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Exclusive: The Emerging New Wave of Theranostics

04 May 2016 | Features

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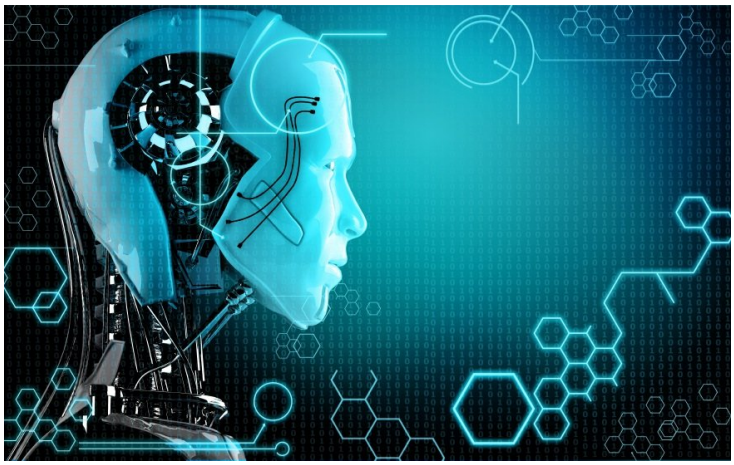

Imagine a very tiny capsule injected just below the skin of your arm. The capsule has a sensor capable of continuously measuring blood glucose levels and sends the information to your phone. Well, let's spice it up one level above the notch. Say, when the blood glucose level crosses its threshold, visualize the tiny little capsule releasing a dose of insulin in your blood stream. What this does is offer total freedom from regular needle pricks to measure blood sugar levels, and frees patients from the anxiety of taking the right insulin doses at the right time.

Science Fiction Or Reality?

Nope, this isn't something straight out of a Steven Spielberg's upcoming science fiction movie. This is Theranostics. A combination of diagnosis with therapy geared to revolutionize and disrupt the world of healthcare diagnostics.

"The idea of Theranostics is old," says Dr Biplab Bose, an Associate Professor in the Department of Biosciences and Bioengineering at the Indian Institute of Technology (IIT), Guwahati. "However, the term was coined and gained popularity in recent times, thanks to the development of targeted drug-delivery, microfluidics, and nanotechnology. Both in India and abroad, extensive work is going on to use targeted nano-delivery systems for Theranostics. A prime focus on this is to create drug loaded nanoparticles that are suitable for both in-vivo imaging and as well as for targeted drug-delivery."

Theranostics is the development and use of molecules for both diagnostics and therapeutic purposes, thereby providing Precision Medicine to patients - first in a clinical setting - for further understanding their diseases at molecular level, and then prescribing specific medicines.

"For example," adds Dr Aman Sharma, the Founder of Pune-based start-up ExoCan Healthcare Technology which focuses on Oncodiagnostics and Therapeutics space. "Fever in different patients has similar symptoms like rise in the body temperature. However, it may occur due to different infections. Hence, detecting the infection, whether bacterial or virus, accurately and then providing specific therapy is addressed by Theranostics."

The classic example is the use of Herceptin drug, a monoclonal antibody (mAb), against HER2 receptor, a specific protein expressed in almost 30% of breast cancer patients, to treat grade IV breast cancer patients.

Theranostics approach would be to first identify HER2 over-expression in breast cancer patients by a diagnostic test, and then prescribe Herceptin as a drug to those who have this over-expression.

In other words, Theranostics deliver customized treatment plan for patients, resulting in the availability of right drug, for the right patient, at the right time.
"This combining of therapeutic and diagnostic modalities for personalized treatment of patients enhances drug efficacy and ensure patients safety," comments Dr Arumugam Muruganandam, MD & CSO of Bangalore-based Affigenix Biosolutions. "At present in India, patient-centered care which focuses on integrating two disciplines such as imaging and therapy for targeted drug-delivery at the site of action is in limited practice except in specialty hospitals for cancer and cardiovascular diseases (CVDs)."

Indian Theranostics Scene

Molecular theranostics is a major field that involves small biochemical moieties and biomacromolecules. India is yet to get its share of modern Theranostics field. There are a few start-up companies in India that are operating in the Theranostics and Personalized Medicine in general.

"Theranostics and Personalized Medicine are very nascent sectors in India, as compared to the West, where personalised medical approaches have reached the clinic on a much larger scale," shares Dr Nilay Lakhkar, Founder & CEO, SynThera Biomedical, a start-up focusing on manufacturing and commercialization of biomaterials-based medical devices.

