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Faculdade de Odontologia

ASSOCIAÇÃO ENTRE A ESTABILIDADE PRIMÁRIA DE MINI-IMPLANTES ORTODÔNTICOS E A QUALIDADE DOS SUBSTRATOS ÓSSEOS RECEPTORES

Mariana Marquezan

CD, MO

Tese submetida ao corpo docente da Faculdade de Odontologia da Universidade do Brasil - UFRJ, como parte dos requisitos, para a obtenção do Título de Doutor em Odontologia (Ortodontia).

Rio de Janeiro

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1 Mini-implante **2 Osso**

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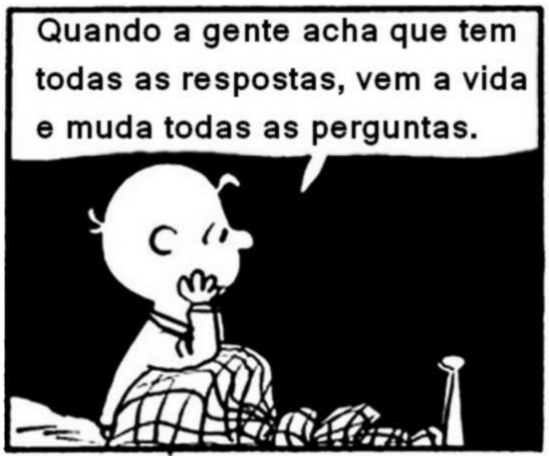

Charlie Brown – criação de Charles Schulz

RESUMO

MARQUEZAN, Mariana. **Associação entre a estabilidade primária de mini-implantes ortodônticos e a qualidade dos substratos ósseos receptores.** Orientadores: Dr[a]. Margareth Maria Gomes de Souza e Dr. Eduardo Franzotti Sant'Anna. Rio de Janeiro: UFRJ/Faculdade de Odontologia, 2013. Tese (Doutorado em Odontologia – Ortodontia). xxii, 110f.

O objetivo dos autores foi verificar a associação da estabilidade primária de mini-implantes ortodônticos (MI) e a qualidade do sítio ósseo receptor. Duas revisões sistemáticas e um experimento foram realizados. A primeira revisão avaliou a associação entre densidade mineral óssea (BMD) e a estabilidade de implantes dentários. A segunda revisão sistemática e meta-análise verificou a associação entre a espessura de cortical e a estabilidade de MI. O experimento teve como objetivo comparar a estabilidade primária de MI inseridos em blocos ósseos com dois tipos de BMD, com e sem cobertura cortical, e investigar se propriedades do osso trabecular podem influenciar na estabilidade. Cinquenta e dois blocos ósseos foram extraídos de ossos pélvicos bovinos frescos. Quatro grupos foram delineados considerando o tipo de osso (ilíaco ou púbico) e a presença ou ausência de cortical. Os espécimes foram escaneados através de

microtomografia computadorizada a fim de avaliar espessura trabecular (Tb.Th), número trabecular (Tb.N), separação trabecular (Tb.S), densidade trabecular (BV/TV), BMD e espessura cortical. MI com 1,4 mm de diâmetro e 6 mm de comprimento foram inseridos nos blocos ósseos e estabilidade primária foi avaliada através de torque de inserção (IT), mobilidade do MI (PTV) e teste de tração (PS). A comparação intergrupos mostrou menor nível de estabilidade primária quando a BMD de osso trabecular foi menor e na ausência de cortical (P≤0,05). Teste de correlação de Pearson mostrou que Tb.N, Tb.Th, BV/TV, BMD trabecular e BMD total, foram correlacionados com IT, PTV e PS. A espessura cortical apresentou correlação positiva com TI e PS (P≤0,05). Com essa tese foi possível concluir que: 1) existe associação positiva entre a estabilidade primária de implantes dentários e a BMD do sítio receptor; 2) há também associação positiva entre a estabilidade primária de MI e espessura cortical do sítio receptor; e 3) o osso trabecular desempenha um papel importante na estabilidade primária de MI na presença ou ausência de osso cortical.

SUMMARY

MARQUEZAN, Mariana. **Associação entre a estabilidade primária de mini-implantes ortodônticos e a qualidade dos substratos ósseos receptores.** Orientadores: Dr[a]. Margareth Maria Gomes de Souza e Dr. Eduardo Franzotti Sant'Anna. Rio de Janeiro: UFRJ/Faculdade de Odontologia, 2013. Tese (Doutorado em Odontologia – Ortodontia). xxii, 110f.

The aim of the authors was to investigate the association between primary stability of orthodontic mini-implants (MI) and the quality of the bone site receiver. Two systematic reviews and a trial were conducted. The first review examined the association between bone mineral density (BMD) and the stability of dental implants. The second systematic review and meta-analysis examined the association between cortical thickness and stability of MI. The experiment aimed to compare the primary stability of miniscrews inserted into bone blocks of different BMD with and without cortical bone, and investigates whether some trabecular properties could influence the primary stability. Fifty-two bone blocks were extracted from fresh bovine pelvic bone. Four groups were designed considering the bone type (iliac or pubic) and presence or absence of cortical. Specimens were microCT imaged to evaluate trabecular thickness (Tb.Th), trabecular number

(Tb.N), trabecular separation (Tb.S), bone volume density (BV/TV), BMD and cortical thickness. MI 1.4 mm in diameter and 6 mm long were inserted into the bone blocks and primary stability was evaluated by insertion torque (IT), MI mobility (PTV) and pullout strength (PS). Intergroup comparison showed lower level of primary stability when BMD of trabecular bone was smaller and in the absence of cortical ($P \leq .05$). Pearson's correlation test showed Tb.N, Tb.Th, BV/TV, trabecular BMD and total BMD were correlated to IT, PTV and PS. Cortical thickness was correlated to IT and PS ($P \leq .05$). This thesis concluded that: 1) there is a positive association between the primary stability of dental implants and BMD of the receptor site; 2) there is also a positive association between the primary stability of MI and cortical thickness of the receptor site; and 3) cancellous bone plays an important role in primary stability of mini-implants in the presence or absence of cortical bone.

RESUMEN

MARQUEZAN, Mariana. **Associação entre a estabilidade primária de mini-implantes ortodônticos e a qualidade dos substratos ósseos receptores.** Orientadores: Dr[a]. Margareth Maria Gomes de Souza e Dr. Eduardo Franzotti Sant'Anna. Rio de Janeiro: UFRJ/Faculdade de Odontologia, 2013. Tese (Doutorado em Odontologia – Ortodontia). xxii, 110f.

El objetivo de los autores fue investigar la asociación de la estabilidad primaria de mini-implantes ortodónticos (MI) y la calidad del sitio óseo receptor. Se realizaron dos revisiones sistemáticas y un experimento. La primera revisión examinó la asociación entre la densidad mineral ósea (BMD) y la estabilidad de los implantes dentales. La segunda revisión sistemática y meta-análisis examinó la asociación entre el espesor cortical y la estabilidad de MI. El experimento tuvo como objetivo comparar la estabilidad primaria de MI insertados en bloques de hueso con dos tipos de BMD con y sin cobertura de cortical, y investigar si las propiedades del hueso trabecular pueden influir en la estabilidad. Cincuenta y dos bloques de hueso fueron extraídos de los huesos pélvicos de bovinos frescos. Cuatro grupos fueron diseñados teniendo en cuenta el tipo de hueso (ilíaco o púbico) y la presencia o ausencia de cortical. Las muestras fueron analizadas por

microtomografía computarizada para evaluar el grosor trabecular (Tb.Th), el número trabecular (Tb.N), la separación trabecular (Tb.S), la densidad ósea trabecular (BV/TV), BMD y el espesor cortical. Fueron insertados MI con 1,4 mm de diámetro y 6 mm de longitud en los bloques de hueso y la estabilidad primaria se evaluó por medio del inserción de torción (TI), movilidad del MI (PTV) y la prueba de depullouT (PS). La comparación entre los grupos mostró una estabilidad primaria más baja cuando la BMD del hueso trabecular fue menos y en la ausencia de hueso cortical (P≤0,05). La prueba de correlación de Pearson mostró que Tb.N, Tb.Th, BV/TV, BMD trabecular y BMD total se correlacionaron con la IT, PTV e PS. El espesor cortical se correlacionó positivamente con la TI y PS (P≤0,05). Con esta tesis se concluyó que: 1) existe una asociación positiva entre la estabilidad primaria de los implantes dentales y BMD del sitio receptor; 2) también hay una asociación positiva entre la estabilidad primaria de los MI y el espesor cortical del sitio del receptor; y 3) el hueso trabecular hace un papel importante en la estabilidad primaria de MI en la presencia o ausencia de hueso cortical.

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DELINEAMENTO DA PESQUISA

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LISTA DE SIGLAS E ABREVIATURAS

ANOVA	Analysis of variance
BMD	bone mineral density
CBCT	cone beam computed tomography
cm	centímetro
DeCS	Descritores em Ciências da Saúde
g/cm^3	grama por centímetro cúbico
HU	Hounsfield Unit
ICC	coeficiente de correlação intraclasse
ISQ	implant stability quotient
IT	insertional torque
kgf	quilograma força
kV	kilovolt
Mand	mandible
Max	maxilla
MeSH	Medical Subject Headings
MI	mini-implante
microCT	microtomografia computadorizada
mL	mililitro

mm	milímetro
mm/s	milímetros por segundo
MPa	megapascal
ms	milisegundo
n	número
Ncm	Newton centímetro
PS	pullout strength
PTV	Periostest value
R^2	coeficiente de determinação
r	coeficiente de correlação linear
RFA	resonance frequency analysis
ROI	region of interest
SD	standard deviation
SIGLE	System for Information on Grey Literature in Europe
Tb.N	trabecular number
Tb.S	trabecular separation
Tb.Th	trabecular thickness
TBA	trabecular bone area
VOI	volume of interest
µA	microampere
µm	micrometro

ÍNDICE

1 INTRODUÇÃO

Desde a criação da especialidade da Ortodontia, o adequado controle de ancoragem é reconhecido como fator importante para se alcançar excelentes resultados nos tratamentos (Angle, 1907). A ancoragem ortodôntica geralmente é obtida por um dente ou grupo de dentes que apoiam a movimentação de outros elementos (Melsen e Verna, 1999). Tradicionalmente, essa pode ser reforçada aumentando-se o número de dentes, utilizando-se aparelhos intra-bucais auxiliares e/ou aparelhos extra-bucais (Lee, Kim *et al.*, 2009). Certos casos, entretanto, como severas assimetrias, perdas múltiplas dentárias ou extenso comprometimento periodontal, podem ser beneficiados pelo uso da ancoragem esquelética (Melsen e Verna, 1999), pois essa permite a realização de movimentos dentários nas três dimensões com mínimos efeitos nos demais dentes (Lee, Kim *et al.*, 2009).

Nas últimas três décadas, têm-se relatado o uso de diferentes dispositivos para ancoragem esquelética: parafusos de vitallium (Creekmore e Eklund, 1983), implantes dentários (Justens e De Bruyn, 2008), *onplants* (Block e Hoffman, 1995), implantes palatais (Wehrbein, Merz *et al.*, 1996) e mini-implantes (Kanomi, 1997). As principais vantagens dos mini-implantes são: tamanho reduzido, baixo custo, fácil inserção e remoção, com pequeno desconforto ao paciente, e possibilidade de aplicação de carga imediata (Serra,

Morais *et al.*, 2008; Luzi, Verna *et al.*, 2009; Wei, Zhao *et al.*, 2011; Topouzelis e Tsaousoglou, 2012).

O sucesso do uso dos mini-implantes (MI) está relacionado à sua estabilidade no tecido ósseo. Classicamente, essa pode ser dividida em primária e secundária. A primeira decorre do estreito contato entre a superfície do mini-implante e o osso (Gedrange, Hietschold *et al.*, 2005; Iijima, Takano *et al.*, 2012), sendo definida como a ausência de mobilidade no leito ósseo após a inserção do dispositivo (Javed e Romanos, 2010). A segunda, dita estabilidade secundária ou tardia, por sua vez, ocorre após a cicatrização (Gedrange, Hietschold *et al.*, 2005).

Na técnica de inserção de MI, a estabilidade primária destaca-se como um importante indício de êxito (Motoyoshi, Hirabayashi *et al.*, 2006; Chaddad, Ferreira *et al.*, 2008), visto que a maioria das falhas ocorre nos estágios iniciais pós-inserção (Miyawaki, Koyama *et al.*, 2003; Lim, Cha *et al.*, 2008). A falta de estabilidade imediata pode levar à mobilidade progressiva do dispositivo e sua subsequente perda (Mischkowski, Kneuertz *et al.*, 2008). Dada sua relevância, têm-se sugerido inclusive que, se a retenção mecânica inicial do MI não for observada, esse seja substituído por um dispositivo de maior diâmetro ou o sítio de inserção seja modificado (Garfinkle, Cunningham *et al.*, 2008). Por outro lado, tensões exageradas durante a inserção podem resultar em aquecimento e danos ao tecido ósseo (Park, Jeong *et al.*, 2006), incluindo isquemia e necrose, ou até fratura do mini-implante (Wilmes, Rademacher *et al.*, 2006)

Segundo revisão sistemática, a taxa de insucesso dos MI varia de 13,4 a 20,1% (Schatzle, Mannchen *et al.*, 2009). Em meta-análise recente, confirmou-

se que os MI ortodônticos possuem baixa taxa de falha (13,5%), sendo, portanto, indicados para a prática clínica (Papageorgiou, Zogakis *et al.*, 2012). Especula-se, entretanto, que a taxa de sucesso em adolescentes seja menor devido a maior taxa de metabolismo e menor densidade óssea nesses pacientes (Miyawaki, Koyama *et al.*, 2003; Topouzelis e Tsaousoglou, 2012).

Imediatamente após a instalação de implantes dentários e mini-implantes ortodônticos, a estabilidade primária tem sido tradicionalmente verificada através de teste manual (Merheb, Van Assche *et al.*, 2010). Métodos menos subjetivos de avaliação da estabilidade primária, são descritos na literatura, como aferição do torque de inserção, do torque de remoção, teste de tração ou de deslocamento lateral, método de frequência de ressonância e percussão. Apesar da variedade de métodos disponíveis, não há padrão ouro para avaliação da estabilidade primária (Cehreli, Karasoy *et al.*, 2009).

Fatores que influenciam a estabilidade imediata de implantes estão relacionados ao desenho do dispositivo (Wilmes, Rademacher *et al.*, 2006; Song, Cha *et al.*, 2007; Wilmes, Ottenstreuer *et al.*, 2008), à quantidade e qualidade óssea (Trisi, Rao *et al.*, 1999; Freudenthaler, Haas *et al.*, 2001; Cheng, Tseng *et al.*, 2004; Wilmes, Rademacher *et al.*, 2006), e à técnica de inserção (Wilmes, Rademacher *et al.*, 2006).

O termo “qualidade óssea”, entretanto, não está claramente definido na literatura. Sugere-se que esse englobe aspectos fisiológicos, estruturais e o grau de mineralização do tecido ósseo (Bergkvist, Koh *et al.*, 2010). Aspectos referentes ao metabolismo ósseo, à renovação celular, à maturação óssea, às propriedades da matriz extracelular e à vascularização do tecido também foram

enfatizados (Molly, 2006), mas o papel de cada um deles não é completamente compreendido (Bergkvist, Koh *et al.*, 2010).

Duas propriedades ósseas, entretanto, já foram relacionadas com a estabilidade de implantes dentários e mini-implantes: a densidade mineral óssea (BMD – do inglês *bone mineral density*) (Turkyilmaz, Tozum *et al.*, 2006; Turkyilmaz, Tumer *et al.*, 2007; Turkyilmaz e Mcglumphy, 2008a; b; Aksoy, Eratalay *et al.*, 2009; Song, Jun *et al.*, 2009; Bergkvist, Koh *et al.*, 2010; Merheb, Van Assche *et al.*, 2010) e a espessura de cortical (Miyawaki, Koyama *et al.*, 2003; Huja, Litsky *et al.*, 2005; Motoyoshi, Yoshida *et al.*, 2007; Motoyoshi, Inaba *et al.*, 2009; Pithon, Nojima *et al.*, 2011). Sabe-se que essas propriedades podem variar de acordo com o paciente e com as regiões da maxila e mandíbula (Deguchi, Nasu *et al.*, 2006), fazendo-se necessário investigar a influência de sua variação na estabilidade dos dispositivos. Além disso, outras propriedades ósseas merecem ser investigadas no que tange à estabilidade dos MI, tais como número de trabéculas (Tb.N), densidade trabecular (BV/TV), espessura trabecular (Tb.Th) e separação trabecular (Tb.S).

2 PROPOSIÇÃO

2.1 Realizar revisões sistemáticas com o objetivo de:

2.1.1 investigar a influência da BMD na estabilidade primária de implantes dentários;

2.1.2 avaliar a associação da espessura de cortical e a estabilidade primária de mini-implantes;

2.2 Realizar experimento com blocos de ossos bovinos a fim de:

2.2.1 comparar a estabilidade primária de mini-implantes inseridos em blocos ósseos de diferentes BMD (com e sem cortical);

2.2.2 investigar se propriedades do ósseas, tais como densidade mineral óssea, densidade trabecular, número de trabéculas, espessura trabecular, espessura de cortical e separação trabecular, podem influenciar a estabilidade primária de mini-implantes.

3 DELINEAMENTO DA PESQUISA

3.1 REVISÃO SISTEMÁTICA E META-ANÁLISE

A qualidade do tecido ósseo receptor, que tem influência na estabilidade primária de implantes, tem sido definida nas pesquisas odontológicas como duas principais propriedades: a densidade mineral óssea (Turkyilmaz, Tozum *et al.*, 2006; Turkyilmaz, Tumer *et al.*, 2007; Turkyilmaz e Mcglumphy, 2008a; b; Aksoy, Eratalay *et al.*, 2009; Song, Jun *et al.*, 2009; Bergkvist, Koh *et al.*, 2010; Merheb, Van Assche *et al.*, 2010) e a espessura de cortical (Miyawaki, Koyama *et al.*, 2003; Huja, Litsky *et al.*, 2005; Motoyoshi, Yoshida *et al.*, 2007; Motoyoshi, Inaba *et al.*, 2009; Pithon, Nojima *et al.*, 2011). Dessa maneira, foram realizadas duas revisões sistemáticas a fim de avaliar a associação dessas propriedades ósseas com a estabilidade primária.

Na primeira delas (Artigo 1, página 17), avaliou-se a correlação entre a estabilidade primária de implantes dentários com a BMD. Optou-se por trabalhar com implantes dentários em vez de MI ortodônticos por não haver trabalhos suficientes na literatura e com metodologias padronizadas para execução de uma revisão sistemática. Além disso, o campo da ancoragem esquelética tem se beneficiado da literatura de implantodontia desde seu surgimento. A segunda revisão sistemática avaliou a associação da espessura

de cortical e estabilidade primária de mini-implantes e deu origem a uma meta-análise (Artigo 2, página 40).

3.2 EXPERIMENTO

Essa pesquisa constituiu um estudo experimental *ex vivo*. Previamente à execução do experimento final, projeto piloto foi desenvolvido a fim de definir os substratos ósseos a serem utilizados (osso pélvico bovino) e o tamanho amostral. Cálculo amostral para diferença entre médias (α=5%, poder do estudo= 80%), sugeriu o uso de 13 amostras por grupo. Os resultados do piloto ainda geraram dois artigos científicos (APÊNDICE A e B, páginas 90 e 100).

3.2.1 AMOSTRA

3.2.1.1 SUBSTRATO ÓSSEO

A amostra foi constituída de treze ossos pélvicos bovinos (*Bos taurus*) da raça Angus, abatidos para consumo humano e obtidos imediatamente após o sacrifício em frigorífico registrado na ANVISA (Figura 1, página 9). Duas secções teciduais foram excisadas da face glútea da asa do ilíaco, e outras duas do púbico, regiões que possuem aproximadamente 1mm de espessura de cortical. Essas foram excisadas do osso pélvico através de fresa trefina (8 mm ø, SIN- Sistema de Implante e Nacional Ltda, São Paulo, Brasil) adaptada em motor de baixa rotação (Beltec LB100, Araraquara, Brasil) sob irrigação com soro fisiológico. Das secções ósseas removidas de cada região, uma teve sua cortical removida e outra teve a cortical preservada, sendo ambas armazenadas por congelamento (-20ºC) em soro fisiológico (Liu, Broucek *et al.*, 2012) até o momento da inserção dos MI. A divisão dos grupos experimentais

se deu de acordo com a região do osso pélvico excisada e a presença de cortical (Quadro 1).

Quadro 1: Divisão dos grupos experimentais de acordo com a região excisada e presença de cortical.

Grupo	Região da excisão	n. de amostras	Cortical óssea
GI0	Ilíaco	13	Ausente
GI1	Ilíaco	13	Presente
GP0	Púbico	13	Ausente
GP1	Púbico	13	Presente

3.2.1.2 MINI-IMPLANTES

Cinquenta e dois MI cônicos autoperfurantes com grau de pureza do tipo V (liga de Ti-6Al-4V) da marca INP (INP®, Sistema de Implantes Nacionais e próteses Comércio Ltda, São Paulo, Brasil), medindo 1,4 mm de diâmetro por 6 mm de comprimento (Figura 2, página 9), foram inseridos nos blocos ósseos. Foi realizada perfuração prévia dos sítios de inserção com broca broca helicoidal de 1mm de diâmetro (INP®, Sistema de Implantes Nacionais e próteses Comércio Ltda, São Paulo, Brasil), em baixa rotação, controlando-se a profundidade de inserção com *stops* de borracha para obter 2 mm. Durante a inserção dos MI, foi realizada aferição do torque de inserção (ver capítulo 3.2.3, página 12). Na sequência, procedeu-se à avaliação da micromobilidade (capítulo 3.2.3) e o escaneamento das peças para avaliação da qualidade óssea (capítulo 3.2.2).

