HealthManagement
Promoting Management and Leadership

Volume 4 / Issue 2 / 2009 - Features

Nanotechnology and Healthcare

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Recent years have witnessed unprecedented growth of research and applications in the area of Nanoscience and Nanotechnology. There is increasing optimism that nanotechnology, as applied to medicine, will bring significant advances in the diagnosis and treatment of disease. Anticipated applications in medicine include drug delivery, diagnostics, cell therapy and production of biocompatible materials. Examples and visions make up of front pages of scientific top journals. But when will we be able to master its potential and the risks involved, so that the patient can start to profit?

Nanotechnology concentrates on the manipulation and fabrication of materials in a bottom-up approach. Using principles often mimicking the processes of nature, we are gradually becoming capable of building highly organised molecules, that have very specific properties. The fascinating side of nanotechnology is that it integrates physics, biology and chemistry and needs open minds by researchers and technology developers in this field. Using the principle of DNA copying in a cell to develop quick calculations is not a straightforward application, but is proving to be very efficient for IT.

Since nanotechnology involves bottomup fabrication, hopes are also there that sustainable and clean production processes can finally be developed without producing waste.

Market Expectations

Analysts estimate that the European market for nano-based products is currently around 2.5 billion but could rise to hundreds of billions of Euros by 2015 and one trillion in a few years thereafter. Lux Research reports that corporations spent 3.8 billion dollars globally on nanotechnology research and development in 2004. Approximately 900 million dollars in venture capital has gone to nanotechnology companies since 1999, with386 million dollars invested in 2003. Furthermore, Lux predicts that by 2014, nanotechnology will be associated with 15 % of all manufactured goods, roughly worth 2.6 trillion dollars. Products incorporating emerging nanotechnologies would constitute 920 billion dollars in value added, accounting for 2% of global gross domestic product. Manufacturing, incorporating nanotechnology, will be responsible for 10 million jobs worldwide, comprising 11% of total manufacturing jobs.

However there is also considerable debate about nanotechnology, as is (and should be) the case occur for every new technology. The complicating fact is that nanotechnology is not a single technology such as biotech, or silencing RNA. Nanotechnology is a foundational technology which in turn enables developments in many sectors and industries. When are we to expect effects or breakthroughs on Health Care?

Nanotechnology and Healthcare: Opportunities

Personalized medicine is key to all perspectives about the future of health care and many developments in science and industry are seeking to make this happen. The vision here is that a personal diagnosis can be complemented with a personalised treatment using customised minimal invasive surgery or medication targeted and tailored to the specific needs of a particular patient. This vision will clearly have a considerably

impact on the development of health care, its costs and on insurance models. Nanomedicine is the term that is being used to describe the field that is generated by interaction of nanotechnologies and a vast range of medical and diagnostic fields (see Table 1).

Regenerative Medicine

Regenerative medicine involves smart biomaterials on the one hand, and on the other nanotechnology enabling cell-based therapies and tissue growth. The imminent growth of this field is explained by the need for "repair and enhancement" of cells and tissue in a rapidly aging population. With the emergence of stem cell therapy a decade ago, this field is expected to grow into a more mature phase where rapid and customized production is likely to be commonplace within a decade from now.

Biosensors

Biosensors is another field that is rapidly changing due to inputs from nanotechnology sensors and has relevance for several other major areas such as in vivo and in vitro diagnostics. At the moment nanotechnology has an enormous effect on the speed and specificity of determinations of biomarkers in body fluids.

Although initial progress has been made in the genomics area using PCR and microarray- technology, it is expected that in the years to come, the analysis of proteins (proteomics) will receive an enormous boost. Proteomics and genomics will then be equal and complimentary tools to detect the risk for and status of biological adverse effects, which lead to diseases.

Drug Delivery

Drug delivery using smart materials and nanoparticles is a research area that may help to restore the continuously decreasing output of new drugs by pharmaceutical companies, and help to improve the efficacy of existing drugs and revitalize drop-out drugs since local delivery may eliminate earlier systemic side effects.

Smart drugs, that consist of assemblies of carrying agents (nanoparticles), imaging devices and drugs are being developed to target affected tissues and at the same time monitor the process.

Magnetic Nanoparticles: Iron Oxide Becoming a Useful Tool.

To date, most interest in the clinical use of magnetic nanoparticles has focused on iron oxide. This is because of the chemical stability, biological compatibility, and relative ease of manufacture of magnetite (Fe3O4) and maghemite (_- Fe2O3) nanoparticles.

The in vivo use of magnetic nanoparticles is attracting considerable interest as a means of delivering personalized medicine. Biocompatible nanoparticles that can be drawn toward a magnet are being investigated as site-specific drug delivery agents. Polymers or silica-shells filled with iron oxide and a drug have been made by and tested in animal tumour models to show increased efficacy and less side-effects (review: Borm & Muller-Schulte, 2006). In addition, paramagnetic iron oxide nanoparticles can be heated in an alternating magnetic field, and in this way be used to create local hyperthermia. This is being applied to treat brain tumours that are not operable, and this application is ongoing in clinical trails (Maier-Hauff, 2007).

