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The Application of Nano/Micro-CT to Preclinical Dental Research and Dental Device Development

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Abstract

The application of Micro-Computed Tomography (micro-CT) and novel Nano-Computed Tomography (nano-CT), 3D X-ray technique to biomedical research including dental research and dental materials development are considerable and growing. This technique can provide high resolution and detailed 3D images for researchers to gain more insight into their samples nondestructively. The samples remain incessantly for further mechanical test and histological analysis. In this article we will highlight the recent applications for dental and endodontic studies.

Introduction

Computed Tomography (CT) technique is used frequently as a non-invasive Three-Dimensional (3D) method which can image internal and external 3D geometry and structure information. Recent years, they are widely used in many fields, especially for dental research, orthopedic research, tissue engineering and the development of biomedical devices. This technique can investigate the internal 3D feathers without sample destruction and this character is really important for clinical application. The market size of CT instrument approached 4 billion in 2017. For clinical application, doctors use CT technique to diagnose disease and it plays an important role in orthopaedic and dental fields. Compared to clinical CT, micro-CT was developed in early 1980s and it has a better spatial resolution. In early 2010s, the voxel resolution is improved to 5-50 μm [1]. The micro-focus X-ray source allows for projections rotated through 180-360 degrees scan to produce 3D reconstructed images and perform 3D structures inside or outside the samples. Nowadays, the evolution of micro-focus and nano-focus X-ray tube in addition to novel high sensitive detectors make high resolution laboratory CT systems possible, the voxel resolution can be improved to sub-μm scale [2]. Combination of micro/nano-CT system with histology or SEM (Scanning Electron Microscope) is quite popular in this field especially in bone and dental applications. The most important advantage of this technique is using this 3D technology to discover the 3D structure information, pore information, pore connectivity and osseointegration between implants and bone in animal models. For orthopaedic research, many researchers used micro-CT to get 3D information for disease models like osteoporosis [3], rheumatoid arthritis [4] and osteoarthritis [5]. In this topic, we will introduce how researchers use this novel technology in preclinical dental research and dental device development including novel dental implants development, dentin hypersensitive treatment, pulp damage treatment.

Dental Implant Development

Dental implant treatment is used to help replace a missing tooth. It needs to be successfully fixed in the bone and it is necessary to determine the implant stabilization and osseointegration, the connection between the living bone and the artificially placed implant. Researchers are going to proceed detailed 3D analysis especially for osteointegration during the development of dental implants. Previously, researchers used to use other conventional methods such as histology, Scanning Electron Microscopy (SEM), and Atomic Force Microscopy (AFM) which are available to study the bone–implant interface. Because metal material such as titanium in dental implants/screws may cause scattering problems during 3D scan. Recently, the improved software algorithms and hardware contribute better Signal Noise Ratio (SNR) and solve many image issues like reconstruction artifacts, beam hardening artifacts, reconstruction center errors and metal scattering. For example, we inserted the porous metal implants into rabbits and then use micro-CT to monitor the bone ongrowth, BIC (bone-implant contact) and bone ingrowth on bone/dental implants (Figure1)[6]. Researchers used to combine the internal 3D information with 2D histology and EDS (Energy Dispersive Spectrometer) for material mapping. This action can accelerate the progress of novel dental device development.

