lingual treatment of skeletal Class II malocclusion. J Clin Orthod 2001;35(10):643-7;quiz 20.
- 65. Leung MT-C, Lee TC-K, Rabie ABM, Wong RW-K. Use of miniscrews and miniplates in orthodontics. Journal of Oral & Maxillofacial Surgery 2008;66(7):1461-6.
- 66. Kuroda S, Katayama A, Takano-Yamamoto T. Severe Anterior Open-Bite Case Treated Using Titanium Screw Anchorage. The Angle orthodontist 2004;74(4):558-67.
- 67. Lee J, Park H-S, Kyung H. Micro-implant anchorage for lingual treatment of a skeletal Class II malocclusion Journal of Clinical Orthodontics 2001;35(10):643-7.
- 68. Wehrbein H, Göllner P. Skeletal anchorage in orthodontics–basics and clinical application. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2007;68(6):443-61.
- 69. Melsen B. Mini-Implants: Where Are We? Journal of Clinical Orthodontics 2005;39(9):539-47; quiz 31-2.

- 70. Baik HS. Limitations in orthopedic and camouflage treatment for Class III malocclusion. Paper presented at, 2007.
- 71. Yamada K, Kuroda S, Deguchi T, Takano-Yamamoto T, Yamashiro T. Distal movement of maxillary molars using miniscrew anchorage in the buccal interradicular region. The Angle Orthodontist 2009;79(1):78-84.
- 72. Chamberland S, Proffit WR. Closer Look at the Stability of Surgically Assisted Rapid Palatal Expansion. Journal of Oral and Maxillofacial Surgery 2008;66(9):1895-900.
- 73. Harzer W, Schneider M, Gedrange T, Tausche E. Direct bone placement of the Hyrax fixation screw for surgically assisted rapid palatal expansion (SARPE). Journal of Oral and Maxillofacial Surgery 2006;64(8):1313-17.
- 74. Umemori M, Sugawara J, Mitani H, Nagasaka H, Kawamura H. Skeletal anchorage system for open bite correction. Am J Orthod Dentofacial Orthop. 1999;115:166-74.
- 75. Gerlach KL, Zahl C. Transversal palatal expansion using a palatal distractor. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2003;64(6):443-49.
- 76. Saltaji H, Major MP, Altalibi M, Youssef M, Flores-Mir C. Long-term skeletal stability after maxillary advancement with distraction osteogenesis in cleft lip and palate patients: A systematic review. The Angle orthodontist 2012;82(6):1115-22.
- 77. Cope JB, Owens SE. Historical Development and Evolution of Temporary Anchorage Devices. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 3-20.
- 78. Buschang PH, Kim KB. Considerations for Optimizing the Use of Miniscrew Implants in Orthodontic Practice. Temporary Skeletal Anchorage Devices: Springer; 2014. p. 1-27.
- 79. Lin J, Liou E, Yeh CL, Evans CA. A comparative evaluation of current orthodontic miniscrew systems. World Journal of Orthodontics 2007;8(2):136.
- 80. Block MS, Hoffman DR. A new device for absolute anchorage for orthodontics. American Journal of Orthodontics and Dentofacial Orthopedics 1995;107(3):251-58.
- 81. Chen Y-J, Chang H-H, Lin H-Y, Lai EH-H, Hung H-C, Yao C-CJ. Stability of miniplates and miniscrews used for orthodontic anchorage: experience with 492 temporary anchorage devices. Clinical Oral Implants Research 2008;19(11):1188-96.
- 82. Wehrbein H, Feifel H, Diedrich P. Palatal implant anchorage reinforcement of posterior teeth: A prospective study. American Journal of Orthodontics and Dentofacial Orthopedics 1999;116(6):678-86.
- 83. Takaki T, Tamura N, Yamamoto M, Takano N, Shibahara T, Yasumura T, et al. Clinical study of temporary anchorage devices for orthodontic treatment-stability of micro/mini-screws and mini-plates: experience with 455 cases. Bulletin of Tokyo Dental College 2010;51(3):151-63.
- 84. Melsen B, Godtfredsen LM. Factors in the Decision to Use Skeletal Anchorage. Temporary Anchorage Devices in Orthodontics: Mosby; 2009. p. 73-89.
- 85. Labanauskaite B, Jankauskas G, Vasiliauskas A, Haffar N. Implants for orthodontic anchorage.Meta-analysis. Stomatologija, Baltic Dental and Maxillofacial Journal 2005;7:128-32.

- 86. Jenner J, Fitzpatrick B. Skeletal anchorage utilising bone plates. Aust Orthod J 1985;9:231-33.
- 87. Sugawara J, Baik UB, Umemori M, Takahashi I, Nagasaka H, Kawamura H, et al. Treatment and posttreatment dentoalveolar changes following intrusion of mandibular molars with application of a skeletal anchorage system (SAS) for open bite correction. Int J Adult Orthodon Orthognath Surg. 2002;17:243-53.
- 88. Sugawara J, Daimaruya T, Umemori M, Nagasaka H, Takahashi I, Kawamura H, et al. Distal movement of mandibular molars in adult patients with the skeletal anchorage system Am J Orthod Dentofacial Orthop. 2004;125:130-38.
- 89. White L, Sugawara J. Dr. Junji Sugawara on the skeletal anchorage system. J Clin Orthod 1999;33:689-96.
- 90. Chung K-R, Kim S-H, Kook Y-A. The C-Palatal Plate. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 431-38.
- 91. Ritto AK. Skeletal Anchorage: Different Approaches. Temporary Anchorage Devices in Orthodontics: Mosby; 2009. p. 238-59.
- 92. Chung K-R, Kim S-H, Kook Y-A. The C-Tube. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 439-48.
- 93. Sugawara J, Umemori M, Takahashi I, Nagasaka H, Kawamura H. The Skeletal Anchorage System. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 449-61.
- 94. Liou EJ-W, Lin JC-Y. Appliances, Mechanics, and Treatment Strategies Toward Orthognatic-Like Treatment Results. temporary anchorage devices in orthodontics: Mosby; 2009. p. 167-97.
- 95. Park H-S. Clinical Application of Microimplants. temporary anchorage devices in orthodontics: Mosby; 2009. p. 260-86.
- 96. Park H-S. Micro-implant anchorage for treatment of skeletal Class I bialveolar protrusion. Journal of clinical orthodontics 2001;35(7):417-22.
- 97. Fortini A, Cacciafesta V, Sfondrini MF, Cambi S, Lupoli M. Clinical Applications and Efficiency of Miniscrews for Extradental Anchorage. Orthodontics 2004;1(2):1-12.
- 98. Schätzle M, Männchen R, Zwahlen M, Lang N. Survival and failure rates of orthodontic temporary anchorage devices: a systematic review. Clinical Oral Implants Research 2009;20(12):1351-9.
- 99. Cornelis MA, Scheffler NR, Nyssen-Behets C, De Clerck HJ, Tulloch JFC. Patients' and orthodontists' perceptions of miniplates used for temporary skeletal anchorage: a prospective study. American Journal of Orthodontics & Dentofacial Orthopedics 2008;133(1):18-24.
- 100. Chen Y-J, Chang H-H, Huang C-Y, Hung H-C, Lai EH-H, Yao C-CJ. A retrospective analysis of the failure rate of three different orthodontic skeletal anchorage systems. Clinical Oral Implants Research 2007;18(6):768-75.
- 101. Ohnishi H, Yagi T, Yasuda Y, Takada K. A Mini-Implant for Orthodontic Anchorage in a Deep Overbite Case. The Angle orthodontist 2005;75(3):444-52.
- 102. Rodriguez JC, Suarez F, Chan H-L, Padial-Molina M, Wang H-L. Implants for Orthodontic Anchorage: Success Rates and Reasons of Failures. Implant Dentistry 2014;23(2):155-61.
- 103. Maino B, Mura P, Bednar J. Miniscrew implants: The Spider Screw anchorage system. Seminars Orthod 2005;11(1):40-46.

