Journey to the Nano World

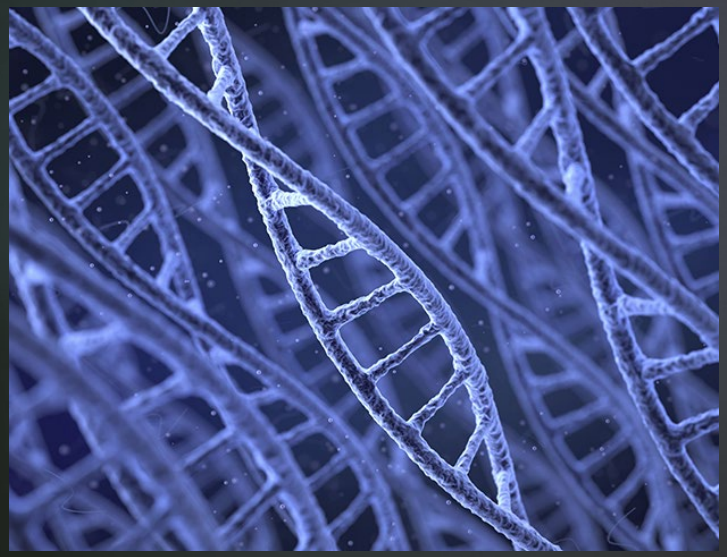
CHAPTER 3: APPLICATIONS OF NANOTECHNOLOGY

What you will be learning in this chapter…

- **Part 1: Consumers Electronics Products**
- **Part 2: Water Technology**
- **Part 3: Defence and Security**
- **Part 4: Life Science and Medical**
  - Biopharmaceutics
  - Implantable materials and devices
  - Diagnostic Tools
  - Textile and Wound Care products

Nanotechnology in Life Science and Medical Industry

- According to BCC Research (www.bccresearch.com), the global market for nanoparticles in the life sciences is estimated at over $29.6 billion for 2014.
- Market is forecast to grow to more than $79.8 billion by 2019. The biggest increase will come in the area of drug delivery systems.



Nanotechnology in Life Science and Medical Industry

Biopharmaceutics

Drug Delivery

1. Drug Encapsulation
2. Functional Drug Carrier

Diagnostic Tools

1. Concentris Nanocantilever
2. Nanomix, Inc.
3. Imaging
   - Nanoparticle probes
   - CNT X-Ray

Implantable Materials and Devices

Tissue Repair and Replacement

1. Implant Coating
2. Tissue Regeneration Scaffolds

Implantable Devices

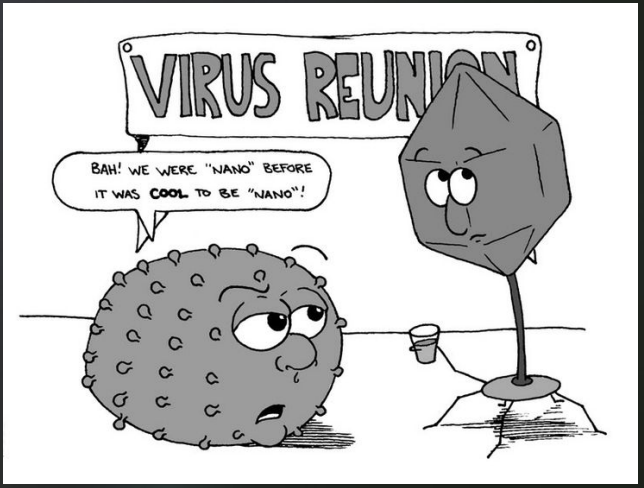
1. Cancer Detection Sensor
2. Pacemakers and hearing aids
3. Microchip-based drug delivery system

Textiles and Wound Care Product

Antimicrobial textile surfaces

Wound care products

1. Alltracel's m·doc™



Biopharmaceutics

Drug delivery

Flaws in conventional drug delivery system:

- Highly toxic drugs cause **harsh side effects** due to decomposition during delivery to the targeted site in the body.
- Rate of release at destination not well controlled leads to **decrease in efficiency** of the drug.

Nanoscale particles/molecules are developed to improve the bioavailability and pharmacokinetics of therapeutics.

Drug encapsulation -- Incorporation of Nanotechnology:

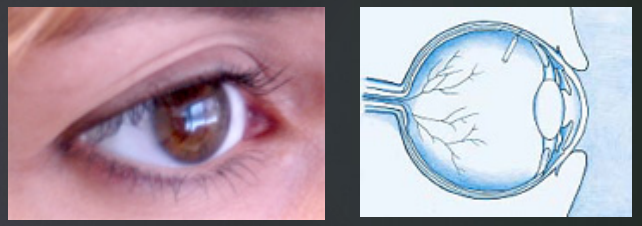
- Materials are made up of Nanoparticles in the size of 1-100nm
- larger surface area for same volume
- smaller pore size
- improved solubility
- improved diffusion and degradation characteristics.

Biopharmaceutics

Drug delivery - Drug encapsulation – Neurotech

Delivery of therapeutic factors (proteins) to the back of eye to treat:

- Retinal degeneration
- Vascular proliferation
- Ocular inflammation



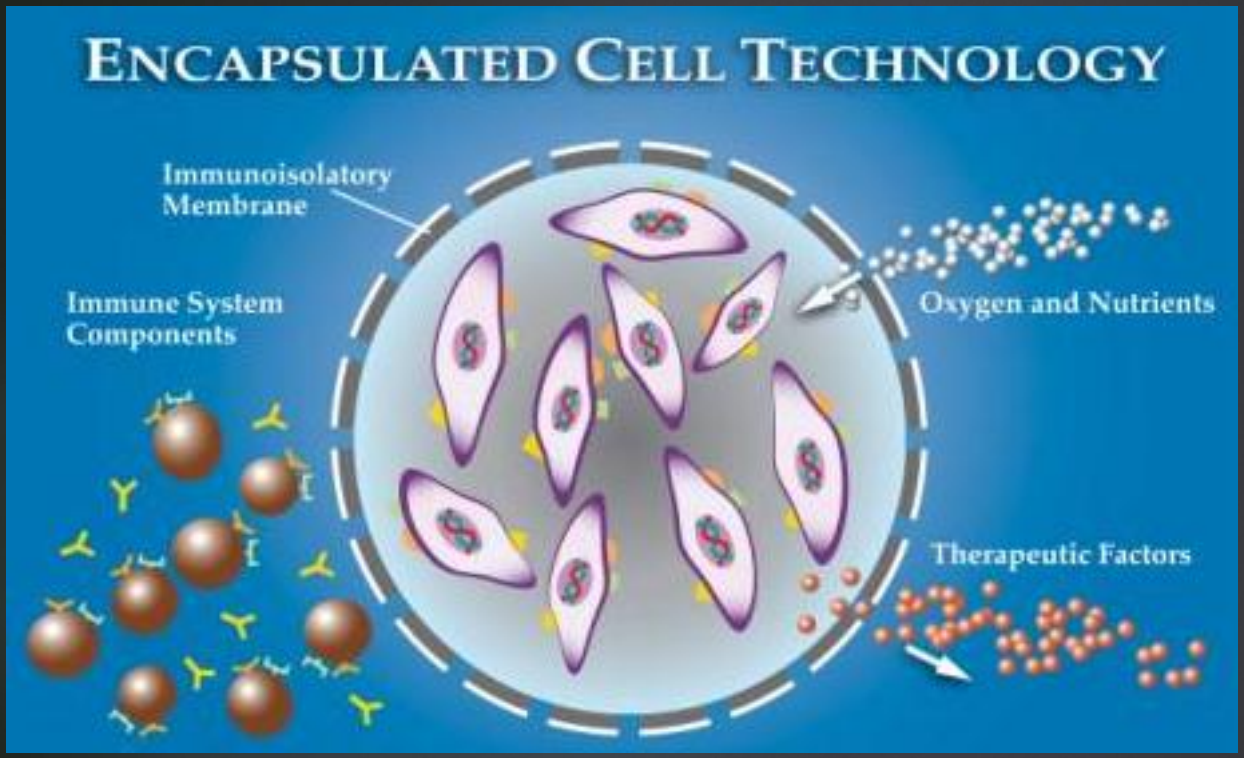
Neurotech drug delivery

Semi-permeable hollow fiber membrane allows:

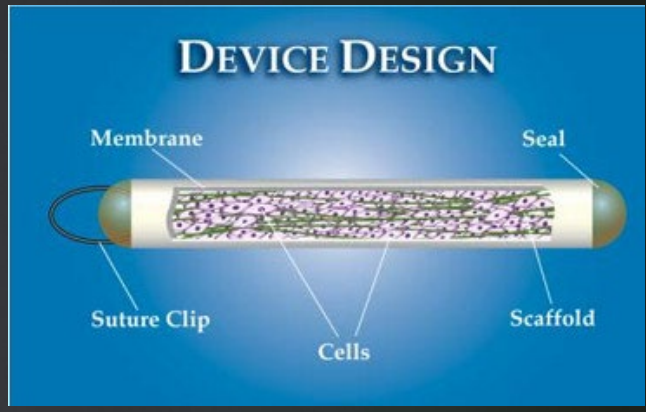
- Influx of oxygen and nutrients to encourage long-term cell survival
- Prevention of direct contact of encapsulated cells with the cellular and molecular elements of the target site.
- Controlled continuous delivery of protein to retina (up to 18 months).

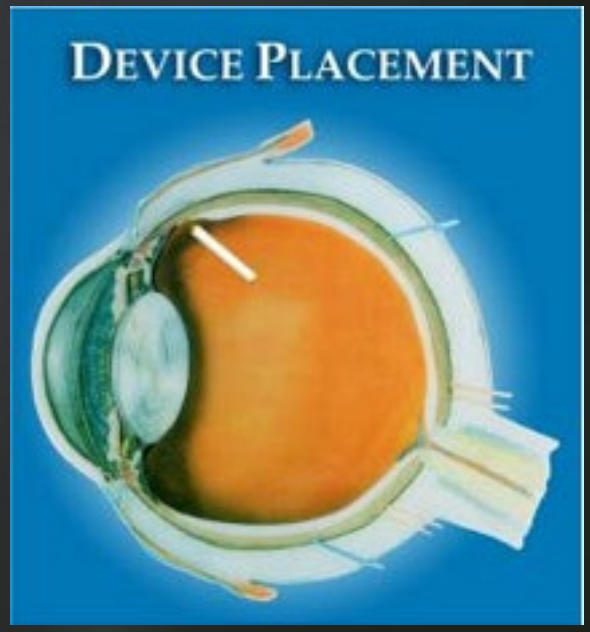
http://www.neurotechusa.com/product_tech.asp

Biopharmaceutics



Features of Encapsulated Cell Therapy

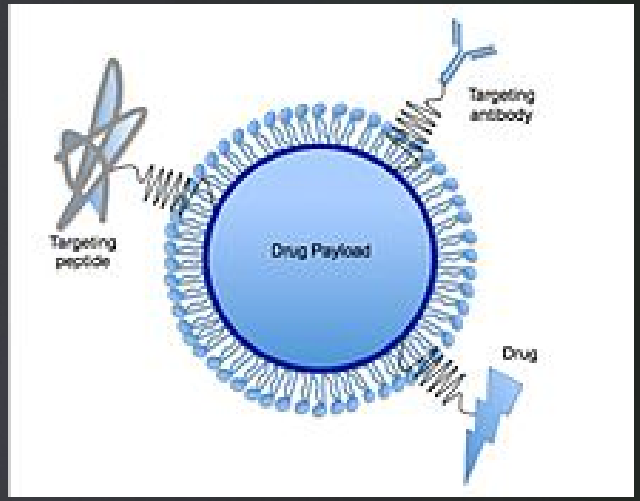




Biopharmaceutics

Drug delivery - Functional Drug Carriers

- Nanostructures (fullerenes, dendrimers and Nanoshells) exhibit functional properties.
- They can be controlled to link with:
    - a drug
    - a targeting molecule
    - an imaging agent
    - Attract specific cells
    - Release payload when required

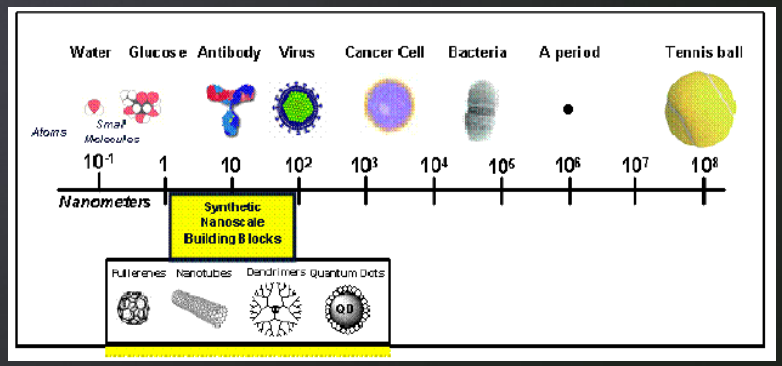


- Cells typically internalize materials below 100nm easily
- Some commercial players in this field:
    - Dendritic Nanotechnologies (http://dNanotech.com/)
    - Nanospectra Biosciences, Inc. (http://www.Nanospectra.com/)

Biopharmaceutics

Drug delivery - Functional Drug Carriers - Dendritic Nanotechnologies Inc.

