A COMPARISON OF IMPLANT STABILITY BETWEEN IMPLANT PLACED WITHOUT BONE GRAFT VERSUS WITH BONE GRAFT USING GBR TECHNIQUE : A RESONANCE FREQUENCY ANALYSIS

Miss Rueangsiri Janyaphadungpong

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Esthetic Restorative and Implant Dentistry
Faculty of Dentistry
Chulalongkorn University
Academic Year 2016

การเปรียบเทียบเสถียรภาพของรากเทียมโดยคลื่นความถี่เรโซแนนซ์ ระหว่างรากเทียมฝังในกระดูกที่ไม่ได้รับการปลูกกระดูก กับรากเทียมฝังในกระดูกที่ได้รับการปลูกกระดูกด้วยเทคนิคจีบีอาร์

นางสาวเรืองศิริ จรรยาผดุงพงศ์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาทันตกรรมบูรณะเพื่อความสวยงามและทันตกรรมรากเทียม
คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2559

Thesis Title	A COMPARISON OF IMPLANT STABILITY BETWEEN IMPLANT PLACED WITHOUT BONE GRAFT VERSUS WITH BONE GRAFT USING GBR TECHNIQUE : A RESONANCE FREQUENCY ANALYSIS
By	Miss Rueangsiri Janyaphadungpong
Field of Study	Esthetic Restorative and Implant Dentistry
Thesis Advisor	Associate Professor Atiphan Pimkhaokham, Ph.D.

Accepted by the Faculty of Dentistry, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

.....Dean of the Faculty of Dentistry
(Assistant Professor Suchit Poolthong, Ph.D.)

THESIS COMMITTEE

.....Chairman
(Associate Professor Chalermpol Leevailoj)

.....Thesis Advisor
(Associate Professor Atiphan Pimkhaokham, Ph.D.)

.....Examiner
(Chanchai Wongchuensoontorn, Ph.D.)

เรืองศิริ จรรยาผดุงพงศ์ : การเปรียบเทียบเสถียรภาพของรากเทียมโดยคลื่นความถี่เรโซแนนซ์ ระหว่างรากเทียมฝังในกระดูกที่ไม่ได้รับการปลูกกระดูก กับรากเทียมฝังในกระดูกที่ได้รับการปลูกกระดูกด้วยเทคนิคจีบีอาร์ (A COMPARISON OF IMPLANT STABILITY BETWEEN IMPLANT PLACED WITHOUT BONE GRAFT VERSUS WITH BONE GRAFT USING GBR TECHNIQUE : A RESONANCE FREQUENCY ANALYSIS) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: รศ. ทพ. ดร. อาทิพันธุ์ พิมพ์ขาวขำ, 81 หน้า.

วัตถุประสงค์: เพื่อเปรียบเทียบเสถียรภาพของรากเทียมด้วยการวัดค่า insertion torque (IT) ในการใส่รากเทียม และการเปลี่ยนแปลงค่า implant stability quotient (ISQ) ในช่วง 12 สัปดาห์แรกหลังการผ่าตัด ระหว่างรากเทียมฝังในกระดูกที่ไม่ได้รับการปลูกกระดูก(กลุ่มควบคุม) กับรากเทียมฝังในกระดูกร่วมกับการปลูกกระดูกด้วยเทคนิคจีบีอาร์(กลุ่มศึกษา) และส่วนที่สองเป็นการหาความสัมพันธ์ระหว่างค่า IT และค่า ISQ

วิธีการศึกษา: ผู้ป่วยจำนวน 15 ราย ในกลุ่มควบคุม ได้รับการฝังรากเทียมจำนวน 20 ราก ในกระดูกที่ไม่ได้รับการปลูกกระดูก และผู้ป่วยจำนวน 7 ราย ในกลุ่มศึกษา ได้รับการฝังรากเทียมจำนวน 10 ราก ในกระดูกที่มีความวิการและได้รับการปลูกกระดูกด้วยเทคนิคจีบีอาร์ โดยผู้วิจัยจะวัดค่า IT เมื่อรากเทียมได้รับการใส่ในกระดูกอย่างสมบูรณ์แล้ว และวัดค่า ISQ ในวันที่ฝังรากเทียม และ 2, 4, 8, 12 สัปดาห์หลังการฝังรากเทียม การเปรียบเทียบค่า IT ในการใส่รากเทียม และการเปรียบเทียบการเปลี่ยนแปลงค่า ISQ ถูกวิเคราะห์ทางสถิติด้วยการวิเคราะห์ t-test, Mann-Whitney U test และ Repeated measures ANOVA ความสัมพันธ์ระหว่างค่า IT และค่า ISQ ถูกวิเคราะห์ทางสถิติด้วยการวิเคราะห์ Pearson และ Spearman correlation ที่ระดับนัยสำคัญ 0.05

ผลการศึกษา: จากการศึกษาพบว่าค่า IT ของกลุ่มควบคุมมีค่า 27.75 ± 8.96 Ncm และกลุ่มศึกษามีค่า 30.5 ± 8.96 Ncm ผลการวิเคราะห์ไม่พบความแตกต่างกันอย่างมีนัยสำคัญของค่า IT (P = 0.502) ค่า ISQ ของกลุ่มควบคุมมีค่า 74.30 ± 6.01, 69.58 ± 5.30, 71.10 ± 5.80, 75.08 ± 3.93, 77.85 ± 3.18 และค่า ISQ ของกลุ่มศึกษามีค่า 69.85 ± 7.00, 63.40 ± 8.47, 59.90 ± 10.23, 72.55 ± 3.10, 76.20 ± 2.68 ISQ ในวันที่ฝังรากเทียม และ 2, 4, 8, 12 สัปดาห์หลังการฝังรากเทียมตามลำดับ โดยกลุ่มควบคุมมีค่า ISQ แตกต่างจากกลุ่มศึกษาอย่างมีนัยสำคัญ ในสัปดาห์ที่ 2 (P = 0.021) และ 4 หลังการผ่าตัด (P = 0.007) ไม่พบความสัมพันธ์ระหว่างค่า IT และค่า ISQ ระหว่างกลุ่มควบคุมและกลุ่มศึกษา

สรุป: การศึกษานี้พบว่ารากเทียมที่ได้รับการฝังในกระดูกที่ไม่ได้รับการปลูกกระดูก และรากเทียมฝังในกระดูกที่มีความวิการและได้รับการปลูกกระดูกด้วยเทคนิคจีบีอาร์ มีค่า IT ไม่แตกต่างกัน แต่พบรูปแบบการเปลี่ยนแปลงของค่า ISQ ที่ระยะเวลา 12 สัปดาห์หลังการผ่าตัดต่างกัน และไม่พบความสัมพันธ์ระหว่างค่า IT กับค่า ISQ

สาขาวิชา ทันตกรรมบูรณะเพื่อความสวยงามและทันตกรรมรากเทียม ลายมือชื่อนิสิต .....

ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ปีการศึกษา 2559

5675832132 : MAJOR ESTHETIC RESTORATIVE AND IMPLANT DENTISTRY
KEYWORDS: DENTAL IMPLANT / FAVORABLE BONE DEFECT / GUIDED BONE REGENERATION TECHNIQUE / INSERTION TORQUE VALUE / IMPLANT STABILITY / RESONANCE FREQUENCY ANALYSIS

RUEANGSIRI JANYAPHADUNGPONG: A COMPARISON OF IMPLANT STABILITY BETWEEN IMPLANT PLACED WITHOUT BONE GRAFT VERSUS WITH BONE GRAFT USING GBR TECHNIQUE : A RESONANCE FREQUENCY ANALYSIS. ADVISOR: ASSOC. PROF. ATIPHAN PIMKHAOKHAM, Ph.D., 81 pp.

Objective : To compare the implant stability using the insertion torque (IT) and implant stability quotient (ISQ) values over the 12 weeks period between implant placement in bone without bone graft (control group) and with bone graft using the guided bone regeneration (GBR) technique (study group). The secondary objective was to assess the correlation between the IT and ISQ values of the two groups

Materials and Methods : In the control group, 20 implants were placed in bone without bone regeneration in 15 patients, whereas in the study group, 10 implants were placed in favorable bone defects at buccal aspect with simultaneous guided bone regeneration in 7 patients. IT (Ncm) of each implant was recorded when fully inserted. ISQ values were obtained from the Osstell® ISQ at the time of implant placement, and at 2, 4, 8, and 12 weeks. The differences between two groups were analyzed by the t-test, the Mann-Whitney U test and the Repeated measures ANOVA. The Pearson and the Spearman correlation tests were used to analyze statistical correlations. All of the analyses were performed using a 95% confidence level.

Results : The mean IT values of the control group was 27.75 ± 8.96 Ncm and the study groups was 30.5 ± 8.96 Ncm. No difference in IT was found between the two groups (P = 0.502). The mean ISQ values at baseline and at 2, 4, 8, and 12 weeks of the control group were 74.30 ± 6.01, 69.58 ± 5.30, 71.10 ± 5.80, 75.08 ± 3.93 and 77.85 ± 3.18, respectively, and the mean ISQ values of the control group were 69.85 ± 7.00, 63.40 ± 8.47, 59.90 ± 10.23, 72.55 ± 3.10 and 76.20 ± 2.68. Statistically significant differences in the mean ISQ values between the control and study groups were found at 2 weeks (P = 0.021) and at 4 weeks (P = 0.007). There was no significant correlation between the IT and ISQ values of the control and study groups.

Conclusions: There was no difference in IT between the control and study groups, while the difference in the changes of ISQ values during the 12 weeks healing period between implant placement without bone graft and with bone graft using the guided bone regeneration (GBR) technique were found. There was no correlation between the IT and ISQ values.

Field of Study: Esthetic Restorative and Implant Dentistry Student's Signature .....
Advisor's Signature .....

Academic Year: 2016

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my thesis advisor, Associate Professor Atiphan Pimkhaokham, Ph.D. for the useful comments, for his guidance, patience and kindness through the time of my master degree thesis.

I would also like to express my gratitude to Associate Professor Chalermpol Leevailoj and Assistant Professor Sirivimol Srisawasdi, Ph.D. for their encouragement, valuable instructions and helpfulness.

I am grateful to my thesis supervisory committee, Dr. Chanchai Wongchuensoontorn , Ph.D. for sharing their expertise and providing precious comments to improve the methodology of this research. My thanks also go to Assistant Professor Tewarit Somkotra, Ph.D. and Associate Professor Chanchai Hosawaun for their great comments and discussions on statistic choice.

My sincere thanks also go to all the teachers, staffs and dental assistants of Esthetic Restorative and Implant Dentistry program for providing a great knowledge and support. Also, I would like to thank the participants in my research, who have willingly shared their precious time entire the process. I would like to thank my friends, my seniors, my juniors who always beside and support me through the difficult time of my graduate study.

Finally, I must express very gratitude to my parents for providing me with their love, support and understanding through my years of study. This accomplishment of my master degree would have not been possible without them.

This research is supported by the 90th Anniversary of Chulalongkorn University, Ratchadaphisek Somphot Endowment Fund.

CONTENTS

Page

Page

Page

LIST OF TABLES

LIST OF FIGURES

CHAPTER I

INTRODUCTION

Rationale and Significance of the Problem

Oral rehabilitation using titanium dental implant has been increasingly performed since osseointegration concept was introduced by Brånemark and associates [1]. Long term successful osseointegration was supported by several studies [2-4]. Implant stability has been defined as an absence of implant mobility. Maintaining of implant stability is a prerequisite to achieve osseointegration [5, 6]. In addition, it has been proposed as one of the factors influencing the timing of functional loading [7-9]. Stability of dental implant depends on the bone-related factors, the surgical technique and the implant characteristics [10, 11]. Nevertheless, reduction in alveolar ridge width after tooth extraction may cause horizontal bone defects at the planned implant site. Horizontal bone defects include a dehiscence and a fenestration defects, which can compromise, the stability of implant, the long term success rate and the esthetic outcomes of the definitive restoration. To overcome this problem, different bone augmentation techniques have been generated. A guided bone regeneration (GBR) is a surgical technique using grafting

materials combined with barrier membranes to maintain and stimulate growth of new bone into the defect sites [12, 13].

Various methods have been developed for accessing implant stability including the invasive and the non-invasive clinical test methods. One of the objective and non-invasive measurement methods is an insertion torque (IT). Insertion torque is a torque values generated during the thread placement procedure into the osteotomy site [14]. Previously, there are some studies reported the stability of implant using IT measurement [15, 16]. High torque number (Ncm) is determined as high implant stability. However, this method could not be reproduced after implantation.

Resonance frequency analysis (RFA) is a recent non-invasive electronic devices monitoring changes in implants stability with high repeatability and reliability results [10, 17, 18]. The stiffness of the implant-bone complex was determined by the Osstell apparatus (Integration Diagnosis AB, Gothenberg, Sweden) and displays as an implant stability quotient (ISQ) value, ranges from 1 (lowest stability) to 100 (highest stability). The acceptable ISQ is between 55 to 85 with the average of 70 [19-21]. An ISQ value below 55 should be regarded as a warning sign, unloading and allowing a longer period of healing should be considered.

For the last ten years, the RFA has been performed increasingly to provide a quantitative measurement of implant stability. The repeated measurements of the ISQ values over the healing period were performed to monitor the changes in implant stability during the osseointegration process [22-27]. Arnotharom in 2011 [28] reported the difference in the ISQ values in different bony structure. Thongborisoot in 2012 [29] compared the changes in implant stability between implant with SLA and SLActive surface using the RFA. The knowledge in the development of implant stability is important to verify the optimal healing time prior implant loading.

The effect of peri-implant bone defect on implant stability measured by RFA was previously reported. An experimental researches suggested a correlation between the peri-implant bone defects and the ISQ values [30-32]. However, the study of the IT value and the development of implant stability measuring by RFA over the healing period of implant placed in favorable bone defect with simultaneous GBR have not been well-documented.

Therefore, the primary objectives of the present study were to compare the IT values and monitor the longitudinal changes in ISQ values as a reflection of the stability between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique. The secondary objective was to assess the relationship between the IT and ISQ values.

Research Question

1) Are there any significant difference in the insertion torque values and the changes of ISQ values of the implant placement in bone without bone graft versus implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique ?

2) Is there any significant correlation between the insertion torque values and ISQ values of the implant placement in bone without bone graft versus implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique ?

