Felipe Eduardo Baires Campos

# Efeito da geometria do implante dentário e do protocolo de fresagem óssea na estabilidade primária e na osseointegração inicial:
## Estudo experimental em cães

Tese apresentada à Faculdade de Odontologia da Universidade Federal de Uberlândia, como parte dos requisitos para obtenção do Título de Doutor em Odontologia na Área de concentração: Clínica Odontológica Integrada.

Uberlândia, 2014

Felipe Eduardo Baires Campos

# Efeito da geometria do implante dentário e do protocolo de fresagem óssea na estabilidade primária e na osseointegração inicial:
## Estudo experimental em cães

Tese apresentada à Faculdade de Odontologia da Universidade Federal de Uberlândia, como parte dos requisitos para obtenção do Título de Doutor em Odontologia na Área de concentração: Clínica Odontológica Integrada.

Orientador: Prof. Dr. Darceny Zanetta Barbosa
Co-orientador: Prof. Dr. Paulo Guilherme Coelho
Banca Examinadora:
Prof. Dr. Darceny Zanetta Barbosa
Prof. Dr. Carlos José Soares
Profa. Dra. Paula Dechichi
Prof. Dr. Wagner Henriques de Castro
Prof. Dr. Rodrigo Granato
Prof. Dra. Claudia Jordão Silva
Prof. Dra. Camila Christian Gomes Moura
Uberlândia, 2014

Dados Internacionais de Catalogação na Publicação (CIP)
Sistema de Bibliotecas da UFU, MG, Brasil.

---

C198e
2014

Campos, Felipe Eduardo Baires,
Efeito da geometria do implante dentário e do protocolo de fresagem óssea na estabilidade primária e na osseointegração inicial: estudo experimental em cães / Felipe Eduardo Baires Campos. - 2014.
72 f.

Orientador: Darceny Zanetta Barbosa.
Tese (doutorado) - Universidade Federal de Uberlândia, Programa de Pós-Graduação em Odontologia.
Inclui bibliografia.

1. Odontologia - Teses. 2. Implantes dentários - Teses. 3. Osseointegração - Teses. I. Zanetta-Barbosa, Darceny. II. Universidade Federal de Uberlândia. Programa de Pós-Graduação em Odontologia. III. Título.

CDU: 616.314

# ***DEDICATÓRIA***

À minha família, meu pai, minha mãe e meu irmão por sempre estarem ao meu lado e fornecerem apoio a este longo caminho pelo qual decidi tomar na Área da Cirurgia e Traumatologia Buco-Maxilo-Facial.

À Renata, minha esposa pelo carinho, amor e dedicação depositados em nossa união durante todo este tempo. Te amo muito!

Aos amigos Wagner Castro e Luiz Felipe, por terem me acolhido na vida profissional e por fazerem parte diária dela.

# AGRADECIMENTOS

Ao meu orientador, prof. Dr. Darceny Zanetta-Barbosa pelo exemplo, orientação, ensinamentos e dedicação durante estes anos.

Ao meu co-orientador, prof. Dr. Paulo Guilherme Coelho pelos ensinamentos e dedicação irrestrita.

Aos professores e funcionários do Programa de Pós Graduação em Odontologia pelos ensinamentos e apoio.

A Faculdade de Odontologia da Universidade Federal de Uberlândia, na pessoa do Coordenador de Pesquisa e Pós-Graduação, Prof. Carlos José Soares pelos ensinamentos.

Ao colega Marcelo Suzuki por ter me acolhido de forma exemplar em Boston, pelos ensinamentos passados no laboratório da BICON.

Aos colegas da pós graduação que participaram desta caminhada.

À FAPEMIG pelo apoio financeiro para execução do projeto de Tese de doutorado.

# SUMÁRIO

# RESUMO

**Capítulo 1.** O presente estudo histológico avaliou dois implantes de macrogeometrias distintas: implantes com roscas tradicionais em comparação com implantes com desenho específico para criação de câmaras de osseointegração, inseridos com dois protocolos de instrumentação. Quarenta implantes dentários (4.1mm de diâmetro) foram inseridos na tIbia de 10 cães Beagle, o torque de inserção máximo foram anotados para todas amostras. As técnicas de instrumentação utilizadas nos dois tipos de implantes foram: instrumentação com diâmetro final de fresagem de 3.75mm (grupo regular); e instrumentação final com 4.0mm de diâmetro (grupo de sobre-instrumentação). Após 2 e 4 semanas, as amostras foram processadas para avaliação histomorfométrica. Para o torque de inserção, BIC e BAFO, um modelo linear geralizado foi aplicado, incluindo técnica de instrumentação e tempo in vivo como fatores independentes. O torque de inserção registrado para cada tipo de implante diminuiu significativamente em função do aumento do diâmetro da perfuração para ambos os desenhos de implantes ($p <0,001$). Não foram detectadas diferenças significativas entre os tipos de implantes para cada técnica de perfuração ($p> 0,18$). Foi observado um aumento significativo em BIC a partir de 2 semanas para 4 semanas de implantação para os dois modelos de implantes utilizados com a técnica de sobrefresagem ($p <0,03$). Quando ambos os implantes foram colocados nos locais de fresagem de 3,75 mm, não foram detectadas diferenças significativas em BIC ao longo do tempo ($p> 0,32$). Apesar das diferenças entre macrogeometrias dos implantes e da técnica de fresagem óssea o tipo de osseointegração prevalente foi a intramembranosa.

**Capítulo 2.** O objetivo deste estudo histológico preliminar foi determinar se alterações nos protocolos de instrumentação (sub-instrumentação, intermediária, sobre-instrumentação) determinam respostas biológicas distintas no estágio inicial de 02 semanas de osseointegração. Foram adiquiridos dez cães, os quais foram submetidos a cirurgia na tibia, e após 02 semanas foi realizada a euthanasia. Durante a cirurgia três implantes

de 4mm de diâmetro por 10mm de comprimento, foram inseridos em sítios cirúrgicos com diâmetro final de 3.5mm, 3.75mm e 4.0mm. Os torques de inserção e remoção foram anotados para todas as amostras. A avaliação estatística foi realizada com 95% de nível de significância e o número de cães foi considerado como a unidade estatística para todas as comparações. Para o torque, BIC e BAFO, modelo geral linear foi utilizado incluindo técnica de instrumentação e tempo *in vivo.* Em geral, com a diminuição do diâmetro final de fresagem houve aumento do torque de inserção de 4.0mm, para 3.75mm, para 3.5mm, com diferenças estatesticas significantes entre todos os grupos ($p<0.001$). Avaliação estatística para BIC e BAFO demosntrou maiores valores significativos para o grupo de 3.75mm de instrumentação em comparação aos outros dois grupos ($p<0.001$). As diferentes técnicas de instrumentação resultaram em variações nos torques de inserção (estabilidade primária) e em distintas vias de osseointegração foram observadas entre os grupos.

**Capítulo 3.** O presente trabalho avaliou o efeito de diferentes dimensões de fresagem (sub-instrumentação, regular, sobre-instrumentação) no torque de inserção e remoção de implantes dentários inseridos em cães beagle. Foram utilizados seis cães com realização de cirurgia em ambos os ossos radio nos períodos de 1 e 3 semanas prévios a euthanasia. Durante a cirurgia, 3 implantes de 4.0mm de diâmetro por 10mm de comprimento foram inseridos em sítios cirúrgicos de diâmetro final de fresagem de 3.2mm, 3.5mm, e 3.8mm. Os torque de inserção e remoção foram avaliados para todas amostras. Avaliação estatística foi realizada por teste *t* pareado para medições repetidas (nível de significância de 95%). Em geral, os torques de inserção e remoção foram inversamente proporcionais a dimensão de fresagem, sendo detectada diferença significativa entre grupos de 3.2mm e 3.5mm em relação ao de 3.8mm ($P<0.03$). Na avaliação pareada para torque de inserção e remoção não foram encontradas diferenças significativas entre grupos de 3.5mm e 3.8mm. Apesar disto, foi observado uma diminuição significativa do torque de remoção em comparação ao torque de inserção para o grupo de

3.2mm. Entre os diferentes grupos foram observadas distintas formas de osseintegração e da interface de remodelação.

## ABSTRACT

**Capítulo 1.** This study histologically evaluated two implant designs: a classic thread design versus another specifically designed for healing chamber formation placed with two drilling protocols. Forty dental implants (4.1 mm diameter) with two different macrogeometries were inserted in the tibia of 10 Beagle dogs, and maximum insertion torque was recorded. Drilling techniques were: until 3.75 mm (regular-group); and until 4.0 mm diameter (overdrilling-group) for both implant designs. At 2 and 4 weeks, samples were retrieved and processed for histomorphometric analysis. For torque and BIC (bone-to-implant contact) and BAFO (bone area fraction occupied), a general-linear model was employed including instrumentation technique and time in vivo as independent. The insertion torque recorded for each implant design and drilling group significantly decreased as a function of increasing drilling diameter for both implant designs ($p<0.001$). No significant differences were detected between implant designs for each drilling technique ($p>0.18$). A significant increase in BIC was observed from 2 to 4 weeks for both implants placed with the overdrilling technique ($p<0.03$) only, but not for those placed in the 3.75 mm drilling sites ($p>0.32$). Despite the differences between implant designs and drilling technique an intramembranous-like healing mode with newly formed woven bone prevailed.

**Capítulo 2.** The objective of this preliminary histologic study was to determine whether the alteration of drilling protocols (oversized, intermediate, undersized drilling) present different biologic responses at early healing periods of 2 weeks *in vivo* in a beagle dog model. Ten beagle dogs were acquired and subjected to surgeries in the tibia 2 weeks before euthanasia. During surgery, 3 implants, 4 mm in diameter by 10 mm in length, were placed in bone sites drilled to 3.5 mm, 3.75 mm, and 4.0 mm in final diameter. The insertion and removal torque was recorded for all samples. Statistical significance was set to 95% level of confidence and the number of dogs was considered as the statistical unit for all comparisons. For the torque and BIC and BAFO, a general linear model was employed including instrumentation technique and time in vivo

as independent. Overall, the insertion torque increased as a function of drilling diameter from 4.0 mm, to 3.75 mm, to 3.5 mm, with a significant difference in torque levels between all groups ($p<0.001$). Statistical assessment of BIC and BAFO showed significantly higher values for the 3.75 mm (recommended) drilling group was observed relative to the other two groups ($p<0.001$). Different drilling dimensions resulted in variations in insertion torque values (primary stability) and different pattern of healing and interfacial remodeling was observed for the different groups.

**Capítulo 3.** The present study evaluated the effect of different drilling dimensions (undersized, regular, and oversized) in the insertion and removal torques of dental implants in a beagle dog model. Six beagle dogs were acquired and subjected to bilateral surgeries in the radii 1 and 3 weeks before euthanasia. During surgery, 3 implants, 4 mm in diameter by 10 mm in length, were placed in bone sites drilled to 3.2 mm, 3.5 mm, and 3.8 mm in final diameter. The insertion and removal torque was recorded for all samples. Statistical analysis was performed by paired t tests for repeated measures and by t tests assuming unequal variances (all at the 95% level of significance). Overall, the insertion torque and removal torque levels obtained were inversely proportional to the drilling dimension, with a significant difference detected between the 3.2 mm and 3.5 mm relative to the 3.8 mm groups ($P < 0.03$). Although insertion torque–removal torque paired observations was statis- tically maintained for the 3.5 mm and 3.8 mm groups, a significant decrease in removal torque values relative to insertion torque levels was observed for the 3.2 mm group. A different pattern of healing and interfacial remodeling was observed for the different groups. Different drilling dimensions resulted in variations in insertion torque values (primary stability) and stability maintenance over the first weeks of bone healing.

## OBJETIVO GERAL

Os presentes trabalhos têm como objetivo a avaliação dos estágios iniciais da osseointegração de implantes dentários com diferentes macrogeomterias inseridos em sítios cirúrgicos com diâmetro final de instrumentação distintos.

## OBJETIVOS ESPECÍFICOS

**Capítulo 1.** Avaliar histológicamente dois sistemas de implantes distintos, um com desenho de roscas tradicionais em comparação com implantes especialmente desenhados para criar câmaras de osseointegração. Implantes estes inseridos com dois protocolos de instrumentação que conferiram diferentes níveis de estabilidade primária assim como na relação da interface implante-osso.

**Capítulo 2.** Determinar se alterações nos protocolos de instrumentação (sobre-instrumnetação, intermediária, sub-instrumentação) apresentam diferentes respostas biológicas nos eságios iniciais de 02 semanas *in vivo* em um modelo de estudo animal.

**Capítulo 3.** Investigar a relação entre torque de inserção e remoção de de implantes dentários inseridos em sítios cirúrgicos com diferentes diâmetros finais de fresagem, após 1 e 3 semanas *in vivo.*

# 1. INTRODUÇÃO E REFERENCIAL TEÓRICO

Após o surgimento de nova tecnologia, indiferente de sua aplicabilidade, quanto mais usual ela for, mais rápido os seus limites serão testados, assim como haverá aumento na demanda quanto a necessidade de ocorrerem refinamentos e melhoras nessa tecnologia (Davies, 2003). Na área da implantodontia isso não pode ser diferente. A necessidade de diminuir o tempo clínico de tratamento e melhorar a resposta óssea em torno de implantes para otimizar o tratamento em regiões de qualidade óssea comprometida. A partir da década de 90 do século passado, estudos relacionados à microtopografia dos implantes iniciaram nova era dos implantes dentários: as modificações de superfície, apresentando resultados promissores, que aceleram a velocidade de osseointegração e modulam positivamente a resposta do tecido ósseo (Wennerberg *et al.,* 1993; Wennerberg *et al.,* 1997, Albrektsson *&* Wennerberg, 2004; Albrektsson *et al*, 2008). A osteogênese na região peri-implante ocorre em duas direções, havendo formação óssea do sítio receptor em direção ao implante (osteogênese a distância), assim como do implante em direção às paredes ósseas adjacentes, denominada de osteogênese de contato (Puelo & Nanci, 1999; Davies, 2000; Marco *et al.,* 2005). Existem evidências de que a osteogênese de contato apresente velocidade de formação óssea 30% maior em relação à osteogênese a distância (Puelo & Nanci, 1999). Por meio da alteração do formato dos implantes e da técnica cirúrgica de fresagem pode se direcionar entre estes dois tipos de formação óssea peri-implante nos estágios iniciais da osseointegração.

Na pratica clínica atual, os implantes dentários parafusados são os mais utilizados, outro tipo empregado, em menor escala, são os implantes em forma de platôs. As taxas de sucesso para estes dois tipos são semelhantes (Chuang *et al.* 2002a). Os implantes na forma de platôs se diferem dos convencionais pela presença de pequenas câmaras de osseointegração na interface com o osso. Nas câmaras observa-se predominância da osteogênese de contato. Este tipo de implante não é parafusado no osso previamente fresado, mas sim pressionado na loja cirúrgica que apresenta diâmetro igual ao do implante. Esta associação permite a criação das câmaras de osseointegração entre as paredes ósseas e o diâmetro interno do implante (Granato *et al.,* 2008; Coelho *et al.,* 2009b; Leonardo *et al.,* 2009). A utilização dos implantes parafusos aliado a técnica cirúrgica é uma alternativa para a criação das câmaras de osseointegração (Coelho *et al.,* 2009b). Na interface entre as paredes ósseas e a superfície destes implantes predominam as osteogêneses de contato e osteogênese a distância.

