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Smart Materials and Structures for *In Vivo* Applications: Overview

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Summary

Smart behaviour occurs when a material can sense some stimulus from its environment and react to it in a useful, reliable, reproducible and usually reversible manner. A really smart material will use its reaction to the external stimulus to initiate or actuate an active response, for example to provide feedback via an active control system. This report provides an overview of the state of the art review on smart materials and structures for *in vivo* applications (Reference Number QINETIQ/EMEA/S&DU/TRP0801284). Information is provided on the active mechanism of the material, typical devices for which that material may be used, and the limitations of using the materials for *in vivo* applications. The full review also provides specific examples of smart devices and research teams currently involved in this area with associated references.

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1 Introduction

The field of *in vivo* applications and devices is extremely broad and an in-depth review of each subject area is beyond the scope of the review. In the context of this report, the term 'smart material' is used to describe a material that can respond in a useful way such as by shape change, release of drugs, or a change in the properties of an implanted device. The stimuli that such materials can respond to within the body, include changes in temperature or pH, amongst others.

For *in vivo* applications, the materials and devices in current use or under development that could be deemed to exhibit smart behaviour include the following themes:

- Shape Memory Materials – including the use of shape memory alloys (SMA) in surgery, therapeutics, cardiovascular, neurovascular, orthopaedic and orthodontic applications, and novel shape memory polymers (SMP) and foams, including biodegradable SMP's and magnetic shape memory materials.
- Hydrogels - including both regenerative medicine and tissue engineering (e.g. scaffolds for bio-artificial skin, bone, cartilage or substrates for tissue and cell engineering) and new therapeutics and intelligent delivery systems for drugs etc (e.g. controlled release systems that can be triggered magnetically, ultrasonically or enzymatically).
- Smart Responsive Polymers - including biodegradable polymers that respond to specific biological conditions, high purity polymers and tailored co-polymers with desirable functional groups, polymers precisely replicating selected properties, biomimetic polymers and hybrid and synthetic extracellular matrices.
- Devices and sensors - including hybrid sensor/biomaterial combinations that provide direct feedback on implant performance by monitoring (potentially wirelessly) physical and biochemical parameters at the bio-artificial interface. It also includes implantable micro-devices for medical diagnostics applications and imaging.
- Nanomaterials – including colloidal nanoparticles, dendrimers, semiconductor Q-dots, and tailored nanosurfaces.
- Surface coatings and treatments – including smart surfaces and surface coatings for biointegration, e.g. polymeric coatings for joint implants.

2 The use of Smart Materials *In Vivo*

This section comprises a summary of the key areas for applications involving smart materials and provides an overview of material type, typical devices incorporating each material and the issues that may limit the exploitation of each material for *in vivo* applications.

2.1 Shape memory materials: alloys

2.1.1 Mode of Operation

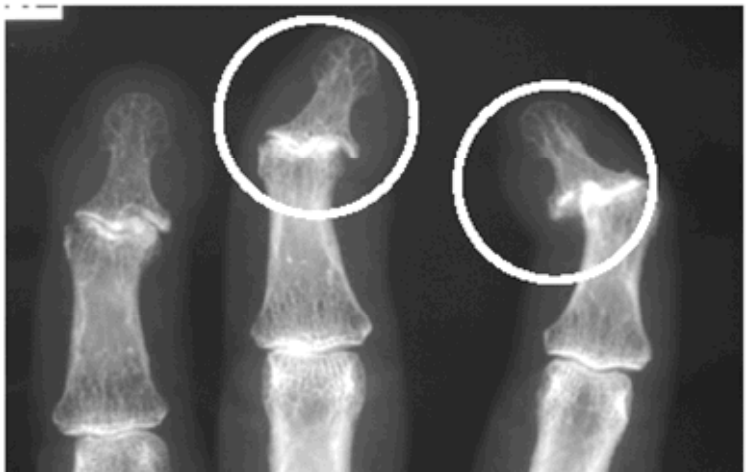
Shape memory alloys (SMAs) are metallic materials that can undergo a significant physical deformation upon the application of either a temperature or a magnetic field.

