

## Nanotubes: A step further in implants

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### Abstract

Understanding the biocomplexity of cell behavior in relation to the topographical characteristics of implants is essential for successful osseointegration with good longevity and minimum failure. The aim of a brighter, better and long-lasting dental implant has led to the entry of nanotubes that can battle infection, improve healing, and help dental implants last a lifetime. Nanotubes have been in use in orthopedic implants but have not found its way yet into dental implants. This article reviews the advantages and application of nanotubes in dental implants.

**Keywords:** Carbon nanotubes, Drug delivery, Nanotechnology, Osseointegration, Titanium nanotubes.

### Introduction

The emerging fields of nanoscale science, engineering and technology, the ability to work at molecular level, atom by atom, to create large structures with fundamentally new properties and functions are leading to unprecedented understanding and control over the basic building blocks and properties of natural and man-made things. Understanding the biocomplexity of cell behavior in relation to the topographical characteristics of implants is essential for successful osseointegration with good longevity and minimum failure. The success of a dental implant largely depends upon the successful osseointegration.

#### History of nanotechnology in dentistry

Various predictions have been made based on the potential applications of nanotechnology in the field of dentistry. Nanotechnology's definition and vision is that the atomic-level precision afforded by molecular devices operating at the nanoscale was an inevitable technologic eventuality. This concept was first put forth by late physicist Richard P Feynman in the year 1959 but was echoed by Freitas in the year 2000.

The first nanotubes to be discovered by L. V. Radushkevich and V. M. Lukyanovich were the carbon nanotubes.

#### Nanotubes- What are they??

Nanotubes are nanometer scale tube like structures, which is a kind of nanoparticle. It may serve as a conductor or insulator depending upon the material it is fabricated with. It may be large enough to serve as a channel through which other nanoparticles may be channeled.

#### Need for Nanotubes<sup>(3)</sup>

The need for newer inventions and their application plays a major role in combating the failures of conventional techniques and materials associated with implant dentistry. So far it has been noticed that implant failures are mainly due to loss of osseointegration which is triggered by infections due to poor surgical technique of contamination of the host site, impaired healing

exhibited by the host site, and improper prosthesis and occlusion leading to overloading and ultimately failure of the implant.

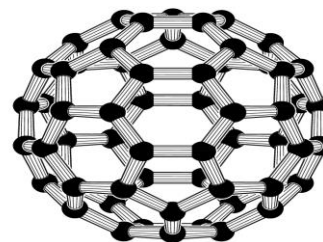
The entry of nanotubes into the field of implants is with the aim and vision of "brighter, better and a more long lasting implant restoration."

#### Types of nanotubes

There are various types of nanotubes available in the market, of which 2 types are of major importance in the field of implantology. They are:

1. Carbon nanotubes
2. Titanium dioxide nanotubes

Carbon nanotubes<sup>(4)</sup>: (Fig. 1)



**Fig. 1: Structure of carbon nanotube**

They were first synthesized by Endo in 1976 and in 1991; their detailed structural characterization was given by Iijima. They have found their way into various fields including the medical field. But their application in dental field remains limited due to lack of ability to control their diameter chirality, number of layers and their purity, since all these factors play a crucial role in their success.

There are various methods used for their manufacturing were put forth by Endo, which are:

1. Seeding method (Fig. 2)
2. Tip growth model (Fig. 3)
3. Floating reactant method. (Fig. 4)

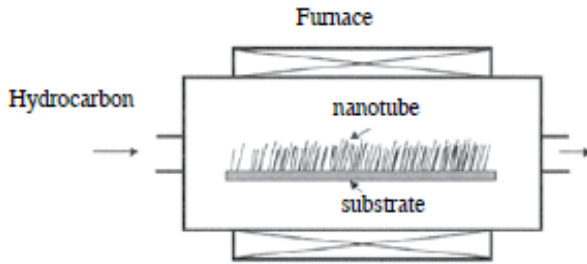


Fig. 2: Seeding method of carbon nanotube synthesis

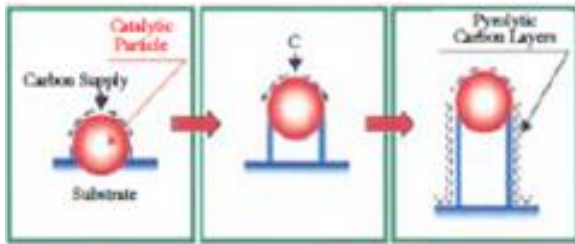


Fig. 3: Tip growth model

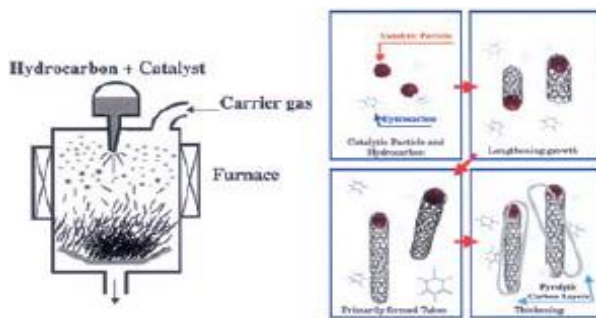


Fig. 4: Floating reactant method

Titanium oxide nanotubes (TiO<sub>2</sub>-Nt)<sup>(5)</sup> (Fig. 5)

TiO<sub>2</sub> is known to be a very useful non-toxic, environmentally friendly, corrosion-resistant material. They have a diameter of about 10-250nm and they exhibit size dependent cell interactions. Those with a diameter of 15nm have shown to strongly promote cell adhesion, proliferation and differentiation, whereas those with a diameter of 100nm were found to be detrimental as they induce apoptosis.

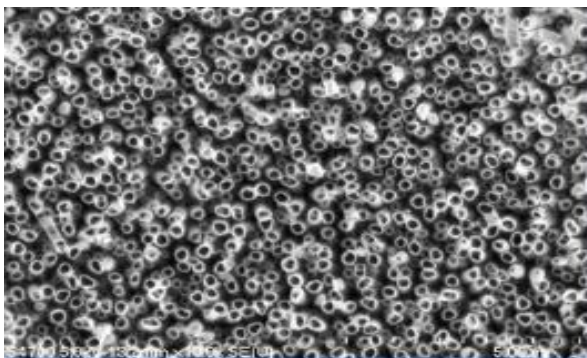


Fig 5: Cluster of TiO<sub>2</sub> tubes

TiO<sub>2</sub>-Nt is synthesized by electrochemical oxidation reaction of metallic titanium substrate under a specific set of environmental conditions. The synthesis is carried out by a low-cost parallel process: conventional electrochemical anodization<sup>(9)</sup> (Fig. 6).

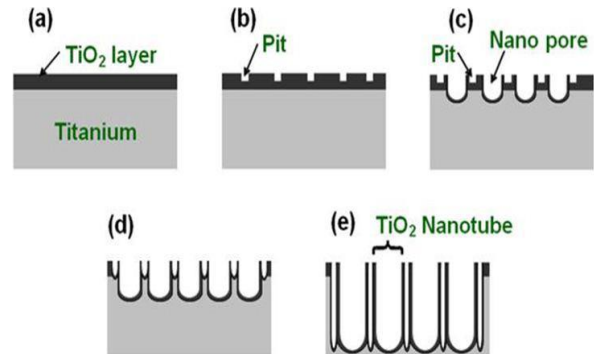


Fig. 6: Electrochemical anodization

The metals when, exposed to a sufficiently anodic voltage in an electrochemical configuration an oxidation reaction  $M \rightarrow M^{n+} + ne^-$  will be initiated.

Depending mainly on the electrolyte and the particular anodization parameters, essentially three possibilities for reactions exist:

- The  $M^{n+}$  ions are solvated in the electrolyte; that is, the metal is continuously dissolved.
- The  $M^{n+}$  ions formed react with  $O^{2-}$  and form a compact oxide (MO) layer if MO is not soluble in the electrolyte.
- Under some electrochemical conditions, competition between solvatization and oxide formation is established (leading to porous MO).
- Under even more specific experimental conditions, a situation is established where selforganization during the growth of porous oxide takes place; furthermore, under some specific conditions, disorganized rapid growth of TiO<sub>2</sub> nanotube bundles.
- Or formation of thick self-organized mesoporous layers can be observed.

