

1

Innovations in Medical Technology

Nanotechnology



A microscopic view of numerous red blood cells, appearing as small, circular, reddish-orange structures with a darker center, densely packed together. The background is a lighter, warm orange color.

Introduction

This is part of a short series of Eucomed booklets which are intended to be of assistance in informing stakeholders of innovation and developments in various fields of medical technology, and in communicating the importance and value of medical technology innovation for the patient, for the economy and for society in general.

What is Nanotechnology?

Nanotechnology is a term widely talked and written about today but what exactly does it mean? In one sense, nanoparticles and nanostructures are not new. They have been part of nature and of life for thousands of millions of years. What is relatively new, however, is our ability as humans to work, measure and manipulate at the nano-level across a range of disciplines like physics, chemistry and biology, and to be able to create new materials and products with novel nano-level characteristics.

“Nano” comes from the Greek word meaning “dwarf” and, in a mathematical or scientific sense, means one billionth (10^{-9}). Therefore, one nanometre (nm) is the same as one billionth of a metre (or about one eighty thousandth the width of an average human hair). In science and technology it is generally taken to mean working with structures in the size range 5 to 100nm.

“Nanotechnologies” refer to technological fields concerning the controlled manufacturing of functional “nanosystems” or the deliberate creation of nanostructures that results in the production of entities with at least one dimension in the “nano” scale.

Nanotechnology is rapidly becoming a ubiquitous technology with a potential to impact on every aspect of modern human civilization. Almost every aspect of human endeavour will be affected, such as agriculture and food, communication, computers, environmental monitoring, textiles, robotics, healthcare and medical technology. Indeed, it is in the final two areas that many observers consider that nanotechnology will have its most immediate and dramatic impact.

Why is Nanotechnology so Important for Medical Technology?



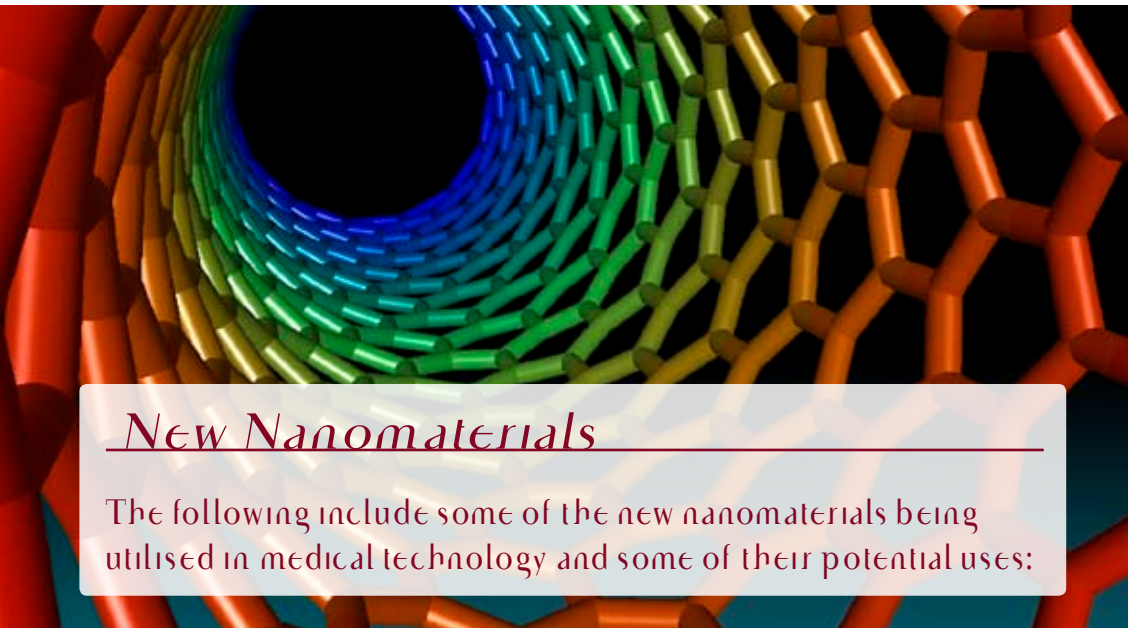
Nanotechnology will provide huge opportunities not only to improve materials and medical devices but also to create new “smart” devices and technologies. Nanotechnology is expected to accelerate scientific as well as economic activities in medical research and development.

