

# **Nanomaterials for Imaging Technology**

**Nadeem A. Kizilbash, *Ph.D.***

**Assistant Professor**

**Department of Chemistry**

**Quaid-i-Azam University**

**Islamabad**

# Introduction

- **Nanotechnology, most basically put, is the molecular manufacture of small things; “nano” being Greek for dwarf.**
- **For purposes of biological applications, a good working definition of nanotechnology is that it employs components that range from approximately five to 500 nanometers in diameter.**
- **These components form the base for delivery systems that can ferry therapeutics or diagnostic agents to specific sites in the body, allowing for highly targeted treatments that minimize side effects.**

- **Applications of nanotechnology are being developed for cancer therapies and diagnostics.**
- **Specific tissue targeting of nanoparticles for diagnostic enhancement or drug delivery is critical and is the subject of much research.**
- **In the diagnostic realm, nanoparticles have been used to enhance the efficacy of magnetic resonance imaging (MRI) to detect the spread of cancer.**

# Discovery and Early Research

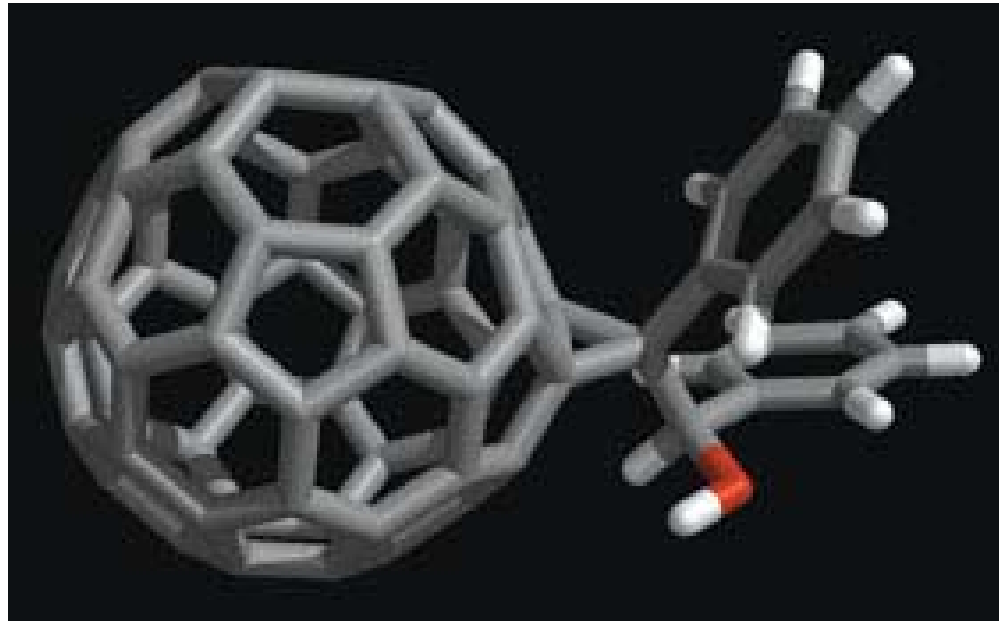
- **The birth of nanotechnology is usually attributed to physicist Richard Feynman's 1959 talk, "There's plenty of room at the bottom." Although he did not actually use this term in the talk delivered to the American Physical Society.**
- **Among other proposals, Feynman suggested developing a 1/25,000 reduction in type size that would permit the entire Encyclopedia Britannica to be contained on the head of a pin. He offered \$1,000 to anyone who could develop a method to do so and, in 1985, a Stanford graduate student claimed the prize by reducing the first paragraph of "A Tale of Two Cities."**

- **Feynman also described his vision of mechanical robots, each programmed to build a set of tools that could construct a smaller robot to build even smaller tools, eventually culminating in a billion tiny factories.**
- **This idea was picked up and expanded on by one of Feynman's students, K. Eric Drexler, whose 1986 book, *Engines of Creation: the coming age of nanotechnology*, brought the field to wide popular attention.**
- **Drexler himself received the first doctorate degree "in the field of nanotechnology" from MIT in 1991, under the supervision of Marvin Minsky, a renowned artificial intelligence pioneer.**

- **Dexler also founded the Foresight Institute in Palo Alto, California, which has as its mission to increase public understanding of the risks and benefits of nanotechnology.**
- **The first scientific conference on nanotechnology in biology, "Biological Approaches and Novel Applications for Molecular Nanotechnology" was held in later 1996, in San Diego, and sponsored by International Business Communications.**
- **In 1999, Robert Freitas, Jr., a senior research fellow at the Institute for Molecular Manufacturing in Palo Alto, published the first in his book series, Nanomedicine, describing how molecular machine systems can be engineered to address medical problems.**

