Nanomedicine Changing the Way Cancer Is Detected and Treated

Introduction:

Nanotechnology promises remarkable advances in electronics and information technology, sustainable energy, environmental remediation, transportation, and even medicine (National Nanotechnology Initiative, para. 2). The nanoscale, in engineering, refers to materials between one and 100 nanometers (nm), one nm equaling one billionth of a meter. To put this in perspective, a human hair is 50,000 nm across and a fingernail grows approximately one nm per second (Ben-Ari, 2003, p.502). Constructing materials on this scale requires years of research and new equipment, especially in the field of medicine. In the future nanorobots may reside in the body, working to locate and treat disease without causing side effects, in essence creating a mechanical immune system. These theoretical robots may seem futuristic; however, currently researchers are working on individual nanoparticles which have the potential to alter the way cancer is detected and treated. Quantum dots, which are semiconducting nanocrystals, possess properties that make them optimal candidates for biomarkers in the detection and imaging of cancerous cells. Once cancer is detected, nanoparticles can be used to deliver drugs, allowing for the treatment of cancer without the side effects of conventional chemotherapy. However, scientists continue to question the toxicity of nanoparticles because, due to strict regulations on human testing, little is known about the actual effects of nanoparticles in the body. These unresolved concerns are preventing potential treatments for patients in dire need.

According to the Centers for Disease Control and Prevention (2013), the second leading cause of death in the United States was cancer, killing 574,443 people in 2013. In the near future cancer treatments utilizing nanotechnology will drastically improve these statistics, secondary to

higher specificity and sensitivity. This paper explains how quantum dots could greatly enhance medical imaging, describes how drugs could be delivered efficiently using nanoparticles, and, most importantly, considers how nanoparticles may be dangerous to the human body.

Statement of the Problem:

Currently devices for medical imaging and disease detection within the human body are limited because organic dyes last only a short time, and, as a result, are restricted in their ability to contrast tumors when medical professionals are using imaging such as Computed (Axial) Tomography (CT) or Magnetic Resonance Imaging (MRI). Current biomarkers only last a matter of seconds before dissipating to concentrations lower than imaging requires; this limits the information medical professionals can gather through imaging as they can only see the cells at a single point in time. Detailed, accurate images of specific parts of the body are essential for doctors to detect cancer at an earlier stage, when treatment is more effective.

Once a cancerous tumor is detected in the body, drugs must be transported to treat the tumor. Current treatment methods release medication into the bloodstream and circulate it throughout the body; eventually the medicine reaches the tumor. Chemotherapeutic drugs are designed to destroy cells that rapidly reproduce, such as cancer cells. Unfortunately, other cells in the body also reproduce rapidly and, consequently, are harmed by chemotherapy treatments. Chemotherapeutic drugs cause temporary and sometimes permanent damage to many organ systems including the hematopoietic, cardiovascular, and nervous systems. Currently, when medication is required in a single location, it is delivered to the entire body. "Bioavailability refers to the presence of drug molecules where they are needed in the body and where they will do the most good" (Raghvendral, Yadev, & Saxera, 2010, p. 662). Not only does poor

bioavailability cause detrimental side effects to patients, but ineffective bioavailability also contributes to tremendous waste and higher costs. The United States annually spends $65 billion on drugs that never reach their targeted destination. Furthermore, poor bioavailability results in drugs leaving the body too rapidly, thus requiring high dosages of medication (Raghvendral, Yadev, & Saxera, 2010, p. 662). With more efficient and effective methods to transport drugs, treatments will be safer for patients and reduce medical costs.

The Advantages of Quantum Dots in Medical Imaging:

With the discovery of nanotechnology, a new door has been opened in the field of medical imaging. Quantum dots are "fluorescent semiconductor nanocrystals. . . which range from about 2 to 10 nanometers across" (Ben-Ari, 2003, p. 502). When first discovered, these particles were believed to have enormous potential in computer and electronic development; however, their first application has actually been in medicine. These particles possess properties which make them optimal candidates for biomarkers: they "have a broad absorption spectrum," "can be excited by a wide range of wavelengths," and "have a narrow emission spectrum" (Jiang, Gnanasammandhan, & Zhang, 2009, "Quantum Dots," para. 1). Those characteristics mean that quantum dots will emit the same frequency of light when exposed to a large variation of light frequencies; in addition, different kinds of quantum dots will emit a different frequency of light when hit with the same light source. Current biomarkers need to be exposed to specific light frequencies to be illuminated; however, quantum dots allow medical professionals to image a wide variety of biomarkers at one time, utilizing only one light source (Jiang, Gnanasammandhan, & Zhang, 2009, "Quantum Dots," para. 1).