- 104. Wiechmann D, Meyer U, Büchter A. Success rate of mini- and micro-implants used for orthodontic anchorage: a prospective clinical study. Clinical Oral Implants Research 2007;18(2):263-67.
- 105. Park H-S, Jeong S-H, Kwon O-W. Factors affecting the clinical success of screw implants used as orthodontic anchorage. American Journal of Orthodontics and Dentofacial Orthopedics 2006;130(1):18-25.
- 106. Topouzelis N, Tsaousoglou P. Clinical factors correlated with the success rate of miniscrews in orthodontic treatment. International Journal of Oral Science 2012.
- 107. Kravitz ND, Kusnoto B. Risks and complications of orthodontic miniscrews. American Journal of Orthodontics and Dentofacial Orthopedics 2007;131(4, Supplement 1):S43-S51.
- Fritz UB, Diedrich PR. Clinical Suitability of Titaniun Microscrews for Orthodontic Anchorage. Temporary Anchorage Devices in Orthodontics: Mosby; 2009. p. 287-94.
- 109. Lim H-J, Choi Y-J, Evans CA, Hwang H-S. Predictors of initial stability of orthodontic miniscrew implants. The European Journal of Orthodontics 2011.
- 110. Park HC. Clinical study on success rate of microscrew implants for orthodontic anchorage. Korean journal of orthodontics 2003;33:151-56.
- 111. Rygh P, Reitan K. Ultrastructural changes in the periodontal ligament incident to orthodontic tooth movement. Transactions. European Orthodontic Society 1972:393.
- 112. Poggio P IC, Velo S, Carano A. Safe zones: a guide for miniscrew positioning in the maxillary and mandibular arch. Angle Orthod 2006;76:191-7.
- 113. Costa A, Pasta G, Bergamaschi G. Intraoral hard and soft tissue depths for temporary anchorage devices. Seminars in Orthodontics 2005;11(1):10-15.
- 114. Schnelle MA, Beck FM, Jaynes RM, Huja SS. A radiographic evaluation of the availability of bone for placement of miniscrews. The Angle orthodontist 2004;74(6):832-37.
- 115. Ludwig B BSaBS. Mini-implants in orthoodntics: Innovative anchorage concepts. Berlin: Quintessence Publishing Co Ltd; 2007.
- 116. Dalstra M CP, Melsen B. Load transfer of miniscrews for orthodontic anchorage. Orthodontics 2004;1:53-62.
- 117. Fabbroni G, Aabed S, Mizen K, Starr DG. Transalveolar screws and the incidence of dental damage: a prospective study. International journal of oral and maxillofacial surgery 2004;33(5):442-46.
- 118. Asscherickx K VB, Wehrbein H, Sabzevar MM. Root repair after injury from mini-screw. Clinical Oral Implants Research 2005;16:575-8.
- 119. Park H-C. The skeletal cortical anchorage using titanium microscrew implants. Korean journal of orthodontics 1999;29(6):699-706.
- 120. Kadioglu O, Büyükyilmaz T, Zachrisson BU, Maino BG. Contact damage to root surfaces of premolars touching miniscrews during orthodontic treatment. American Journal of Orthodontics and Dentofacial Orthopedics 2008;134(3):353-60.
- 121. Maino BG, Weiland F, Attanasi A, Zachrisson BU, Buyukylmaz T. Root damage and repair after contact with miniscrews. Journal of Clinical Orthodontics 2007;41:762–66.

- 122. Hwang Y-C, Hwang H-S. Surgical repair of root perforation caused by an orthodontic miniscrew implant. American Journal of Orthodontics and Dentofacial Orthopedics 2011;139(3):407-11.
- 123. Bargholz C. Perforation repair with mineral trioxide aggregate: a modified matrix concept. International endodontic journal 2005;38(1):59-69.
- 124. Mortensen MG, Buschang PH, Oliver DR, Kyung HM, Behrents RG. Stability of immediately loaded 3-and 6-mm miniscrew implants in beagle dogs: a pilot study. American Journal of Orthodontics and Dentofacial Orthopedics 2009;136(2):251-59.
- 125. Wang Y-C, Liou EJW. Comparison of the loading behavior of self-drilling and predrilled miniscrews throughout orthodontic loading. American Journal of Orthodontics and Dentofacial Orthopedics 2008;133(1):38-43.
- 126. Genant HK, Cooper C, Poor G, Reid I, Ehrlich G, Kanis J, et al. Interim report and recommendations of the World Health Organization task-force for osteoporosis. Osteoporosis International 1999;10(4):259-64.
- 127. Park J-B, Kim E-Y, Paek J, Kook Y-A, Jeong D-M, Cho I-S, et al. Primary Stability of Self-Drilling and Self-Tapping Mini-Implant in Tibia of Diabetes-Induced Rabbits. International Journal of Dentistry 2014;2014.
- 128. Marquezan M, Trindade Mattos C, Franzotti Sant'Anna E, Gomes de Souza MM, Cople Maia L. Does cortical thickness influence the primary stability of miniscrews? A systematic review and meta-analysis. The Angle Orthodontist 2014;84(6):1093-103.
- 129. Wilmes B, Rademacher C, Olthoff G, Drescher, D. Parameters affecting primary stability of orthodontic mini-implants. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2006;67(3):162-74.
- 130. Glasl B, Björn L, Lietz T, Bowman SJ, Baumgaertel S. Risks and prevention strategies. In: Baumgaertel S, Bowman SJ, editors. Mini-implants in orthodontics: innovative anchorage concepts. Berlin: Quintessence; 2008. p. 123-25.
- 131. Bergkvist G, Koh K-J, Sahlholm S, Klintström E, Lindh C. Bone density at implant sites and its relationship to assessment of bone quality and treatment outcome. The International journal of oral & maxillofacial implants 2009;25(2):321-28.
- 132. Gracco A, Lombardo L, Cozzani M, Siciliani G. Quantitative cone-beam computed tomography evaluation of palatal bone thickness for orthodontic miniscrew placement. American Journal of Orthodontics and Dentofacial Orthopedics 2008;134(3):361-69.
- 133. Ten Cate AR. Oral histology : development, structure, and function St. Louis : Mosby; 2007.
- 134. Gong JK, Arnold JS, Cohn SH. Composition of trabecular and cortical bone. The Anatomical Record 2005;149(3):325-31.
- 135. Melsen B, Graham J, Baccetti T, Koga M, Boyd R, Park J, et al. Factors contributing to the success or failure of skeletal anchorage devices: an informal JCO survey. Journal of Clinical Orthodontics 2010;44(12):714-8; quiz 43.
- 136. Lietz T. Mini-screws Aspects of Assessment and Selection Among Different Systems. In: Baumgaertel S, Bowman SJ, editors. Mini-implants in orthodontics: innovative anchorage concepts. Berlin: Quintessence; 2008. p. 188.

- 137. Zitzmann NU, Berglundh T, Ericsson I, Lindhe J. Spontaneous progression of experimentally induced periimplantitis. Journal of Clinical Periodontology 2004;31(10):845-49.
- 138. Ericsson I, Berglundh T, Marinello C, Liljenberg B, Lindhe J. Long-standing plaque and gingivitis at implants and teeth in the dog. Clinical Oral Implants Research 1992;3(3):99-103.
- 139. Lee J-H, Frias V, Lee K-W, Wright RF. Effect of implant size and shape on implant success rates: A literature review. The Journal of Prosthetic Dentistry 2005;94(4):377-81.
- 140. Wilmes B, Rademacher C, Olthoff G, Drescher D. Parameters Affecting Primary Stability of Orthodontic Mini-implants. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2006;67(3):162-74.
- 141. Huja SS. Mechanisms of Bone Adaptation to miniscrew Implants. ORTHOTADs The Clinical Guide and Atlas. Dallas: Under Dog Media; 2007. p. 537.
- 142. Aerssens J, Boonen S, Lowet G, Dequeker J. Interspecies Differences in Bone Composition, Density, and Quality: Potential Implications for in Vivo Bone Research. Endocrinology 1998;139(2):663-70.
- 143. Farnsworth D, Rossouw PE, Ceen RF, Buschang PH. Cortical bone thickness at common miniscrew implant placement sites. American Journal of Orthodontics & Dentofacial Orthopedics 2011;139(4):495-503.
- 144. Kokich VG, Shapiro PA, Oswald R, Koskinen-Moffett L, Clarren SK. Ankylosed teeth as abutments for maxillary protraction: a case report. American Journal of Orthodontics 1985;88(4):303-07.
- 145. Jamilian A, Haraji A, Showkatbakhsh R, Valaee N. The effects of miniscrew with Class III traction in growing patients with maxillary deficiency. International journal of orthodontics (Milwaukee, Wis.);22(2):25.
- 146. Wilmes B, Nienkemper M, Ludwig B, Kau C, Drescher D. Early class III treatment with a hybrid hyrax-mentoplate combination. Journal of clinical orthodontics 2011;45(1):15.
- 147. Shroff B, Yoon W, Lindauer S, Burstone C. Simultaneous intrusion and retraction using a three-piece base arch. The Angle Orthodontist 1997;67(6):455.
- 148. Bishara S. How orthodontic appliances work. Textbook of orthodontics. Philadelphia; 2001. p. 208-31.
- 149. Baccetti T, De Clerck H, Cevidanes L, Franchi L. Morphometric analysis of treatment effects of bone-anchored maxillary protraction in growing Class III patients. The European Journal of Orthodontics 2010:cjq170.
- 150. Şar Ç, Şahinoğlu Z, Özçırpıcı AA, Uçkan S. Dentofacial effects of skeletal anchored treatment modalities for the correction of maxillary retrognathia. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(1):41-54.
- 151. Melsen B, Costa A. Immediate loading of implants used for orthodontic anchorage. Clinical Orthodontics and Research 2000;3(1):23-28.
- 152. Fritz U, Diedrich P, Kinzinger G, Al-Said M. The Anchorage Quality of Miniimplants towards Translatory and Extrusive Forces. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2003;64(4):293-304.