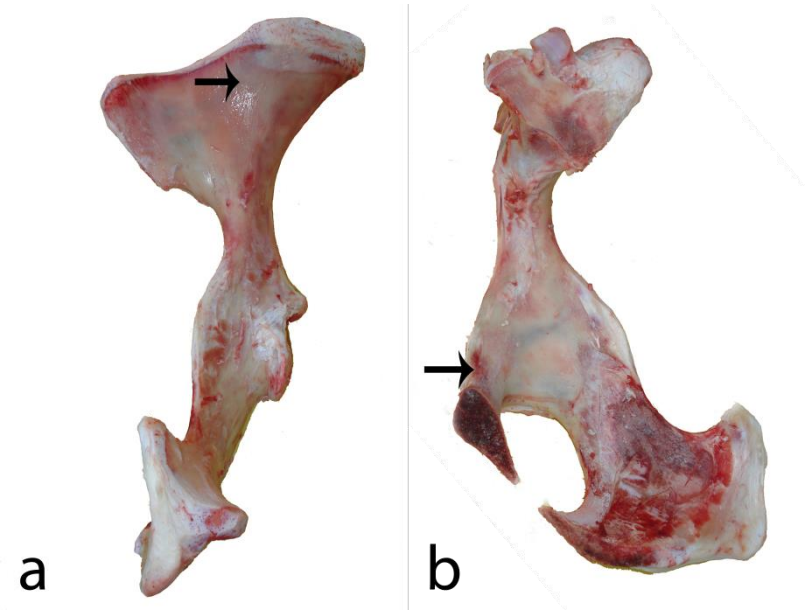

Figura 1: Aspecto macroscópico da metade direita do osso pélvico. (a) Vista caudal: a seta indica a asa glútea do osso ilíaco. (b) Vista medial: a seta indica a porção caudal do osso púbico.

Figura 2: Mini-implante utilizado na pesquisa, cônico, autoperfurante, com 1,4 mm de diâmetro e 6 mm de comprimento (INP®, Sistema de Implantes Nacionais e próteses Comércio Ltda, São Paulo, Brasil).

3.2.2 AVALIAÇÃO DA QUALIDADE ÓSSEA

A avaliação da qualidade do tecido ósseo receptor foi realizada através dos exames de microtomografia computadorizada (microCT), sendo assim possível aferir a densidade mineral e a micro-arquitetura ósseas.

O *scanner* utilizado para obter as imagens de microCT foi o SkyScan 1173 (Bruker micro-CT, Kontich, Bélgica, software versão 1.6). Para aquisição das imagens, as peças foram inseridas em tubos *eppendorf* de 2 mL, contendo soro fisiológico, e posicionadas de modo manter o longo eixo do implante perpendicular à fonte de raios-X. Entre a fonte e o receptor *flat panel*, um filtro de alumínio de 1 mm foi interposto. Os parâmetros de aquisição foram: 80 kV de tensão, 90 µA de corrente elétrica, matriz de aproximadamente 2 cm x 2 cm, resolução de 9,3 µm (Cha, Lim *et al.*, 2009; Cha, Song *et al.*, 2009), exposição de 800 ms.

Na sequência, as imagens foram reconstruídas com software NRecon, versão 1.6.4.1, e avaliadas no software CT-Analyser (version 1.10, Bruker micro-CT, Kontich, Bélgica).

A espessura de cortical foi medida em imagens bidimensionais. Cortes sagitais e coronais foram obtidos no software DataViewer (Bruker micro-CT, Kontich, Bélgica), contendo o centro do mini-implante. Esses foram transportados para o CT-Analyser, onde as mensurações foram realizadas e registradas em milímetros (Wilmes, Rademacher *et al.*, 2006; Suzuki, Suzuki *et al.*, 2010). Duas medidas foram realizadas em cada corte, anterior e posterior ao parafuso. Das quatro medidas realizadas foi obtida uma média, considerada a espessura de cortical. Trinta por cento da amostra foi remedida com intervalo de uma semana para aferir a concordância intra-examinador através do coeficiente de correlação intraclasse (ICC= 0,97).

Propriedades histomorfométricas como: volume trabecular – razão entre o volume de tecido ósseo e volume total da amostra (BV/TV), expresso em percentual; espessura trabecular (Tb.Th), expresso em mm; separação das

trabéculas (Tb.S), expresso em mm; e número de trabéculas por mm da amostra (Tb.N), expresso em 1/mm, foram aferidos em imagem tridimensional no CT-Analyser. Para isso, as imagens escaneadas foram abertas no software de análise com redimensionamento (Resize 3) a fim de reduzir seu tamanho original e permitir o adequado funcionamento do software.

Previamente à análise, para a aferição da BMD, foi necessário realizar a calibração do software através do escaneamento de um padrão de osso artificial (Sawbones® Pacific Research Laboratories Inc., Washington, EUA), composto de osso trabecular com densidade de 0,32 g/cm^3 e osso cortical com 1,64 g/cm^3. Esse padrão possuía as mesmas dimensões da amostra e continha um mini-implante inserido em seu centro. O escaneamento foi realizado em frasco *eppendorf* contendo soro fisiológico, de modo a reproduzir as condições de escaneamento das amostras. A BMD dos blocos ósseos foi então calculada pelo software a partir dos valores de coeficiente de atenuação dos ossos naturais e artificiais e registrada em g/cm^3. Foram aferidas as BMDs dos blocos ósseos considerando porção trabecular e cortical em conjunto (BMD total), do osso trabecular em separado (BMD trabecular) e do osso cortical (BMD cortical).

O processo de análise de aferição dos parâmetros histomorfométricos e da BMD se iniciou pela seleção do volume de interesse (VOI- do inglês *volume of interest*). Um cilindro de 3,4 mm de diâmetro foi selecionado em torno do mini-implante, cobrindo pelo menos 1 mm além das dimensões do parafuso, partindo de seu perfil transmucoso até a sua ponta. O centro desse cilindro, contendo o parafuso e os 6 voxels de osso adjacente a ele (54 µm) foram excluídos do VOI a fim de reduzir o efeito do artefato sobre as análises (Brinley,

Behrents *et al.*, 2009). A imagem selecionada foi binarizada por meio de histograma de tons de cinza, onde o valor de cinza é proporcional ao coeficiente de atenuação (áreas mais densas aparecem mais claras, enquanto áreas menos densas, mais escuras). O processamento da imagem foi então realizado automaticamente para calcular os parâmetros histomorfométricos desejados e a BMD.

3.2.3 AVALIAÇÃO DA ESTABILIDADE PRIMÁRIA

Para avaliação da estabilidade primária, o torquímetro digital (Lutron TQ-8800, Taipei, Taiwan) foi adaptado à chave de inserção dos MI, possibilitando a mensuração do pico do torque de inserção (IT, do inglês *intersional torque*). O torquímetro e os blocos ósseos, por sua vez, foram adaptados a um dispositivo especialmente desenhado para essa finalidade, que permitiu a inserção dos mini-implantes perpendicularmente aos blocos ósseos e ao solo (Figura 3, página 15). Os valores obtidos foram registrados em newtons.centímetro (Ncm).

A mobilidade dos mini-implantes foi aferida imediatamente após sua instalação através do aparelho Periotest (modelo 3218, Medizintechnik Gulden, Modautal, Alemanha), que realiza mensuração eletromecânica (Figura 4, página 15). O aparelho foi calibrado com a luva de calibração fornecida pelo fabricante previamente à mensuração de cada amostra. O aparelho e a amostra foram então acoplados a um dispositivo acrílico construído para manter a ponteira do aparelho paralela ao solo e perpendicular ao mini-implante, garantindo ainda uma distância de 2 mm entre a ponteira e a cabeça

do mini-implante, segundo recomendações do fabricante. Para cada análise, o aparelho foi acionado e a ponteira realizou 16 percussões, levando cerca de 4 segundos. Na sequência, um valor (*Periotest Value*- PTV) foi gerado no monitor do aparelho dentro da escala de -8 a +50. Quanto menor o PTV, menor a mobilidade e maior a estabilidade do implante (Kim, Ahn *et al.*, 2005). Para cada amostra, 2 medidas do PTV foram realizadas e a média delas foi tabulada. Se a diferença entre as medidas fosse maior que 2 pontos, essas eram desprezadas, o aparelho recalibrado e as medidas refeitas, seguindo-se o protocolo sugerido pelo fabricante.

Ainda para aferir a estabilidade primária, ensaio mecânico de tração (PS, do inglês *pull-out strength*) foi realizado em máquina universal (Emic DL 2000, São José dos Pinhais, Brasil). Esse é um ensaio destrutivo que consiste em extrair o mini-implante do tecido ósseo a uma velocidade constante, avaliando-se dessa forma, a força máxima necessária para remoção do dispositivo do tecido ósseo (Huja, Litsky *et al.*, 2005). Para tal, dois dispositivos foram acoplados à máquina: um em forma de pé de cabra, acoplado na parte superior e usado para prender o mini-implante; o outro na porção inferior, que serviu de base para fixar o bloco ósseo e manter o mini-implante perpendicular ao solo (Figura 5, página 15). Para o tracionamento dos mini-implantes foi utilizada velocidade de 0,05 mm/s (Huja, Litsky *et al.*, 2005; Salmoria, Tanaka *et al.*, 2008) e célula de carga de 500 kgf. O valor da carga e do deslocamento foram registrados e a força máxima (Fmax) alcançada foi registrada em Newtons (N).

3.2.4 ANÁLISE ESTATÍSTICA

As análises estatísticas foram realizadas por meio do programa Statistical Package for the Social Science (version 18, SPSS Inc., USA). Os valores obtidos foram tabulados e submetidos a estatísticas descritivas. A verificação da normalidade e da homogeinedade das variáveis foi realizada por meio do teste de Shapiro-Wilk e do teste de Levene, respectivamente. A diferença entre grupos foi avaliada através dos testes T-student (para as variáveis espessura de cortical e BMD cortical) e ANOVA/Tukey (para as demais variáveis). Por fim, para verificar se existe correlação entre as variáveis referentes à qualidade óssea e àquelas que indicam o comportamento mecânico dos mini-implantes foi realizado teste de correlação de Pearson. O nível de significância adotado foi de 0,05.

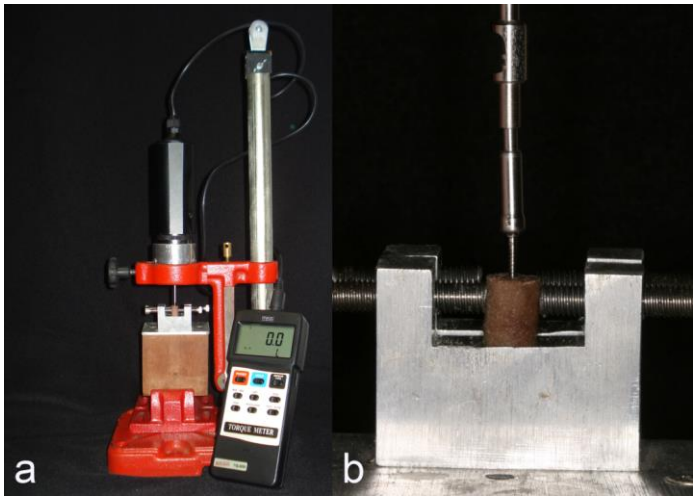

Figura 3: Avaliação do torque de inserção. (a) torquímetro digital e bloco ósseo adaptados ao dispositivo confeccionado para permitir a inserção dos mini-implantes perpendicularmente aos blocos ósseos e ao solo. (b) Visão aproximada da inserção do mini-implante ao bloco ósseo.

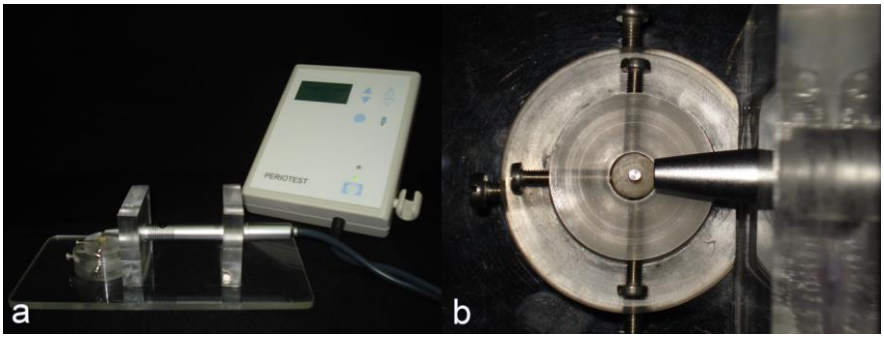

Figura 4: Avaliação da mobilidade do mini-implante. (a) Aparelho Periostest e amostra acoplados ao dispositivo acrílico desenvolvido para manter a ponteira do aparelho paralela ao solo e perpendicular ao parafuso. (b) vista aproximada da ponteira do Periostest, mantida a 2 mm da cabeça do mini-implante.

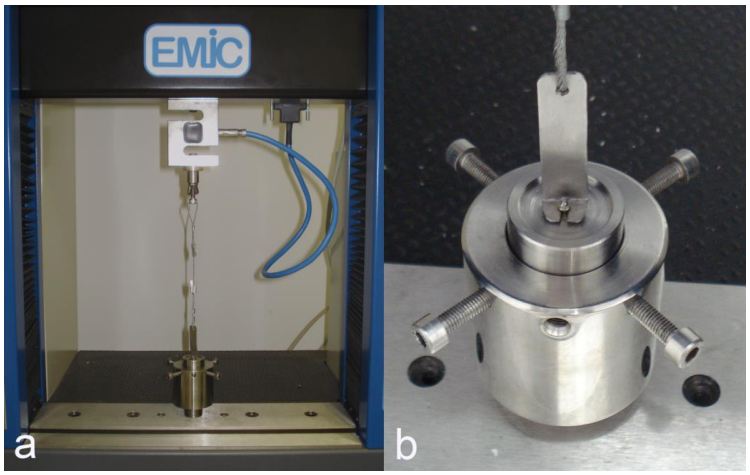

Figura 5: Teste de tração. (a) máquina universal com os dispositivos acoplados para prender o bloco ósseo, na parte inferior, e extrair o mini-implante, na parte superior. (b) vista aproximada dos dispositivos usados no teste de tração.

4 DESENVOLVIMENTO DA PESQUISA

4.1 ARTIGO 1

Marquezan M, Osório A, Sant'Anna E, Souza MM, Maia L. Does bone mineral density influence the primary stability of dental implants? A systematic review. Clin Oral Implants Res. 2012 Jul;23(7):767-74.

4.2 ARTIGO 2

Marquezan M, Mattos CT, Sant'Anna EF, Souza MMG, Maia LC. Does cortical thickness influence the primary stability of mini-implants? A systematic review and meta-analysis. *Submitted to The Angle Orthodontist.*

4.3 ARTIGO 3

Marquezan M, Lima I, Lopes RT, Sant'anna EF, de Souza MM. Is trabecular bone related to primary stability of miniscrews? *Accepted in The Angle Orthodontist* (ANEXO 1, página 110).

Artigo 1

Does bone mineral density influence the primary stability of dental implants?
A systematic review.

ABSTRACT

Objective: the aim of this systematic review was to investigate the influence of bone mineral density on the primary stability of dental implants.

Material and Methods: A search of health science databases (Cochrane Library, MEDLINE-PubMed, ISI Web of Knowledge, EMBASE, LILACS) and grey literature was performed, including papers published until January 2011. The main key words used were “bone density” (MeSH/ DeCS), “dental implant” (MeSH/ DeCS), “implant stability”, “implant stability quotient”, “ISQ”, “resonance frequency analysis”, “RFA”, “Ostell”, “Periotest value”, “PTV”, “Periostest”, “insertion torque”, “placement torque”, “cutting torque”. The inclusion criteria comprised observational clinical studies performed in patients who received dental implants for rehabilitation; studies that evaluated the association between bone mineral density and implant primary stability; bone density assessment performed by measurement of Hounsfield units using cone beam computed tomography; and dental implant primary stability evaluated by ISQ value, PTV value or Insertion torque measurement. The articles selected were carefully read and classified as low, moderate and high methodological quality, and data of interest were tabulated.

Results: Ten articles met the inclusion criteria, but only seven were included because of overlapping patients. They were classified as low or moderate methodological quality and control of bias, and presented positive association between primary stability and bone density.

Conclusions: There is a positive association between implant primary stability and bone mineral density of the receptor site. However, the methodological quality and control of bias of the studies should be improved to produce stronger evidences.

INTRODUCTION

Implants have been increasingly used in two fields of dentistry: dental rehabilitation and skeletal anchorage. The implants used for oral rehabilitation are called dental implants, and if these have already been inserted in the patient's oral cavity, they can be used for skeletal anchorage. Otherwise, specific temporary devices, such as mini-implants, onplants or miniplates, can be used for this purpose in Orthodontics. Various implant designs, diameters and lengths are available on the market to perform different functions at different sites in the oral cavity, and the characteristics of these devices are associated with their primary stability (Wilmes et al. 2006, Song et al. 2007). Primary stability is the absence of mobility in the bone bed after implant placement (Javed & Romanos 2010). It also depends on the technique used to insert the device (Wilmes et al. 2006) and bone quality and quantity at the receptor site (Trisi et al. 1999, Freudenthal et al. 2001, Cheng et al. 2004, Wilmes et al. 2006).

The term "bone quality" is not clearly defined in the literature. This includes physiological and structural aspects and the degree of bone tissue mineralization (Bergkvist et al. 2010). Aspects such as bone metabolism, cell turnover, maturation, intracellular matrix and vascularity have also emphasized (Molly 2006). But the role of each of these aspects is not completely understood (Bergkvist et al. 2010). In Implant dentistry, the most accepted classification of bone quality has been the one proposed by Lekholm & Zarb (1985), based on the amount of cortical and trabecular bone shown in preoperative radiographs generating four scores. This classification, however, depends on operator subjectivity. Thus, in Implant dentistry, it has been assumed that bone quality is equivalent to bone mineral density (Bergkvist et al. 2010). In endocrinology and traumatology, bone densitometry is taken as the gold standard for the quantification of bone mineral density (Carey et al. 2007).

Whereas in implant dentistry, cone beam computed tomography (CBCT), introduced as a preparatory exam by Scharz (1987), has been used for this purpose. It has become increasingly popular in dentistry because it is a three-dimensional and cross sectional analysis that allows the mineral density of jaw bones in specific sites to be quantified, and expressed in Hounsfield units (HU), in addition to allowing the measurement of bone dimensions.

Primary stability plays an important role in successful osseointegration of dental implants (Meredith 1998) and in the secondary stability of miniscrews, since the lack of immediate stability can lead to progressive mobility of the device and its subsequent loss (Mischkowski et al. 2008). Primary stability has traditionally been assessed by the practitioner by manual verification (Merheb et al. 2010). In researches, however, two less subjective methods, based on implant vibration produced by two electronic appliances (Ostell - Integration Diagnostics, Sweden - and the Periotest - Medizintechnik Gulden, Germany) are now being used. Ostell gives the implant stability quotient (ISQ) through resonance frequency analysis on a scale from 1 to 100. The higher the ISQ number, the higher the stability. The Periotest produces percussion of the implant and also provides a stability number on a scale ranging from -8 to +50. The lower the Periotest value (PTV), the higher the stability. These methods are noninvasive and offer the possibility of checking implant stability *in vivo* at different times (Cehreli et al. 2009). Another non-subjective and non-invasive method for assessing primary stability that is used extensively in clinical practice is the measurement of insertion torque (IT) in Newton.centimeter (Ncm) during implant placement (Pagliani et al. 2010). This method, however, allows a single measurement of primary stability. It cannot be used for evaluating secondary stability.

Considering that the bone quality of the receptor site might influence the primary stability of implants, and that bone density can be considered bone quality, the aim of this systematic review was to investigate the influence of bone mineral density on the primary stability of dental implants.

The present systematic review was focused on this question: is there scientific evidence to support the influence of bone mineral density on the primary stability of dental implants?

MATERIAL AND METHODS

Study selection criteria

The inclusion criteria comprised observational clinical studies conducted in patients who received dental implants for rehabilitation; studies that evaluated

the association between bone mineral density (prognostic factor) and implant primary stability (outcome); bone density assessment performed by measurement of Hounsfield unit (HU) using cone beam computed tomography (CBCT); and dental implant primary stability evaluated by ISQ value (Ostell, Integration Diagnostics, Sweden), PTV value (Periotest (Medizintechnik Gulden, Germany) or Insertion torque (IT) measurement. Studies that evaluated implant stability and bone density but did not verify their association were excluded from this systematic review.

Search strategy and screening of articles

The search process was performed independently by two examiners (MM and AOAF) under the guidance of a librarian. The Cochrane Library, MEDLINE-PubMed, ISI Web of Knowledge, EMBASE, LILACS and grey literature (SIGLE) databases were searched for articles published until January 2011, without language restriction. The search strategy included appropriate changes in the key words and followed the syntax rules of each database. The main key words used were “bone density” (MeSH/ DeCS), “dental implant” (MeSH/ DeCS), “implant stability”, “implant stability quotient”, “ISQ”, “resonance frequency analysis”, “RFA”, “Ostell”, “Periotest value”, “PTV”, “Periostest”, “insertion torque”, “placement torque”, “cutting torque”. Specific related terms used for each database are described in Table 1. Experts were also contacted to identify unpublished and ongoing studies. The searches were complemented by screening the references of selected articles to find any that did not appear in the database search. Two examiners independently evaluated the titles and the abstracts of all the studies identified. If the abstract contained insufficient information to allow decision-making as regards inclusion or exclusion, the full article was obtained and reviewed before making a final decision. Articles appearing in more than one database search were considered only once. Any differences between the two readers were solved by consensus. The selected articles were then carefully read for quality assessment and control of bias and data extraction.

Quality assessment and control of bias

The quality assessment and control of bias was realized by the two authors using the Methodological checklist for prognostic studies developed by the National Institute for Health and Clinical Excellence of the United Kingdom (Table 2). Checklist items are worded so that a 'yes' response always indicates that the study has been designed and conducted in such a way as to minimize the risk of bias for that item. An 'unclear' response to a question may arise when the answer to an item is not reported or is not reported clearly. A study was classified as having high methodological quality if at least 5 of the 6 parameters received the answer "yes"; moderate methodological quality if at least 3 of the parameters received the answer "yes"; or low methodological quality if 2 or less parameters received the answer "yes". None of the articles was excluded from the systematic review after this classification, except for articles on studies conducted by the same author and having some overlapping patients. In this case, after ranking the studies, the one with the highest score was included in the systematic review, the others were excluded.