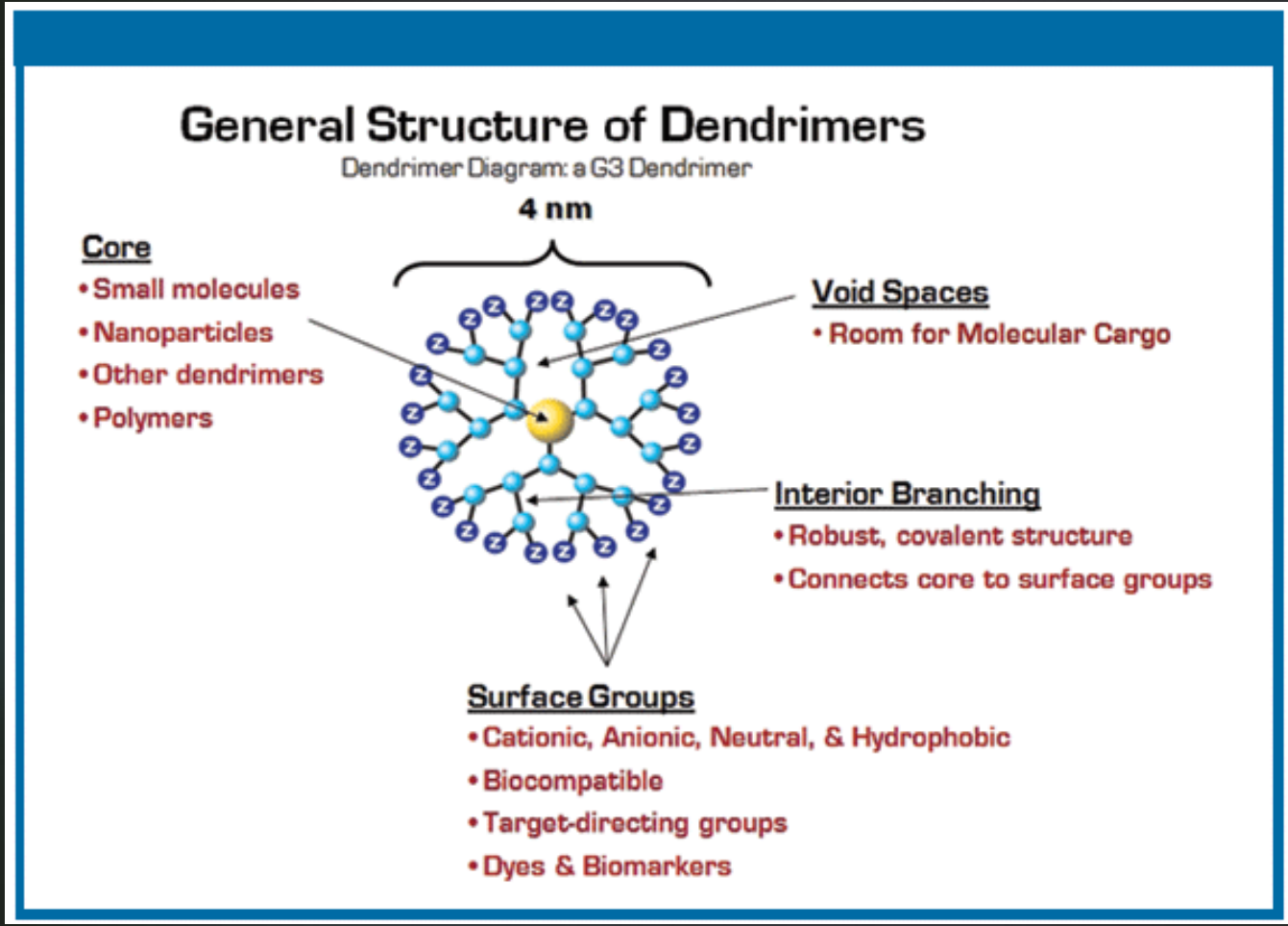
- Dendrimers are spheroid or globular Nanostructures that are precisely engineered to carry molecules encapsulated in the interior void spaces or attached to the surface.
- Size, shape and reactivity are determined by generations (shells) and chemical composition of the core, interior branching and surface functionalities.
- Drugs stored within dendrimers can be transported to specific sites for therapeutic healing



Size of dendrimers

http://dNanotech.com/catalog.php

Biopharmaceutics



COURTESY OF DENDRITIC NANOTECHNOLOGIES

Because of their **small size** and **branched structure**, dendrimers are being studied to transport genetic material or tumor-destroying therapies into a cell without triggering an immune response.

Drug delivery dendrimers

Biopharmaceutics

Functional Drug Carriers - Dendritic Nanotechnologies Inc. - Application

Commercialized applications:

Product	Purpose	Company
VivaGel™	Prevention of HIV	Starpharma
Stratus® CS	Cardiac marker diagnostic	Dade Behring
SuperFect®	Gene transfection	Qiagen
Alert Ticket™	Anthrax detection	U.S. Army Research Laboratory

Applications of dendrimers

Implantable Materials - Tissue Repair and Replacement

Hard Tissue

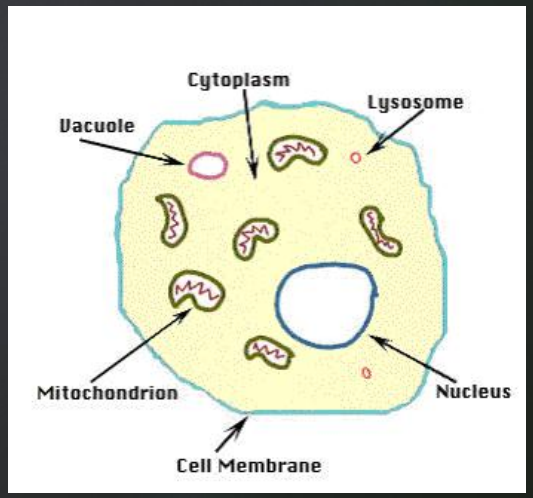
- "Hard" tissues : Bone and teeth repair by reproduction of tissues similar to original ones.
- Artificial implants are to be bio-compatible, otherwise they may cause adverse effects such as immune rejection, corrosion in the body or loss of adherence to the host, etc.

