





# Rajiv Gandhi Cancer Institute and Research Centre

A Unit of Indraprastha Cancer Society Registered under "Societies Registration Act 1860"



# EDITORIAL CAN MALES DEVELOP BREAST CANCER?

You may think, men don't have breast, so how can they get breast cancer? The truth is that boys and girls, men and women, all have breast tissues. The various hormones in girls and women stimulate the breast tissue to grow into full breast. Boys and men's bodies normally don't make much of the breast stimulating hormones. As a result, their breast tissues usually stay small and flat. But sometimes, you see boys and elderly males with medium size or large breasts. Usually these breasts are just mound of fat.

Male Breast Cancer is a relatively rare cancer. Almost 1% of breast cancers develop in males. In an Indian study, eight out of 1200 (0.7%) male cancer diagnoses in a pathology review represented breast cancer. The relative risk of breast cancer for a female with an affected brother is approximately 30% higher than for a female with an affected sister. For men, the life time risk of being diagnosed with breast cancer is about 1 in 1000.

The risk of male breast cancer is related to an increased lifelong exposure to estrogen or to reduced androgens. The strongest association in men is with Klinefelter Syndrome (XXY), they have a 14 to 50 fold increased risk of developing male breast cancer and account for 3% of all male breast cancer cases.

Men who carry a BRCA-1 or particularly a BRCA-2 mutation have an increased risk of developing breast cancer. Certain conditions have been associated with an increased risk of breast cancer in men; chronic liver disorder (cirrhosis, schistosomiasis), history of mumps orchitis, undescended testis and feminization (genetically or by environmental exposure). In contrast it is important to note that gynecomastia is not a risk factor. Chronic alcoholism has been linked to male breast cancer.

There are significant differences between male and female breast cancers. Lesions are easier to find in men due to smaller breast size, however, lack of awareness may postpone seeking medical attention. The presence of gynecomastia may mask the condition. Lesions are less contained in men as they don't have to travel far to infiltrate skin, nipple or muscle tissue. These lesions tend to be more advanced. Indeed, more than half of male breast cancers are stage III or IV.

The median age of male breast cancer onset is 10 yrs later than in women. Diagnosis of breast cancer is often not considered as promptly in men and screening mammography is not used. Men often present with more advanced stage than do women. All histological types have been described with IDC accounting for more than 70%. However, infiltrating lobular carcinoma in men is rare but lobular carcinoma in-situ has not been seen in men. Majority of male breast cancers are ER, PR positive.

Primary local treatment is total mastectomy. Theoretically, BCT is a viable option but subareolar location of tumor and small amount of breast tissue present in most men limit eligibility for BCT. The use of post-op. RT follows the same guidelines as for female breast cancer. Use of systemic therapy in adjuvant setting follows same principles as in female breast cancer. Tamoxifen is the mainstay of adjuvant systemic therapy in ER + male breast cancer. However, treatment may be associated with hot flashes and impotence. There is no data on the efficacy of aromatase inhibitors as adjuvant treatment in male breast cancer. Adjusted for age and stage, the prognosis of breast cancer in men is similar to that in women.

Never ignore a lump in male breast. It could be cancer!

**Dr. Dewan A. K.** Medical Director

# NEW AVENUES IN RADIONUCLIDE THERAPY IN ONCOLOGY

In the present century, advances in cancer diagnosis & treatment have increased many folds. Currently, molecular diagnostic techniques coupled with biological targeted therapy has changed many facets of the disease, namely, the disease free interval, disease free survival, quality of life etc. Tremendous advances have been made in Radionuclide diagnostic techniques in Positron Emission Tomography (PET), whereby, bringing in objectivity and clarity in detection, diagnosis and response assessment. Keeping in pace with this, the scope of Radionuclide Therapy in the treatment of cancer has also taken significant steps forward from the "bench" to the "bed side".

The main ingredients of this form of the treatment are a tracer in the form of a radio isotope which has cell killing potential and a ligand which can be labeled with the isotope to target the specific areas of interest and sparing the rest of the body completely. The beauty of this form of treatment is its specific nature of radiation delivery and simplicity without any immediate or long term effects.