In thermally activated SMAs, the deformation is not caused simply by thermal expansion, but by a phase change in the material between austenitic (high temperature) and martensitic (low temperature) phases. Each of these crystalline phases contains unit cells of a different size and shape and hence conversion from one phase from the other results in a macroscopic physical deformation of the material. This deformation can be designed into devices to provide, for example, a change in length of a rod or radius of a ring, etc. By careful selection of the alloy composition, devices can be designed that switch phases at a temperature around that of the body, with potential strains of around 5-8%. The most common alloy used for thermal SMAs, Nitinol (a nickel-titanium alloy) is also biocompatible and hence can be used in a range of *in vivo* applications.

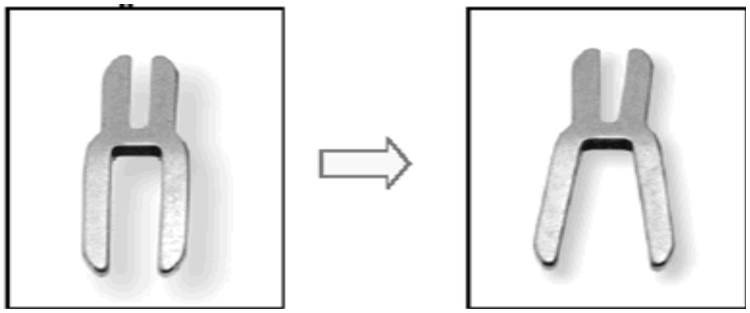
Magnetic shape memory alloys (MSMAs), also known as Ferromagnetic shape memory alloys (FSMAs) are stimulated by an external magnetic field. These materials are relatively immature in comparison to thermally activated SMAs, but potentially offer intrinsic strain levels of up to 11%. These materials exhibit both ferromagnetism, where a shape change is induced by a magnetic field and a two-way shape memory effect, caused by the presence of an austenitic/martensitic phase transformation regime in the material that forces the crystal structure into a tetragonal phase. Expansion in the material occurs in one direction (with a corresponding contraction in others) when the magnetic vectors in the tetragonal unit cells are forced to align with an external magnetic field. Typical MSMA alloys are based on the nickel-manganese-gallium system.

2.1.2 Typical devices:

SMAs have been used extensively in medicine for a number of decades. Early applications included bone clamps, guidewires and orthodontic wires. More recent developments have seen Nitinol alloys employed for use with self-expanding cardiovascular stents, stent grafts, catheters, filters (e.g. for use with carotid angioplasty for the safe extraction of embolisms), valve correctors and permanent implants for the dissolution of blood clots. Figure 1 shows an example of an SMA device used to correct deformation in the fingers caused by conditions such as arthritis. In contrast, the use of FSMAs in devices is currently limited. It is currently under research in a porous form to assess its potential for devices such as biomedical pumps.



a)



b) hot b) cold

Figure 1: a) X-ray showing deformation in finger joints b)ADS® implant in hot and cold shape, courtesy of Bernard Prandi, Memometal Technologies, Proceedings Of the International Conference on Shape Memory and Superelastic Technologies, Oct 3-7, 2004

2.1.3 Limitations:

SMAs are limited by a relatively low (~80GPa) modulus of elasticity. This makes the material unsuitable for applications where high elastic forces may be experienced. However, porous Nitinol has been developed with an elastic modulus comparable with that of bone. This has been developed to enable orthopaedic implants with optimised load transfer between the bone and the implant. Mechanical fatigue is a factor in high-frequency devices, but most *in vivo* applications tend to require only a few transformation cycles. SMA devices can suffer from thermal lag, where it takes the device some time to reach the activation temperature once the stimulus is applied. However, this is primarily dependent on device size; due to the small sizes inherent in *in vivo* applications, this should not be a serious problem.

Corrosion resistance is also an important factor that has been found to be dependent on the surface condition of the implant in question. Corrosion resistance can be dramatically improved by electropolishing to provide a protective surface coating of pure titania (TiO_2). Corrosion can be accelerated by the presence of dissimilar metals, so care has to be taken with the selection of, for example, radio-opaque markers or rivets made from materials such as gold or platinum.

FSMAs are still extremely immature and require significant development before *in vivo* devices are likely to be realised. In addition, the need to apply a high (~0.5-1T) external magnetic field will limit the applications such devices could be used. The

use of such a material as a permanent implant may also be prevented due the possible effect that common diagnosis techniques, such as MRI scanners, could have on an implanted device.

