

Editorial

A Quixotic journey with a fairy tale ending? A brief history of hyperthermia

Hyperthermia (HT) as a therapeutic option is mentioned in early medical texts from India. However, it is in the early eighties of the last century that the first wave of technology backed HT, which was tested in clinics. There is a vast body of laboratory data as an evidence for the utility of heat in treating cancer. The ability to sterilize hypoxic cells, induce apoptosis, inhibit DNA repair, influence temperature dependent intracellular processes, immune stimulation induction for changes and many other biological rationale, formed a formidable rationale for combining HT with radiation and later with chemotherapy. The late seventy's and the eighty's saw a surfeit of papers with mixed results. Interest started waning as clinicians who had hoped for a quantum leap, but witness a modest change. Biology was on the side of scientists but adequate technology was not with clinicians. The modality of HT got restricted to silos in a few countries of Europe and Japan. It was nearly a decade later that HT got approved by insurance agencies in USA. However, remuneration was not attractive to enthuse radiation oncologists. Hence, HT never was popular.

Developments in technology continued albeit at a slow pace. Publication of a seminal paper by Vander Zee in the *Nature* in 2002^[1] galvanized the resurgence in interest, but, in a small group of clinicians. There were also new recruits to the field. Many of the trials are small, but collectively did indicate the effectiveness of HT. High-intensity focused ultrasound (HIFU) for ablation and thermal range HT have grown in popularity. Both microwave and radiofrequency based heating technology has improved. Computed tomography (CT) scan based treatment planning systems have enhanced the understanding of specific absorption rate (SAR) distribution prior to HT. Online magnetic resonance (MR)-based thermometry has added a new dimension to technological capabilities. Overtime, considerable data including positive randomized trials have raised the level of evidence.^[2] Nagraj G Huilgol, Sapna Gupta, CR Sridhar. Hyperthermia with radiation in the treatment of locally advanced head and neck cancer: A report of randomized trial. *Journal of Cancer Research and Therapeutics* 2010, 6 (4):492-496.

Earlier laboratory studies in HT in India were conducted at Bhabha Atomic Research centre in the seventies. They were at the time when hypoxic cell sensitizers, ruled the roost in most research heating system from Japan and was installed in Chennai and later in Mumbai in 2000. Another capacitive heating system from Germany was installed in Bangalore in 2010. Indian association of hyperthermic oncology and medicine has been in existence since two decades. Indigenous development of technology failed to take off for the lack of support from funding agencies and earlier opinion makers. Nano gold and iron particles for cellular HT are being developed at Indian Institute of Technology, Bombay. However, the technology has not been marketed or tested in the clinics. IIT Madras has developed microwave based surface heating system, which is awaiting clinical validation.

The dynamics of progress in medicine is complex. The truth in medicine is many a times ephemeral but always contextual. Evidence-based medicine is only a part of the story. The dominant personality's market forces and pressure groups influence the trends in many instances. Angioplasty was implemented without the benefit of randomized trials. The push for protons for routine clinical use in India and elsewhere is an example of persuasive power of the industry.

The mistake of recommending hormone replacement therapy for all women was based on ghost written articles in some prestigious journals. The subsequent clinical trials have shown the perils of HRT like increased chance of stroke and breast cancer.^[3] Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women Principal Results From the Women's Health Initiative Randomized Controlled Trial, *AMA*. 2002;288 (3):321-333. doi: 10.1001/jama.288.3.321. The market forces primarily driven by pharmaceutical giants have compelled medical science to pursue false leads. Hyperthermia suffered for lack of support from such giants.

It is indeed sad that opinion makers in India also have been reluctant to pursue HT while eagerly embracing proton and hadron-therapy, which will be a huge drain on the national exchequer without

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Access this article online

Website: www.cancerjournal.net

DOI: 10.4103/0973-1482.136528

PMID: ***

Quick Response Code:



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any proportional benefits both tangible and intangible. The way forward is to develop the technology for HT indigenously and make it available to clinicians. Most international venders are reluctant to enter India. So, it is a good idea to develop skills in engineering and clinical HT. The quixotic journey will have a fairy tale end if more clinicians adopt an inexpensive but effective therapy to treat cancer. This is a brief history of HT.

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Cite this article as: Huilgol NG. A Quixotic journey with a fairy tale ending? A brief history of hyperthermia. *J Can Res Ther* 2014;10:225-6.

Source of Support: Nil, **Conflict of Interest:** No.

