

**Assessment of Chemically Modified  
Roughened Titanium Implants in Diabetic  
Patients: A Clinical Study**

**A Thesis**

Submitted to the Faculty of Dentistry, Ain Shams University in partial fulfilment  
for Master Degree in Oral and Maxillofacial Surgery

By

**Ahmed AbdAllah Mohammed Attia**

B.D.S. (2007)

**Faculty of Dentistry**

**Ain Shams University**

**(2019)**

# **Supervisors**

**Mohamed Daa Zein El Abdien Ismaeil**

Professor of Oral and Maxillofacial Surgery

Dean of Faculty of Dentistry, Ain Shams University

**Karim Mohamed Mahmoud AbdelMohsen**

Lecturer of Oral and Maxillofacial Surgery

Faculty of Dentistry, Ain Shams University

# *Dedication*

*To my family; father, mother and sisters  
for their inspiration for me to be the best.*

*To my wife who supports me in every  
step throughout our life.*

*To my beloved son and daughter*

*To my supervisors who helped me to  
succeed and supported me during my  
study*

## ***Acknowledgement***

*I would like to thank Dr. May Hussain Dental Photography, for the quality of the images and her complete professionalism.*

*I would also like to acknowledge the contribution of Photon Dental Radiographic Center, for their highly detailed CBCT images and their accurate crestal bone measurements.*

## Contents

Subject	Page
List of abbreviations	I
List of figures	III
List of tables	VI
Introduction	1
Review of literature	3
Aim of the study	30
Materials and methods	31
Results	52
Discussion	67
Summary and conclusion	78
Recommendations	83
References	84
Appendix 1	--
Appendix 2	--
Appendix 3	--
Appendix 4	--
Arabic summary	--

## List of Abbreviations

<b>AGE</b>	: Advanced Glycation End Products.
<b>BMP</b>	: Bone Morphogenic Proteins.
<b>BIC</b>	: Bone Implant Contact.
<b>CBCT</b>	: Cone Beam Computerized Tomography.
<b>DM</b>	: Diabetes Mellitus.
<b>HbA1c</b>	: Glycated Hemoglobin A1c.
<b>HO<sup>•</sup></b>	: Hydroxyl.
<b>H<sub>2</sub>O<sub>2</sub></b>	: Hydrogen Peroxide.
<b>IAJ</b>	: Implant Abutment Junction.
<b>IL-1</b>	: Interleukin One.
<b>IL-6</b>	: Interleukin Six.
<b>ISQ</b>	: Implant Stability Quotient.
<b>N</b>	: Newton.
<b>NO</b>	: Nitric Oxide.
<b>O<sub>2</sub><sup>•-</sup></b>	: Superoxide.
<b>ONOO<sup>•-</sup></b>	: Peroxynitrite.
<b>PD</b>	: Periodontal Disease.
<b>PDGF</b>	: Platelet Derived Growth Factor.
<b>RAGE</b>	: Receptor for Advanced Glycation End Products.
<b>RANKL</b>	: Receptor Activator for Nuclear Factor Kappa-B Ligand.

## **List of Abbreviations** (Cont.)

<b>RFA</b>	: Resonance Frequency Analysis.
<b>ROS</b>	: Reactive Oxygen Species.
<b>SLA</b>	: Sand Blasted, Large Grit, Acid Etched.
<b>TGF-<math>\beta</math></b>	: Tumour Growth Factor Beta.
<b>TNF-<math>\alpha</math></b>	: Tumour Necrosis Factor Alpha.
<b><math>\mu\text{m/N}</math></b>	: Micrometer per Newton.