- 153. Wehrbein H, Yildirim M, Diedrich P. Osteodynamics around orthodontically loaded short maxillary implants. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 1999;60(6):409-15.
- 154. Meredith N, Shagaldi F, Alleyne D, Sennerby L, Cawley P. The application of resonance frequency measurements to study the stability of titanium implants during healing in the rabbit tibia. Clinical Oral Implants Research 1997;8(3):234-43.
- 155. Glauser R SL, Meredith N, Ree A, Lundgren A, Gottlow J, et al. . Resonance frequency analysis of implants subjected to immediate or early functional occlusal loading. Successful vs. failing implants. Clinical oral implant research 2004;15:428-34.
- 156. Katsavrias G. Reliability and validity of measuring implant stability with resonance frequency analysis [Saint Louis University; 2009.
- 157. Florvaag B, Kneuertz P, Lazar F, Koebke J, Zöller J, Braumann B, et al. Biomechanical Properties of Orthodontic Miniscrews. An In-vitro Study. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie 2010;71(1):53-67.
- 158. Motoyoshi M, Hirabayashi M, Uemura M, Shimizu N. Recommended placement torque when tightening an orthodontic mini-implant. Das empfohlenen Drehmoment beim Festziehen eines orthodontischen Mini-Implantats. Clinical Oral Implants Research 2006;17(1):109-14.
- 159. Friberg B, Sennerby L, Roos J, Lekholm U. Identification of bone quality in conjunction with insertion of titanium implants. A pilot study in jaw autopsy specimens. Clinical Oral Implants Research 1995;6(4):213-19.
- 160. Kim J-W, Ahn S-J, Chang Y-I. Histomorphometric and mechanical analyses of the drill-free screw as orthodontic anchorage. American Journal of Orthodontics and Dentofacial Orthopedics 2005;128(2):190-94.
- 161. Klokkevold PR, Johnson P, Dadgostari S, Davies JE, Caputo A, Nishimura RD. Early endosseous integration enhanced by dual acid etching of titanium: a torque removal study in the rabbit. Clinical Oral Implants Research 2001;12(4):350-57.
- 162. Favero LG, Pisoni A, Paganelli C. Removal torque of osseointegrated miniimplants: an in vivo evaluation. The European Journal of Orthodontics 2007;29(5):443.
- 163. Shah AH, Behrents RG, Kim KB, Kyung H-M, Buschang PH. Effects of screw and host factors on insertion torque and pullout strength. The Angle orthodontist 2011;82(4):603-10.
- 164. Shigeeda T. Root proximity and stability of orthodontic anchor screws. Journal of oral science 2014;56(1):59-65.
- 165. Uemura M, Motoyoshi M, Yano S, Sakaguchi M, Igarashi Y, Shimizu N. Orthodontic mini-implant stability and the ratio of pilot hole implant diameter. The European Journal of Orthodontics 2012;34(1):52-56.
- 166. Roberts W. Bone tissue interface. J Dent Educ 1988;52(12):804-09.
- 167. Roberts WE, Helm FR, Marshall KJ, Gongloff RK. Rigid endosseous implants for orthodontic and orthopedic anchorage. Angle Orthodontist 1989;59:247–56.
- 168. Ono A, Motoyoshi M, Shimizu N. Cortical bone thickness in the buccal posterior region for orthodontic mini-implants. International Journal of Oral & Maxillofacial Surgery 2008;37(4):334-40.

- 169. Motoyoshi M, Yoshida T, Ono A, Shimizu N. Effect of cortical bone thickness and implant placement torque on stability of orthodontic mini-implants. The International journal of oral & maxillofacial implants 2006;22(5):779-84.
- 170. Frost HM. A 2003 Update of Bone Physiology and Wolff's Law for Clinicians. The Angle orthodontist 2004;74(1):3-15.
- 171. Kuroda S, Yamada K, Deguchi T, Hashimoto T, Kyung H-M, Takano-Yamamotod T. Root proximity is a major factor for screw failure in orthodontic anchorage. Am J Orthod Dentofacial Orthop 2007;131(4 Supp 1):S68-S73.
- 172. Hyde JD, King GJ, Greenlee GM, Spiekerman C, Huang GJ. Survey of Orthodontists' Attitudes and Experiences Regarding Miniscrew Implants. Journal of clinical orthodontics: JCO 2010;44(8):481.
- 173. Mah JK, Huang JC, Choo H. Practical applications of cone-beam computed tomography in orthodontics. Journal of the American Dental Association (1939) 2010;141:7S-13S.
- 174. Watanabe H, Deguchi T, Hasegawa M, Ito M, Kim S, Takano-Yamamoto T. Orthodontic miniscrew failure rate and root proximity, insertion angle, bone contact length, and bone density. Orthodontics & Craniofacial Research 2013;16(1):44-55.
- 175. Kim S-H, Choi Y-S, Hwang E-H, Chung K-R, Kook Y-A, Nelson G. Surgical positioning of orthodontic mini-implants with guides fabricated on models replicated with cone-beam computed tomography. American Journal of Orthodontics and Dentofacial Orthopedics 2007;131(4):S82-S89.
- 176. Kim S-H, Kang S-M, Choi Y-S, Kook Y-A, Chung K-R, Huang JC. Cone-beam computed tomography evaluation of mini-implants after placement: is root proximity a major risk factor for failure? American Journal of Orthodontics and Dentofacial Orthopedics 2010;138(3):264-76.
- 177. Duaibis RB. Factors affecting the stability of miniscrew implants: A stepwise three dimensional finite element study [Chicago: University of Illinois. ; 2010.
- 178. Duaibis R, Kusnoto B, Natarajan R, Zhao L, Evans C. Factors affecting stresses in cortical bone around miniscrew implants. The Angle orthodontist 2012;82(5):875-80.
- 179. Motoyoshi M, Yoshida T, Ono A, Shimizu N. Effect of cortical bone thickness and implant placement torque on stability of orthodontic mini-implants. The International journal of oral & maxillofacial implants 2007;22(5):779.
- 180. McManus MM, Qian F, Grosland NM, Marshall SD, Southard TE. Effect of miniscrew placement torque on resistance to miniscrew movement under load. American Journal of Orthodontics and Dentofacial Orthopedics 2011;140(3):e93-e98.
- 181. Motoyoshi M, Hirabayashi M, Uemura M, Shimizu N. Recommended placement torque when tightening an orthodontic mini implant. Clinical Oral Implants Research 2006;17(1):109-14.
- 182. Meredith N. Assessment of implant stability as a prognostic determinant. The International journal of prosthodontics 1998;11(5):491.
- 183. Gupta N, Kotrashetti SM, Naik V. A Comparitive Clinical Study Between Self Tapping and Drill Free Screws as a Source of Rigid Orthodontic Anchorage. Journal of Maxillofacial and Oral Surgery 2012;11(1):29-33.