Data extraction

From the selected articles, data on the following issues were extracted and tabulated by the two authors: a) author and year publication; b) geographical location; c) type of study; d) sample (sample size, age and gender); e) implant name and manufacturer; f) implant dimensions and surface treatment (if present); g) number of implants evaluated; h) regions of implant insertion; i) bone density of the receptor sites (HU value) and type of bone evaluated (if cortical and trabecular bones together or only trabecular); j) implant primary stability number (ISQ, PTV and/or IT (Ncm); k) confounders included in the analysis (cortical thickness and/or implant dimensions); l) association between stability and bone density.

RESULTS

The search procedures retrieved 519 articles from EMBASE, 343 articles from MEDLINE-PubMed, 219 articles from ISI Web of Knowledge, 1338 articles from the Grey Literature (SIGLE) and 18 articled from the Cochrane Library. No

articles were found in LILACS, or any extra articles by hand search (Figure 1). After the duplicate articles were removed, 13 articles were selected by title and abstract reading according to the inclusion and exclusion criteria (Aksoy et al. 2009; Bergkvist et al. 2010; Farré-Pagés et al. 2010; Ikumi & Tsutsumi, 2005; Merheb et al. 2010; Pagliani et al. 2010; Sencimen et al. 2010; Song et al. 2009; Turkyilmaz et al. 2006; Turkyilmaz et al. 2007; Turkyilmaz & McGlumphy 2008A; Turkyilmaz & McGlumphy 2008B). After complete text reading, two articles were excluded because did not meet the inclusion criteria (Sencimen et al. 2010; Song et al. 2009). Four of selected articles were on studies conducted by the same author and there were some overlapping patients, as confirmed by the author during contact by e-mail (Turkyilmaz et al. 2006; Turkyilmaz et al. 2007; Turkyilmaz & McGlumphy 2008A; Turkyilmaz & McGlumphy 2008B). Using the quality assessment and control of bias, the article that received the highest classification among the four written by the same researcher was included in the systematic review (Turkyilmaz & McGlumphy 2008A). This article was also the one recommended by the author during the contact. The other three were excluded (Table 3).

Seven clinical series were included in the systematic review and data extracted from them were tabulated (Table 4) (Aksoy et al. 2009; Bergkvist et al. 2010; Farré-Pagés et al. 2010; Ikumi & Tsutsumi, 2005; Merheb et al. 2010; Pagliani et al. 2010; Turkyilmaz & McGlumphy 2008A). Some missing data were asked to the authors by e-mail contact and were included in Table 4.

The quality assessment and control of bias showed that the articles had low to moderate methodological quality. This result was mainly due to unclear definition of inclusion and exclusion criteria (first question in the quality assessment), no reporting of blinding of examiners (third and fourth questions), no confounders included in analysis (fifth question) and inadequate interpretation of statistical analysis (sixth question) in some studies (Table 3).

The extracted data showed that the selected clinical series were developed from 2005 to 2010 in seven different countries: Turkey, Sweden, Spain, Japan, Belgium, Italy and United States of America (Table 4).

Samples comprised patients that received dental implants for rehabilitation. The number of patients varied from 4 (Ikumi & Tsutsumi 2005) to 111 (Turkyilmaz & McGlumphy 2008A), and the number of implants, considered

the unit analysis, ranged from 23 (Aksoy et al. 2009) to 300 (Turkyilmaz & McGlumphy 2008A) (Table 4). Seven types of implants from six different manufacturers were used: Swiss plus (Zimmer Dental), Standard Plus SLActive (Straumann), Astra (Astra Tech), Mis-Seven (Biodenix Tech Inc), Mis-Biocom (Biodenix Tech Inc), TiUnite MK III (Nobel Biocare) and Neoss Dental Implant System (Neoss Ltd.). They presented different surface treatments, and their dimensions varied from 3.3 to 5.5 mm in diameter and from 6 to 15 mm in length (Table 4).

Density values (HU) were higher in men than in women (Aksoy et al. 2009; Turkyilmaz & McGlumphy 2008A). The jaw bone also showed difference, the mandible presented higher values than maxilla (Aksoy et al. 2009). On the other hand, the stability value according gender differences, evaluated only by Aksoy et al. (2009), was lower for men (Table 4).

The IT values ranged from 4 Ncm (Ikumi & Tsutsumi, 2005) to 42.34 Ncm (Farré-Pagés et al. 2010), being higher in the mandible than maxilla, and in the anterior than posterior region (Farré-Pagés et al. 2010) (Table 4).

Although the implant dimensions were cited in all of the studies, the only study that included this factor and other confounders in the analysis was the one conducted by Merheb et al (2010) (Table 4).

Despite methodological differences and weak to moderate methodological quality (Table 3), all of the selected articles presented a positive association between primary stability of implants and bone density (Table 4).

DISCUSSION

There was positive association between bone density and dental implant stability in the selected articles. When evaluating the correlation between ISQ and HU values, correlation coefficients ranged from 0.46 (moderate correlation- Merheb et al. 2010) to 0.882 (high correlation- Turkyilmaz & McGlumphy 2008A). Methodological differences might be responsible for this difference. Even though all of the articles quantified HU in CBCT images, some studies evaluated the cortical bone and trabecular bone density together (Aksoy et al. 2009, Pagliani et al. 2010, Turkyilmaz & McGlumphy 2008A), a factor that probably increased the HU value of the unit. Other authors considered only the

trabecular bone (Bergkvist et al. 2010, Merheb et al. 2010). Merheb et al. (2010), who considered only the trabecular bone for density evaluation, found one of the lower values (r=0.46). Authors who considered the cortical and trabecular bone as a unit when evaluating bone density observed stronger correlations (Aksoy et al., 2009; Pagliani et al. 2010, Turkyilmaz & McGlumphy 2008A).

The cortical thickness has been related to primary stability of miniscrews (Miyawaki et al. 2003; Huja et al. 2005; Motoyoshi et al. 2007; Motoyoshi et al. 2009). Data extracted from one of the selected articles also showed this correlation: r=0.57 (Merheb et al. 2010). It seems logical that when there was increased cortical thickness, there would also be an increase in the area of highly mineralized tissue when bone density was measured. It can be inferred that the density measured by the sum of cortical and trabecular bone might be strongly influenced by cortical thickness.

When evaluating the correlation between IT and HU values, only one study revealed the type of bone evaluated (Turkyilmaz & McGlumphy 2008A-evaluated cortical and trabecular bone together). The IT values ranged from 4 Ncm (Ikumi & Tsutsumi 2005) to 42.34 Ncm (Farré-Pagés et al. 2010). This big difference can be explained by methodological differences. Ikumi & Tsutsumi (2005), who found a low value for IT, evaluated the cutting torque during the entire implant placement procedure. On the other hand, Farré-Pagés et al. (2010) evaluated the insertion torque only in the final phase of insertion. The values for IT in different parts of jaw bones was evaluated only by Farré-Pagés et al. (2010), who found higher values in the mandible than maxilla and in the anterior than posterior region, in agreement with their findings for HU values.

Primary stability depends on the implant design, insertion technique and bone quality (Wilmes et al. 2006). The aim of this systematic review was to verify the influence of bone quality, considered as bone mineral density, on primary stability of dental implants. It was also possible to extract some data concerning the implant design from the selected articles. All of the selected studies reported the type of implant used and its dimensions, but only one of them investigated its influence on the results. Merheb et al. (2010) discovered an important influence of implant dimension on stability when using a multivariable model. In a stepwise multiple regression analysis an inverse

interaction was verified between cortical thickness and implant length. Implant shape, design and surface characteristics also are important for primary stability (Javed & Romanos 2010). Each study selected had used only one type of implant (with only the diameter or length varying), so these characteristics were not evaluated.

The HU, ISQ and IT values were related to variation of the jaw (maxilla or mandible) and gender (female or male) in four of the articles involved in this review (Aksoy et al. 2009, Bergkvist et al. 2010, Farré-Pagés et al. 2010, Turkyilmaz & McGlumphy 2008A). They revealed different HU values for men and women, being higher in men (Aksoy et al. 2009, Turkyilmaz & McGlumphy 2008A). On the other hand, the ISQ, evaluated by gender only by Aksoy et al. (2009), was lower for men. Consequently, the correlation coefficient was not statistically significant for men in this study. The result might be influenced by the small number of the sample. The HU values were higher in the mandible than maxilla (Aksoy et al. 2009, Farré-Pagés et al. 2010) and IT was also higher in the mandible than maxilla (Farré-Pagés et al. 2010). Even though it is interesting to look for the influence of these categorical variables on stability of implants, the bone density and implant stability values might be more related to the site of observation, because there is a great variation among the different sites of analysis (Turkyilmaz et al. 2007).

Despite the positive association found between primary stability and bone density, the methodological quality and control of bias of the studies could be improved to produce stronger evidences. Inclusion and exclusion criteria for the sample selection were not clearly defined in some studies. Calibration, error calculation and blinding of examiners were rarely mentioned by the authors. Finally, confounders were considered for analysis in only one of the studies (Merheb et al. 2010). Therefore, the quality assessment and control of bias ranked six articles as “moderate” and four as “low”.

The purpose of this systematic review was to evaluate whether there was scientific evidence to support the association between bone density and implant primary stability. The search was focused on dental implants instead of miniscrews, or both, because no observational clinical studies evaluating the primary stability of miniscrews and correlating it to bone density were found in the consulted literature. Moreover, there were few laboratory studies on this

subject and there was no standard to evaluate the stability. As the field of skeletal anchorage has been improved by the literature on oral rehabilitation to support clinical procedures, this systematic review might enrich both fields.

Primary stability, known as the absence of mobility in the bone bed, has traditionally been assessed by the practitioner by manual verification (Merheb et al. 2010). To avoid subjectivity, three methods for the clinical verification of primary stability were chosen for analysis in this review: the resonance frequency method, which generated the ISQ value, the percussion method, which generates the PTV value, and the insertion torque measurement that provided the IT value in Ncm. IT was previously considered as a parameter to assess bone quality during implant surgery (Meredith 1998), but recently many authors have considered this measurement as an indicator of primary stability (Homolka et al. 2002; Wilmes et al. 2006; Pithon & Nojima 2007; Lim et al. 2008; Mischkowski et al. 2008; Brinley et al. 2009; Trisi et al. 2009; Cha et al. 2010; Farré-Pagés et al. 2010). Despite the controversy, the three methods were chosen to cover the maximum number of clinical articles on this subject and to avoid subjectivity. Although “Periotest value”, “PTV” and “Periotest” were used as key words none of the selected articles used this method to assess primary stability.

The data extraction process revealed that there were some items of missing information in the selected articles. Several of them were filled by e-mail contact with corresponding authors, however others related to HU values and HU measurement remained unclear. Although the articles that provided this information led one to the conclusion that the HU values are higher when cortical bone and trabecular bone are measured together, we assume that the lack of complete information in all of the selected articles is a limitation of this systematic review because there is a possibility of the information omitted by some studies being in disagreement with the data reported by the other studies.

All the articles presented some indication of positive correlation between primary stability of dental implants and bone density of receptor site: as the bone density increases, the primary stability of implants also increases. This information has clinical relevance. If an implant has to be placed in a site with little bone density, little primary stability is expected, unless other resources are resorted to with regard to the implant dimensions and insertion technique.

The evidence to support the relationship between bone density and implant primary stability is still weak to moderate according to the quality assessment and control of bias of the series of clinical studies found. The methodological quality of the studies needs to be improved to produce stronger evidences preferably with the use of multivariate analysis including confounders.

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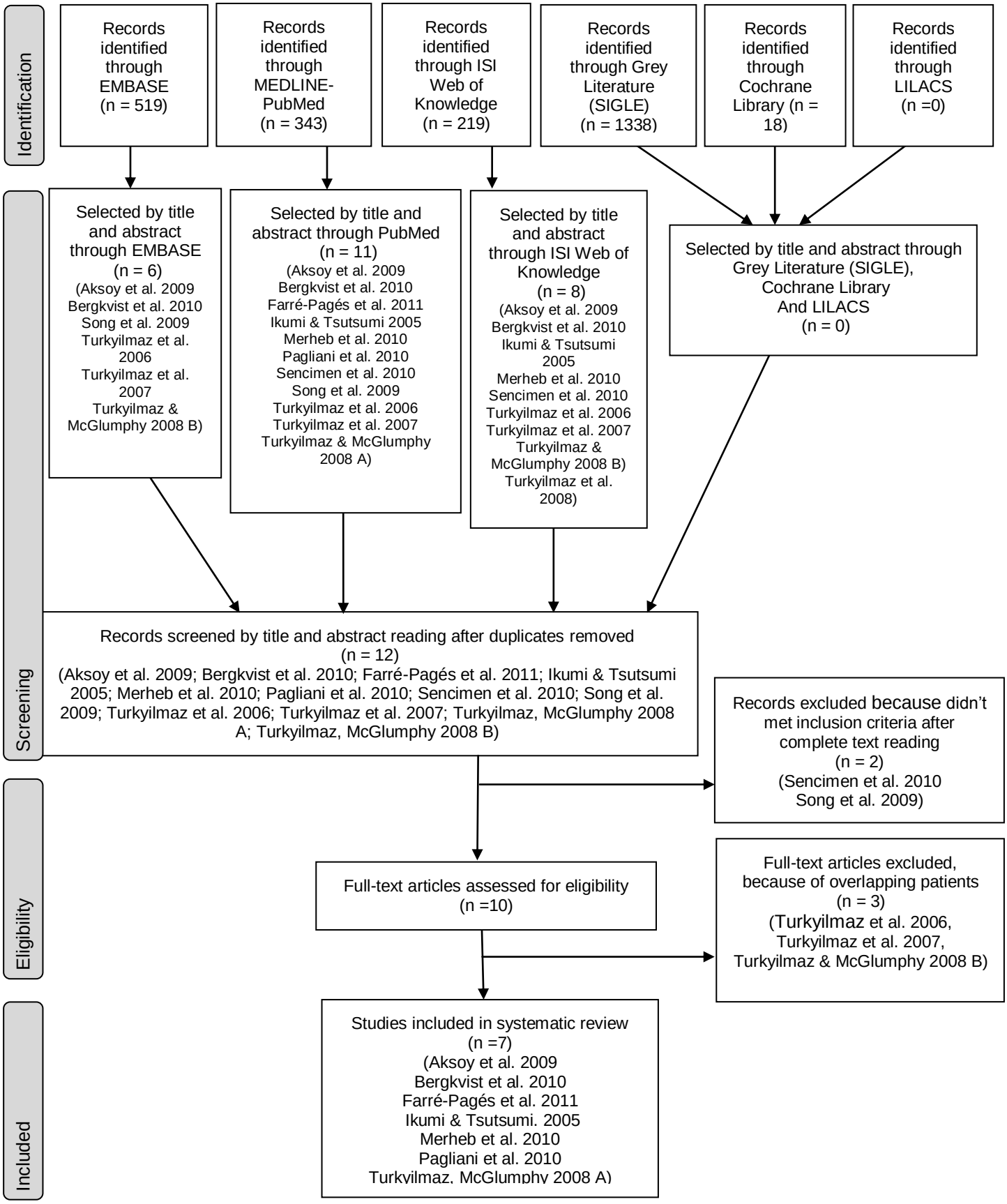

Figure 1: Flow diagram of literature search.

Table 1 Electronic database used and search strategy.

Database	Key words
Cochrane Library http://cochrane.bvsalud.org/portal/php/index.php	bone density AND dental implant AND implant stability
MEDLINE-PubMed http://www.ncbi.nlm.nih.gov/pubmed	"bone density" AND ("dental implant" OR "implant stability" OR "implant stability quotient" OR "ISQ" OR "resonance frequency analysis" OR "RFA" OR "Ostell" OR "Periotest value" OR "PTV" OR "Periostest" OR "insertion torque" OR "placement torque" OR "cutting torque")
ISI Web of Knowledge http://apps.isiknowledge.com	bone density AND (dental implant OR implant stability OR implant stability quotient OR ISQ OR resonance frequency analysis OR RFA OR Ostell OR Periotest value OR PTV OR Periostest OR insertion torque OR placement torque OR cutting torque)
EMBASE http://embase.com/search	'bone density'/de AND ('dental implant'/de OR 'implant stability' OR 'implant stability coefficient' OR 'isq' OR 'resonance frequency analysis' OR 'rfa' OR 'ostell' OR 'periotest value' OR 'ptv' OR 'periostest' OR 'insertion torque' OR 'placement torque' OR 'cutting torque') AND [humans]/lim
LILACS http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/	bone density AND (dental implant OR implant stability OR implant stability quotient OR ISQ OR resonance frequency analysis OR RFA OR Ostell OR Periotest value OR PTV OR Periostest OR insertion torque OR placement torque OR cutting torque)
grey literature (SIGLE) http://www.cardiff.ac.uk/insrv/eresources/databases/sigle.html	bone density AND (dental implant OR implant stability OR implant stability quotient OR ISQ OR resonance frequency analysis OR RFA OR Ostell OR Periotest value OR PTV OR Periostest OR insertion torque OR placement torque OR cutting torque)

Table 2: Methodological checklist for prognostic studies developed by the National Institute for Health and Clinical Excellence from United Kingdom. It was used to perform the quality assessment and control of bias.

Study identification:				
Circle one option for each question				
1.1	The study sample represents the population of interest with regard to key characteristics, sufficient to limit potential bias to the results? To minimise bias, the study population should be clearly defined and described and should represent the source population of interest. Points to consider include the following: • Are the source population or the population of interest adequately described with respect to key characteristics? • Are the sampling frame and recruitment adequately described, possibly including methods to identify the sample (number and type used; for example, referral patterns in healthcare), period of recruitment and place of recruitment (setting and geographical location)? • Are inclusion and exclusion criteria adequately described (for example, including explicit diagnostic criteria or a description of participants at the start of the follow-up period)? • Is participation in the study by eligible individuals adequate? • Is the baseline study sample (that is, individuals entering the study) adequately described with respect to key characteristics?	Yes	No	Unclear
1.2	Loss to follow-up is unrelated to key characteristics (that is, the study data adequately represent the sample), sufficient to limit potential bias? To minimise bias, completeness of follow-up should be described and adequate. Points to consider include the following: • Is the response rate (that is, proportion of study sample completing the study and providing outcome data) adequate? • Are attempts to collect information on participants who dropped out of the study described? • Are reasons for loss to follow-up provided? • Are the key characteristics of participants lost to follow-up adequately described? • Are there any important differences in key characteristics and outcomes between participants who completed the study and those who did not?	Yes	No	Unclear
1.3	The prognostic factor of interest is adequately measured in study participants, sufficient to limit potential bias? To minimise bias, prognostic factors should have been defined and measured appropriately. Points to consider include the following: • Is a clear definition or description of the prognostic factor(s) measured provided (including dose, level, duration of exposure, and clear specification of the method of measurement)? • Are continuous variables reported, or appropriate cut-off points (that is, not data-dependent) used? • Are the prognostic factor measured and the method of measurement valid and reliable enough to limit misclassification bias? (This may include relevant outside sources of information on measurement properties, as well as characteristics such as blind measurement and limited reliance on recall.) • Are complete data for prognostic factors available for an adequate proportion of the study sample?	Yes	No	Unclear

	• Are the method and setting of measurement the same for all study participants? • Are appropriate methods employed if imputation is used for missing data on prognostic factors?			
1.4	The outcome of interest is adequately measured in study participants, sufficient to limit bias? • Is a clear definition of the outcome of interest provided, including duration of follow-up? • Are the outcome that was measured and the method of measurement valid and reliable enough to limit misclassification bias? (This may include relevant outside sources of information on measurement properties, as well as characteristics such as 'blind' measurement and limited reliance on recall.) • Are the method and setting of measurement the same for all study participants?	Yes	No	Unclear
1.5	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest? • To minimise bias, important confounders should be defined and measured, and confounding should be accounted for in the design or analysis. Points to consider include the following: • Are all important confounders, including treatments (key variables in the conceptual model), measured? Are clear definitions of the important confounders measured (including dose, level and duration of exposures) provided? • Is measurement of all important confounders valid and reliable? (This may include relevant outside sources of information on measurement properties, as well as characteristics such as 'blind' measurement and limited reliance on recall.) • Are the method and setting of measurement of confounders the same for all study participants? • Are appropriate methods employed if imputation is used for missing data on confounders? • Are important potential confounders accounted for in the study design (for example, matching for key variables, stratification or initial assembly of comparable groups)? • Are important potential confounders accounted for in the analysis (that is, appropriate adjustment)?	Yes	No	Unclear
1.6	The statistical analysis is appropriate for the design of the study, limiting potential for the presentation of invalid results? To minimise bias, the statistical analysis undertaken should be clearly described and appropriate for the design of the study. Points to consider include the following: • Is the presentation of data sufficient to assess the adequacy of the analysis? • Where several prognostic factors are investigated, is the strategy for model building (that is, the inclusion of variables) appropriate and based on a conceptual framework or model? • Is the selected model adequate for the design of the study? • Is there any selective reporting of results? • Are only pre-specified hypotheses investigated in the analyses?	Yes	No	Unclear

Table 3: Articles ranked according the quality assessment and control of bias.

	Aksoy et al. 2009	Bergkvist et al. 2010	Farré-Pagés et al. 2010	Ikumi & Tsutsumi 2005	Merheb et al. 2010	Pagliani et al. 2010	Turkyilmaz et al. 2006	Turkyilmaz et al. 2007	Turkyilmaz & McGlumphy 2008 A	Turkyilmaz & McGlumphy 2008B
The study sample represents the population of interest with regard to key characteristics, sufficient to limit potential bias to the results.	yes	yes	unclear	unclear	unclear	unclear	unclear	unclear	yes	unclear
Loss to follow-up is unrelated to key characteristics (that is, the study data adequately represent the sample), sufficient to limit potential bias.	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
The prognostic factor of interest is adequately measured in study participants, sufficient to limit potential bias. (In these studies the prognostic factor was the BMD).	yes	unclear	unclear	unclear	unclear	unclear	yes	yes	yes	yes
The outcome of interest is adequately measured in study participants, sufficient to limit bias. (The outcome was the primary stability).	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear
Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest. (For example: implant dimensions and cortical thickness).	no	no	no	unclear	yes	no	no	no	no	no
The statistical analysis is appropriate for the design of the study, limiting potential for the presentation of invalid results	yes	yes	yes	yes	yes	yes	no	yes	yes	yes
Category and situation of the article	4 “yes”: Moderate methodol quality Included	3 “yes”: Moderate methodol quality Included	2 “yes”: Low methodol quality Included	2 “yes” : Low methodol quality Included	3 “yes”: Moderate methodol quality Included	2 “yes”: Low methodol quality Included	2 “yes”: Low methodol quality Excluded*	3 “yes”: Moderate methodol quality Excluded*	4 “yes”: Moderate methodol quality Included	3 “yes”: Moderate methodol quality Excluded*

*The articles conducted by the same author had some overlapping patients. After ranking these studies, the one with the highest score was included in the systematic review, the others were excluded.

methodol= methodological

Table 4: Summarized data collected from the selected articles.