# Current Research Directions

- Applications of nanotechnology are being developed for cancer therapies and diagnostics.
- In the diagnostic realm, nanoparticles have been used to enhance the efficiency of Magnetic Resonance Imaging (MRI) to detect the spread of cancer.
- In one study, lymphotropic iron oxide nanoparticles were demonstrated to act as effective contrast agents and allowed the detection of small nodal metastases in men with prostate cancer that would otherwise have been overlooked. Such imaging with nanoparticles might also help eliminate invasive biopsy procedures as the only means to monitor a cancer's spread.
- Nanoparticle contrast agents for Ultrasound have also been developed, which may enhance the sensitive detection of vascular and cardiac thrombi, as well as solid tumors of the colon, liver and breast, in a noninvasive manner.



**Nanotechnology is no stranger to oncology: nanoscale-targeted magnetic resonance imaging contrast agents illustrate the application of nanotechnology to diagnostics.**



- **Recently developed nanowires -- silicon strands containing receptors for tumor markers such as prostate specific antigen (PSA) -- were shown to be sensitive enough to detect markers from as few as ten tumor cells. They can test a drop of blood in a few minutes, providing a simultaneous scan for multiple cancers.**
- **Nanotubes, developed by materials science engineers and used to increase the strength and elasticity of concrete and plastics, have also been shown to be capable of crossing cell membranes and ferrying proteins into cells.**
- **Because eliminating specific RNA molecules has been shown to down-regulate cancer growth, attaching RNA-degrading enzymes to nanotubes is one approach under development.**
- **In addition to the enzymes, additional drugs can be inserted inside the tubes as secondary payloads.**

- **Nanoparticles can be constructed from a number of materials and employing various methods. Liposomes, small bubbles of lipid membrane, have been used to ferry short-chain ceramide, an analog of a naturally occurring compound that can trigger cell death, or apoptosis, in a variety of cancer cell types.**
- **When given intravenously to mice with breast adenocarcinoma, the liposomes carrying ceramide inhibited solid tumor growth. Over the course of three weeks, a more than six-fold reduction in tumor size was observed, as compared to tumors in animals treated with empty liposomes.**

- **Developments in emulsions are also being employed in nanotechnology efforts. Under high pressures of approximately 10,000 pounds, aqueous droplets are stabilized inside a lipid wrapper. Drugs or imaging molecules can then be inserted into the lipid membrane.**
- **An advantage to emulsion technology is that it is relatively simple, involving only a few steps, and, therefore, highly scalable. The end product is inexpensive and easy to store, as it is stable at room temperature.**

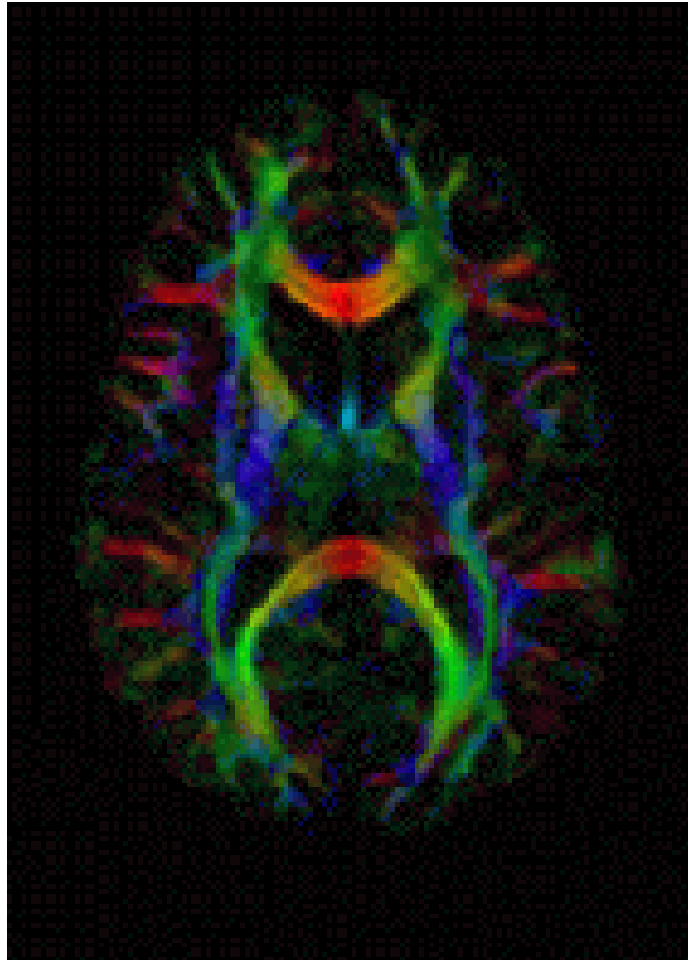
# Nanotechnology and MRI Contrast Agents

