
CANCER RESEARCH INSTITUTE

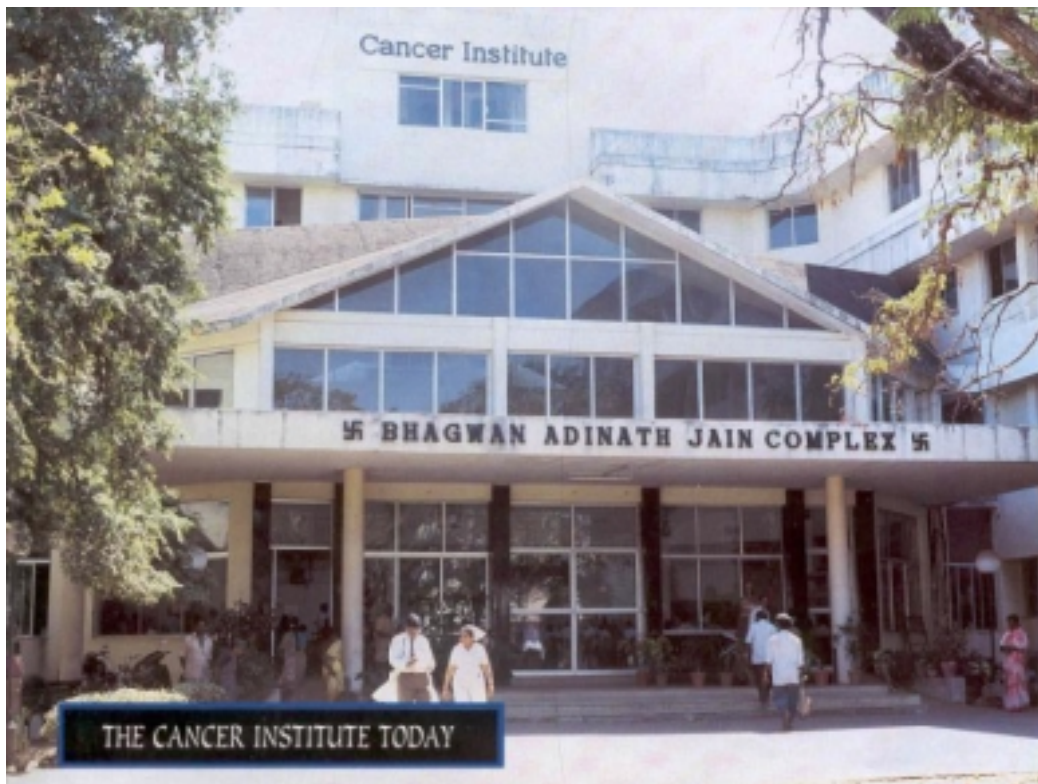
Cancer Institute (WIA), Chennai (Madras)

The Institute Today

The Cancer Institute today comprises of a hospital, a research centre, a centre of preventive oncology and the Dr.Muthulakshmi College of Oncologic Sciences. The Hospital has 428 beds of which 297 are free. Annually over 70,000 cancer patients (old and new) pass thro' the portals of the Institute. Over 2/3 of them are indigent and come from all over India. Hardly 0.5% may be covered by Health Insurance. The financial burden of treatment of the 66% indigent is no different from the best in the world.

Radiation and surgical oncology are as old as the Institute. Medical Oncology was introduced as a distinct speciality in 1970. The division of radiation oncology is the largest in the country with a great tradition. It has an array of 4 linear accelerators, 2 cobalt-60 units and 3 remote after loading brachytherapy units and supporting ancillary facilities like a treatment planning system, an interfaced CT scanner, and simulators. One of the brachytherapy units is a product of the Engineering and Physics department of the Institute, the first indigenous remote after loading unit to be built in India, at a tenth of the cost of an imported one. A high dose rate interstitial brachytherapy unit is under development.

As a trend setter, the Institute pioneered a number of programmes on radiosensitisation of oral and cervical cancers and has collaborated in global international trials with the Medical Research Council of U.K., the IAEA, Vienna and others. It also introduced multimodality treatment in the management of advanced oral and breast cancers as early as 1958, an evolution born out of necessity and which today is the accepted state of the art the world over.



Cancer Institute (WIA), Regional Cancer Centre, 38, Sardar Patel Road, Chennai 600036, India Fax: +91-4912085 E-mail: caninst.md2.vsnl.net.in

Research

Clinical, Basic and Translational Research are being carried out at the Institute.

Clinical research has focussed on oral cancer, breast cancer, gastric cancer, cervical cancer, bone and soft tissue sarcomas.

Radiosensitization Trials

The Institute has been a trend setter in Radiosensitisation in oral and cervical cancers using chemical and physical sensitisation techniques and has participated in several International trials in this area, initiated by the Medical Research Council of United Kingdom and the International Atomic Energy Agency (IAEA).