Recentemente a carga imediata em implantes dentários ganhou popularidade devido a redução no tempo de tratamento e da morbidade, assim como benefícios estéticos e psicológicos para o paciente (Javed & Romanos, 2010). Tradicionalmente os implantes dentários são colocados em função após 3 a 6 meses de osseointegração na interface osso-implante (Branemark, 1977), já os que são submetidos a carga imediata são colocados em função logo após a sua inserção, sem esse longo período de espera. O sucesso do tratamento da carga imediata tem sido relacionado ao estabelecimento de uma boa estabilidade primária, que pode ser definida pela criação de rígida interface entre osso-implante, em outras palavras, a falta de mobilidade do implante após sua inserção (Javed & Romanos, 2010). A percepção clínica de estabilidade primária do implante é comumente relacionada à resistência rotacional (torque de inserção) durante a colocação do implante. Alguns fatores estão relacionados à aquisição da estabilidade primária, como a técnica de inserção (velocidade de fresagem, tamanho das fresas, proporção entre diâmetro final das fresas e diâmetro do implante, parafusos auto-perfurantes ou não, etc.), a geometria do implante (implantes cônicos, sólidos, diâmetro do implante), a qualidade (proporção entre osso compacto e trabecular) e quantidade óssea (Sennerby *et al.,* 1992; Meredith, 1998; O'Sullivan *et al.,* 2000; O'Sullivan *et al.,* 2004).

Para adquirir maior estabilidade primária é prática comum realizar dimensões de fresagem menores em relação ao diâmentro do implante (O'Sullivan *et al.,* 2000). Entretanto, apesar de adquirirem maiores valores de torque de inserção por meio da colocação de implantes em sítios cirúrgicos de menor dimensão, a resposta inicial da área hospedeira poderá ser afetada pelos maiores níveis de compressão óssea. No estágios iniciais de osseointegração os fatores biológicos e biomeânicos variam ao longo do tempo. Mais precisamente, observa-se uma queda da estabilidade em implantes inseridos com alto torque de inserção. Em contrapartida, os implantes com baixa estabilidade primária observa-se aumento na estabilidade com a evolução da osseointegração (Coelho *et al., 2014*). Portanto, a transição entre a estabilidade primária (mecânica) e secundária (biológica) deve ser avaliada nos estágios iniciais da osseoitegração. Comumente, se utiliza os períodos de 1 a 6 semanas de osseointegração no cães, pois é hipotetizado que nos estágios tardios da osseointegração as formações ósseas se tornam equivalentes.

Teoricamente, tem sido sugerido que o tecido ósseo é um material elástico previamente ao seu ponto de deformação, o que indica ser capaz de suportar determinados níveis de forças de compressão (Jimbo *et al.,* 2013). Em contrapartida, quando a tensão exercida excede o módulo de elasticidade óssea, ocorrem pequenas microfraturas ósseas. Em associação, a compressão capilar, que leva a necrose óssea isquêmica, associado ou não a fratura óssea (Bashutski *et al.,* 2009).

## 2. CAPÍTULOS

# Capítulo 1 (Artigo 1)

**Referência do Artigo segundo normas do programa:**

Campos FEB, Bonfante E, Jimbo R, Oliveira MTF, Moura CCG, Barbosa DZ, Coelho PG. Drilling dimension effects in early stages of osseointegration and implant stability in a canine model. (Artigo enviado para publicação na revista International Journal of Oral and Maxillofacial Surgery)

Manuscript Number:

Title: Drilling Dimension Effects in Early Stages of Osseointegration and Implant Stability in a Canine Model

Article Type: Research Paper

Keywords: histomorphometry; biomechanical; in vivo; initial stability; insertion torque; osseointegration

Corresponding Author: Dr. Estevam A Bonfante, DDS, MS, PhD

Corresponding Author's Institution: University of São Paulo - Bauru School of Dentistry

First Author: Felipe E Campos, DDS, MS

Order of Authors: Felipe E Campos, DDS, MS; Ryo Jimbo, DDS, PhD; Estevam A Bonfante, DDS, MS, PhD; Maiolino T Oliveira, DDS, MS; Camila C Moura, DDS, PhD; Darceny Z Barbosa, DDS, PhD; Paulo G Coelho, DDS, MS, BS, MSMtE, PhD

Abstract: This study histologically evaluated two implant designs: a classic thread design versus another specifically designed for healing chamber formation placed with two drilling protocols. Forty dental implants (4.1 mm diameter) with two different macrogeometries were inserted in the tibia of 10 Beagle dogs, and maximum insertion torque was recorded. Drilling techniques were: until 3.75 mm (regular-group); and until 4.0 mm diameter (overdrilling-group) for both implant designs. At 2 and 4 weeks, samples were retrieved and processed for histomorphometric analysis. For torque and BIC (bone-to-implant contact) and BAFO (bone area fraction occupied), a general-linear model was employed including instrumentation technique and time in vivo as independent. The insertion torque recorded for each implant design and drilling group significantly decreased as a function of increasing drilling diameter for both implant designs ($p<0.001$). No significant differences were detected between implant designs for each drilling technique ($p>0.18$). A significant increase in BIC was observed from 2 to 4 weeks for both implants placed with the overdrilling technique ($p<0.03$) only, but not for those placed in the 3.75 mm drilling sites ($p>0.32$). Despite the differences between implant designs and drilling technique an intramembranous-like healing mode with newly formed woven bone prevailed.

New York University College of Dentistry

Department of Biomaterials & Biomimetics
Arnold and Marie Schwartz Hall of Dental Sciences
345 East 24th Street (Rm 813a) New York, NY 10010 212-998-9368, FAX: 212-995-4244

New York, January 8th, 2014

Dr. Nabil Samman,
Editor-in-chief
International Journal of Oral and Maxillofacial Surgery

Dear Dr. Samman,

Attached please find our latest work entitled: **“Drilling Dimension Effects in Early Stages of Osseointegration and Implant Stability in a Canine Model** “ which we submit for possible publication in International Journal of Oral and Maxillofacial Surgery. In this work we have investigated the effect of different implant designs and drilling protocols on selected osseointegration parameters. Classic thread and experimentally designed implants with healing chambers were used under a drilling protocol either recommended by the manufacturer or a controlled overdrilling. Results and discussion are presented along with the clinical significance of our findings and interpretation of osseointegration pathways occurring when healing chambers are allowed. We hope that the manuscript fits the content of the journal and we look forward to hearing back from the referees.

We confirm that our study has not been submitted simultaneously to another journal, has been read and approved by all authors, and that the work has not been published before.

Paulo G. Coelho et al

# Drilling Dimension Effects in Early Stages of Osseointegration and Implant Stability in a Canine Model.

Felipe Eduardo B. Campos[a], Ryo Jimbo[b], Estevam Augusto Bonfante*[c], Maiolino Thomaz. F. Oliveira[a], Camila Christian G. Moura [a],[d], Darceny Z. Barbosa[a], Paulo G. Coelho[e,f,g]

a- Division of Oral and Maxillofacial Surgery, Department of Oral Surgery, School of Dentistry, Federal University of Uberlândia, Uberlândia, MG, Brazil

b- Department of Prosthodontics, Faculty of Odontology, Malmö University, Malmö, Sweden

c- Department of Prosthodontics, University of Sao Paulo – Bauru College of Dentistry, Bauru, SP, Brazil

d- Department of Histology, Federal University of Triângulo Mineiro, Uberaba, MG, Brazil

e- Department of Biomaterials and Biomimetics, New York University, New York, NY, USA

f- Director for Research, Department of Periodontology and Implant Dentistry New York University College of Dentistry, New York, NY, USA

g- Division of Engineering, New York University Abu Dhabi, Abu Dhabi, United Arab Emirates

*** Corresponding author**:

Estevam A. Bonfante / Department of Prosthodontics

Alameda Octávio Pinheiro Brisola, 9-75, Bauru, SP, Brasil, 17012-901.

Phone: 55(14) 3235-8349. / FAX: 55(14)3234-2566 / e-mail: estevamab@gmail.com

**Keywords**: histomorphometry; biomechanical; *in vivo;* initial stability; insertion torque; osseointegration

**Short Title**: Primary Stability and Osseointegration

## Introduction

Osseointegration has been thoroughly reported in literature and has become one of the most effective treatments in medicine and dentistry. While highly successful for anchoring load bearing capable metallic devices through established surgical and prosthetic techniques, a plethora of scientific work regarding osseointegration's fundamental mechanisms as a function of multiple variables has been published over the last decade[1].

Being the implant surface the first part of the implant to interact with the host, a large amount of work has established surface modifications as one possible design parameter capable of substantially decrease osseointegration time[2, 3]. For that purpose, surface texturing has become the most utilized approach and work regarding texturing at both micrometer scale and nanometer scale is ongoing in an attempt to find the optimal pattern to hasten early osseointegration[4-6]. In addition, recent work on how the dimensional interplay between implant macro-geometry and surgical instrumentation affects the bone healing pathway has provided new insight regarding how implant systems can be further modified to provide scenarios where implant stability can be immediately achieved and temporally maximized[7-10].

While it has been previously demonstrated that surgical instrumentation and implant design may result in high degrees of contact between implant and bone immediately after placement providing higher resistance to micromotion (thus improving the likelihood of osseointegration compared to fibrous integration)[11], several studies have shown that this initially contacting bone gradually resorbs resulting in an implant stability dip[7, 8, 12]. Such decrease in implant resistance to micromotion has been experimentally demonstrated to be posteriorly compensated by new bone formation at regions where bone resorption occurred [13-15]. Such scenario has been suggested to arise from the excessive strain or compression that the implant exerts on the surrounding bone that exceeds the physiological limit and triggers bone resorption/remodeling[13].

Alternatively, void spaces left between bone and implant bulk that will fill with a blot clot immediately after placement and will not contribute to primary stability are known to rapidly fill with woven bone, being a key contributor to secondary stability as it does not have to undergo remodeling due to its different healing pattern [16, 17]. The mode and kinetics of bone formation in such healing chambers has been discussed in detail by Berglundh et al. [14] while the effect of healing chamber size and shape on bone formation has been explored by Marin et al.[9]. In addition, studies comparing implants that were tightly fit into their drilling sites with implants that were simply taped into oversized drilling sites or lightly screwed in larger drilling sites have shown that at the same time that bone resorption was occurring in regions that were compressed by the implant, bone filling was already occurring in healing chambers [7, 8, 12, 18]. Altogether, these studies have led to an initial platform for designing implant systems that combine instrumentation and implant geometrical configurations that attempt to maximize implant stability over time. For this purpose, several investigators have employed either experimental implant designs with an outer thread design that provided stability while the inner thread and osteotomy dimensions allowed healing chambers[14, 19, 20] or alterations in osteotomy dimensions in large thread pitch implant designs[7, 8, 12]. While it is obvious that most threaded implant systems may present healing chambers if expanded drilling dimensions are utilized, the combination of the initial mechanical stability and related healing may not necessarily lead to satisfactory degrees of atemporal stability. Thus, the objective of the present study was to histologically evaluate two different implant systems, a classic thread design versus another specifically designed for healing chamber formation along with primary stability, placed into two drilling schemes that allowed different initial stability and interplay between implant and bone.

## Materials and Methods

Implants of 4.1 mm diameter and 10 mm length of two different macrogeometries (n=40 of each type) were utilized in the present study, namely Strong SW and Unitite (SIN, São Paulo, SP, Brazil). Both implants presented similar conical profiles and the main difference between the designs comprised the thread profile, where the SW presented a single thread design and the Unitite presented a dual thread (thread within thread profile). Both implants presented a dual acid etched surface that has been previously characterized[21]. Two drilling techniques were utilized for each of the implant designs, a technique to the final diameter recommended by the manufacturer (3.75 mm- regular group) and a technique where the final diameter was larger than recommended by the manufacturer (4.0 mm- overdrilling group). For the laboratory *in vivo* model, ten adult male beagle dogs with approximately 1.5 years of age were acquired following the approval of the Ethics Committee for Animal Research at "Institution's name can not be mentioned accoding to author's guidelines", (protocol/approval number CEUA/UFU 082/12).

Prior to general anesthesia, IM atropine sulfate (0,044 mg/kg) and xilazyne chlorate (8 mg/kg) were administered. A 15mg/Kg ketamine chlorate dose was then utilized to achieve general anesthesia.

The surgical site was the proximal tibia. Following hair shaving, skin exposure, and antiseptic cleaning with iodine solution at the surgical and surrounding area, a 5 cm length incision to access the periosteum was performed and a flap reflected for bone exposure.

Four implants were placed along the tibia from proximal to distal in an alternated implant design and drilling technique distribution, being interchanged in every tibia to minimize bias from different implantation sites (sites 1 to 4 from proximal to distal). Therefore, the 40 implants of each design in each drilling technique remained *in vivo* for either 2 or 4 weeks, respectively, and were thus allocated in sites 1 to 4 in an equal distribution. This approach resulted in balanced surgical procedures that allowed the comparison of the same number of implant design and drilling technique per time *in vivo*, limb, surgical site (1 through 4), and animal. The implants were placed at distances of 1 cm from each other along the central region of the bone. The implants were inserted in the drilled sites and the maximum insertion torque was recorded with a portable digital torquemeter (Tohnichi, Tokyo, Japan) with a 200 Ncm load cell for each implant placed.

Following placement, each implant received its proprietary cover screw to avoid tissue overgrowth. The soft tissue was sutured in layers following standard procedures, where the periosteum was sutured with vicryl 4-0 (Ethicon Johnson, Miami, FL, USA) and the skin with 4-0 nylon (Ethicon Johnson, Miami, FL, USA).

Post-operative anti-biotic and anti-inflammatory medication included a single dose of Benzyl Penicillin Benzatine (20.000 UI/Kg) IM and Ketoprofen 1%

(1ml/5Kg). The animals were euthanized by anesthesia overdose and the limbs were retrieved by sharp dissection. The soft tissue was removed by surgical blades, and initial clinical evaluation was performed to determine implant stability. If an implant was clinically unstable, it was excluded from the study.

The bones containing the implants were reduced to blocks and immersed in 10% buffered formalin solution for 24h. The blocks were then washed in running water for 24h, and steadily dehydrated in a series of alcohol solutions ranging from 70-100% ethanol. Following dehydration, the samples were embedded in a methacrylate-based resin (Technovit 9100, Heraeus Kulzer GmbH, Wehrheim, Germany) according to the manufacturer's instructions. The blocks were then cut into slices (~300 μm thickness) aiming the center of the implant along its long axis with a precision diamond saw (Isomet 2000, Buehler Ltd., Lake Bluff, USA), glued to acrylic plates with an acrylate-based cement, and a 24h setting time was allowed prior to grinding and polishing. The sections were then reduced to a final thickness of ~30 μm by means of a series of SiC abrasive papers (400, 600, 800, 1200 and 2400) (Buehler Ltd., Lake Bluff, IL, USA) in a grinding/polishing machine (Metaserv 3000, Buehler Ltd., Lake Bluff, USA) under water irrigation[22]. The sections were then toluidine blue stained and referred to optical microscopy at 50X-200X magnification (Leica DM2500M, Leica Microsystems GmbH, Wetzlar, Germany) for histomorphologic evaluation.

The bone-to-implant contact (BIC) was determined at 50X-200X magnification (Leica DM2500M, Leica Microsystems GmbH, Wetzlar, Germany) by means of computer software (Leica Application Suite, Leica Microsystems GmbH, Wetzlar, Germany). The regions of bone-to-implant contact along the implant perimeter were subtracted from the total implant perimeter, and calculations were performed to determine the BIC. The bone area fraction occupied (BAFO) between threads in trabecular bone regions was determined at 100X magnification (Leica DM2500M, Leica Microsystems GmbH, Wetzlar, Germany) by means of a computer software (Leica Application Suite, Leica Microsystems GmbH, Wetzlar, Germany). The areas occupied by bone were subtracted from the total area between threads, and calculations were performed to determine the BAFO (reported in percentage values of bone area fraction occupied)[16].

For all outcomes, statistical significance was set to 95% level of confidence and the number of dogs was considered as the statistical unit for all comparisons. For the torque and histomorphometric dependent variables BIC and BAFO, a general linear model was employed including implant design, instrumentation technique, and time *in vivo* as independent variables (surgical site position was preliminarily evaluated and due to a lack of effect on Torque, BIC, and BAFO was excluded from further analysis) (IBM SPSS Statistics, v. 19 IBM, New York, NY, USA).

## Results

No complications regarding procedural conditions or other immediate clinical concerns were observed during immediate follow up and throughout the entire study *in vivo* period. No post-operative complication was detected and no implant was excluded from the study due to clinical instability of all implants after euthanization.