2.2 Shape Memory Polymers:

2.2.1 Mode of operation:

Shape Memory Polymers (SMP) are linear chain copolymers that change their shape to correspond to changes in temperature or changes in stress. SMPs have been developed more recently than SMAs and have several advantages over the alloys, providing larger deformation (~300%), ease of processing, shape stability, flexibility and ease of delivery. Their transition temperatures and mechanical properties can be varied to a wide range with only small changes to their chemical structure and composition. The polymers contain two or more types of regions with different thermal properties and generally have a very sharp transition between their glassy and rubbery states. These materials work by being 'trained' in their high temperature state (above their glass transition temperature, Tg). Once cooled below the Tg, these materials can be mechanically deformed into temporary shapes, but can revert back to their original trained shape on heating back through their Tg. As with SMAs, these materials can be designed to transition at, or slightly above, body temperature, making them suitable for *in vivo* applications. To ensure biocompatibility, much of the ongoing development work is looking at producing co-polymers from materials that are already used for applications such as drug release.

In addition to thermally-activated SMPs, research is underway in the US on SMPs that can be activated via stimulation with ultraviolet (UV) light. These materials contain photosensitive groups that are grafted onto a polymer network. Upon application of both a mechanical stress and UV of a specific wavelength, temporary cross-links are formed in the structure. Upon removal of the stimuli, the cross-links cause the polymer to maintain its elongated structure. The polymer can be returned to its original state by exposing it to light of a different wavelength that destroys the cross-links. Development work is also underway in Germany on SMPs that can be triggered remotely by magnetic fields.

Shape memory rubbers are under development in the US, that maintain their rubbery state at room temperature, as opposed to going through their glass transition temperature around this point. These offer the potential for a very slow, controlled transition from their deformed shape to their trained 'memory' shape, by utilising the formation of temporary hydrogen bonds in the material under mechanical stress. The degree of hydrogen bonding that can be produced in the material can be adjusted by tailoring the composition of the rubber, as bonds are formed by the presence of specific active groups in the material. The speed of transition from deformed to trained shape is dependent on natural degradation of the hydrogen bonds.

2.2.2 Typical devices:

SMPs are very much in their infancy when compared with SMAs, so little information is available on devices approved for *in vivo* applications. However, areas under development include 'smart' sutures for optimised knot tightening to prevent tissue necrosis and intelligent stents. These stents are capable of taking many different forms which allows shape optimisation throughout a medical

procedure (i.e. a different shape for insertion, deployment and withdrawal). Shape memory rubbers (a distinct form of SMPs) are also being developed with applications such as 'smart' sutures in mind.

2.2.3 Limitations:

'Traditional' SMPs (i.e. those that go through the Tg for transformation) can be limited whilst in their glassy phase by brittleness and opacity, therefore will not be suited to many permanent implant applications. Although they are capable of much higher strains than SMAs (300% cf ~5-8%), their blocked force capability is very low, therefore they are unsuitable for load-bearing applications. These materials are also relatively immature, and significant de-risking needs to be undertaken for them to be approved for *in vivo* use. Much of this risk is, however, mitigated when the systems under development are based on known biocompatible and biodegradable materials.

2.3 Hydrogels:

2.3.1 Mode of operation:

Hydrogels are engineered materials that absorb or release fluid in response to physical or chemical stimuli such as humidity, pH, temperature, pressure, solvent composition or electrical fields. They are three-dimensional (3D) cross-linked polymers, or interpenetrating networks, containing hydrophilic material. They may be neutral, ampholytic or anionic or cationic gels and may be amorphous, semi-crystalline or have a hydrogen bonded 3D structure. Hydrogels can be genetically engineered, reversibly self-assembled in precisely defined three-dimensional structures (as depicted in Figure 2) and manufactured to have controlled degradability. These materials are most effective for controlled drug release, and as scaffolds and substrates for tissue regeneration, since they can be used to encapsulate and release items such as chemicals, cells and growth factors. The gels are insoluble in water but are hydrophilic polymers that are highly absorbent, have high water solvent content and have high porosities that enable the diffusion of cells and molecules.