Research Objectives

The Primary Objectives of the present study were

1) To compare the insertion torque values between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

2) To monitor the longitudinally changes in ISQ values as a reflection of the implant stability between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

The Secondary Objective of the present study was

1) To assess the correlation between the insertion torque values and ISQ values of the implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

Primary Hypothesis

Null Hypothesis

1) There is no significant difference in the insertion torque values between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

2) There is no significant difference in the longitudinally changes in ISQ values between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

Alternative Hypothesis

1) There is a significant difference in the insertion torque values between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

2) There is a significant difference in the longitudinally changes in ISQ values between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

Secondary Hypothesis

Null Hypothesis

1) There is no correlation between the insertion torque values and ISQ values of the implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

Alternative Hypothesis

1) There is a correlation between the insertion torque values and ISQ values of the implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

Conceptual Framework

Population : 30 OsseoSpeed™ EV Implants placed in the posterior mandible.

Intervention : The use of GBR technique to correct favorable bone defect

The insertion torque measurements at the time of implant placement

The ISQ measurements at day 0, and 2, 4, 8 and 12 weeks

Outcome measurement :

1) The insertion torque (IT) values (Ncm) from calibrated torque wrench were measured at the time of implant placement [33].

2) The Implant Stability Quotient (ISQ) values from resonance frequency analysis (Osstell ISQ : Osstell AB, Integration Diagnosis, Gothenburg, Sweden) were measured at day 0, and 2, 4, 8 and 12 weeks [23-25, 27].

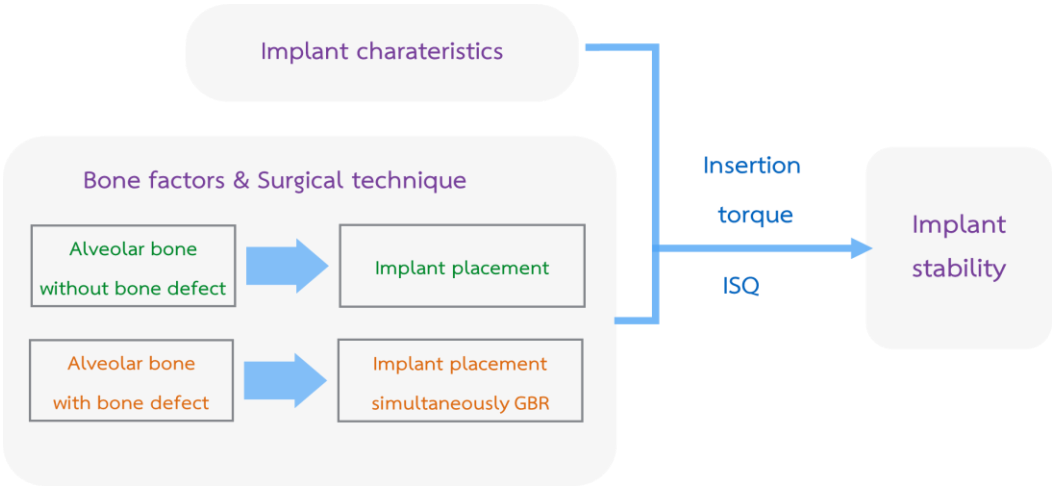

Figure 1: The conceptual framework in normal clinical situation

In clinical situation, lots of factors affected implant stability including insufficient alveolar bone, fenestration or dehiscence defect at the implant site, poor bone quality, implant geometry, improper and traumatic surgical technique.

In the present study, all implants were placed in a single center (Faculty of Dentistry, Chulalongkorn University, Thailand) using the same surgical protocol. The OsseoSpeed™ EV implant (OsseoSpeed, ASTRA TECH EV Implant System, DENTSPLY Implants, Mölndal, Sweden) 4.2 mm in diameter were placed in the posterior mandible. Therefore, the favorable bone defect simultaneously grafted with GBR technique being one of the major variable affected the insertion torque and the ISQ values. All the insertion torque values and the ISQ values were measured by one-trained evaluator in order to decrease confounding factors, systemic bias and increase validity.

Variations

- Favorable bone defect which the width of the defect was less than one third of the mesio-distal dimension as described by Sclar in 2003 [34] simultaneously grafted with the GBR technique

Method of Testing

- The insertion torque measurement
- The resonance frequency analysis

Assumption

Every implants were assumed to be placed strictly according to the manufacturer's instruction. Furthermore, all the GBR procedures were considered the same in all cases.

Limitations

The populations included in this study were patients needed of implant therapy at the posterior mandible. Patients must have adequate bone volume at the planned implant site to placed the OsseoSpeed™ EV implant, 4.2 mm in diameter, in a prosthetically ideal position and achieve optimum primary stability.

Key Words

Dental implant, favorable bone defect, guided bone regeneration technique, insertion torque value, implant stability, resonance frequency analysis

Expected Benefit of the Study

The results from the study will be the background for a further clinical study in the same field of interest. If there were no significant difference in the insertion torque value and the pattern of the changes in ISQ values between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique, these could be inferred that loading the OsseoSpeed™ EV implant placed with simultaneous GBR at favorable bone defect, could be the same time as implants placed in bone without bone graft.

If there were significant difference in the insertion torque value and the pattern of changes in ISQ values between implant placement in bone without bone graft and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique, these could be inferred that loading the OsseoSpeed™ EV implant placed with simultaneous GBR at favorable bone defect, should be extended to ensure implant stability and osseointegration.

CHAPTER II

REVIEW OF THE LITERATURES

The literature in the following topics were reviewed.

2.1) Dental implant and osseointegration

2.2) Implant stability

- Definition of implant stability
- Factors influencing implant stability
- Implant stability evaluation methods

2.3) Resonance frequency analysis

- The resonance frequency analysis method
- Factors influencing resonance frequency analysis

2.4) Guided bone regeneration technique

- Concept of Guided bone regeneration
- Barrier membrane : Bio-Gide
- Grafting material : Bio-Oss

2.1) Dental implant and osseointegration

Oral implant supporting dental prosthesis has been extensively performed since osseointegration concept was introduced by Brånemark and associates [1]. Osseointegration has been defined as " a direct bone to implant contact without interposed soft tissue layers " or " a direct structural and functional connection between living bone and the surface of a load-carrying implant " [5]. When the implant is stable in the bone site, new bone which has similarly appearance to that found in the mature original bone, will form and remodel direct on the implant surface [6, 35, 36]. A direct bone to implant contact (BIC) increases with time during the healing period. A histologic analysis of the 1 to 16 years functioned implants on humans revealed the bone tissue inside the threads of implants with the average BIC and surface around 80% [37].

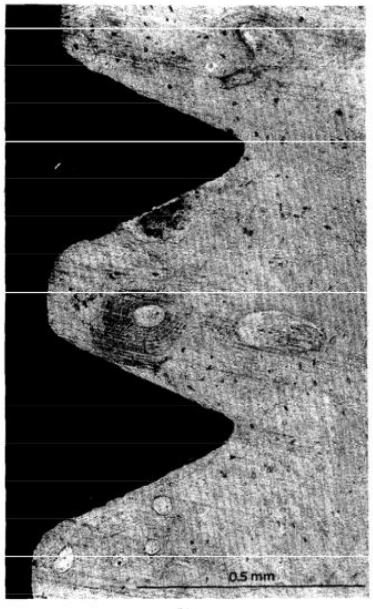

Figure 2: A Histologic section presented a well organized lamella and osteocyte lacunae with canaliculae close to the implant surface.

Reprinted from Albrektsson T, Eriksson AR, Friberg B, Lekholm U, Lindahl L, Nevins M, et al. Histologic investigations on 33 retrieved Nobelpharma implants. Clin Mater. 1993; 12 (1): 1-9. [37]

One of the important factors for achieving and maintaining osseointegration is an implant stability which was defined as an absence of implant mobility. For a recent years, the studies of implant stability have been increasingly focused.

2.2) Implant stability

2.2.1) Definition of implant stability

A clinical definition of osseointegration termed by Zarb and Albrektsson is " a process whereby clinically asymptomatic rigid fixation of alloplastic materials is achieved, and maintained, in bone during functional loading "[7]. In other words, a clinical manifestation of osseointegration is an absence of implant mobility [38]. The rigid fixation of implant or implant stability has been identified as a prerequisite to achieve osseointegration and proposed as one of the factors affecting implant loading and long-term success.

Implant stability can be divided into 2 phases, primary (mechanical) and secondary (biological) stability. The proportion of mechanical and biological stability varies during the healing period. At the time of implant installation, implant stability is based purely on the mechanical retention between the implant and the bony bed. The mechanical or primary stability decreases with time by the osteoclastic activity. Lack of the primary stability may lead to

less bone to implant contact compared to the stable implant [39]. An excessive micromovement during healing period may disrupt bone formation on the implant surface and may lead to fibrous tissue encapsulation instead of osseointegration [40]. Three weeks after implant placement is considered a critical period. The lowest implant stability is expected during this period due to the loss of mechanical stability and the biological stability has not yet achieved [41, 42]. Following this, biological stability increases owing to the formation of newly form bone on the implant surface [17, 27, 41, 43]. Finally, for the oseeointegrated implant, implant stability relies on the biologic component [26, 44]. Therefore, the knowledge in the development of implant stability during healing period is important in order to verify the optimal healing time prior functional loading. Non integrated implant can be defined by a clinically mobility [2].

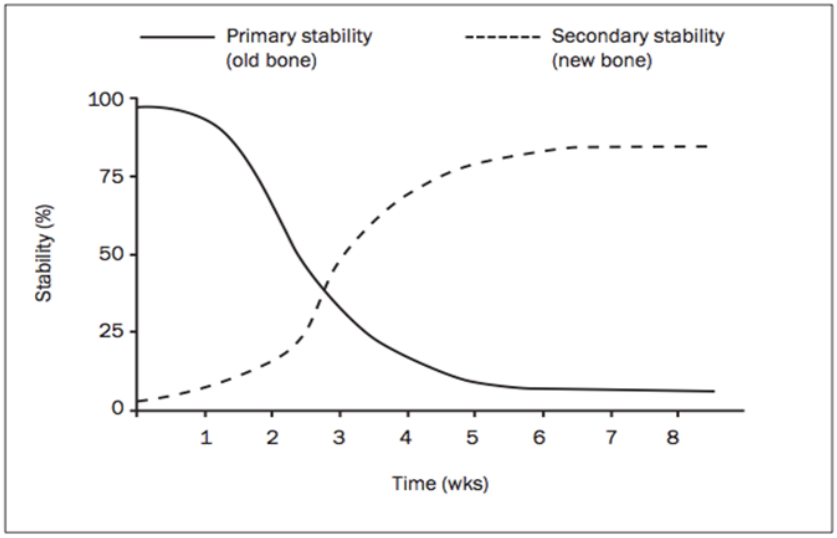

Figure 3: A schematic drawing of the changeover from primary stability to secondary stability by osseointegration in humans.

Reprinted from Raghavendra S, Wood MC, Taylor TD. Early wound healing around endosseous implants: a review of the literature. Int J Oral Maxillofac Implants. 2005 ; 20 (3) : 425-431. [42]

2.2.2) Factors influencing implant stability

Implant stability is depended on the bone-related factor, the surgical technique and the implant [6, 10, 11].

Alveolar bone loss can occur due to congenitally missing tooth, periodontal disease, periapical pathology, trauma and tooth extraction. Schropp and coworkers [45] demonstrated that the width of the alveolar ridge could reduce by 50% from the original site following 12 months after tooth extraction. Reduction in alveolar ridge width may cause horizontal bone defects at the planned implant site, including dehiscence and fenestration defects which can compromise the long-term success rate, the stability of the implant and the esthetic outcome of the definitive restoration. Moreover, the resorption occurs most at the buccal side of the jaw and maxillary sites resorbs greater than mandibular site. Sclar in 2003 [34] classified an osseous defect of the buccal alveolar crest that " defects are considered either favorable or unfavorable when the width of the defect is less than or greater than one third of the mesio-distal dimension between the adjacent teeth ". A site with favorable defect has a better potential for bone regeneration and reconstruction by guided bone regeneration procedure.

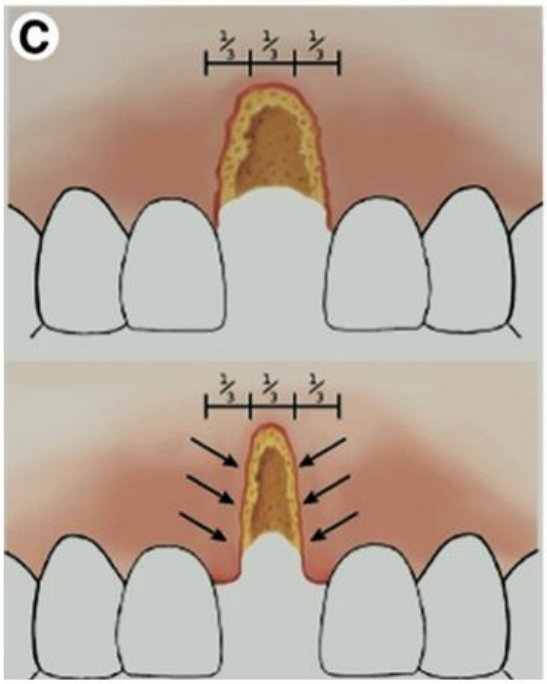

Figure 4: A schematic illustrating of favorable and unfavorable bone defects.

Reprinted from Sclar AG. The Bio-Col technique, soft tissue and esthetic considerations in implant therapy. Chicago, Quintessence : 2003 ; 75-112. [46]

Numerous studied have reported an association between bone quality and implant stability [47, 48]. Lekholm and Zarb in 1985 [49] developed a bone classification system based on the amount of compact bone and trabecular bone into 4 type : Type I bone is a hard and dense homogenous compact bone. This type of bone has less blood supply and tends to increase risk of overheating during implant site preparation. Therefore it can lead to bone necrosis and non-integrated implant ; Type II bone has a thick layer of compact bone with a dense trabecular bone inside. It provides lots of blood supply and good initial stability ; Type III bone has a thin layer of compact bone surrounded a dense trabecular bone and ; type IV bone has a thin layer of cortical bone with a low density trabecular core. This type provides less primary stability due to its poor quality.

A correlation between bone quality and regions of the jaws have reported in many studies. Mandibles are generally denser than maxillas and both jaws tend to decrease in bone quality when they are in posteriorly. Most of the posterior mandible has bone quality in type II and III and theses two types of bone are difficult to predict the differences either by computed tomography scans (CT) or a histomorphometric analysis [50, 51].