## List of Figures

<i>Figure</i>	<i>Subject</i>	<i>Page</i>
1	An implant placed in soft trabecular bone.	5
2	Over time the trabecular bone is transformed to a more cortical bone structure, which results in an increased stiffness of the implant–bone interface.	6
3	An implant placed in dense cortical bone.	6
4	No major changes of the bone density occur over time. The interfacial voids have been filled with bone.	7
5	Possible alterations in bone healing in diabetic patients.	9
6	Mechanism of diabetes induced osteoclastogenesis.	10
7	Relation between HbA1c levels (%) and plasma glucose levels (mg/dl).	17
8	Preoperative CBCT to determine adequacy of bone stock.	37
9	Preoperative HbA1c measurements to allocate each patient to one of the two groups.	38
10-11	Occlusal views showing crestal incision and a full thickness mucoperiosteal flap.	38
12	Lateral view of implant osteotomies	39
13	SLActive implant stored in isotonic solution (sodium chloride) to avoid surface contamination with molecules from	39



<b><i>Figure</i></b>	<b><i>Subject</i></b>	<b><i>Page</i></b>
	atmosphere and to maintain its hydrophilic surface.	
14	Lateral view showing implant insertion.	40
15	Lateral view of transducer attached to implant via screw to collect ISQ values in order to measure primary stability by a frequency response analyser.	40
16	Occlusal view of cover screws after being screwed to implants.	41
17	Occlusal view showing the flap repositioned and sutured over cover screws.	41
18	Occlusal view of healing abutments after being placed for 2 weeks.	46
19	Occlusal view showing impression posts with locating plastic caps screwed to the implant in preparation for a closed tray impression technique.	47
20	An audible click confirms successful reattachment of impression posts with their respective caps inside the additional silicone impression.	47
21	Channel drilled into crowns directly above the abutment's screw.	48
22	Channel is closed by Teflon temporarily in preparation for cementation on cast.	48
23	Cementation of crowns to the abutments on the cast by resin modified glass ionomer cement.	49

<b><i>Figure</i></b>	<b><i>Subject</i></b>	<b><i>Page</i></b>
24	Unscrewing of an abutment with the cemented crown through the channel to remove any remaining excess cement and to screw it to the implant fixture.	49
25	Occlusal view of channel after closure with Teflon and composite.	50
26	Measuring crestal bone levels on CBCT.	50
27	Superimposition of two CBCT images (one taken immediately after implant placement and the other after one year).	51
28	Bar chart representing mean and standard deviation for HbA1c in the two groups.	57
29	Line chart representing changes by time in mean HbA1c levels.	59
30	Bar chart representing mean and standard deviation for ISQ scores in the two groups.	61
31	Line chart representing changes by time in mean ISQ scores.	62
32	Box plot representing median and range values for amounts of bone loss in the two groups.	64
33	Line chart representing median crestal bone height changes in each group (An increase in measurement indicates bone loss).	65
34	Crestal bone levels measured on CBCT images.	66

## List of Tables

<i><b>Table</b></i>	<i><b>Subject</b></i>	<i><b>Page</b></i>
1	Number of cases, gender, age, preoperative HbA1c values and ISQ values recorded at time of implant insertion for group 1.	54
2	Number of cases, gender, age, preoperative HbA1c values and ISQ values recorded at time of implant insertion for group 2.	54
3	Comparisons of the demographic data for the two groups.	55
4	Descriptive statistics and results of repeated measures ANOVA test for comparison between HbA1c in the two groups.	57
5	Descriptive statistics and results of repeated measures ANOVA test for comparison between HbA1c levels at different time periods within each group.	58
6	Descriptive statistics and results of repeated measures ANOVA test for comparison between ISQ scores in the two groups.	60
7	Descriptive statistics and results of repeated measures ANOVA test for comparison between ISQ scores at different time periods within each group.	62
8	Descriptive statistics and results of Mann-Whitney U test for comparison between amounts of bone loss after 1 year in the two groups.	63
9	Descriptive statistics and results of Wilcoxon signed-rank test for comparison between crestal bone height changes within each group.	65

## Introduction

*Oates and Ba*<sup>1</sup> published that, diabetes mellitus is a chronic metabolic disorder that is reaching epidemic proportions, recently projected as affecting over 350 million individuals worldwide.

*Hegazi et al*<sup>2</sup> stated that, in Egypt, Diabetes mellitus is a fast-growing health problem with a significant impact on morbidity, mortality, and health care resources. Currently, the prevalence of Diabetes Mellitus is around 15.6% of all adults aged 20 to 79.