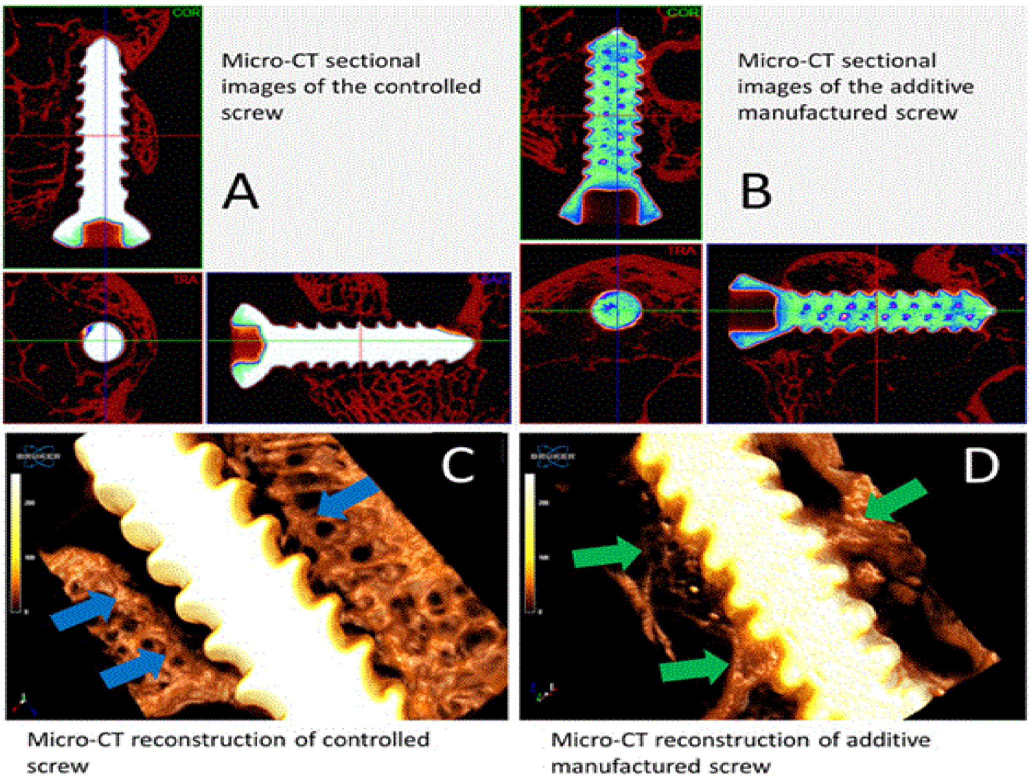

Figure 1: Micro-CT revealed the BIC (Bone-Implant Contact) in 3D images

Dentin Hypersensitivity Treatment Development

Dentin is a hydrated hard tissue and is the major portion of the tooth which protects the pulp. Dentin is the substance that lies beneath the enamel and the cementum in the tooth. Root sensitivity is a common disease due to gingival recession in which dentin was directly exposed to oral environment [7]. The hydrodynamic theory asserts that when dentin is exposed to thermal, chemical, tactile or evaporative stimuli, the movement of the fluid within dentinal tubule stimulates the mechanical receptors which are sensitive to fluid pressure, resulting in the transmission of the stimuli to the pulpal nerves ultimately causing the pain response [8].

There are many commercial products to prevent dental hypersensitivity, most of them try to block the dentinal tubule to inhibit the stimuli of oral environment. However, most of them can only superficially cover the surface of dentinal tubule (2-10 μm) and after the daily brushing, chewing or food erosion, the covered material would be lost and dentinal tubule would be exposed again. Researchers are investigating novel biomimetic materials which can be stable in the deep area of the tiny dentinal tubules. To achieve the goal, researchers need to monitor the whole 3D structure of dentinal tubule. SEM analysis showed that the diameter of dentinal tubule of human teeth is about 2.44 – 2.99 μm [9]. Recently, Zanette et al., used the phytography X-ray nano-CT to clearly demonstrate the 3D structure of dentinal tubule with the diameter of 1-2 μm [10]. This size range is a proper target for a high-resolution micro/nano-CT. In order to develop new long-lasting anti-dentin hypersensitive material, we previously used Sub-micron-CT (Bruker Skyscan 1272) combined SEM to display the 3D structure of dentinal tubule and find the developed bioactive calcium phosphate precipitated in dentinal tubule and found that novel mesoporous silica biomaterial derived crystallization blocked the dentinal tubule efficiently with the depth of 40-60 μm (Figure2) [11].