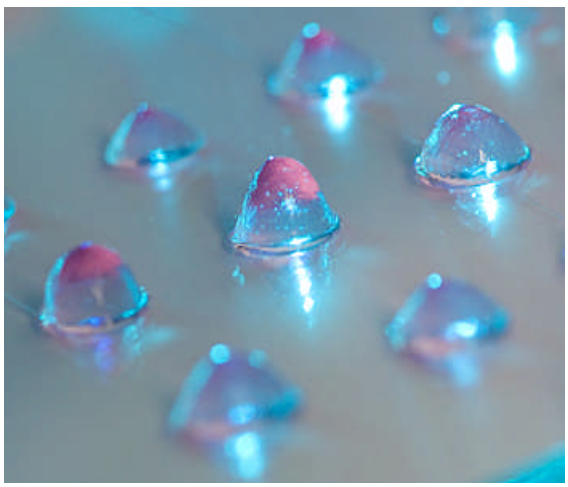


Figure 2: Self-assembling Peptide Hydrogel

Courtesy: University of Delaware

Considerable research is underway on hydrogels based on either polysaccharides or peptides. These materials can be engineered to respond to one or more of the stimuli listed above in addition to being able to respond to specific molecules, such as glucose, enzymes or antigens. In addition to their ability to contain and release chemicals, these materials are also of interest for their ability to assemble and disassemble in the presence of particular stimuli.

2.3.2 Typical devices:

Hydrogels have the potential to be used in a range of applications, including cosmetics, prosthesis, artificial valves, artificial tendon materials, wound-healing, artificial skin, biosensors and prosthetic reconstruction materials. 'Oscillating' hydrogels are under development for potential future use in pulse generators or micro-pumps.

2.3.3 Limitations:

By their nature, hydrogels are only capable of providing small amounts of mechanical force. This has been overcome to some extent by developments in hydrogels formed from dextran (a polysaccharide) with maleic acid for the release of high molecular weight proteins. Response times can also be fairly slow, which can be an advantage for some drug delivery requirements, but is a significant hurdle to be overcome if the materials are to be used for example as biopumps. Biocompatibility has also been resolved for some systems, but not all.

2.4 Smart Responsive Polymers

Whilst not inherently 'smart' by the definition of this report, the materials described in this section are triggered by external stimuli such as a biological or chemical effect. These materials are of critical importance for *in vivo* applications and hence are included in this review.

2.4.1 Mode of operation:

A number of system responsive, or "smart", polymer materials and polymer-based "devices" are under active development and currently exist at various levels of technological maturity. These include:

- Biodegradable polymers that respond to specific biological conditions,
- High purity polymers and tailored co-polymers with desirable functional groups
- Polymers precisely replicating selected properties ('tailored polymer')
- Biomimetic polymers
- Hybrid and synthetic extracellular matrices

Natural and synthetic biodegradable polymers have been developed that incorporate controlled copolymerisation areas. These degrade in the presence of specific biological materials and can therefore be used for applications such as absorbable sutures and drug-release systems.

High purity polymers are bioresorbable materials that are under development for implanted products. In these materials, the properties of the polymer are highly

tailored for specific applications and are produced by a combination of genetic engineering and selective polymerisation of a wide range of monomers and are under investigation for degradable products.

Tailored polymers that mimic the self-assembly techniques used in nature are under investigation. Polymer scaffolds are placed into a chemical solution containing the molecules required to attach to the scaffold. These molecules can be selected depending on the application for which the material is to be used; hence the polymers can be optimised. Polyrotaxane supramolecular structures are a group of intelligent biomaterials with architecture designed to perform dynamic molecular functions similar to those of natural tissue. Such molecular assemblies are under investigation for applications such as artificial muscles, whereby the functional groups are excited to move along the polymeric backbone under the application of a stimulus such as temperature.

Biomimetic polymers, such as those based on spider silk are under development for applications such as nerve regeneration and microvascular networks. The nature of biomimetic polymers varies on the application under consideration. An example of how these materials could be employed includes the effort being made to replicate proteins such as 'host-defence peptides' which are produced as part of the immune response to hostile bacteria. In this instance, the polymers produced are attracted to the bacteria's negatively charged membranes, which are subsequently destroyed by polymeric re-ordering. These polymers do not attack neutrally charged animal cells, and are currently under examination for approval by the US Food and Drug Administration.