- 184. Son S, Motoyoshi M, Uchida Y, Shimizu N. Comparative study of the primary stability of self-drilling and self-tapping orthodontic miniscrews. American Journal of Orthodontics and Dentofacial Orthopedics 2014;145(4):480-85.
- 185. Tachibana R, Motoyoshi M, Shinohara A, Shigeeda T, Shimizu N. Safe placement techniques for self-drilling orthodontic mini-implants. International journal of oral and maxillofacial surgery 2012;41(11):1439-44.
- 186. Heidemann W GK, Grobel KH, Kollner HG. Influence of different pilot sizes on torque measurements and pulllout analysis of osteosynthesis screws. Journal of Craniofacial Surgery 1998;26:50-55.
- 187. Wilmes B, Ottenstreuer S, Su Y-Y, Drescher D. Impact of Implant Design on Primary Stability of Orthodontic Mini-implants. Journal of Orofacial Orthopedics 2008;69(1):42-50.
- 188. Hong C, Lee H, Webster R, Kwak J, Wu BM, Moon W. Stability comparison between commercially available mini-implants and a novel design: Part 1. The Angle Orthodontist 2011.
- 189. Hong C, Truong P, Song HN, Wu BM, Moon W. Mechanical stability assessment of novel orthodontic mini-implant designs: part 2. The Angle Orthodontist *In Press*.
- 190. Shah AH. Effect of miniscrew characteristics and bone properties in insertion torque and pullout strength [Saint Louis: Saint Louis University 2011.
- 191. Reigstad O, Johansson CB, Stenport V, Wennerberg A, Reigstad A, Røkkum M. Different patterns of bone fixation with hydroxyapatite and resorbable CaP coatings in the rabbit tibia at 6, 12, and 52 weeks. journal of Biomedical Materials Research Part B: Applied Biomaterials; 2011.
- 192. Herman RJ, Currier GF, Miyake A. Mini-implant anchorage for maxillary canine retraction: a pilot study. American Journal of Orthodontics and Dentofacial Orthopedics 2006;130(2):228-35.
- 193. Reynders R, Ronchi L, Bipat S. Mini-implants in orthodontics: A systematic review of the literature. American Journal of Orthodontics and Dentofacial Orthopedics 2009;135(5):564.e1-64.e19.
- 194. Büchter A, Wiechmann D, Koerdt S, Wiesmann HP, Piffko J, Meyer U. Loadrelated implant reaction of mini-implants used for orthodontic anchorage. Clinical Oral Implants Research 2005;16(4):473-79.
- 195. Park HS, Lee K-J. Biomechanical Principles in Miniscrew-Driven Orthodontics. Temporary Anchorage Devices in Orthodontics: Mosby; 2009. p. 93-144.
- 196. MELSEN B, VERNA C, LUZI C. Mini-implants and their clinical applications: The Aarhus Experience; 2013. p. 104.
- 197. Baek S-H, Kim B-M, Kyung S-H, Lim JK, Kim YH. Success rate and risk factors associated with mini-implants reinstalled in the maxilla. The Angle orthodontist 2008;78(5):895-901.
- 198. Wu T-Y, Kuang S-H, Wu C-H. Factors associated with the stability of miniimplants for orthodontic anchorage: a study of 414 samples in Taiwan. Journal of Oral and Maxillofacial Surgery 2009;67(8):1595-99.
- 199. Melsen B, Verna C. Miniscrew implants: The Aarhus anchorage system. Seminars in Orthodontics 2005;11(1):24-31.
- 200. Ma PX. Biomimetic materials for tissue engineering. Advanced drug delivery reviews 2008;60(2):184-98.

- 201. Kim TG, Shin H, Lim DW. Biomimetic scaffolds for tissue engineering. Advanced Functional Materials 2012;22(12):2446-68.
- 202. Masala S, Nano G, Marcia S, Muto M, Fucci FPM, Simonetti G. Osteoporotic vertebral compression fractures augmentation by injectable partly resorbable ceramic bone substitute (Cerament[™]| SPINE SUPPORT): a prospective nonrandomized study. Neuroradiology 2012;54(6):589-96.
- 203. Ryu K-S, Shim J-H, Heo H-Y, Park C-K. Therapeutic efficacy of injectable calcium phosphate cement in osteoporotic vertebral compression fractures: prospective nonrandomized controlled study at 6-month follow-up. World neurosurgery 2010;73(4):408-11.
- 204. Becker S, Franz K, Wilke I, Ogon M. Injectable bone cements in the treatment of spinal fractures, osteopromotive capacity and surgical considerations. Eur Cells Mater 2006;11(Suppl 1):1.
- 205. Larsson S, Hannink G. Injectable bone-graft substitutes: current products, their characteristics and indications, and new developments. Injury 2011;42:S30-S34.
- 206. Masaki T, Sasao Y, Miura T, Torii Y, Kojima A, Aoki H, et al. An experimental study on initial fixation strength in transpedicular screwing augmented with calcium phosphate cement. Spine 2009;34(20):E724-E28.
- 207. Wolff K-D, Swaid S, Nolte D, Böckmann RA, Hölzle F, Müller-Mai C. Degradable injectable bone cement in maxillofacial surgery: indications and clinical experience in 27 patients. Journal of Cranio-Maxillofacial Surgery 2004;32(2):71-79.
- 208. Ko C, Kohn D, Hollister S. Micromechanics of implant/tissue interfaces. The Journal of oral implantology 1991;18(3):220-30.
- 209. Cho BC, Park JW, Baik BS. Clinical application of injectable calcium sulfate on early bony consolidation in distraction osteogenesis for the treatment of craniofacial microsomia. Journal of Craniofacial Surgery 2002;13(3):465-75.
- 210. Guarnieri R, Aldini NN, Pecora G, Fini M, Giardino R. Medial-grade calcium sulfate hemihydrate (surgiplaster) in healing of a human extraction socket--histologic observation at 3 months: a case report. The International journal of oral & maxillofacial implants 2004;20(4):636-41.
- 211. Kim JY, Cho BC. Effect of calcium sulfate pellets on early bone mineralization in distraction osteogenesis for craniofacial microsomia in adults. Journal of Craniofacial Surgery 2007;18(6):1309-21.
- 212. Apelt D, Theiss F, El-Warrak A, Zlinszky K, Bettschart-Wolfisberger R, Bohner M, et al. In vivo behavior of three different injectable hydraulic calcium phosphate cements. Biomaterials 2004;25(7):1439-51.
- 213. Charrière E, Terrazzoni S, Pittet C, Mordasini P, Dutoit M, Lemaître J, et al. Mechanical characterization of brushite and hydroxyapatite cements. Biomaterials 2001;22(21):2937-45.
- 214. Ryf C, Goldhahn S, Radziejowski M, Blauth M, Hanson B. A new injectable brushite cement: first results in distal radius and proximal tibia fractures. European Journal of Trauma and Emergency Surgery 2009;35(4):389-96.
- 215. Keating J, Hajducka C, Harper J. Minimal internal fixation and calciumphosphate cement in the treatment of fractures of the tibial plateau A PILOT STUDY. Journal of Bone & Joint Surgery, British Volume 2003;85(1):68-73.

- 216. Mattsson P, Larsson S. Unstable trochanteric fractures augmented with calcium phosphate cement A prospective randomized study using radiostereometry to measure fracture stability. Scandinavian journal of surgery 2004;93(3):223-28.
- 217. Mattsson P, Alberts A, Dahlberg G, Sohlman M, Hyldahl H-C, Larsson S. Resorbable cement for the augmentation of internally-fixed unstable trochanteric fractures A PROSPECTIVE, RANDOMISED MULTICENTRE STUDY. Journal of Bone & Joint Surgery, British Volume 2005;87(9):1203-09.
- 218. Moore DC, Maitra RS, Farjo LA, Graziano GP, Goldstein SA. Restoration of pedicle screw fixation with an in situ setting calcium phosphate cement. Spine 1997;22(15):1696-705.
- 219. Russell TA, Leighton RK. Comparison of autogenous bone graft and endothermic calcium phosphate cement for defect augmentation in tibial plateau fracturesA multicenter, prospective, randomized study. The Journal of Bone & Joint Surgery 2008;90(10):2057-61.
- 220. De Leonardis D, Pecora GE. Prospective study on the augmentation of the maxillary sinus with calcium sulfate: histological results. Journal of Periodontology 2000;71(6):940-47.
- 221. Guarnieri R, Grassi R, Ripari M, Pecora G. Maxillary sinus augmentation using granular calcium sulfate (surgiplaster sinus): radiographic and histologic study at 2 years. International Journal of Periodontics and Restorative Dentistry 2006;26(1):79.
- 222. Schneider G, Blechschmidt K, Linde D, Litschko P, Körbs T, Beleites E. Bone regeneration with glass ceramic implants and calcium phosphate cements in a rabbit cranial defect model. Journal of Materials Science: Materials in Medicine 2010;21(10):2853-59.
- 223. Von Rechenberg B, Génot OR, Nuss K, Galuppo L, Fulmer M, Jacobson E, et al. Evaluation of four biodegradable, injectable bone cements in an experimental drill hole model in sheep. European Journal of Pharmaceutics and Biopharmaceutics 2013;85(1):130-38.
- 224. Gómez E, Martín M, Arias J, Carceller F. Clinical applications of Norian SRS (calcium phosphate cement) in craniofacial reconstruction in children: our experience at Hospital La Paz since 2001. Journal of Oral and Maxillofacial Surgery 2005;63(1):8-14.
- 225. Goodman SB, Bauer TW, Carter D, Casteleyn PP, Goldstein SA, Kyle RF, et al. Norian SRS cement augmentation in hip fracture treatment: laboratory and initial clinical results. Clinical orthopaedics and related research 1998;348:42-50.
- 226. Welkerling H, Raith J, Kastner N, Marschall C, Windhager R. Painful soft-tissue reaction to injectable Norian SRS calcium phosphate cement after curettage of enchondromas. Journal of Bone & Joint Surgery, British Volume 2003;85(2):238-39.
- 227. Thomas MV, Puleo DA, Al-Sabbagh M. Calcium sulfate: a review. Journal of long-term effects of medical implants 2005;15(6).
- 228. Su-Gwan K, Hak-Kyun K, Sung-Chul L. Combined implantation of particulate dentine, plaster of Paris, and a bone xenograft (Bio-Oss< sup>®</sup>) for bone regeneration in rats. Journal of Cranio-Maxillofacial Surgery 2001;29(5):282-88.