Author and year	**Geographical location**	**Sample**	**Implant and manufacturer**	**Implant dimensions (mm) and surface**	**N. of implants**	**Regions of implant insertion**	**HU mean (SD) and type of bone evaluated**	**Stability: ISQ, PTV and/or IT (Ncm) mean (SD)**	**Confounders included in analysis**	**Association between stability and bone density**
Aksoy et al. 2009	Turkey	*number:* 10 *gender:* 5 ♀, 5 ♂ *mean age:* 46.28	Swiss plus (Zimmer Dental)	*Diameters:* 3.75, 4.1, 4.8 *Lengths:* 8, 10, 12, 14 *Surface:* 1-2 µm roughness	23	Anterior and posterior areas of maxilla and mandible	554.87 (302,045 ♀440 (171.16) ♂612 (340.08) Max 409.92 (141.87) Mand 699.83 (353.24) Measured trabecular + cortical bone	*ISQ:* 72.28 (6.194) ♀77.63 (2.32) ♂70.20 (6.08) Max 74.36 (5.73) Mand 71.33 (6.48)	*Implant dimensions:* cited, but not included in analysis *Cortical thickness:* not evaluated	*bone density- ISQ*: Only verified in women r=0.807 p=0.015
Bergkvist et al. 2010	Sweden	*number:* 31 *gender:* 13 ♀, 8 ♂ *mean age:* 70.1	Standard Plus SLActive (Straumann)	*Diameters:* 3.3 and 4.1 *Lengths:* 10 and 12 *Surface:* 2-4 µm roughness - sandblasted and acid etched	137	Regions of upper and lower incisors, canines and premolars	Not mentioned Measured only trabecular bone	*ISQ:* Max 51.6 (7.5) Mand 66.5 (6.0)	*Implant dimensions:* cited, but not included in analysis *Cortical thickness:* not evaluated	*bone density- ISQ*: there is correlation in the maxilla, but the r coefficient was not mentioned
Farré-Pagés et al. 2010	Spain	*number:* 10 *gender:* 4 ♀, 6 ♂ *mean age:* 53	25 Astra (Astra Tech), 22 Mis-Seven (Biodenix Tech Inc),	*Diameters:* 3.5 to 5 *Lengths:* 8 to 13	54	Anterior and posterior mandible regions	Anterior mandible 776 Posterior mandible	*ISQ: not mentioned* *IT (Ncm):* Max 40.22	*Implant dimensions:* cited, but not included in analysis	*bone density- ISQ:* r=0.0474 p<0.05

			7 Mis-Biocom (Biodenix Tech Inc)	*Surface:* Astra - chemically modified titanium surface; Mis-seven - sandblasted and acid etched; Mis-Biocom - sandblasted and acid etched			746.72 Anterior maxilla 431.6 Posterior maxilla 193.286 Didn't mentioned if only trabecular bone or trabecular + cortical bone were measured	Mand 42.34 anterior region 42.22 posterior region 40	*Cortical thickness:* not evaluated	*bone density- IT:* r=0.0859 p>0.05
Ikumi & Tsutsumi 2005	Japan	*number:* 13 *gender:* 7 ♀, 6 ♂ *mean age:* not mentioned	TiUnite MK III (Nobel Biocare)	*Diameters:* 3.75 *Lengths:* 10, 11.5, 13, 15 *Surface:* layer of titanium oxide	56	Maxilla and madible	625.421 (262.629)* Didn't mentioned if only trabecular bone or trabecular + cortical bone were measured	*IT (Ncm): 4 (2.62)**	*Implant dimensions:* cited, but not included in analysis *Cortical thickness:* not evaluated	*bone density- IT:* r=0.77 p=0.01
Merheb et al. 2010	Belgium	*number:* 24 *gender:* 16 ♀, 8 ♂ *mean age:* 58	SLActive (Straumann)	*Diameters:* 3.3 and 4.1 *Lengths:* 6, 8, 10,12,14 *Surface:* 2-4 μm roughness - sandblasted and acid etched	136	Anterior and posterior regions of maxilla	428 (212.69)** Measured only trabecular bone	*ISQ:* 67.98 (7.64)**	*Implant dimensions:* diameter and length influenced the stability (multi-variable model) *Cortical thickness:* correlated with stability r=0.57 p=0.000	*bone density- ISQ*: r=0.46 p=0.000
Pagliani et al. 2010	Italy	*number:* 4 *gender:* 2 ♀, 2 ♂	Neoss Dental Implant System	*Diameters:* 3.5, 4, 4.5 and 5.5	26	Anterior and posterior regions	657.6 (240.7)	*ISQ:* 75 (5.9)	*Implant dimensions:* cited,	*bone density- ISQ:* r=0.54

		mean age: 67.3	(Neoss Ltd.)	*Lengths:* 11, 13, 15 *Surface:* Biomodal surface-multistage blasted**		of maxilla and mandible	Measured trabecular + cortical bone	*IT (Ncm):* 12.2 (6.6)	but not included in analysis *Cortical thickness:* not evaluated	p=0.004 *bone density- IT:* r=0.73 p=0.002
Turkyilmaz & McGlumphy 2008 A	USA	*number:* 111 *gender:* 55 ♀, 56 ♂ *mean age:* 55±11	TiUnite MK III (Nobel Biocare)	*Diameters:* 3.75 and 4 *Lengths:* 8.5,10, 11.5, 13, 15 *Surface:* layer of titanium oxide	300	Anterior and posterior regions of maxilla and mandible	620 (251) ♀542 (20) ♂692 (271) Measured trabecular + cortical bone	*ISQ:* 65.7 (9) ♀64 (9) ♂67.3 (8) *IT (Ncm):* 36.1 (8) ♀34.5 (8) ♂37.6 (8)	*Implant dimensions:* cited, but not included in analysis *Cortical thickness:* not evaluated	*bone density- ISQ:* r =0.882 p<0.001 *bone density- IT:* r=0.768 p<0.001

* values calculated by the authors of the present review because the crude data were presented in the article.
** values provided by the corresponding author.
Max= maxilla; mand= mandible; ISQ= implant stability quotient; PTV= Periotest value; IT= insertion torque

Artigo 2

Does cortical thickness influence the primary stability of miniscrews? A systematic review and meta-analysis

ABSTRACT

The aim of this study was to investigate whether there is evidence to support the association between cortical thickness (Ct.Th) and mini-implants (MI) primary stability. A search was performed including papers published until September 2013. The inclusion criteria comprised observational clinical studies conducted in patients who received monocortical MI for orthodontic anchorage, and *in vivo* or *ex vivo* experimental studies performed to evaluate primary stability of MI; studies that evaluated the association between Ct.Th and MI primary stability; Ct.Th measurement performed numerically; and MI primary stability evaluated by ISQ value, PTV value, Pull-out strength (PS) or Insertion torque (IT). Studies conducted exclusively in artificial bone or finite elements were excluded. Abstract and title reading identified fifteen possible articles to be included. After reading the complete text, three were excluded. One article was found by hand searching and another excluded for overlapping sample. Then, twelve articles were selected. A positive correlation was found between primary stability and Ct.Th when studies that evaluated primary stability through PS were grouped (r=0.409) and when studies that evaluated stability in humans were grouped (r=0.338). There is a positive association between mini-implant primary stability and Ct.Th of the receptor site. However, there is still a lack of well-designed clinical trials.

INTRODUCTION

The success of MI is related to primary stability, which is defined as the absence of mobility in the bone bed after mini-implant placement[1]. Lack of immediate stability can lead to progressive mobility of the device and its subsequent loss[2]. Primary stability depends on the MI design[3], insertion technique[3], and bone quality and quantity at the receptor site[3-6]. The term bone quality has not been clearly defined in the literature, including physiological and structural aspects and the degree

of bone tissue mineralization. Additionally, the role of each of these aspects is not completely understood[7]. While some authors assumed that bone quality is equivalent to bone mineral density (BMD)[7], others have considered that the bone quality refers to Ct.Th[3].

The present systematic review and meta-analysis was focused on the following question: is there scientific evidence to support the influence of Ct.Th on the primary stability of MI?

MATERIALS & METHODS

Study design

This is a Systematic Review of Prognosis that evaluated the association between Ct.Th (prognostic factor) and MI primary stability (outcome). It is not a Systematic Review of Intervention, as described by Cochrane Handbook and PRISMA. Therefore, PRISMA statement was followed as possible.

Study selection criteria

The inclusion criteria comprised observational clinical studies conducted in patients who received monocortical MI for orthodontic anchorage, and *in vivo* or *ex vivo* experimental studies performed in animals to evaluate primary stability of MI; studies that evaluated the association between Ct.Th and MI primary stability; the Ct.Th measurement should have been performed numerically; and MI primary stability should have been evaluated by ISQ value (Ostell, Integration Diagnostics, Gothenburg, Sweden), PTV value (Periotest, Medizintechnik Gulden, Modautal, Germany), PS or IT measurement. Studies conducted exclusively in artificial bone or finite elements were excluded.

Search strategy and screening of articles

The search process was performed independently by two examiners (MM and CTM) under the guidance of a librarian. Articles were searched without language restriction until September 2013. Appropriate changes in the key words were done to follow the syntax rules of each database (Table 1).

The two examiners evaluated the titles and abstracts of all the studies identified. If the abstract contained insufficient information to allow decision-making as regards inclusion or exclusion, the full article was obtained and reviewed before making a final decision. Articles appearing in more than one database search or containing overlapping samples were considered only once. Any differences between the two readers were solved by consensus. Screening the reference lists of the selected articles complemented the search. The selected articles were then carefully read for quality assessment and control of bias and for data extraction.

Quality assessment and control of bias

The quality assessment and control of bias was performed using the Methodological checklist for prognostic studies developed by the National Institute for Health and Clinical Excellence of the United Kingdom[8] (Supplemental Appendices 1).

Data extraction

Data extracted from the selected articles were tabulated. When missing data were identified, the authors where contacted through e-mail.

Meta-analysis

A meta-analysis was performed to combine comparable results. Studies were grouped according the primary stability measurement method (IT and PS) and bone substrate (humans). The software used in the analyses was the Comprehensive Meta Analysis (version 2, Biostat, Englewood, USA).

The individual correlation coefficient from each study was used along with the sample size of screws, discarding the losses. Results were pooled using the random-effects method because the studies compared were not considered to have the same effect size. Heterogeneity was assessed (I^2) and publication bias was examined with the use of funnel plots.

RESULTS

The flow diagram (Figure 1) describes the results of search queries. The two studies conducted by Wilmes et al.[3,9] presented some overlapping sample (information confirmed by the author through e-mail contact). During the ranking of

these studies (Table 2), it was verified that they had the same score. Therefore, the study that presented more complete data on the results was elected[9]. Data obtained from the articles and e-mail contact were tabulated in Table 3.

The majority of the selected articles presented a positive correlation between primary stability and Ct.Th [10,11,12,13,14,15,16,17,18,19]. The studies that evaluated the primary stability through IT presented high heterogeneity (I^2=97,23%) and meta-analysis was not performed. The studies that used the PS indicated a statistically significant moderate correlation of primary stability and Ct.Th (r=0.409) (Figure 2). When evaluating only studies performed in human beings (Figure 3), the correlation was weaker (r=0.338).

DISCUSSION

The association between Ct.Th and MI primary stability in the selected articles was evaluated by correlations tests or linear regression analysis and the majority of them have demonstrated a significant positive association. Correlation coefficients ranged from 0.32[12-15] (moderate correlation) to 0.91[9] (high correlation). When linear regression was performed[9], it was found that 83% of the variation in insertion torque could be explained by Ct.Th (R^2=0.83).

When using PTV for evaluating primary stability[17], the correlation was negative because PTV decrease as stability increases.

Some associations did not present a statistical significance [11,13,14,18] (Table 3). Methodological differences, such as methods of primary stability and Ct.Th measurements, MI design and dimensions, and sample size might be responsible for this difference.

During meta-analysis calculation, the studies that evaluated the primary stability through IT showed a very high heterogeneity (I^2=97,23%), invalidating the meta-analysis for this group of studies.

When grouping studies that evaluated primary stability through PS, it was found a moderate positive correlation (r=0,409) (Figure 2). When studies were combined by bone substrate, it was found a weaker positive correlation when human beings were evaluated (r= 0,338) (Figure 3). This fact corroborates the assertion that the results of researches with animals are applicable to humans with reservations[20].

The MI design and dimensions are important parameters for the primary stability of MI[21]. All of the selected studies reported the characteristics and dimensions of the MI used, but few of them used more than one type and investigated their influence on the result[9,10,11]. It was verified that the diameter of the MI seemed to have a bigger influence on primary stability of MI than its length[3, 9]. This fact can reinforce the importance of the Ct.Th in primary stability: as the MI diameter increases, the contact surface between MI and cortical bone also increases. On the other hand, when the length of MI increases, its contact with the trabecular bone increases and the stability is not improved to the same extent.

Even though it was found that Ct.Th and primary stability are associated, it's important to remember that a very high primary stability is not desirable in clinical practice because of the risk of bone necrosis and subsequent stability loss[3]. Motoyoshi et al[16] recommended placement torques between 5 and 10 Ncm. Chaddad et al[22] found higher success rates at torque values above 15 Ncm. However, Meursinge Reynders et al[23] performed a systematic review and stated that no evidence indicates that specific maximum insertion torque levels are associated with higher success rates for orthodontic MI mainly because insertional torque measures are not very accurate[24].

There is still a lack of studies with good methodological design evaluating the relationship between Ct.Th and primary stability of MI. From the selected studies, only two were conducted in living humans, convenience samples were used, and no sample size calculation was made. One study was conducted in human cadavers, without sample size calculation. The other studies were conducted in animals and only one performed sample size calculation. The authors did not mention calibration, error calculation and blinding. Therefore, the quality assessment ranked all the articles as "low" considering the quality of evidence and control of bias. Another factor that might have contributed to the low methodological quality was the quality assessment checklist used: The Methodological checklist for prognostic studies developed by the National Institute for Health and Clinical Excellence from United Kingdom. This established checklist focused on clinical studies, while the majority of selected studies were laboratorial.

The evidence to support the relationship between Ct.Th and MI primary stability is still weak. It is recommended that well-designed clinical trials be conducted

to support this question, showing stronger evidence, preferably with the use of multivariate analysis.

CONCLUSION

There is a positive association between MI primary stability and Ct.Th of the receptor site. However, there is still a lack of well-designed clinical trials.

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Table 1 Database and search strategy used.

Database	Key words
Cochrane Library http://cochrane.bvsalud.org/portal/php/index.php	(cortical OR compacta) AND (miniscrew OR "mini implant" OR "mini-implant") AND stability
MEDLINE-PubMed http://www.ncbi.nlm.nih.gov/pubmed	(cortical OR compacta) AND (miniscrew OR "mini implant" OR "mini-implant") AND (“stability” OR “implant stability quotient” OR “ISQ” OR “resonance frequency analysis” OR “RFA” OR “Ostell” OR “Periotest value” OR “PTV” OR “Periostest” OR “insertion torque” OR "insertional torque" OR “placement torque” OR “cutting torque”)
Web of Knowledge http://apps.webofknowledge.com	((cortical OR compacta) AND (miniscrew OR mini implant OR mini-implant) AND (stability OR implant stability quotient OR ISQ OR resonance frequency analysis OR RFA OR Ostell OR Periotest value OR PTV OR Periostest OR insertion torque OR insertional torque OR placement torque OR cutting torque)) Refined by: Subject Areas=(DENTISTRY ORAL SURGERY MEDICINE OR SURGERY)
EMBASE http://embase.com/search	(cortical OR compacta) AND (miniscrew OR 'mini implant') AND (stability OR 'implant stability quotient' OR isq OR 'resonance frequency analysis' OR rfa OR ostell OR 'periotest value' OR ptv OR periostest OR 'insertion torque' OR 'insertional torque' OR 'placement torque' OR 'cutting torque')
VHL http://regional.bvsalud.org/php/index.php	(cortical OR compacta) AND (miniscrew OR "mini implant") AND (stability OR "implant stability quotient" OR ISQ OR "resonance frequency analysis" OR RFA OR Ostell OR "Periotest value" OR PTV OR Periostest OR "insertion torque" OR "insertional torque" OR "placement torque" OR "cutting torque")
Grey literature (SIGLE) http://www.cardiff.ac.uk/insrv/eresources/databases/sigle.html	(cortical OR compacta) AND (miniscrew OR "mini implant" OR "mini-implant") AND(“stability” OR “implant stability quotient” OR “ISQ” OR “resonance frequency analysis” OR “RFA” OR “Ostell” OR “Periotest value” OR “PTV” OR “Periostest” OR “insertion torque” OR "insertional torque" OR “placement torque” OR “cutting torque”)

Table 2: Articles ranked according to the quality assessment and control of bias.

	The study sample represents the population of interest with regard to key characteristics, sufficient to limit potential bias.	**Loss to follow-up is unrelated to key characteristics sufficient to limit potential bias.**	**The prognostic factor of interest is adequately measured, sufficient to limit potential bias.**	**The outcome of interest is adequately measured, sufficient to limit bias.**	**Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.**	**The statistical analysis is appropriate for the design of the study, limiting potential for the presentation of invalid results**	**Category of the article according methodological quality**
Cha et al. 2010	No	Unclear	Unclear	Unclear	Unclear	Yes	1 yes Low
Cehreli et al. 2012	No	Unclear	No	Yes	No	Yes	2 yes Low
Cehreli et al. 2013	No	Unclear	No	Yes	No	Yes	2 yes Low
Huja et al. 2005	No	Unclear	No	Yes	No	Yes	2 yes Low
McManus et al. 2011	No	Unclear	No	Unclear	No	Yes	1 yes Low
Migliorati et al. 2012	No	Unclear	No	No	No	Yes	1 yes Low
Motoyoshi et al. 2007	No	Unclear	Unclear	Unclear	No	Yes	1 yes Low
Motoyoshi et al. 2010	No	Unclear	Unclear	Unclear	No	Yes	1 yes Low
Nienkemper et al. 2012	No	Unclear	No	No	No	Yes	1 yes Low
Salmória et al. 2008	No	Unclear	No	Yes	No	Yes	2 yes Low
Su et al. 2009	No	Unclear	No	No	No	Yes	1 yes Low
Wilmes et al. 2006	No	Unclear	No	Yes	No	Yes	2 yes Low
Wilmes et al. 2011	No	Unclear	No	Yes	No	Yes	2 yes Low

Up to 5 “yes“: high; up to 3 “yes“: moderate; 2 or less “yes“: low.

Table 3: Summarized data collected from the selected articles.