Overall torque (when both drilling techniques were collapsed for each separate implant design) showed no significant difference between implant designs (Figure 1a). The insertion torque recorded for each implant design and drilling group is presented in Figure 2, where the torque significantly decreased as a function of increasing drilling diameter for both implant designs ($p<0.001$). No significant differences were detected between implant designs for each drilling technique ($p>0.18$).

Qualitative evaluation of the biological response showed intimate contact between cortical and trabecular bone for all groups at both implantation times, including regions that were in close proximity or substantially away from the osteotomy walls (Figures 3 and 4). For both implant designs and all drilling techniques employed, the toluidine blue stained thin sections presented an appositional bone healing mode at regions where intimate contact existed between implant surfaces and bone immediately after placement (Figures 3 and

## Results

No complications regarding procedural conditions or other immediate clinical concerns were observed during immediate follow up and throughout the entire study *in vivo* period. No post-operative complication was detected and no implant was excluded from the study due to clinical instability of all implants after euthanization.

Overall torque (when both drilling techniques were collapsed for each separate implant design) showed no significant difference between implant designs (Figure 1a). The insertion torque recorded for each implant design and drilling group is presented in Figure 2, where the torque significantly decreased as a function of increasing drilling diameter for both implant designs ($p<0.001$). No significant differences were detected between implant designs for each drilling technique ($p>0.18$).

Qualitative evaluation of the biological response showed intimate contact between cortical and trabecular bone for all groups at both implantation times, including regions that were in close proximity or substantially away from the osteotomy walls (Figures 3 and 4). For both implant designs and all drilling techniques employed, the toluidine blue stained thin sections presented an appositional bone healing mode at regions where intimate contact existed between implant surfaces and bone immediately after placement (Figures 3 and

4). These regions comprised the vast majority of the perimeter of the SW implants placed into 3.75 mm drilling sites (Figure 3a and 4a), and the outer aspects of the threads of the Unitite implants placed into the 3.75 (recommended, Figures 3b and 4b) and both Unitite and SW implants placed in 4.0 mm (overdrilling, Figures 3c-d and 4c-d) drilling sites.

At two weeks, the SW implants placed into the 3.75 mm drilling sites presented necrotic spots and bone remodeling sites (Figure 3a) along the perimeter of the implant/bone contact especially in regions in close proximity with the implant inner diameter. At 4 weeks *in vivo*, the SW implants placed into the 3.75 mm drilling sites presented initial bone formation in the void space between threads that originated from remodeling of the necrotic spots, and remodeling sites were observed at bone regions in proximity with the thread tips (Figure 4a).

For both Unitite groups and the SW implant placed in the 4.0 mm drilling sites, where a mismatch occurred between the implant inner diameter and the larger drilling site diameter (forming healing chambers), bone healing followed an intramembranous-type healing mode (Figures 3b-d and 4b-d). At the 2 week time point, these implant groups presented spots of necrotic bone/ remodeling areas with bone resorption, and a chamber filled with osteogenic tissue between the implant inner diameter and the drilled wall along with newly formed woven bone (Figure 3b-d). Primary engagement by the threads outer region without extensive necrotic bone areas was observed (Figure 3b-d). At 4 weeks, the healing chamber regions presented higher amounts of newly formed woven bone, and regions where primary engagement between implant and bone occurred presented newly formed bone partially filling void regions where bone remodeling occurred (Figure 4b-d).

Statistical assessment of overall BIC as collapsed over implant design did not show significant differences between implant design groups ($p=0.92$, Figure 1b). Within the different implantation times and drilling techniques, no significant differences were observed between implant designs (Figure 5). A significant increase in BIC was observed from 2 weeks to 4 weeks implantation time for the both implant designs placed with the overdrilling technique ($p<0.03$). When both implants were placed in the 3.75 mm drilling sites, no significant differences were detected in BIC over time ($p>0.32$) (Figure 5).

A significant effect ($p=0.044$) of implant design was detected for BAFO measurements, where the Unitite implant presented higher values compared to the SW implants (Figure 1c). An overall significant increase in BAFO was observed as a function of time *in vivo* ($p<0.01$). A significant increase in BAFO as a function of time was observed for all groups (all $p<0.02$) except for the Unitite implant design placed in 3.75 mm drilling sites ($p>0.40$), group that presented the highest BAFO levels at both evaluation times (Figure 6). At 2 weeks, the Unitite implant design presented higher values at both drilling techniques (statistically significant for the recommended 3.75 mm drilling sites, $p<0.03$) (Figure 6). At 4 weeks, no significant differences in BAFO were observed between implant designs for each drilling technique ($p>0.35$) (Figure 6).

The present study evaluated two different implant designs placed into two different drilling dimensions, one recommended by the manufacturer and another drilling scheme where a larger final drill outer diameter was utilized. Since the implant designs selected were from the same implant manufacturer and presented the same body diameter and overall shape, the surgical drills were exactly the same. Both implants, as per the manufacturer, have the exact same indications and placement sequence. In general, the overall histometric results obtained in the present study were not surprising since BIC and BAFO were larger for the recommended drilling technique relative to the overdrilling for both implants. Not surprisingly, higher insertion torque values were observed for the smaller diameter instrumentation relative to the larger diameter instrumentation. However, osseointegration pathways and kinetics substantially varied between designs depending on the drilling scheme utilized.

The rationale for the selection of the two drilling schemes on the two selected implant designs is that recent experimental preclinical work has shown the feasibility of achieving primary stability of dental implants through engagement of the implant thread outer portions while allowing for the formation of void spaces between implant and bone immediately after placement (healing chambers)[12]. Since no bone resorption occurs in healing chambers and healing at those regions take place in an intramembranous-like rapid woven bone formation[23], such rapid bone growth may compensate for the implant stability loss due to compression regions where implant contacts bone for primary stability. From a clinical perspective, this phenomenon is of special interest in the rehabilitation with immediate/early functional loading of single implant crowns at regions of poor quality bone biomechanics, such as type IV bone. Theoretically, a higher amount of necrotic dieback and interfacial remodeling will take place, potentially decreasing implant stability over time until secondary stability is achieved through new bone formation between the implant surface and pristine bone. Although a clinical study has shown no differences in survival rates of implants placed in poor bone density under a regular or undersized drilling protocol, no information regarding prostheses loading schedule was provided, except that no immediate loading was performed[24]. Therefore such information warrants further clinical investigation.

Previous studies have shown that healing chamber bone filling happens in tandem with the remodeling process at compression regions [8, 14], and the results obtained in the present study further support this finding since irrespective of implant design and drilling scheme, regions compressed by the implant in close contact with bone underwent resorption and regions where void spaces were formed presented newly formed bone as early as at the 2 weeks time point. However, healing patterns substantially differed between designs and drilling techniques.

These differences in healing pattern were more remarkable between implants for the recommended drilling technique, where healing chambers were formed for the Unitite implant (as per its design rationale – healing chamber formation under the recommended drilling dimension) and direct contact occurred for most of the SW implant perimeter with bone. Thus, while bone was being resorbed between the SW thread regions due to compressive forces, new bone was filling the void spaces that were allowed by the Unitite implant geometry and associated drilling dimension. Therefore, substantial remodeling occurred around the SW implant leading new contact between bone and implant taking place at 4 weeks (after interfacial remodeling). On the other hand, the Unitite implant presented remodeling taking place to lesser extent at the outer thread regions while presenting new bone in intimate contact with the implant as early as 2 weeks *in vivo* at the healing chamber regions. Due to the healing pathway dictated by the interplay between implant and surgical drilling dimension, histomorphometric analysis showed significantly higher BAFO for the Unitite implant relative to the SW at 2 weeks *in vivo*. Such significant difference was not observed at 4 weeks as new bone replaced the necrotic and void areas around the SW implant placed in the recommended drilling sites at 2 weeks. It is worth noting that such BAFO difference at 2 weeks *in vivo* between the SW and Unitite implants provided enough statistical size effect to deem significantly higher BAFO values for the Unitite implant relative to the SW when drilling technique and time *in vivo* were collapsed.

No differences in BIC were detected between implant designs under the recommended drilling procedure at 2 and 4 weeks and these results were likely due to the substantially different healing dynamics between the two different implant designs. It must be noted that while BIC is an important histomorphometric indication of osseointegration, it by no means represents the overall implant in bone system biomechanical competence, especially in cases where different implant designs are directly compared[25, 26].

Healing patterns were similar between the SW and Unitite implants when the overdrilling scheme was employed since larger healing chamber size was allowed for the Unitite implant while a healing chamber was formed for the SW implant. No difference in BIC and BAFO was observed between implant designs placed under both drilling schemes and besides BIC and BAFO values for both implants placed in the overdrilling sites being significantly lower compared to their recommended drilling scheme counterparts at both times *in vivo*, their increase over time was higher, once again suggesting alterations in osseointegration pathway and kinetics between the experimental groups.

**Acknowledgements**:

Funding: None / Competing interests: None declared / Ethical approval: from Ethics Committee for Animal Research at Universidade Federal de Uberlandia, MG, Brazil (protocol/approval number CEUA/UFU 082/12) / Patient permission: Not required

All the named authors agree to publication and each has had significant input into the paper.

## REFERENCES

1. Alfarraj Aldosari A, Anil S, Alasqah M, Al Wazzan KA, Al Jetaily SA, Jansen JA. The Influence of implant geometry and surface composition on bone response. Clin Oral Implants Res 2013. doi: 10.1111/clr.12190. [Epub ahead of print]
2. Coelho PG, Granjeiro JM, Romanos GE, Suzuki M, Silva NR, Cardaropoli G, Thompson VP, Lemons JE. Basic research methods and current trends of dental implant surfaces. J Biomed Mater Res B Appl Biomater 2009;88(2):579-96.
3. Wennerberg A, Albrektsson T. Effects of titanium surface topography on bone integration: a systematic review. Clin Oral Implants Res 2009;20 Suppl 4:172-84.
4. Tomisa AP, Launey ME, Lee JS, Mankani MH, Wegst UG, Saiz E. Nanotechnology approaches to improve dental implants. Int J Oral Maxillofac Implants 2011;26 Suppl:25-44; discussion 45-9.
5. Anselme K, Bigerelle M. Statistical demonstration of the relative effect of surface chemistry and roughness on human osteoblast short-term adhesion. J Mater Sci Mater Med 2006;17(5):471-9.
6. Lee BH, Lee C, Kim DG, Choi K, Lee KH, Kim YD. Effect of surface structure on biomechanical properties and osseointegration. Materials Science and Engineering: C 2008;28(8):1448-61.

7. Campos FE, Gomes JB, Marin C, Teixeira HS, Suzuki M, Witek L, Zanetta-Barbosa D, Coelho PG. Effect of drilling dimension on implant placement torque and early osseointegration stages: an experimental study in dogs. J Oral Maxillofac Surg 2012;70(1):e43-50.

8. Coelho PG, Suzuki M, Guimaraes MV, Marin C, Granato R, Gil JN, Miller RJ. Early bone healing around different implant bulk designs and surgical techniques: A study in dogs. Clin Implant Dent Relat Res 2010;12(3):202-8.

9. Marin C, Granato R, Suzuki M, Gil JN, Janal MN, Coelho PG. Histomorphologic and histomorphometric evaluation of various endosseous implant healing chamber configurations at early implantation times: a study in dogs. Clin Oral Implants Res 2010;21(6):577-83.

10. Coelho PG, Granato R, Marin C, Teixeira HS, Suzuki M, Valverde GB, Janal MN, Lilin T, Bonfante EA. The effect of different implant macrogeometries and surface treatment in early biomechanical fixation: an experimental study in dogs. J Mech Behav Biomed Mater 2011;4(8):1974-81.

11. Brunski JB. Biomaterials and biomechanics in dental implant design. Int J Oral Maxillofac Implants 1988;3(2):85-97.

12. Coelho PG, Marin C, Teixeira HS, Campos FE, Gomes JB, Guastaldi F, Anchieta RB, Silveira L, Bonfante EA. Biomechanical evaluation of

undersized drilling on implant biomechanical stability at early implantation times. J Oral Maxillofac Surg 2013;71(2):e69-75.

13. Bashutski JD, D'Silva NJ, Wang HL. Implant compression necrosis: current understanding and case report. J Periodontol 2009;80(4):700-4.
14. Berglundh T, Abrahamsson I, Lang NP, Lindhe J. De novo alveolar bone formation adjacent to endosseous implants. Clin Oral Implants Res 2003;14(3):251-62.
15. Gomes JB, Campos FE, Marin C, Teixeira HS, Bonfante EA, Suzuki M, Witek L, Zanetta-Barbosa D, Coelho PG. Implant biomechanical stability variation at early implantation times in vivo: an experimental study in dogs. Int J Oral Maxillofac Implants 2013;28(3):e128-34.
16. Leonard G, Coelho P, Polyzois I, Stassen L, Claffey N. A study of the bone healing kinetics of plateau versus screw root design titanium dental implants. Clin Oral Implants Res 2009;20(3):232-9.
17. Coelho PG, Granato R, Marin C, Bonfante EA, Janal MN, Suzuki M. Biomechanical and bone histomorphologic evaluation of four surfaces on plateau root form implants: an experimental study in dogs. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109(5):e39-45.
18. Bonfante EA, Granato R, Marin C, Suzuki M, Oliveira SR, Giro G, Coelho PG. Early bone healing and biomechanical fixation of dual acid-etched and as-machined implants with healing chambers: an experimental study in dogs. Int J Oral Maxillofac Implants 2011;26(1):75-82.

19. Abrahamsson I, Berglundh T, Linder E, Lang NP, Lindhe J. Early bone formation adjacent to rough and turned endosseous implant surfaces. An experimental study in the dog. Clin Oral Implants Res 2004;15(4):381-92.

20. Abrahamsson I, Linder E, Lang NP. Implant stability in relation to osseointegration: an experimental study in the Labrador dog. Clin Oral Implants Res 2009;20(3):313-8.

21. Marin C, Granato R, Bonfante EA, Suzuki M, Janal MN, Coelho PG. Evaluation of a nanometer roughness scale resorbable media-processed surface: a study in dogs. Clin Oral Implants Res 2012;23(1):119-24.

22. Donath K, Breuner G. A method for the study of undecalcified bones and teeth with attached soft tissues. The Sage-Schliff (sawing and grinding) technique. J Oral Pathol 1982;11(4):318-26.

23. Witek L, Marin C, Granato R, Bonfante EA, Campos FE, Gomes JB, Suzuki M, Coelho PG. Surface characterization, biomechanical, and histologic evaluation of alumina and bioactive resorbable blasting textured surfaces in titanium implant healing chambers: an experimental study in dogs. Int J Oral Maxillofac Implants 2013;28(3):694-700.

24. Alghamdi H, Anand PS, Anil S. Undersized implant site preparation to enhance primary implant stability in poor bone density: a prospective clinical study. J Oral Maxillofac Surg 2011;69(12):e506-12.

25. Jimbo R, Anchieta R, Baldassarri M, Granato R, Marin C, Teixeira HS, Tovar N, Vandeweghe S, Janal MN, Coelho PG. Histomorphometry and

bone mechanical property evolution around different implant systems at early healing stages: an experimental study in dogs. Implant Dent 2013;22(6):596-603.

26. Bougas K, Jimbo R, Vandeweghe S, Tovar N, Baldassarri M, Alenezi A, Janal M, Coelho PG, Wennerberg A. In Vivo Evaluation of a Novel Implant Coating Agent: Laminin-1. Clin Implant Dent Relat Res 2013.