The use of Radioactive Iodine  $I^{131}$  is known to all and its potential in the treatment of differentiated thyroid cancer is well established. In this article I am going to describe two other such forms of treatment which is already used in patients elsewhere in the world and is gradually gathering evidence in its favour. We plan to introduce these two modalities of treatment for our patients in this year. These treatments are the ones as described below;

- (i) Peptide Receptor Radionuclide Therapy (PRRT)
- (ii) Intra-operative avidination for Radionuclide treatment as a radiotherapy boost for breast cancer (IART)

#### Peptide Receptor Radionuclide Therapy (PRRT)

PRRT is a new treatment modality and is well established in Europe for patients with unresectable somatostatin receptor positive neuroendocrine tumors and thousands of patients have been treated there with this approach. In India, currently this form of treatment is gaining popularity among the clinicians and is being discussed in conferences & forums regularly. The availability of <sup>68</sup>Ga labeled compounds for diagnostic imaging of somatostatin receptors and availability of Indian data is responsible for this popularity. However, still only limited centres in India has facilities for PRRT. The results of this form of treatment so far has been convincing as has been published in the literature and a randomized controlled trial is on the cards. Roughly 25 % of all treated patients achieve an objective tumor response with serious side effects been rarely reported. The first radiopharmaceutical used in PRRT was <sup>111</sup>In DTPA octreotide which was initially developed for diagnostic purposes. However, in addition to the y radiation <sup>111</sup>In emits Auger electrons (low-energy electrons with a short tissue penetration range of  $0.02 - 10 \, \text{um}$ ). These Auger electrons exert their cytotoxic potential within the nucleus at close proximity to the DNA after receptor internalization. However, in this aspect a major breakthrough was achieved by the conjugation of somatostatin analogs with the Chelator DOTA which stably binds all M3+ radiometals such as <sup>90</sup>Y (high energy B+ emitters), 2.28 Mey, half life of 64 hrs & <sup>177</sup>Lu (low energy  $\beta$ -emitter, 0.5 Mev, half life of 6.7 days) as well as some positron ( $\beta$ +) emitters (eg <sup>68</sup>Ga) and permits the use of such nuclides for therapy & imaging purposes. The first report on PRRT using <sup>90</sup>Y DOTATOC was published in 1997 and since then number of Phase I & Phase II trials have established the therapeutic potential of the modality. Recently long term follow-up and survival data for <sup>90</sup>Y DOTATOC was published with encouraging response rates and a significant longer overall survival. At the present moment <sup>177</sup>Lu DOTATOC is the preferred tracer for PRRT and significant literature data is evolving regarding its utility. The effect of <sup>177</sup>Lu-DOTATOC in patients with NET's refractory to conventional therapies is now been tried. Treatment was well tolerated with no adverse events. 66% patients achieved partial response (PR) and stable disease (SD) was found in 27% of patients. To popularize this treatment modality in India the Radiopharmaceuticals Division in Bhabha Atomic Research Centre (BARC) has started the production and supply of <sup>177</sup>Lu for its use in PRRT. This endeavour has significantly reduced the cost of this treatment and more and more patients are expected to be benefitted from this. Generally PRRT can be regarded as a relatively safe treatment and severe side effects are rare, especially when compared with the side effects of chemotherapy. The side effects of PRRT can be categorized as acute effects or as more delayed effects caused by radiation toxicity. The acute effects occurring up to a few days after injection of the therapy include nausea, vomiting and increased pain at tumor sites. These side effects are mild and can be minimized by infusing slowly and also can be prevented or reduced by symptomatic treatment. Severe toxicity as a result of the radiation absorbed dose in healthy organs is a rare phenomenon in case of adequate patient preparation before therapy.

