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Review Article

Nanotechnology in orthopedics

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ABSTRACT

Nanotechnology has revolutionized science and consumer products for several decades. Most recently, its applications to the fields of medicine and biology have improved drug delivery, medical diagnostics, and manufacturing. Recent research of this modern technology has demonstrated its potential with novel forms of disease detection and intervention, particularly within orthopedics. Nanomedicine has transformed orthopedics through recent advances in bone tissue engineering, implantable materials, diagnosis and therapeutics, and surface adhesives. The potential for nanotechnology within the field of orthopedics is vast and much of it appears to be untapped, though not without accompanying obstacles.

1. What is nanotechnology?

Nanotechnology refers to the engineering of matter at a very small, molecular scale.[1] Specifically, nanotechnology deals with "dimensions and tolerances of less than 100 nanometers" and particularly with the "manipulation of individual atoms and molecules."[2] The field of nanotechnology has existed for several centuries but has expanded prolifically with the emergence of the Information Age.[2] In fact, early applications of nanotechnology can be traced back all the way to pre-modern times beginning with the crafting of glass for ceramic antiques.[3,4] By the mid-twentieth century, its use became integral in various fields of science, serving as the basis for instruments such as the field ion and atomic microscopes.[3] The field especially grew in breadth and recognition throughout the twentieth century. Of note, Richard Feynman's description of the field during a historic 1959 talk highlighted the immense capacity and potential of nanotechnology, leading to further exploration of its applications.[5,6]

"Nanotech," as it is often called, found its way into the marketplace by the early 2000s, allowing manufacturers to improve materials such as sunscreens, tennis rackets, and display screens for electronic devices.[3] In practice, the altercation of tiny molecules can make large changes; for instance, changing the girth of a guitar or tennis string can change the sounds and power of the instrument.[7] Today, nanotechnology remains present in various avenues of daily life and has also grown into an increasingly important role within medical research and practice.

2. Nanomedicine

The application of nanotechnology to medicine, commonly referred to as "nanomedicine," has been hailed as nothing short of revolutionary.[8] As most biological molecules are on the nanoscale, this type of technology has had much success and room for growth within the medical field. Nanotechnology has been used in its active state to change the mechanisms by which drugs are delivered and is being explored for its potential to serve as a scaffold for nerve regeneration, among many other applications.[8] Thus far, nanotechnology has proven particularly successful in transforming drug delivery and manufacturing as well as medical diagnostic tools.[9] As researchers learn more about the mechanisms and characteristics of medical nano-particles, these molecules have become increasingly known for their pharmacologic potential in improving drug synthesis and carriers as well as optimizing materials and reducing toxicity.[9]

Some benefits of nanotechnology that have already become apparent in medicine include permanent implantation of small devices, semi-automation of diagnosis and treatment, the quick suspension of new diseases, cheaper surgical tools, and the ability to replace certain organs.[10] Within cancer biology, nanotech has been used to deliver drugs such as doxorubicin in a way that shuts off cancer genes that normally allow cells to escape the drug.[11] Nano-equipped breathalyzers for diabetics have been developed to measure acetone levels in one's breath, providing an alternative to traditional finger-prick glucose testing.[12] Eye surgery has been robotized by nanomedicine, such as by the creation of a

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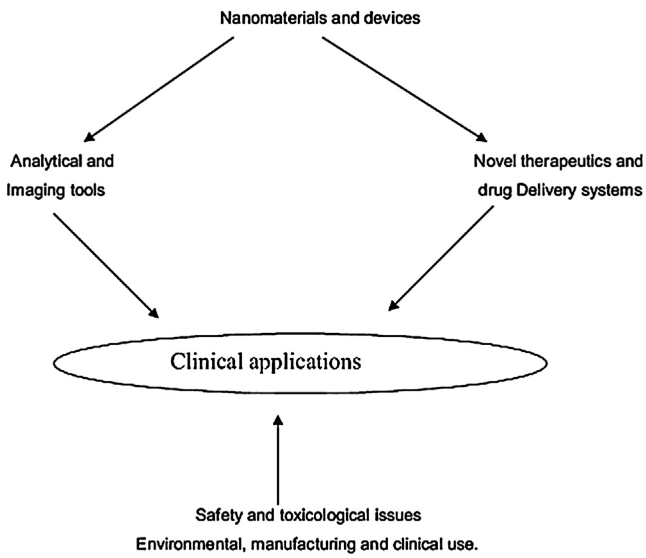

Fig. 1. The main dimensions in which nanotechnology can impact clinical practice. *Source*: J Indian Soc Periodontol. 2008 May–Aug; 12(2): 34–40 (http://creativecommons.org/licenses/by-nc/3.0/).

magnetically guided robot that allows for greater precision in surgery and dosage of drug delivery.[12] Nanotechnology has also been shown to be useful in detection of cardiac arrest, serving as the basis for a sensor that detects heart attacks via screening blood cells.[12] These examples are diverse but yet only represent a small fraction of the capabilities of nanomedicine, which has found a place in nearly every branch of medicine.