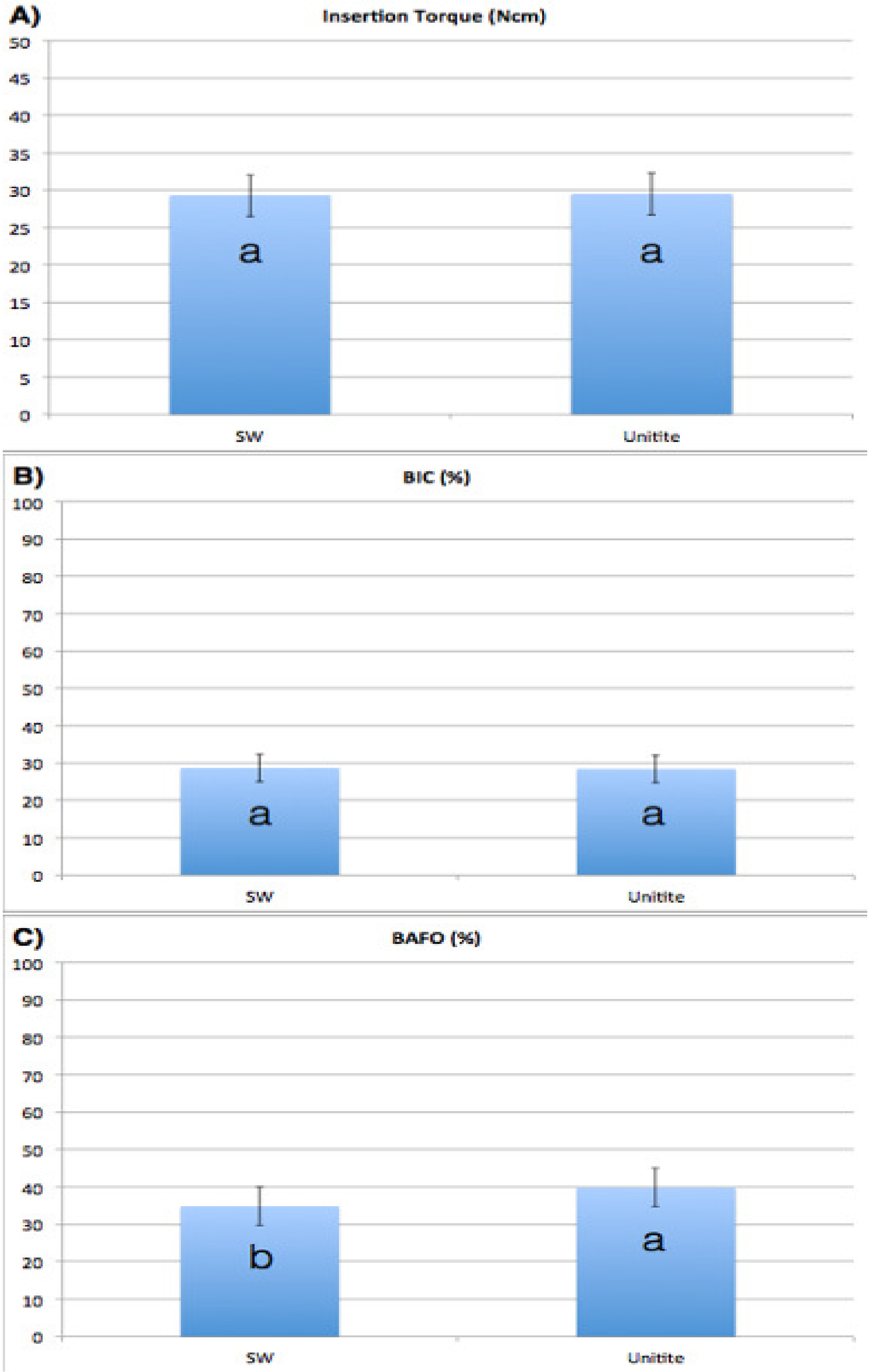


Figure 1: Overall (a) insertion torque, (b) BIC, and (c) BAFO for the two different implant designs. The error bars represent the 95% confidence interval and letters represent statistically homogeneous groups.

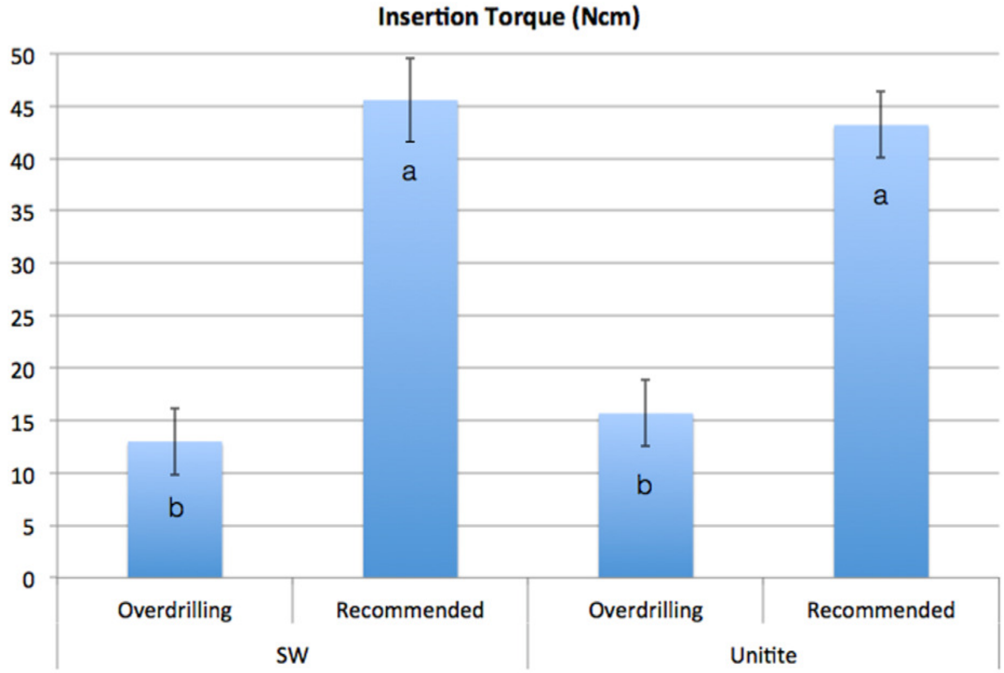


Figure 2: Insertion torque values for the two different implant designs placed with the recommended and the over drilling instrumentation protocol. The error bars represent the 95% confidence interval and letters represent statistically homogeneous groups.

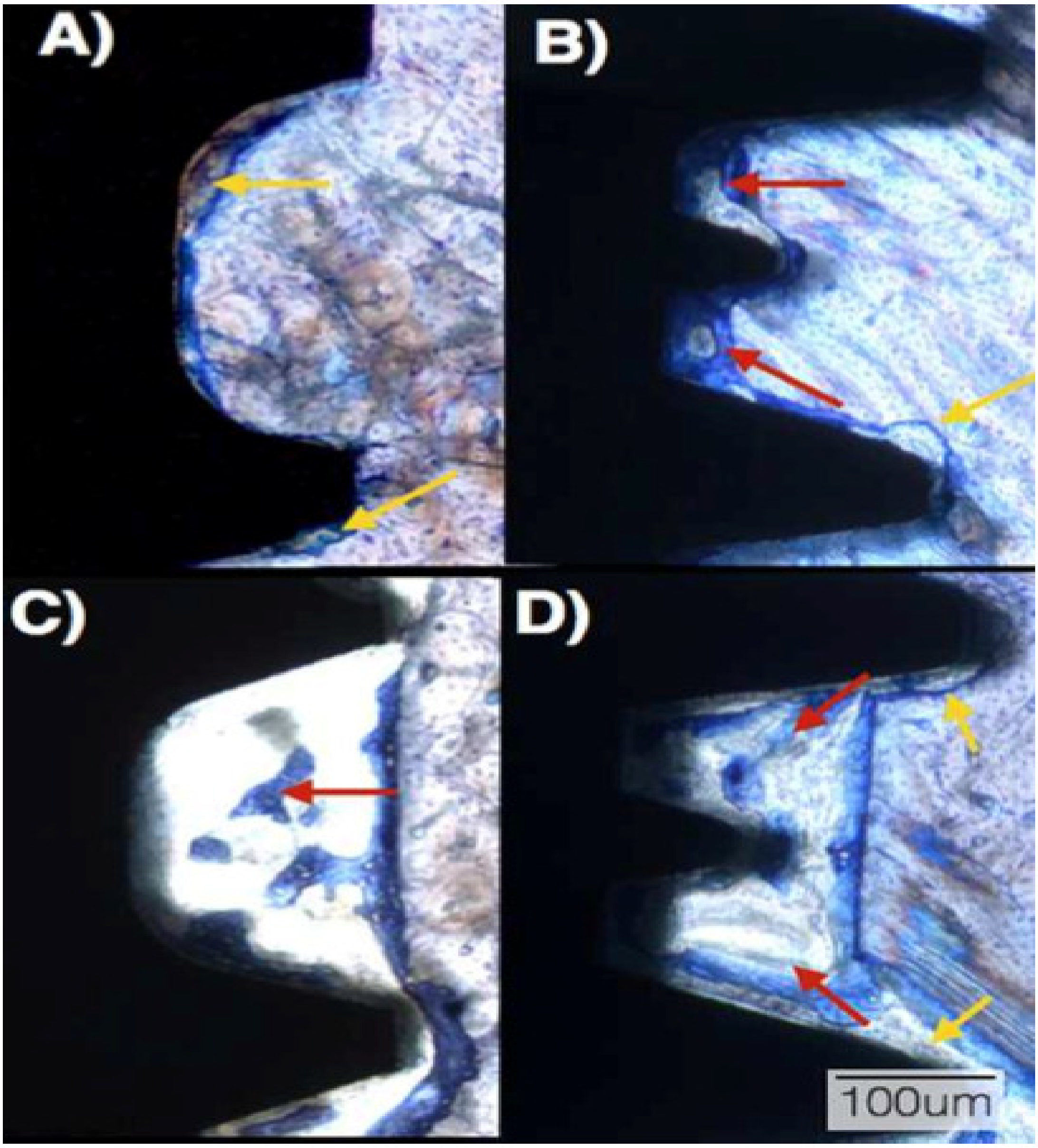


Figure 3: Optical micrographs at 2 weeks in vivo for the (a) SW recommended instrumentation, (b) Unitite recommended instrumentation, (c) SW overdrilling instrumentation, and (d) Unitite overdrilling instrumentation. The red arrows depict newly formed bone at the healing chambers regions; yellow arrows depict bone remodeling regions.

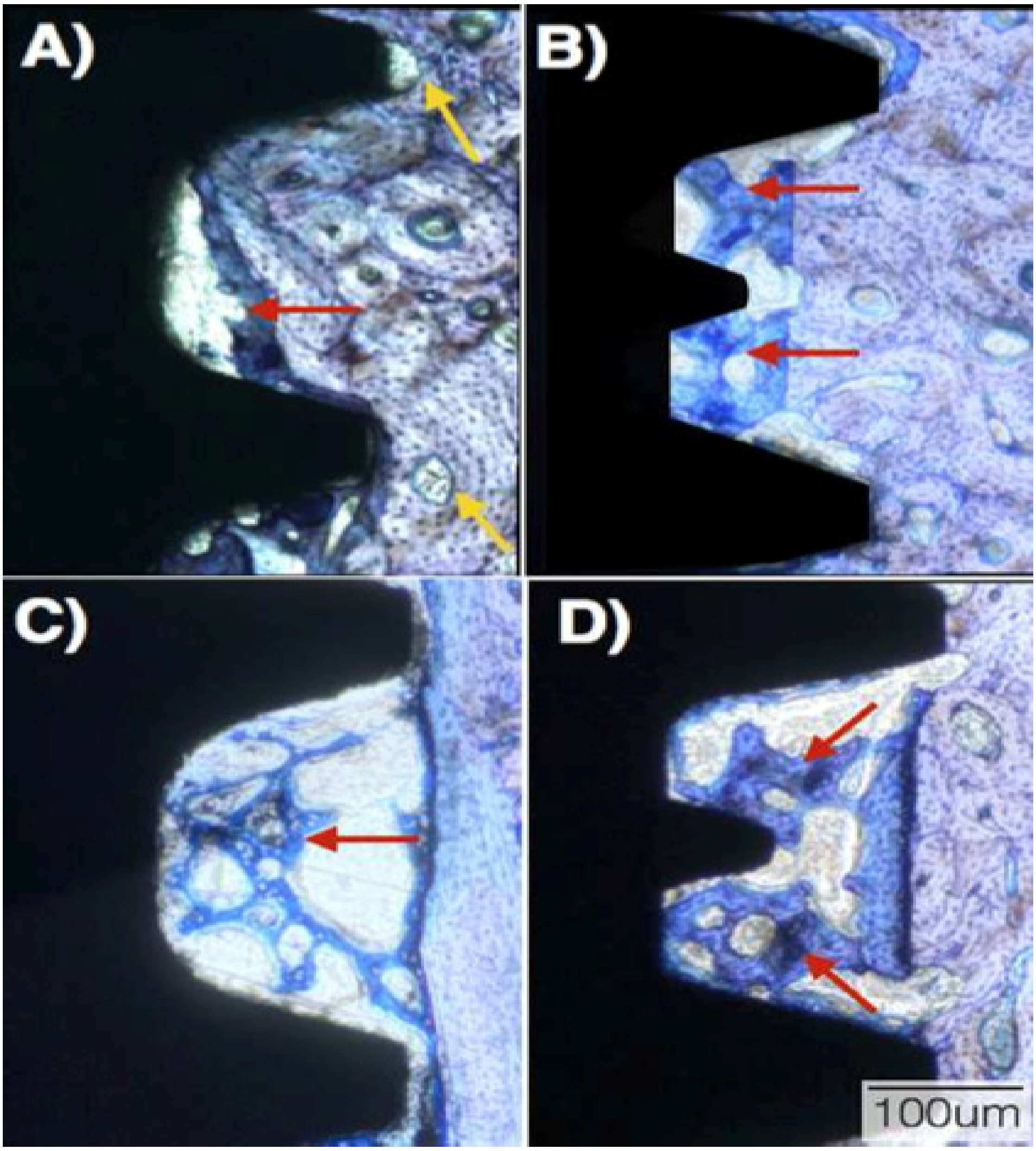


Figure 4: Optical micrographs at 4 weeks in vivo for the (a) SW recommended instrumentation, (b) Unitite recommended instrumentation, (c) SW overdrilling instrumentation, and (d) Unitite overdrilling instrumentation. The red arrows depict newly formed bone at the healing chambers regions.

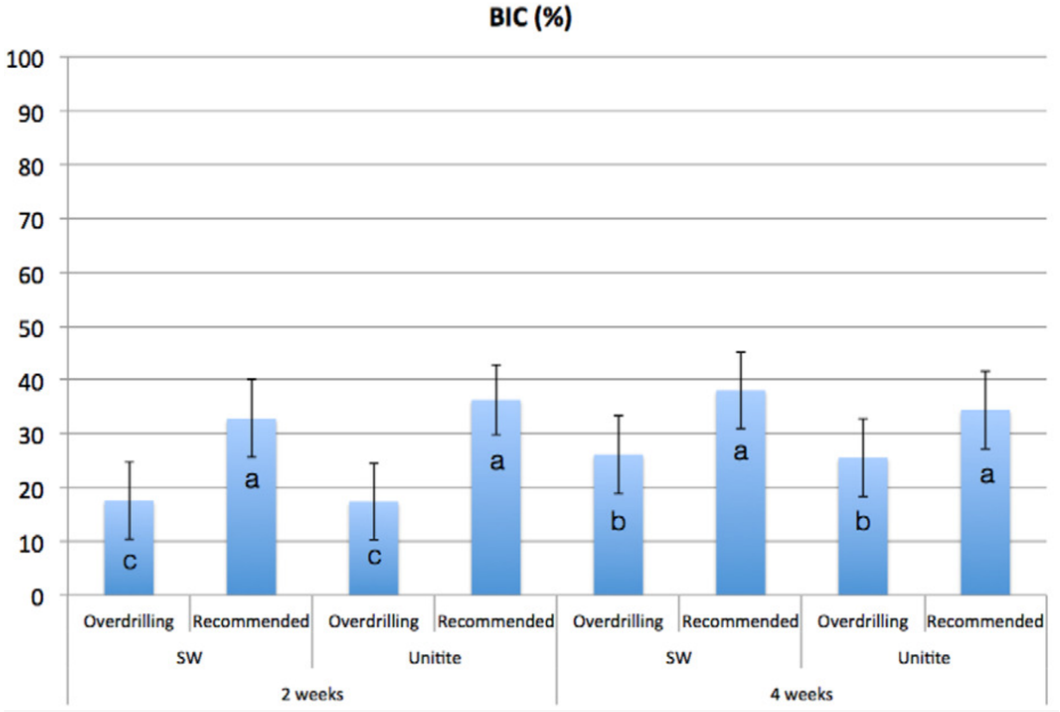


Figure 5: Bone-to-implant contact (BAFO) values for the two different implants placed under the recommended and the over drilling instrumentation protocols at 2 and 4 weeks. The error bars represent the 95% confidence interval and letters represent statistically homogeneous groups.