#### Intra-operative avidination for radionuclide treatment for breast cancer (IART)

Conservative breast surgery, with adequate margins, followed by External Beam Radiotherapy (EBRT) to the residual breast, is considered as the standard treatment for most patients with early breast cancer. The initial treatment is generally followed by a boost to the tumor bed. The total time duration of 5 - 7 weeks for the EBRT schedule, many times is difficult to comply with. Partial breast irradiation techniques using Intra-operative Radiotherapy (IORT), Mammosite & Targetted Intra-operative Radiotherapy (TARGIT) are promising alternatives to conventional whole breast EBRT and have the advantage that they can shorten or perhaps even eliminate the conventional EBRT course. However, partial breast irradiation has two limitations; the limited availability of instruments for delivering the radiation and the restricted irradiation field which may fail to eradicate breast disease beyond the resection site. Possibility & feasibility of irradiating the residual gland using an innovative nuclear medicine approach named IART has been tried with encouraging results. IART is a technology based on the intra-operative injection of avidin (a glycosylated protein) in the operated breast followed by intravenous <sup>90</sup>Y (Yttrium) labeled biotin (radio labeled vitamin H) administration 16 - 24 hrs after surgery. Avidin & biotin have strongest affinity known in nature. The IART procedure is more or less a simple procedure which needs to be standardized in a particular Institution and needs close cooperation between the Surgeon and the Nuclear Physician. The procedure is performed in two steps, the first being avidination of the the anatomical area of the tumor bed with native avidin. The surgeon intra-operatively injects with a syringe, a solution of avidin directly into the tumor area without

margins & depth limitations. Within 24 hrs of surgical intervention BIOTIN–DOTA ligand labeled with 90Y is administered I.V. as a slow bolus injection. This form of treatment in early breast cancer is gradually becoming popular in few European Nations and the data published till date shows that using IART can have the advantages of targeting only the region of interest sparing the vital organs with less external tissue damage & burns. It is also seen that hospital stays can be reduced which will have logistic & economic benefits. IART is also a way of ensuring immediate adjuvant treatment after conservative surgery which may have other long term benefits.

Preliminary results reported from Milan, Italy, by Prof. Paganelli indicate that IART is a safe procedure for delivering 20 - 25 Gy to the tumor bed. There is a possibility of delivering a high dose upto 40-60 Gy by increasing the specific activity of <sup>90</sup>Y biotin to 20 - 30 GBq/mg. IART offers several advantages over other currently available accelerated breast irradiation methods. It could potentially be available to the majority of breast cancers without limitation as to location, size or multi focality. The surgeon plays a very important role in the procedure. After removing the tumor he has the advantage to choose the exact sites to inject avidin around the tumor bed. IART is a procedure which can be carried out in any hospital having a Nuclear Medicine facility.

Radionuclide therapy in oncology initially begun with the treatment of thyroid cancer with radioactive iodine in the sixties which is continuing till date. It has come a long way since then adding newer forms of therapy in its armamentarium regularly. Radionuclide therapy is unique in a way that it delivers high dose of radiation specifically at the target of interest without affecting the normal tissue. It can also be considered as a part of the "multimodality" approach to the treatment of cancer & is part of a team comprising various clinical disciplines. More and more use of this modality is envisaged in the future.

**Dr. P. S. Choudhary** Director - Nuclear Medicine

## **BREASTCON 2013**



The first ever International conference on Early Breast Cancer was organized by the Breast Services Dept. of Rajiv Gandhi Cancer Institute & Research Centre, Delhi. The theme of the conference was **"BREASTCON 2013: Emerging trends and Future Directions in the Management of Early Breast Cancer"**. The conference was held in full grandeur and scientific fervour between 13th - 14th April 2013 at India Habitat Centre, Lodhi Road, New Delhi.

The formal inauguration of the conference was held on 13th April in the evening. The inauguration was auspiciously marked by the lighting of the lamp by Shri Rakesh Chopra, Chairman, Shri D. S. Negi, CEO, Dr. D. C. Doval, Chairman – Organizing Committee and Dr. Kapil Kumar, Organizing Secretary of Breastcon 2013.