Author/year	Study design	Sample/ substrate	N° of MI	MI model, shape, classification of insertion method, dimensions (diameter x length) and manufacturer	Method of Ct.Th evaluation	Main method of primary stability measurement*	Association between stability and Ct.Th	Confounders included in analysis
Cha et al. 2010	Experimental *in vivo* (dogs)	maxilla and mandible of 6 dogs	96	*model 1:* OAS-1507C cylindrical non-drilling 1.4x7mm Biomaterials Korea (Korea) *model 2:* OAS-1507T tapered non-drilling 1.4x7mm Biomaterials Korea (Korea)	CBCT	IT	r=0.476 p=0.001 (Pearson)	BMD of cortical BMD of total bone Screw type Screw position Insertion technique (Multiple regression analysis)
Cehreli et al. 2012	Experimental *ex vivo* (bovine)	16 bovine Iliac crest	72	*model 1:* AbsoAnchor cylindrical self-taping 1.4x7mm Dentos (Korea) *model 2:* AbsoAnchor cylindrical self-drilling 1.4x7mm Dentos (Korea)	CT	IT	*model 1* r=0.516 p=0.001 (Pearson) *model 2* r=0.544 p=0.001 (Pearson)	Evaluated the insertional angle of MI, BMD of cortical and trabecular bones, but no multivariate analysis was performed
Cehreli et al. 2013	Experimental *ex vivo* (bovine)	4 bovine Iliac crest	24	*model:* AbsoAnchor cylindrical self-drilling 1.4x7mm Dentos (Korea)	CT	IT	r=0.194 p>0.05 (not significant) (Spearman)	Evaluated the insertional angle of MI, BMD of cortical and trabecular bones, but no multivariate analysis was performed
Huja et al. 2005	Experimental *ex vivo* (dogs)	maxilla and mandible of 4 dogs	56	*model:* not mentioned *shape:* not mentioned self-drilling 2x6mm Synthes (USA)	Microscope with a grid	PS	r=0.39 p=0.02 (Pearson)	-
McManus et al. 2011	Experimental *ex vivo* (human cadavers)	24 hemi-mandibles and 24 hemi-maxilla	96	*model:* not mentioned nontapered *CIM:* not mentioned 1.5x11mm KLS Martin (USA)	Digital caliper	IT	*Maxilla* r= not mentioned p>0.05 (not significant) *Mandible* r=0.61 p<0.00001 (Pearson)	Evaluated the correlation of IT and bone type (maxilla or mandible), but no multivariate analysis was performed
	Experimental *ex vivo* (pigs)	Pig ribs	20	*model 1:* Orthoeasy cylindrical self-drilling 1.7x10mm Forestadent (Germany)				

Migliorati et al. 2012				*model 2:* Orthoscrew cylindrical self-drilling 1.65x9mm Leader Ortodonzia (Italy) *model 3:* Tomas cylindrical self-drilling 1.6x10mm Dentaurum (Germany) *model 4:* ORTHOImplant tapered self-drilling 1.8x10mm 3M Unitek (USA)	CBCT	PS and IT	*PS:* T=0.36 p=0.027 *IT:* T= 0.27 p=0.18 (not significant) (Kendall rank correlation)	Evaluated BMD of cortical and trabecular bones, but no multivariate analysis was performed considering these aspects
Motoyoshi et al. 2007	Observational (humans)	maxilla and mandible of 32 patients	87	ISA system orthodontics implants tapered *CIM:* not mentioned 1.6x8mm Biodent (Japan)	CT	IT	r=0.32 p=0.002 (Pearson)	-
Motoyoshi et al. 2010	Observational (humans)	maxilla and mandible of 57 patients (5 losen)	148	ISA system orthodontics implants tapered *CIM:* not mentioned 1.6x8mm Biodent (Japan)	CT	IT	*Maxilla* r=0.392 p<0.05 *Mandible* r= -0.019 p>0.05 (not significant) (Pearson)	Evaluated the correlation of placement torque and bone type (maxilla or mandible), but no multivariate analysis was performed
Nienkemper et al. 2012	Experimental *ex vivo* (pigs)	Porcine pelvic bone	110	Benefit s cylindrical self-drilling 2x9mm PSM medical solutions (Germany)	CBCT	RFA and PTV	*RFA* r=0.71 p<0.001 *PTV* r= -0.64 p<0.001 (Pearson)	-
Salmória et al. 2008	Experimental *in vivo* (dogs)	10 mandible of dogs	60	*model:* specially manufactured for this research** cylindrical** self-tapping 1.6x6mm Neodent Implante Osteointegrável (Brazil)	Microscope and a digital caliper rule	PS and IT	*PS:* r=0.44 p=0.05 *IT:* r= not mentioned p>0.05 (not significant) (Pearson)	-
Su et al. 2009	Experimental *ex vivo* (pigs)	1 swine pelvic bone**	15	Dual top tapered** self-drilling** 1.6x8mm Jeil medical Corp (Korea)	Scanned image measurement in Image Pro Plus software	RFA	r=0.9 p<0.0001 (Pearson correlation)	-
Wilmes et al. 2011	Experimental *ex vivo* (pigs)	20 swine pelvic bone	600	*model 1:* Dual top (DT) conical self-drilling	Micro-CT	IT	DT 2x10mm: R^2=0.69 DT 1.6x8mm:	Screw type Screw position Insertion technique

				1.6x8, 1.6x10 and 2x10mm Jeil medical Corp (Korea) *model 2:* Tomas-pin (TP) cylindrical self-tapping 1.6x8 and 1.6x10 mm Dentaurum (Germany)			R^2=0.68 DT 1.6x10mm: R^2=0.73 TP 1.6x8mm: R^2=0.39 TP 1.6x10mm: R^2=0.45 All of them R^2=0.83 and r**=0,9135 p<0.0001 (Linear regression analysis)	(Linear regression analysis)

* Some authors used more than one method to evaluate primary stability, but the main method considered the one used as standard for correlation analysis.
** Information given by authors through e-mail contact.
CIM= classification of insertion method; CI= confidence interval; r= correlation coefficient; R^2= determination coefficient; CBCT= cone beam computed tomography; CT= Computed tomography

Supplemental Appendices 1: Methodological checklist for prognostic studies developed by the National Institute for Health and Clinical Excellence from United Kingdom. It was used to perform the quality assessment and control of bias.

Study identification:				
Circle one option for each question				
1.1	The study sample represents the population of interest with regard to key characteristics, sufficient to limit potential bias to the results? To minimise bias, the study population should be clearly defined and described and should represent the source population of interest. Points to consider include the following: • Are the source population or the population of interest adequately described with respect to key characteristics? • Are the sampling frame and recruitment adequately described, possibly including methods to identify the sample (number and type used; for example, referral patterns in healthcare), period of recruitment and place of recruitment (setting and geographical location)? • Are inclusion and exclusion criteria adequately described (for example, including explicit diagnostic criteria or a description of participants at the start of the follow-up period)? • Is participation in the study by eligible individuals adequate? • Is the baseline study sample (that is, individuals entering the study) adequately described with respect to key characteristics?	Yes	No	Unclear
1.2	Loss to follow-up is unrelated to key characteristics (that is, the study data adequately represent the sample), sufficient to limit potential bias? To minimise bias, completeness of follow-up should be described and adequate. Points to consider include the following: • Is the response rate (that is, proportion of study sample completing the study and providing outcome data) adequate? • Are attempts to collect information on participants who dropped out of the study described? • Are reasons for loss to follow-up provided? • Are the key characteristics of participants lost to follow-up adequately described? • Are there any important differences in key characteristics and outcomes between participants who completed the study and those who did not?	Yes	No	Unclear
1.3	The prognostic factor of interest is adequately measured in study participants, sufficient to limit potential bias? To minimise bias, prognostic factors should have been defined and measured appropriately. Points to consider include the following: • Is a clear definition or description of the prognostic factor(s) measured provided (including dose, level, duration of exposure, and clear specification of the method of measurement)? • Are continuous variables reported, or appropriate cut-off points (that is, not data-dependent) used? • Are the prognostic factor measured and the method of measurement valid and reliable enough to limit misclassification bias?	Yes	No	Unclear

	(This may include relevant outside sources of information on measurement properties, as well as characteristics such as blind measurement and limited reliance on recall.) • Are complete data for prognostic factors available for an adequate proportion of the study sample? • Are the method and setting of measurement the same for all study participants? • Are appropriate methods employed if imputation is used for missing data on prognostic factors?			
1.4	The outcome of interest is adequately measured in study participants, sufficient to limit bias? • Is a clear definition of the outcome of interest provided, including duration of follow-up? • Are the outcome that was measured and the method of measurement valid and reliable enough to limit misclassification bias? (This may include relevant outside sources of information on measurement properties, as well as characteristics such as 'blind' measurement and limited reliance on recall.) • Are the method and setting of measurement the same for all study participants?	Yes	No	Unclear
1.5	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest? • To minimise bias, important confounders should be defined and measured, and confounding should be accounted for in the design or analysis. Points to consider include the following: • Are all important confounders, including treatments (key variables in the conceptual model), measured? Are clear definitions of the important confounders measured (including dose, level and duration of exposures) provided? • Is measurement of all important confounders valid and reliable? (This may include relevant outside sources of information on measurement properties, as well as characteristics such as 'blind' measurement and limited reliance on recall.) • Are the method and setting of measurement of confounders the same for all study participants? • Are appropriate methods employed if imputation is used for missing data on confounders? • Are important potential confounders accounted for in the study design (for example, matching for key variables, stratification or initial assembly of comparable groups)? • Are important potential confounders accounted for in the analysis (that is, appropriate adjustment)?	Yes	No	Unclear
1.6	The statistical analysis is appropriate for the design of the study, limiting potential for the presentation of invalid results? To minimise bias, the statistical analysis undertaken should be clearly described and appropriate for the design of the study. Points to consider include the following: • Is the presentation of data sufficient to assess the adequacy of the analysis? • Where several prognostic factors are investigated, is the strategy for model building (that is, the inclusion of variables) appropriate and based on a conceptual framework or model? • Is the selected model adequate for the design of the study? • Is there any selective reporting of results? • Are only pre-specified hypotheses investigated in the analyses?	Yes	No	Unclear

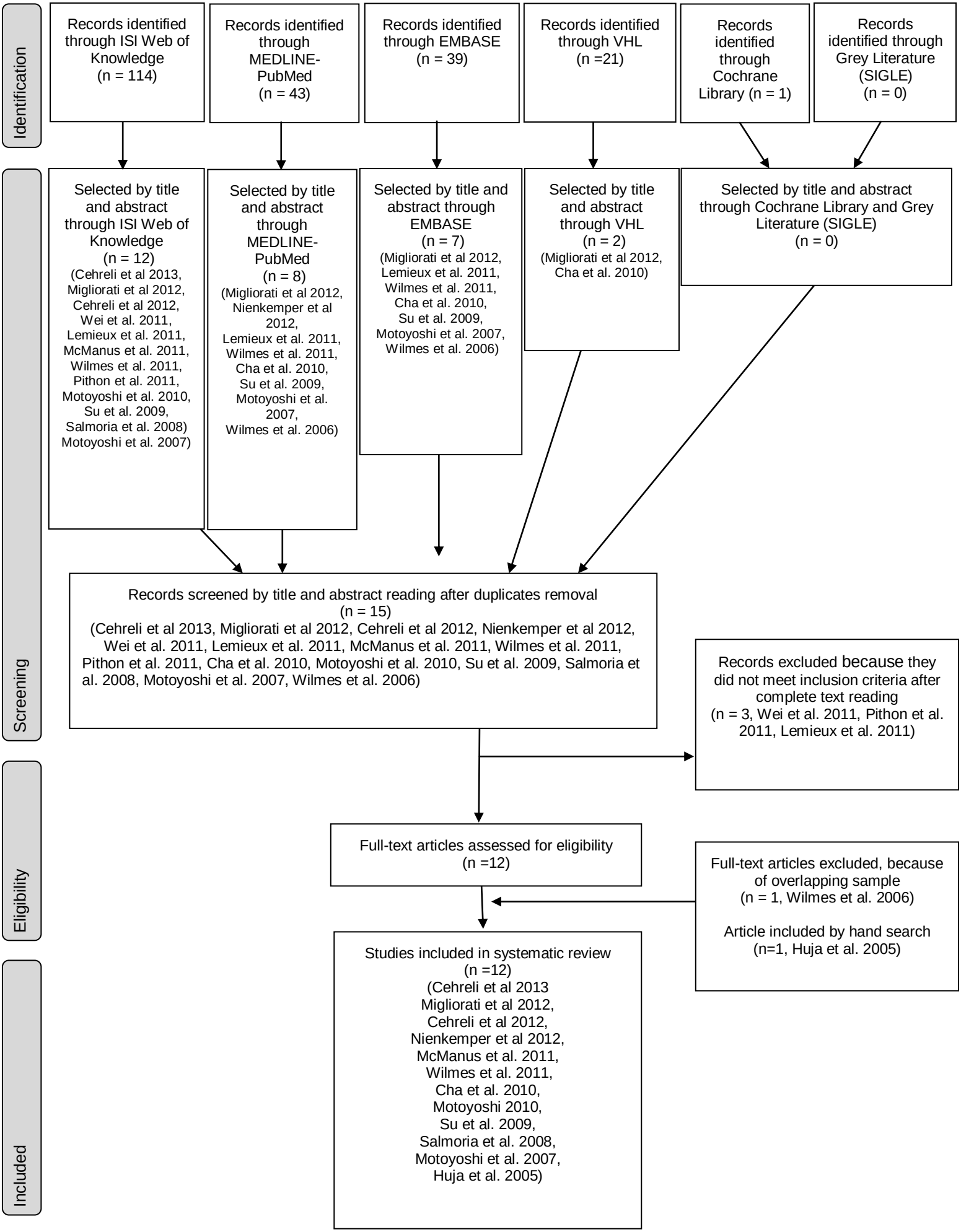
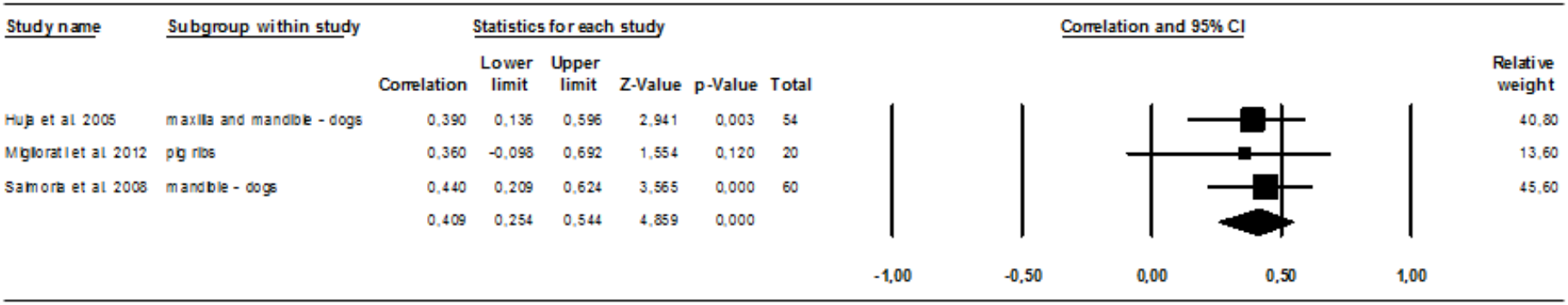
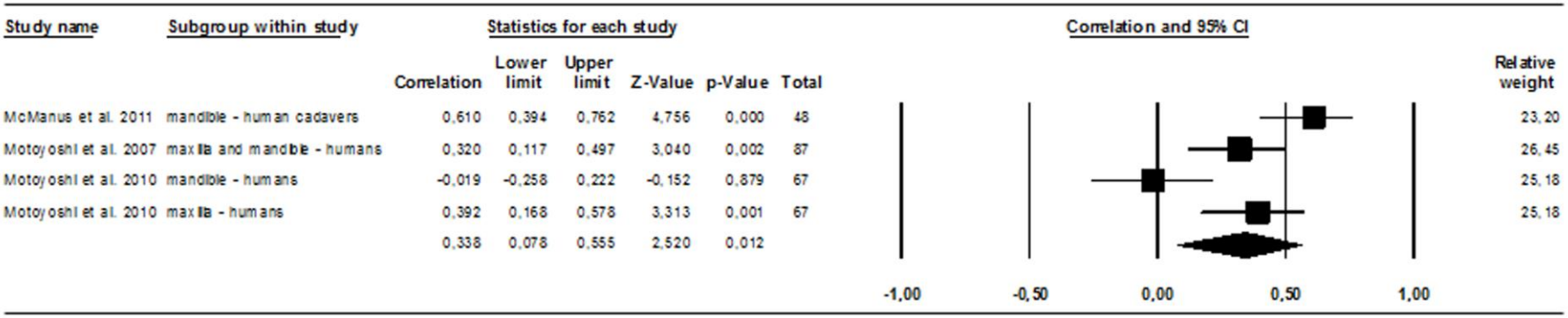


Figure 1: Flow diagram of literature search.



Heterogeneity: Tau2=0.000; Chi2=0.164 df=2 (P=0.921); I2=0.000%
Test for overall effect: Z=4.85 (P< 0.001)

Figure 2: Correlation between Ct.Th and primary stability evaluated through PS.



Heterogeneity: Tau2=0.062; Chi2=14.71 df=3 (P=0.002); I2=79.60%
Test for overall effect: Z=2.52 (P=0.012)

Figure 3: Correlation between Ct.Th and primary stability when only studies in human beings were considered.

Artigo 3

Is trabecular bone related to primary stability of miniscrews?

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Color Figures – no

ABSTRACT

Objective: To compare the primary stability of miniscrews inserted into bone blocks of different bone mineral density (BMD) with and without cortical bone, and investigate whether some trabecular properties could influence primary stability.

Materials and Methods: Fifty-two bone blocks were extracted from fresh bovine pelvic bone. Four groups were created considering the bone type (iliac or pubic region) and presence or absence of cortical. Specimens were microCT imaged to evaluate trabecular thickness, trabecular number, trabecular separation, bone volume density (BV/TV), BMD and cortical thickness. Miniscrews 1.4 mm in diameter and 6 mm long were inserted into the bone blocks and primary stability was evaluated by insertion torque (IT), mini-implant mobility (PTV) and pull-out strength (PS).

Results: Intergroup comparison showed lower level of primary stability when BMD of trabecular bone was lower and in the absence of cortical ($P \leq .05$). Pearson's correlation test showed correlation between trabecular number, trabecular thickness, BV/TV, trabecular BMD, total BMD, and IT, PTV and PS. There was correlation between cortical thickness and IT and PS ($P \leq .05$).

Conclusion: Cancellous bone plays an important role in primary stability of mini-implants in the presence or absence of cortical bone.

KEY WORDS: Trabecular bone; Mini implant; Miniscrew; Stability

INTRODUCTION

The success of skeletal anchorage using miniscrews is related to their stability in the bone. Most of the failures occur immediately after mini-implant placement[1] because the lack of primary stability may lead to progressive mobility of the device and to its subsequent loss[2]. Factors that influence the immediate stability are related to the design of the device, quantity and quality of bone, and insertion technique[3]. The term “bone quality” is not clearly defined in the literature. This includes physiological and structural aspects and the degree of bone tissue mineralization[4]. Some bone properties such as bone mineral density[4-7] and cortical thickness[8-10] have been related to the stability of implants or mini-implants. Although the role of trabecular bone in the stability of dental implants[11]has been investigated, there is still a lack of literature on miniscrews.

The aim of this study was to compare the primary stability of miniscrews inserted into bone blocks of different bone mineral density (BMD), and investigate whether there were any bone properties such as trabecular thickness, trabecular number, trabecular separation, cortical thickness, BMD and bone volume density (BV/TV) that could influence the primary stability of miniscrews in the presence and absence of cortical bone.

MATERIALS AND METHODS

The sample consisted of thirteen bovine pelve (Bos taurus, Angus lineage) obtained from a Slaughterhouse immediately after the animals were slaughtered. Four bone sections were taken from each pelve - two from the pubic and two from the iliac region - with the use of a trephine bur (8mm ø x 20mm long, Sin Implants, São Paulo, Brazil) adapted to a low speed motor handpiece (Beltec LB100, Araraquara, Brazil), under irrigation. In the samples taken from each bone region, the cortical was preserved in one and removed in the other, using a diamond disc under irrigation. The final sample dimension was 8mm ø x 10mm long. The material was immersed in saline solution and stored by freezing (-20ºC)[12]. Division of the groups was based on the bone region and the presence of cortical (Table 1). The number of samples was calculated using the sample size data of a previous pilot study (α=5%, power of study= 80%).

Evaluation of bone quality

Images of the samples were acquired in the microCT system (Bruker/Skyscan micro-CT, model 1173, Kontich, Belgium) at a resolution of 9.3 µm, using a 1 mm thick aluminum filter, 80 kV, 90 µA, and

exposure of 800 ms. The bone sections were kept in 2 ml Eppendorf tubes containing saline solution with the bolt head facing upwards. The diameter of the Eppendorf was very close to that of the sample, so that it was kept stable during image acquisition. The images were reconstructed (NRecon software, InstaRecon, Inc. Champaign, USA) and evaluated using the CT-Analyzer software (Bruker/Skyscan micro-CT, Kontich, Belgium).

The Cortical thickness was measured in two-dimensional images. Sagittal and coronal sections were visualized in DataViewer (Bruker/ Skyscan micro-CT, Kontich, Belgium), containing the center of the mini-implant. Two measurements were taken of each cross-section, one on the left and other on the right side of the screw. The average of these four measurements was considered the cortical thickness. Thirty percent of the sample was measures twice in an interval of 1 week to assess the intra-examiner reliability by means of the intraclass correlation coefficient (ICC=0.97).

In three-dimensional analysis, the volume of interest (VOI) corresponded to a cylinder 3.4 mm in diameter. The center of this cylinder, containing the screw, and the bone 6 voxels adjacent to it (54 μm) were excluded from the VOI in order to reduce the effect of artifact on analyses, a previously reported concern[12-15].

In the imaging analysis process, a global threshold was used in order to distinguish trabecular bone (white pixels) from the background (empty space - black pixels) by means of a histogram analysis of gray-scale images. Histomorphometric parameters such as trabecular thickness, trabecular number and trabecular separation were automatically calculated for cancellous bone. For the total bone block, BV/TV was evaluated.

The BMD, in g/cm^3 HA, was computed from the attenuation values of gray scale in the micro CT images. The phantom used to calibrate the software was an artificial bone block (containing 1 mm thick cortical - 1.64 g/cm^3 - and trabecular bone - 0.32 g/cm^3 - Sawbones®, Washington, USA), with the same dimensions as those of the sample, and containing a miniscrew inserted in its center. Thus, the conditions of the artifact were reproduced. The BMD was measured for the total bone block (total BMD), trabecular bone (trabecular BMD) and cortical bone (cortical BMD).

Insertion torque (IT)

Fifty-two conical self-drilling miniscrews Ti-6Al-4V alloy (INP®, São Paulo, Brazil) 1.4 mm in diameter and 6 mm long were inserted into the bone blocks. The implant sites were predrilled to a depth of 2 mm with a pilot drill 1.0 mm in diameter (INP®, São Paulo, Brazil). The mini-implants were placed by a single operator with the use of a manual key connected to a digital torque meter (Lutron TQ-8800, Taipei, Taiwan). To guarantee perpendicular insertion of the miniscrews into the bone, the torque meter and the bone blocks were adapted to a mechanical device[16] (Figure 1). The peak insertion torque values were recorded in Newton centimeter (Ncm).

Miniscrew mobility

Immediately after miniscrew placement, their mobility was evaluated with the Periotest instrument (Medizintechnik Gulden, Modautal, Germany). A special acrylic device was used to fix the sample and Periotest handpiece, and to standardize the distance between the sleeve and the mini-implant (Figure 2). The handpiece was calibrated before each screw was measured. Two recordings were collected for each mini-implant, and the average value was designated as the Periotest value (PTV), which is on a scale from -8 to +50. The smaller the PTV is, the smaller is the mobility and the higher is the primary stability.

Pull-out Strength (PS)

This mechanical test was performed in a universal test machine (Emic DL 2000, São José dos Pinhais, Brazil), using a 500 Kgf load cell, at a crosshead speed of 0.05 mm per second to remove the miniscrew[16] (Figure 3). The maximum PS was recorded (N).

Statistical Analysis

Data were evaluated with the software SPSS (version 18, SPSS Inc, USA). The normality and homogeneity of variables were verified by Shapiro-Wilk and Levene's tests. Intergroup comparisons were performed by T-test (for cortical thickness and cortical BMD) and ANOVA/ Tukey tests (for the other variables). Pearson's correlation test was applied to verify the correlational relationships between variables. The level of significance was 5%.

RESULTS

Mean, standard deviation and intergroup comparison for the bone properties are described in Tables 2 and 3. Trabecular thickness, trabecular number, trabecular separation and trabecular BMD presented lower values in the iliac than in pubic groups (Figure 4). BV/TV and total BMD presented increasing values from GI0, GI1, GP0 to GP1 (Table 2). For GI1 and GP1, cortical thickness and cortical BMD did not differ (Table 3).