http://www.alphatecspine.com

http://www.emirateshospital.ae

Ultra-Soft Tissue

- "Ultrasoft" tissue: Cell membrane and organelles exhibiting metabolic function
- Replacement of damaged tissue could be done using tissue regeneration scaffolds.



http://www.windsor.edu

Implantable materials and devicesF

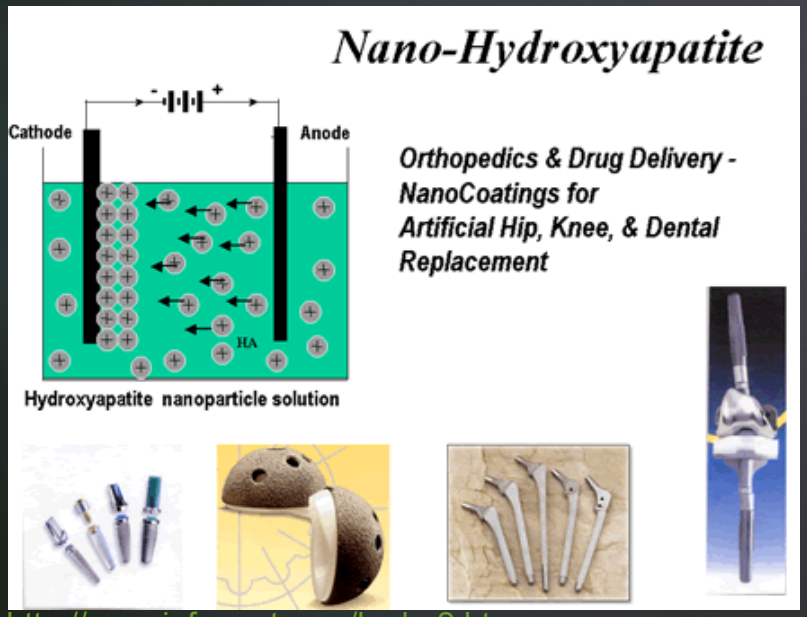
Implant coatings for 'hard' tissues

- Orthopaedic implants – Primary aim is to provide mechanical stabilization.
- Acute and chronic infection are potential complications.
- Coat implants to enhance osseointergration and mitigate adverse effects due to foreign boy response or infection.
- Coatings to enhance osseointergation such as hydroxyapatite (HA) have shown to enhance new bone formation on implant surface

Implantable materials and devices

Implant coatings for 'hard' tissues - Inframat, Inc.

- Developed orthopedic and dental implants using Nano-structured **hydroxyapatite (HA) coatings**
- Electrophoretic deposition technique is used.



http://www.inframat.com/hydro2.htm

Advantages of Nano-structured HA:

- Increased bond strength:
  - greater than 60MPa
  - Conventional thermally sprayed (30MPa)
  - Chemical deposited Hap coatings (14MPa)
- Improved corrosion resistance: Density = 100%, Crystallinity = 100%
- Extended prostheses lifetime
- Broader market applications: - Hips, knee and dental
- Projected Accelerated Healing Rates

Implantable materials and devices

Implant coatings for 'hard' tissues - Spire Biomedical

- Developed new family of "smart" Nanophase (grain sizes < 100nm in at least one direction), Ion-Tite™
- Benefits of Spire's Nanophase hydroxyapatite coating:
    - Discourage soft tissue growth on implants. (Problem faced by conventional hydroxyapatite coating)
    - Encourage hard tissue growth instead.

Implantable materials and devices

Tissue Regeneration Scaffolds for 'ultrasoft' tissues

- Nanotechnology can be used to mobilize the body's own healing abilities to repair or regenerate tissues and organs.
- Hybrid Nanostructures serve as molecular sensors and optical control systems to adjust stiffness and strength of scaffolds.
- Nanocomposite Hydrogels are being researched to produce:-
  - Heart valves implanted with fibroblasts and endothelial cells
  - Hydrogel structure seeded with corneal epithelia cells
- AorTech has developed the Elast-Eon™
  - Patented high silicone content, polyurethane copolymers
  - Surface features are engineered at Nanometer scale
  - Minimal tissue adhesion => Essential for biocompatibility
  - Developed tri-leaflet heart valve.