The second factor associated with implant stability is a surgical technique. At the time of implant site preparation, heat is generated from the bone drilling procedure, especially at the superficial part of the site. Increasing temperature at the time of preparation can cause thermal bone injury. Erikssson and associates demonstrated that human bone has a critical temperature at 47 °C, when the temperature exceeds more than 47 °C for 1 minute, bone necrosis can be occured [52]. Therefore, to minimize the temperature during procedure, saline irrigation must be used. External irrigation with saline solution is proved to decrease temperature below the critical level of 47 °C [53]. In addition, precise drilling technique is also important to get the stable implant. Clinicians who have inadequate skill possible to create ill-fitted implant bed. An oversize preparation may lead to the cause of implant micromotion and non-integrate. On the other hand, undersize preparation, a technique using a smaller drill than the implant size, can cause compression at the implant-bone interface. This compressive stress is called “ Hoop stresses which may be beneficial in enhancing primary implant stability ” [10].

The last factor affected implant stability is an implant surface. The use of titanium as material for dental implant is well-accepted with high predictability result and high success rate of osseointegration [1, 2, 6]. After exposed to oxygen, an oxide layer formed on the titanium surface, this oxide layer is stable and makes the surface bioinert. However, due to long healing time from implant insertion to loading, limited load-bearing capacity of the implant at the initial period and loss of marginal bone, an improvement of the implant surface to motivate bone biological response has been developed.

Two main methods for treating implant surface are addition and subtraction methods. The addition methods add various materials to the titanium surface by titanium plasma spraying, hydroxyapatite coating and calcium phosphate coating. The subtractive methods remove part of titanium surface by blasting and acid etching treatment. The above mentioned treatments create surface microtopography which can be classified into three degree based on the surface area (S_a value) : turned surface or minimally rough surface (S_a value less than 1 μm), moderately rough surface (S_a value between 1 to 2 μm) and very rough surface (S_a value more than 2 μm) [54]. A histologic studies in human revealed a higher bone-to-implant contact (BIC) values of the rough surface than the turned surface [55, 56] and the moderately rough surface showed strongest bone response .

For a recent decades, surface modification with chemical agents has been focused. Fluoride was selected due to its calcium-binding capacity and its effect on osteoblasts. The OsseoSpeed™ Implant System (Dentsply Implants, Mölndal, Sweden) is made of grade 4 titanium, blasted with TiO_2 particles and chemically treated with diluted hydrofluoric acid (HF). The surface roughness S_a is 1.32 - 1.82 μm resulting in a moderately rough surface with a nanoscale structure. The nanoscale structure favours bone regeneration and the remaining fluoride ions, with high electronegative at the TiO_2 surface, have an effect on attracting calcium ions and phosphate groups to the surface. An in vitro and in vivo studies reported the effects of fluoride-modified surface on promoting fibrinogen activation and rapid coagulation resulting in promoting osteoblast migration and differentiation [57, 58]. Furthermore, a histomorphometric analysis on humans demonstrated that the Osseospeed™ implants had a better bone deposit and almost 2 times higher bone-to-implant contact (BIC) values compared to the control implants [59]

2.2.3) Implant stability evaluation methods

Implant stability is an absence of implant mobility. It has been observed that over micromovement during the healing period can disrupt the osseointegration and lead to fibrous tissue formation. Continuous measurement of implant stability from the time at installation is important in order to predict the prognosis and determine the optimum healing period prior to

implant loading. Several different diagnosis methods have been invented for assessing implant stability including the invasive and the non-invasive clinical test methods [10].

Invasive clinical test methods

The histologic and histomorphometric analysis is a gold standard technique to provide the information on the percentage of bone to implant contact and the amount of bone within the threads of implant. However, these procedure needs to take biopsies of the implant and the surrounding bone. Therefore, it is considered a destructive methods and does not seem practical in a clinical practice.

The reverse torque test is a test that apply a counter-clockwise torque to remove implant. Torque is increased until reach the critical torque threshold where bone to implant contact is destroyed [14]. Sullivan and colleagues [60] reported that implant failure occurred in the 45 to 48 Ncm range, whereas reverse torque no greater than 20 Ncm is acceptable as reliable. Nevertheless, Brånemark reported that the reverse torque might result in irreversible plastic deformation leading to implant failure [1].

Non-invasive clinical test methods

The percussion test with a metallic instruments is one of the simplest non-invasive methods to identify osseointegration. This test determines resonance and damping of an implant from the sound created by the percussion. A crystal sound indicate a successful osseointegration.

On the other hand, dull sound may indicate non-integration. However, this method relies on the clinician's experience and is considered insensitivity to detect changes in implant stability.

The radiographic assessment provides information on osseointegration and level of peri-implant bone which can effect implant stability. Precise measurement requires perfectly parallel technique to prevent distortion, but it is difficult to standardize reliable and repeatable radiograph. In addition, radiograph has two-dimension so, changes in facial bone and changes within bone structure are barely detected. Goodson also reported that the correlation between disease activity and radiographic analysis was weak and did not appear to be capable of detecting early changes in bone mineral [61].

The cutting torque resistance test measures the torque during cutting off the bone at the time of preparing the fixture site. Instead of the resistance sensation experienced by the surgeon, a torque gauge connected to a drilling unit is developed to gain more objective assessment. The cutting resistance values demonstrated correlation with bone quality which is one of the factor influencing implant stability [62]. The limitations of this method are it cannot provide pre-operative bone quality assessment and a serial measurement cannot be done.

The insertion torque is the torque forces needed to seat the implant into the prepared bone site. Johansson and Stride described an insertion torque technique whereby " bone quality as a function of density and hardness could be derived from the torque values generated during

the thread placement procedure ". They postulated that " the energy used to place the implant into the site is a combination of the thread placement force from the tip of the instrument and the friction created as the remaining part of a tap or implant enters the site " [14]. Implant insertion and primary stability were standardized with a minimum insertion torque of 20 Ncm [63, 64].

The recent non-invasive electronic measuring devices have been invented to provide an objective changes in implants stability. They are the Periotest® and the resonance frequency analysis (RFA).

Periotest® (Siemen AG, Bensheim, Germany) is designed to measure the degree of periodontal integration of tooth and the stiffness of the implant/bone interface. The technique used in Periotest® bases on the damping characteristics of tissues surrounding tooth or implants [65]. An electronically tapping head percusses the tooth or implant then, the response is measured by a small accelerometer. The contact time of the tapping rod to the object is recorded and transformed to a value called the Periotest values (PTV). The stable tooth and implant gives short contact times, which means the low Periotest values. Natural tooth mobility has a wide range of the Periotest value from -8 to +50. On the contrary, range of implant mobility is narrower due to lack of periodontal ligament. The normal PTV of osseointegrated implant range from -5 to +5. The values above 10 PTV units are considered insufficient/failure of

osseointegrated [66]. However, a number of studies reported factors influencing the PTV including the striking point, the handpiece angulation and the abutment length. An investigation of Meredith demonstrated a greater effect of the striking point ; the variation of the PTV with striking height was approximately 1.5 units per millimeter [67]. Owing to the variable influencing accuracy of Periotest®, the use of this instrument is considered lack of resolution, poor sensitivity and susceptible to operator variables.

2.3) Resonance frequency analysis

2.3.1) The resonance frequency analysis method

Resonance frequency analysis (RFA) was introduced by Meredith and colleagues in 1996 [68] as a recent non-invasive electronic device measuring implant stability. The RFA is designed bases on a flexural test of the implant/bone complex. The RFA system originally composes of an excitation source, a computer analysis and a transducer. The transducer comprises of a small offset cantilever beam which two piezo elements are attached. One of the piezo elements is stimulated by a sinusoidal signal from a frequency response analyzer and the other is a receptor of the signal. The resonance frequency of the system is calculated from the peak amplitude of the signal which can vary from 5 KHz to 15 KHz [68].

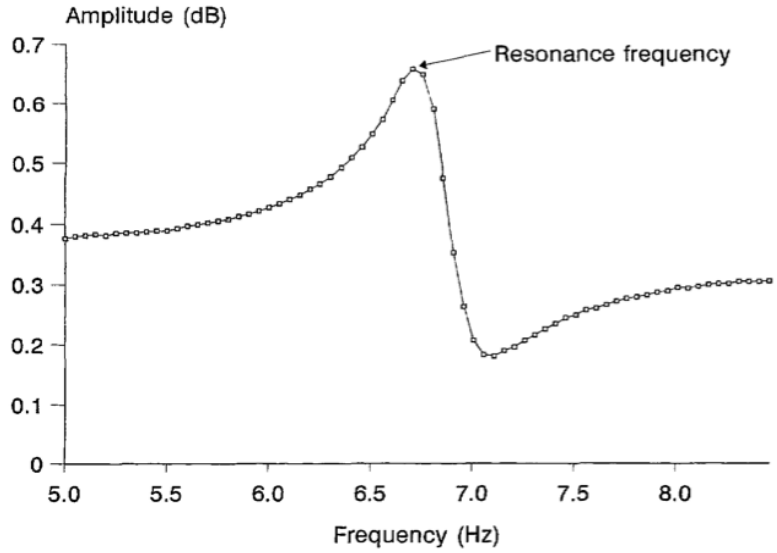

Figure 5: Plot of frequency against amplitude of a transducer attached to implant.

Reprinted from Meredith N, Alleyne D, Cawley P. Quantitative determination of the stability of the implant-tissue interface using resonance frequency analysis. Clin Oral Implants Res. 1996 ; 7 (3) : 261-267. [68]

The first commercially RFA was the Osstell® (Osstell AB, Integration Diagnosis Gothenburg, Sweden). In this generation, a transducer was pre-calibrated from a manufacturer for various implant systems. The second commercially version was the Osstell® Mentor (Osstell AB, Integration Diagnosis, Gothenburg, Sweden) and the latest version was the Osstell® ISQ (Osstell AB, Integration Diagnosis, Gothenburg, Sweden). The transducer or the SmartPeg (SmartPeg, Integration Diagnostics AB) which small magnet has been attached on top, was screwed to a fixture and then stimulated by a magnetic pulses from the Osstell® instrument. An outcome has been given in implant stability quotient (ISQ) units in place of hertz. The ISQ units range from 1

(lowest stability) to 100 (highest stability). The acceptable ISQ level is between 55 to 85 with the average of 70 [19-21]. The ISQ value less than 55 should be regarded as a warning sign, unloading and allowing a period of healing should be considered.

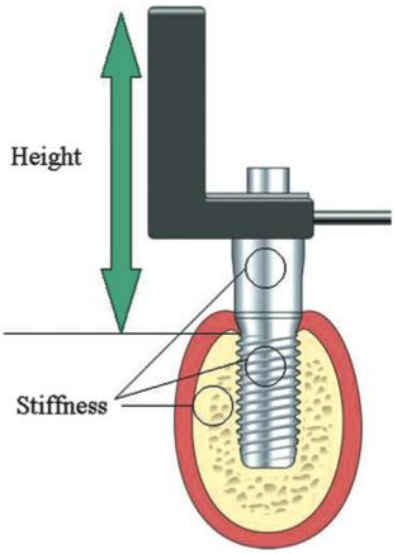

Figure 6: A schematic showing the factors effect resonance frequency : the design of the transducer, the stiffness of the implant-bone junction, the total effective length above the marginal bone level.

Reprinted from Sennerby L, Meredith N. Implant stability measurements using resonance frequency analysis: biological and biomechanical aspects and clinical implications. Periodontol 2000. 2008 ; 47 : 51-66. [43]

2.3.2) Factors influencing resonance frequency analysis

The resonance frequency analysis depends on three main factors ; the design of the transducer, the stiffness of the implant-bone junction and the total effective length [43].

The first factor is the design of the transducer or peg. The SmartPeg have difference in length, thread type, diameter and connection surfaces which are designed for different implant systems. In order to receive a precise ISQ value, the peg must be exactly matched with type of implant and screw in a correct direction.

Secondly, the stiffness of the implant-bone junction which is depended on the stiffness of an implant as a function of its characteristics, the stiffness of the surrounding tissue and the stiffness of the bond between the surface of the implant and the surrounding bone.

Implant characteristics include implant length, diameter and overall shape. The studies of implant length on RFA suggested that there was no impact of implant length on RFA [23, 69, 70]. However, most of the studies indicated that implant diameter have a significant effect on RFA measurement, as wider diameter demonstrated higher ISQ values [69, 70]. Moreover, the results from many studies showed no significant difference on RFA values between different implant designs [28], excepted in the type IV bone, it is showed that tapered implant could be affect RFA value [15].

The stiffness of the surrounding tissue is related with the bone density and the ratio of compact to trabecular bone which an implant engages. Several investigations reported higher ISQ value in denser bone [27, 28, 70]. Typically, mandibles demonstrated higher ISQ value than maxillas and both jaws tend to decrease in ISQ value when they are in posteriorly [51, 69]. This difference in ISQ value has been attributed to the difference in bone morphology and the ratio of compact to trabecular bone.

The stiffness of the implant-bone interface has been evaluated both in vitro and vivo studies. Longitudinal changes in the stiffness of the bond between the implant surface and the surrounding bone were observed. Meredith and colleagues [68] attached the transducer to an implant placed in a self polymerizing acrylic resin to simulate changes of the stiffness of bone during healing and remodeling period. The resonance frequency was measured during polymerization. The experiment resulted that the RFA can monitor the changes in stiffness. Due to the fact that a histological method is a gold standard to evaluate osseointegration, Meredith and colleagues [22] did an animal study to determine a correlation between bone to implant contact (stiffness) and the changes in resonance frequency. The results from the study found that an increase in bone to implant area conformed with an increase in resonance frequency.

The last factor affected the RFA is a total effective length above a marginal bone level. The effective implant length (EIL) is the length of a fixture above a bone combined with the length of a transducer or abutment. In fact that the length of the transducer/abutment is constant, the effective length is depended on the changes in bone level around the fixture (length of fixture exposed) [11, 43]. The results from an experimental study showed that more exposed of implant height resulting in less resonance frequency [68]. Moreover, an in vivo study of resonance frequency measurements on Brånemark implants after 5 years placement

confirmed a correlation between the effective implant length (EIL) and the resonance frequency [17].

