Magnetic Nanoparticles Hyperthermia: An Emerging Cancer Therapy Sans Side Effects

Surojit Ranoo*
Indira Gandhi Centre for Atomic Research
Email: surojit@igcar.gov.in

Cancer, a real threat to human race, is spreading its roots in every organs of the human body. The probability of occurring cancer in different organ varies: in some organs it's quite evident whereas it's rare for some other parts of the human body. With time, scientists and doctors worked together and managed to discover various means for damage control, but still curing cancer remains one of the biggest challenges for mankind. The most effective and popular techniques like chemotherapy, radio therapy, hormonal therapy, have permanent side effects which may be severe for certain cases. In chemotherapy the drug is designed to destroy fast growing cancer cells which besides doing its job, also gets involved in damaging fast growing blood forming cells in the bone marrow, hair follicles, cells in the mouth and digestive tract, etc. leading to anaemia, hair loss, infection and various other side effects. Similarly radio therapy causes permanent skin problems. So the need of the hour is an efficient cancer therapy with minimum side effects.

In cancer treatment the primary goal is to kill the cancer cells. Our human body uses a mechanism to get rid of germs by simply increasing our body temperature which manifests as fever. Why not use the same defensive mechanism to kill cancer cells also in a controlled manner? Yes, it can be done. Cancer cells, like other cells, are susceptible to temperature rise. Research shows that beyond certain temperature regime (>42^{0}C), the growth rates of cancer cells reduce significantly. Further increase in temperature, leads to necrosis of cancer cells. Such temperature sensitive growth rate of cancer cells is tried to exploit in hyperthermia -based cancer treatment, where, initially, hot water circulation was used to cure cancer. But its success rate highly depends on the position of the

* Mr. Surojit Ranoo, Ph.D. Scholar from Indira Gandhi Centre for Atomic Research, Homi Bhabha National Institute, Mumbai, is pursuing his research on "Magnetic Field Induced Heating of Magnetic Nanoparticles for Magnetic Hyperthermia Applications." His popular science story entitled "Magnetic Nanoparticles Hyperthermia: An Emerging Cancer Therapy Sans Side Effects" has been selected for AWSAR Award.

tumour and tolerance of the patient. If the tumour is well within the body it's extremely difficult to use this technique.

The path -breaking developments in the field of nanotechnology, in the last decade, showered new light on the hyperthermia technique. It's well- known that ferro/ferri magnetic material can dissipate heat energy through magnetic hysteresis loss when subjected to an alternating magnetic field. Nano sized magnetic particles (1nm = 10^{-9}m) can easily travel through the blood vessels and reach the cancer affected organs. Once it reaches the desired organ, an alternating magnetic field can be applied around that region externally. In the AC magnetic field, the magnetic nanoparticles (MNP) start dissipating heat energy owing to their inherent loss mechanisms (like hysteresis and relaxation losses). Here, the tiny magnetic nanoparticles act as transducers that converts the externally supplied magnetic energy into heat energy. Magnetic nanoparticles mediated hyperthermia therapy is called magnetic fluid hyperthermia. The major advantage of magnetic fluid hyperthermia is its ability to act as focal therapy due to the smaller sizes of the magnetic nanoparticles. The MNPs can be distally controlled using and external magnetic field and tissue specific targeting can be achieved by selectively coating the MNPs with various bio-compatible moieties. As the entire body is not exposed to the AC magnetic field and a very low amount of MNPs is sufficient to provide a therapeutic dose to the cancer cells, the side effects are substantially lower in the case of magnetic fluid hyperthermia -based cancer treatment. Though originally proposed by Dr. R. K. Gilchrist and his group, in the year 1957, recent advances in nanotechnology resulted in the continued and active research and development in this field.

Out of so many magnetic materials available, iron oxide has been approved by FDA for *in vivo* clinical trials owing to its low level of toxicity in the human body. These MNPs can be directly injected into tumours or it can be guided through the body fluid. For guiding through the body fluid, these MNPs should be coated with biocompatible molecules which ensure less side effects and stable dispersion behaviour in body fluid. However, questions have been raised by several biotechnologists about the side effects arising from the interaction of the magnetic field of MNP with the body's own magnetic field. Upon reducing from bulk to nano size, the property of ferro/ferri magnetic material changes mysteriously and they exhibit superparamagnetic behaviour. In room temperature (~30^0C), they behave as paramagnetic material, i.e., no magnetization unless a magnetic field is applied externally. However, their magnetic response to external magnetic field is ~5000 times more than that of a paramagnetic material.

Here in the Indira Gandhi Center for Atomic Research (IGCAR), we are working on the development of superior MNPs for efficient biomedical and sensing applications. We have, in-house, developed a radio frequency induction heating facility for testing the magneto-thermal conversion efficiency of MNPs dispersed in a suitable base fluid. The efficiency of the dissociated heat energy is described in terms of a dosimitric quantity named as specific absorption rate (SAR). The value of SAR decides the dose for practical applications. We have successfully developed and demonstrated the magnetic fluid hyperthermia in water based magnetic fluid containing phosphate coated iron oxide nanoparticles. Phosphate coating was applied on the surface of the magnetic nanoparticles to ensure bio-compatibility and long- term stability.

We have also carried out experiments on MNP immobilized in a tissue mimicking agar gel, where, ~ 50 % reduction in heating efficiency was observed, as compared to the water based system. This leads to a scary scenario where the nano-particle dose or the amplitude to the AC magnetic field need to increase beyond biologically acceptable levels. To address these issues, we at IGCAR, have demonstrated, for the first time, in-situ orientation of the dispersed MNP using an external DC magnetic field and thereafter, the oriented assembly is subjected to the AC magnetic field, which results in ~ 40-60 % enhancement in heating efficiency, thereby mitigating the practical challenges. Under the influence of the small external DC field (~ 80 Gauss), the MNPs form linear chain like structures along the field direction. These oriented chain-like structures have a larger hysteresis loop area, as compared to the randomly distributed MNPs, which causes the enhancement in heating efficiency.

Using this modified approach to magnetic fluid hyperthermia, the nanoparticle dose and treatment time can be reduced significantly. Here, at IGCAR, we are in the process of continuous development and fine-tuning of magnetic nanoparticles for hyperthermia based cancer treatment. The multi-faceted research team consists of Mr Surojit Ranoo, Mr T. Muthukumaran, Dr B. B. Lahiri and Dr John Philip (team leader). Selected portions of the work are published in the Journal of Magnetism and Magnetic Materials (Vol. 407, 2016, pp 101-113). The latest developments are going to be presented at the International Conference on Magnetic Materials and Applications, at Bhubaneswar, during 9th -13th December 2018.