AorTech

http://www.aortech.com/

Implantable materials and devices

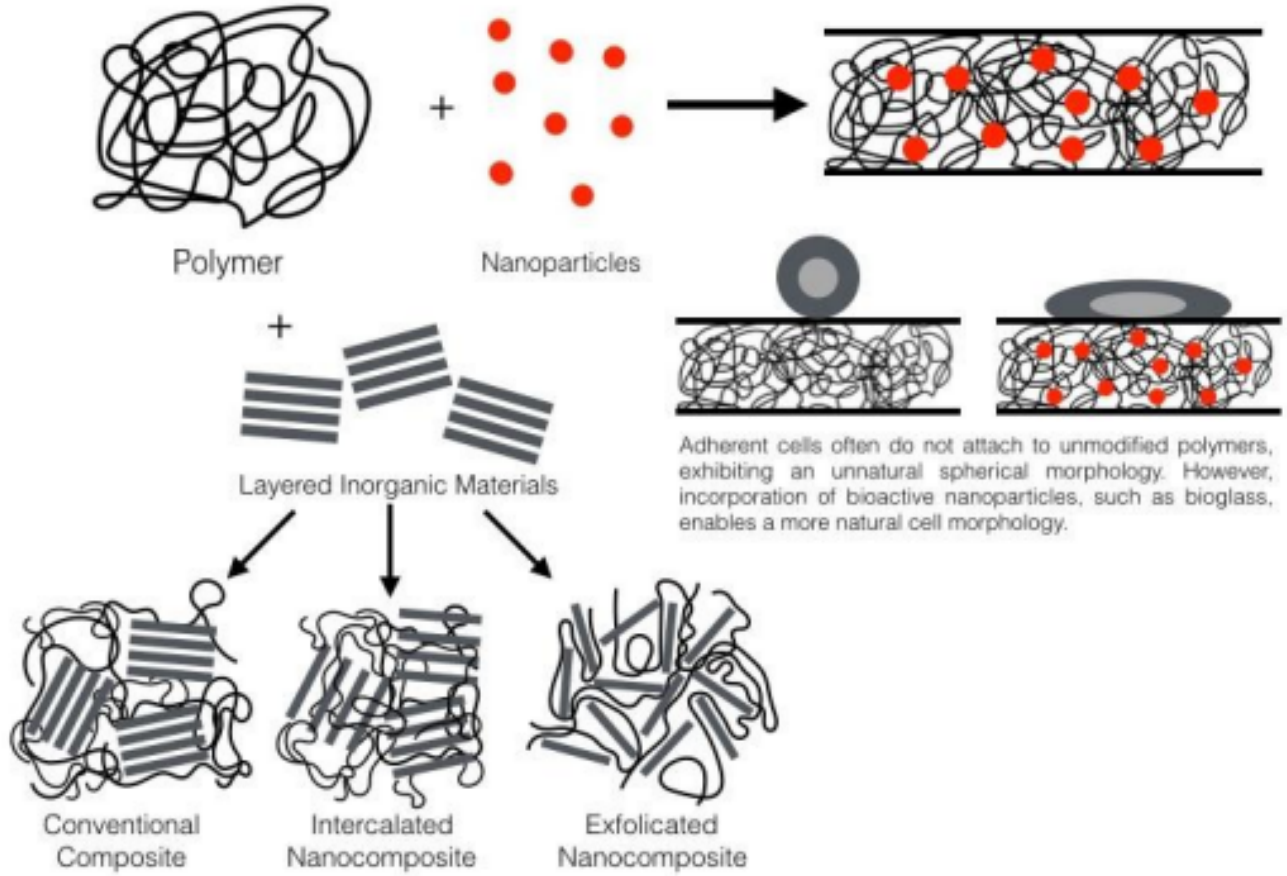


Figure 2. Two types of polymer-based nanocomposites.

Implantable materials and devices

Implantable devices

- Nanotechnology offers novel sensor technologies that provide continuous and extremely accurate medical information.
- Ability to incorporate microprocessors and miniature devices for diagnostic and treatment applications.