Several medical devices that have already benefited from the application of nanotechnology are in use or are currently being commercialised. Examples include:

- contrast agents incorporating nanoparticles for greatly improved imaging
- bone replacement materials incorporating nanostructured materials allowing better integration in the body
- nanostructured biomaterials for use in scaffolds for regenerative medicine
- wound dressings incorporating antibacterial nanoparticles
- orthopaedic implants with nanocontoured surfaces to improve fixation in bone

These and other new “smart” applications will bring huge benefits in terms of early diagnosis, perhaps even at the stage of initial onset of a disease, more effective treatments and therapies, better prognosis, earlier recovery of the patient and return to a contributive role in society. Because of the combination of these factors they will make a contribution towards improved efficiency and use of resources in already stretched healthcare services faced with a demographically ageing population.

Some Novel Medical Technology Applications



New Nanomaterials

The following include some of the new nanomaterials being utilised in medical technology and some of their potential uses:

→ *Carbon-based Nanomaterials such as Carbon Nanotubes*

Carbon nanotubes are essentially elongated molecules, formed entirely from carbon atoms, that possess many very interesting and useful physical characteristics, e.g. electronic, mechanical, thermal and optical, that exceed those of conventional materials. One such property currently under research is their ability to elongate or contract in suitable electrolytes under very low voltages which may render them very useful as actuators or sensors in a variety of medical devices. Other potentially valuable characteristics are their possible use as sensors, e.g. for CO₂ monitoring in anaesthesiology, and their remarkable flexibility and resistance to breaking.

→ *Nanowires*

Nanowires differ from nanotubes in that they have no inner cavity. Semiconducting silicon-based nanowires are showing promise for the detection of viruses in solution and their capabilities in such applications may exceed those of other methods.

→ *Nanoporous Materials*

Nanoporous materials, e.g. of carbon-, silicon-, ceramic- or polymer-based materials, with holes in the region of 100nm have greatly increased surface area and can have extremely useful catalytic, adsorbent and absorbent properties. These may have valuable applications in implant technology or in drug delivery.

→ *Dendrimers*

Dendrimers are macromolecules with a regular and highly branched three-dimensional structure comprising three major components, i.e. core with a central cavity, branches and end groups at the periphery of the molecule. The end groups may be chemically tailored in a variety of ways to provide differing properties. Dendrimers are currently being developed for use in in-vitro diagnostics, as carriers for contrast agents and drugs (given that the end groups may be modified to facilitate targeting within the body), and as light-sensitive carriers where the payload may be activated by carefully-tuned frequencies of light which can be less physically damaging to tissues than other forms of energy.

→ *Quantum Dots*

Quantum dots are spherical nano-sized crystals and can be made from many semi-conducting materials, e.g., CdS, CdSe, CdTe, ZnS, PbS, as well as metals, e.g. Au, and various alloys. They generally range from 2nm to 10nm with a semi-conducting core and outer shell and surface layer, and take advantage of the quantum confinement effect to provide some unique optical and electronic properties. There are many potential applications in imaging and with biophotonic devices enabling diagnosis at very local and specific sites in the body

Surgery

In the surgical field, nanotechnology is already being applied in several areas, including the following examples:



➤ *Nanocoated Surgical Blades*

By means of nanoparticulate coatings onto specially prepared hard metal substrates, e.g. plasma polished diamond nanolayers, it is possible to manufacture surgical blades of extreme sharpness and low friction that are highly suited to optical- and neurosurgery.