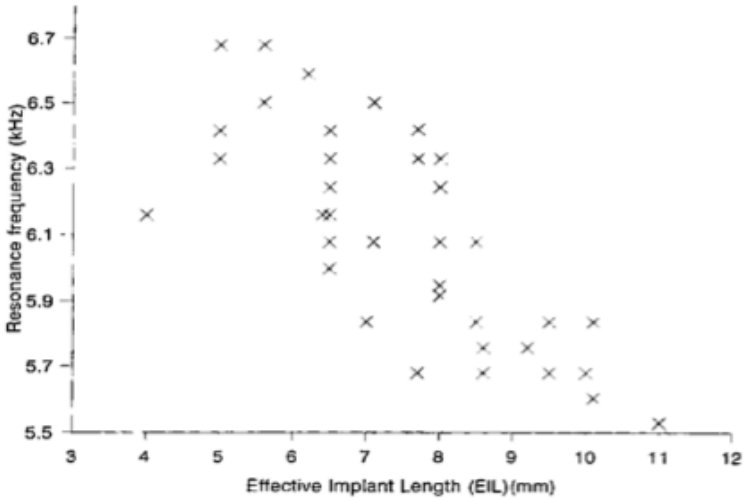

Figure 7: Plot of correlation between resonance frequency and effective implant length (length of abutment and exposed fixture height above bone).

Reprinted from Meredith N, Book K, Friberg B, Jemt T, Sennerby L. Resonance frequency measurements of implant stability in vivo. A cross-sectional and longitudinal study of resonance frequency measurements on implants in the edentulous and partially dentate maxilla. Clin Oral Implants Res. 1997 ; 8 (3) : 226-233. [17]

The Osstell® apparatus has been increasingly performed in clinical research to evaluate the development in implant stability during the healing periods. Arnotharom in 2011 [28] measured the ISQ values in various implant characteristics and bone structure at the time of implant placement and then every week for three months. Thongborisoot in 2012 [29] measured the ISQ values of two different implant surfaces at day 1, day 2 and then at 1, 2, 3 ,4 and 8

weeks. Cassette et al. [71] measured the ISQ values in grafted sites at implant placement, surgical reentry (2 month), each month up to 12 months and each year up to 5 years. Bischof et al. and Nedir et al. [23, 24] measured the ISQ values at the day of implant placement and at 1, 2, 4, 6, 8, 10 and 12 weeks. The results showed that the mean ISQ remained constant or slightly increased during the first 4–6 weeks, then started to increase more noticeably and the ISQ at 12 weeks was significantly higher. In addition, a review literature of Raghavendra and collaegues [42] found that the critical time of implant healing in humans would be 2 to 3 weeks post implant placement, due to the timeline of osseointegration. Therefore, an evaluation of implant stability over the first 3 months is important, in order to evaluate possible changes in implant stability and determine the proper timing for implant loading.

2.4) Guided bone regeneration technique (GBR)

Alveolar bone loss can occur from periodontal disease, periapical lesion, trauma and tooth extraction. Alveolar bone atrophy is a well-known problem for implant placement. Loss of ridge width may cause horizontal bone defects at the planned implant site. Horizontal bone defects may result in a dehiscence or a fenestration defects. An exposing implant surface may be occured which can compromise the long-term success rate, the stability of implant and the

esthetic outcomes of the definitive restoration. However, healing of the bone defects was considered a significant problem. Melcher in 1967 [72] described that " osteogenesis in repair of a bone wound can be inhibited by invasion of the site by non-osteogenic cells that presumably exclude the migrating osteogenic cells ". To overcome this problem, several techniques have been invented, a guided bone regeneration (GBR) technique is the most popular one. The GBR technique uses barrier membranes to protect the blood clot, maintain spaces over the defects, preventing migration of the cells from the soft tissues and promoting ingrowth of osteogenic cells [13]. GBR procedures can be gained with non-resorbable or resorbable membranes with or without grafting materials including autogenous bone, allografts (same species), xenografts (another species) and alloplastic (synthetic) materials. The main disadvantage of the non-resorbable membranes is membrane exposure leading to bacterial contamination, early removal of the membrane and subsequently reduced amount of bone fill at the defects.

Currently, there has been several studies supported the use of Bio-Gide combined with Bio-Oss for GBR procedures at dehisced implant surface at the time of implant placement [73-75]. Bio-Gide® (Geistlich, Wolhusen, Switzerland) is a resorbable non cross-linked porcine derived type I and III collagens membrane. The bilayer membrane provide a double function; the inner surface facing the bone is porous and the collagen fiber is in loose arrangement, allowing coagulation, vascularization and subsequent osteoblasts migration, while the outer surface

contacting the soft tissue is smooth and dense preventing ingrowth of fibroblasts into the bony defect.

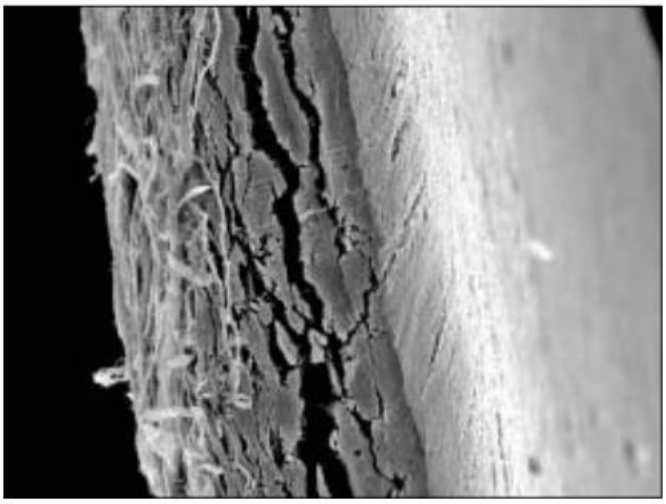

Figure 8: A Scaning electron mircoscope picture under magnification X 100 presents a bilayer structure with a smooth upper surface and a courser bottom surface of Bio-Gide.

Reprinted from Rothamel D, Schwarz F, Fienitz T, Smeets R, Dreiseidler T, Ritter L, Happe A, Zoller J. Biocompatibility and biodegradation of a native porcine pericardium membrane: results of in vitro and in vivo examinations. Int J Oral Maxillofac Implants. 2012 ; 27 (1) : 146-154. [75].

Due to the less stiff of the resorbable membranes, the use of grafting materials seem to be indicated to prevent collapse of the membranes and maintain space for bone regeneration.

Bio-Oss® (Geistlich Pharma AG, Wolhusen, Switzerland) is a bone derived from bovine by which all organic components are removed , but preserves the natural structure of bone. Bio-Oss has an oseteoconductive propertie to provide as scaffold for blood vessel invasion and bone regeneration. Zitzmann and colleagues [76] investigated the healing of bone defects augmented with Bio-Oss and Bio-Gide in humans and reported the mean average percentage of bone fill to the defects was 92%. Moreover, Zitzmann and colleagues [73] presented a histologic outcome of

human alveolar ridge augmentation with Bio-Oss combined with Bio-Gide® which biopsies were obtained 6 to 7 months after augmented. A histologic analysis demonstrated that Bio-Oss particles were surrounded by a newly formed bone with an apposition of osteoid tissue in direct contact, the intimate contact between the Bio-Oss particles and woven bone was about 37% of the particle surfaces. In addition, bone remodelling was also observed with osteoclastic resorption and Howship's lacunae.

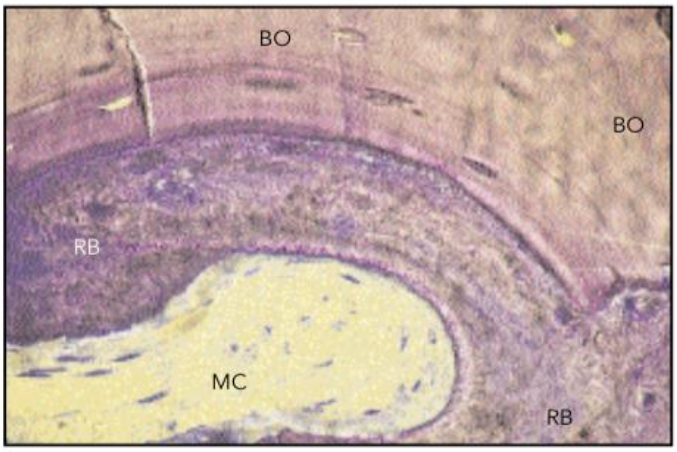

Figure 9: A histologic slide presents a newly formed bone (RB) in contact with Bio-Oss particle (BO) (MC = bone marrow).

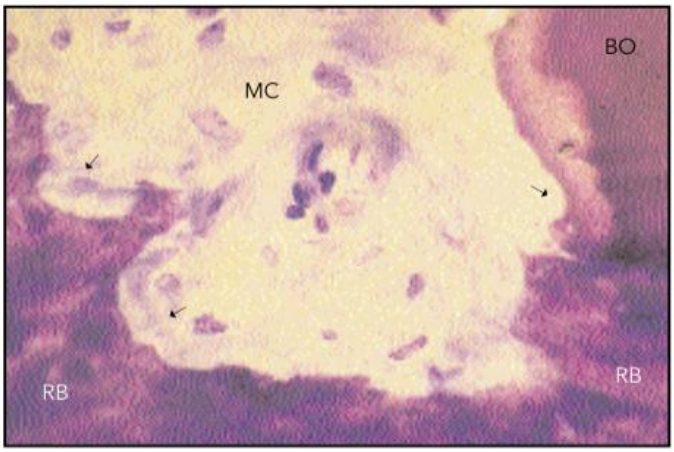

Figure 10: A histologic slide presents a resorption lacunae (arrows) in mineralized regenerated bone (RB) and Bio-Oss particle (BO) (MC = bone marrow).

Reprinted from Zitzmann NU, Scharer P, Marinello CP. Long-term results of implants treated with guided bone regeneration: a 5-year prospective study. Int J Oral Maxillofac Implants. 2001 ; 16(3) : 355-366. [73]

At present, one of the popular non-invasive clinical implant stability test methods are the insertion torque measurement (for primary stability) [33, 70] and the resonance frequency analysis (for primary and secondary stability) [23-25, 27, 71].

A correlation between peri-implant bone defect and implant stability have been reported in many studies [30-32]. However, less clinical studies have been performed in evaluating the IT values and monitoring the development of ISQ values of implant placed in bone without bone defect and implant placement at bone presented with favorable bone defect simultaneously grafted with GBR technique over the healing period.

CHAPTER III

MATERIALS AND METHODS

Research Design

This study was performed as a prospective clinical study. The intervention of the study was the use of GBR technique to correct favorable bone defect.

Independent Variable : Implant placement in bone without bone defect and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique.

Dependent Variables : 1) The insertion torque value (Ncm)

2) The implant stability quotient (ISQ) values

Control Variables : Region of the edentulous ridge, design of implant, diameter of implant, implant surface, surgical technique

Ethical Consideration

This study had been approved by the Ethical committee of the Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand. The study reference ID was HREC-DCU 2015-061 (Appendix A).

Patient Data

The population consisted of patients needed of dental implant in the posterior mandible at the Faculty of Dentistry, Chulalongkorn University, between August 2015 and January 2017. The study protocol was submitted to and approved by the Ethics Committee for Human Research of the Faculty of Dentistry, Chulalongkorn University (HRECDCU 2015-061, Appendix A). Patients were vocally informed about the study protocol and signed informed consent forms prior to starting the treatment.

The preoperative planning was based on clinical examinations and cone-beam computed tomography with radiographic stent. Only patients who met the following inclusion and exclusion criteria were accepted in the study.

Table 1: Groups of the study population

Control group	Implants placed in bone without bone graft (N = 15)
Study group	Implants placed in bone presented with favorable bone defect simultaneously grafted with GBR technique (N = 15)

Inclusion Criteria

1) Age over 21 years

2) Systematically healthy (ASA I or II) with no contraindications against oral surgical interventions

3) A healed posterior mandible ridge with more than 6 months after extraction

4) Sufficient residual bone volume at the planned implant site (the bone height must be adequate to prevent damage to vital structure with sufficient bone width for placement the OsseoSpeed™ EV implant 4.2 mm in diameter in a prosthetically ideal position)

5) Implant placement with the same surgical protocol

6) In the control group, implants must be entirely surrounded by bone

7) In the study group, patients were presented with favorable bone defects as described by Sclar in 2003 [34] which the width of the defect less than one third of the mesio-distal dimension.

8) Achievement of primary stability without clinical implant mobility

9) Ability and willingness to comply the study

Exclusion Criteria

1) Heavy smokers (>10 cigarettes/day)

2) History of alcoholism or drug abuse

3) Severe medical conditions or on medication that affected bone or wound healing (i.e. uncontrolled diabetes mellitus, on intravenous bisphosphonate)

4) Pregnancy

5) The presence of infection at or adjacent to the surgical sites.

6) Implanted placement in bone presented with unfavorable bone defect as described by Sclar in 2003 [34] which the width of the defect greater than one third of the mesio-distal dimension

7) Inadequate primary stability presented with clinical implant mobility

Population

Regarding to the study of Cassette et al. in 2012 [71], 19 implants were placed in sites grafted with autologous bone whereas 17 implants were placed in sites grafted with a combination of 50 autologous : 50 porcine bone. A significant in ISQ values between two groups were observed at 2 months after implant placement (P = 0.0134). Therefore, the estimated sample size of this study decided to set at 15 implants per group due to the limitation in time and participants.

After collected the data of 8 implants per group, the estimated sample size was then confirmed using a statistical software package called GPower. The GPower is a software program with high-precision power and sample size analyses [77, 78]. In fact that the sample size is a function of three factors - the alpha level, beta level and magnitude of the difference (effect size) hypothesized.

$$\text{Pooled variance } s^2 = \frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{(n_1 - 1) + (n_2 - 1)}$$

Where n_1 is the number in group 1, n_2 the number in group 2, s_1^2 the variance in group 1, and s_2^2 the variance in group 2. The square root of s^2 is the combined standard deviation estimate.

The values of n_1, n_2, s_1, s_2 are 8, 8, 10.98 and 3.22 respectively. Pooled variance of 8.1 was calculated from the calculation.

The effect size = $(\bar{y} - \bar{x})/\sigma$

The values of $\bar{y}$, $\bar{x}$, σ are 60.50, 71.69 and 8.1 respectively. From the calculation, the effect size is 1.38. This study set the alpha level probability (Type I error) as p=0.05 and the beta level probability (Type 2 error) as 0.05. Thus, the power of the study was set at 0.95. Using the Gpower, it was estimated that 15 samples would be needed in each of the control and test groups.