Mean, standard deviation and intergroup comparison for the variables used to evaluate miniscrew stability are shown in Table 4. IT values were lower for GI0, followed by GP0 and GI1 (without statistical difference between them), and the highest value was for GP1. PTV values in decreasing order were from GI0, GI1, GP0 to GP1. PS differed statistically among the groups, being higher in GP1, followed by GI1, GP0 and GI0. Pearson's correlation test results are presented in Table 5.

DISCUSSION

Practitioners have traditionally assessed primary stability by manual verification[17]. Nevertheless there are other less subjective methods, such as IT, removal torque, PS – by which mechanical behavior can be assessed in the axial direction; the mobility and lateral displacement test – by which mechanical behavior can be assessed laterally. However, there is still no gold standard for primary stability assessment[17]. In this study, three methods were used for evaluating primary stability of mini-implants: IT, PTV and PS.

The Periotest instrument allows a nondestructive and objective measurement of implant movement[18]. It is probably the method that best reproduces the clinical verification of primary stability: manual verification of mobility. There is no consensus about the reliability of the Periotest for assessing implant stability. Some authors consider the Periotest a good tool for measuring stability in dental implants[19-22] and mini-implants[23,24], others disagree[25]. In our study, there was correlation between the PTV value and the other two stability measures. IT presented a substantial negative correlation with PTV, as has previously been found[20,24,26]. The correlation between PTV and PS was also negative. The two mechanical measures used to evaluate stability axially (IT and PS) presented strong positive correlation, in agreement with previous studies[16].

It is known that a PTV of -8 to +9 corresponds to a mobility index of 0 with no distinguishable movement[27]. In this study, the only group with PTV above +9 was GI0 (PTV=20.19), which indicated palpable mobility[28].

Considering bone properties, values for trabecular thickness, trabecular number and trabecular BMD were higher for pubic bone, and trabecular separation was lower. These findings corroborate the difference between the trabecular characteristics of iliac and pubic bones[29]. When the trabecular number increases, its separation diminishes and its thickness tends to increase. It reflects on BV/TV, and BMD, which also increase. Both bone density measurements of the total block –BV/TV and BMD – showed very strong positive correlation. As previously mentioned[16], the BMD of trabecular bone and the total bone block presented a very strong positive correlation.

Iliac and pubic bone presented similar cortical bone characteristics. No difference was observed for cortical thickness and Cortical BMD in GI1 and GP1. The presence of cortical bone, *per se*, numerically increased the primary stability, corroborating the importance of the cortical effect on primary stability[3,6,8-10,26]. However, when the cortical bone was absent, the importance of the trabecular bone became more apparent. IT, PTV and PS values differed between GI0 and GP0 with higher stability in pubic bone. When GI1 and GP0 were compared, IT and PTV values presented no statistical difference. It seems that the cortical bone plays an important role when trabecular bone has lower BMD, lower trabecular number, thinner and more separated trabeculae. When comparing the stability values for GI1 and GP1, groups with similar cortical coverage, IT, PTV and PS were higher for the pubic bone, which has a higher level of BMD, thicker and less separate trabeculae and has a higher trabecular number

A positive correlation was found between cortical thickness and IT[3,10,26,30-33], and between cortical thickness and PS[8,34]. Cortical thickness did not influence the PTV value. It was believed that cortical thickness had a greater influence on axial than on lateral measures. Cortical BMD presented no valid correlation with IT, PS, or PTV, in disagreement with previous studies[16,24,16]. However, the methodology of BMD evaluation differed. While this study evaluated BMD three dimensionally by means of microCT, a more accurate method[35], the others used computed tomography slices.

Although the results of the present study cannot be directly extrapolated to clinical practice, because of the animal model and ex vivo methodology used, it was found that cancellous bone plays an important role in the primary stability of miniscrews, redirecting the spotlight that was previously focused only on the cortical bone.

CONCLUSIONS

- As the BMD of the receptor site increases, the primary stability increases numerically as well;
- In the presence and in the absence of cortical bone, trabecular number, trabecular thickness, BV/TV, trabecular BMD and total BMD are correlated with the primary stability of mini-implants, showing the importance of trabecular bone in the stability of miniscrews.

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Table 1: Division of the groups based on the bone region, the presence and the thickness of the cortical bone

Group	Bone region	n. of sample	cortical
GI0	Iliac	13	absent
GI1	Iliac	13	1mm
GP0	Pubic	13	absent
GP1	Pubic	13	1mm

Table 2: Descriptive analysis and ANOVA/Tukey result for bone quality.

Group	Mean (± sd)					
	Tb.Th (mm)	**Tb.N (mm^{-1})**	**Tb.S (mm)**	**Tb.BMD (g/cm^3)**	**total BMD (g/cm^3)**	**BV/TV (%)**
GI0	0.14 (0.01) a	1.20 (±0.23) a	0.45 (±0.06) a	0.69 (±0.12) a	0.69 (±0.12) a	17.69 (±4.38) a
GI1	0.15 (0.01) ab	1.23 (±0.14) a	0.49 (±0.02) a	0.76 (±0.13) a	0.93 (±0.15) b	20.39 (±4.07) ab
GP0	0.16 (0.02) b	1.49 (±0.16) b	0.38 (±0.05) b	0.97 (±0.18) b	0.97 (±0.18) b	25.18 (±6.19) bc
GP1	0.17 (0.02) b	1.61 (±0.22) b	0.40 (±0.04) b	1.15 (±0.25) b	1.27 (±0.26) c	30.32 (±7.96) c

Each column presents an independent result for ANOVA/ Tukey. Different letters indicate statistical significant difference at α=0.05%
Tb.Th = trabecular thickness; Tb.N = trabecular number; Tb.S = trabecular separation; Tb.BMD = bone mineral density of trabecular bone; total BMD = bone mineral density of the total bone block; BV/TV = bone volume density.

Table 3: Descriptive analysis and T-test result for bone quality.

Group	Mean (± sd)	
	Ct.Th (mm)	**Ct.BMD (g/cm^3)**
GI1	1.01 (±0.64)	5.31 (±0.54)
GP1	1.07 (±0.92)	4.89 (±0.30)
P-value	0.32	0.06

Each column presents an independent result for T-test.
Ct.Th = cortical thickness; Ct.BMD = bone mineral density of cortical bone.

Table 4: Descriptive analysis and ANOVA/Tukey result for primary stability.

Group	Mean (± sd)		
	IT (N.cm)	**PTV**	**PS (N)**
GI0	3.22 (±1.03) a	20.19 (±4.48) a	46.27 (±19.61) a
GI1	7.70 (±1.38) b	9.76 (±3.84) b	197.75 (±25.88) b
GP0	5.76 (±1.55) b	8.96 (±5.20) bc	117.20 (±27.43) c
GP1	10.65 (±3.44) c	5.30 (±2.59) c	258.30 (±89.81) d

Each column presents an independent result for ANOVA/ Tukey. Different letters indicate statistical significant difference at α=0.05%
IT = insertional torque; PTV = Periotest value; PS = pull-out strength

Table 5: Pearson correlation test.

		Tb.Th	Tb.N	Tb.S	BMD.trab	BMD.total	BV/TV	Ct.Th	Ct.BMD	IT	PTV	PS
Tb.Th	r	1	,536*	-,228	,566*	,610*	,745*	,251	-,109	,570*	-,487*	,578*
	P-value		,000	,115	,000	,000	,000	,226	,638	,000	,000	,000
Tb.N	r	,536*	1	-,657*	,619*	,561*	,846*	,275	,088	,541*	-,481*	,423*
	P-value	,000		,000	,000	,000	,000	,175	,697	,000	,000	,002
Tb.S	r	-,228	-,657*	1	-,521*	-,373*	-,533*	-,109	,122	-,238	,308*	-,145
	P-value	,115	,000		,000	,011	,000	,604	,597	,096	,029	,320
BMD.trab	r	,566*	,619*	-,521*	1	,950*	,786*	,353	-,038	,628*	-,532*	,521*
	P-value	,000	,000	,000		,000	,000	,107	,868	,000	,000	,000
BMD.total	r	,610*	,561*	-,373*	,950*	1	,763*	,512*	,063	,763*	-,604*	,700*
	P-value	,000	,000	,011	,000		,000	,015	,782	,000	,000	,000
BV/TV	r	,745*	,846*	-,533*	,786*	,763*	1	,385	,098	,688*	-,568*	,553*
	P-value	,000	,000	,000	,000	,000		,052	,663	,000	,000	,000
Ct.Th	r	,251	,275	-,109	,353	,512*	,385	1	,413	,651*	-,154	,501*
	P-value	,226	,175	,604	,107	,015	,052		,056	,000	,454	,009
Ct.BMD	r	-,109	,088	,122	-,038	,063	,098	,413	1	,008	,077	,120
	P-value	,638	,697	,597	,868	,782	,663	,056		,972	,733	,595
IT	r	,570*	,541*	-,238	,628*	,763*	,688*	,651*	,008	1	-,680*	,835*
	P-value	,000	,000	,096	,000	,000	,000	,000	,972		,000	,000
PTV	r	-,487*	-,481*	,308*	-,532*	-,604*	-,568*	-,154	,077	,680*	1	,655*
	P-value	,000	,000	,029	,000	,000	,000	,454	,733	,000		,000
OS	r	,578*	,423*	-,145	,521*	,700*	,553*	,501*	,120	,835*	-,655*	1
	P-value	,000	,002	,320	,000	,000	,000	,009	,595	,000	,000	

* Indicates statistical significant difference at α=0.05%

Tb.Th = trabecular thickness; Tb.N = trabecular number; Tb.S = trabecular separation; Tb.BMD = bone mineral density of trabecular bone; total BMD = bone mineral density of the total bone block; BV/TV = bone volume density; Ct.Th = cortical thickness; Ct.BMD = bone mineral density of cortical bone; IT = insertional torque; PTV = Periotest value; PS = pull-out strength.

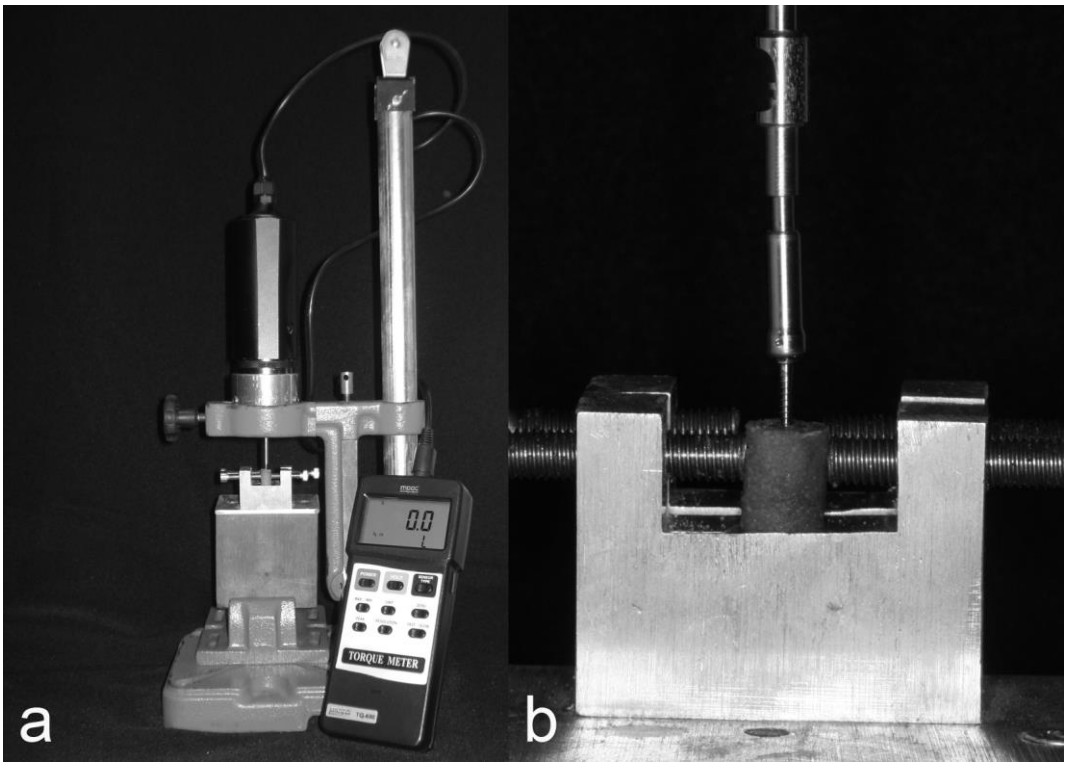

Figure 1. Evaluation of IT. (a) digital torque meter and bone block adapted to the device that was developed to allow insertion of mini-implants into the bone blocks perpendicular to the floor (b) Approximate view of the process of mini-implant insertion.

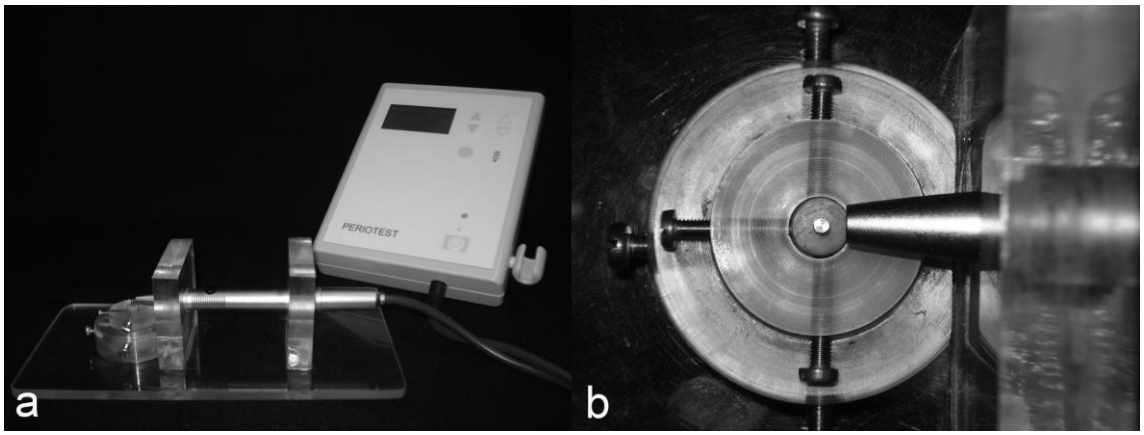

Figure 2. Evaluation of the mini-implant mobility. (a) Periostest and sample adapted to the acrylic apparatus to maintain the tip of the Periotest handpiece parallel to the floor and perpendicular to the screw. (b) Close view of the Periostest tip maintained 2 mm away from the head of the mini-implant.

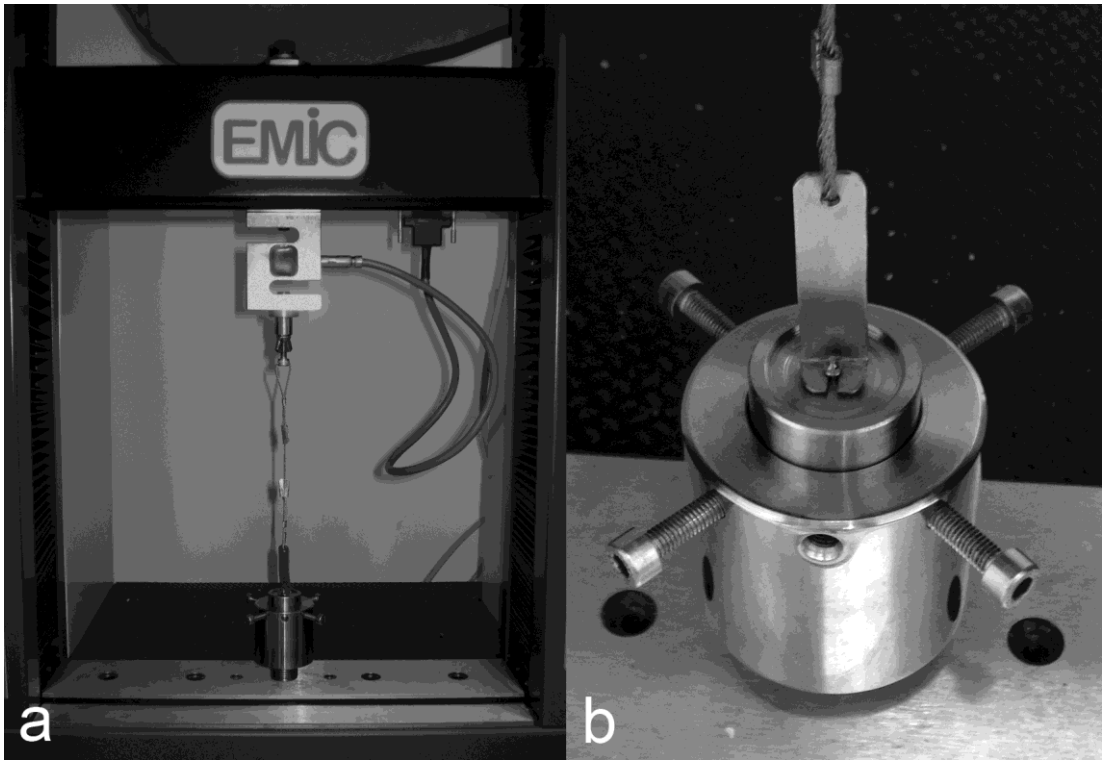

Figure 3. Pull-out strength test. (a) Universal test machine during the test. (b) Close view of the devices manufactured to adapted the small sample to the machine: the lower one – used to fix the sample; and upper one, used to extract the miniscrew.

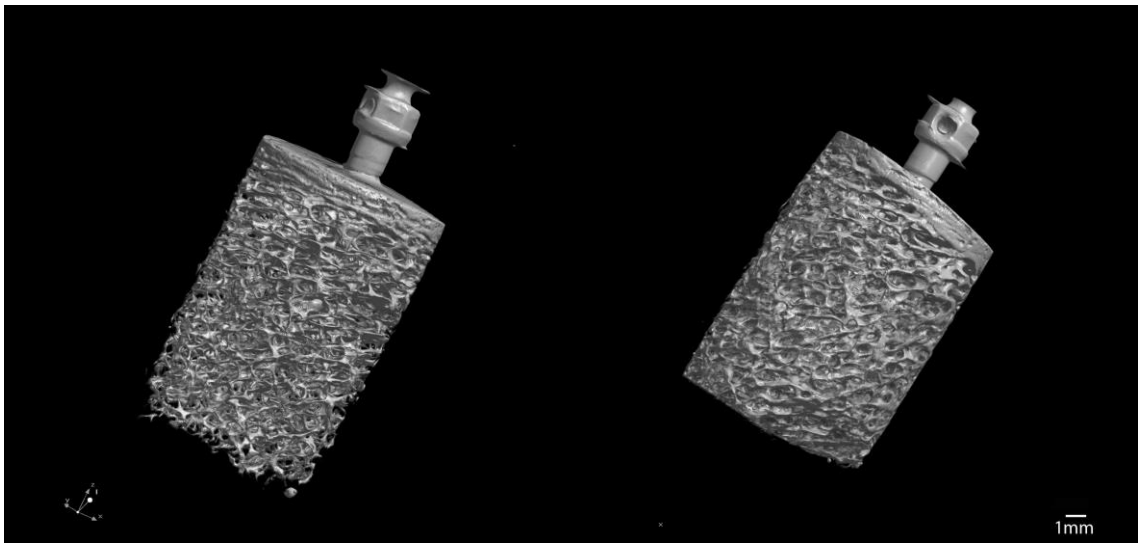

Figure 4. Reconstruction of specimens from GI1 and GP1, respectively, showing the different architecture in trabecular bone.

5 DISCUSSÃO

A qualidade do osso receptor é um dos fatores a ser considerado para o estabelecimento do prognóstico da estabilidade de implantes dentários e ortodônticos. Sendo o termo "qualidade óssea" subjetivo, buscamos avaliar a associação entre a estabilidade primária de mini-implantes e diferentes propriedades ósseas.

As revisões sistemáticas e meta-análise mostraram haver carência de estudos clínicos observacionais, assim como de estudos laboratoriais de alta qualidade metodológica, que avaliem a associação entre a estabilidade primária de MI e a qualidade do sítio receptor.

A primeira revisão sistemática (Artigo 1, página 17) focou, inclusive, na associação entre a BMD do leito ósseo receptor e a estabilidade de implantes dentários (em vez de mini-implantes) por não terem sido encontrados, nas bases de dados consultadas, estudos clínicos observacionais que avaliassem essa associação. Além disso, naquele momento, apenas poucos estudos laboratoriais haviam sido publicados com esse objetivo, e esses apresentavam importantes diferenças metodológicas. Como o ramo da ancoragem esquelética se beneficiou da literatura de implantodontia, essa revisão visou enriquecer ambas as áreas.

Verificou-se que existe associação positiva entre a estabilidade primária de implantes dentários e a BMD do sítio receptor. Entretanto, alguns estudos avaliaram a BMD apenas do osso trabecular, outros avaliaram o conjunto de osso cortical e trabecular, e outros, ainda, não especificaram em que região óssea a BMD foi avaliada. Dentre os estudos incluídos na revisão sistemática, aquele que apresentou o segundo menor valor de correlação entre BMD e estabilidade primária foi um dos que avaliou apenas o osso trabecular (Merheb, Van Assche *et al.*, 2010). O estudo que apresentou menor valor de correlação não relatou se avaliou a cortical em conjunto com o trabeculado (Farre-Pages, Auge-Castro *et al.*, 2011). Esse dado vem corroborar a importância da cortical na estabilidade, uma vez que os valores de correlação são mais altos quando a cortical é envolvida no ROI (*region of interest*) de análise da BMD.

A segunda revisão sistemática e meta-análise (Artigo 2, página 40) visou verificar a influência da espessura de cortical na estabilidade primária de mini-implantes ortodônticos. Para essa segunda revisão, estudos clínicos observacionais e experimentais foram considerados, sendo apenas dois dos doze artigos incluídos na revisão, estudos clínicos observacionais. A qualidade metodológica dos estudos foi considerada baixa, não sendo descritos em muitos deles os critérios de inclusão e exclusão da amostra, calibragem e cegamento, e inclusão de fatores de confundimento na análise estatística.