*Bianchi et al*<sup>3</sup> concluded that, diabetes mellitus affects the blood circulations and is associated with many complications such as retinopathy, ischemic heart disease, nephropathy, cerebrovascular disease, neuropathy and peripheral arterial diseases. Consequently there are several oro-dental manifestations. Marginal periodontitis with subsequent alveolar bone loss is one of the most common oro-dental complications especially in case of uncontrolled diabetes, which may lead to tooth loss and partial or total edentulism.

*Casap et al*<sup>4</sup> reported that, dental implants are usually used with excellent success rates in generally healthy individuals to replace their missing teeth; on the other hand, their use in diabetic patients remains controversial.

Recent studies indicate that diabetic patients might significantly benefit from implant supported rehabilitation allowing for an improved capacity for nutrition and metabolic control of the disease <sup>5, 29, 37</sup>.

*Kotsovilis et al* <sup>5</sup> stated that diabetes mellitus could contribute to implant failure as a result of impairment of wound healing, decreased vascular supply due to microangiopathies, decreased host defences, formation of advanced glycation end products (AGEs), reduction in collagen production and increased collagenase activity.

*Nobre et al* <sup>6</sup> published that, given the high number of affected individuals, an urgent need to understand the effects of diabetes on dental implants in order to improve the care for those patients.

A chemically modified hydrophilic titanium implant has been developed which enhances osteoblasts – surface and cell – surface interactions, resulting in a reduction of healing time to three to four weeks in healthy population. *Mamalis et al* <sup>7</sup> concluded that, this hydrophilic surface had a positive effect on osteoblasts differentiation and mineralization which might counteract the cellular effects caused by diabetes.

## Review of literature

*Mavrogenis et al*<sup>8</sup> published that, the concept of osseointegration as described by Brånemark is a direct and structural functional connection between ordered living bone and the surface of a load carrying implant. In other words, there is no relative progressive motion as a result of intimate direct contact between the implant and native bone. Osseointegration starts by a cascade of cellular and extracellular biological events which initiates the bone healing process at the bone - implant interface until the implant surface is finally covered with bone.

This cascade of events is regulated by growth and differentiation factors released by activated blood cells at bone – implant interface.

*Marcianni et al*<sup>9</sup> described the phases of bone healing. The first phase of bone healing around implants is coagulation and inflammation. A hematoma is formed first by blood contents escaping injured vessels and marrow at implant site. It is formed by platelets and coagulation factors. Inflammatory mediators as Tumour Growth Factor beta (TGF-B) and Platelet Derived Growth Factor (PDGF) are released due to platelets degranulation; these mediators recruit mesenchymal cells and osteoblasts into the area during the first 24 hours.

During this time, macrophages and neutrophils produce cytokines such as Tumour Necrosis Factor Alpha (TNF-  $\alpha$ ), Interleukin one (IL-1) and Interleukin six (IL-6). These cytokines further recruits mesenchymal cells, osteoblasts and chondroblasts. As healing transitions into the next phase which is proliferation phase, fibroblasts secrete their matrix which acts as a scaffold for recruitment of endothelial cells to produce granulation tissue. Osteoblasts differentiation from mesenchymal cells is directed by TGF-B and Bone Morphogenic Proteins (BMP). Immature osteoblasts secrete osteoid which is the organic part of bone matrix and produce growth factors as TGF-B, while mature osteoblasts produce alkaline phosphatase and BMP. Alkaline phosphatase initiates osteoid matrix mineralization and formation of hydroxyapatite crystals. The newly formed woven bone which is disorganized calcified osteoid provides biological stabilization of the implant (**Fig. 1**).

As the mineralization process ends, most osteoblasts undergo apoptosis, while the remaining osteoblasts entrench themselves in lacunae, or rest on bone surface. These remaining osteoblasts are now osteocytes and responsible for maintenance (**Fig 2**). The bone healing process is terminated by the remodelling phase which is controlled by osteoblasts which not only produce the components of bone, but also, influence osteoclasts differentiation. Osteoclasts