Combinations of iron-oxides have already been approved for clinical use as MRI contrast agents. MRI agents work by altering the relaxation rates of water protons that are trying to realign with a static magnetic field following the application of radio frequency (RF) pulses. Iron oxide-based contrast agents affect transverse relaxation times, or what is known as T2 decay.

This leads to 'negative contrast', or dark spots, on T2-weighted MR images. The agents tend to be termed super-paramagnetic iron oxides (SPIO) if individual particles are larger than 50 nm and called ultra- small (USPIO) when particles are smaller then 50 nm. This application is mainly used to enhance contrast in inflammatory regions or regions characterized by leaky vessels, such as in tumours. A new application is passive imaging of medical devices in MRI by marking devices on the surface with a coating containing iron oxide nanoparticles.

However, its clear that one size does not necessarily fit all. Realizing the clinical potential of these novel nanocarriers means finding the correct magnetic nanoparticle and its properties for each particular application.

This means that the exact functional demands needs to be disentangled into the needed physicochemical properties and coupled to a biological behaviour that allows these things to happen.

Despite the tremendous amount of work the only registered applications of iron oxide particles are (U)SPIO as contrast agents. Of course there is also the ex-vivo application of iron oxide in magnetic beads that are used in diagnostic platforms for rapid and automated determination of biomarkers.

A Classical Dilemma

The flood of consumer nano products tells us that nanoproducts are already on the market without a life cycle analysis or sufficient toxicity testing. What emerges is that for implementation for engineered nanoparticles in healthcare, a risk-benefit evaluation is needed per individual material and application. At the moment there is incomplete information on the risk side and we may discover the same occurs on the benefit side of the equation as well. This is typically the dilemma for many applications of nanoparticles. It appears that we do not have a full understanding or appreciation of the longer term implications or toxic effects of free, as opposed to fixed or biodegradable, nanoparticles.

Nanotechnologies therefore pose a classical dilemma for modern society: use its potential and go full speed ahead or perform the necessary risk assessment and technology assessments before stepping into this. Application in the field of health care is the ultimate challenge but has already started and will move from carefully controlled conditions such as contrast agents to more day to day products and applications.

Healthcare IT and Nanotechnology

Given the huge volumes of data that will be generated by nanomedicine, and require realtime capture, access, management and interpretation, it is inevitable that healthcare IT will be closely involved in the making of such a vision real.

In healthcare IT, the first significant impact of nanotechnology is likely to be in the area of medical diagnostics and Laboratory Information Management Systems.

Diagnosis is today still a lengthy and complicated business, with tests having to be scheduled and conducted, and samples then having to be sent for analysis, after which results can take days or even weeks to reach. Nanotechnology is accelerating the entire process, and enabling more precise diagnosis, via what has come to be known as a ‘lab-on-a-chip’ – a small, handheld device which not only requires tiny sample but permits near-immediate processing and analysis.

Nano-sized probes and biosensors will continue to enhance the speed of in vitro diagnostic testing. Nanoparticle formulations of iron oxides and specialty polymers will, on their part, broaden in vivo imaging capabilities by enabling the far-earlier detection of genetic anomalies, tumours and a whole spectrum of disease states, using lower and more effective doses of diagnostic compounds.

Concerns About Nanomedicine

Like biotechnology, there have been concerns about nanomedicine in some quarters, especially with regard to safety and privacy. So far, most such concerns have been raised by NGOs and technology watchdogs rather than the general public, which remains sanguine about its prospects. An exception is the Netherlands, where the Health Council has highlighted the need for rules and laws on privacy, the doctor-patient relationship and the possibility of a widening gap between diagnostics and access to therapy (Betekenis van Nanotechnologies voor de Gezondheid. No. 2006/06, Health Council of the Netherlands).

And yet, nanomedicine is hardly an everyday word. Nor, it seems, is nanotechnology. Various surveys (e.g. by the EU’s Eurobarometer) show about half of the general public had not heard about nanotechnology.

The European Commission has published a Recommendation for a Code of Conduct on responsible nano-research [C(2008) 424 final, dated February 7, 2008]. This urges research labs, companies, government bodies and NGOs to make a ‘public consultation on nanosciences’. One of its key planks is that “researchers and research organisations should remain accountable for the social, environmental and human health impacts” which their research “may impose on present and future generations.”

Some of the other points urged by the Recommendation for nanotechnology research include the following:

Ó Comprehensibility to the public.

Ó Safe, ethical and contributing to sustainable development.

Ó Anticipating potential environmental, health and safety impacts.

Ó Conforming to best scientific standards, including Good Laboratory Practices (GLP).

O Encouraging creativity, innovation and growth.

Led by Britain's Royal Society, Europe's private sector has also been developing a Responsible Nanocode of good practices, which would establish guiding principles rather than strict rules.

In the United States, chemicals giant DuPont and the Environmental Defense Fund (EDF) have jointly published a Nano Risk Framework in 2007, which seeks to identify and evaluate potential risks of nanomaterials throughout the product cycle.

Published on : Wed, 4 Feb 2009