

ORTHO KINETIC TECHNOLOGIES, LLC **ORTHO KINETIC TESTING TECHNOLOGIES, LLC**

NANOTECHNOLOGY

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DISCLOSURES

- OKT – Strategic Planning & Regulatory Consulting
- OKT² – ISO 17025 A2LA Accredited Test Facility











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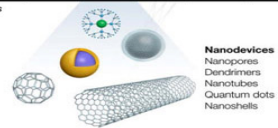
NANO

- Nanotechnology deals with sizes from 1-100nm range
- 10^{-9} m.

How Small Is Small?

Water	Glucose	Antibody	Virus	Bacterium	Cancer cell	A period	Tennis ball
							
10^{-1}	1	10	10^2	10^3	10^4	10^5	10^7

Nanometers



Nanodevices
Nanopores
Dendrimers
Nanotubes
Quantum dots
Nanoshells

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NANOMETERS - SIZE PERSPECTIVE

- Nanotechnology - 10^{-9} m.


DNA - 2 nm RBC - 750 nm Ant - 5 million nm



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DEFINITION OF NANOMEDICINE

- Monitor, repair, construct, control of human biological systems at molecular level via engineered nanodevices




"An Engineered Nanodevice for RBC"

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NANOMEDICINE STRUCTURAL COMBINATION

- Macro + Micro + Nano

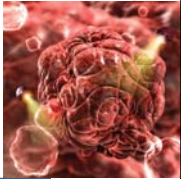
↑ ↑
Cellular Molecular



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APPLICATION OF NANOMEDICINE

- **Diagnostic**
Imaging & identification
Detect cancer cells - very early- could increase survival
- **Therapeutic**
Delivering medication to the exact location
Killing of bacteria, viruses & cancer cells
Repair of damaged tissues.



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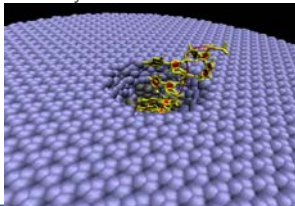
EXAMPLES OF NANOTECHNOLOGY IN FUTURE MEDICAL APPLICATIONS



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NANOPORES

- Create structures that control molecular passage
- Nanosized pores allow passage of molecules to target tissue
 - O₂, Glucose, Insulin
- Impede passage of larger immune system molecules
 - Immunoglobulin
 - Viruses



Nanopores & DNA

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MEMS+NANO = Early Cancer Detection

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Example - Cancer Detection

- Cantilever Beam
 - coated with antibody to PSA
 - exposed to sample with PSA
 - better than 0.2 ng/ml
 - bending of cantilever
 - deflection monitored by laser

Microcantilever Biosensor
 Wu et al., *Nature Biotechnology*, 19, p. 856 (2001)

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DENTAL ROBOTS


Remote-controlled nanorobots examine & clean subocclusal surfaces of a patient's teeth, near gumline.

Copyright 2001 American Dental Association

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NANOROBOTS

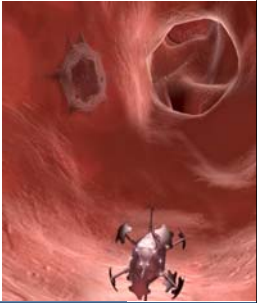
- Nanodevices used for purpose of maintaining & protecting body against pathogens.
- Total Size = 0.5 to 3 μm
- Component Size 1-100nm



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NANOROBOT EXAMPLE - 2


A single inhaled nanorobot reaches deeply into lungs, enters an alveolar duct, & attaches to the tissue surface.



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NANOROBOTS – HOW ARE THEY POWERED?

- Through metabolizing local glucose and oxygen for energy
- Other sources of energy within the body can also be used
- Simple onboard computers capable of performing 1000 or fewer computations per second.





HOW ARE THEY TRACKED (MONITORED)?

- A navigational network installed in body, which may provide high positional accuracy to all moving nanorobots
- This will enable the physician to keep track of the various devices in the body

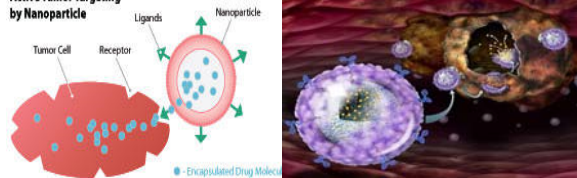




TUMOR SEEKING NANOPARTICLES

- 1/100th the size of human cell
- Deliver high dose chemotherapy to cancer cells
- Target specific cells
- Precise delivery

Active Tumor Targeting by Nanoparticle





RESORBABLE NANO-SCAFFOLDS

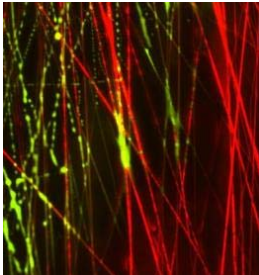
- Scaffolds 3D porous structures need to fulfil the following criteria for tissue engineering ([Spaans et al. 2000](#); [Boccaccini et al. 2002](#)).
- Material must be biocompatible and degradation non-cytotoxic.
- Must be biodegradable and resorb at same rate as tissue is repaired.
- Must possess highly interconnected porous network, formed by a combination of macro- and micropores -enable proper tissue ingrowth, vascularization, nutrient delivery.
- Less toxic – nanoparticles????.