Fig 15: Implant cartoon

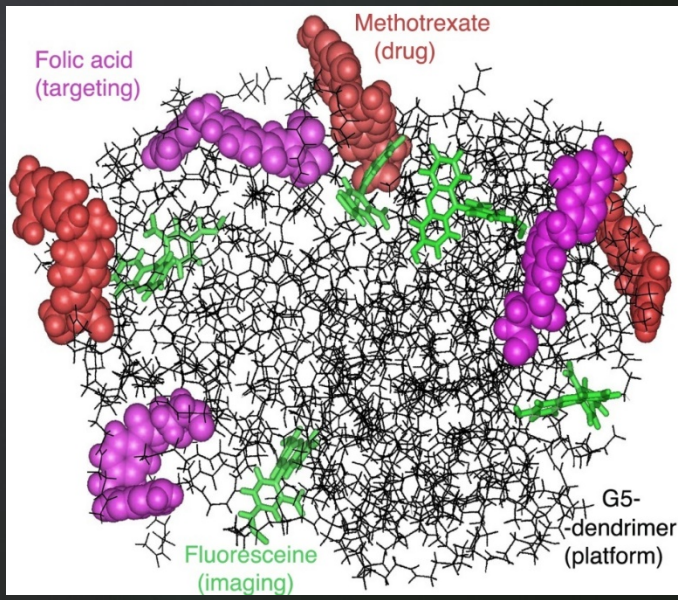
http://www.washingtonpost.com/

1. Cancer detection sensor
2. Pacemakers and hearing aids
3. Microchip-based drug delivery system

Implantable materials and devices

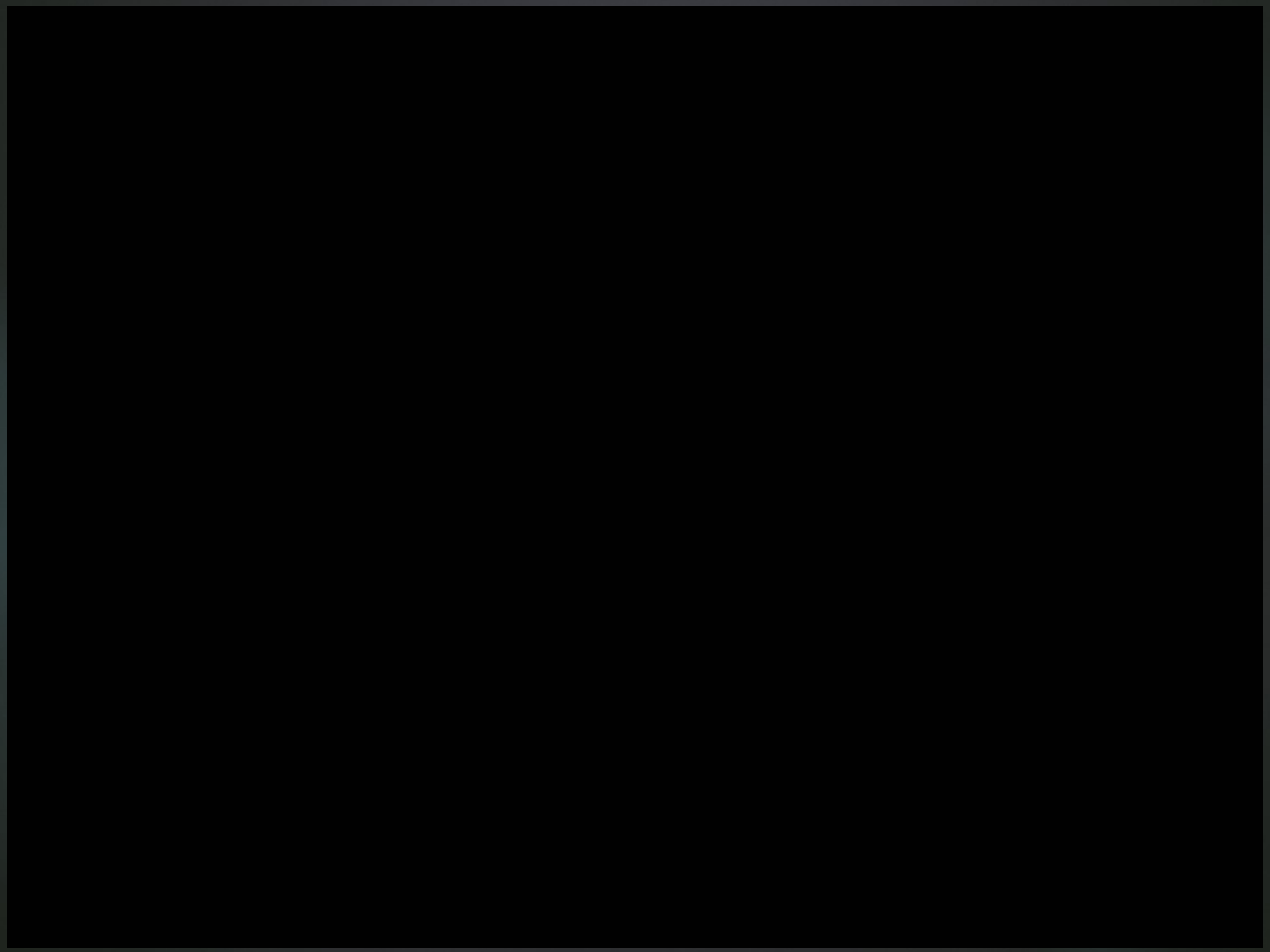
Cancer detection sensor

- **Dendrimers** (< 5nm in diameter) are able to pass through membranes into white blood cells to detect early signs of biochemical changes from radiation or infection.
- Fluorescent tags on their branches will glow in the presence of death cells using a laser scanning device.
- Besides **radiation and cancer detection**, it serves as a **drug delivery vehicle** when drugs are attached to other branches.
- Targets infected cells locally and minimize damage to normal cells.



http://www.med.umich.edu/opm/newspage/2005/Nanoparticles.htm

Implantable materials and devices



Implantable materials and devices

Pacemakers and hearing aids

- NVE, Corp. produces Spintronic-based sensors for both pacemaker and hearing aid market.
- Giant magneto resistance (GMR) effect is used in these solid state devices - produce "giant" changes in resistance when subjected to magnetic fields.
- Advantages of using Spintronic sensors:
  - Non-invasive
  - High speed communication
  - Miniaturization of devices
  - Power enhancement
  - Better reliability as they are solid state devices and do not suffer from mechanical failures.

Frontier CRT-P
Three-port, multi-chamber device capable of biventricular or left-ventricular stimulation to promote resynchronization and improved hemodynamic performance in heart failure patients

From St Jude Medical

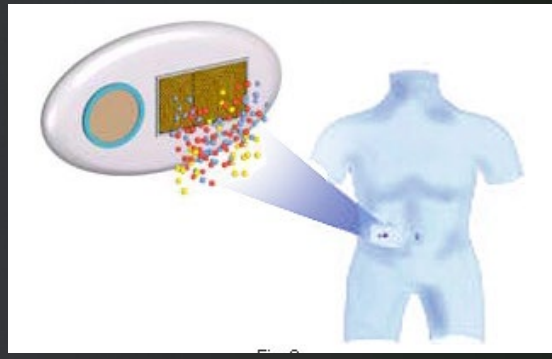
Implantable materials and devices

Microchip-based drug delivery system

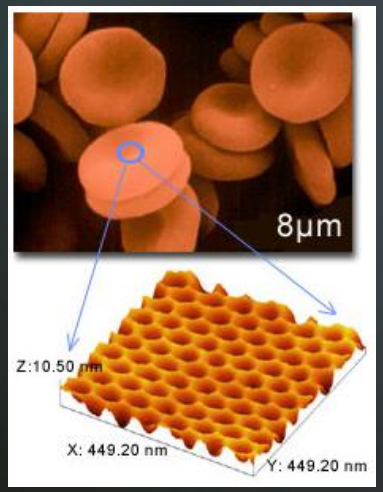
- Incorporation of micrometer-scale pumps, valves and flow channels.
- Controlled delivery of drugs could also be achieved through pumps and actuators.

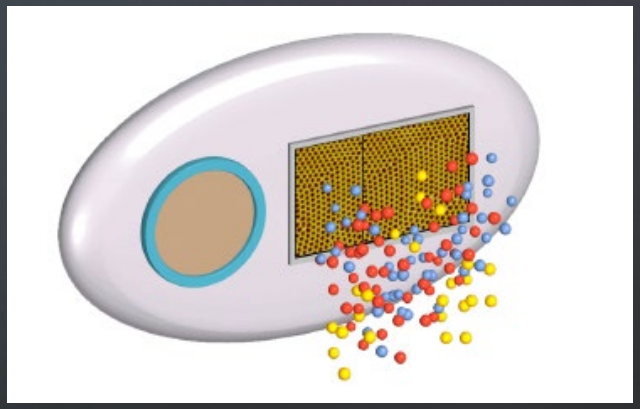
Product: DebioSTAR™ development by Debiotech SA

- Nanoporous membrane (pore size up to 250nm)
- Drug release precisely controlled.
- Can be passive or active pressurized.



Debiostar by Debiotech





Nanoporous membranes

Nanoporous membrane is able to deliver drugs in the body over several weeks to several months.

http://www.debiotech.com/products/drugdd/debiostar.html

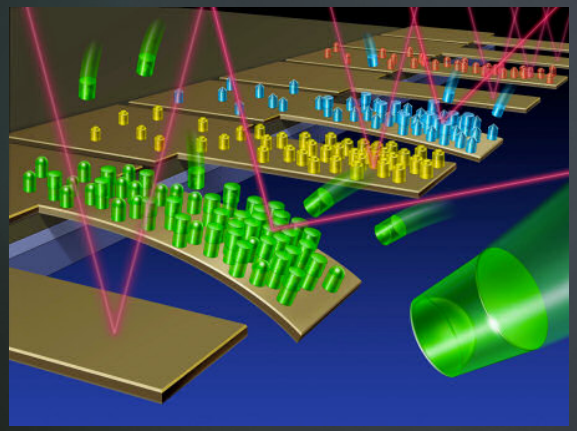
Diagnostic tools

1. Concentris Nanocantilever
2. Nanomix, Inc.
3. Imaging
    a. Nanoparticle probes
    b. CNT X-Ray

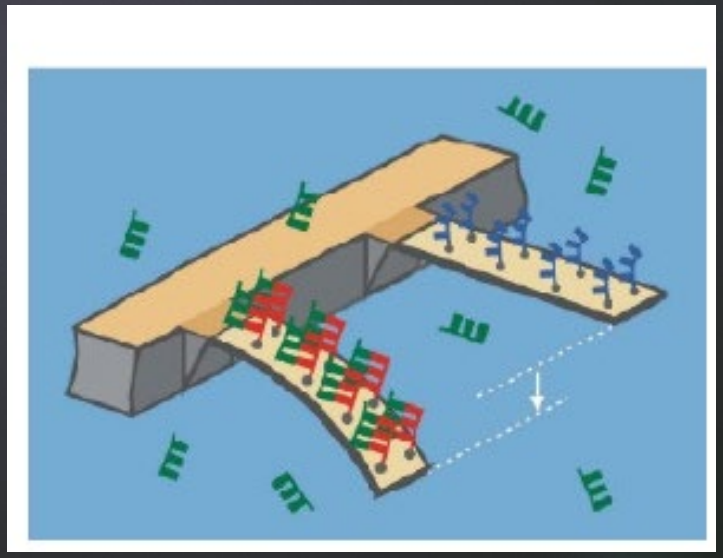
Diagnostic tools

Concentris Nanocantilever

- The Nanocantilever are coated with a thin film (several nm) of Au.
- They are then functionalized with a single stranded DNA.
- As the complementary strand of DNA is attached to it, the nanocantilever bends due to surface stress.
- Response is in the form of deflection in nm or change in resonance frequency.