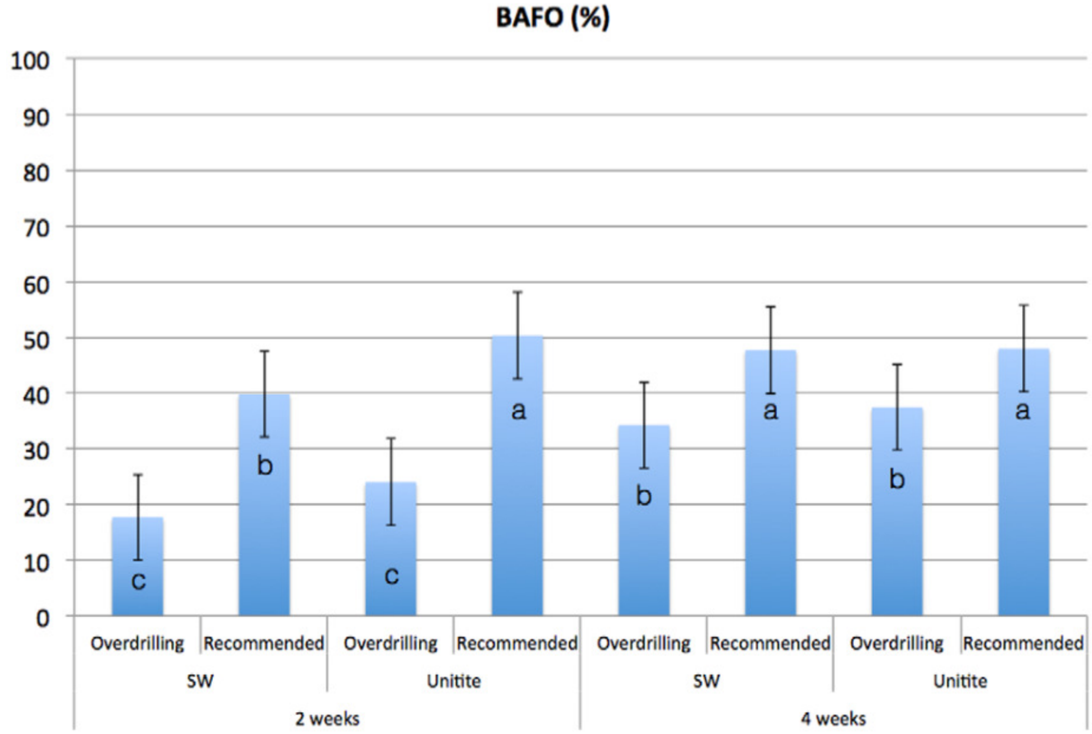


Figure 6: Bone area fraction occupancy (BAFO) values for the two different implants placed under the recommended and the over drilling instrumentation protocols at 2 and 4 weeks. The error bars represent the 95% confidence interval and letters represent statistically homogeneous groups.

# Capítulo 2 (Artigo 2)

**Referência do Artigo segundo normas do programa:**

Campos FEB, Bonfante E, Jimbo R, Oliveira MTF, Moura CCG, Barbosa DZ, Coelho PG. Is insertion torque and early osseointyegration proportional? A histologic evaluation. (Artigo enviado para publicação na revista Clinical Oral Implants Research).

# Is insertion torque and early osseointegration proportional? A histologic evaluation.

Felipe E. B. Campos[a] D.D.S., M.S., Ryo Jimbo[b] D.D.S., Ph.D., Maiolino T. F. Oliveira[a] D.D.S., M.S., Camila C. G. Moura[c] D.D.S., Darceny Z. Barbosa[d] D.D.S., Ph.D., Paulo G. Coelho[e] D.D.S., Ph.D., B.S., Ms.Mt.E.

a- Doctoral Student, Division of Oral and Maxillofacial Surgery, Department of Oral Surgery, School of Dentistry, Federal University of Uberlândia, Uberlândia, MG, Brazil

b- Associate Professor, Department of Prosthodontics, Faculty of Odontology, Malmö University, Malmö, Sweden

c- Professor, Department of Histology, Federal University of Triângulo Mineiro; and Researcher, School of Dentistry, Federal University of Uberlândia, Uberlândia, MG, Brazil

d- Professor, Division of Oral and Maxillofacial Surgery, Department of Oral Surgery, School of Dentistry, Federal University of Uberlândia, Uberlândia, MG, Brazil

e- Associate Professor, Department of Biomaterials and Biomimetics, New York University; and Director for Research, Department of Periodontology and Implant Dentistry New York University College of Dentistry, New York, NY, USA

Running Title: Primary Stability and Osseointegration

Keywords: histomorphometry, initial stability, insertion torque, osseointegration

* Corresponding author: Paulo G Coelho
345 E 24th Street, 10010, Dept. Biomaterials and Biomimetics, room 314a, New York University, New York, NY, USA

Phone: (212) 998-9214. / FAX: 212-995-4244 / e-mail: pc92@nyu.edu

## Abstract

**Purpose:** The objective of this preliminary histologic study was to determine whether the alteration of drilling protocols (oversized, intermediate, undersized drilling) present different biologic responses at early healing periods of 2 weeks *in vivo* in a beagle dog model.

**Materials and Methods:** Ten beagle dogs were acquired and subjected to surgeries in the tibia 2 weeks before euthanasia. During surgery, 3 implants, 4 mm in diameter by 10 mm in length, were placed in bone sites drilled to 3.5 mm, 3.75 mm, and 4.0 mm in final diameter. The insertion and removal torque was recorded for all samples. Statistical significance was set to 95% level of confidence and the number of dogs was considered as the statistical unit for all comparisons. For the torque and BIC and BAFO, a general linear model was employed including instrumentation technique and time in vivo as independent.

**Results:** Overall, the insertion torque increased as a function of drilling diameter from 4.0 mm, to 3.75 mm, to 3.5 mm, with a significant difference in torque levels between all groups ($p<0.001$). Statistical assessment of BIC and BAFO showed significantly higher values for the 3.75 mm (recommended) drilling group was observed relative to the other two groups ($p<0.001$).

**Conclusions:** Different drilling dimensions resulted in variations in insertion torque values (primary stability) and different pattern of healing and interfacial remodeling was observed for the different groups.

## Introduction

Obtaining an adequate stability (primary stability) after implant placement has been regarded as one of the essential factors for the achievement of secondary stability (osseointegration). Insufficient primary stability levels results in increased micromotion and micromotion of more than 50-150 µm results in subsequent soft tissue encapsulation of the implant [1].

Theoretically, it has been suggested that the bone is an elastic material before its yielding point, which is an indication that a certain level of strain can be tolerated due to a relaxation effect [2]. On the other hand, once the strain in the bone exceeds the yielding point, numerous microfractures along with blood capillary overcompression provokes ischemic necrosis or in the worst scenario, complete bone fracture [3]. It has been acknowledged that ischemia and/or pressure necrosis have an impact on rapid bone resorption [4], however, reports suggest that the living bone can tolerate certain levels of overcompression (beyond the yield strain) without provoking negative bone responses [5, 6]. Based on this theoretical and experimental knowledge and the emerging clinical demands for an implant to be loaded immediately, a number of different implant macro designs challenge the limit in order to obtain maximum primary stability [7-9], however, the definite level that would provoke rapid bone loss is uncertain.

In general, the contact area between the implant and the bone influences primary stability, since the primary stability is a pure mechanical interaction involving friction and compression to the bone. Clinically, the friction and compression by the implant insertion has been controlled by altering the drilling protocol. In brief, the discrepancy between the size of the osteotomy site and the implant diameter creates different contact situations between the implant and the bone, which the implant macrodesign acts as an influential factor [10-12]. Hypothetically, the undersized drilling, which provides the largest initial contact area between the implant presents the highest primary stability. Moreover, in many of the cases, these implants present high insertion torque values. Thus, if the degree of insertion torque is considered equivalent to the primary stability, the alteration of drilling protocols may have a great impact on the subsequent biological (secondary) stability.

Thus, the objective of this preliminary histologic study was to determine whether the alteration of drilling protocols (oversized, intermediate, undersized drilling) present different biologic responses at early healing periods of 2 weeks *in vivo* in a beagle dog model. It was hypothesized that the higher levels of insertion torque would present lower micromotion and the degree of osseointegration would be proportional to the insertion torque values.

## Materials and Methods

Thirty Unitite (SIN, Sao Paulo, Brazil) implants of 4.1 mm diameter and 10 mm length were utilized in the present study. All implants presented a dual acid etched surface that has been previously characterized. Three drilling/instrumentation techniques were utilized, a technique to the final diameter recommended by the manufacturer (to a final diameter of 3.75 mm- regular group), a technique where the final diameter was smaller than recommended by the manufacturer (to a final diameter of 3.5 mm- tight group), and a technique where the final diameter was larger than recommended by the manufacturer (to a final diameter of 4.0 mm- overdrilling group). For the laboratory in vivo model, ten adult male beagle dogs with approximately 1.5 years of age were acquired following the approval of the Ethics Committee for Animal Research at Universidade Federal de Uberlandia, Brazil (protocol/approval number CEUA-UFU 082/12).

Prior to general anesthesia, IM atropine sulfate (0,044 mg/kg) and xilazyne chlorate (8 mg/kg) were administered. A 15mg/Kg ketamine chlorate dose was then utilized to achieve general anesthesia.

The surgical site was the proximal tibia. Following hair shaving, skin exposure, and antiseptic cleaning with iodine solution at the surgical and surrounding area, a 5 cm length incision to access the periosteum was performed and a flap reflected for bone exposure.

Three implants were placed along the left tibia from proximal to distal in an alternated drilling technique distribution, being interchanged in every tibia to minimize bias from different implantation sites (sites 1 to 3 from proximal to distal). The implants remained in vivo for a period of 2 weeks, and were allocated in sites 1 to 3 in an equal distribution. This approach resulted in balanced surgical procedures that allowed the comparison of the same number of implants placed under the different drilling technique per time *in vivo*, surgical site (1 through 3), and animal. The implants were placed at distances of 1 cm from each other along the central region of the bone. The implants were inserted in the drilled sites and the maximum insertion torque was recorded with a portable digital torquemeter (Tohnichi, Tokyo, Japan) with a 200Ncm load cell for each implant placed.

Following placement, each implant received its proprietary cover screw to avoid tissue overgrowth. The soft tissue was sutured in layers following standard procedures, where the periosteum was sutured with vicryl 4-0 (Ethicon Johnson, Miami, FL, USA) and the skin with 4-0 nylon (Ethicon Johnson, Miami, FL, USA).

Post-operative anti-biotic and anti-inflammatory medication included a single dose of Benzyl Penicillin Benzatine (20.000 UI/Kg) IM and Ketoprofen 1% (1ml/5Kg). The animals were euthanized by anesthesia overdose and the limbs were retrieved by sharp dissection. The soft tissue was removed by surgical blades, and initial clinical evaluation was performed to determine implant stability. If an implant was clinically unstable, it was excluded from the study.

The bones containing the implants was reduced to blocks and immersed in 10% buffered formalin solution for 24h. The blocks were then washed in running water for 24h, and steadily dehydrated in a series of alcohol solutions ranging from 70-100% ethanol. Following dehydration, the samples were embedded in a methacrylate-based resin (Technovit 9100, Heraeus Kulzer GmbH, Wehrheim, Germany) according to the manufacturer's instructions. The blocks were then cut into slices (~300 μm thickness) aiming the center of the implant along its long axis with a precision diamond saw (Isomet 2000, Buehler Ltd., Lake Bluff, USA), glued to acrylic plates with an acrylate-based cement, and a 24h setting time was allowed prior to grinding and polishing. The sections were then reduced to a final thickness of ~30 μm by means of a series of SiC abrasive papers (400, 600, 800, 1200 and 2400) (Buehler Ltd., Lake Bluff, IL, USA) in a grinding/polishing machine (Metaserv 3000, Buehler Ltd., Lake Bluff, USA) under water irrigation.(20) The sections were then toluidine blue stained and referred to optical microscopy at 50X-200X magnification (Leica DM2500M, Leica Microsystems GmbH, Wetzlar, Germany) for histomorphologic evaluation.

The bone-to-implant contact (BIC) was determined at 50X-200X magnification (Leica DM2500M, Leica Microsystems GmbH, Wetzlar, Germany) by means of computer software (Leica Application Suite, Leica Microsystems GmbH, Wetzlar, Germany). The regions of bone-to-implant contact along the implant perimeter were subtracted from the total implant perimeter, and calculations were performed to determine the BIC. The bone area fraction occupied (BAFO) between threads in trabecular bone regions was determined at 100X magnification (Leica DM2500M, Leica Microsystems GmbH, Wetzlar, Germany) by means of a computer software (Leica Application Suite, Leica Microsystems GmbH, Wetzlar, Germany). The areas occupied by bone were subtracted from the total area between threads, and calculations were performed to determine the BAFO (reported in percentage values of bone area fraction occupied) (21).

For all outcomes, statistical significance was set to 95% level of confidence and the number of dogs was considered as the statistical unit for all comparisons. For the torque and histomorphometric dependent variables BIC and BAFO, a general linear model was employed including instrumentation technique and time in vivo as independent variables (surgical site position was preliminarily evaluated and due to a lack of effect on Torque, BIC, and BAFO was excluded from further analysis).

## Results

The surgical procedures and follow-up throught the length of the study demonstrated no complications regarding procedural conditions or other immediate clinical concerns. No post-operative complication was detected and no implant was excluded from the study due to clinical instability of all implants after euthanization.

The insertion torque recorded for each drilling group is presented in Figure 1, where the torque increased as a function of drilling diameter from 4.0 mm (overdrilling), to 3.75 mm (recommended), to 3.5 mm (tight). A significant difference in torque levels was observed between all groups ($p<0.001$).

Qualitative evaluation of the biological response showed intimate contact between cortical and trabecular bone for all groups at 2 weeks in vivo, including regions which were in close proximity or substantially away from the osteotomy walls (Figure 2).

The toluidine blue stained thin sections presented an appositional bone healing mode at regions where intimate contact existed between implant surfaces and bone immediately after placement (Figures 2a-c). These regions comprised the vast majority of the perimeter of implants placed into 3.5 mm (tight) sites (Figure 2a), and the outer aspects of the threads of implants placed into the 3.75 (recommended, Figure 2b) and 4.0 mm (overdrilling, Figure 2c) drilling sites. In contrast to implants placed into 3.5 mm (tight) sites that presented substantial bone remodeling along the perimeter of the implant/bone contact (Figure 2a), the initial healing pattern observed in proximity of the implant inner thread diameter and drilled walls (forming healing chambers) when implants were placed into the 3.75 mm and 4.0 mm drilling sites followed an intramembranous-type healing mode (Figures 2b-c).

At the 2 week time point, the implants placed into 3.5 mm (tight) drilling sites presented extensive necrotic bone/remodeling areas with bone resorption areas in the region between the implant threads (Figure 2a). The 3.75 mm (recommended) and 4.0 mm (overdrilling) presented spots of necrotic bone/ remodeling areas with bone resorption, and a chamber filled with osteogenic tissue between the implant inner diameter and the drilled wall along with newly formed woven bone (Figure 2b-c). Primary engagement by the threads outer region without extensive necrotic bone areas was observed (Figure 2a-c).