The molecular engineering of cell-instructive artificial extracellular matrices is a powerful tool in the investigation of cell behaviour, enabling the complex processes of tissue formation and regeneration to be studied. The extracellular matrix (ECM) is a vital component of cellular microenvironments, providing cells and tissues the 3-D architecture they need for normal growth and development. The function of the ECM is to promote key signalling pathways for enabling cell proliferation, differentiation, and cell-cell and cell-tissue interactions. Tissue engineering, stem cell biology, and cancer biology rely critically on ECM and the correct three-dimensional microenvironment for the development and success relevant therapies. A new class of biologically-inspired polypeptide biomaterials has been developed and tested in the context of cell culture, stem cell biology and tissue engineering.

2.4.2 Typical devices:

Biodegradable polymers are under development for a wide range of applications including degradable sutures, drug delivery microspheres and stents, gene carriers for stimulated or accelerated healing and scaffolds for the regeneration of damaged tissues.

High purity polymers are under evaluation for use in a variety of medical devices such as bioengineered heart valves, orthopaedic fixation devices and general surgical products such as sutures, patches and meshes. Subsequent products are expected to include degradable stents, tissue engineering scaffolds, drug delivery systems, ultrasound agents, nerve guides and medical adhesives.

Tailored polymers are being synthesised for applications such as drug delivery systems, biosensors, artificial muscle and for *in vivo* oximetry. The range of applications for biomimetic materials is huge, including artificial muscle, nerve conduits and artificial lumbar discs with graduated modulus to replicate the physiological transfer of loads to adjacent vertebrae.

2.4.3 Limitations:

With any degrading material, toxicity is a prime concern as the degraded products will be released into the body. Materials such as polylactic acid may contain regions with a high degree of crystallinity that can result in undissolved regions, potentially leading to an inflammatory reaction. Reduction in crystallinity results in a corresponding reduction in mechanical strength. Many polymers are also not compatible with cell-attachment, so the number of applications for which they can be used are limited. For example, degradable copolymers of polyglycolic acid and polylactic acid have been developed for sutures and bone pins, but these are unsuitable for tissue-engineering scaffolds due to their inability to support and sustain cell attachment and growth. Some synthetic polymers can change the pH of the local area through erosion, which can adversely affect proteins. Natural polymers can suffer from high solubility in water, causing, for example, faster drug release than required, though this area is being addressed with the development of microspheres that can provide a sustained controlled release of drugs via enzyme degradation.

2.5 Devices and Sensors

The following section describes some of the many devices that are either commercially available or under development that either incorporate traditional 'smart materials', or offer the potential for smart behaviour. The materials incorporated in these devices include piezoelectrics, electroactive polymers (EAPs), fibre optics, electrorheological fibres, MEMS and colour-changing materials.

2.5.1 Mode of operation:

Piezoelectric materials can operate in one of two ways; they either produce an electrical charge when exposed to mechanical force, or can produce an intrinsic strain under the application of an electric field. In the field of *in vivo* medical devices, this has led to them being used predominantly as sensor devices. There is interest in using piezoelectric materials as microactuators, but the materials that are suitable for *in vivo* use (lead-free, generally polymeric or thin-film) do not have a high load-carrying capacity.

Electroactive polymers (EAPs) operate in one of two ways. So-called 'dry' EAPs produce an intrinsic strain on the application of an applied electric field. 'Wet' EAPs produce an intrinsic strain as a result of ion migration when in the presence of certain chemicals, for example the strain can be stimulated by a change in local pH.

Fibre optics can be used for the detection of, for example, intrinsic strain (the change in diameter of a fibre induces a change in the wavelength of transmitted light), but they have also been developed for use as pH sensors. These generally work by cladding the fibre with a pH sensitive chromophore. This material changes light absorption characteristics as a result of a change in pH (for example, absorbed light may change from purple to green). These changes in absorbance spectrum can be measured to give a direct measurement of pH. As fibre optic sensors have a smaller diameter than traditional amperometric devices, they are suitable for insertion, for example, into arteries for real-time blood pH monitoring.