- 229. Kutkut A, Andreana S. Medical-grade calcium sulfate hemihydrate in clinical implant dentistry: a review. Journal of long-term effects of medical implants 2010;20(4).
- 230. Li Y, Rodrigues J, Tomas H. Injectable and biodegradable hydrogels: gelation, biodegradation and biomedical applications. Chemical Society Reviews 2012;41(6):2193-221.
- 231. Urban RM, Turner TM, Hall DJ, Infanger SI, Cheema N, Lim T-H, et al. Effects of altered crystalline structure and increased initial compressive strength of calcium sulfate bone graft substitute pellets on new bone formation. Orthopedics 2004;27(1 Suppl):s113-8.
- 232. Sbordone L, Bortolaia C, Perrotti V, Pasquantonio G, Petrone G. Clinical and histologic analysis of calcium sulfate in treatment of a post-extraction defect: a case report. Implant Dentistry 2005;14(1):82-87.
- 233. Peltier LF, Bickel EY, Lillo R, Thein MS. The use of plaster of Paris to fill defects in bone. Annals of surgery 1957;146(1):61.
- 234. Juillet J. Use of plaster of Paris in implantology. Inf Dent 1976;58:51-3.
- 235. Johansson L-Å, Isaksson S, Lindh C, Becktor JP, Sennerby L. Maxillary sinus floor augmentation and simultaneous implant placement using locally harvested autogenous bone chips and bone debris: a prospective clinical study. Journal of Oral and Maxillofacial Surgery 2010;68(4):837-44.
- 236. De Leonardis D, Pecora GE. Augmentation of the maxillary sinus with calcium sulfate: one-year clinical report from a prospective longitudinal study. The International journal of oral & maxillofacial implants 1998;14(6):869-78.
- Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: Part

 The influence of stability of fixation and soft-tissue preservation. Clinical
 orthopaedics and related research 1989;238:249-81.
- 238. Sariibrahimoglu K, Wolke JG, Leeuwenburgh SC, Yubao L, Jansen JA. Injectable biphasic calcium phosphate cements as a potential bone substitute. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2014;102(3):415-22.
- 239. Yetkinler DN, Ladd AL, Poser RD, Constantz BR, Carter D. Biomechanical Evaluation of Fixation of Intra-Articular Fractures of the Distal Part of the Radius in Cadavera: Kirschner Wires Compared with Calcium-Phosphate Bone Cement*. The Journal of Bone & Joint Surgery 1999;81(3):391-9.
- 240. Larsson S. Calcium phosphates: what is the evidence? Journal of orthopaedic trauma 2010;24:S41-S45.
- 241. Gisep A, Wieling R, Bohner M, Matter S, Schneider E, Rahn B. Resorption patterns of calcium-phosphate cements in bone. Journal of Biomedical Materials Research Part A 2003;66(3):532-40.
- 242. Barralet JE, Grover LM, Gbureck U. Ionic modification of calcium phosphate cement viscosity. Part II: hypodermic injection and strength improvement of brushite cement. Biomaterials 2004;25(11):2197-203.
- 243. Xia Z, Grover LM, Huang Y, Adamopoulos IE, Gbureck U, Triffitt JT, et al. In vitro biodegradation of three brushite calcium phosphate cements by a macrophage cell-line. Biomaterials 2006;27(26):4557-65.
- 244. Constantz BR, Ison IC, Fulmer MT, Poser RD, Smith ST, VanWagoner M, et al. Skeletal repair by in situ formation of the mineral phase of bone. Science 1995;267(5205):1796-99.

- 245. Frakenburg EP, Goldstein SA, Bauer TW, Harris SA, Poser RD. Biomechanical and Histological Evaluation of a Calcium Phosphate Cement*. The Journal of Bone & Joint Surgery 1998;80(8):1112-24.
- 246. Khan SN, Tomin E, Lane JM. Clinical applications of bone graft substitutes. Orthopedic Clinics of North America 2000;31(3):389-98.
- 247. Da Costa G, Pare A, Goga D, Sury F, Laure B. [CT-scan evaluation of calvarial bone donor site reconstruction using calcium phosphate cement.]. Revue de stomatologie, de chirurgie maxillo-faciale et de chirurgie orale 2014.
- 248. Thordarson DB, Bollinger M. SRS cancellous bone cement augmentation of calcaneal fracture fixation. Foot & ankle international 2005;26(5):347-52.
- 249. Gal P, Ondrus S, Skvaril J, Straka M, Jochymek J, Planka L. [Synthetic biocompatible degradable material for juvenile bone cyst treatment]. Acta chirurgiae orthopaedicae et traumatologiae Cechoslovaca 2009;76(6):495-500.
- 250. Deramond H, Depriester C, Galibert P, Le Gars D. Percutaneous vertebroplasty with polymethylmethacrylate: technique, indications, and results. Radiologic clinics of north america 1998;36(3):533-46.
- 251. Doria C, Tranquilli Leali P. Percutaneous techniques in the treatment of osteoporotic, traumatic and neoplastic fractures of thoraco-lumbar spine: our institutional experience. Injury 2010;41(11):1136-39.
- 252. Klazen CA, Lohle PN, de Vries J, Jansen FH, Tielbeek AV, Blonk MC, et al. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. The Lancet 2010;376(9746):1085-92.
- 253. Stankewich C, Swiontkowski MF, Tencer AF, Yetkinler DN, Poser RD. Augmentation of femoral neck fracture fixation with an injectable calcium-phosphate bone mineral cement. Journal of Orthopaedic Research 1996;14(5):786-93.
- 254. Hillmeier J, Meeder PJ, Nöldge G, Kasperk C. Minimal invasive Reposition und innere Stabilisierung osteoporotischer Wirbelkörperfrakturen (Ballonikyphoplastie). Operative Orthopädie und Traumatologie 2003;15(4):343-62.
- 255. Betz RR. Limitations of autograft and allograft: new synthetic solutions. Orthopedics 2002;25(5 Suppl):s561-70.
- 256. Hornicek FJ, Gebhardt MC, Tomford WW, Sorger JI, Zavatta M, Menzner JP, et al. Factors affecting nonunion of the allograft-host junction. Clinical orthopaedics and related research 2001;382:87-98.
- 257. Mitchell N, Shepard N. The resurfacing of adult rabbit articular cartilage by multiple perforations through the subchondral bone. The Journal of Bone & Joint Surgery 1976;58(2):230-33.
- 258. Wozney JM, Rosen V, Celeste AJ, Mitsock LM, Whitters MJ, Kriz RW, et al. Novel regulators of bone formation: molecular clones and activities. Science 1988;242(4885):1528-34.
- 259. Hannink G, Wolke JGC, Schreurs BW, Buma P. In vivo behavior of a novel injectable calcium phosphate cement compared with two other commercially available calcium phosphate cements. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2008;85B(2):478-88.