Os resultados da meta-análise mostraram haver correlação positiva entre a espessura de cortical e a estabilidade primária de mini-implantes ortodônticos (r=0.409), quando essa foi aferida através de teste de tração, confirmando a importância da espessura de cortical para a estabilidade

primária (Motoyoshi, Hirabayashi *et al.*, 2006; Papageorgiou, Zogakis *et al.*, 2012). Quando a estabilidade foi aferida através de torque de inserção, a heterogeneidade dos estudos foi muito alta (I^2=97,23%), não sendo recomendável a execução da meta-análise. Já quando os estudos foram agrupadas através do substrato ósseo humano, a meta-análise mostrou também que a associação entre a espessura de cortical e a estabilidade foi positiva, porém mais fraca (r= 0.338). Este fato corrobora a afirmação de que os resultados de pesquisas com animais são aplicáveis a seres humanos com reservas. Estes estudos têm contribuído grandemente para o conhecimento na área da prevenção, etiologia e tratamento de doenças orais, tendo as vantagens de melhor controle das variáveis, menor diversidade genética, facilidade de obtenção da amostra, possibilidade de maior número de repetições e facilidade para executar análise microscópica (Neto, 2001). No entanto, não é possível extrapolar os resultados para os seres humanos. A experimentação animal é um degrau, na pirâmide científica, que antecede os estudos em seres humanos, mas não os substitui.

Na parte experimental da pesquisa, optou-se por trabalhar com amostras de ossos pélvicos bovinos, considerando-se as vantagens e desvantagens supracitadas. O osso pélvico de bovinos (Trisi, Rao *et al.*, 1999; Cehreli e Arman-Ozcirpici, 2012; Cehreli, Yilmaz *et al.*, 2013) e suínos (Wilmes, Rademacher *et al.*, 2006; Wawrzinek, Sommer *et al.*, 2008; Wilmes, Ottenstreuer *et al.*, 2008; Su, Wilmes *et al.*, 2009) havia sido previamente utilizado em pesquisas que avaliaram o comportamento biomecânico de mini-implantes. Esse é composto de três ossos: ísquio, ilíaco e púbico. Durante a exploração para retirada das secções ósseas, no projeto piloto, pôde-se

observar que as três regiões apresentavam diferentes características de coloração, textura e até resistência ao corte. A região do púbico era mais escura e mais resistente ao corte em relação ao ilíaco e ísquio, sendo esse último menos abundante. Esses fatos levaram à investigação das duas diferentes regiões quando da instalação de mini-implantes. Avaliação histológica desses ossos revelou que a densidade trabecular (TBA, do inglês *trabecular bone area*) do púbico se assemelha a dos maxilares humanos (APÊNDICE A, página 92), conforme descrito previamente (Aksoy, Eratalay *et al.*, 2009).

Clinicamente, a classificação de qualidade óssea mais aceita em Implantodontia foi proposta por Lekholm e Zarb (Lekholm e Zarb, 1985). Essa se baseia na quantidade de osso cortical e trabecular verificada em radiografias pré-operatórias. Por essa classificação depender da subjetividade do operador, alguns autores assumiram que o termo qualidade óssea equivale a BMD (Bergkvist, Koh *et al.*, 2010). Outros autores, ainda, atribuem à qualidade óssea à espessura (Wilmes, Rademacher *et al.*, 2006; Iijima, Takano *et al.*, 2012) e densidade mineral da cortical (Cha, Kil *et al.*, 2010; Iijima, Takano *et al.*, 2012). Outra propriedade óssea que tem ganhado maior destaque nos últimos anos é a microarquitetura trabecular (Zhao, Xu *et al.*, 2009; Ikeda, Rossouw *et al.*, 2011; Wirth, Goldhahn *et al.*, 2011; Zhao, Xu *et al.*, 2011). Buscou-se, assim, abranger o estudo de todas as propriedades ósseas supracitadas: BMD, espessura de cortical e microarquitetura trabecular, todas avaliadas através de microCT.

A aferição da BMD por micro CT foi validada em 2007 (Macneil e Boyd, 2007), tendo as vantagens de permitir a avaliação da BMD em imagens

tridimensionais de alta resolução (Ito, Nishida *et al.*, 2002) em sítios específicos selecionados pelo operador (VOI).

Estima-se que a resistência óssea é dependente da BMD em cerca de 70 a 75% e que o restante é explicado por fatores como arquitetura óssea e composição do tecido (Krug, Burghardt *et al.*, 2010). Por isso, a mensuração isolada da BMD não traduz completamente a qualidade óssea, sendo a estabilidade de implantes afetada também pela qualidade micro-estrutural do osso trabecular adjacente ao implante (Wirth, Goldhahn *et al.*, 2011). Faz-se, portanto, interessante avaliar ambas as propriedades ósseas, sendo a microCT o exame de eleição já que permite ambas avaliações com uma única tomada. Infelizmente, o atual estágio tecnológico não permite a utilização clínica da microCT para os ossos maxilares, sendo possível utilizá-la apenas em estudos laboratoriais.

Um importante parâmetro da arquitetura trabecular é a sua densidade. A densidade trabecular pode ser medida com técnica histológica (TBA), em 2D, ou microtomografia (BV/TV), em 3D. A microCT foi validada como um método para avaliação tridimensional do osso trabecular em 1998 através da comparação de seus resultados com os de histomorfometria (Muller, Van Campenhout *et al.*, 1998). Ela apresenta a vantagem de ser mais rápida e precisa que a análise histológica convencional, que requer o trabalhoso, demorado e destrutivo preparo histotécnico (Ruegsegger, Koller *et al.*, 1996; Ito, Nishida *et al.*, 2002; Lima, Lopes *et al.*, 2009). Enquanto a análise na micro CT é automatizada, a análise histológica é dependente do examinador e sujeita a seu erro. Além disso, são requeridos muitos cortes até que uma conclusão sobre a qualidade óssea seja atingida.

Um problema das imagens de microCT, quando o osso apresenta um metal inserido, é o artefato gerado. Foi demonstrado que até mesmo 9 mm distante do mini-implante a BMD é influenciada pelo artefato do parafuso (Sabo, Pollmann *et al.*, 2009), e que pelo menos 5 voxels de osso adjacentes aos parafusos devem ser descartados para avaliação da BV/TV (Cha, Song *et al.*, 2009). Dessa maneira, nessa pesquisa os 6 voxels (54 μm) de osso adjacente ao mini-implante foram excluídos do VOI e o padrão de osso artificial utilizado para calibração do software para avaliação da BMD continha um mini-implante inserido em seu centro. Assim, as condições de artefato foram reproduzidas.

Para a aferição da estabilidade primária, não há padrão ouro estabelecido (Cehreli, Karasoy *et al.*, 2009). Dessa maneira, foram realizados a mensuração do torque de inserção dos mini-implantes (Kim, Choi *et al.*, 2008; Mischkowski, Kneuertz *et al.*, 2008; Pithon, 2008; Salmoria, Tanaka *et al.*, 2008; Wilmes, Ottenstreuer *et al.*, 2008; Brinley, Behrents *et al.*, 2009; Wilmes e Drescher, 2009; Florvaag, Kneuertz *et al.*, 2010), a avaliação da micro-mobilidade com Periotest (Kim, Ahn *et al.*, 2005; Inaba, 2009; Su, Wilmes *et al.*, 2009; Cehreli e Arman-Ozcirpici, 2012), e o teste de tração (Huja, Litsky *et al.*, 2005; Kim, Choi *et al.*, 2008; Mischkowski, Kneuertz *et al.*, 2008; Pithon, 2008; Salmoria, Tanaka *et al.*, 2008; Brinley, Behrents *et al.*, 2009; Florvaag, Kneuertz *et al.*, 2010; Liu, Broucek *et al.*, 2010).

O Periostest é um instrumento eletrônico, originalmente desenvolvido para medir, através de percussão, as características de amortecimento do periodonto de dentes naturais traumatizados (Inaba, 2009; Cehreli e Arman-Ozcirpici, 2012). Seu uso tem sido expandido para verificar a mobilidade de

implantes e mini-implantes, em micro escala, através do fornecimento de um número contido numa escala de -8 a +50. Quanto maior o número fornecido, maior a mobilidade e menor a estabilidade. Como a estabilidade primária é comumente avaliada clinicamente através da verificação manual da mobilidade do parafuso, a aferição da mobilidade do implante com o Periotest parece ser o teste que melhor reproduz a condição clínica.

O aparelho Periotest permite a avaliação da mobilidade do mini-implante de maneira objetiva e não destrutiva (Jividen e Misch, 2000). Entretanto, o aparelho é muito sensível às condições de uso. Durante a mensuração, a peça de mão do aparelho deve ser mantida paralela ao solo e perpendicular ao parafuso. A cabeça do aparelho não deve tocar o parafuso, e a sua distância deve ser de 0,7 à 2 mm. Assim, para esse experimento, um dispositivo acrílico foi construído a fim de fixar a peça de mão e a amostra, mantendo uma distância de 2 mm entre a cabeça da peça de mão e o parafuso. A confiabilidade do Periostest já foi relatada em estudos com mini-implantes (Su, Wilmes *et al.*, 2009; Cehreli e Arman-Ozcirpici, 2012; Uemura, Motoyoshi *et al.*, 2012) e implantes dentários (Tricio, Van Steenberghe *et al.*, 1995; Lachmann, Laval *et al.*, 2006; Alsaadi, Quirynen *et al.*, 2007). Entretanto, sua confiabilidade para essa finalidade não é consenso na literatura (Caulier, Naert *et al.*, 1997). Nessa pesquisa, os valores de PTV apresentaram correlação negativa com os valores de IT e PS, testes já consagrados na literatura, concordando com estudos prévios (Tricio, Van Steenberghe *et al.*, 1995; Cha, Kil *et al.*, 2010; Cehreli e Arman-Ozcirpici, 2012) e indicando seu sucesso na avaliação da estabilidade primária. IT e PS apresentaram forte correlação positiva entre si,

concordando com estudos anteriores (Brinley, Behrents *et al.*, 2009; Marquezan, Lau *et al.*, 2012).

Os resultados dessa pesquisa mostraram que a densidade óssea – tanto a mineral (BMD total) como a trabecular (BV/TV) – possui correlação com as medidas de estabilidade. Esses achados concordam com (Wang, Zhao *et al.*, 2010), que encontraram correlação positiva entre PS e as propriedades ósseas de BV/TV e BMD quando avaliaram a diferença da estabilidade primária de mini-implantes inseridos na mandíbula de cães jovens e adultos.

Tanto o papel do osso trabeculado quanto do osso cortical foram evidenciados. A presença de cortical por si só aumentou os valores de estabilidade (Tabela 2, Artigo 3, página 67) corroborando sua importância na estabilidade (Turkyilmaz, Tozum *et al.*, 2006; Wilmes, Rademacher *et al.*, 2006; Motoyoshi, Yoshida *et al.*, 2007; Su, Wilmes *et al.*, 2009; Cha, Kil *et al.*, 2010). Entretanto, quando a cortical esteve ausente, a importância do osso trabecular se tornou mais evidente. Os valores de IT, PTV e PS diferiram para os grupos GI0 e GP0, havendo maior estabilidade no osso púbico. Quando comparados os grupos GI1 e GP0, IT e PTV não mostraram diferença estatisticamente significativa. Esses resultados sugerem que quando a cortical esteve ausente, a responsabilidade da estabilidade dos parafusos recaiu sobre as propriedades do osso trabecular. Já quando a cortical esteve presente, ela demostrou seu papel, especialmente quando o osso trabecular possuía menores valores de BMD, Tb.N, Tb.Th e maior valor de Tb.S. Essa responsabilidade da cortical sobre as propriedades mecânicas do osso havia sido relata anteriormente (Ito, Nishida *et al.*, 2002). Em estudo com elementos finitos, esses autores encontraram forte correlação entre propriedades mecânicas do tecido ósseo e

a microarquitetura trabecular. Entretanto, quando a estrutura trabecular estava deteriorada (simulando osteoporose), as propriedades mecânicas dependiam principalmente da cortical.

Para que não se dependa exclusivamente da cortical, quando mini-implantes são inseridos em ossos de baixa BMD, de pacientes osteoporóticos ou adolescentes, as propriedades dos mini-implantes (diâmetro, comprimento, superfície) e o tempo de reparo devem ser considerados (Wang, Zhao *et al.*, 2010).

Considerando as propriedades da cortical óssea em relação às demais propriedades do osso, a espessura de cortical apresentou correlação positiva apenas com a BMD total, corroborando a crença de que quando a espessura de cortical aumenta, a BMD total também aumenta porque a cortical é a porção mais mineralizada do osso (Marquezan, Osorio *et al.*, 2012).

Já avaliando a espessura de cortical com relação à estabilidade primária, foi observada correlação positiva entre a espessura de cortical e o IT (Wilmes, Rademacher *et al.*, 2006; Motoyoshi, Yoshida *et al.*, 2007; Cha, Kil *et al.*, 2010; Motoyoshi, Uemura *et al.*, 2010; Mcmanus, Qian *et al.*, 2011; Wilmes e Drescher, 2011; Wirth, Goldhahn *et al.*, 2011), e entre a espessura de cortical e o PS (Huja, Litsky *et al.*, 2005; Salmoria, Tanaka *et al.*, 2008). Entretanto, a espessura de cortical não influenciou o PTV. Acredita-se que a espessura de cortical tenha maior influência nas medidas axiais de estabilidade que nas laterais.

O teste de correlação de Pearson mostrou não haver correlação entre a BMD da cortical e a estabilidade dos mini-implantes, discordando de Marquezan, Lau *et al.* (Marquezan, Lau *et al.*, 2012) (APÊNDICE B, página

100). Tal discordância provavelmente deve-se à diferença metodológica. Enquanto em Marquezan, Lau *et al.* (Marquezan, Lau *et al.*, 2012) a avaliação da BMD da cortical foi realizada em cortes de CBCT, nesse experimento foi utilizada microCT, um método de avaliação tridimensional e mais preciso (Wang, Boyd *et al.*, 2011). A CBCT, entretanto, é atualmente utilizada na clínica ortodôntica, ao contrário da microCT.

Considerando os três trabalhos que compõe essa tese, ficou evidente que a qualidade do sítio ósseo receptor tem influência sobre a estabilidade primária de mini-implantes. Sugere-se que futuras pesquisas confirmem tais achados através de estudos clínicos.

6 CONCLUSÃO

6.1 Nas revisões sistemáticas foi verificado que:

6.1.1 existe associação positiva entre a estabilidade primária de implantes dentários e da BMD do sítio receptor;

6.1.2 existe associação positiva entre a estabilidade primária de MI e espessura cortical do sítio receptor;

6.2 No trabalho experimental:

6.2.1 a estabilidade primária (IT, PS e PTV) diferiu estatisticamente entre os ossos ilíaco e púbico na presença e na ausência de cortical;

6.2.2 a densidade trabecular, a espessura trabecular, a espessura de cortical, o número de trabéculas, a BMD trabecular e a BMD total, aferidas com microCT, apresentaram correlação com a estabilidade primária dos MI.

7 RECOMENDAÇÕES

Para futuras pesquisas sobre a relação entre qualidade óssea e a estabilidade primária de MI, sugere-se a utilização de espessuras de cortical entre 0,1 e 1 mm. Sugere-se ainda a realização de estudos clínicos que verifiquem a influência da qualidade óssea na estabilidade primária e secundária.

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9 APÊNDICES

9.1 APÊNDICE A: Marquezan M, Souza MM, Araújo MT, Nojima LI, Nojima MC. Is miniscrew primary stability influenced by bone density? Braz Oral Res. 2011 Sep-Oct;25(5):427-32.

Is miniscrew primary stability influenced by bone density?

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ABSTRACT

Primary stability is absence of mobility in the bone bed after mini-implant placement and depends on bone quality among other factors. Bone quality is a subjective term frequently considered as bone density. The aim of this preliminary study was to evaluate bone density in two bovine pelvic regions and verify the primary stability of miniscrews inserted into them. Forty bone blocks were extracted from bovine pelvic bones, 20 from iliac and 20 from pubic bone, all of them containing cortical about 1 mm thick. Half of the sections extracted from each bone were designated for histological evaluation of bone density (trabecular bone area - TBA) and the other half for bone mineral density (BMD) evaluation by means of central dual-energy X-ray absorptiometry (DEXA). Then, twenty self-drilling miniscrews (INP®, São Paulo, Brazil) 1.4 mm in diameter and 6 mm long were inserted into the bone blocks used for BMD evaluation. Peak implant insertion torque (IT) and pull-out strength (PS) were used for primary stability evaluation. It was found that iliac and pubic bones present different bone densities, iliac bone being less dense considering BMD and TBA values ($P>0.05$). However, the miniscrew primary stability was not different when varying the bone type ($P<0.05$). IT and PS were not influenced by these differences in bone density when cortical thickness was about 1 mm thick.

Descriptors: Bone and Bones; Bone Density; Orthodontic Anchorage Procedures.

INTRODUCTION

Primary stability is absence of mobility in the bone bed after implant or mini-implant placement [1, 2]. It is achieved by mechanical contact between the miniscrew surface and bone [3] and depends on the characteristics of devices [4, 5], insertion technique [4] and bone quality and quantity of the receptor site [4, 6-8].

The primary stability plays an important role in the successful secondary stability of miniscrews, since lack of immediate stability can lead to progressive mobility of the device and its subsequent loss [9]. In clinical use, the initial stability of miniscrews is also considered essential, because of immediate or early load applied on them in many patients [10]. It has been suggested that if initial

mechanical retention of the mini-implant is not observed, it should be replaced by a thicker device, or its insertion site should be changed [11]. Primary stability has traditionally been assessed by the practitioner through manual verification [12]. Several other less subjective methods are described in the literature: histological (BIC-bone to implant contact), which assesses the percentage of bone to implant contact; mechanical, which assesses insertion and removal torque or pullout strength of mini-implants, and the percussion method (Periotest value). However, there is still no gold standard to assess the primary stability of miniscrews [13].

The term “bone quality” is not clearly defined in the literature. This includes physiological and structural aspects and degree of bone tissue mineralization [14]. Aspects such as bone metabolism, cell turnover, maturation, intracellular matrix and vascularity have also been emphasized [1]. Nevertheless, the role of each of these aspects is not completely understood [14]. In Implant dentistry, the most accepted classification of bone quality has been the one proposed by Lekholm and Zarb [15]. This was based on the amount of cortical and trabecular shown in preoperative radiographs. This classification, however, depends on the operator’s subjectivity during radiographic evaluation.

A less subjective method for evaluating cortical and trabecular bone quality is to verify bone mineral density (BMD) [14]. Bone densitometry is taken as the gold standard for quantifying BMD in Endocrinology and Traumatology [16]. The bone mineral content of tissue is measured and divided by the area of tissue to obtain bone mineral density. Another parameter of bone quality evaluated in Implant dentistry is trabecular bone density. For this measurement, however, the percentage of trabecular bone area in the total biopsy area is calculated. The trabecular bone area (TBA) instead of mineral content is evaluated. For TBA analysis, histological and morphometrical methods are considered the gold standard [1].

Considering the above, the aim of this study was to evaluate the primary stability of miniscrews inserted in two bovine pelvic regions with different densities, to verify the influence of bone density on stability.

METODOLOGY

The sample comprised 40 bone sections extracted from bovine pelvis (*Bos taurus*), Angus lineage. Ten pelvic bones were obtained from a Slaughterhouse (registered with ANVISA – the Brazilian Health Surveillance Agency) immediately after slaughter. From each bone, two small bone sections were taken from the gluteal wing of the iliac and from the pubic bone (Figure 1). Tissue sections were removed by means of a trephine bur (8 mm in diameter x 20 mm long, Sin Implantes, São Paulo, Brazil) adapted to a low speed motor (Beltec LB100, Araraquara, Brazil) under irrigation. The bone sections were taken from a region in which cortical bone was about 1 mm thick (measured with an orthodontic caliper, Odin, Ortho-pli, Philadelphia, USA). One of the two bone sections taken from each region was used to measure bone mineral density and evaluate primary stability. These samples were immersed in sterile physiological solution and stored by freezing (-20 ºC) until the tests were performed. The other section removed from each bone was used for histomorphometric analysis. These samples were immersed in 10% buffered formalin solution for 2 days for fixation.

Bone mineral density evaluation (BMD)

The bone mineral content of specimens was measured and divided into areas to obtain bone mineral density by means of central dual-energy X-ray absorptiometry (DEXA) Prodigy (GE/LUNAR, Madison, USA), calibrated for small animals. To perform the exam, the bone blocks were thawed at room temperature and were put into plastic boxes (6x11x4 cm) containing raw rice to simulate soft tissue during irradiation. After this the samples were irradiated by DEXA for 30 seconds [17].

Histomorphometric evaluation

After being immersed in 10% buffered formalin solution for 2 days, the samples were decalcified in Morse solution[18] (equal parts of 50% formic acid and 20% sodium citrate - Vetec Química Fina Ltda., Rio de Janeiro, Brazil) by immersion for 7 days and then embedded in paraffin. Longitudinal sections were cut into 5 µm slices and stained with picrosirius for histologic evaluation.

Histomorphometric analysis of bone samples was performed using Image J software (National Institute of Mental Health, Bethesda, USA). Digitized photomicrographs (microscope Nikon Eclipse E600, magnification X40, camera DS-U2, Nikon Corporation, Tokyo, Japan) were taken and analyzed by the same examiner (ICC= 0.971). The histomorphometric evaluation was measured as a percentage of trabecular bone area (TBA).

Primary Stability evaluation

Primary stability was evaluated by means of insertion torque (IT) measurement and pull-out strength (PS). Twenty miniscrews (INP®, São Paulo, Brazil) 1.4 mm in diameter and 6 mm long were inserted into the bone blocks used for BMD evaluation. This was done with the use of a manual placement key connected to a digital torque meter (Lutron TQ-8800, Taipei, Taiwan), to allow the measurement of peak implant placement torque. The values were recorded in Newton centimeter (Ncm). After this, the pull-out test, which consists of extracting the miniscrew from bone at a constant velocity, was performed to evaluate the maximum force required to remove it [19]. The mechanical test was performed in a universal test machine (Emic DL 2000, São José dos Pinhais, Brazil), using a 500 kgf load cell at a crosshead speed of 0.05 mm per second [19] to remove the miniscrew. The maximum pull-out strength was recorded.