➤ *Needles*

Nanocoated needles are now available for very fine suturing in demanding applications. Such needles have good ductility, exceptional strength and corrosion resistance.

➤ *Catheters for Minimally Invasive Surgery*

Nanomaterials, e.g. carbon nanotubes, have been successfully added to catheters used in minimally invasive surgery to increase their strength and flexibility and reduce their thrombogenic effect.

➤ *Optical Nanosurgery*

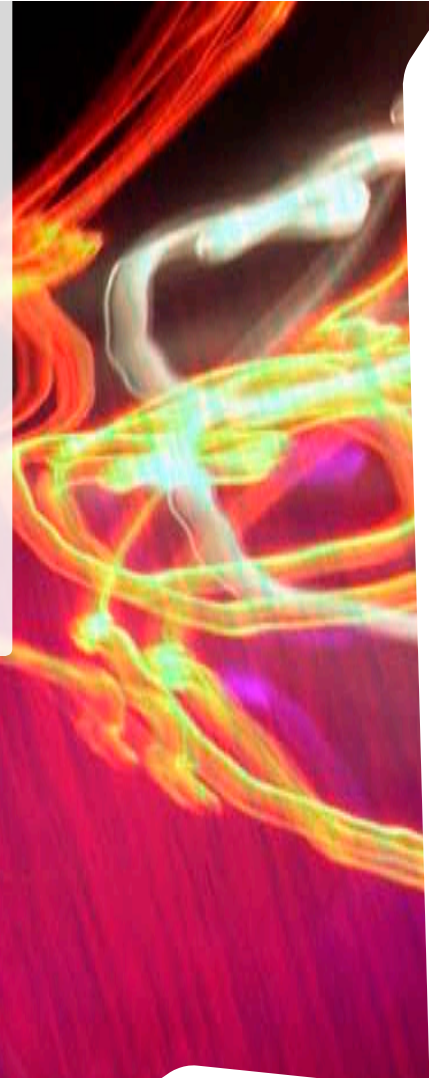
Nanotechnological tools such as “optical tweezers” and “nanoscissors” can be used at the cellular level for cell manipulation and immobilisation. Essentially these devices use the forces arising from the momentum of, for example, laser light at particular tuned wavelengths to precisely reposition minute objects by steering the laser beam. This opens up the possibility of medical or surgical procedures at the cellular level.

➤ *Nanocoated or Nanocontoured Implant Surfaces*

New coatings are being developed at a nanotech level that will greatly improve the wear characteristics, fixation and biocompatibility of surgical implants. Similarly, in combination with cells and tissues in the area of regenerative medicine, nanocontoured implant or scaffold surfaces can greatly influence the growth and proliferation of cells in beneficial ways.

➤ *Wound Management*

Nanoformulated materials, e.g. silver nanoparticles, are already being incorporated into “smart” textiles that can be used for improved wound dressings with antibacterial properties.



Biosensors and Biodetection

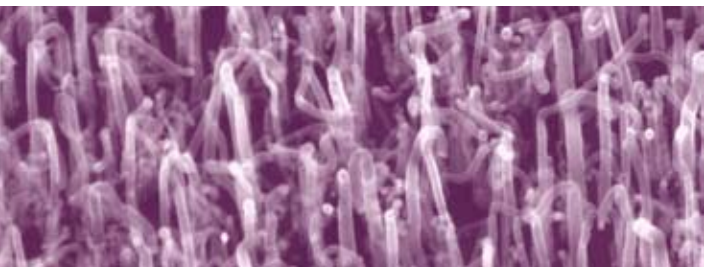
Nanotechnology is becoming increasingly used to detect metabolic changes very locally within the body with improved specificity and minimal invasiveness to the patient. The following illustrate some examples:

→ *Cantilever Arrays*

Nanomechanical cantilever arrays can be used to detect diabetes mellitus and cancer, as well as viruses, bacteria and fungi. Biomarkers are bound to the cantilevers and cause them to bend. Deflection of the cantilever beams can be directly observed with lasers or electronically. Alternatively, the shift in resonant frequencies caused by the binding can be electronically detected. Nanocantilevers that are able to detect a large number of different proteins at the same time, in real time, are under development and will greatly improve diagnostic capacities.