- 260. Hayashi C, Kinoshita A, Oda S, Mizutani K, Shirakata Y, Ishikawa I. Injectable calcium phosphate bone cement provides favorable space and a scaffold for periodontal regeneration in dogs. J Periodontol 2006.
- 261. Horstmann WG, Verheyen CCPM, Leemans R. An injectable calcium phosphate cement as a bone-graft substitute in the treatment of displaced lateral tibial plateau fractures. Injury 2003;34(2):141-44.
- 262. Low KL, Tan SH, Sharif Zein SH, Roether JA, Mouriño V, Boccaccini AR. Calcium phosphate-based composites as injectable bone substitute materials J Biomed Mater Res B Appl Biomater 2010;94(1):273-86.
- 263. Sanzana ES, Navarro M, Macule F, Suso S, Planell JA, Ginebra MP. Of the in vivo behavior of calcium phosphate cements and glasses as bone substitutes. Acta Biomaterialia 2008;4(6):1924-33.
- 264. Kelly CW, Ross; Gitelis, Steven; Hartjen, Charles; Watson, J. Tracy; Kim, Poong Taek. The use of surgical grade calcium sulfate as a bone graft substitute: results of a multicenter trial. Clinical Orthopaedics & Related Research 2001;382:42-50.
- 265. Bohner M. Design of ceramic-based cements and putties for bone graft substitution. European Cells and Materials 2010;20:1-12.
- 266. Temenoff JS, Mikos AG. Injectable biodegradable materials for orthopedic tissue engineering. Biomaterials 2000;21(23):2405-12.
- 267. Yang H, Zou J. Filling materials used in kyphoplasty and vertebroplasty for vertebralcompression fracture: a literature review. Artificial Cells, Blood Substitutes, & Immobilization Biotechnology 2011;39(2):87-91.
- 268. Zhu X, Zhang Z, Mao H, Geng D, Zou J, Wang G, et al. A novel sheep vertebral bone defect model for injectable bioactive vertebral augmentation materials. Journal of Materials Science: Materials in Medicine 2011;22(1):159-64.
- 269. Komath M, Varma HK. Development of a fully injectable calcium phosphate cement for orthopedic and dental applications. Bulletin of Materials Science 2003;26(4):415-22.
- 270. Yu X-W, Xie X-H, Yu Z-F, Tang T-T. Augmentation of screw fixation with injectable calcium sulfate bone cement in ovariectomized rats. journal of Biomedical Materials Research Part B: Applied Biomaterials 2009;89B(1):34-44.
- 271. Panchbhavi VK, Vallurupalli S, Morris R, Patterson R. The Use of Calcium Sulfate and Calcium Phosphate Composite Graft to Augment Screw Purchase in Osteoporotic Ankles. Foot & ankle international 2008;29(6):593-600.
- 272. Bowen JA, Mellonig JT, Gray JL, HT. T. Comparison of decalcified freezedried bone allograft and porous particulate hydroxyapatite in human periodontal osseous defects. J Periodontol 1989;60(12):647-54.
- 273. El Deeb M, Holmes RE. Tissue response to facial contour augmentation with dense and porous hydroxylapatite in rhesus monkeys. Journal of Oral and Maxillofacial Surgery 1989;47(12):1282-89.
- 274. Rosen HM, McFarland MM. The Biologic Behavior of Hydroxyapatite Implanted into the Maxillofacial Skeleton. Plastic and Reconstructive Surgery 1990;85(5):718-23.
- 275. Mercier P. Failures in ridge reconstruction with hydroxyapatite: Analysis of cases and methods for surgical revision. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 1995;80(4):389-93.

- 276. Jansen J, Ooms E, Verdonschot N, Wolke J. Injectable calcium phosphate cement for bone repair and implant fixation. Orthopedic Clinics of North America 2005;36(1):89-95.
- 277. Leung KS, Siu WS, Li SF, Qin L, Cheung WH, Tam KF, et al. An in vitro optimized injectable calcium phosphate cement for augmenting screw fixation in osteopenic goats. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2006;78B(1):153-60.
- 278. Baroud G, Cayer E, Bohner M. Rheological characterization of concentrated aqueous [beta]-tricalcium phosphate suspensions: The effect of liquid-to-powder ratio, milling time, and additives. Acta Biomaterialia 2005;1(3):357-63.
- 279. Phillips F. Minimally invasive treatments of osteoporotic vertebral compression fractures. Spine 2003;28:S45–S53.
- 280. Heini P, Berlemann U. Bone substitutes in vertebroplasty. Eur Spine J 2001;10:S205–S13.
- 281. Thomson R, Wake M, Yaszemski M, Mikos A. Biodegradable polymer scaffolds to regenerate organs. Biopolymers II. In: Peppas N, Langer R, editors: Springer Berlin / Heidelberg; 1995. p. 245-74.
- 282. Lu JX, Flautre B, Anselme K, Hardouin P, Gallur A, Descamps M, et al. Role of interconnections in porous bioceramics on bone recolonization in vitro and in vivo. Journal of Materials Science: Materials in Medicine 1999;10(2):111-20.
- 283. Karageorgiou V, Kaplan D. Porosity of 3D biomaterial scaffolds and osteogenesis. Biomaterials 2005;26(27):5474-91.
- 284. von Doernberg M-C, von Rechenberg B, Bohner M, Grünenfelder S, van Lenthe GH, Müller R, et al. In vivo behavior of calcium phosphate scaffolds with four different pore sizes. Biomaterials 2006;27(30):5186-98.
- 285. Libicher M, Hillmeier J, Liegibel U, Sommer U, Pyerin W, Vetter M, et al. Osseous integration of calcium phosphate in osteoporotic vertebral fractures after kyphoplasty: initial results from a clinical and experimental pilot study. Osteoporosis International 2006;17(8):1208-15.
- 286. Ikenaga M, Hardouin P, Lemaître J, Andrianjatovo H, Flautre B. Biomechanical characterization of a biodegradable calcium phosphate hydraulic cement: A comparison with porous biphasic calcium phosphate ceramics. Journal of Biomedical Materials Research 1998;40(1):139-44.
- 287. Gisep A, Kugler S, Wahl D, Rahn B. Mechanical characterisation of a bone defect model filled with ceramic cements". Journal of materials science. Materials in medicine 2004;15(10):1065.
- 288. Morgan JP, Dauskardt RH. Notch strength insensitivity of self-setting hydroxyapatite bone cements. Journal of Materials Science: Materials in Medicine 2003;14(7):647-53.
- 289. Yaszemski MJ, Payne RG, Hayes WC, Langer R, Mikos AG. In vitro degradation of a poly(propylene fumarate)-based composite material. Biomaterials 1996;17(22):2127-30.
- 290. Thompson R, Wake M, Yaszemski M, Mikos A. Biodegradable Polymer scaffolds to regenerate organs Adv Polym Sci 1995;122:245-74.
- 291. Moseley J, Blum B. PRO-DENSE® Injectable regenerative graft: *in vitro* and *in vivo* observations, and a proposed mechanism of action 2008.

- 292. Thomas MV, Puleo DA. Calcium sulfate: Properties and clinical applications. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2009;88B(2):597-610.
- 293. Coetzee A. Regeneration of bone in the presence of calcium sulfate. Arch Otolaryngol 1980;106:405–09.
- 294. Lim SA, Cha JY, Hwang CJ. Insertion torque of orthodontic miniscrews according to changes in shape, diameter and length. The Angle orthodontist 2008;78(2):234-40.
- 295. Wilmes B, Drescher D. Impact of bone quality, implant type, and implantation site preparation on insertion torques of mini-implants used for orthodontic anchorage. International journal of oral and maxillofacial surgery 2011;40(7):697-703.
- 296. Cehreli MC, Karasoy D, Akca K, Eckert SE. Meta-analysis of methods used to assess implant stability. The International journal of oral & maxillofacial implants 2008;24(6):1015-32.
- 297. Hench LL, Polak JM. Third-Generation Biomedical Materials. Science 2002;295(5557):1014-17.
- 298. Yaszemski MJ, Payne RG, Hayes WC, Langer R, Mikos AG. Evolution of bone transplantation: molecular, cellular and tissue strategies to engineer human bone. Biomaterials 1996;17(2):175-85.
- 299. Kotnis N, Parasu N, Finlay K, Jurriaans E, Ghert M. Chronology of the radiographic appearances of the calcium sulphate–calcium phosphate synthetic bone graft composite following resection of bone tumours—a preliminary study of the normal post-operative appearances. Skeletal Radiology 2011;40(5):563-70.
- 300. Gitelis S, Urban RM, Turner TM, Hall DJ, Neel M. Early radiological results with a bio-engineered degradable bone graft substitute for bone tumors. Musculoskeletal Tumor Society. St. Louis, MO, USA; 2007.
- 301. Urban RM, Turner TM, Hall DJ, Inoue N, Gitelis S. Increased Bone Formation Using Calcium Sulfate-Calcium Phosphate Composite Graft. Clinical Orthopaedics & Related Research 2007;459:110-17.
- 302. Gbureck U, Barralet JE, Spatz K, Grover LM, Thull R. Ionic modification of calcium phosphate cement viscosity. Part I: hypodermic injection and strength improvement of apatite cement. Biomaterials 2004;25(11):2187-95.
- 303. Michael S. A mechanical and histomorphological analysis into the healing and osseointegration of 3 mm miniscrews with and without surface treatment in the femurs of New Zealand rabbits: A pilot study [The University of Sydney; 2012.
- 304. Woods PW, Buschang PH, Owens SE, Rossouw PE, Opperman LA. The effect of force, timing, and location on bone-to-implant contact of miniscrew implants. European Journal of Orthodontics 2009;31(3):232-40.
- 305. Fleszar TJ, Knowles JW, Morrison EC, Burgett FG, Nissle RR, Ramfjord SP. Tooth mobility and periodontal therapy. Journal of Clinical Periodontology 1980;7(6):495-505.
- 306. Liu T-C, Chang C-H, Wong T-Y, Liu J-K. Finite element analysis of miniscrew implants used for orthodontic anchorage. American Journal of Orthodontics and Dentofacial Orthopedics 2012;141(4):468-76.
- 307. Cehreli M, Duyck J, Cooman MD, Puers R, Naert I. Implant design and interface force transfer. Clinical Oral Implants Research 2004;15(2):249-57.