The West may be early adopters of the evolving field of Theranostics in to their routine healthcare as it promotes safer and more efficacious pharmacotherapies to patients which is supported by patients, and encouraged by Insurance companies.

"Whereas in India, we may gradually implement Theranostics across urban areas as it becomes affordable with appropriate testing systems, and expertise becomes available," remarks Dr Arumugam.

Currently in the West, a severe disease like cancer is treated through precision medicine. For example, mutational typing of a cancer is first performed and the right therapy or drug is then prescribed based on the mutation.

Nanoparticles made of Iron Oxide and Gold are increasingly adapted for both in vivo diagnosis and treating cancer.

Here the diagnosis is performed by using existing clinical imaging techniques such as MRI (iron oxide) and X-ray or CT (Gold), where in following the intravenous injection, the nanoparticles accumulate in the tumor tissue to provide precise contrast thereby differentiating it from normal tissue.

Considering the Indian population and its disease burden, Theranostics will eventually enter the Indian healthcare market in a big way in the next couple of years.

"In the next 5 or 6 years, we would see some form of Theranostics in clinical use, particularly for solid tumours. I believe oncologists along with radiologists will probably be the first to introduce Theranostics in clinics," Dr Biplab predicts.

However, the key question is whether India will be able to develop any such products indigenously?

There are several lacking factors, points Dr Biplab. "Factors include lack of access to advanced instruments. India is lacking in the development of real-life microfluidic devices. However, Indian scientists have gained reputation in the field of nano-materials, including nano-drug delivery systems. Unfortunately, Indian pharma companies are slow to pick the thread from laboratories, and have not yet built upon the developments that have happened in our academic labs," he stresses.

Also, the patients in India are not much clinically educated. "One of the fundamental issue is cost factor, and the absence of active clinical trials and proper counselling in Government hospitals; and lack of high throughput facilities are among many reasons which retard the development of opportunities in Theranostics in our country," highlights Dr Aman.

The key areas of Theranostics have developed rapidly in the last few years including Photo-Immunotherapy (PIT), and nano-particle-based drug-delivery and imaging systems. "We may soon see some successful clinical trials in these two segments," reveals Dr Biplab.

In a way, Personalized Medicine, Theranostics and Precision Medicine are all interlinked from the view point of treatment.

Dr Arumugam explains, "It is all about the right drug, at the right time, for the right patients. Theranostics mainly refers to treatment strategy that combines therapeutics with diagnostics as one treatment unit. Personalized Medicine imply that drugs are being customized for each individual patient. In Precision Medicine, the dosing regimen is designed for patients based on drugs used, condition to be treated, genetics, environmental and lifestyle factors."

Theranostics is important for both Personalized as well Precision Medicine, feels Dr Biplab.

"I would say, it is important more for Precision Medicine. Take the example of a drug-delivery system that combines targeted drug-delivery and imaging of drug-delivery. Such drug-delivery system would allow the physician to deliver the drug to specific location as well as confirm it by imaging," he notes.

The field of Theranostics is aided by Genomics, Proteomics, Organic or Inorganic Chemistry and Pharmacology. This makes it a broader field of interest, which cannot be catered by one researcher.

"In a global perspective, active collaboration is very important for rational and innovative ideas to be seeded for true emergence of Theranostics. In Indian scenario, this is building up with many thematic inter-institutional and industry-academia proposals being funded by DBT, DST, ICMR and the likes. India ranks 3rd, with 1st and 2nd being China and USA, in research outcome in field of Nanotechnology, and a significant percent of publication is related to Nanotheranostics, funded mostly by DST's Nano Mission. India can be a global leader in the field, if collaboration between scientists in the above mentioned field is made stronger and sustained for a significant period of time," elaborates Dr Asifkhan Shanavas, Scientist, Institute of Nano Science and Technology (INST), Department of Science & Technology (DST), Government of India.

Theranostics and Personalized Medicine is bridged by Pharmacogenomics, a field that studies the effect of genes on a person's response to drugs.

This relatively new field combines Pharmacology and Genomics to develop effective, safe medications and doses that will be tailored to a person's genetic makeup.

Personalized Medicine also takes all non-genetic and environmental factors in to account, including gender, age, diet, lifestyle, and even the intestinal microflora.