Nano-mechanical response of cantilever

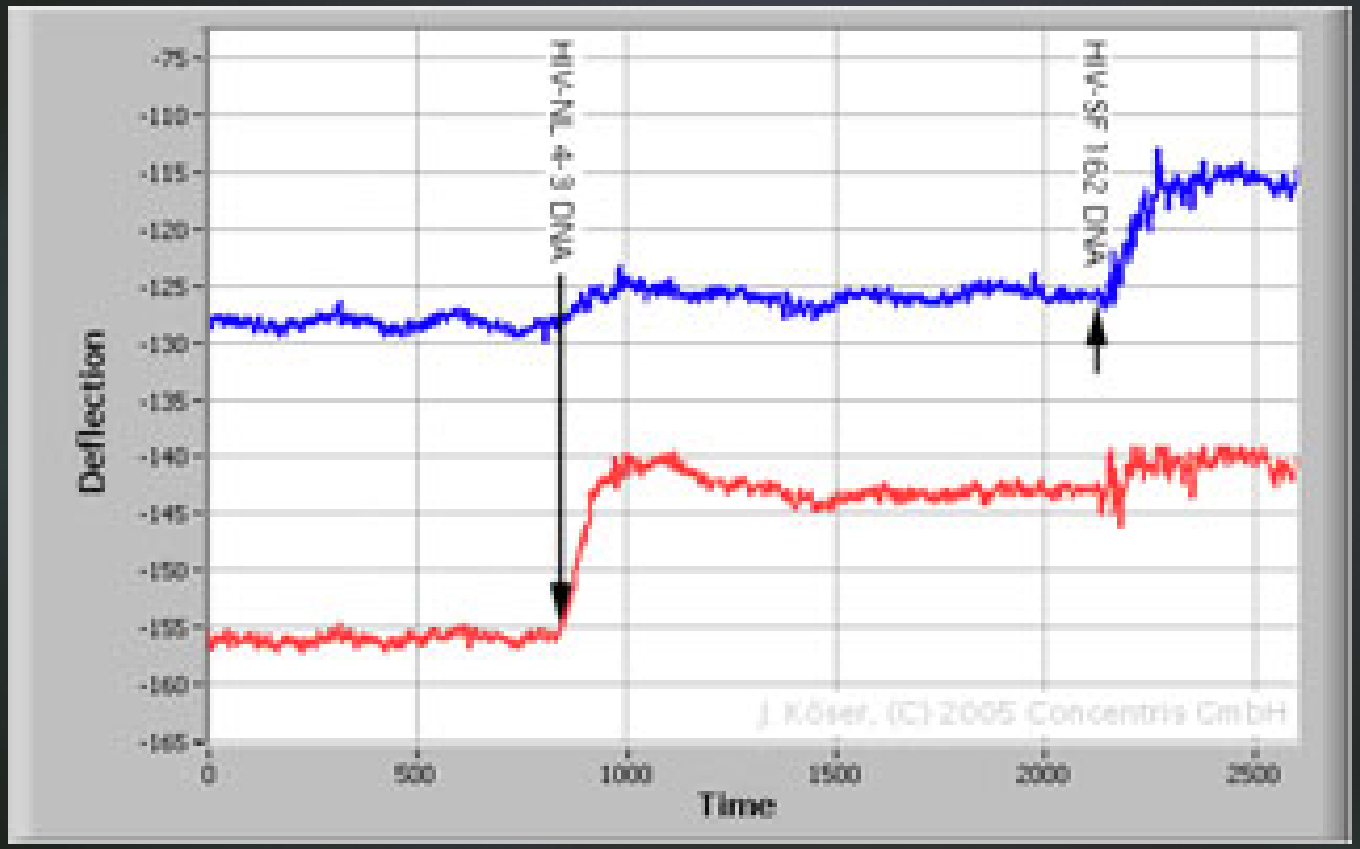


http://www.concentris.ch/

Diagnostic tools

Concentris Nanocantilever

- HIV DNA sequence detection results.



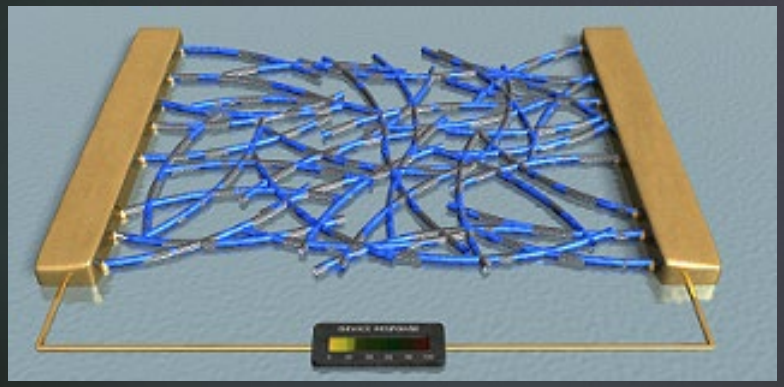
http://www.concentris.ch/

Diagnostic tools

Nanomix, Inc.

Nanomix Sensation™ technology has targeted three different market:

- Unique hydrogen sensor for industrial gas segment
- Capnography respiratory monitoring device for medical.
- Nanoelectronic bio molecule detection.