- 308. Kelly CM, Wilkins RM. Treatment of benign bone lesions with an injectable calcium sulfate-based bone graft substitute. Orthopedics 2004;27(1 Suppl):s131-5.
- 309. Calvo Guirado J, Ortiz Ruiz A, Negri B, López Marí L, Rodriguez Barba C, Schlottig F. Histological and histomorphometric evaluation of immediate implant placement on a dog model with a new implant surface treatment. Clinical Oral Implants Research 2010;21(3):308-15.
- 310. Canè V, Marotti G, Volpi G, Zaffe D, Palazzini S, Remaggi F, et al. Size and density of osteocyte lacunae in different regions of long bones. Calcified tissue international 1982;34(1):558-63.
- 311. Deguchi T T-YT, Kamoni R, Hartsfield JK, Roberts WE, Garetto LP. The use of small titanium screws for orthodontic anchorage. Journal of Dental Research 2003;82:377-81.
- 312. Ohmae M, Saito S, Morohashi T, Seki K, Qu H, Kanomi R, et al. A clinical and histological evaluation of titanium mimi-implants as anchors for orthodontic intrusion in the beagle dog. Am J Orthod Dentofac Orthop 2001;119:489-97.
- 313. H W. Bone-to-implant contact of orthodontic implants in humans subjected to horizontal loading. Clinical oral implant research 1998;9(5):348-54.
- 314. Gantous A, Phillips JH. The Effects of Varying Pilot Hole Size on the Holding Power of Miniscrews and Microscrews. Plastic and Reconstructive Surgery 1995;95(7):1165-69.
- 315. Majzoub Z, Finotti M, Miotti F, Giardino R, Aldini NN, Cordioli G. Bone response to orthodontic loading of endosseous implants in the rabbit calvaria: early continuous distalizing forces. The European Journal of Orthodontics 1999;21(3):223-30.
- 316. Wennerberg A, Albrektsson T, Andersson B, Krol J. A histomorghometric study of screw-shaped and removal torque titanium implants with three different surface topographies. Clinical Oral Implants Research 1995;6(1):24-30.
- 317. Albrektsson T BP, Hansson HA and Lindstrom J. Osseointegrated titanium implants: requirements for ensuring a long lasting direct bone to implant anchorage in man. Acta Odontol Scand 1981;52:155-70.
- 318. Albrektsson T, Brånemark P-I, Eriksson A, Lindström J. The preformed autologous bone graft: An experimental study in the rabbit. Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery 1978;12(3):215-23.

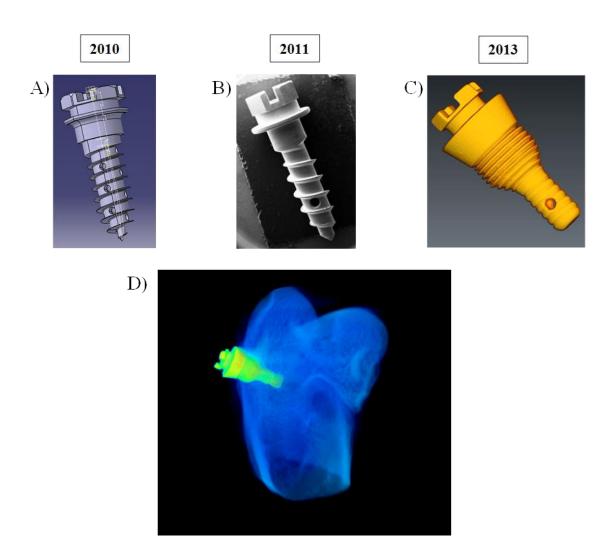


Figure 1. The Sydney Miniscrew design. (A) Initial implant introduced in 2010 (B) Implant modification in 2011 (C) Current implant design tested in this study (D) Micro CT view of current implant design in femur specimen.

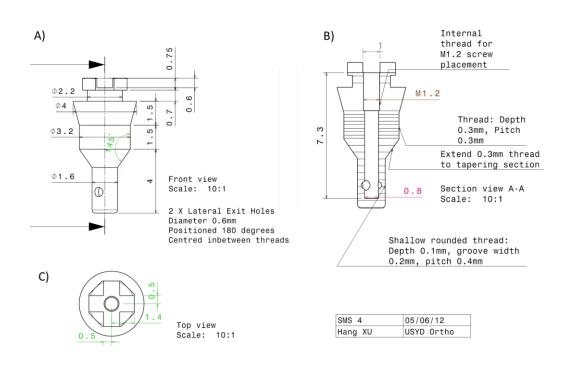


Figure 2. The Sydney Miniscrew (A) Front view dimensions and port hole location; (B) Section view dimensions; (C) Cross sectional view of the miniscrew head. (Unit: mm).

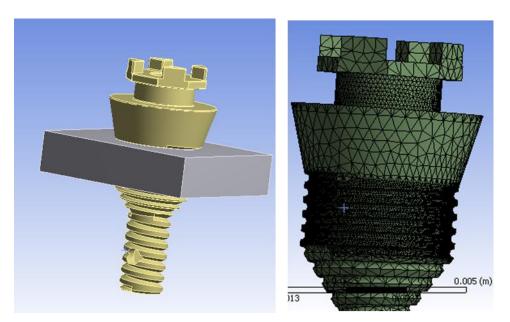


Figure 3. A 3-dimensional model of the mini-screw integrated with cortical bone (displaying in Ansys) (L) and a refined mesh creation in regions expected of larger stresses (R).

A comparative histomorphological and micro CT study of the primary stability and the osseointegration of the Sydney Mini-Screw; an animal study using New Zealand rabbits

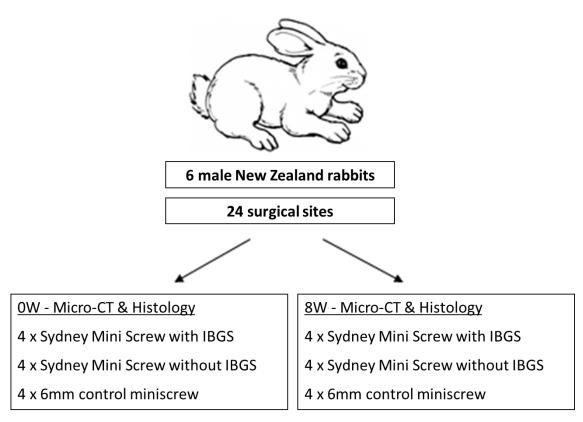


Figure 4. Animal Study Design.

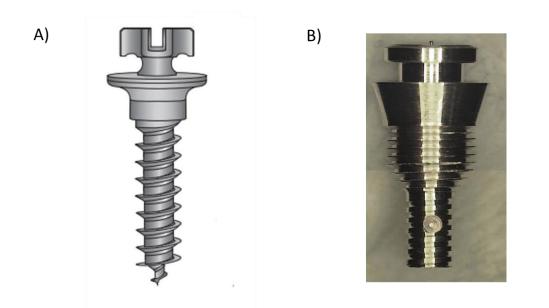


Figure 5. (A) The Arhus anchorage system, (B) The Sydney Miniscrew.

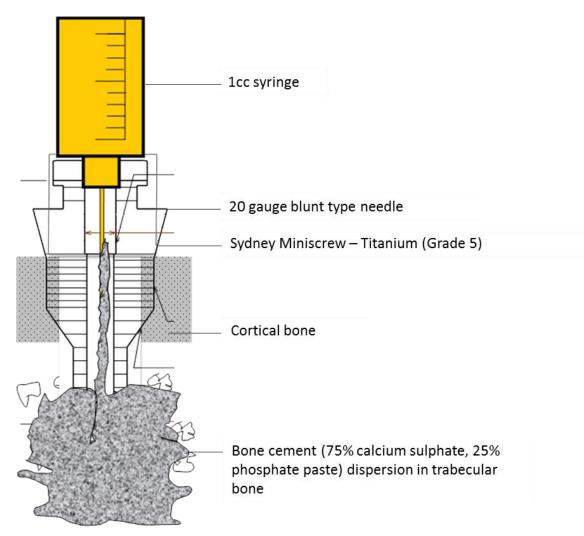


Figure 6. Bone Graft Substitute delivery through the Sydney Miniscrew. (Figure courtesy of Prof Ali Darendeliler, modified by Anastacia Bacopulos).