Materials

The ASTRA TECH EV Implant System™ (OsseoSpeed, ASTRA TECH EV Implant System, DENTSPLY Implants, Mölndal, Sweden) 4.2 mm in diameter was used in the study. The OsseoSpeed™ implant is made of grade 4 titanium, blasted with TiO_2 particles and chemically treated with diluted hydrofluoric acid (HF). The surface roughness S_a is 1.32 - 1.82 μm resulting in a moderately rough surface with a nanoscale structure.

Bio-Gide® (Geistlich, Wolhusen, Switzerland) is a resorbable non cross-linked porcine derived type I and III collagens membrane. The bilayer membrane provide a double function; the

inner surface facing the bone is porous and the collagen fiber is in loose arrangement, allowing coagulation, vascularization and subsequent osteoblasts migration, while the outer surface contacting the soft tissue is smooth and dense preventing ingrowth of fibroblasts into the bony defect.

Bio-Oss® (Geistlich Pharma AG, Wolhusen, Switzerland) is a bone derived from bovine by which all organic components are removed, but preserves the natural structure of bone. Bio-Oss has an oseteoconductive properties to provide as scaffold for blood vessel invasion and bone regeneration.

Methods

Clinical Protocol

Patients who met all the inclusion and exclusion criteria were accepted in the study. All patients performed CBCT scan with radiographic stent prior to the surgery in order to demonstrate the bone quality and quantity and plan for the implant position. All implants were placed in the Faculty of Dentistry, Chulalongkorn University, Thailand. Implant placement was performed as a one-staged procedure following the manufacturer's protocol.

Surgical Procedure

All patients received systemic antibiotic (1 g of Amoxycillin) and analgesic (500 mg of Ponstan®) prior to the surgery. The surgical area was anesthetized locally and a crestal incision with a full thickness mucoperiosteal flap was raised to access the site. The alveolar site was prepared according to the manufacturer's drilling sequence with external irrigation. The OsseoSpeed™ EV implant (OsseoSpeed, ASTRA TECH EV Implant System, DENTSPLY Implants, Mölndal, Sweden) 4.2 mm in diameter was inserted in a prosthetically ideal position. A healing abutment was installed into the fixture, followed by repositioning and suturing the mucoperiosteal flap. Patients were given 1 g of amoxycillin for 5 days (500 mg two time a day) and 500 mg of Ponstan for severe pain for 3 days. Oral hygiene was controlled with chlorhexidine 0.1% mouth rinse for 7 days.

Guided Bone Regeneration Procedure

In case of exposed implant surface and presented with a favorable bone defect, which was the width of the defect less than one third of the mesio-distal dimension as described by Sclar in 2003 [34]. The GBR procedure was performed following the protocol outlined by Buser *et al*. in 2008 [79]. Small autogenous bone chips collected at the time of the osteotomy site preparation were soaked in blood and placed directly on the exposed implant surface. The

deproteinized bovine bone mineral (Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland) mixed with blood was then used as a second layer over the autogenous bone. Non-crosslinked collagen membrane (Bio-Gide®, Geistlich Pharma AG, Wolhusen, Switzerland) was cut into two strips, moistened with blood, applied with a double-layer technique to improve membrane stability and extended 2–3 mm onto the intact bony borders of the defect. Releasing incisions were performed for primary closure with a tension-free flap.

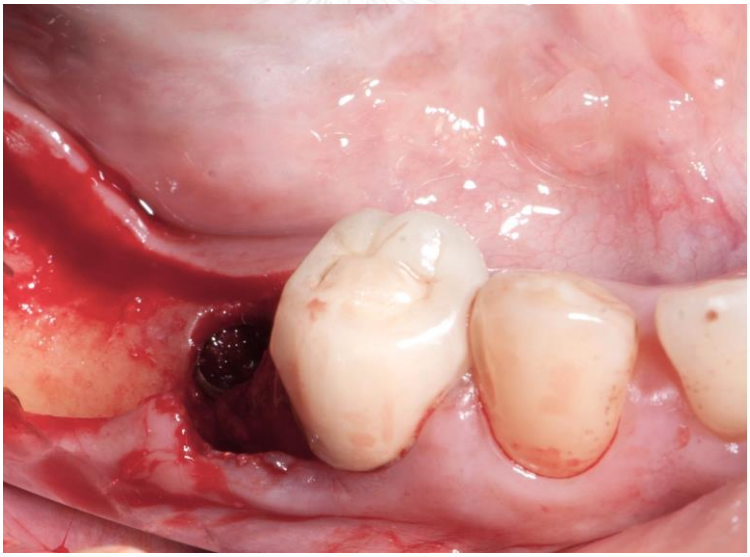

Figure 11: Implant presented with favorable bone defect as described by Sclar in 2003 [34] which the width of the defect less than one third of the mesio-distal dimension. The exposed implant surface was covered with small autogenous bone chips as a first layer.

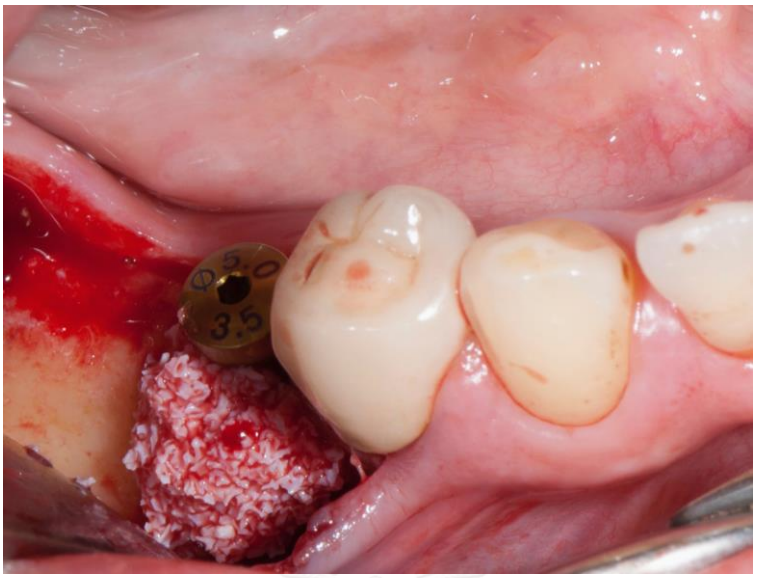

Figure 12: Bio-Oss mixed with blood was placed as a second layer over the autogenous bone.

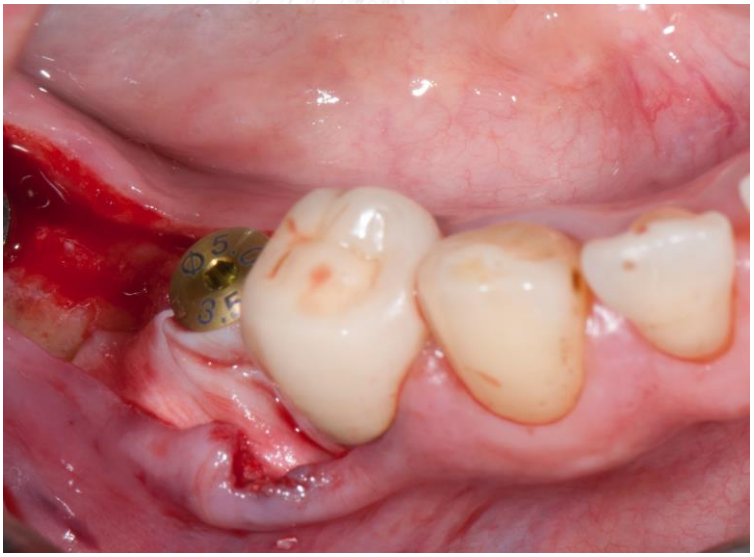

Figure 13: Bio-Gide with a double-layer technique was placed over the bone particles and extended 2–3 mm onto the intact bony borders of the defect.

Insertion Torque Value Measurement

During the implant installation, the insertion torque value was recorded with a calibrated torque wrench attached to the fixture. The technique of the insertion torque measurement is described in the study of Gomez-Polo et al. [70], as the initial torque was set at 10 Ncm and increased in steps of 5 Ncm. The final IT value (Ncm) of each implant was recorded when it was fully inserted.

Resonance Frequency Analysis : ISQ Measurement

Implant stability was measured by an Osstell® ISQ (Osstell AB, Integration Diagnosis, Gothenburg, Sweden). A standardized SmartPeg (type 49, SmartPeg, Integration Diagnostics AB) was hand-screwed into the implant fixture with amount of 4–5 Ncm of torque. Immediately after implant placement, the probe of the device was held close to the peg in buccal and mesial direction, and the ISQ measurement was performed and served as baseline. Thereafter, the ISQ was further recorded at 2, 4, 8, and 12 weeks after implant placement [23, 24]. To perform the measurement at each time point, the healing abutment was gently removed and the peg was hand-screwed into the fixture. All measurements were performed by one trained evaluator.

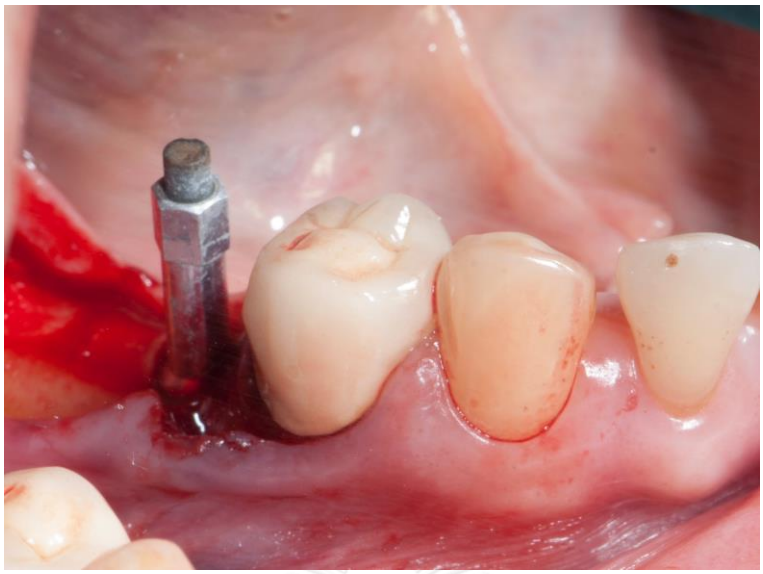

Figure 14: Resonance frequency analysis measurement

Clinical Complication Observation

Any complication after implant placement and GBR procedure in both group were be recorded ; implant failure, graft failure, wound dehiscence, infection, severe pain and swelling.

In case of implant and/or graft failure, patients were be excluded from the study and were retreated using the same protocol. Patients who lost follow-up were excluded from the study.

Data Collection and Analysis

The data were analyzed using the SPSS statistical software (IBM SPSS Statistics 18.0, IBM Corp, Armonk, NY). The data was summarized using means and standard deviations. The normality of the data was tested with the Shapiro-Wilk W-test. The data distribution was normal and the t-test was used to compare the difference between two groups. If the data is not normally distributed, the Mann-Whitney U test was used. For repeated measurements, the Repeated measures ANOVA was used. Statistical correlations were analyzed with the Pearson and the Spearman correlation test. Statistical significance was set with a P-value of 0.05.

CHAPTER IV

RESULTS

Demographic Results

A total of 30 implants in 22 patients were included in the study. The control group consisted of 20 implants in 15 patients with a mean age of 56.20 $\pm$ 8.29 years while the study group consisted of 10 implants in 7 patients with a mean age of 52.10 $\pm$ 8.21 years. There was no significant difference in the mean age between two groups (P = 0.211). All implants were the Osseospeed™ EV implants (OsseoSpeed, ASTRA TECH EV Implant System, DENTSPLY Implants, Mölndal, Sweden) 4.2 mm in diameter. Most of the implants were 9 mm in length (24 implants) while 6 implants were 11 mm in length. All implants achieved good stability and healing was uneventful in all cases. None of the implants failed during the 12 weeks healing period, and the overall implant survival rate was 100%. Demographic data of the control and study groups were presented in Table 2 and 3.

Table 2: Demographic data of the control group

No.	Age	Gender	Tooth No.	Implant length
Control 1	57	F	35	9
Control 2	60	F	36	11
Control 3	66	F	45	11
Control 4	64	F	36	9
Control 5	64	F	37	9
Control 6	58	M	36	9
Control 7	58	M	37	9
Control 8	57	F	45	9
Control 9	64	F	36	9
Control 10	64	F	37	9
Control 11	39	M	36	9
Control 12	39	M	37	9
Control 13	54	F	45	9
Control 14	60	F	45	9
Control 15	45	M	36	9
Control 16	45	M	46	9
Control 17	59	F	45	9
Control 18	61	F	44	11
Control 19	50	F	36	9
Control 20	60	F	35	9

Table 3: Demographic data of the study group

No.	Age	Gender	Tooth No.	Implant length
Study 1	57	F	44	11
Study 2	45	F	45	11
Study 3	45	F	46	9
Study 4	45	F	47	9
Study 5	57	M	45	11
Study 6	39	M	34	9
Study 7	65	F	45	9
Study 8	52	F	36	9
Study 9	58	F	36	9
Study 10	58	F	47	9

Insertion Torque Values

In the control group, the insertion torque (IT) value ranged from 15 to 45 Ncm with a mean value of 27.75 ± 8.96 Ncm. In the study group, the IT value ranged from 20 to 45 Ncm with a mean value of 30.5 ± 8.96 Ncm. There was no significant difference in the insertion torque values between the control and the study groups (P = 0.502).

Table 4: The insertion torque values of the control and study groups (mean ± standard deviation, P-value)

	Control group	**Study group**
N	20	10
Range of IT (Ncm)	15 - 45	20 - 45
IT (Mean ± SD)	27.75 ± 8.96	30.50 ± 8.96
P-value	0.502	
The Mann-Whitney U test was used to compare the difference in IT between two groups.		

Implant Stability Quotient Values

The mean ISQ values at baseline and in the subsequent time points are presented in Table 5 and the longitudinal development of the ISQ values of the implants in the control and study groups were presented in Figure 15 and 16, respectively.