Nanotechnology has infiltrated a particularly successful niche within orthopedic surgery, where bench and translational research have uncovered several applications for manipulating nanoparticles.[13] Through many different avenues, these innovations allow for improved clinical capabilities. The main dimensions through which nanotechnology can be employed to make an impact in medicine and orthopedic surgery are displayed in Fig. 1.[14]

3. Current applications to orthopedic surgery

3.1. Nanotechnology for bones: implants and scaffolds

Implantable biomaterials have become essential components of orthopedic surgery, largely due to their ability to provide for osteointegration and to better stimulate healthy bone processes, especially in comparison to their standard material counterparts.[15] These essential improvements come at a time of great importance, as the aging population demands an increasing amount of orthopedic implants. For instance, the use of joint implants in the US is estimated to be over 600,000 per annum and growing.[16] Implants in orthopedics are used in a variety of ways across many areas of the body, but across the board, the functioning and purpose of implants are well served by the addition of nanomaterials.

Older methods of bone defect treatment, such as bone allografts and autografts, are still often employed, estimated to compose nearly 80% of surgeries related to bone defects.[17] However, these techniques are accompanied by many risks including infection, rejection by the immune system, and lengthy times for complete repair, especially for minor defects.[17] Implants using nanomaterials have improved upon many of those risks, but still, are not without fail. Implants derived from nanomaterials are not yet able to provide restoration of full functionality, nor do they often have longevity beyond a decade or two, at best.[16] Complete failure of implants may occur and can be particularly challenging, requiring extensive and expensive re-operations.[16]

Nevertheless, nanotechnology has proven incredibly beneficial for use in orthopedic implants, improving the treatment of many types of bone defects and orthopedic traumas. Several materials have been investigated and applied, leading to the use of a wide array of potential materials with their own unique properties and benefits. Examples of materials include gelatin, bioactive ceramics, biodegradable polymers, and polysaccharides such as agarose.[17] These nanomaterials are able to work well within the human body, as their physical properties and nanoscale features allow them to promote cell growth and tissue regeneration. The ability of these nanomaterials to mimic cellular environment is key in replicating mechanisms of cells, which also have nanometer dimensions and come together to form extra-cellular matrices.[17] Furthermore, implants with nanomaterials are able to form a greater surface area, which helps cultivate a healthy environment for bone growth and reduce infection rates.[17]

Oftentimes, the use of nanomaterials for implants will involve a coating to provide for scaffolding. Extracellular adhesion proteins have been shown to better interact with nanophase implant scaffolds than conventional implant surfaces. Greater absorption of these proteins provides an environment that is well-suited for osteoblast adhesion, as well as for bone formation and for fusion between implant and bone.[17] Furthermore, the use of nanotechnology for implants has been demonstrated to have many positive effects on clinical outcome, including decreasing the likelihood of infection and improving scar appearance.[18,19]

There are many instances in which nanomaterials have been shown to work effectively. For instance, they have been integral in total joint replacements (TJRs), for which aseptic loosening is a major cause of failure.[13] Nanotextured material has been shown to reduce this risk, particularly through improving osteoblast adhesion and osteointegration. Similarly, implants and scaffolds made of nanomaterials have shown to be effective across the body for bone defects. One study by Kon et al. demonstrated the effectiveness of nanocomposite implants in the treatment of osteochondral knee defects.[20] Scaffolds from nanomaterials have also been used to improve treatment of peripheral nerve injuries. Collagen scaffolds that are impregnated with silver are used to increase the amount of absorbed proteins that are useful for nerve healing, which ultimately speeds up the rate of nerve regeneration.[21] A study comparing the silver (nanotechnology) scaffolds to standard collagen scaffolds found that the use of nanotechnology increased the thickness of myelin sheaths and bettered nerve conduction.[21]

Nanomaterials have a wide array of uses for implants and scaffolding in orthopedics, ultimately contributing to faster recoveries, decreasing risks of surgery, and improving overall health of the affected area. However, many potential uses are yet to be investigated and there is still a lack of clarity surrounding long-term safety and clinical benefits.

4. Diagnosis

Another major use of nanotechnology in orthopedics is in the realm of detection. Specifically, nanotechnology has been used to diagnose bone diseases, such as Paget's disease, renal osteodystrophy, and osteoporosis.[15,22] This is often done using biosensors. These sensors are available in many designs and forms and can be implanted. Often, biosensors employ carbon nanotubes (CNTs), as their unique properties make the sensors strong and electrically conductive.[24]

There is a diversity of detection products employing nanotechnology and revolutionizing the field of orthopedics. For instance, for osteoporosis, techniques for diagnosis have great importance in