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NANOFIBERS

- Dynamic transition in fibrous biomaterial
- Electrospun polymeric nanofibers.
- Slow-degrading polymer
- Water-soluble polymer
 - Selectively removed to increase or decrease the spacing between fibers
- Stretchable fiber (textile)
- Seed with cells
- 3D Scaffold
- Brendon M. Baker, Ph.D.; Perelman School of Medicine, University of Pennsylvania



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CURRENT: NANOSURFACES



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NANOSURFACES & MECHANOTRANSDUCTION

- To understand nanosurfaces
- Must understand Mechanotransduction
 - Macro level
 - Micro level (cellular)
 - Nano level



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MECHANOTRANSDUCTION - MOA

- Process where mechanical energy is converted in electrical and biochemical signals.
- Mechanical stimuli ↔ Tissue ↔ individual Cells
- Cellular Mechanotransduction – the mechanism by which cells convert mechanical signals into biochemical responses.

The diagram illustrates the process of mechanotransduction. It shows a cell with various components: 'Mechanical response (force generation)', 'Adhesion and stiffness', 'Cytoskeleton network (cellular organization and contractility program)', 'Mechanotransduction (force transduction)', 'Mechanical stimulus (shear force)', and 'Chemical response (change in cellular organization, cell-cellular protein expression, etc.)'. A hand holding a bone is shown in the background.

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Surface Textures - Mechanotransduction

- Induce mechanotransduction
- Guide cellular growth
- Increased cell proliferation – or -
- Increased cell function
- On Metals: use of surface textures
 - Increase fatigue performance of implant
 - Careful not to compromise strength
 - Titanium = improve osseointegration

The image shows a microscopic view of a textured surface, likely a metal implant, with a hand holding a bone in the background.

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SURFACE- CELL DIFFERENTIATION & AFFINITY

- Materials & Geometrical design
- Interface surfaces
 - (open architecture, pores, textured surfaces)
- Extent & planes of motion
- Frictional surface
- Surface area
- Biomechanics of region
- Cells have affinity for certain geometries, preferred sizing, shape, repetition, mechanical stimuli
- **Chondrocytes - 10µm posts**


The bar chart shows the relative cell number for different surface geometries. The y-axis is 'Relative cell number (%)' ranging from 0 to 700. The x-axis shows different surface types: 'Posts', 'Pores', 'Ridges', 'Grooves', 'Random', and 'Smooth'. The 'Posts' bar is the highest, reaching approximately 450%. Below the chart is a microscopic image of a surface with 10µm posts.

Surface Geometry	Relative Cell Number (%)
Posts	~450
Pores	~250
Ridges	~200
Grooves	~150
Random	~100
Smooth	~100

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PEEK + BONE APPPOSITION

thinking Different

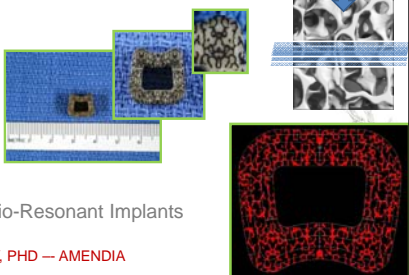


A blue-tinted image of a PEEK implant and a 3D model of a hand joint.

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Laser Etch Nanosurface - Variable Depth in Single Pass

New material

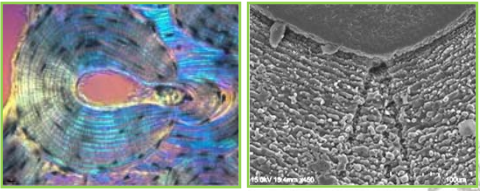


Bio-Resonant Implants

TIM GANEY, PHD — AMENDIA

A collage of images showing a laser etched surface, a bio-resonant implant, and a microscopic view of a porous structure.

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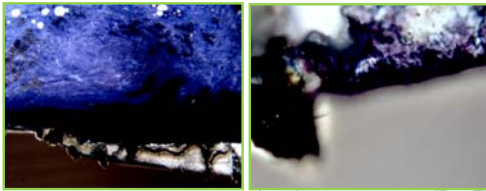


Mimic Lamellar Bone Structures

Offering Dimension as Substrate

Two images showing lamellar bone structures.

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MIMETIC **PEEK**

Early Bone Formation & Apposition
3 mos.

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Summary 6-month Histology

Mimetic

1. More extensive bone contact
2. Less evidence of fibrous tissue interface
3. Well-modeled lamellar bone
4. Highly cellular bone matrix

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BUT.....

WHAT ABOUT SAFETY OF NANOTECHNOLOGY

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RISKS & SAFETY OF NANOTECHNOLOGY

- Must understand toxic effects on nanosized elements in vivo
 - Shape, size, material, surface area, electric charge, other physicochemical structures
 - Dosage
 - Mode of application
 - Concentration in the target organ
 - Duration of action



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TYPES OF TOXICITY


- Bio-degradation
- Bio-accumulation
- Animal toxicity
- Genotoxicity
- Ecotoxicity
- Cytotoxicity
- Primary vs. Secondary (leeching or residual products toxic)
- Local vs. Peripheral Tissue Reactions



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MEASURING NANO EFFECTS

- Early stage equipment & methods to quantify nano effects
- Developing processes
- Still learning the technology and Effects




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THANK YOU