→ *Nanosensors*

The use of carbon nanotubes for blood glucose and CO₂ monitoring, and of nanowires for virus detection, has already been mentioned. Nanowire sensors have also been developed that can detect peptides associated with cystic fibrosis and, indeed, peptide nanosensors are capable of detecting a wide range of biomolecules and disease markers, e.g. dopamine and ascorbic acid for the diagnosis of Parkinson's Disease.



→ *Optical Sensors*

Surface enhanced Raman spectroscopy has many advantages for the chemical analysis in vivo of molecular substances including high specificity and the ability to use micromolar to picomolar concentrations of analyte. Raman spectrometry substrates could, in the longer term, be miniaturized to nanoscale devices that can be implanted subcutaneously enabling, for example, highly effective non-invasive glucose monitoring via the eye in diabetic patients.

→ *Nanoparticle Sensors and Detectors*

Single nanoparticles, e.g. of gold, iron oxide or silica functionalised with poly- or monoclonal antibodies, can be used for the detection of pathogenic biochemical markers or of individual bacteria.





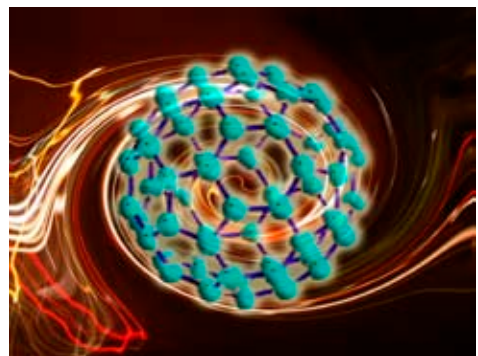
Imaging, in-vivo Diagnosis and Theranostics

Nanotechnology is set to play a massive role in the development of more specific, accurate and less invasive diagnosis of diseases and metabolic states. The size range enabled by new tracing and imaging agents based on nanotechnology allows for imaging down to the cellular, or even molecular, level. The most promising areas for imaging using nanotech-based agents are magnetic resonance imaging (MRI), ultrasonic imaging and optical imaging. These technologies offer the possibility of safer, less invasive and much more targeted and precise imaging and diagnosis. Combined with suitable targeting molecules and either drugs or other nanoparticulate or encapsulated materials, e.g. semi-metallics, this opens up also the possibility of combining, possibly very early, diagnosis with treatment, so-called theranostics.



In-vitro Diagnostics

The area of in-vitro diagnostic medical devices is one of great growth and potential for nanotechnology. The development of micro- and nano-fluidic systems allows for the use of tiny amounts of analyte and the degree of miniaturisation possible will allow for the development of true “lab-on-a-chip” devices capable of simultaneously carrying out dozens, or even hundreds, of analyses in virtually real time. Linked to other devices, this will allow for continuous monitoring of the patient’s condition and variations in treatment, e.g. drug delivery, to take account of the patient’s actual needs.





Summary

Nanotechnology is set to have an enormous impact on many areas in medical technology. It is providing tremendous opportunities not only to improve materials and medical technology products but also to create novel “smart” devices and technologies.

Set alongside this, further work is required, and is being carried out, to fully establish the risk/benefit characteristics of some novel nanomaterials, particularly the behaviour of nanoparticulate materials in the human body, due to the different characteristics of such materials to bulk materials. Such a systematic approach to safety is both normal practice in the medical technology industry and is required by regulation and should therefore reassure patients and medical professionals alike that the exciting new products becoming available are not only delivering better treatment but have been fully characterised in terms of risk and benefit.