Statistical Analysis

The data were evaluated using the Statistical Package for Social Sciences (version 17, SPSS Inc., Chicago, USA). The values obtained were tabulated and submitted to descriptive analysis. The normality and homogeneity of variables were verified by Shapiro-Wilk and Levene's tests. Intergroup comparisons of mean values were performed by the paired T-test at a level of significance of 5%.

RESULTS

Under light microscopy, the histological sections revealed the presence of trabecular bone with osteocytes and marrow spaces filled with fat marrow. The

marrow spaces were larger in Iliac bone. Descriptive statistics and the paired T-test results are shown in Table 1.

Table 1: Descriptive analysis and paired T-test comparing the four variables for iliac and pubic bones.

	Iliac (mean and SD)	Pubic (mean and SD)	paired T-test
BMD g/cm²	0.13 (0.01)	0.16 (0.00)	P = 0.000*
Trabecular bone density (%)	24.23 (6.12)	39.01 (7.95)	P = 0.002*
IT (Ncm)	7.13 (0.75)	6.23 (0.20)	P = 0.071
PS (N)	203.33 (91.11)	164.33 (23.07)	P = 0.387

* Indicates statistical significant difference at α=0.05%

Statistical difference was observed for the variables that evaluated bone quality: BMD – P=0.000; TBA – P=0.002. The difference in trabecular bone density between the iliac and pubic bones is shown in Figure 2. The variables that evaluated primary stability (IT and PS) showed no statistical difference (P=0.071 and P=0.387, respectively).

DISCUSSION

Pelvic bone has previously been used in studies with miniscrews [4, 20, 21, 22]. During exploration of this bone, it was observed that some characteristics such as color, texture and drill resistance differed in its various regions. Pubic bone was darker and more resistant when compared with iliac bone. Therefore, these two regions of the pelvic bone were chosen for this study. The BMD results showed that they are less dense than human jaw bones, as previously related in the literature by Devlin et al. [23], indicating the following values: maxilla anterior region=0.55 g/cm^2; maxilla posterior region=0.31 g/cm^2; mandible=1.11 g/cm^2; and by Choel et al. [24], indicating values for dentate mandible =0.604 g/cm^2; and edentulous mandible=0.521 g/cm^2. However, the two cited studies presented a large variation in values for mandibular BMD. Trabecular bone density evaluation, however, showed that the TBA value for pubic bone was

similar to the result previously described by Aksoy et al. [25] for maxilla=38.20±9.65; mandible=44.08±14.97. The results of this study showed that the iliac and the pubic bones (which the pelvis is composed), present different bone qualities: bone mineral density and trabecular bone density. These characteristics, however, had no influence on primary stability of mini-implants inserted in bone when the cortical was 1mm thick.

Mean values for IT ranged from 6.23 to 7.13 Ncm, representing adequate primary stability according to Motoyoshi et al. [26], who stated that these values should range from 5 to 10 Ncm.

Pull-out strength values ranged from 164.33 to 203.33 N, being within the range found by Huja et al. [19] in a study with dog jaws: 134.5 N, for anterior mandible, and 388.3 N for posterior mandible. Nevertheless, no landmark for adequate pull-out strength value was found in the literature.

A previous study evaluated the influence of BMD on primary stability of miniscrews and despite methodological differences, found a similar result [27]. No correlation was found between BMD, verified by cone beam computed tomography, and miniscrew stability assessed by placement torque. The authors also investigated the influence of cortical bone and found that cortical thickness and cortical BMD were positively correlated with miniscrew stability [27]. No studies evaluating the influence of TBA on miniscrew stability were found.

Two hypotheses were formulated to explain the results of the present study. The first is that the presence of a cortical thickness of 1 mm in all of the specimens had an important influence on miniscrew stability, masking the influence of bone mineral density and trabecular density. Cortical thickness has been related to primary stability of miniscrews and implants [5, 12, 28, 29, 30]. However, there is a lack of studys isolating these two factors: bone density and cortical thickness. The second hypothesis is that the difference in bone quality verified statistically may not be clinically relevant. A bigger difference between BMD and TBA values in bones could perhaps reflect differences in mini-implant stability.

Despite the limitations of this in vitro study, it can be inferred that in clinical practice, a cortical thickness of 1mm is sufficient to guarantee the primary stability of miniscrews, as previous supposed by Motoyoshi et al. [30], even when there are variations in BMD and TBA values.

Further researches are suggested isolating the cortical effect and increasing difference in density between different types of bone.

CONCLUSIONS

- Iliac and pubic bones present different BMD and TBA values, the iliac being less dense when considering the two parameters;
- Miniscrew primary stability was not influenced by these differences in bone density.

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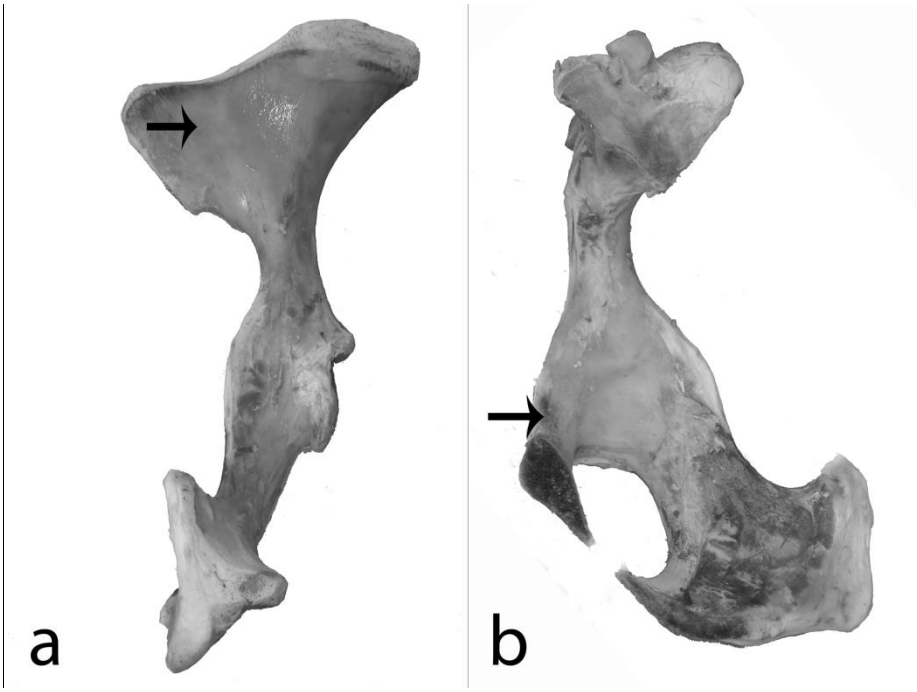

Figure 1: Macroscopic view of the right hemi pelvis. (a) caudal view: the arrow indicates the gluteal wing of iliac bone. (b) medial view: the arrow indicates the caudal portion of pubic bone.

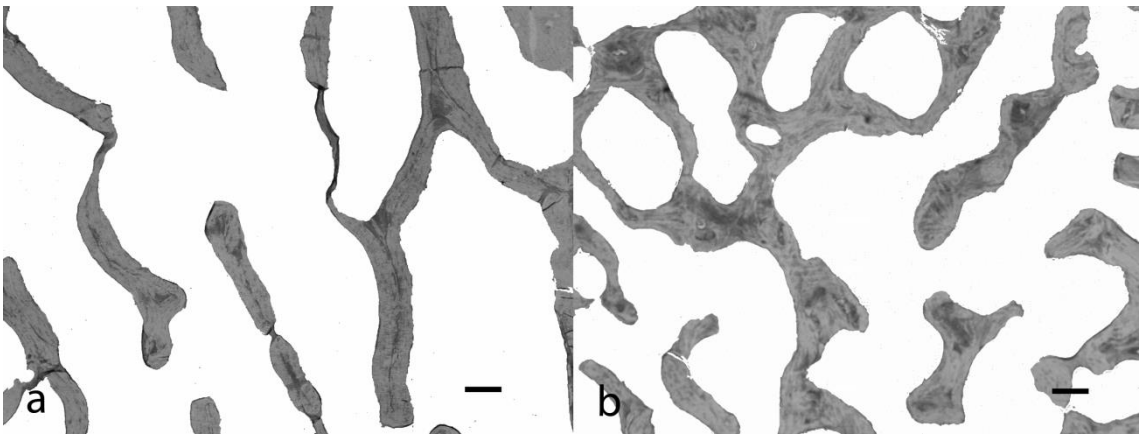

Figure 2: Micrograph of iliac (a) and pubic (b) bones (picrosirius, 40X, bars=100µm). Note that the marrow spaces are larger in iliac bone (a).

9.2 APÊNDICE B: Marquezan M, Lau TC, Mattos CT, Cunha AC, Nojima LI, Sant'anna EF, Souza MM, Araújo MT. Bone mineral density. *Angle Orthod*. 2012 Jan;82(1):62-6.

Bone mineral density: methods of measurement and its influence on primary stability of miniscrews

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ABSTRACT

Objective: To verify whether bone mineral density (BMD) of cortical bone, trabecular bone and total bone influences the primary stability of orthodontic miniscrews and to verify whether there is correlation between the measurement of BMD by Cone-Beam Computed Tomography (CBCT) and Central Dual-energy X-ray Absorptiometry (DEXA).

Material and Methods: Twenty bovine bone sections were extracted from the pubic and iliac bones from regions with cortical thickness of approximately 1mm. The BMD of the total bone block was evaluated by two methods: CBCT and DEXA. The BMD of cortical, trabecular and total bone in the region of interest (ROI) were also evaluated by CBCT. After scanning the bone blocks, twenty self-drilling miniscrews (INP®) 1.4 mm in diameter and 6 mm long were inserted into them. The peak implant insertion torque (IT) was registered. After this, the pull-out test (PS) was performed and the maximum force registered. Pearson's correlation test was applied to verify the correlations between variables. **Results:** The BMD of the total bone block verified by CBCT and DEXA showed a positive and strong correlation (r=0.866, p=0.000). The BMD of the ROI for cortical bone influenced the IT (r=0.518, p=0.40) and the PS of miniscrews (r=0.615, p=0.015). However, the total bone BMD (verified by CBCT and DEXA) and trabecular bone BMD presented weak and not statistically significant correlations with primary stability.

Conclusions: There was a positive correlation between total bone block BMD measured by DEXA and CBCT. The cortical BMD influenced the IT and PS.

Keywords: Bone density; Cone-Beam Computed Tomography; Dual-energy X-ray Absorptiometry; Miniscrew

INTRODUCTION

The primary stability of miniscrews depends on the characteristics of the device, insertion technique and bone quality and quantity of the receptor site [4]. The bone quality classification most accepted in Implant dentistry has been that proposed by Lekholm and Zarb [15], based on the amount of cortical and trabecular bone shown in preoperative radiographs. However, this classification depends on the operator's subjective evaluation of the radiograph. A less

subjective method for evaluating the quality of cortical and trabecular bone is to verify the bone mineral density (BMD) [14].

The quantification of bone mineral density taken as the gold standard in endocrinology and traumatology is bone densitometry by means of central dual-energy X-ray absorptiometry (DEXA)[16]. In implant dentistry, however, cone-beam computed tomography (CBCT) has been used for this purpose because it is a three-dimensional analysis that allows the quantification of the mineral density of jaw bones in specific sites in Hounsfield units (HU). When evaluating the bone mineral density of the receptor site by CBCT, it is possible to verify the cortical BMD and trabecular BMD separately or the total bone BMD which is the measurement of mineral density of trabecular bone and cortical bone together.

The aims of this study were to verify how these parameters influence the primary stability of orthodontic miniscrews and to verify whether there is correlation between the measurement of BMD by CBCT and DEXA.

MATERIALS AND METHODS

The sample consisted of twenty bone sections extracted from bovine pelvic bone (Bos taurus, Angus lineage). The bones were obtained from a slaughterhouse (registered with ANVISA – the Brazilian Health Surveillance Agency) immediately after slaughter. The bone sections were extracted from the caudal portion of the pubic bone and from the gluteal wing of iliac bone with the use of a trephine bur (8mm in diameter x 20mm long, Sin Implantes, São Paulo, Brazil) adapted to a low speed motor (Beltec LB100, Araraquara, Brazil) under irrigation. The bone sections (8mm in diameter x 12mm long) were taken from regions in which there was a mean cortical thickness of 1mm (measured with an orthodontic caliper, Odin, Ortho-pli, Philadelphia, USA). The extracted material was immersed in sterile physiological solution and stored by freezing (-20ºC).

BMD evaluation

The BMD was evaluated by two methods: DEXA and CBCT. First, the bone mineral content of specimens was measured and divided by the area to obtain the BMD by means of central dual-energy X-ray absorptiometry (DEXA) Prodigy (GE/LUNAR, Madison, USA), calibrated for small animals. To perform the exam, the bone blocks were thawed at room temperature and put into plastic boxes (6x11x4 cm) containing raw rice to simulate soft tissue [17]. After this, the samples were irradiated by DEXA for 30 seconds[17] . This analysis comprised the entire bone block (cortical and trabecular bones).

After this, CBCT (I-CAT 3D Dental Imaging System, Pennsylvania, USA) was used to obtain tomographs in accordance with a standard protocol (120 KV, 47 mA, FOV of 22 cm, voxel of 0.4 mm, and scan time of 30 s). All the samples were arranged identically in a Styrofoam box with the cortical bone perpendicular to the floor for the purpose of scanning. Data were imported in DICOM format (Digital Imaging and Communications in Medicine) and handled by I-CAT Vision (Dental Imaging System, Pennsylvania, USA). Once imported, CT data were reconstructed into 1-mm thick transaxial images. The BMD was obtained using the multiplanar reconstruction screen and measuring the HU (Hounsfield Unit) of the selected area. First, a sagittal section was obtained in the center of the bone block . To verify whether the data of CBCT measurement of BMD were correlated with the data acquired from DEXA, the total area of the bone block in this section was evaluated (total bone block BMD) . After this, the region of interest (ROI) was isolated. The ROI was considered the area in the center of the block that would surround the miniscrew after its placement (2.4 mm X 7 mm). The BMD of cortical bone, trabecular bone and total bone were measured separately in the ROI (Figure 1).

Primary Stability Evaluation

The primary stability was evaluated by means of insertion torque (IT) measurement and pull-out strength (PS). Twenty miniscrews (INP®, São Paulo, Brazil) 1.4 mm in diameter and 6 mm long were inserted into the bone blocks with the use of a manual placement key connected to a digital torque meter (Lutron TQ-8800, Taipei, Taiwan) to allow measurement of the peak implant placement torque. The values were recorded in Newton centimeter (Ncm). After this, the pull-out

test, which consists of extracting the miniscrew from the bone at a constant speed, was performed to evaluate the maximum force required to remove it [19]. The mechanical test was performed in a universal test machine (Emic DL 2000, São José dos Pinhais, Brazil), using a 500 kgf load cell at a crosshead speed of 0.05 mm per second [19] to remove the miniscrew. The maximum pull-out strength was recorded.

Statistical Analysis

The variables total bone BMD (evaluated by DEXA and CBCT), cortical BMD, trabecular BMD and total BMD in ROI (evaluated by CBCT), IT and PS were evaluated using the Statistical Package for Social Sciences (version 17, SPSS Inc., USA). The values obtained were tabulated and submitted to normality and homogeneity tests (Shapiro-Wilk and Levene). Pearson's correlation test was applied to verify the correlations between variables. The level of significance was 5%.

RESULTS

Descriptive statistics are presented in Table 1. The result of Pearson's correlation test is shown in Table 2. The cortical bone BMD in the ROI (CBCT) influenced the insertion torque (r=0.866, p=0.000, positive and strong correlation) and the pull out strength of miniscrews (r=0.615, p=0.015, positive and substantial correlation). However, the total bone block BMD, measured by means of DEXA and CBCT, the total BMD in the ROI and the trabecular BMD in the ROI presented weak and non statistically significant correlation with primary stability. The two variables that measured the primary stability, IT and PS, presented a positive and substantial correlation (r=0.615, p=0.015).

DISCUSSION

Although DEXA[16] is used as the gold standard method for measuring BMD in traumatology and endocrinology, Cone Beam CT is often used in implant dentistry. Computed tomography was introduced as a preparatory exam for prosthodontic implant placement by Scharz[31] in 1987 and became popular in dentistry. The CT three-dimensional analysis allows the quantification of the mineral density of jaw bones in specific sites in cross sections. The BMD is measured in

Hounsfield units (HU) by the difference in grayscale. The CBCT also allows bone dimensions to be measured before miniscrew placement. The results of this study showed that the BMD of the total bone block, verified by CBCT and DEXA, had a positive and strong correlation (r=0.866, p=0.000).

The results of this study showed that the BMD of the ROI of cortical bone influences the primary stability of miniscrews measured by the insertion torque and pull out strength tests. The total bone block BMD and the total BMD ROI did not influence the insertion torque and pull-out strength of miniscrews. Similar result was previously described by Cha et al[27]. They evaluated the primary stability of miniscrews inserted in the jaws of beagle dogs. As in the present study, the bone density was assessed by CBCT and the primary stability was verified by means of insertion torque and also by the Periotest value (Periotest - Medizintechnik Gulden, Modautal, Germany). They found a positive association between cortical BMD and miniscrew primary stability, but the BMD for the total bone was weak and non statistically significant.

The importance of the cortical in miniscrew stability has previously been established by assessing the cortical thickness, and a positive association was verified between cortical thickness and the primary stability of miniscrews [4, 19, 22, 27, 29, 30]. The evaluation of cortical BMD corroborates its importance in initial stability.

The ROI of total BMD has previously been related to the primary stability of prosthodontic implants [25, 32, 33], but it was not verified for miniscrews in the present study or by Cha et al [27]. The ROI of trabecular BMD also plays an important role in the primary stability of prosthodontic implants, as verified by Bergkvist et al [14] and Merheb et al [12]. However, in this study, with cortical thickness of 1mm, there was no association between ROI of trabecular BMD and the primary stability of mini-implants.

Despite the limitations of our laboratory study, the CBCT proved to be a useful exam for noninvasive assessment of bone density at the preoperative stage of mini-implant placement. Moreover, the cortical thickness and the cortical BMD can be measured to estimate the primary stability of miniscrews.

It is suggested that future researches should investigate the influence of total BMD and trabecular BMD on primary stability when there is a cortical thickness of less than 1mm.

CONCLUSION

- The total bone block BMD measured by DEXA and CBCT presented a positive and strong correlation;
- The ROI of cortical BMD presented a positive and substantial correlation with IT and PS, however, the ROI of trabecular BMD, ROI of total BMD and total bone block BMD was not correlated with the primary stability of miniscrews.

ACKNOWLEDGEMENTS

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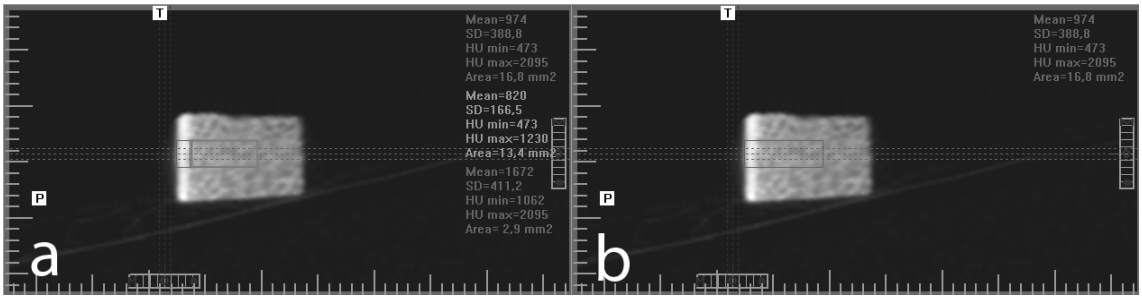

Figure 1. ROI delimitation in the sagittal section. a) Smaller rectangle on the left indicates the cortical ROI. Larger rectangle on the right indicates the trabecular ROI; b) total bone ROI.

Table 1: Descriptive statistics.

	Unit	Minimum	Maximum	Mean	Standard Deviation
Total bone block BMD (DEXA)	g/cm²	.106	.193	.14815	.026502
Total bone block BMD (CBCT)	HU	705.00	1140.00	938.3500	142.88614
ROI total BMD (CBCT)	HU	611.00	1161.00	874.5000	141.67550
ROI cortical BMD (CBCT)	HU	1175.00	2153.00	1651.0000	295.95786
ROI trabecular BMD (CBCT)	HU	431.00	953.00	722.0000	158.72154
IT	Ncm	5.80	18.80	7.5875	3.42323
PS	N	115.00	369.00	231.2222	88.05717

Table 2: Pearson correlation test.

	Total Bone Block BMD (DEXA)	Total Bone Block BMD (CBCT)	ROI Total BMD (CBCT)	ROI Cortical BMD (CBCT)	ROI Trabecular BMD (CBCT)	IT	PS
Total bone block BMD (DEXA)							
Pearson correlation	1	.866*	.309	.232	.339	.334	.050
P value		.000	.186	.325	.144	.206	.843
Total bone block BMD (CBCT)							
Pearson correlation	.866*	1	.569*	.299	.564*	.314	.064
P value	.000		.009	.201	.010	.237	.802
ROI total BMD (CBCT)							
Pearson correlation	.309	.569*	1	.519*	.852*	.489	.334
P value	.186	.009		.019	.000	.055	.175
ROI cortical BMD (CBCT)							
Pearson correlation	.232	.299	.519*	1	.146	.518*	.713*
P value	.325	.201	.019		.540	.040	.001
ROI trabecular BMD (CBCT)							
Pearson correlation	.339	.564*	.852*	.146	1	.172	.073
P value	.144	.010	.000	.540		.524	.774
IT							
Pearson correlation	.334	.314	.489	.518*	.172	1	.615*
P value	.206	.237	.055	.040	.524		.015
PS							
Pearson correlation	.050	.064	.334	.713*	.073	.615*	1
P value	.843	.802	.175	.001	.774	.015	

* Correlation is significant at the 0.05 level.

10 ANEXOS

10.1 ANEXO 1: Aceite do Artigo 3.

Manuscript052513-395R Decision Letter

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