In the control group, immediately after implant placement (baseline), the ISQ values were ranged from 58 to 82 with a mean values of 74.30 $\pm$ 6.01. At 2 weeks, the ISQ values were ranged from 55.5 to 79 with the mean ISQ values decrease to 69.58 $\pm$ 5.30. Thereafter, the mean ISQ values continuously increased to 71.10 $\pm$ 5.80 at 4 weeks (ranged from 56 to 79.5) and 75.08 $\pm$ 3.93 at 8 weeks (ranged from 66 to 81). At the end of the observation, the mean ISQ values increased to 77.85 $\pm$ 3.18 within a range of 70.50 to 83 (Table 5). Statistically significant differences were found between the mean ISQ values at 2 weeks and 8 weeks (P = 0.000), at 2 weeks and 12 weeks (P = 0.000) and at 4 weeks and 12 weeks (P = 0.001) (Figure 15).

Regarding to the study group, at the first measurement (after surgery), the ISQ values were ranged from 57 to 77 with a mean value of 69.85 $\pm$ 7.00. Subsequently, the mean ISQ values decreased to 63.40 $\pm$ 8.47 at 2 weeks (ranged from 48 to 73.5). The lowest mean ISQ values of 59.90 $\pm$ 10.23 were reached at 4 weeks (ranged from 51 to 71). After that, the mean ISQ values increased to 72.55 $\pm$ 3.10 at 8 weeks (ranged from 68 to 77) and 76.20 $\pm$ 2.68 at 12 weeks

(ranged from 72 to 79.5) (Table 5). Statistically significant differences were found between the mean ISQ values at 2 weeks and 12 weeks (P = 0.019) and at 4 weeks and 12 weeks (P = 0.011) (Figure 16).

It was evidence that the development of the ISQ values over the 12 weeks healing period of two groups displayed different pattern as presented in Table 5 and Figure 17. In addition, a statistically significant differences in mean ISQ values between the control and study groups were found at 2 weeks (P = 0.021) and at 4 weeks (P = 0.007).

Table 5: The ISQ values of the control and study groups during the observation period (mean ± standard deviation, P-value)

	ISQ values				
	Control group (N = 20)		Study group (N = 10)		
	Range	Mean ± SD	Range	Mean ± SD	P-Value
Baseline	58 - 82	74.30 ± 6.01	57 -77	69.85 ± 7.00	0.081
2 weeks	55.5 - 79	69.58 ± 5.30	48 - 73.5	63.40 ± 8.47	**0.021***
4 weeks	56 - 79.5	71.10 ± 5.80	51 -71	59.90 ± 10.23	**0.007***
8 weeks	66 - 81	75.08 ± 3.93	68 -77	72.55 ± 3.10	0.088
12 weeks	70.5 - 83	77.85 ± 3.18	72 - 79.5	76.20 ± 2.68	0.171

• Refer to the corresponding statistically significant groups

The repeated measures ANOVA and the unpaired t-test were used to analyzed the data.

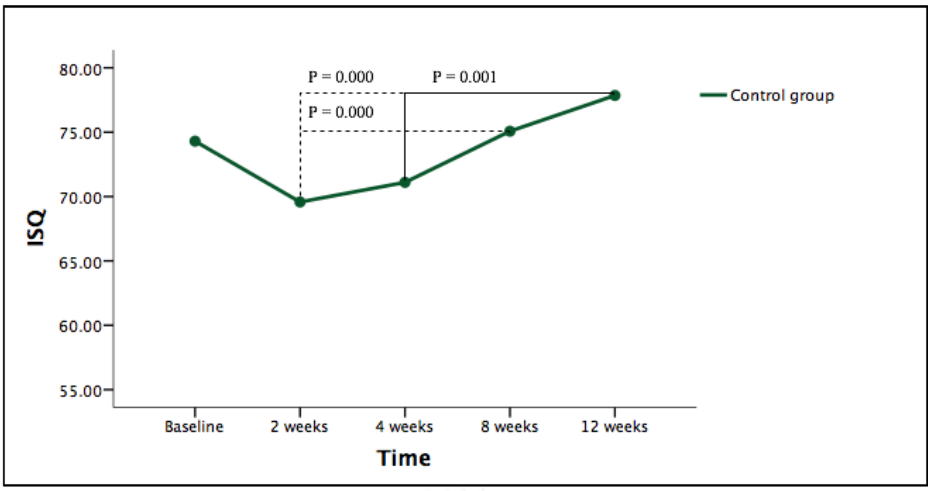

Figure 15: The development of implant stability quotient (ISQ) values of the implants in the control group over the observation period. Statistically significant differences in the mean ISQ values were found between at 2 weeks and 8 weeks (P = 0.000), at 2 weeks and 12 weeks (P = 0.000) and at 4 weeks and 12 weeks (P = 0.001).

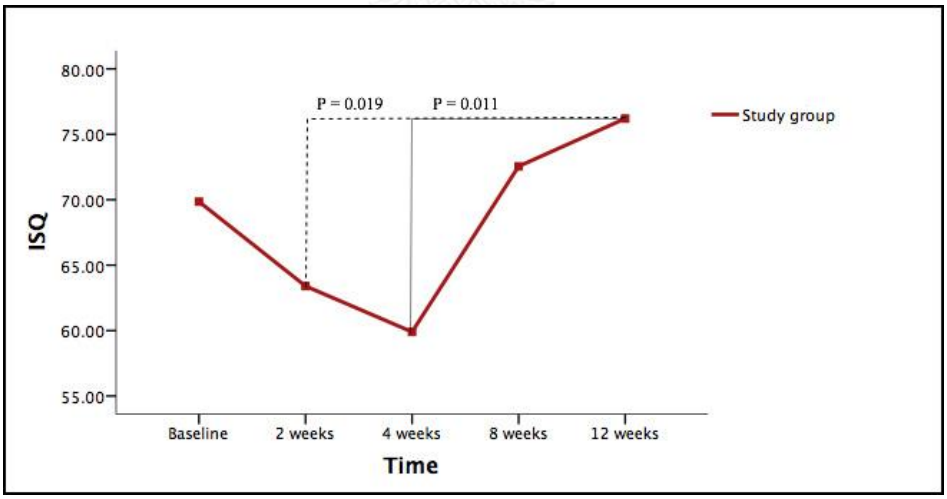

Figure 16: The development of implant stability quotient (ISQ) values of the implants in the study group over the observation period. Statistically significant differences in the mean ISQ values were found between at 2 weeks and 12 weeks (P = 0.019) and at 4 weeks and 12 weeks (P = 0.011)

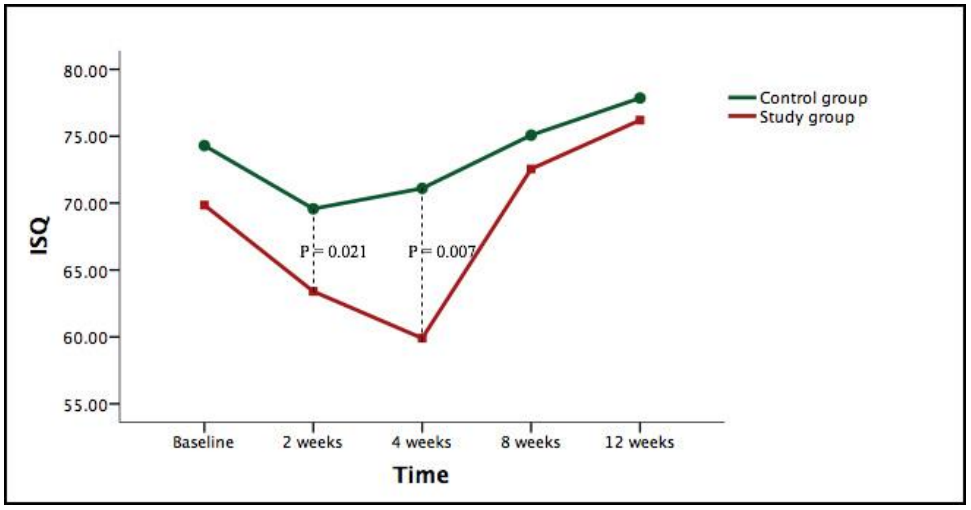

Figure 17: The development of implant stability quotient (ISQ) values of the implants in the control and study groups over the observation period. Statistically significant differences in the mean ISQ values between two groups were found at 2 weeks (P=0.021) and at 4 weeks (P = 0.007).

Correlation between Insertion Torque and Implant Stability Quotient Values

A correlation between the IT and ISQ values was analyzed by the Pearson and Spearman correlation test. A low positive correlation was found between the IT and ISQ values at baseline of the control group. However, there was no significant different (r = 0.147, N = 20, P = 0.537). A slightly negative correlations between the IT and ISQ values were found at baseline of the study group and at 12 weeks for both groups as presented in Table 6. Therefore, these statistical findings do not collaborate the relation between these 2 variables.

Table 6: Analysis of the data for the insertion torque value, ISQ values at baseline and ISQ values at 12 weeks of the control and study groups (mean ± standard deviation, correlation, P-value).

	N	Insertion torque value	At baseline			At 12 weeks		
			ISQ	r	P-value	ISQ	r	P-value
Control group	20	27.75 ± 8.96	74.30 ± 6.01	0.147	0.537	77.85 ± 3.18	-0.026	0.912
Study group	10	30.50 ± 8.96	69.85 ± 7.00	-0.013	0.972	76.20 ± 2.68	-0.269	0.452

The Mann-Whitney U test was used to compare the difference in IT between two groups.
The Pearson and the Spearman correlation tests were used to analyze the correlations between IT and ISQ values.

CHAPTER V

DISCUSSION AND CONCLUSIONS

Discussion

The insertion torque (IT) measurement provides an information on implant stability as a torque values generated during the thread placement procedure into the osteotomy site [14]. High torque value (Ncm) is determined as high implant stability. The resonance frequency analysis (RFA) is a recent non-invasive electronic device which has been proven as a reliable and repeatable method for measuring implant stability over the healing period [17, 24, 26, 67]. The RFA determine the stiffness of the implant-bone complex and displays as an implant stability quotient (ISQ) value. The ISQ value depends on 3 main factors; the design of the transducer, the stiffness of the implant-bone junction (the implant characteristics, the ratio of cancellous to cortical bone, the stiffness of the implant-tissue interface) and the total effective length [17, 24, 27, 43].

The present study was designed to standardize the experimental conditions. Therefore, the same implant design, diameter and surface were placed in the same area of jaw (posterior

mandible) using the same surgical protocol, resulting in favorable bone defect simultaneously grafted with GBR technique being one of the major variable. As a result of the specific inclusion and exclusion criteria, the control group consisted of 20 implants whereas the study group consisted of 10 implants. The power of the study was estimated using the GPower software [77, 78]. The result from the Gpower estimated that if the control and study groups consisted of 20 and 10 implants, when the alpha level probability was set at 0.05, the power of the present study was 0.95 (the beta level probability = 0.05).

The present study reported the data of the insertion torque (IT) values and implant stability quotient (ISQ) values obtained from the OsseoSpeed™ EV implant 4.2 mm in diameter placed in the posterior mandible area over the 12 weeks healing period. The primary objectives of the study were to determine the IT and ISQ values as a reflection of the implant stability between implant placement in bone without bone graft (control group) and implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique (study group). The secondary objective was to assess the correlation between the IT and ISQ values of the two groups.

Insertion Torque Values

The insertion torque (IT) value was considered relative to the primary implant stability to prevent any micromovement. Previous studies reported the IT value of implants placed in bone defect. Turkyilmaz *et al*. [30] reported that the mean IT value of 84 implants placed in human cadaver mandibles with vertical defects was 28.9 $\pm$ 7 Ncm. In addition, they demonstrated a relation between the IT value and the depth of marginal bone defects as the IT value decreased when the amount of defect size increased. Shin *et al*. [32] and Akca *et al*. [16] demonstrated a significant higher IT value in no defect group compare to defect group.

In the present study, statistically significant difference in the IT values were not found between implants placed in bone without bone graft and implants placed in bone presented with favorable bone defect simultaneously grafted with GBR technique. Disagreement between these results could be associated with the different in bone type and defect characteristics. The present study placed implant in patient who have favorable bone defect which the width of the defect less than one third of the mesio-distal dimension as described by Sclar in 2003 [34]. On the other hand, Shin *et al*. placed implant in 3 wall, 1 wall and circumferential defect in bovine rib bone and Akca *et al*. placed implants in 6 mm deep circumferential defects in human cadavers [16, 32].

Implant Stability Quotient Values

The objective of this study was to monitor the longitudinally changes in ISQ values of implants placed in bone with and without dehiscence bone defects over the 12 weeks healing period. In the control group, implants were placed in posterior mandible with adequate surrounding bone. The results of the present study demonstrated the mean ISQ values of 74.30 $\pm$ 6.01 at the time of implant installation. The lowest ISQ values of 69.58 $\pm$ 5.30 were found at 2 weeks and then, the mean ISQ values continuously increased. The development in ISQ values as presented in the study was in accordance with the earlier studies. The study of Geckili *et al.* in 2009 [80] and Schliephake *et al.* in 2012 [81] placed the Oseeospeed™ implant in the region of the mandible and reported the mean ISQ values of 75.5 $\pm$ 8.9 and 73.3 $\pm$ 6.8, respectively, at the time of implant placement. The two studies found the lowest stability at 2 weeks similar to the present study. The decrease in the ISQ values at 2 weeks may be the result of the resorption in the pitch regions which provided retention of the mechanical stability and the newly formed woven bone with low mineral density appeared to be less intense [41, 82].

The influence of bone defect on the primary ISQ value has been previously reported in many experimental studies [16, 30, 32]. However, in the present study, there were no significant differences in the mean ISQ values at baseline between the control and study groups.

Disagreement between the results could possibly be the different in the bone type, the defect characteristics, the implant design and diameter which were used in the studies. On the contrary, Chan *et al.* in 2010 [31] reported no correlation between the narrow dehiscence defect type and the primary ISQ value. Merheb *et al.* (2010) demonstrated that a significant differences in initial ISQ values was found in a constant 3 mm wide dehiscence defect after removal of bone more than 10 mm depth. The narrow dehiscence defect and the constant 3 mm wide dehiscence defect with a height less than 10 mm could be similar to the favorable defect of the present study.