Not only do quantum dots possess optimal florescent properties, quantum dots can

remain in the body without dispersing like organic dyes; this means medical professionals and researchers can watch the movement of markers for minutes or even days (Ben-Ari, 2003, p. 503). Biophysicist Jeeseong Hwang, the lead scientist for the National Institute of Standards and Technology (NIST), has said, "They [quantum dots] also have the advantage of monitoring changes in cellular processes while most high-resolution techniques like electron microscopy only provide images of cellular processes frozen at one moment. Using quantum dots, we can now elucidate cellular processes involving the dynamic motions of proteins" (Boutin, 2010, para. 3). This technology has the potential to enhance the understanding of how cells work by allowing scientists to image specific cells over extended periods of time, therefore gaining an in-depth understanding of cellular function.

History of Quantum Dots:

When first discovered, quantum dots were made entirely of chemicals that were toxic to the human body and were not soluble in water, rendering them impractical for any medical application. In 1998 this problem was resolved through "various surface modifications such as silica encapsulation, ligand exchange, conjugation to mercaptohydrocarbonic acids, dithiothretol and oligomeric ligands are carried out to make them soluble in water, which is essential for biological applications" (Jiang, Gnanasammandhan, & Zhang, 2009, "Quantum Dots," para. 2). The coatings also allowed the crystals to bind to certain cells, including tumor cells. When the crystals are illuminated with a specific light source, medical professionals can identify tumor locations.

Soon other discoveries were made. "By filling tiny polymer beads with multiple colors and intensities of dots in various combinations, the researchers created 'quantum beads' with

distinct optical signatures analogous to merchandise barcodes," (Ben-Ari, 2003, p. 502). The distinct optical signatures allow researchers to monitor each bead and its specific location. Researchers have also discovered that "quantum dot optical properties are altered as the nanoscale environment changes, offering greater possibility of using quantum dots to sense the local biochemical environment inside cells" (Boutin, 2010, para. 6). This property is key when medical professionals are monitoring single proteins within a cell. At first, UV light was widely used to image the markers; however, UV rays cause damage to human tissue. Since quantum dots can be illuminated by a broad array of light frequencies, with the same result, near-infrared light has now been used to eliminate radiation exposure.

One example of the application of biomarkers used today is in the detection of breast and ovarian cancer. "The overexpression of HER2 protein has been observed on the plasma membrane of tumors ... Fluorescent NPS [nanoparticles] are conjugated with the intact or derived forms of mAb directed against the extracellular domain of HER2 and used to label cancer cells" (Jiang, Gnanasammandhan, & Zhang, 2009, "In Vitro Imaging of Cancer," para. 3). Scientists have created biomarkers that will selectively bind to proteins found on cancerous tumors, making it possible to image the tumors and decide on further treatment. However, the HER2 protein is only present in about 25 percent of breast cancer (Ben-Ari, 2003, p. 502). Further research is necessary to discover methods for binding biomarkers to specific cells that are intended for imaging. A large number of proteins that exist on tumors, including chemicals that can bind to them, have yet to be discovered. This technology opens new opportunities to understand the body in ways research has never imagined.

How Drug Delivery Works:

Once cancerous tumors are detected, nanoparticles can transport medication to diseased locations in the body. “A drug can be encapsulated in particles or attached to the surfaces of capsules” (Liu, Miyoshi, Nakamura, 2007, p. 2527). Tumors have unique pathophysiology; they possess “a high density of abnormal blood vessels that are dilated and poorly differentiated.” After intravenous administration, nanoparticles become entrapped in these abnormal vessels (Liu, Miyoshi, & Nakamura, 2007, p. 2528). Once the particles are in the tumor, they slowly release medication, destroying the cancer over a period of hours or days. This means that less medicine is needed to treat diseases, healthy cells are not harmed, and more concentrated dosages can be directed to the tumor--resulting in rapid treatment. There are three prominent methods by which drugs can be delivered using nanotechnology. The first method introduces nanoparticles which become entrapped in the tumor, evading the healthy tissue, due to inefficient pathophysiology of the blood vessels in the tumor. The second approach utilizes drug delivery through encapsulation; these capsules slowly release drugs over a period of time. The third proposed solution is ligand-targeted nanoparticles, which carry medication on the outside of the particles, then bind with cancerous cells, and finally release the drugs once inside the cancer (Liu, Miyoshi, & Nakamura, 2007, pp. 2527-2529).