Root Canal Damage Treatment Development

Vital pulp therapy is now considered a pivotal treatment for pulp/root damage due to the development of Minimally Invasive Dentistry (MID), regeneration medicine and novel dental materials. However, we still need to develop the more efficiency and pulp capping material. Novel pulp capping material with growth factor to enhance the recovery of reparative dentin. Pulpotomy in rats is a good animal model for this research. Researchers can use the in vivo micro-CT (Bruker Skyscan 1176) to check the status including volume and calcium content of calcified tissue in rats. We can find that the increase of calcified area in different time periods (Figure 3) [12]. In addition, ex vivo nano-CT (Bruker Skyscan 2211)" can provide nano-scale resolution and better contrast, this character can be used for the development of

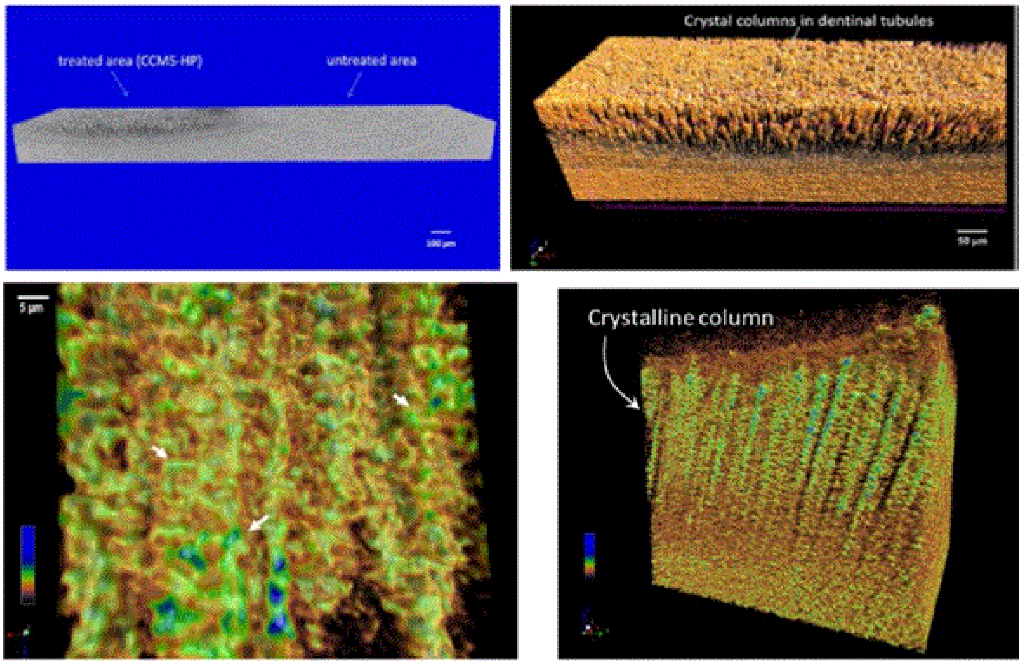

Figure 2: Micro-CT images showed the 3D information of crystal columns in dentinal tubules.

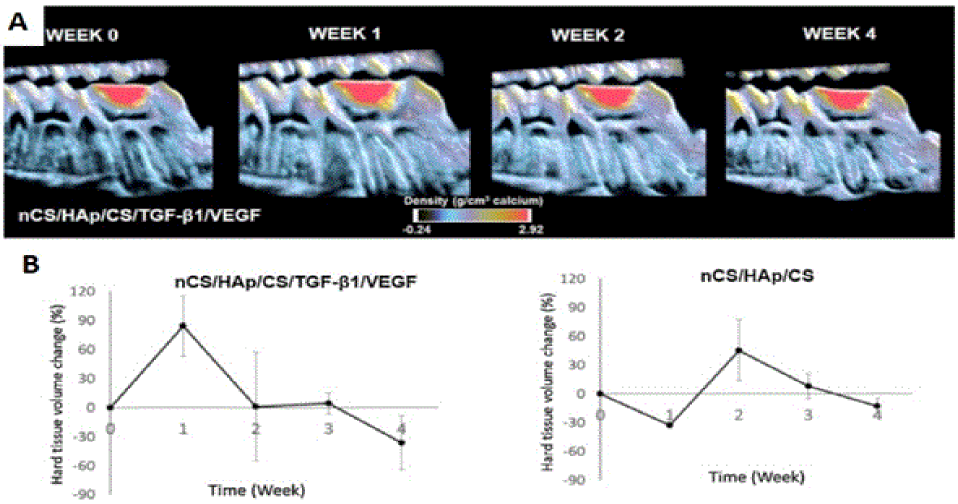

Figure 3: In vivo micro-CT showed 3D information of the calcified hard tissue volume and distribution at different time point.