Prof. Robert Mansel, Head of Surgery, Cardiff University School of Medicine, U.K., the man who pioneered the concepts of sentinel lymph node in the United kingdom and steered the ALMANAC & the much awaited AMAROS trials delivered key note address on topics most pertinent to India today "Accredition of Breast Centres". The other thought provoking concept was "Is there a future for breast surgery or will it be the technologist?"

Prof. Ismail Jatoi, Professor & Chief - Surgical Oncology, University of Texas, San Antonio, U.S.A., a renowned breast surgeon spoke on a contrarian perspective of mammographic screening. He also updated the audience on the current status and indications of MR Mammogram and the implication of age on breast conservation.

Dr. Amit Goyal, Consultant - Oncoplastic Breast Surgeon, Royal Derby Hospital, U.K., showed his videos on Therapeutic Mammoplasty and explained the technique in detail for the benefit of the younger surgeons. Dr. Jayant Vaidya, Consultant Surgeon, Whittington Hospital, London, U.K., introduced the concept of IORT in the setting of Breast Conservation emphasized by the recent results of the TARGIT trial. Dr. Christine Brezden Mansley, Medical Oncologist from the University of Toronto, updated the recent advances on targeted therapy in breast cancer.

Renowned National Faculty from all over the country presented the very much valuable Indian data on the various aspects of management of early breast cancer. It was a feast to the minds, to hear the stalwarts in the field of breast oncology, interact, argue, and draw to a consensus on the most burning issues in the purest of scientific spirit. The conference was tailored to cater to recent advances in imaging, diagnostic dilemmas in in-situ cancers, role of genomic profiling techniques of breast conservation and reconstructive challenges, neoadjuvant strategies to optimize breast conservation and adjuvant radiation and systemic therapy in the management of early breast cancer.

The panel discussions and "Meet the Professor" session were well appreciated. It was attended by over 250 delegates from all over the country with great enthusiasm and about 50 students presented poster and oral papers in the competitive session.

Dr. Kapil Kumar, Organizing Secretary Dr. Ashish Goel, Co-organizing Secretary Dr. S. Veda Padma Priya, Co-organizing Secretary Date of Printing – 25th April 2013 Date of Publishing – 30th April 2013

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# **QUALITY WEEK**



Quality lies at the core of all organizations and so is with us. RGCI & RC is committed to continually improve the quality and strives to provide Quality Healthcare to all the patients and society at large.

RGCI & RC, Delhi, had organized its 'Ist Quality Week' between 11th to 16th March 2013, to instill the importance of delivering Quality Care for improved Patient Care outcomes. The Theme for the Week was "Healthcare Quality and Risk Management".

The Quality week was full of educational activities and awareness programs. Everyday, during the week, a different theme was chosen. The six day program included a series of guest lectures and interactive sessions on Quality Improvement Strategies in Healthcare Sector and how implementing them is essential to enhance patient experience?

There were enriching sessions by industry experts on Quality and Patient Safety, Disaster Management in Healthcare, Medication Safety, Measuring and Monitoring Quality Indicators and Prevention of Hospital Acquired Infection. The focus of all the sessions was to provide information on the best practices that need to be adopted for Continuous Quality Improvement. There were a host of sessions by Internal Quality Champions from different Departments to discuss Quality Initiatives taken at various fronts.

There was a Quality Quiz where staff from different Departments enthusiastically participated to answer questions about quality tools, processes and practices. A Poster Competition was held to highlight the work of employees who have taken quality initiatives in their Department to enhance our Healthcare Delivery System. The Best posters were selected by the Jury and cash prizes were awarded to the winners. Overall, more than 450 staff members, from all the departments, participated in the event and it was appreciated by all.

The event was concluded by a vote of thanks from our Chief Executive Officer, Shri D. S. Negi, who stated that Quality can be taken a step forward if all the employees learn, imbibe and develop a Quality Improvement Culture where all the team members work together and take measures to provide Quality Service to our Valuable Patients.

The Quality Week provided an ideal opportunity to reinforce our commitment to Quality Improvement. The commitment portrayed by the hospital staff was commendable and reflected their passion to do things right first time, every time and with empathy!

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