A number of materials exist that are capable of changing their flow properties when exposed to external stimuli of electric (electrorheological) or magnetic (magnetorheological) fields, or by changes in pH in the immediate area. An example is that of polyacrylonitrile (PAN) fibres; these are under investigation for use as artificial muscle as they are capable of undergoing deformation when

stimulated by a change in pH, and are capable of load-bearing when bundled together. Magnetorheological fluids have also been investigated for feedback and correction devices for prosthetic knees. These fluids are free to flow under normal conditions but, when subjected to a magnetic field, their magnetic particles align to stiffen the fluid.

Polymers capable of mimicking cell membranes are under development, some of which can respond to the presence of pathogens by displaying a change in colour. One example is polydiacetylenic materials with cell surface receptor gangliosides and sialic acid residues. This has been used for the colourimetric detection of bacterial toxins and the influenza virus.

Sensors incorporating small amounts of DNA are under development to enable the continuous and selective detection of biological molecules. Such devices can be used for the identification of specific gene sequences, to enable early detection of illness. It is hoped that they may also be developed sufficiently to enable tailoring of medication to match a patient's specific genetic profile.

Microelectromechanical systems (MEMS) are of interest for applications such as blood flow monitoring and drug delivery. Drug delivery is enabled by the use of microprocessors or wireless telemetry to open reservoirs in materials such as silicon, in order to release the drug or substance contained therein. As this mechanism is completely controlled *ex vivo*, it is possible to vary the dosage with time as required. Similar mechanisms can be employed for the production of microactuators.

Kinesins are tiny motors that run along tubulin protein polymer tracks (microtubule highways about 25nm in diameter), powered by hydrolysing adenosine triphosphate (ATP). They are of interest for powering MEMS devices and for manipulating and assembling nanoparticles into useful structures. One application under investigation has used DNA oligonucleotides attached to the surfaces of microtubules to enable the transport of kinesin-coated silica beads. It is expected that 2D and 3D structures can be built from microtubules that will allow kinesins to transport biomolecules, nanoparticles, cells and other objects. The building of parallel arrays will also enable many more MEMS operations.

2.5.2 Typical devices:

Piezoelectric materials are currently in use as feedback sensors for monitoring the loads in an artificial knee and sensors for monitoring cardiac activity for pacemaker control. EAPs are of interest for steerable vascular devices, releasable clamps, electrically controlled substance release and micro-muscles. Fibre optic pH sensors are of use for the real-time monitoring of blood pH during surgery and critical care, gastro-oesophageal pH monitoring for the assessment of peptic ulcers, cerebrospinal fluid monitoring and monitoring of exocrine glandular sections. Electro and magnetorheological systems are of interest for artificial muscle and prosthetic control and for artificial sphincters and pacemakers. MEMS are of interest for drug release, blood flow monitoring, pace makers and microactuators.

2.5.3 Limitations:

Piezoelectric polymers and EAPs are limited in the amount of mechanical force they are able to apply. In addition, if they are required to act as actuators, rather than as sensors, they require high electrical drive fields (of the order of kV/mm). However, in micro-actuators, where the active material in question is relatively thin, the amount of voltage required can be reduced to realistic levels. Many of the devices listed above require a complicated feedback system, for example apparatus

capable of detecting the shift in absorbance spectrum of the pH sensitive fibre optic sensors. In many cases, these are not stand-alone devices. As with any *in vivo* device, all of the devices and sensors described herein are subject to strict regulatory control.

2.6 Nanomaterials

2.6.1 Mode of operation:

Nanomaterials have the potential to be used in an extremely wide range of *in vivo* applications due to the advantages of their high surface area to volume ratio. They can be used as substrates for the attachment of active materials, such as enzymes, antibodies and nucleic acids. One mechanism employed by such devices is the generation of an electrical charge by a biochemical reaction, caused when the active materials are triggered by a target molecule. The addition of luminescent markers enables the detection of such modified nanoparticles when stimulated by single wavelength light. As the nanoparticles can be designed to be selectively absorbed by tumours, for example, they can be used for the early detection of cancers.

Carbon nanotubes are under development for use as microactuators for *in vivo* applications. These materials are capable of producing intrinsic strains under the application of an electric field. These generally require low power, are efficient at converting electrical energy to mechanical energy and have a low mass.