In the present study, the development in the ISQ values over the 12 weeks period of the control and study groups displayed different decreasing and increasing patterns. In the control group, the mean ISQ values decreased at 2 weeks after that, started to increase whereas in the study group, the mean ISQ values decreased up to 4 weeks and then started to increase. It may be speculated that the decreasing and increasing in the ISQ values may represent the bone resorption and formation of a biological bonding. The different in the increasing pattern of the ISQ values between two groups could possibly be explained by the different bone formation pattern. The histologic studies demonstrated that, at 4 week, the parallel-fibered bone and the lamellar bone appeared to be the most elaborate type of bone in the implants placed in pristine bone [41]. In contrast, these two types of bone seem to take place too slowly in the implant

presented with dehiscence-type defect and received guided bone regeneration. In the implants with dehiscence-type defect grafted with GBR technique, the parallel-fibered bone and a nearly complete bone fill into the defect area were found at 6 weeks [83]. The parallel-fibered and the lamellar bone were more mature bone of the initially formed woven bone resulting in improvement in bone quality [41, 82]. Therefore, the development in ISQ values may reflect the changes in the stiffness of the implant-bone junction during the osseointegration process.

The RFA has been used to assess implant stability in several studies. The results of previous studies and the manufacturer's guideline suggested that an ISQ value more than 70 is a safe level of stability and served as a threshold level [19-21]. During the 12 weeks period, the mean ISQ values of the control group appealed to show slightly unaltered. The ISQ values of the implants in the control group reached a threshold level of 70 at every time point, except at 2weeks (69.58 $\pm$ 5.30) and the statistically significant increase was found at 8 weeks or more. On the contrary, the study group with low primary ISQ values, secondary ISQ values tended to increase after osseointegration. The mean ISQ values of the study group reached the threshold level of 70 at 8 weeks and reached a statistically significant differences at 12 weeks. Some previous studies reported similar results which was the implants with high primary ISQ value more than 70 seem not to increase with time while implants with lower ISQ value exhibited increase in stability [24, 26, 27, 43].

Relationship between Insertion Torque and Primary and Secondary Implant Stability Quotient Values

The results from the present study demonstrated no significant correlation between the Insertion torque (IT) values with either the primary or secondary implant stability quotient (ISQ) values. The results dissented from several studies reported correlation between the IT and the primary ISQ value [30, 70, 84]. One possible explanation was the presence of bone defect eliminating contact at the cortical level. Therefore, a relationship between the IT and ISQ value could not be observed.

Few authors have studied in the relation between the IT and the secondary ISQ value. However, Gomez-Polo *et al*. [70] reported no correlation between them, similar to the results presented in the study.

Based on the results of the development of implant stability within the 12 weeks follow-up period, , implants placement in bone presented with favorable bone defect simultaneously grafted with GBR technique were as stable as implants with no bone defect at the end of observation. However, a significantly lower implant stability can be occurred in the implants treated with GBR technique in the initial weeks of healing. Moreover, loading of the implant with

a definitive restoration should be waited at least 8 weeks to ensure greater stability and osseointegration.

Limitations of the study were that only the Osseospeed™ EV implants 4.2 mm in diameter were placed in the posterior mandible which actually have bone in type 2 and 3 [49, 51]. This results may not infer to the other types of implant and bone. Future study with different implant design, implant diameter or bone type would be beneficial for the knowledge in clinical treatments with dental implants.

Conclusions

With in the limitations of the present study, the data of the insertion torque (IT) values and implant stability quotient (ISQ) values were obtained from the OsseoSpeed™ EV implants over the 12 weeks healing period. The following conclusion could be drawn.

1) There was no difference in the IT values between two groups.

2) The ISQ values of implant placement in bone without bone defect were significantly higher than implant placement in bone presented with favorable bone defect simultaneously grafted with GBR technique at 2 weeks and 4 weeks after implant placement.

3) There were no correlations between the IT and the ISQ values at baseline and after the 12 weeks healing period.

Clinical Implications

After 12 weeks healing, implant placement in bone presented with favorable bone defect grafted with GBR technique was as stable as implant placement in bone without bone graft. However, loading of the implant with a definitive restoration of implant with augmentation should be waited at least 8 weeks to ensure greater stability and osseointegration.

Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Branemark, P.I., et al., *Intra-osseous anchorage of dental prostheses. I. Experimental studies.* Scand J Plast Reconstr Surg, 1969. **3**(2): p. 81-100.
2. Adell, R., et al., *A 15-year study of osseointegrated implants in the treatment of the edentulous jaw.* Int J Oral Surg, 1981. **10**(6): p. 387-416.
3. Albrektsson, T., et al., *The long-term efficacy of currently used dental implants: a review and proposed criteria of success.* Int J Oral Maxillofac Implants, 1986. **1**(1): p. 11-25.
4. Buser, D., et al., *10-year survival and success rates of 511 titanium implants with a sandblasted and acid-etched surface: a retrospective study in 303 partially edentulous patients.* Clin Implant Dent Relat Res, 2012. **14**(6): p. 839-51.
5. Branemark, P.I., *Introduction to Osseointegration. In Branemark P-I, Zarb G, Albrektsson T (eds): Tissue Integrated Prosthesis. Chicago.* Quint Publishing, 1985: p. 11-76.
6. Albrektsson, T., et al., *Osseointegrated titanium implants. Requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man.* Acta Orthop Scand, 1981. **52**(2): p. 155-70.
7. Albrektsson, T. and G.A. Zarb, *Current interpretations of the osseointegrated response: clinical significance.* Int J Prosthodont, 1993. **6**(2): p. 95-105.
8. Albrektsson, T., J. Brunski, and A. Wennerberg, *'A requiem for the periodontal ligament' revisited.* Int J Prosthodont, 2009. **22**(2): p. 120-2.
9. Fischer, K., M. Backstrom, and L. Sennerby, *Immediate and early loading of oxidized tapered implants in the partially edentulous maxilla: a 1-year prospective clinical, radiographic, and resonance frequency analysis study.* Clin Implant Dent Relat Res, 2009. **11**(2): p. 69-80.
10. Meredith, N., *Assessment of implant stability as a prognostic determinant.* Int J Prosthodont, 1998. **11**(5): p. 491-501.
11. Atsumi, M., S.H. Park, and H.L. Wang, *Methods used to assess implant stability: current status.* Int J Oral Maxillofac Implants, 2007. **22**(5): p. 743-54.
12. Hammerle, C.H., et al., *The effect of a deproteinized bovine bone mineral on bone regeneration around titanium dental implants.* Clin Oral Implants Res, 1998. **9**(3): p. 151-62.
13. Wang, H.L. and M.J. Carroll, *Guided bone regeneration using bone grafts and collagen membranes.* Quintessence Int, 2001. **32**(7): p. 504-15.
14. Johansson, B. and C. Strid, *Assessment of bone quality from cutting resistance during implant surgery.* Int J Oral Maxillofac Implants, 1994. **9**: p. 279-288.

15. O'Sullivan, D., et al., *A comparison of two methods of enhancing implant primary stability.* Clin Implant Dent Relat Res, 2004. **6**(1): p. 48-57.
16. Akca, K., et al., *Torque-fitting and resonance frequency analyses of implants in conventional sockets versus controlled bone defects in vitro.* Int J Oral Maxillofac Surg, 2010. **39**(2): p. 169-73.
17. Meredith, N., et al., *Resonance frequency measurements of implant stability in vivo. A cross-sectional and longitudinal study of resonance frequency measurements on implants in the edentulous and partially dentate maxilla.* Clin Oral Implants Res, 1997. **8**(3): p. 226-33
18. Lachmann, S., et al., *Resonance frequency analysis and damping capacity assessment. Part 2: peri-implant bone loss follow-up. An in vitro study with the Periotest and Osstell instruments.* Clin Oral Implants Res, 2006. **17**(1): p. 80-4.
19. Kokovic, V., et al., *Immediate vs. early loading of SLA implants in the posterior mandible: 5-year results of randomized controlled clinical trial.* Clin Oral Implants Res, 2014. **25**(2): p. e114-9.
20. Bornstein, M.M., et al., *Early loading of nonsubmerged titanium implants with a chemically modified sand-blasted and acid-etched surface: 6-month results of a prospective case series study in the posterior mandible focusing on peri-implant crestal bone changes and implant stability quotient (ISQ) values.* Clin Implant Dent Relat Res, 2009. **11**(4): p. 338-47.
21. Glauser, R., et al., *Resonance frequency analysis of implants subjected to immediate or early functional occlusal loading. Successful vs. failing implants.* Clin Oral Implants Res, 2004. **15**(4): p. 428-34.
22. Meredith, N., et al., *The application of resonance frequency measurements to study the stability of titanium implants during healing in the rabbit tibia.* Clin Oral Implants Res, 1997. **8**(3): p. 234-43.
23. Bischof, M., et al., *Implant stability measurement of delayed and immediately loaded implants during healing.* Clin Oral Implants Res, 2004. **15**(5): p. 529-39.
24. Nedir, R., et al., *Predicting osseointegration by means of implant primary stability.* Clin Oral Implants Res, 2004. **15**(5): p. 520-8.
25. Huwiler, M.A., et al., *Resonance frequency analysis in relation to jawbone characteristics and during early healing of implant installation.* Clin Oral Implants Res, 2007. **18**(3): p. 275-80.

26. Simunek, A., et al., *Development of implant stability during early healing of immediately loaded implants.* Int J Oral Maxillofac Implants, 2012. **27**(3): p. 619-27.
27. Sim, C.P. and N.P. Lang, *Factors influencing resonance frequency analysis assessed by Osstell mentor during implant tissue integration: I. Instrument positioning, bone structure, implant length.* Clin Oral Implants Res, 2010. **21**(6): p. 598-604.
28. Arnotharom, V., *Influence of bony structure and implant characteristics on implant stability during healing period measured by Resonance Frequency Analysis (RFA) : Randomized Controlled Trial (Unpublished master's thesis).* 2011. Chulalongkorn University, Bangkok, Thailand.
29. Thongborisoot, S., *The Comparison of Implant Stability between Two Implant Surfaces Using the Resonance Frequency Analysis Measurement : Randomized Controlled Trial (Unpublished master's thesis).* 2012. Chulalongkorn University, Bangkok, Thailand.
30. Turkyilmaz, I., et al., *Influence of defect depth on resonance frequency analysis and insertion torque values for implants placed in fresh extraction sockets: a human cadaver study.* Clin Implant Dent Relat Res, 2009. **11**(1): p. 52-8.
31. Chan, H.L., et al., *Implant primary stability determined by resonance frequency analysis in surgically created defects: a pilot cadaver study.* Implant Dent, 2010. **19**(6): p. 509-19.
32. Shin, S.Y., et al., *The Effects of Defect Type and Depth, and Measurement Direction on the Implant Stability Quotient Value.* J Oral Implantol, 2015. **41**(6): p. 652-6.
33. Tozum, T.F., I. Turkyilmaz, and E.A. McGlumphy, *Relationship between dental implant stability determined by resonance frequency analysis measurements and peri-implant vertical defects: an in vitro study.* J Oral Rehabil, 2008. **35**(10): p. 739-44.
34. Sclar, A.G., *: The Bio-Col technique, Soft Tissue and Esthetic Considerations in Implant Therapy.* Chicago, IL, Quintessence, 2003: p. 75-112.
35. Davies, J.E., *Mechanisms of endosseous integration.* Int J Prosthodont, 1998. **11**(5): p. 391-401.
36. Sennerby, L. and L. Ericson, *Early tissue response to titanium implants inserted in rabbit cortical bone.* J Mater Sci-Mater M, 1993. **4**: p. 240-250.
37. Albrektsson, T., et al., *Histologic investigations on 33 retrieved Nobelpharma implants.* Clin Mater, 1993. **12**(1): p. 1-9.
38. Albrektsson T, I.F., *Consensus report of session V. In: Lang NP, Karring T, eds. Proceedings of 1st European Workshop on Periodontology.* 1993, Quintessence: London. p. 365-369.
39. Ivanoff, C.J., L. Sennerby, and U. Lekholm, *Influence of initial implant mobility on the integration of titanium implants. An experimental study in rabbits.* Clin Oral Implants Res, 1996. **7**(2): p. 120-7.

40. Aspenberg, P., et al., *Intermittent micromotion inhibits bone ingrowth. Titanium implants in rabbits.* Acta Orthop Scand, 1992. **63**(2): p. 141-5.
41. Berglundh, T., et al., *De novo alveolar bone formation adjacent to endosseous implants.* Clin Oral Implants Res, 2003. **14**(3): p. 251-62.
42. Raghavendra, S., M.C. Wood, and T.D. Taylor, *Early wound healing around endosseous implants: a review of the literature.* Int J Oral Maxillofac Implants, 2005. **20**(3): p. 425-31.
43. Sennerby, L. and N. Meredith, *Implant stability measurements using resonance frequency analysis: biological and biomechanical aspects and clinical implications.* Periodontol 2000, 2008. **47**: p. 51-66.
44. Sennerby, L. and N. Meredith, *Resonance frequency analysis: measuring implant stability and osseointegration.* Compend Contin Educ Dent, 1998. **19**(5): p. 493-8, 500, 502; quiz 504.
45. Schropp, L., et al., *Bone healing and soft tissue contour changes following single-tooth extraction: a clinical and radiographic 12-month prospective study.* Int J Periodontics Restorative Dent, 2003. **23**(4): p. 313-23.
46. Sclar, A.G., *Guidelines for flapless surgery.* J Oral Maxillofac Surg, 2007. **65**(7 Suppl 1): p. 20-32.
47. Friberg, B., T. Jemt, and U. Lekholm, *Early failures in 4,641 consecutively placed Branemark dental implants: a study from stage 1 surgery to the connection of completed prostheses.* Int J Oral Maxillofac Implants, 1991. **6**(2): p. 142-6.
48. Morris, H.F., et al., *AICRG, Part V: Factors influencing implant stability at placement and their influence on survival of Ankylos implants.* J Oral Implantol, 2004. **30**(3): p. 162-70.
49. Lekholm, U. and G. Zarb, *Patient selection and preparation. In: Branemark PI, Zarb GA, Albrektsson T, eds. Tissue-Integrated Prostheses : Osseointegration in Clinical Dentistry.* Chicago : Quintessence, 1985: p. 199-209.
50. Trisi, P. and W. Rao, *Bone classification: clinical-histomorphometric comparison.* Clin Oral Implants Res, 1999. **10**(1): p. 1-7.
51. Norton, M.R. and C. Gamble, *Bone classification: an objective scale of bone density using the computerized tomography scan.* Clin Oral Implants Res, 2001. **12**(1): p. 79-84.
52. Eriksson, A.R. and T. Albrektsson, *Temperature threshold levels for heat-induced bone tissue injury: a vital-microscopic study in the rabbit.* J Prosthet Dent, 1983. **50**(1): p. 101-7.
53. Sener, B.C., et al., *Effects of irrigation temperature on heat control in vitro at different drilling depths.* Clin Oral Implants Res, 2009. **20**(3): p. 294-8.