Under this regime, the doctor will advise the patient to first take an in vitro diagnostic test or a single in vivo imaging protocol with the Theranostic agent to identify its efficiency to selectively accumulate and act in the pathological site.

"According to the therapeutic outcome," explains Dr Asifkhan, "the physician decides the course of treatment for the patient. Furthermore, information from non-invasive imaging on the accumulation of nanomedicine formulations in potentially endangered healthy tissues such as heart and brain may help in excluding patients from further treatment. Consequently, combination of non-invasive imaging and disease-targeted drug delivery has significant potential for Personalized Nanomedicine-based chemotherapeutic interventions, to achieve delivery of the right drug, to the right location, in the right patient, at the right time."

India's Opportunities At Hand

Indian population is genetically very diverse. Scientifically, the West-built Theranostics tools may not work well for Indian population.

Moreover, the mutations or genomic anomalies present in the Western population may not be harbored by the Indian patients due to different genetic makeup.

Dr Aman explains, "Hence, development of indigenous pool of databases for Theranostics in various diseases is what we should start with. Three vital opportunities lie ahead for Theranostics in India. Firstly, disease-specific database (diabetes, heart disease, and cancer can be taken on priority) generation for personalized medicine by genotyping known mutations and validation of existing biomarkers.

"Secondly, setting up minimal infrastructure for Theranostics tests in hospital level settings. Lastly, there must be patient counselling centres inside hospitals to make patients aware of their disease type. Economically, we are one of the biggest markets for Theranostics as mentioned earlier due to very divergent genetic makeup of the population. The Government can encourage public-private partnerships to promote Theranostics research in collaboration with pharma and biotechnology giants and improve infrastructure for such opportunities."

For advanced diseases like cancer, the greater diversity in Indian population creates a window of opportunities for Theranostics or Precision Medicine.

Dr Nilay opines that opportunities do exist for Indian companies to focus on cutting-edge Theranostics products and services with demands being driven by a growing, affluent, and knowledgeable patient pool.

"However, the Indian market for Personalised Medicine is still very much a niche market focused on high-net-worth individuals (HNWIs), and upper middle-class consumers, since these therapies are highly expensive, and not yet easily scalable," he justifies.

Dr Biplab believes that the first use of Theranostics would probably be in oncology clinics, where physicians would use targeted drug-delivery for solid tumours, and would be able to image or monitor such delivery in real-time.

"Cancer is one of the leading causes of death in India, and its burden is increasing. Unlike many other disease, Precision Medicine is crucial in cancer. In near future, we may see several players in cancer Theranostics to enter the Indian market," adds Dr Biplab.

India also has vast potential to exploit the Theranostics especially in nano Theranostics for patient care, provided the regulation and funding support system helps in the discovery by academic sector; development by biopharma sector; and adoption by healthcare providers for personalized treatment.

"The middle income group population is growing in India, and medical tourism is on the rise, and my guess is that wealthy patients may be more willing to pay for personalized treatments," Dr Arumugam says.

The sub-continent has significant population affected by both communicable (infectious disease of bacteria, fungi and virus) and non-communicable (cancer, myocardial infarction etc) diseases.

Dr Asifkhan states that a significant percentage of these patients fail to respond to standard treatments due to emergence of drug resistance, which warrants newer effective strategies with rapid molecular diagnosis followed by rationally designed treatment.

"Early detection and treatment is also vital to reduce such disease burden. Theranostic approach can have tremendous impact in this line along with appreciable reduction in cost involved due to the selective treatment protocol, i.e., Personalized Medicine," he highlights.

Overcoming Obstacles

Therapy and diagnosis go hand-in-hand, and both are expensive for a country like India,

"Patient affordability is going to be a big challenge," stresses Dr Arumugam. "There is also perceived loss of opportunity by drug manufacturers for particular drug to be used by cherry-picking patients for treatments as it reduces the market potential of the drug. Educating doctors, patients, Insurers and regulators will be a challenge as Theranostics does not provide guaranteed outcome yet."

Theranostics is closely related to patients. "Hence we should educate more patients about their disease types and right therapies, and how it can enhance lifesaving chances in case of a deadly disease," recommends Dr Aman.

There is a need for the existence of certain private equity bodies, venture capitalists and Government schemes who can invest in high-risk upcoming areas like Theranostics.