- **More than 25 million patients in the U.S. undergo MRIs each year. Doctors use contrast agents in about 30% of MRIs. The contrast agents increase the sensitivity of the scans, making it easier for doctors to deliver a diagnosis. Gadolinium agents are the most effective agents and the most commonly used.**
- **Carbon nanotubes have become an unexpected source of highly effective contrast agents for enhancing MRI scans. The new agents - dubbed gadonanotubes - use the same highly toxic metal, gadolinium, that is given to more than a quarter of MRI patients today, but the metal atoms are encased inside a hollow nanotube of pure carbon. Shrouding the toxic metals inside the benign carbon is expected to significantly reduce or eliminate the metal's toxicity to patients.**

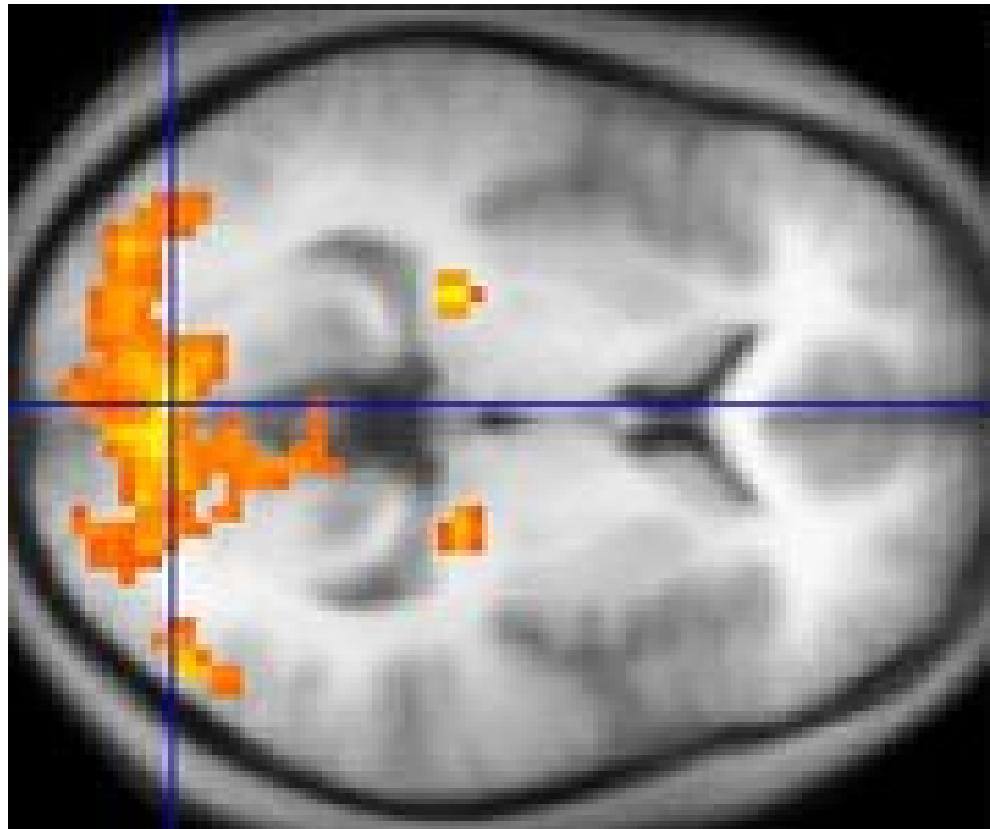
- **The gadonanotubes were created by researchers at Rice University, the Baylor College of Medicine and the University of Houston, all in the USA, and the *Ecole Polytechnique Fédérale de Lausanne* in Switzerland. They have succeeded in creating a new class of magnetic resonance imaging (MRI) contrast agents that are at least 40 times more effective than the best in current clinical use.**



A modern 3 tesla clinical MRI scanner.