54. Albrektsson, T. and A. Wennerberg, *Oral implant surfaces: Part 1--review focusing on topographic and chemical properties of different surfaces and in vivo responses to them.* Int J Prosthodont, 2004. **17**(5): p. 536-43.

55. Ivanoff, C.J., et al., *Histologic evaluation of bone response to oxidized and turned titanium micro-implants in human jawbone.* Int J Oral Maxillofac Implants, 2003. **18**(3): p. 341-8.

56. Ivanoff, C.J., et al., *Histologic evaluation of the bone integration of TiO(2) blasted and turned titanium microimplants in humans.* Clin Oral Implants Res, 2001. **12**(2): p. 128-34.

57. Cooper, L.F., et al., *Fluoride modification effects on osteoblast behavior and bone formation at TiO2 grit-blasted c.p. titanium endosseous implants.* Biomaterials, 2006. **27**(6): p. 926-36.

58. Isa, Z.M., et al., *Effects of fluoride-modified titanium surfaces on osteoblast proliferation and gene expression.* Int J Oral Maxillofac Implants, 2006. **21**(2): p. 203-11.

59. Rocci, M., et al., *Comparing the TiOblast and Osseospeed surfaces. Histomorphometric and histological analysis in humans.* Oral Implantol (Rome), 2008. **1**(1): p. 34-42.

60. Sullivan, D.Y., et al., *The reverse-torque test: a clinical report.* Int J Oral Maxillofac Implants, 1996. **11**(2): p. 179-85.

61. Goodson, J.M., A.D. Haffajee, and S.S. Socransky, *The relationship between attachment level loss and alveolar bone loss.* J Clin Periodontol, 1984. **11**(5): p. 348-59.

62. Friberg, B., et al., *On cutting torque measurements during implant placement: a 3-year clinical prospective study.* Clin Implant Dent Relat Res, 1999. **1**(2): p. 75-83.

63. Ottoni, J.M., et al., *Correlation between placement torque and survival of single-tooth implants.* Int J Oral Maxillofac Implants, 2005. **20**(5): p. 769-76.

64. Turkyilmaz, I. and E.A. McGlumphy, *Influence of bone density on implant stability parameters and implant success: a retrospective clinical study.* BMC Oral Health, 2008. **8**: p. 32.

65. Schulte, W. and D. Lukas, *The Periotest method.* Int Dent J, 1992. **42**(6): p. 433-40.

66. Olive, J. and C. Aparicio, *Periotest method as a measure of osseointegrated oral implant stability.* Int J Oral Maxillofac Implants, 1990. **5**(4): p. 390-400.

67. Meredith, N., et al., *Relationship between contact time measurements and PTV values when using the Periotest to measure implant stability.* Int J Prosthodont, 1998. **11**(3): p. 269-75.

68. Meredith, N., D. Alleyne, and P. Cawley, *Quantitative determination of the stability of the implant-tissue interface using resonance frequency analysis.* Clin Oral Implants Res, 1996. **7**(3): p. 261-7.

69. Ostman, P.O., et al., *Resonance frequency analysis measurements of implants at placement surgery.* Int J Prosthodont, 2006. **19**(1): p. 77-83; discussion 84.

70. Gomez-Polo, M., et al., *Does Length, Diameter, or Bone Quality Affect Primary and Secondary Stability in Self-Tapping Dental Implants?* J Oral Maxillofac Surg, 2016. **74**(7): p. 1344-53.

71. Cassetta, M., et al., *Resonance frequency analysis of implants inserted with a simultaneous grafting procedure: a 5-year follow-up study in man.* Int J Periodontics Restorative Dent, 2012. **32**(5): p. 581-9.

72. Melcher, A.H., *On the repair potential of periodontal tissues.* J Periodontol, 1976. **47**(5): p. 256-60.

73. Zitzmann, N.U., P. Scharer, and C.P. Marinello, *Long-term results of implants treated with guided bone regeneration: a 5-year prospective study.* Int J Oral Maxillofac Implants, 2001. **16**(3): p. 355-66.

74. Hammerle, C.H., et al., *Ridge augmentation by applying bioresorbable membranes and deproteinized bovine bone mineral: a report of twelve consecutive cases.* Clin Oral Implants Res, 2008. **19**(1): p. 19-25.

75. Rothamel, D., et al., *Biocompatibility and biodegradation of a native porcine pericardium membrane: results of in vitro and in vivo examinations.* Int J Oral Maxillofac Implants, 2012. **27**(1): p. 146-54.

76. Zitzmann, N.U., R. Naef, and P. Scharer, *Resorbable versus nonresorbable membranes in combination with Bio-Oss for guided bone regeneration.* Int J Oral Maxillofac Implants, 1997. **12**(6): p. 844-52.

77. Cunningham, J.B., McCrum-Gardner, E., *Power, effect and sample size using GPower: practical issues for researchers and members of research ethics committees.* Evidence Based Midwifery, 2007. **5**(4): p. 132-6.

78. McCrum-Gardner, E., *Sample size and power calculations made simple.* International Journal of Therapy and Rehabilitation, 2010. **17**(1): p. 10-14.

79. Buser, D., et al., *Early implant placement following single-tooth extraction in the esthetic zone: biologic rationale and surgical procedures.* Int J Periodontics Restorative Dent, 2008. **28**(5): p. 441-51.

80. Geckili, O., H. Bilhan, and T. Bilgin, *A 24-week prospective study comparing the stability of titanium dioxide grit-blasted dental implants with and without fluoride treatment.* Int J Oral Maxillofac Implants, 2009. **24**(4): p. 684-8.

81. Schliephake, H., et al., *Early loading of surface modified implants in the posterior mandible - 5 year results of an open prospective non-controlled study.* J Clin Periodontol, 2012. **39**(2): p. 188-95.

82. Schenk, R.K. and D. Buser, *Osseointegration: a reality.* Periodontol 2000, 1998. **17**: p. 22-35.

83. Schwarz, F., et al., *Immunohistochemical characterization of guided bone regeneration at a dehiscence-type defect using different barrier membranes: an experimental study in dogs.* Clin Oral Implants Res, 2008. **19**(4): p. 402-15.

84. Ohta, K., et al., *Influence of factors related to implant stability detected by wireless resonance frequency analysis device.* J Oral Rehabil, 2010. **37**(2): p. 131-7.

REFERENCES

APPENDIX

Appendix A. Study protocol and consent form approval

No.068/2015

Study Protocol and Consent Form Approval

The Human Research Ethics Committee of the Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand has approved the following study to be carried out according to the protocol and patient/participant information sheet dated and/or amended as follows in compliance with the **ICH/GCP**

Study Title	: A COMPARISON OF IMPLANT STABILITY BETWEEN IMPLANT PLACED WITHOUT BONE GRAFT VERSUS WITH BONE GRAFT USING GBR TECHNIQUE: A RESONANCE FREQUENCY ANALYSIS
Study Code	: HREC-DCU **2015-061**
Study Center	: Chulalongkorn University
Principle Investigator	: Dr. Rueangsiri Janyaphadungpong
Protocol Date	: May 22, 2015
Date of Approval	: August 4, 2015
Date of Expiration	: August 3, 2017

V. Lertchirakarn

(Associate Professor Dr. Veera Lertchirakarn)
Chairman of Ethics Committee

K. Bhalang

(Assistant Professor Dr. Kanokporn Bhalang)
Associate Dean for Research

*A list of the Ethics Committee members (names and positions) present at the Ethics Committee meeting on the date of approval of this study has been attached (upon requested). This Study Protocol Approval Form will be forwarded to the Principal Investigator.

Approval is granted subject to the following conditions: (see back of the approval)

Appendix B. Demographic data and measurement form

Subject No.....Gender.....Age.....

Implant site..... **Date of Surgery.....**

Implants placement with guided bone regeneration technique ☐ Yes ☐ No

Implant brand ASTRA TECH Implant System™ EV **Diameter** 4.2 mm **Length.....**mm

At the day of implant surgery

Insertion torque value..... Ncm

Implant stability quotient (ISQ) values

Healing duration	ISQ values		
	Buccal side	Mesial side	Mean
Day 0			
Week 2			
Week 4			
Week 8			
Wekk 12			

Complication

Appendix C. Insertion torque values and mean implant stability quotient values of the control group

Implant	IT	ISQ				
		day 0	2 weeks	4 weeks	8 weeks	12 weeks
1	15	71	55.50	67.50	70.00	75.50
2	20	78.50	74	75	80	79.50
3	35	76	73	74.50	80	81
4	30	79	72	67	76	74
5	25	74	71.50	70	77	78.50
6	25	79	66	74.50	72.50	76.00
7	25	71	68	73.50	76	78.50
8	35	82	66.50	71.50	70	70.50
9	15	75	68.50	68	69.50	76.50
10	25	78.50	73.50	63.50	76	79
11	25	78	60	56	75	81
12	35	81	71.50	73	77.50	79
13	45	72	68	78	76	82
14	35	75	72.50	69	75	80.50
15	45	63	68	74.50	75	75
16	20	58	71	73	75	75
17	25	75.50	67	73.50	66	76.50
18	35	70	76.50	62.50	74	75
19	15	70	69.50	78	80	81
20	25	79.50	79	79.50	81	83

Appendix D. Insertion torque values and mean implant stability quotient values of the study group

Implant	IT	ISQ				
		day 0	2 weeks	4 weeks	8 weeks	12 weeks
1	20	68	65.50	63	75.50	79.50
2	25	60.50	66.50	58.50	72.50	74.50
3	25	75	67	70.50	71	78.50
4	25	65.50	51	38.50	77	78.50
5	45	76.50	73.50	51.50	75	79
6	25	76	73.50	71	71	73.50
7	35	72	65	63.50	68.50	73.50
8	45	57	59	67.50	71.50	76.50
9	25	77	48	64	75.50	76.50
10	35	71	65	51	68	72

Appendix E. Implant stability quotient values at the buccal and mesial aspect of the control group

Implant	Buccal day 0	Mesial day 0	Buccal 2 weeks	Mesial 2 weeks	Buccal 4 weeks	Mesial 4 weeks	Buccal 8 weeks	Mesial 8 weeks	Buccal 12 weeks	Mesial 12 weeks
1	73.00	69.00	58.00	53.00	67.00	68.00	69.00	71.00	75.00	76.00
2	77.00	80.00	72.00	76.00	75.00	75.00	80.00	80.00	79.00	80.00
3	74.00	78.00	75.00	71.00	74.00	75.00	80.00	80.00	81.00	81.00
4	79.00	79.00	71.00	73.00	65.00	69.00	76.00	76.00	74.00	74.00
5	75.00	73.00	72.00	71.00	70.00	70.00	77.00	77.00	79.00	78.00
6	79.00	79.00	62.00	70.00	76.00	73.00	75.00	70.00	75.00	77.00
7	71.00	71.00	70.00	66.00	75.00	72.00	75.00	77.00	80.00	77.00
8	81.00	83.00	67.00	66.00	74.00	69.00	70.00	70.00	70.00	71.00
9	75.00	75.00	68.00	69.00	68.00	68.00	70.00	69.00	76.00	77.00
10	79.00	78.00	73.00	74.00	67.00	60.00	75.00	77.00	79.00	79.00
11	78.00	78.00	60.00	60.00	60.00	52.00	75.00	75.00	81.00	81.00
12	80.00	82.00	67.00	76.00	75.00	71.00	79.00	76.00	79.00	79.00
13	72.00	72.00	68.00	68.00	78.00	78.00	76.00	76.00	82.00	82.00
14	75.00	75.00	75.00	70.00	69.00	69.00	75.00	75.00	81.00	80.00
15	63.00	63.00	68.00	68.00	75.00	74.00	75.00	75.00	75.00	75.00
16	58.00	58.00	71.00	71.00	73.00	73.00	75.00	75.00	75.00	75.00
17	77.00	74.00	70.00	64.00	73.00	74.00	66.00	66.00	77.00	76.00
18	62.00	78.00	73.00	80.00	55.00	70.00	71.00	77.00	70.00	80.00
19	70.00	70.00	69.00	70.00	78.00	78.00	80.00	80.00	81.00	81.00
20	79.00	80.00	80.00	78.00	80.00	79.00	82.00	80.00	84.00	82.00

Appendix F. Implant stability quotient values at the buccal and mesial aspect of the study group

Implant	Buccal day 0	Mesial day 0	Buccal 2 weeks	Mesial 2 weeks	Buccal 4 weeks	Mesial 4 weeks	Buccal 8 weeks	Mesial 8 weeks	Buccal 12 weeks	Mesial 12 weeks
1	63.00	73.00	60.00	71.00	56.00	70.00	74.00	77.00	80.00	79.00
2	51.00	70.00	64.00	69.00	59.00	58.00	72.00	73.00	74.00	75.00
3	72.00	78.00	64.00	70.00	66.00	75.00	65.00	77.00	78.00	79.00
4	66.00	65.00	51.00	51.00	40.00	37.00	77.00	77.00	79.00	78.00
5	75.00	78.00	71.00	76.00	51.00	52.00	75.00	75.00	78.00	80.00
6	75.00	77.00	73.00	74.00	71.00	71.00	71.00	71.00	72.00	75.00
7	75.00	69.00	65.00	65.00	66.00	61.00	70.00	67.00	75.00	72.00
8	57.00	57.00	66.00	52.00	66.00	69.00	68.00	75.00	76.00	77.00
9	74.00	80.00	53.00	43.00	70.00	58.00	76.00	75.00	77.00	76.00
10	69.00	73.00	59.00	71.00	51.00	51.00	69.00	67.00	72.00	72.00

VITA

NAME Rueangsiri Janyaphadungpong

DATE OF BIRTH May 13, 1987

PLACE OF BIRTH Sukhothai, Thailand

ADDRESS 299/101 Patcha2 Village, Mueang, Nongkhai, Thailand

INSTITUTIONS ATTENDED 2005-2010 Doctor of Dental Surgery, Faculty of Dentistry, Khon Kaen University, Khon Kaen, Thailand