It also calls for setting up infrastructure to create biobanks, tissue banks, and minimal research setups in hospitals and medical colleges for creating our own indigenous databases.

Dr Aman continues, "One of the most important shortcomings is the lack of good research in this area in our country. The Government should setup special grants schemes to promote biological research in Theranostics, and should also make a provision to bring research entities, medical colleges, and hospitals under one umbrella to make the best use of existing knowledge and resources."

Just like drug development, work on Theranostics requires clarity on specific clinical requirements, understanding market dynamics, and the limitations of current technologies.

"Therefore, successful development of a Theranostics requires active collaboration between academia, clinicians and the industry. In India such collaborations are rare, if not absent," Dr Biplab mentions.

Dr Asifkhan also believes that cost will play a major role in translation of new Theranostic agents to clinics.

He opines, "The foremost challenge is to develop these agents at lower costs, so that their industrial scalability will not have profound effect on its marketing costs, if they clear clinical trials.

"Secondly, time is a crucial player in bringing some of the promising agents into market, as pre-clinical and clinical trial takes years to complete, demanding simple and efficient models such as organ-on-a-chip that provides quicker results on par to human trials. It is also important for Indian researchers to take up innovation as a key element to provide state-of-the-art Theranostic solutions."

Strict Competition?

Experts believe that the real completion is yet to begin perhaps due to great investments required in any Theranostics programs.

One of the reasons is that it requires a huge sample base to start with, and compilation of information to reach statistical end-points.

"Subsequently, that information is then put-up into R&D to design effective therapies for patients. The whole process is far more costly than just developing a common drug which would be used by bulk and unsorted population. Though, the field has far reaching implications for mankind, it is yet to take off to reach to its newer heights," says Dr Aman.

Dr Arumugam also believes that though Theranostics has good potential it does not have any competitions at the moment.

"In India, both doctors and patients may prefer to go with 'one-size-fits-all' approach, and continue with trial-and-error method for treating patients. Potential impact on revenues by the 'slice-and-dice' approach in selecting patients for personalized treatment will prevent wide acceptability by bigger hospital managements and biopharma companies, and may resist to change," he emphasizes.

The Future

While there are several advancements in molecular Theranostics to quote, the most attracting is in the field of Radiopharmaceuticals.

They are successfully being used at Indian premier institutes such as Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC) among others.

Dr Shailaditya Sengupta of Massachusetts Institute of Technology's (MIT) Brigham and Women's Hospital (BWH) developed nanoparticles which first delivers an anticancer drug specifically to tumour tissues, and if the tumour starts dying or regressing, it then starts lighting up the tumour in real-time.

This is a major finding to first treat and then have a follow-up on the course of a disease.

In longer terms, Theranostics would pave the way for a healthier world around us.

Advancement in Nanotechnology, Biosensors, Bioelectronics, Pharmacogenetics, Cancer Immunotherapy, Biomarker Profiling, Companion Diagnostics, and the ability to combine therapeutic and diagnostic capabilities into one single agent (nanomaterials) have already started a ripple effect in healthcare.

"The only limiting factor is going to be the affordability for personalized treatment," states Dr Arumugam.

In the future, patients who suffer from chronic diseases will have a combination of wearable devices and implantable Theranostics.

Dr Biplab observes, "These will monitor our critical health parameters in real-time and intervene at the right time. Considering the speed in development of micro-fabrication and micro-electronics, I believe, such devices will be in our homes within the next 10 years."

Five years down the line, breakthroughs in Theranostics R&D may bring down treatment costs, and increase scale-up potential.

"A focus on building strategic partnerships with global players in the pharma and diagnostics sectors may be the way forward for Indian companies in this space," suggests Dr Nilay.

Through Theranostics, the treatment costs might go up initially, but a faster disease recovery would be ensured.

Dr Aman voices, "Theranostics might improve patient survival chances especially in cancer and heart disease patients. In totality, a greater health, emotional, and life security is what the goal of Theranostics is."

At the moment, India does not have a statistical data on molecular nature of disease(s) among the Indian population.

Nevertheless, combining the three major diseases including diabetes, heart disease, and cancer, Theranostics market should value anywhere between US $300-500 billion in the next 5 years.

In the coming years, a better collaboration between the fields of molecular or nano Theranostics and OMICs -- Genomics, Epigenomics, Transcriptomics, Proteomics and Metabolomics -- is expected to realize the dream of personalizing medical interventions, especially for evading disorders such as cancer.