**An image of brain obtained via Diffusion Tensor Imaging (a technique of MRI).**



**An image of brain obtained via Functional MRI.**



# Examples of Nanotechnology from Analytical Diagnostics

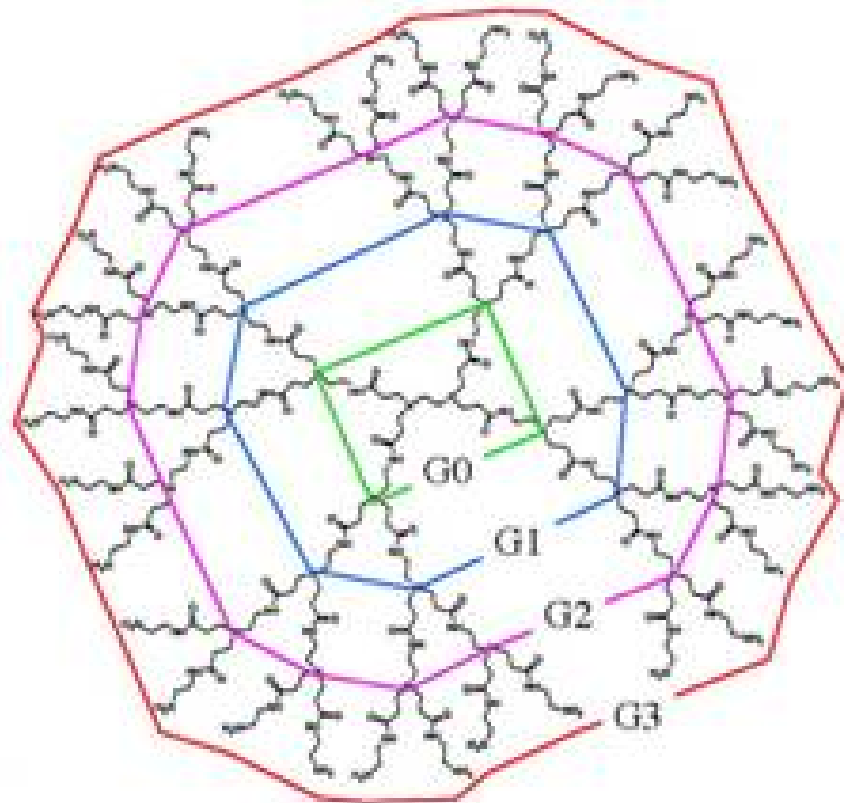
- **Surface Enhanced Raman Scattering (SERS)** is an ultra-sensitive technique for detecting tumor markers.
- **SERS uses "tags" to link to the target cancer tumor marker. A low-cost Raman spectrometer is then used to detect the SERS tag.**
- **The optimum SERS excitation wavelength is dependent on the chemical/physical properties of the enhancing substrate and not the photophysics of the scatterer, facilitating multi-label readout by requiring only one excitation wavelength and the Raman responses are much less susceptible to photobleaching than fluorescence, enabling the use of extended signal averaging to lower detection limits.**

# Nanotechnology and Cancer Research

- Nanoparticles can be engineered to target cancer cells for use in the molecular imaging of a malignant lesion. Large numbers of gold nanoparticles are safely injected into the body (unlike Quantum Dots that are toxic) and preferentially bind to the cancer cell, defining the anatomical contour of the lesion and making it visible.
- These nanoparticles give us the ability to see cells and molecules that we otherwise cannot detect through conventional imaging. The ability to pick up what happens in the cell - to monitor therapeutic intervention and to see when a cancer cell is mortally wounded or is actually activated - is critical to the successful diagnosis and treatment of the disease.