There are different ways in which drug delivery systems release medication. Research has been done by the Massachusetts Institute of Technology (2009) with gold nanoparticles, "The team built two different shapes of nanoparticles, which they call ‘nanobones’ and ‘nanocapsules.’ Nanobones melt at light wavelengths of 1,100 nanometers, and nanocapsules at 800 nanometers" (para. 7). Medication can be encapsulated in these nanoparticles until infrared light is used to illuminate the cancer specifically; at this point the capsule melts and the

medication is released. The application of nanotechnology, in the area of drug delivery, has the potential to increase bioavailability, create treatments with fewer side effects, improve success rates, and decrease costs.

Toxicity:

Nanotechnology could greatly alter the field of health care, but are nanoparticles safe? That nanoparticles exhibit properties different from macroparticles could compromise safety. According to the Department of Environmental Medicine, "The greater surface area per mass compared with larger-sized particles of the same chemistry renders NSPs [nanosized particles] more active biologically. This activity includes a potential for inflammatory and pro-oxidant, but also antioxidant, activity, which can explain early findings showing mixed results in terms of toxicity of NSPs to environmentally relevant species" (Oberdörster, Oberdörster, & Oberdörster, 2005, "Abstract," para. 1). This could be detrimental. "Because mitochondria are redox active organelles, there is a likelihood of altering ROS production and thereby overloading or interfering with antioxidant defenses" (Oberdörster, Oberdörster, & Oberdörster, 2005, "Concepts of Nanotoxicology," para. 10). Not only do these particles react faster, causing potential damage to cell mitochondria, but these particles can pass through cell membranes and enter areas of the body that they are not intended for, "sensitive target sites such as bone marrow, lymph nodes, spleen, and heart" (Oberdörster, Oberdörster, & Oberdörster, 2005, "Abstract," para. 1). The effect of these particles is dangerous not only for the patients but for also the manufacturer. In the process of making nanotechnology, such as quantum dots, nanoparticles may be inhaled or absorbed transdermally in far greater amounts than medical professionals recommend. This could be extremely dangerous for people working or living close to where

these nanotechnologies are produced. Before nanoparticles can be utilized in medicine, researchers need to discover a technique to make these products safe for the producer and the consumer.

Conclusion:

Nanoparticles could change the way diseases are detected, monitored, studied, and treated. They have the potential to make medical images brighter and more specific; they could also allow continuous screening for many hours or even days. Treatment could be specifically directed, reducing costs as well as side effects. When researchers learn more about the effects of nanoparticles, the industry of medicine could be changed forever. This process must not be rushed, since the medical community must first understand the long-term effects these particles have on humans and the environment.

References

American Cancer Society. (2013). Chemotherapy principles: An in-depth discussion of the techniques and its role in cancer treatment. Retrieved April 5, 2013, from http://www.cancer.org/acs/groups/cid/documents/webcontent/002995-pdf.pdf

Ben-Ari, E.T. (2003). Nanoscale quantum dots hold promise for cancer applications. *Journal of the National Cancer Institute, 95* (7), 502-504. doi. 10.1093/jnci/95.7.502

Boutin, C. (2010, October 6). Small nanoparticles bring big improvement to medical imaging. Retrieved April 5, 2013, from http://www.nist.gov/pml/div685/imaging_111709.cfm

Centers for Disease Control and Prevention. (2013, January 11). Leading causes of death. Retrieved April 5, 2013, from http://www.cdc.gov/nchs/fastats/lcod.htm

Jiang, S., Gnanasammandhan, M.K., & Zhang, Y. (2009, September 16). Optical imagine-guided cancer therapy with fluorescent nanoparticles. *Journal of the Royal Society Interface, 7*, 3-18. doi: 10.1098/rsif.2009.0243

Liu, Y., Miyoshi, H., & Nakamura, M. (2007). Nanomedicine for drug delivery and imaging: A promising avenue for cancer therapy and diagnosis using targeted functional nanoparticles. *International Journal of Cancer, 120*, 2527-2537. doi: 10.1002/ijc.22709

Oberdörster, G., Oberdörster, E., & Oberdörster, J. (2005, July). Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles. *Environmental Health Perspectives, 113* (7), 823-839. doi: 10.1289/ehp.7339

Massachusetts Institute of Technology. (2009, January 6). Gold nanoparticles for controlled drug delivery. ScienceDaily. Retrieved from http://www.sciencedaily.com/releases/2008/12/081231005359.htm

National Nanotechnology Initiative. (n.d.). Benefits and applications. Retrieved from http://www.nano.gov/you/nanotechnology-benefits

Raghvendra1, S.T., Yadav, P., & Saxena, S. (2010, August-October). Clinical applications of nanomedicines: A review. *International Journal of Applied Biology and Pharmaceutical Technology*, *1* (2), 6600-665. Retrieved from http://www.ijabpt.com/pdf/8757-Tyagi[1].pdf