Statistical assessment of BIC showed significantly higher BIC values for the

3.75 mm (recommended) drilling group was observed relative to the other two groups (Figure 3) ($p<0.001$). The overdrilling group presented significantly higher BIC values relative to the tight group (Figure 3). The BAFO results (Figure 4) showed a trend identical to the BIC results, where significantly higher BAFO values for the 3.75 mm (recommended) drilling group was observed relative to the other two groups (Figure 4) ($p<0.001$). The overdrilling group presented significantly higher BAFO values relative to the tight group (Figure 4).

## Discussion

This preliminary study investigated the effect of different drilling protocols on early osseointegration. The early time point of 2 weeks was selected in order to observe the transition from the mechanical (primary) stability to the biologic stability, since it is thought that at later timepoints, the bone formation around the implant would be comparable. It was hypothesized that the higher levels of primary stability expressed clinically as higher insertion torque values positively influenced osseointegration.

The insertion torque testing showed that the final drill size significantly influenced the insertion torque values with the oversized drilling group presenting the lowest values and the undersized drilling group (Tight) presenting the highest values. However, the histologic micrographs clearly presented that new bone formation was most active in proximity of the implant surface for the implants placed with the intermediate drilling protocols. Moreover, both the BIC and the BAFO showed that the intermediate drilling protocols presented the highest histomorphometric values suggesting that the alteration from primary to biologic stability was most active for this group.

The reasons for the unproportional biologic response could be that the insertion torque values may not be fully representing the primary stability of this specific implant design. It has been suggested by Norton that depending on implant systems, the low levels of rotational stability at the time of implant insertion is may not be an indication for high micromotion [13, 14]. Thus, concerning the implant design utilized in the current study, the application of intermediate drilling could have provided the lowest micromotion, which resulted in an active bone apposition at an early healing stage of 2 weeks.

Furthermore, due to the low micromotion and the adequate space provided between the implant and the bone for the intermediate drilling group seemed to have created a possibility for direct bone apposition. This is in accordance with several reports where it was suggested that a closed chamber between the implant and the bone allowed blood fill and subsequent new bone formation compared to the press-fit group [15, 16]. The authors suggested that the bone in direct contact to the implant initially for the press-fit group seemed to first undergo bone resorption before new bone was formed. Therefore, the biologic process observed for the undersized drilling in the current study at the time of 2 weeks *in vivo* might have been an ongoing bone remodeling procedure.

The oversized drilling group presented the lowest histomorphometric values and this may be due to the gap generated between the implant to the osteotomy wall, which is evident in the histologic micrograph. The distance between the implant and the bone was wider than the intermediate group, which may require more time for bone regeneration; furthermore, the low levels of primary stability may not have been the optimal basis for bone formation. This has been indicated in our previous study that the less stable implant created by overdrilling do not contribute to subsequent osseointegration [10].

The results of this current preliminary study suggested that at the early time point of 2 weeks, the insertion torque values and osseointegration is unproportional and the initial hypothesis was rejected. However, it must be stressed that the results obtained can only be applied for this specific implant design and cannot be directly applied to all implant designs. More information is needed to clarify the influence of implant design and drilling protocols to obtain an optimal surgical setup for different implants.

[1] Szmukler-Moncler S, Salama H, Reingewirtz Y, Dubruille JH. Timing of loading and effect of micromotion on bone-dental implant interface: review of experimental literature. Journal of biomedical materials research. 1998;43:192-203.

[2] Jimbo R, Anchieta R, Baldassarri M, Granato R, Marin C, Teixeira HS, et al. Histomorphometry and bone mechanical property evolution around different implant systems at early healing stages: an experimental study in dogs. Implant dentistry. 2013;22:596-603.

[3] Bashutski JD, D'Silva NJ, Wang HL. Implant compression necrosis: current understanding and case report. Journal of periodontology. 2009;80:700-4.

[4] Kalebo P, Johansson C, Albrektsson T. Temporary bone tissue ischemia in the hind limb of the rabbit. A vital microscopic study. Archives of orthopaedic and traumatic surgery Archiv fur orthopadische und Unfall-Chirurgie. 1986;105:321-5.

[5] Perren SM, Huggler A, Russenberger M, Allgower M, Mathys R, Schenk R, et al. The reaction of cortical bone to compression. Acta orthopaedica Scandinavica Supplementum. 1969;125:19-29.

[6] Halldin A, Jimbo R, Johansson CB, Wennerberg A, Jacobsson M, Albrektsson T, et al. The effect of static bone strain on implant stability and bone remodeling. Bone. 2011;49:783-9.

[7] Chowdhary R, Halldin A, Jimbo R, Wennerberg A. Influence of Micro Threads Alteration on Osseointegration and Primary Stability of Implants: An FEA and In Vivo Analysis in Rabbits. Clinical implant dentistry and related research. 2013.

[8] Trisi P, Perfetti G, Baldoni E, Berardi D, Colagiovanni M, Scogna G. Implant micromotion is related to peak insertion torque and bone density. Clinical oral implants research. 2009;20:467-71.

[9] Irinakis T, Wiebe C. Initial torque stability of a new bone condensing dental implant. A cohort study of 140 consecutively placed implants. The Journal of oral implantology. 2009;35:277-82.

[10] Jimbo R, Tovar N, Yoo DY, Janal MN, Anchieta RB, Coelho PG. The effect of different surgical drilling procedures on full laser-etched microgrooves surface-treated implants: an experimental study in sheep. Clinical oral implants research. 2013:n/a-n/a.

[11] Donati M, La Scala V, Di Raimondo R, Speroni S, Testi M, Berglundh T. Marginal Bone Preservation in Single-Tooth Replacement: A 5-Year Prospective Clinical Multicenter Study. Clinical implant dentistry and related research. 2013:n/a-n/a.

[12] Coelho PG, Marin C, Teixeira HS, Campos FE, Gomes JB, Guastaldi F, et al. Biomechanical Evaluation of Undersized Drilling on Implant Biomechanical Stability at Early Implantation Times. Journal of Oral and Maxillofacial Surgery. 2013;71:e69-e75.

[13] Norton MR. The influence of insertion torque on the survival of immediately placed and restored single-tooth implants. The International journal of oral & maxillofacial implants. 2011;26:1333-43.

[14] Norton M. Primary stability versus viable constraint--a need to redefine. The International journal of oral & maxillofacial implants. 2013;28:19-21.

[15] Berglundh T, Abrahamsson I, Lang NP, Lindhe J. De novo alveolar bone formation adjacent to endosseous implants. Clinical oral implants research. 2003;14:251-62.

[16] Coelho PG, Suzuki M, Guimaraes MV, Marin C, Granato R, Gil JN, et al. Early bone healing around different implant bulk designs and surgical techniques: A study in dogs. Clinical implant dentistry and related research. 2010;12:202-8.

# Capítulo 3 (Artigo 3)

**Referência do Artigo segundo normas do programa:**

Coelho PG, Teixeira HS, Campos FE, Gomes JB, Guastaldi F, Anchieta RB, Silveira L, Bonfante EA. Biomechanical evaluation of undersized drilling on implant biomechanical stability at early implantation times. Journal of Oral Maxillofac Surg. 2013 Feb;71(2):e69-75.

# Biomechanical Evaluation of Undersized Drilling on Implant Biomechanical Stability at Early Implantation Times

*Paulo G. Coelho, DDS, PhD,[*] Charles Marin, DDS, PhD,[†] Hellen S. Teixeira, DDS, MS,[‡]*
*Felipe E. Campos, DDS, MS,[§] Julio B. Gomes, DDS, MS,[||] Fernando Guastaldi, DDS, MS,[¶]*
*Rodolfo B. Anchieta, DDS, MS,[#] Lucas Silveira, DDS, MS,[**]*
*and Estevam A. Bonfante, DDS, PhD[††]*

**Purpose:** The present study evaluated the effect of different drilling dimensions (undersized, regular, and oversized) in the insertion and removal torques of dental implants in a beagle dog model.

**Methods:** Six beagle dogs were acquired and subjected to bilateral surgeries in the radii 1 and 3 weeks before euthanasia. During surgery, 3 implants, 4 mm in diameter by 10 mm in length, were placed in bone sites drilled to 3.2 mm, 3.5 mm, and 3.8 mm in final diameter. The insertion and removal torque was recorded for all samples. Statistical analysis was performed by paired $t$ tests for repeated measures and by $t$ tests assuming unequal variances (all at the 95% level of significance).

**Results:** Overall, the insertion torque and removal torque levels obtained were inversely proportional to the drilling dimension, with a significant difference detected between the 3.2 mm and 3.5 mm relative to the 3.8 mm groups ($P < 0.03$). Although insertion torque–removal torque paired observations was statistically maintained for the 3.5 mm and 3.8 mm groups, a significant decrease in removal torque values relative to insertion torque levels was observed for the 3.2 mm group. A different pattern of healing and interfacial remodeling was observed for the different groups.

**Conclusions:** Different drilling dimensions resulted in variations in insertion torque values (primary stability) and stability maintenance over the first weeks of bone healing.

*J Oral Maxillofac Surg 71:e69-e75, 2013*

Long-term implant success is dependent on both the biologic tissue response and mechanical factors.[1-4] For achieving successful osseointegration, implant stability is one of the fundamental prerequisites and must be maintained for the entire healing period to avoid micromovements, which could lead to fibrous tissue formation around the fixture.[5-7]

The implant stability over time can be considered a variable combination of primary and secondary stability. Primary implant stability is a mechanical

---

[*] Assistant Professor, Department of Biomaterials and Biomimetics, New York University, New York, NY, USA / Director for Research, Department of Periodontology and Implant Dentistry, New York University College of Dentistry, New York, NY.

[†] Assistant Professor, Postgraduate Program in Dentistry, UNIGRANRIO University, School of Health Sciences, Duque de Caxias, RJ, Brazil.

[‡] PhD Candidate, Department of Biomaterials and Biomimetics, New York University, New York, NY.

[§] PhD Candidate, Department of Oral and Maxillofacial Surgery, Universidade Federal de Uberlandia, MG, Brazil.

[||] PhD Candidate, Department of Oral and Maxillofacial Surgery, Universidade Federal de Uberlandia, MG, Brazil.

[¶] PhD Candidate, Department of Biomaterials and Biomimetics, New York University, New York, NY.

[#] PhD Candidate, Department of Biomaterials and Biomimetics, New York University, New York, NY.

[**] PhD Candidate, Department of Biomaterials and Biomimetics, New York University, New York, NY.

[††] Assistant Professor, Postgraduate Program in Dentistry, UNIGRANRIO University, School of Health Sciences, Duque de Caxias, RJ, Brazil.

Address correspondence and reprint requests to Dr Bonfante: UNIGRANRIO University, School of Health Sciences, Postgraduate Program in Dentistry. Rua Prof. José de Souza Herdy, 1.160 - 25 de Agosto, Duque de Caxias, RJ, Brazil, 25071-202; e-mail: estevamab@gmail.com

0278-2391/12/7008-0/$36.00/0
http://dx.doi.org/10.1016/j.joms.2012.10.008

phenomenon influenced by the combination of multiple variables that include the quality and quantity of bone at the recipient site, the surgical technique used to place the implant, and macro-microscopic morphology of the implant.[4,8,9]

Secondary stability is the progressive increase in stability as a consequence of the dynamic interrelationship between new bone formation and remodeling occurring at the bone-implant interfacial zone.[4,10] A substantial body of research supports that achievement of secondary stability is also dependent on the site bone quality along with instrumentation and implant design interplay that result in different bone-to-implant healing patterns.[11-14] For instance, it is known that regions that are in direct contact with bone will render primary stability to the system for a given period of time and, because of compression, will suffer cell-mediated activity and remodeling with the potential to decrease the initial system stability.[15-17] On the other hand, void spaces—left between bone and implant bulk that will fill with a blood clot immediately after placement and will not contribute to primary stability—are known to rapidly fill with woven bone. This is a key contributor to secondary stability, as the bone does not have to undergo remodeling because of its different healing pattern.[15,16,18,19]

It is well known by researchers and clinicians that implant stability immediately and early after placement is desirable, mainly in immediate loading protocols, in an attempt to decrease the relative motion between implant and bone, which could risk osseointegration.[20-22] Thus, it is common practice to clinically adapt the surgical approach by undersizing implant drilling preparation.[2] However, although such an approach will render a perceived higher stability (previous work has shown that high torque levels will not necessarily lead to lower system micromotion),[23] such approach may, in fact, be detrimental to osseointegration kinetics because of bone modeling/remodeling pattern changes due to higher mechanical strain in the system.[15]

In a recent investigation by our group,[24] in which 4-mm implants were inserted in bone sites drilled to 3.2 mm, 3.5 mm, and 3.8 mm, substantially different insertion torque levels and healing patterns were observed. When implants were placed in sites drilled to 3.2 mm and 3.5 mm, insertion torque was significantly higher compared with implants placed in sites drilled to 3.8 mm. Our histologic results at both 1 week and 3 weeks in vivo after implantation showed significant interfacial remodeling along with minimal new bone formation for the implants placed in sites drilled to 3.2 mm and 3.5 mm. On the other hand, we found that, although lower insertion torque levels were observed for implants placed in sites drilled to 3.8 mm, new bone formation onset was detected at 1 week, and substantial new bone formation in proximity and in contact with the implant surface was observed. Although the primary stability levels and healing patterns observed by our previous study indicate that, depending on drilling protocol and the insertion torque levels obtained, scenarios that will result in higher primary stability (lower drilling diameters) and higher potential for secondary stability achievement (larger drilling diameters resulting in bone healing chambers due to the void spaces created because of surgical instrumentation and implant geometric interplay) may occur, no biomechanical evaluation was performed after different time periods in vivo. Thus, the present study investigated the relationship between insertion torque and removal torque of implants placed in bone sites drilled to different dimensions after 1 week and 3 weeks in vivo. The research hypothesis tested was that discrepancies in biomechanical fixation would be more pronounced for implants placed in sites drilled to smaller diameters. It was our specific aim to evaluate the effect of drilling dimensions for implant placement in torque at early observation periods as well as in bone healing pathways.

## Materials and Methods

Thirty-six commercially pure grade 2 threaded endosseous implants, 4 mm in diameter and 10 mm in length (Colosso, Emfils, Itu, Brazil), with a grit-blasted and acid-etched surface, were used. For the laboratory in vivo model, 6 adult male beagle dogs approximately 1.5 years old were acquired after the approval of the Ethics Committee for Animal Research at Universidade Federal de Uberlandia, Brazil.

Before general anesthesia, intramuscular atropine sulfate (0.044 mg/kg) and xylazine chlorate (8 mg/kg) were administered. A 15 mg/kg ketamine chlorate dose was then used to achieve general anesthesia.

The surgical site was the central region of the radius diaphysis. After hair shaving, skin exposure, and antiseptic cleaning with iodine solution at the surgical site and surrounding area, an ~5 cm length incision was performed to access the periosteum and a flap reflected for bone exposure.

Three implants were placed along the radius from proximal to distal in an alternated distribution, with starting drilling dimension (3.2 mm, 3.5 mm, and 3.8 mm final drill diameter) interchanged in every radius to minimize bias from the different implantation sites (sites 1 to 3 from proximal to distal). Therefore, the 36 implants of the drilling technique, remaining in vivo for either 1 week or 3 weeks (right and left radii provided samples that remained in vivo for 1 week and 3 weeks, respectively), were allocated to sites 1 to 3 in an equal distribution. This approach resulted in balanced surgical procedures that allowed the comparison of the same number of implant surfaces per time in vivo, limb, surgical site (1 through 3), and animal. The implants were placed at distances of 1 cm from each other along the central region of the bone. The implants were inserted in the drilled sites, and the maximum insertion torque was recorded with a portable digital torquemeter (Tohnichi, Tokyo, Japan), with a 200-N-cm load cell for each implant placed.

After placement, each implant received its proprietary cover screw to avoid tissue overgrowth. The soft tissue was sutured in layers according to standard procedures, with the periosteum sutured with Vicryl 4-0 (Ethicon, Johnson & Johnson, Miami, FL) and the skin sutured with 4-0 nylon (Ethicon).