2.6.2 Typical devices:

The addition of active materials to nanosize particles can ensure that they are selectively absorbed by specific areas of the body. A good example is that of cancer therapy, whereby the nanoparticles are selectively absorbed by a tumour. Once absorbed, the particles can be heated by the action of an alternating current, resulting in the destruction of the tumour cells without causing damage to peripheral tissue. The absorption of active nanoparticles can also be used for cancer detection and for the detection of neurotransmitters in the case of e.g. Parkinson's disease. Carbon nanotubes are of interest for actuation mechanisms, such as for artificial muscle. Carbon nanofibres are also used as tissue engineering supports.

2.6.3 Limitations:

Toxicity is of prime concern with nanoparticles, as their small size is of concern when interacting with biological components such as cells, particularly with regard to potential long-term effects of the particles (e.g. do they stay where they are supposed to be, what happens when the cells they are absorbed in are destroyed etc). There is also a public preconception regarding the use of nanoparticles that may need to be overcome (the so-called 'grey goo' effect, whereby the end of the world is caused by self-replicating robots based on molecular nanotechnology). Nanoparticles and carbon nanotubes can also be extremely costly to produce, particularly in large, reproducible quantities. Low cost alternatives are under development. As with any emerging field, toxicity, biocompatibility and biodegradation effects need to be addressed.

2.7 Surfaces and Coatings

Surface coatings play an important role in promoting biocompatibility and biointegration. Coatings have been demonstrated that, for example, can provide

hydrating lubricating layers for hip implants. Diamond has been coated onto devices such as artificial heart valves, prosthetics and joint replacements for improved tribological characteristics. However, this can lead to clotting problems as diamond attracts coagulating proteins, plus its hardness can cause damage to peripheral tissue. Work is progressing on producing a biocompatible surface based on water molecules for use in conjunction with diamond. Polymeric coatings are also under development to improve the biocompatibility of e.g. haemodialysers, oxygenators and percutaneous glucose sensors.

3 Conclusions

Currently, cardiovascular and orthopaedic products make up the largest segment in the medical devices market while wound care therapies represent a growing market. Bioresorbable scaffolding for tissue engineering and cell research are finding their way into the medical marketplace. Targeted and controlled release drug delivery is becoming more established. The next generation of therapies will depend on smart delivery concepts that make use of the regenerative potential of stem cells, morphogenetic growth factors and biomimetic materials in order to expand clinical potential. In addition, there is a trend towards making implants or drug delivery devices that are immunogenic and those that promoting healing and biointegration.

It is evident that devices for *in vivo* applications can be manufactured from a range of materials using a variety of techniques including self-assembly, guided growth and bio-nanotechnology methods. The range of applications of these materials in the biomedical field has become increasingly diverse. Shape memory materials continue to provide an important basis for a range of smart applications. The methods for controlling shape change have widened to include heat, light and magnetic actuation allowing greater scope in device design and flexibility. Hydrogels are an increasingly valuable technology for smart delivery systems and the creation and control of biodegradable scaffolds for tissue engineering. They are made from a variety of novel materials, such as peptides and polyrotaxanes, using a number of fabrication techniques including guided self-assembly. It is likely that they will remain a central platform for the design and delivery of new smart therapeutic applications.

A number of system responsive, or “smart”, polymer materials and polymer-based “devices” are under active development and currently exist at various levels of technological maturity. Such materials can be designed and synthesized at the molecular level by attaching well characterised and tailored functionalities. Devices and sensors for bio-monitoring of *in vivo* processes remain an area of active development. Hybrid sensor/biomaterial combinations are being developed to provide direct feedback on implant performance by the monitoring (potentially wirelessly) of physical and biochemical parameters at the bio-artificial interface.

Nanotechnology and bio-nanotechnology is leading to improved medical treatments from targeted drug delivery and improved diagnosis to better materials for sensors and implants. Biodegradable nano-engineered scaffolds and surfaces made from a range of materials are being used to improve implant performance, such as better biocompatibility or fixation into tissues such as bone, in order to encourage cell growth and differentiation into more complex tissues. Alongside the undoubted advances in both materials and devices there remains a need to better inform investors, the medical profession and the public of the potential for smart biomaterials in order to expedite the commercial exploitation of these technologies. Smart biomaterials can help to improve the quality of life for patients through a diverse range of medical applications by providing the means for better integration and reducing trauma. Networking with medical professionals to better understand their healthcare requirements will help to further exploit the current and emerging range of smart biomaterials.