Journal of Cranio-Maxillo-Facial Surgery 42 (2014) 801–805

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Synchrotron μCT imaging of bone, titanium implants and bone substitutes – A systematic review of the literature

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ARTICLE INFO

Article history:
Paper received 17 May 2013
Accepted 4 November 2013

Keywords:
Synchrotron
Bone microarchitecture
Imaging
Dental implants

ABSTRACT

Today X-ray micro computer tomography (μCT) imaging is used to investigate bone microarchitecture. μCT imaging is obtained by polychromatic X-ray beams, resulting in images with beam hardening artifacts, resolution levels at 10 μm, geometrical blurring, and lack of contrasts. When μCT is coupled to synchrotron sources (SRμCT) a spatial resolution up to one tenth of a μm may be achieved. A review of the literature concerning SRμCT was performed to investigate its usability and its strength in visualizing fine bone structures, vessels, and microarchitecture of bone. Although mainly limited to *in vitro* examinations, SRμCT is considered as a gold standard to image trabecular bone microarchitecture since it is possible in a 3D manner to visualize fine structural elements within mineralized tissue such as osteon boundaries, rods and plates structures, cement lines, and differences in mineralization.

1. Introduction

Osseointegration of dental implants has been evaluated by classic 2D histomorphometry for many years. The advantage of this method has been the ease of access to observe and evaluate bone-to-implant contact, the ratio of hard and soft tissue in proximity to the implant, vessels, and different cells in a light microscope. The major disadvantage is that the preparation for microscopy is a destructive process with grinding of the sample to a preferred thickness of 10–30 μm (Donath, 1993). This omits a lot of information as only a few samples can be evaluated compared to the evaluation of the entire bone sample in 3D. Hence, there is an uncertainty whether the 2D histological section analyzed represents the actual osseous integration of an implant (Sarve et al., 2011).

In conventional radiography the X-ray beam passes through bone and implant, and is recorded as a 2D image. The information obtained in the radiograph depends on the absorption density of the object perpendicular to the direction of the X-ray beam (White and Pharoah, 2006). Since the microarchitecture and degree of mineralization of hard tissues are not possible to evaluate by histomorphometry and conventional radiography, additional 3D evaluations are necessary. Four main sources of 3D imaging modalities are available; Magnetic Resonance Imaging (MRI) which is mainly used for comparing 3D data sets of soft tissues (Reinbacher et al., 2012), conventional third generation CT-scanners are well-established tools for hard tissue imaging (Sauerbier et al., 2013), cone-beam computer tomography (CBCT) which is a suitable tool for bone mass evaluation (Hohlweg-Majert et al., 2011), and X-ray micro computed tomography (μCT). Conventional third generation CT-scanners are well-established tools for hard tissue imaging (Sauerbier et al., 2013). μCT imaging is obtained by polychromatic X-ray beams, resulting in images with beam hardening artifacts, resolution levels at 10 μm, geometrical blurring, and lack of contrast (Feldkamp et al., 1989; Ruegsegger et al., 1996; Wiedemann, 2002; Ritman, 2004; Ruhli et al., 2007). When μCT is combined with synchrotron sources (SRμCT) a spatial resolution up to one tenth of μm may be achieved (www.esrf.eu, ESRF, 2013). Although mainly limited to *in vitro* examinations, it is considered as a gold standard to image trabecular bone microarchitecture in 3D (Peyrin et al., 2010). The evaluation of bone microarchitecture has traditionally been performed by measuring 2D histomorphometric parameters from bone slices obtained from iliac crest bone biopsies (Parfitt et al., 1987) and by algorithms turning these parameters into 3D volumetric estimations (Gundersen and Jensen, 1987).

Synchrotron-based microtomography is an established technique available at various synchrotron light sources worldwide. Synchrotron radiation (SR) has a monochromatic beam, high photon flux, coherence, collimation, and sufficiently high spatial

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http://dx.doi.org/10.1016/j.jcms.2013.11.015

resolution to evaluate the implant-to-bone contact (Kim et al., 2001a, 2001b). Utilizing volume images obtained with SR, the different material phases i.e. bone, titanium implant, cavities, and ceramic particles within a specimen may be distinguished by different absorption densities (Rack et al., 2006, 2011; Stiller et al., 2009). SRμCT uses the absorption of X-rays in order to detect density differences inside solid matter (Bernhardt et al., 2004). The information obtained is reconstructed by mathematical algorithms using the different absorption coefficients obtained by multiple tomography at different exposing angles of the samples resulting in a 3D image (Bernhardt et al., 2004).