Postoperative antibiotic and anti-inflammatory medications included a single dose of benzyl penicillin benzatine (20,000 UI/kg) intramuscularly and ketoprofen 1% (1 mL/5 kg). The dogs were euthanized by an anesthesia overdose, and the limbs were retrieved by sharp dissection. The soft tissue was removed by surgical blades, and an initial clinical evaluation was performed to determine implant stability. If an implant was clinically unstable, it was excluded from the study.

After the experimental periods of 1 and 3 weeks, the implants were exposed, and a specially designed key was connected to both the implant and the same portable digital torquemeter. A counterclockwise movement was performed to remove the implant. The maximum removal torque value for breakage of bone-implant interaction was measured with a 200-N-cm load cell for each implant placed.

For descriptive purposes, the histologic sections previously published by our group under an identical study design are presented in the results section.[24]

Statistical evaluation of insertion and removal torque values for each implant was performed by paired *t* tests. Statistical evaluation of the overall insertion and removal torque values for the different groups and times in vivo was performed by *t* tests assuming unequal variances. Statistical significance was set at 95%.

## Results

The surgical procedures and follow-up showed no complications regarding the procedural conditions or other immediate clinical concerns. No postoperative complications were detected, and no implant was excluded from the study because of clinical instability.

The overall insertion torque recorded for each drilling group and healing period is presented in Figure 1. Overall, the highest insertion torque values were observed for implants placed in sites drilled to 3.2 mm and 3.5 mm compared with implants placed to sites drilled to 3.8 mm (Fig 1) ($P < 0.001$ when both 3.2 mm and 3.5 mm groups are compared with the 3.8 mm group). When comparing implants placed in sites drilled to the same diameter that remained for different times in vivo (implants placed in the right and left limbs, respectively) slight, nonsignificant variations were detected (Fig 2) ($P = 0.73$, $P = 0.61$, and $P = 0.50$ for the 3.2 mm, 3.5 mm, and 3.8 mm groups, respectively).

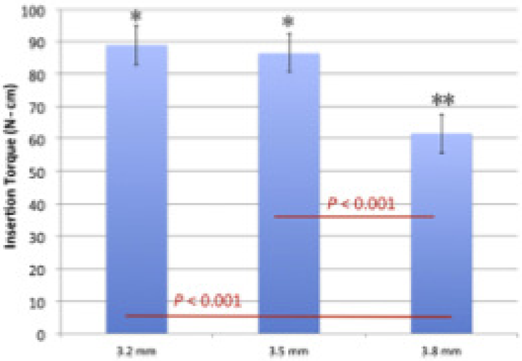


**FIGURE 1.** Mean insertion torque values (± SD) for different experimental groups. Significantly higher insertion torque values were observed for implants placed in sites drilled to 3.2 mm and 3.5 mm compared with implants placed to sites drilled to 3.8 mm ($P < 0.001$). Same number of asterisks indicates no statistical significant difference between groups.

*Coelho et al. Drilling Dimension and Implant Biomechanical Stability. J Oral Maxillofac Surg 2013.*

The insertion and removal torque recorded for each drilling group and healing period, statistically evaluated by paired *t* tests, are presented in Figure 3. The only significant differences observed were between the insertion and removal torque values in the 3.2 mm drilling

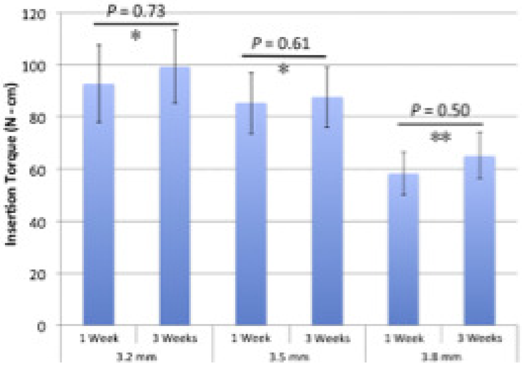


**FIGURE 2.** Mean insertion torque values (± SD) for different experimental groups as a function of time that the implants remained in-vivo (1 and 3 weeks, left and right limbs). The number of asterisks depicts statistically homogeneous groups.

*Coelho et al. Drilling Dimension and Implant Biomechanical Stability. J Oral Maxillofac Surg 2013.*

diameter group ($P = 0.04$ and $P = 0.02$ for implants that remained for 1 and 3 weeks in vivo, respectively). Nonsignificant differences between the insertion and removal torque values were observed for the other groups and times in vivo. However, slight decreases in between insertion and removal torque values were detected for implants placed in sites drilled to 3.5 mm, and remarkably similar insertion and removal torque values were observed for implants placed in sites drilled to 3.8 mm (Fig 3).

The overall removal torque results recorded for each drilling group is presented in Figure 4. A significant difference in removal torque values was observed between the 3.2 mm and 3.5 mm group relative to the 3.8 mm group.

The histologic micrographs for the different groups at 1 and 3 weeks in vivo are presented in Figures 5 and 6. Temporal morphologic changes were observed for the different experimental groups. At 1 week, implants placed into 3.2 mm and 3.5 mm drilling sites presented extensive necrotic bone areas in the region between the first 3 implant threads (Fig 5A,B). These necrotic regions evolved to remodeling sites that were present along with restricted amounts of newly formed bone at 3 weeks implantation time (Fig 6A,B). At 1 week, the implants placed into 3.8 mm drilling sites presented a chamber filled with osteogenic tissue between the implant inner diameter and the drilled wall (Fig 5C). Initial osteoid nucleation was observed in minor amounts within the healing chamber (Fig 5C). Primary engagement by the thread's outer region without extensive necrotic bone areas was observed (Fig 5C). At 3 weeks, extensive woven bone formation was observed at the drilled bone walls, implant surface, and within the healing chamber volume (Fig 6C).

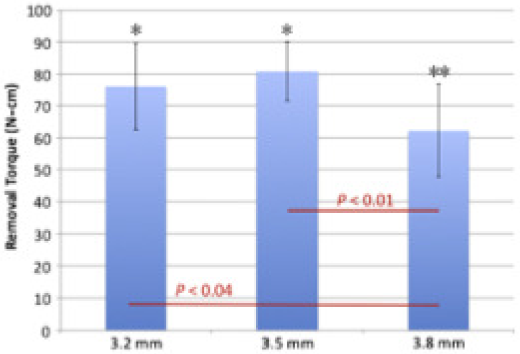


**FIGURE 4.** Mean removal torque values (± SD) for different experimental groups. Significantly higher removal torque values were observed for the 3.2 mm and 3.5 mm groups relative to the 3.8 mm. Number of asterisks depicts statistically homogeneous groups.

*Coelho et al. Drilling Dimension and Implant Biomechanical Stability. J Oral Maxillofac Surg 2013.*

## Discussion

Variable levels of predictability in implant dentistry have been shown with early and immediate loading protocols, as reported by an increasing number of clinical and experimental studies.[12,23] For such treatment modalities, primary stability has been regarded as a key factor for treatment success.[12,23]

The ideal condition of implant stability during the early healing periods has been questioned, as several

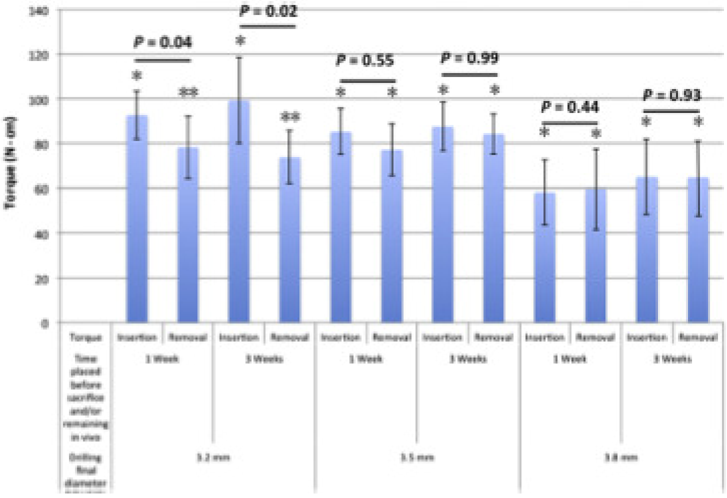


**FIGURE 3.** Mean insertion and removal torque values (± SD) for different experimental groups as a function of time in vivo. The $P$ values were derived from paired $t$ tests, and the number of asterisks depicts statistically homogeneous groups.

*Coelho et al. Drilling Dimension and Implant Biomechanical Stability. J Oral Maxillofac Surg 2013.*

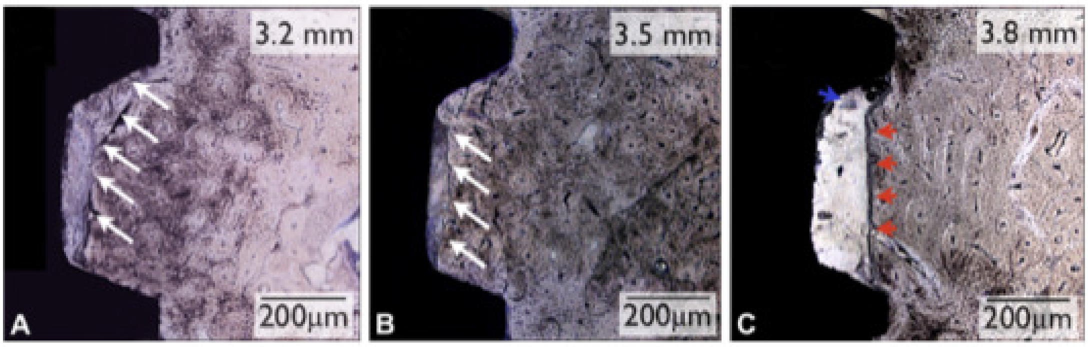


**FIGURE 5.** Week 1 optical micrographs of the implant-bone interface showing that implants placed into (*A*) 3.2-mm and (*B*) 3.5-mm drilling sites presented necrotic bone areas in the region between the first 3 implant threads (*white arrows*). Implants placed into (*C*) 3.8-mm drilling sites presented a chamber (*red arrows*) filled with osteogenic tissue between the implant inner diameter and the drilled wall. Initial osteoid nucleation was observed in minor amounts within the healing chamber (*blue arrow*).

*Coelho et al. Drilling Dimension and Implant Biomechanical Stability. J Oral Maxillofac Surg 2013.*

biomechanical and histologic studies have shown that even if implant primary stability is rendered during placement and because of the initial remodeling and subsequent bone apposition, a decrease in implant stability is likely to be observed before the bridging of the old bone and implant surface renders the system with secondary stability.[1,25,26]

Specific to dental implants, insertion torque has been perceived as a reliable measurement of the implant ability to resist micromotion.[27] Thus, to increase torque values during placement (especially in cases where lower bone density is encountered), clinicians have undersized the recommended drilling sites before implant placement despite the fact that basic engineering mechanics and in vitro testing of various implant designs in bone-like mechanical property materials have shown that high insertion torque values may not necessarily correlate with lower micromotion levels.[23] In fact, multiple studies have shown that the healing kinetics and mode around the same implant system may substantially change depending on the interplay between drilled site and implant macrogeometry dimensions.[17,24,28,29] For the implants tested in the present study, the smaller the drilled site, the more pronounced was the amount of remodeling at the interface region, a condition that may be detrimental to dental implant stability, as new bone formation is necessary to replace bone that is remodeled away. Supplementing the histologic findings from our previous study,[24] the present investigation evaluated the relationship between insertion and removal torques after 1 week and 3 weeks of placement for implants placed to sites drilled to the same 3 different dimensions.

The results of the insertion torque for the different groups are in agreement with our previous study,[24] where significantly higher values were observed for the 3.2 mm and 3.5 mm groups relative to the 3.8 mm groups. The overall lower values obtained in the present study were due to the level of insertion,

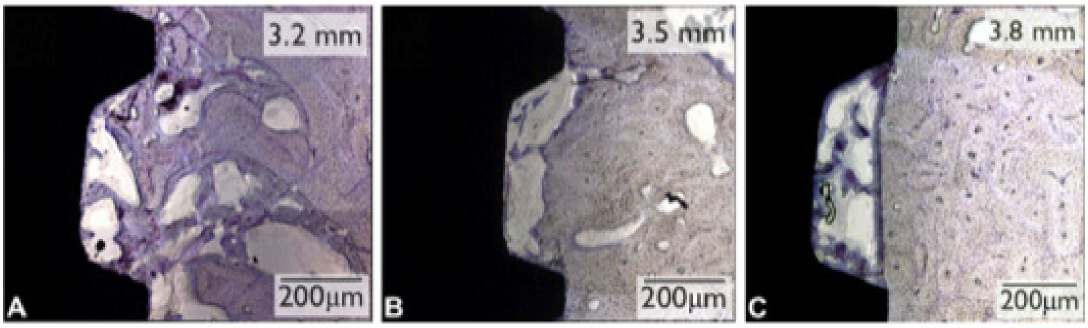


**FIGURE 6.** Week 3 optical micrographs of the implant-bone interface showing that implants placed into (*A*) 3.2-mm and (*B*) 3.5-mm drilling sites presented extensive remodeling along with a restricted amount of newly formed bone. At 3 weeks, implants placed into (*C*) 3.8-mm drilling sites presented extensive woven bone formation at the drilled bone walls, implant surface, and within the healing chamber volume.

*Coelho et al. Drilling Dimension and Implant Biomechanical Stability. J Oral Maxillofac Surg 2013.*

which, in the present study, was down to the first thread, whereas they were all the way to the implant cervical in the previous study. The consistency of the insertion torque values between the implants that were placed to remain in vivo for 1 and 3 weeks was remarkably similar, and allowed appropriate evaluation of the potential decrease/increase in torque values as a function of time in vivo. The results of the present investigation unequivocally indicate that under-dimensioned drilling enhances the primary stability, which is in agreement with previous studies.[13,14,27,30]

Although insertion torque values were inversely proportional to drilling dimension, decreases in torque values were significant for the 3.2 mm group and also decreased for the 3.5 mm group. Virtually no change between insertion and removal torque values was observed for the 3.8 mm group.

The significant decrease in torque values noticed for the 3.2 mm group is in agreement with the histology presented as a function of implantation time, where high degrees of bone remodeling occurred along with a restricted amount of new bone formation at both 1 week and 3 weeks, respectively. The same scenario was observed for the 3.5 mm group, for which slight decreases between insertion and removal torque values were recorded, in agreement with the remodeling interface with little new bone formation taking place at the bone-implant interfacial region. The 3.8 mm group was substantially different from the 3.2 mm and 3.5 mm groups when both torque and histologic features are considered together. This group presented stable insertion and removal torque values as a function of time, along with little to nonexistent interfacial remodeling where the implant was engaging bone for its primary stability in tandem with remarkable amounts of new bone formation at the bone-implant interfacial region.

Considering the tight fit scenario (3.2 mm and 3.5 mm groups), losses in implant biomechanical stability, because of necrotic dieback or interfacial remodeling, may negatively influence the time necessary to new bone formation render the system secondary stability.[24] Worth noting is the fact that although high torque values are still in place for the 3.2 mm and 3.5 mm groups at both 1 and 3 weeks relative to implants placed in sites drilled to 3.8 mm, such high torque values may not translate into the implant-bone system's ability to effectively resist micromotion,[23] potentially jeopardizing the early osseointegration process in treatment modalities such as early implant loading. Recently, a clinical study of implants placed into fresh extraction sockets with an insertion torque of no more than 25 N-cm and immediately loaded showed an overall survival rate of 95.5% in 1.25 years to 9.5 years.[31] Given that not only such a torque value may be considered small and that primary stability during immediate implantation is mainly held apically, the high survival rates suggests that the insertion torque value per se is important, but may present one among several other relevant parameters for the restoration survival such as implant design, bone density, surgical technique, and occlusal stability.