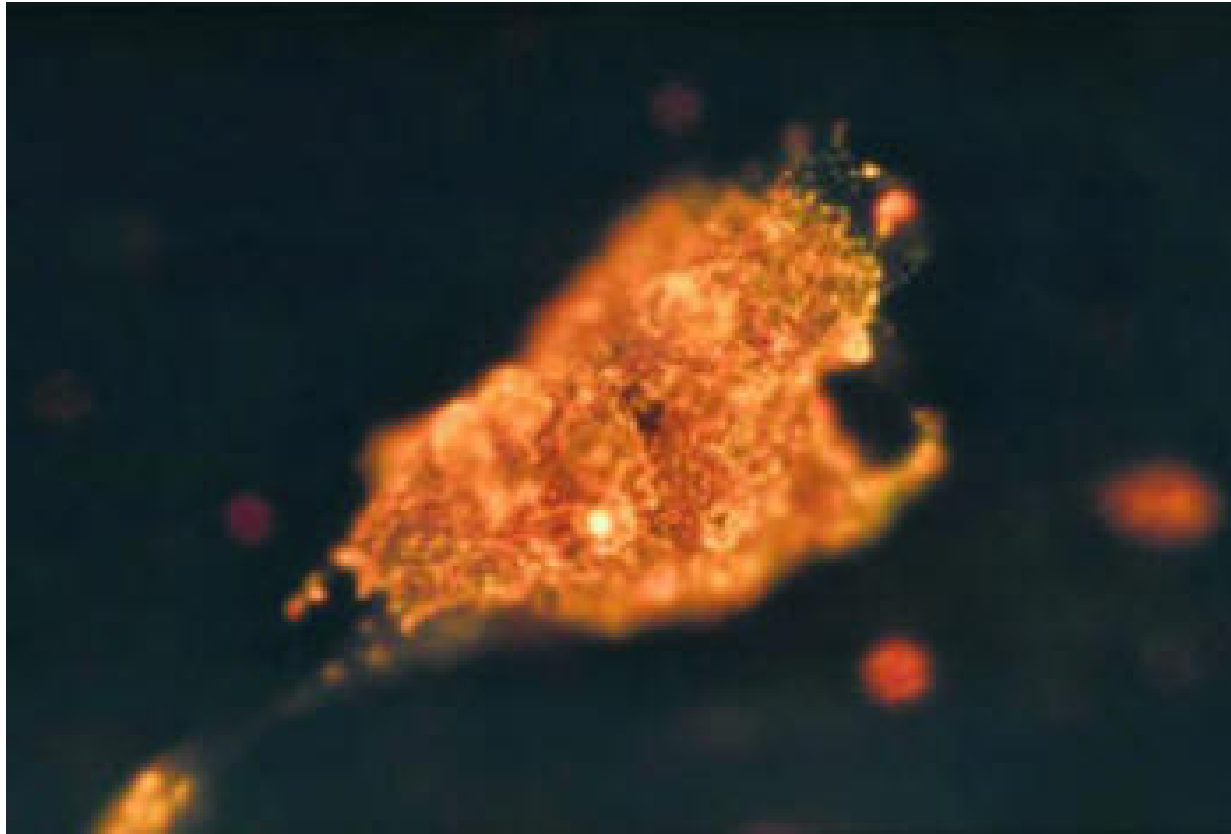
**Dendrimers are of particular interest for cancer applications because of their defined and reproducible size, but more importantly, because it is easy to attach a variety of other molecules to the surface of a dendrimer.**

**Dendrimers are complex, branched molecules that can be built up layer by layer, offering investigators a great deal of flexibility in designing specific shapes and sizes and in attaching various functional groups.**



# Gold Nanorods

- **Gold Nanorods function much like spherical gold nanoparticles in that they may be engineered to target cancer cells for use in the molecular imaging of a malignant lesion.**
- **Large numbers of nanoparticles are safely injected into the body and preferentially bind to the cancer cell, making it visible using different imaging moieties including Two Photon Fluorescence, Optical Coherence Tomography, and Photoacoustic Imaging.**



**Cancer cell illuminated by gold nanorods bound to anti-EFGR anti-body**

- **The added advantages of gold nanorods is their ability to provide these imaging abilities at near-infrared wavelengths. At these wavelengths, skin and tissue are most transparent, so deep tissue imaging is possible.**
- **Further, gold nanorods possess strong absorption features at these same wavelengths and are very efficient photothermal converters. That is, a simple low power diode laser may be used outside the body to heat the gold nanorods to high enough temperatures that the attached cancer tumor is destroyed.**

# Conclusions

- **In the fight against cancer, nanotechnology introduces unique approaches to diagnosis and treatment that could not even be imagined with conventional technology. New tools engineered at sizes much smaller than a human cell will enable researchers and clinicians to detect cancer earlier, treat it with much greater precision and fewer side effects, and possibly stop the disease long before it can do any damage.**
- **Nanoparticulate technology can prove to be very useful in cancer therapy allowing for effective and targeted drug delivery by overcoming the many biological, biophysical and biomedical barriers that the body stages against a standard intervention such as the administration of drugs or contrast agents.**

- **The small size of nanoparticles endows them with properties that can be very useful in oncology, particularly in imaging. Quantum dots (nanoparticles with quantum confinement properties, such as size-tunable light emission), when used in conjunction with MRI (magnetic resonance imaging), can produce exceptional images of tumor sites.**
- **A very exciting research question is how to make these imaging nanoparticles do more things for cancer. For instance, is it possible to manufacture multifunctional nanoparticles that would detect, image, and then proceed to treat a tumor? This question is currently under vigorous investigation; the answer to which could shape the future of cancer treatment.**



**Thank You!**