Due to its high resolution, SRμCT has been used to visualize the vascular canals in cortical bone in humans (Bousson et al., 2004) and in rats (Matsumoto et al., 2011a). The medical application of SRμCT is increasing, since SRμCT has been used to visualize the microarchitecture of osteoporotic bone and fractures (Ito, 2005; Kazakia et al., 2008; Cooper et al., 2011a), bone microcracks (Voide et al., 2009; Larrue et al., 2011), and bone changes after orthodontic treatment of teeth (Dalstra et al., 2006). SRμCT makes it possible to see fine structural elements within mineralized tissue such as osteon boundaries, rods and plate structures, cement lines, differences in mineralization of trabeculae (Nuzzo et al., 2002; Chappard et al., 2006), and of individual bone lamellae (Peyrin et al., 2010; Cooper et al., 2011b; Larrue et al., 2011).

The aim of this study was to compare and analyze the literature on high resolution scans on bone microarchitecture and dental implants visualized by SRμCT and to discuss its usability in contrast to conventional μCT and histology.

Hypothesis: The null hypothesis of this study is that there is no difference between SRμCT and μCT and that the studies are comparable so a meta-analysis can be performed.

2. Material and methods

A Medline search (PubMed) was conducted, and studies published in English from 2000 to 2012 were included in the review. The inclusion and exclusion criteria are listed in Table 1. The MeSH words used for the literature search as well as the search results are listed in Table 2.

From the identified studies, the following variables were extracted: author, journal, year of publication, type of synchrotron μCT, which type of animal, human yes/no, body part, resolution, histology, μCT, and graft material.

3. Results

The combination of synchrotron μCT and used MeSH words resulted in 118 articles. Some of the articles appeared multiple times during the different combination of MeSH words and are subsequently only accounted for once. Following screening of titles and abstracts by defining the chosen inclusion and exclusion criteria, 41 potentially relevant publications were found and full text analysis was performed by one author (CAN). Out of the 41 articles 17 articles were included in the study. The studies were divided into human studies (Table 3), studies reporting only graft or dental implant (Table 4), and animal studies (Table 5) for analyzing purposes.

3.1. Human studies

Four human studies (Nuzzo et al., 2002; Nogueira et al., 2010; Cooper et al., 2011b; Larrue et al., 2011) described bone microarchitecture in cortical and trabecular bone of the extremities, osteons, microcracks and lacunae in bone, trabecular bone volume fraction and mineral content comparisons in cortical and trabecular bone evaluated by SRμCT and μCT, respectively (Nuzzo et al., 2002; Nogueira et al., 2010; Cooper et al., 2011b; Larrue et al., 2011). The studies comprise evaluation of different types of bone (Nuzzo et al., 2002; Cooper et al., 2011b; Larrue et al., 2011), while the fourth study (Nogueira et al., 2010) analyzed femoral bone tibia-, fibula-, humerus-, cuboid-, and calcaneus bone (Table 3).

Table 1
Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Studies published after January 2000	Studies published before January 2000
Published in English	Published in other languages than English
Grafting material in connection with bone	Lack of parameters of bone structure
High resolution synchrotron scans	Medical induced bone disease
Human bone	Lack of parameters of bone
Animal bone	Orthodontic treatment
Bone structure	Osteoporotic bone
Dental implants in bone	Osteoporosis

Table 2
Results of the MeSH search, results represent number of articles.

Search	MeSH word	MeSH word	Results	Full text analysis	Included
#1	Synchrotron	Maxillofacial surgery	0	0	0
#2	Synchrotron	Tricalcium phosphate	1	1	1
#3	Synchrotron	MicroCT/μCT	40	5	2
#4	Synchrotron	Dental implant	2	1	1
#5	Synchrotron	Alveolar ridge augmentation	0	0	0
#6	Synchrotron	Osseointegration	7	7	7
#7	Synchrotron	Porosity	23	6	3
#8	Synchrotron	Bone density	25	16	3
#9	Synchrotron	HA–TCPβ	0	0	0
#10	Synchrotron	Electron microscope tomography	1	0	0
#11	Synchrotron	Jaw	4	3	0
#12	Synchrotron	Bone transplantation	2	2	0
#13	Synchrotron	Histology	13	0	0
Total			118	41	17

3.2. Graft and dental implant studies

Two studies were included reporting the degradation of porous bone substitute tricalcium phosphate (TCP) foam with poly(DL-lactic acid) (PDLLA), and the microgap between a dental implant and the abutment, respectively (Ehrenfried et al., 2010; Rack et al., 2010) (Table 4).

3.3. Animal studies

11 animal studies were included comprising six different animal species and various types of bone (Table 5). Bernhardt et al. (Bernhardt et al., 2004, 2005, 2012) described the use of high photon flux energies to evaluate titanium dental implants and compared it to histology and μCT.

4. Discussion

In a literature search comprising SRμCT, histology, and μCT only a few publications are available (Nuzzo et al., 2002; Gauthier et al., 2003; Jung et al., 2003; Weiss et al., 2003; Bernhardt et al., 2004, 2005, 2012; Tzaphlidou et al., 2006; Ehrenfried et al., 2010; Morelhao et al., 2010; Nogueira et al., 2010; Rack et al., 2010;