Although all scenarios tested in the present investigation resulted in successful osseointegration, even with different healing patterns, the extrapolation that they would also lead to the same survival rates if clinically loaded early or immediately should not be taken for granted. In fact, whereas it is virtually general consensus that a high insertion torque is necessary for immediate loading, it is not intriguing that early loading (2 months) has shown a trend toward lower survival rates when compared with both immediate and conventional loading according to a systematic review.[32] At early loading stages (2 months), bone remodeling, especially in undersized drilled implant sites, is at its highest peak, along with extensive loss of primary stability and initial secondary stability gain.[29,33] Loading in such a scenario seems challenging especially in nonsplinted single units. Most importantly, when the number of variables involved in insertion torque is considered, such as the implant system's macrogeometric configurations available worldwide, surface treatment, surgical techniques, bone density, and others, the proposal of a target value for insertion torque as a decision-making guide for the time of implant loading seems unsound, empirical, and should be reconsidered because it is too generic. Therefore, future multivariate analyses considering clinical values for insertion torque of specific implant systems and their survival under different loading time protocols and prosthesis configurations are warranted.

Specific to the 3.8 mm group, where virtually atemporal torque values stability was achieved, little to no dieback was observed, along with rapid bone formation from placement to 3 weeks in vivo. From a theoretical standpoint, such lack of interfacial remodeling may provide the same levels of micromotion resistance during early implantation times where extensive new bone formation is not yet in place and void spaces are under-filling by woven bone. From an engineering perspective, the results obtained for different implant/instrumentation dimension scenarios warrant studies concerning macrogeometries that, while allowing empty spaces between implant and bone for rapid bone formation that will ultimately result in secondary stability, will also present thread designs that will maximize primary stability. Such implant design may minimize detrimental bone remodeling at its interface at regions in which the implant engages bone immediately after placement.

The research hypothesis that discrepancies in biomechanical fixation would be more pronounced for implants placed in sites drilled to smaller diameters was accepted.

### *Acknowledgments*

The present study was partially funded by Emfils, Itu, Brazil.

## References

1. Abrahamsson I, Berglundh T, Linder E, et al: Early bone formation adjacent to rough and turned endosseous implant surfaces. An experimental study in the dog. Clin Oral Implants Res 15: 381, 2004
2. Alghamdi H, Anand PS, Anil S: Undersized implant site preparation to enhance primary implant stability in poor bone density: A prospective clinical study. J Oral Maxillofac Surg 69:e506, 2011
3. Chuang SK, Wei LJ, Douglass CW, Dodson TB: Risk factors for dental implant failure: A strategy for the analysis of clustered failure-time observations. J Dent Res 81:572, 2002
4. Stacchi C, Vercellotti T, Torelli L, et al: Changes in implant stability using different site preparation techniques: Twist drills versus piezosurgery. A single-blinded, randomized, controlled clinical trial. Clin Implant Dent Relat Res 2011 [Epub ahead of print]
5. Brunski JB: Biomechanical factors affecting the bone-dental implant interface. Clin Mater 10:153, 1992
6. Leucht P, Kim JB, Wazen R, et al: Effect of mechanical stimuli on skeletal regeneration around implants. Bone 40:919, 2007
7. Szmukler-Moncler S, Salama H, Reingewirtz Y, Dubruille JH: Timing of loading and effect of micromotion on bone-dental implant interface: Review of experimental literature. J Biomed Mater Res 43:192, 1998
8. Martinez H, Davarpanah M, Missika P, et al: Optimal implant stabilization in low density bone. Clin Oral Implants Res 12:423, 2001
9. Moon SH, Um HS, Lee JK, et al: The effect of implant shape and bone preparation on primary stability. J Periodontal Implant Sci 40:239, 2010
10. Raghavendra S, Wood MC, Taylor TD: Early wound healing around endosseous implants: A review of the literature. Int J Oral Maxillofac Implants 20:425, 2005
11. Marquezan M, Osório A, Sant'Anna E, et al: Does bone mineral density influence the primary stability of dental implants? A systematic review. Clin Oral Implants Res 23:767, 2012
12. Trisi P, Todisco M, Consolo U, Travaglini D: High versus low implant insertion torque: A histologic, histomorphometric, and biomechanical study in the sheep mandible. Int J Oral Maxillofac Implants 26:837, 2011
13. Tabassum A, Meijer GJ, Wolke JG, Jansen JA: Influence of surgical technique and surface roughness on the primary stability of an implant in artificial bone with different cortical thickness: A laboratory study. Clin Oral Implants Res 21:213, 2010
14. Tabassum A, Meijer GJ, Wolke JG, Jansen JA: Influence of the surgical technique and surface roughness on the primary stability of an implant in artificial bone with a density equivalent to maxillary bone: A laboratory study. Clin Oral Implants Res 20:327, 2009
15. Coelho PG, Suzuki M, Guimaraes MV, et al: Early bone healing around different implant bulk designs and surgical techniques: A study in dogs. Clin Implant Dent Relat Res 12:202, 2010
16. Leonard G, Coelho P, Polyzois I, et al: A study of the bone healing kinetics of plateau versus screw root design titanium dental implants. Clin Oral Implants Res 20:232, 2009
17. Marin C, Granato R, Suzuki M, et al: Histomorphologic and histomorphometric evaluation of various endosseous implant healing chamber configurations at early implantation times: A study in dogs. Clin Oral Implants Res 21:577, 2010
18. Bonfante EA, Granato R, Marin C, et al: Early bone healing and biomechanical fixation of dual acid-etched and as-machined implants with healing chambers: An experimental study in dogs. Int J Oral Maxillofac Implants 26:75, 2011
19. Coelho PG, Granato R, Marin C, et al: Biomechanical and bone histomorphologic evaluation of four surfaces on plateau root form implants: An experimental study in dogs. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 109:e39, 2010
20. Albrektsson T, Sennerby L, Wennerberg A: State of the art of oral implants. Periodontol 2000(47):15, 2008
21. Brånemark PI, Hansson BO, Adell R, et al: Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. Scand J Plast Reconstr Surg Suppl 16:1, 1977
22. Lemons JE: Biomaterials, biomechanics, tissue healing, and immediate-function dental implants. J Oral Implantol 30:318, 2004
23. Freitas AC Jr, Bonfante EA, Giro G, et al: The effect of implant design on insertion torque and immediate micromotion. Clin Oral Implants Res 23:113, 2012
24. Campos FE, Gomes JB, Marin C, et al: Effect of drilling dimension on implant placement torque and early osseointegration stages: An experimental study in dogs. J Oral Maxillofac Surg 70:e43, 2012
25. Berglundh T, Abrahamsson I, Albouy JP, Lindhe J: Bone healing at implants with a fluoride-modified surface: An experimental study in dogs. Clin Oral Implants Res 18:147, 2007
26. Coelho PG, Cardaropoli G, Suzuki M, Lemons JE: Early healing of nanothickness bioceramic coatings on dental implants. An experimental study in dogs. J Biomed Mater Res B Appl Biomater 88:387, 2009
27. Friberg B, Sennerby L, Gröndahl K, et al: On cutting torque measurements during implant placement: A 3-year clinical prospective study. Clin Implant Dent Relat Res 1:75, 1999
28. Coelho PG, Suzuki M, Guimaraes MV, et al: Early bone healing around different implant bulk designs and surgical techniques: A study in dogs. Clin Implant Dent Relat Res, 2009
29. Coelho PG, Granato R, Marin C, et al: The effect of different implant macrogeometries and surface treatment in early biomechanical fixation: An experimental study in dogs. J Mech Behav Biomed Mater 4:2011, 1974
30. Lioubavina-Hack N, Lang NP, Karring T: Significance of primary stability for osseointegration of dental implants. Clin Oral Implants Res 17:244, 2006
31. Norton MR: The influence of insertion torque on the survival of immediately placed and restored single-tooth implants. Int J Oral Maxillofac Implants 26:1333, 2011
32. Esposito M, Grusovin MG, Achille H, et al: Interventions for replacing missing teeth: Different times for loading dental implants. Cochrane Database Syst Rev CD003878, 2009
33. Berglundh T, Abrahamsson I, Lang NP, Lindhe J: De novo alveolar bone formation adjacent to endosseous implants. Clin Oral Implants Res 14:251, 2003

# 3. CONCLUSÕES

Nos estágios imediato e precoce (02 meses) de colocação de carga sobre inplantes dentários, a remodelação óssea esta em grande atividade. Em sítios cirúrgicos de sub-instrumentação este fenômeno é mais relevante. O “turn over’’ ósseo leva a perda significativa na estabilidade primária, desta maneira, colocar implantes em função neste cenário específico torna-se um grande desafio. Levando em consideração o número de variáveis envolvidas neste episódio como sistemas de implantes com diferentes macrogeometrias, tratamento de superfície, técnica cirúrgica, densidade óssea, entre outros, o objetivo de se conseguir um determinado valor de torque de inserção para se decider quando colocar o implante em função parece ser empírico. Por ser um fator de avaliação muito genérico, deve ser reconsiderado. Desta maneira, enfatiza-se a necessidade da realização de futuros trabalhos clínicos multivariáveis considerando os valores de torque de inserção de um especícfico sistema de implantes e o seu sucesso a partir de diferentes protocolos de colocação em função e opções protéticas

**Capítulo 1.** As vias de osseointegração foram similares entre os implantes testados (SW e Unitite) quando utilizado a técnica de sobre-instrumentação. Haja vista que, foram criadas maiores câmaras de osseointegração para os implantes Unitite, enquanto para os SW foram formadas, em menor tamanho, câmaras de osseointegração. Não foram observadas diferenças significativas entre os implantes testados para os parâmetros BIC e BAFO independente da têcnica cirúrgica. Considerando ambas geometrias de implantes utilizadas e tempos cirúrgicos, foram encontrados menores valores de BIC e BAFO quando inseridos nas áreas de sobre-instrumentação em comparação aos colocados conforme normas do fabricante. Apesar disso, os implantes inseridos na técnica de sobre-instrumentação tiveram maior crescimento nos parâmetros de osseointegração ao longo do tempo. Permitindo, mais uma vez, sugerir que ocorreram alterações nas vias e na cinética da osseointegração entre os grupos experimentais.

**Capítulo 2.** Os resultados deste estudo preliminar sugerem que no estágio inicial de 02 semanas de osseointegração, os valores de torque de inserção e osseointegração não são proporcionais. Entretanto, deve ser enfatizado que os resultados obtidos devem ser aplicados apenas a este específico tipo de implante, não devendo ser diretamente aplicado a outros desenhos de implantes. Mais informação é necessária para clarificar a influência da geometria do implante e os protocolos de instrumentação na tentativa de maximizar a osseointegração precocemente.

**Capítulo 3.** Considerando os valores de torque encontrados para o grupo de 3.8mm, independente do período, foram observados pouca ou nenhuma áreas de reabsorção óssea. Neste grupo ocorreu rápida formação óssea do momento da inserção até o período de 03 semanas *in vivo.* Os diferentes cenários avalidados obtiveram sucesso na osseointegração, mesmo com distintas vias de formação óssea. Apesar disto, não pode ser extrapolado que clinicamente eles teriam as mesmas taxas de sucesso clínico quando precocemente ou imediatamente colocados em função.

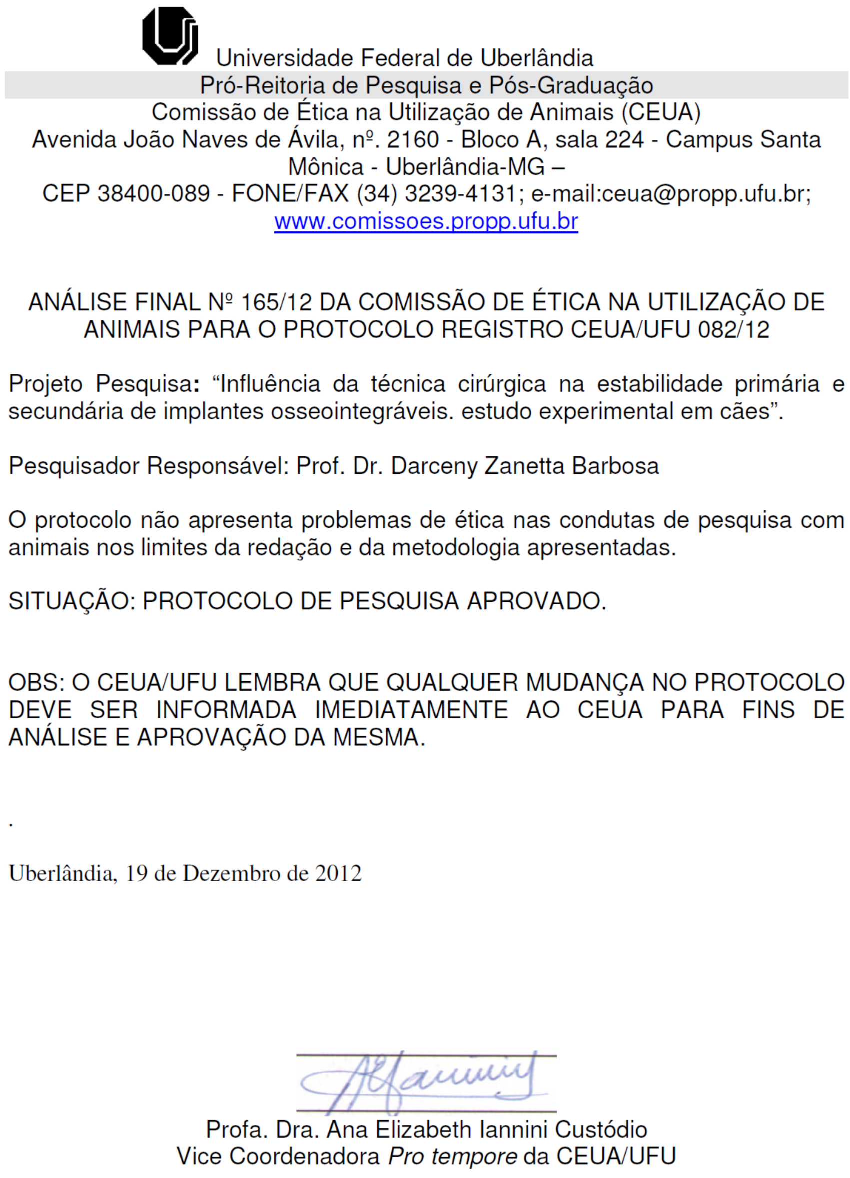
## REFERÊNCIAS

ALBREKTSSON, T.; WENNERBERG, A. Oral implant surfaces: Part 1--review focusing on topographic and chemical properties of different surfaces and in vivo responses to them. **Int J Prosthodont**, v 17, n° 5, p. 536-43, Sep-Oct. 2004.

BRANEMARK, P.I., et al. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. **Scand J Plast Reconstr Surg Suppl**, v 16, p. 1-132, 1977.

# Anexo 1

## Comissão de Ética na Utilização de Animais



Universidade Federal de Uberlândia
Pró-Reitoria de Pesquisa e Pós-Graduação
Comissão de Ética na Utilização de Animais (CEUA)
Avenida João Naves de Ávila, nº. 2160 - Bloco A, sala 224 - Campus Santa Mônica - Uberlândia-MG –
CEP 38400-089 - FONE/FAX (34) 3239-4131; e-mail:ceua@propp.ufu.br;
www.comissoes.propp.ufu.br

ANÁLISE FINAL Nº 165/12 DA COMISSÃO DE ÉTICA NA UTILIZAÇÃO DE ANIMAIS PARA O PROTOCOLO REGISTRO CEUA/UFU 082/12

Projeto Pesquisa**:** “Influência da técnica cirúrgica na estabilidade primária e secundária de implantes osseointegráveis. estudo experimental em cães”.

Pesquisador Responsável: Prof. Dr. Darceny Zanetta Barbosa

O protocolo não apresenta problemas de ética nas condutas de pesquisa com animais nos limites da redação e da metodologia apresentadas.

SITUAÇÃO: PROTOCOLO DE PESQUISA APROVADO.

OBS: O CEUA/UFU LEMBRA QUE QUALQUER MUDANÇA NO PROTOCOLO DEVE SER INFORMADA IMEDIATAMENTE AO CEUA PARA FINS DE ANÁLISE E APROVAÇÃO DA MESMA.

.

Uberlândia, 19 de Dezembro de 2012

Profa. Dra. Ana Elizabeth Iannini Custódio
Vice Coordenadora *Pro tempore* da CEUA/UFU