Webster et al. reported that osteoblasts showed significantly greater adhesion to a nanophase surface compared to conventional aluminum and titanium surfaces.<sup>(2)</sup>

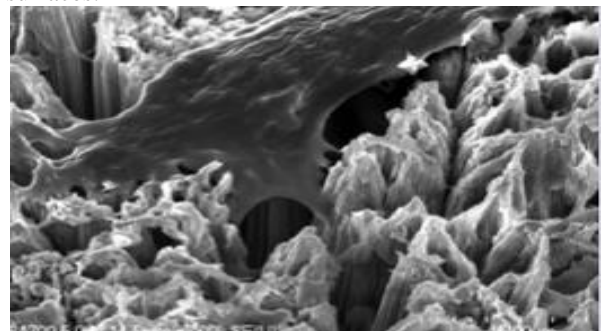


Fig. 7: Bone cell anchoring to a surface of titanium dioxide nanotubes

## Properties of TiO<sub>2</sub>

### 1. Cell response.<sup>(6)</sup>

Not only mesenchymal stem cells but also hematopoietic stem cells, endothelial cells, and also osteoblasts and osteoclasts show this size-selective response. Studies have shown that HAp formation can strongly be accelerated on TiO<sub>2</sub> nanotube surfaces compared with flat TiO<sub>2</sub> surfaces.

They are also shown to have the ability to modulate the macrophage and inflammatory responses.<sup>(7)</sup>

β-titanium oxide nanotubes promote faster acquisition and development of osteoblasts and bone tissues and have better bone regenerating ability after one week.<sup>(10)</sup>

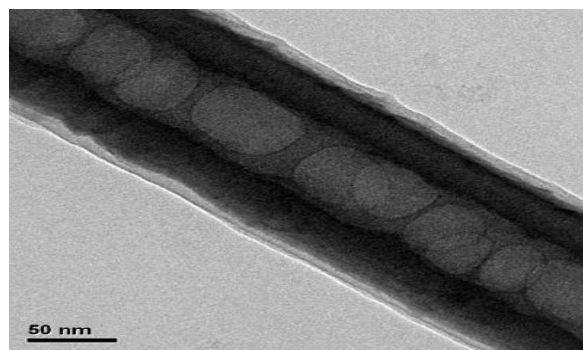
The adhesion/propagation of the osteoblast cells is significantly improved by the topography of the nanotubes with the filopodia of the growing cells actually going into the nanotube pores, producing an interlocked cell structure. Webster et al. reported that osteoblasts showed significantly greater adhesion to a nanophase surface compared to conventional aluminum and titanium surfaces. Nanotube surfaces can enhance collagen type I and BMP-2- higher implant bone contacts can be established.<sup>(11)</sup>

Nanotubes(50 nm diameter) were found to trigger the expression of the osteoblast-specific transcription factors, sp7 and Dlx and upregulate the expression of alkaline phosphatase (ALP).

Studies have revealed that miRNAs can help regulate osteoblast differentiation and osteogenesis. The expression level of miR-488 was significantly higher in cells grown on 50nm nanotubes.

### 2. Drug delivery system (Fig. 8)

The nanotubes can also be used to deliver drugs faster. Nanotube delivery assures direct release into the area where it is needed most, without much adverse side effects as seen with oral intake. The geometry of the TiO<sub>2</sub> nanotube arrays it can be used as a drug-delivery capsule if nanotube layers are separated (singled-out) and stabilized or it may be used as a drug-eluting coating on biomedical implant materials.<sup>(8)</sup> It takes advantage of the fact that long molecules attached to a TiO<sub>2</sub> surface can be released photocatalytically. Most recent work demonstrates that to achieve slow release, capping of drug-loaded tubular or porous systems with a biopolymer, such as poly (lactic acid), is required.



**Fig. 8: TiO<sub>2</sub> nanotube as drug delivery system**

The use of electrochemical anodization and Ag doping provides the required antibacterial surface properties against the selected periodontal pathogens, *A. actinomycetemcomitans*, *T. forsythia*, and *C. rectus*, resulting in reproducible antibacterial coatings on transmucosal parts of dental implants.<sup>(12)</sup>

### 3. Esthetics

The aesthetically enticing advantage of the TiO<sub>2</sub> nanotube is its **transparency**, especially when it comes to the white zirconia device.

## Conclusion

The advancement of dental implant technology has indeed come a long way since its experimental era 25 or 30 years ago. The world of dental implantology is constantly evolving and we will expect to marvel at more advanced technology, materials, and techniques. Nanotechnology not only offers a considerable reduction in healing time, rapid bone adhesion, and faster recovery, it also offers to improve the prevailing standards of dental care and overall quality of life.

Nanotechnology is an idea that most people simply don't believe - Ralph Merkle

But, if we can reduce the cost and improve the quality of medical technology through advances in nanotechnology, we can more widely address the medical conditions that are prevalent and reduce the level of human suffering.

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