complex micro-porous scaffold in this field. Researchers using nano-CT with SEM to monitor the 3D pore distribution and structure distribution for novel scaffold investigation (Figure 4) [13].These results showed 3D information of porosity, pore size distribution, closed pores, open pores and pore connectivity. This new scaffold will be used to endodontic therapy and researchers can used the in vivo system for the upcoming animal experiments. This is a good example to combine both high resolution ex vivo nano-CT and in vivo micro-CT

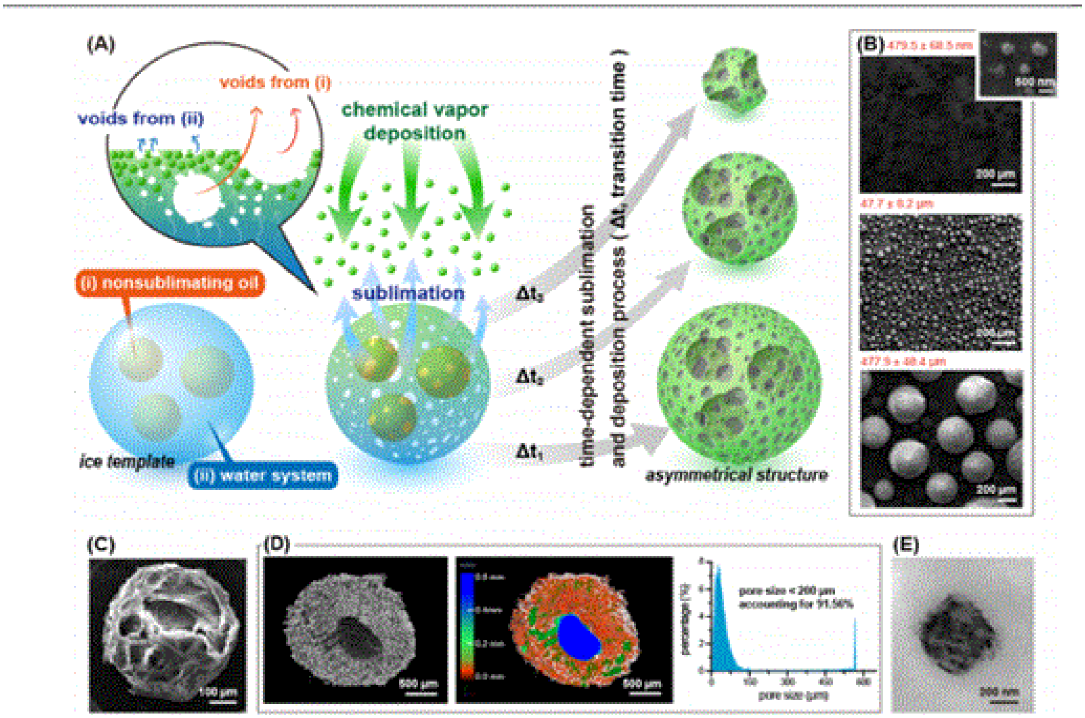

Figure 4: Nano-CT combined SEM showed the detail morphometric information of the pores.

Conclusion

Multiscale micro/nano-CT can provide 3D structure information and 3D analysis, researchers can also perform histology/SEM/mechanical test after non-destructive CT scan. Combining this technique with advanced 3D software can help professional researchers and clinical dentists to overcome the obstacle and achieve the goal for preclinical dental research and dental device development.

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