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

A Thesis

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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

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List of Abbreviations

AGE	**:**	Advanced Glycation End Products.
BMP	**:**	Bone Morphogenic Proteins.
BIC	**:**	Bone Implant Contact.
CBCT	**:**	Cone Beam Computerized Tomography.
DM	**:**	Diabetes Mellitus.
HbA1c	**:**	Glycated Hemoglobin A1c.
HO^-	**:**	Hydroxyl.
H_2O_2	**:**	Hydrogen Peroxide.
IAJ	**:**	Implant Abutment Junction.
IL-1	**:**	Interleukin One.
IL-6	**:**	Interleukin Six.
ISQ	**:**	Implant Stability Quotient.
N	**:**	Newton.
NO	**:**	Nitric Oxide.
O_2^-	**:**	Superoxide.
$ONOO^-$	**:**	Peroxynitrite.
PD	**:**	Periodontal Disease.
PDGF	**:**	Platelet Derived Growth Factor.
RAGE	**:**	Receptor for Advanced Glycation End Products.
RANKL	**:**	Receptor Activator for Nuclear Factor Kappa-B Ligand.

List of Abbreviations (Cont.)

RFA	**:**	Resonance Frequency Analysis.
ROS	**:**	Reactive Oxygen Species.
SLA	**:**	Sand Blasted, Large Grit, Acid Etched.
TGF-B	**:**	Tumour Growth Factor Beta.
TNF-α	**:**	Tumour Necrosis Factor Alpha.
µm/N	**:**	Micrometer per Newton.

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Introduction

Oates and Ba [1] 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 [2] 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 [3] 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 [4] 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 [5, 29, 37].

Kotsovilis et al [5] 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 [6] 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*** [7] 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 [8] 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 [9] 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- α), 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