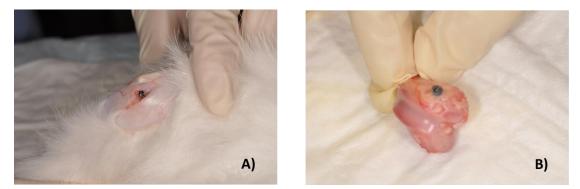


Figure 7. (A) Surgical site at 8W; (B) Bone section at 8W.

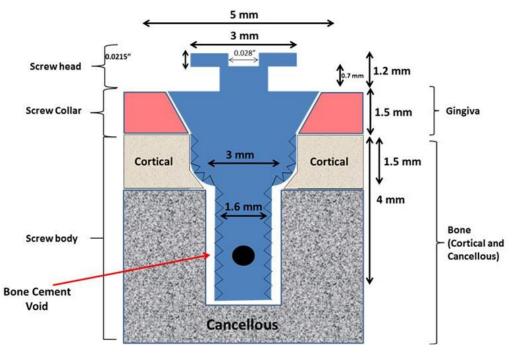


Figure 8. Schematic representation: bone sections.

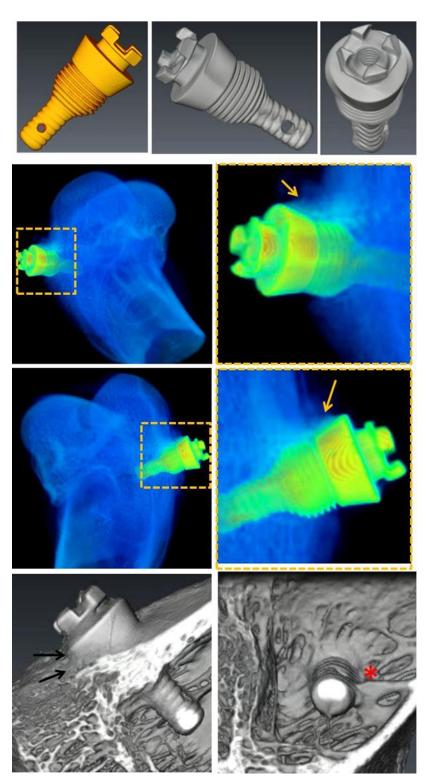


Figure 9. 3D Micro CT mapping of the Sydney Miniscrew showing superior adhesion and adoption of the miniscrew with the surrounding periosteum and hard tissue (arrow: periosteum membrane adhesion, asterisk: hard tissue).

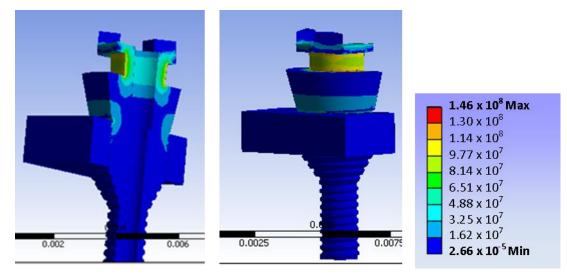


Figure 10. Equivalent (Von Mises') Stress (Pascals) contours on interior (L) and exterior (R) Mini-screw system.

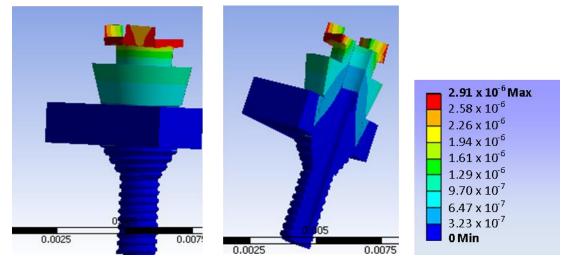


Figure 11. Total Deformation (metres) contours on exterior (L) and interior (R) Mini-screw system.

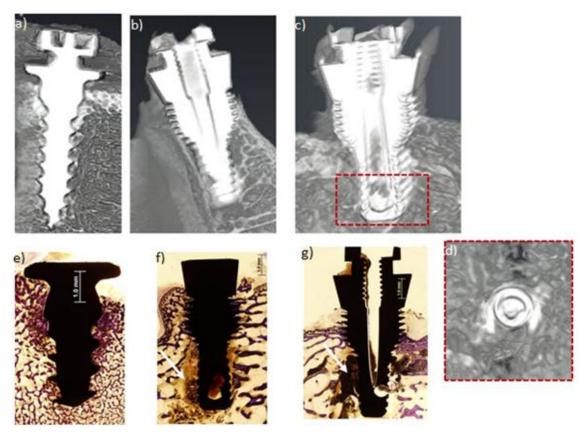


Figure 12. Micro CT scanning (a, b, c, d) and histologic (e, f, g) images of 0W Insertion of: Aarhus positive control (a, e), Sydney Miniscrew (b, f), Sydney Miniscrew with injectable bone graft substitute (c, g), axial view of Sydney Miniscrew with injectable bone graft substitute (d). Scale bar: 1 mm, arrows show the pre-drilling site in the application of Sydney Miniscrew.

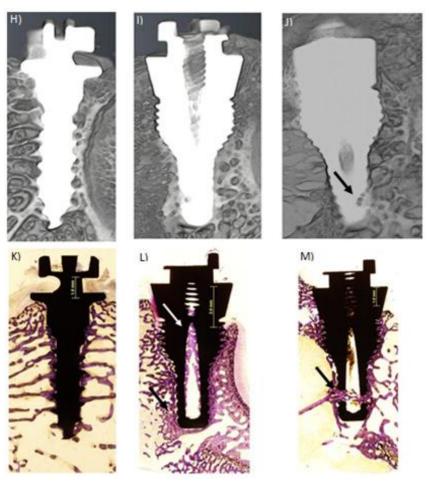


Figure 13. Micro CT scanning (H, I, J) and histologic (K, L, M) images of 8W healing of: Aarhus positive control (H, K), Sydney Miniscrew (I, L), Sydney Miniscrew with injectable bone graft substitute (J, M). Scale bar: 1 mm, arrows show the osseointegration at pre-drilling site in the application of Sydney Miniscrew.

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•	Compound	•	Mechanical Properties	•	Degradation Rate/	•	Ref
					Mechanism		
٠	CSC	•	Compression Modulus:	•	Resorb by desolation	٠	205, 209
		•	10 to 15 MPa		in body fluid in 3-6		211
					months,		
٠	BCPC	٠	Tension mod: .6±0.4	•	Macrophage or	٠	212-214
			GPa		Osteoblast		
		•	Compression mod:7.9		medicated process in		
			±0.3 GPa		6 months		
•	ACPC	٠	Tension mod: 12.3±0.8	•	Osteoclast mediated	٠	206, 213
			GPa		process,		215-219
		•	Compression mod:	•	Might be not fully		
			13.5±0.8 GPa		resorbable		

• CSC: Calcium Sulphate Cemenet; BCPC: Brushite Calcium Phosphate Cement;

ACPC: Apatite Calcium Phosphate Cement

Table 2: General properties of apatite and brushite calcium phosphate and calcium sulphate cements.

Titanium Ti-6AI-4V Grade 5 (Miniscrew)	Density = 4.43 g/cm^2		
	Elastic Modulus = 114 GPa		
	Poisson's Ratio = 0.33		
Cortical Bone	Elastic Modulus = 14.7 GPa*		
	Poisson's Ratio = 0.30*		

Table 3. Material properties of the mini-screw and attached cortical bone.*Field et. al. 2009.

		Surgery Site			
	Rabbit #	_	=	=	IV
	1	SMS-iBGS	SMS-iBGS	SMS	AC
0 week	2	SMS	AC	SMS-iBGS	SMS
	3	AC	SMS	AC	SMS-iBGS
	4	SMS	AC	SMS-iBGS	SMS
8 weeks	5	AC	SMS	AC	SMS-iBGS
	6	SMS-iBGS	SMS-iBGS	SMS	AC

Table 4. Rabbit randomization in time period 0W and 8W. I: left tibia, II: right tibia, III: left femur, IV right femur. AC: Arhus positive control, SMS: Sydney miniscrew, SMS-iBGS: Sydney miniscrew with injectable bone graft substitute.