Medical capnography sensor

http://www.Nano.com/about/sensation_technology.html

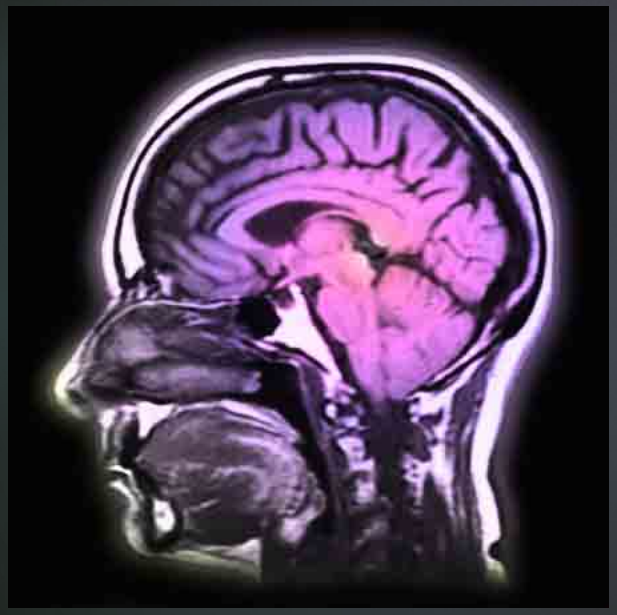
Detection Principle

- CNT are combined with silicon microstructures on the Si substrate.
- CNT are coated with recognition layer that interacts with CO_2 analyte.
- This interaction results in a change of electrical impedance across the network.
- Electrical impedance measured by application of voltage.
- Response is displayed on a colored scale.

Diagnostic tools

Imaging

- High quality images are essential for detection of malignant tumors which are localized at early stage of development.
- Nanotechnology offers new solutions for early detection of cancer and other diseases.



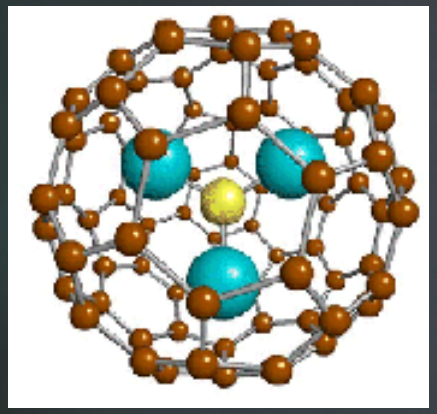
A MRI image

1. Nanoparticle probes
2. CNT X-Ray

Diagnostic tools

Nanoparticle probes

- **Luna Innovations** claimed that the contrast of MRI images could be enhanced by 50 times by using Trimetasphere™ carbon Nanomaterial.
- These fullerenes form a molecular cage with up to 80 carbon atoms and are used to encapsulate contrast agents such as gadolinium.



Trimetasphere carbon Nanomaterial

http://www.lunainnovations.com/research/Nanotechnology.htm

Contracting agents such as Gadolinium increases MRI signal and improves contrast.

Current contrast agents made of Gadolinium chelates do not provide sufficient relativity for doctors to visualize everything.

Solution: Enclose the heavy metals with carbon atoms => Trimetasphere.

Able to improve relativity by 25 times.

Diagnostic tools

CNT X-Ray - Xintek, Inc.

- Advances in X ray technology have been made with Nanotechnology.
- Xintek utilized carbon Nanotubes (CNT) field emitters as the electron source.
- Advantages:
    - Faster response time
    - Programmable electron and x-ray intensity distribution
    - Ultra fine focal spot
    - Rapid pulsation capability
    - Longer lifetime
    - Potential for **miniaturization** of x-ray machines

CNT X ray tube

http://www.xintek.com/products/xray/index.htm

Diagnostic tools

CNT X-Ray - Xintek, Inc.

Images acquired:

Leaf

Micro CT of mouse

Possible Applications:

Medical diagnostics

Security checks

Textile and wound care products

- Natural or synthetic textile fibers offer poor resistance to bacterial or pathogenic fungi.
- A number of products, with the incorporation of Nanotechnology, offers good antibacterial disinfection.

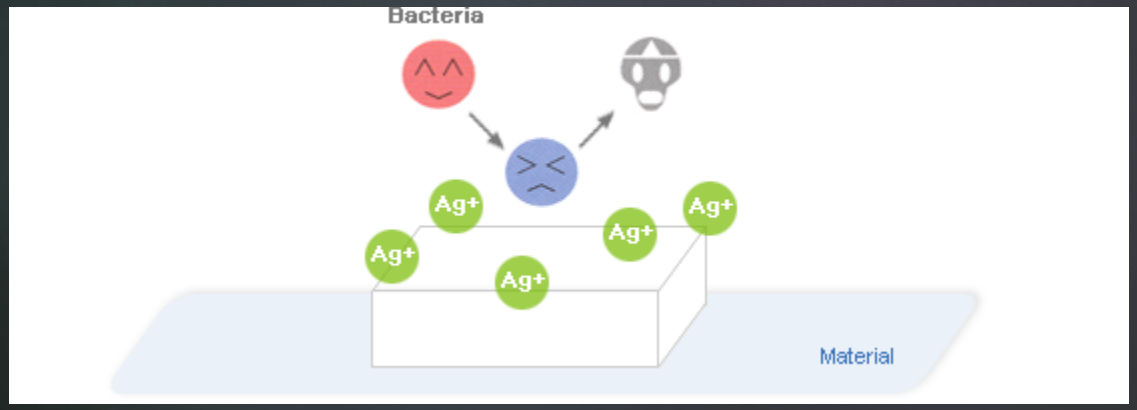
1. Antimicrobial textile surfaces
2. Wound care products

   i.Alltracel's m·doc™

Textile and wound care products

Antimicrobial textile surfaces

- BIOSILVER/Mipan Nano-Magic Silver® contains Nano-sized silver ions in the fabric.
- Kills harmful germs and bacteria.
- Emission of far infrared rays beneficial to body and promotes blood circulation.



Ag+ ions in action

http://pi.hyosung.com/pi_eng/textile/textile/clothing_02.jsp

Textile and wound care products

Wound care products - Alltracel's m·doc™

- **Alltracel's m·doc™** (micro-dispersed oxidized cellulose) technology has produced efficient wound care products.
- Joint collaboration between Alltracel Pharmaceuticals and ELMARCO.
- A novel process is used to spin polymers into Nanofibrous non-woven materials.
- Advantages of m·doc™ :
    - Stops bleeding fast
    - Reduces risk of renewed bleeding
    - No adverse effects or contraindications

http://www.stopbleedingfast.com/mdoc/

Nanotechnology in Life Science and Medical Industry

- Nanotechnology is poised to influence the future of life sciences and medical products.
- It has enabled breakthroughs by going beyond the limitations of other current technology.
- Nano-products discussed here form only the 'tip of the iceberg'.
- Many more products are still in the pipeline and research phase.
- Some of these products may one day revolutionize our medical health care system.