Oral Cancer trials

Roles of chemical agents like synkavit, metronidazole and methotrexate in enhancing the effect of radiotherapy was studied in separate, properly designed, randomized trials. Synkavit nearly doubled the 5-year survivals but the other two agents did not improve the results. The bleomycin (BLM) studies were initiated in 1971. The first phase of this study was supported by Indian Council of Medical Research and the second phase by the Medical Research Council of the United Kingdom. Radiotherapy combined with BLM was proved to be useful, yielding a complete response rate of 70-80%, a recurrence free rate of 60-70% and a 5-year disease-free survival of around 60%. These results were reliable, consistent and reproducible in both an unselected series and subsequent trials. There was, however, a persistent failure rate of about 40% in all these studies. In an effort to improve the results, five more clinical trials were undertaken in which various chemical and physical agents were added to the combination of radiotherapy and bleomycin and evaluated in carefully designed trials. The hyperbaric oxygen trial was a 3-arm trial in which radiotherapy was combined with either BLM or hyperbaric oxygen or both. The Indian Council of Medical Research supported this trial. Hyperbaric oxygen did not improve the results. Another 3-arm trial was carried out in which radiotherapy was combined with BLM or cisplatin or both. BLM and CDDP did seem to have an additive therapeutic effect, the combination eliciting a significantly superior therapeutic effect than either drug alone. In the next trial, which was supported by the International Atomic Energy Agency, Vienna, a combination of radiotherapy, BLM, 5-fluorouracil and vincristine was compared with radiotherapy-BLM combination. The three-drug combination considerably augmented both the local and systemic morbidities, without much added therapeutic benefit. The last two trials in this series were again 3-arm trials, in the first study, which was supported by the Department of Science and Technology, Govt. of India, radiotherapy was combined with either peploemycin (an analogue of BLM) or hyperthermia or both. In the last study, which as supported by the Department of Atomic Energy,

Govt. of India is my country, radiotherapy was compared the combination of radiotherapy with either hydroxyurea, a radiation sensitizer, or BLM. Both these trials showed only marginal benefit by the addition of either hyperthermia or hydroxyurea.

Cervical Cancer trials

A clinical trial supported by the Department of Atomic Energy, Govt. of India was carried out to assess the radiopotentiating effect of hydroxyurea in uterine cervical cancer. Addition of hydroxyurea did not improve the results much.

The International Atomic Energy Agency (IAEA) and the Dept. of Atomic Energy, India have funded a study to assess the role of Hyperthermia in cervical cancer, which is currently on-going.

For gastric cancer, the role of intraoperative radiotherapy using electrons is being evaluated in a two arm study. Both these studies are unique and significant, in that, these facilities are available only at the Institute in India.

Basic and Translational Research

The Research Departments at the Institute include the Dept. of Molecular Oncology, Dept. of Cytogenetics, Hybridoma Unit, Dept. of Tumour Microbiology, Dept. of Bio-Medical Engineering, Dept. of Medical Physics.

Department of Molecular Oncology

This Department has been working on Biologic characterisation of T-cell Acute lymphoblastic leukemias (T-ALL) and detection of minimal residual leukaemia disease in T-ALL using Polymerase chain reaction. The Department has also started a Hereditary Cancer Detection and Prevention programme focussing on the Population of Madras Metropolitan area as well as patients seen at the Institute. Projects on cell cycle regulatory molecules in normal, dysplastic and malignant cervical epithelium and identification of genes involved in radio-responsiveness using differential display are ongoing. Molecular characterisation is also being done on Non-Hodgkin's lymphoma and osteosarcoma. In collaboration with IARC, Lyon case control studies have been conducted to assess the role of Human papilloma virus in the causation of oral and cervical cancer. Our studies have shown that HPV does not play a major role in the causation of oral cancer. The study on cervical cancer has shown that as in the earlier reports, High risk HPV plays a major role in cervical tumourigenesis.

Department of Biochemical Oncology

This Department is engaged in research work pertaining to Immunodiagnosis of cancer using Monoclonal antibodies especially for cancers most prevalent in India like Breast, Head and Neck, Cervix, and Ovary. This study involves isolation, purification and characterization of tumour antigens, growth factors and their receptors, hormones and their receptors, human milk fat globule membrane etc., With a view to develop immunoassay procedures like in vitro

Immunocytochemical assay and serological assay and In vivo radio immunodetection and localization of occult malignancies, monoclonal antibodies have generated against

Cama antigen and HMFG have been to exhibit specific reactivity with a high molecular weight glycoprotein(PEM) expressed on breast tumours and have useful application in the Immunophenotyping of these cancers. The level of circulating PEM was found to increase with the stage of disease in these patients. Mabs CIBCNSH3 and 115c1 generated against human EGFR have potential application to study the over-expression of this receptor in malignancies like Squamous cell carcinoma of the Head and Neck, Breast carcinoma etc which are associated with poor prognosis and thus serve as a predictor of early recurrence and patient survival. The anti-tumour activity of this Mab demonstrated by its ability to block the binding of EGF to its receptor using cell lines in culture and animals tumour models with high expression of EGFR has potential therapeutic application. Two Mabs CIBCgp185 and CIBCHER-2 generated against C-erbB-2 oncoprotein have been extensively characterized and their clinical application evaluated. These antibodies stained specifically the membranes in Frozen tissue sections of Breast and Ovarian tumours over-expressing the C-erbB-2 product. The In vivo diagnostic and therapeutic application of these monoclonal antibodies generated against EGFR and C-erbB-2 is being evaluated using animal tumour models. Using these monoclonal antibodies, serological assay has been developed to study the circulating level of EGFR and C-erbB-2 oncoprotein in cancer patients.

Mabs 23B7 and 7D6 generated against Lymphoma Associated Antigen (LAA) which has been identified as a unique biomarker for B-cell NHL, the expression of this antigen has been found to be high as also the circulating levels in these patients. These immunoassay procedures revealed that LAA is useful marker to differentiate between lymphoma and Lymphadenitis. This department has perfected Immunoscintigraph procedures for In vivo radioimmunodetection and localization of experimental lymphomas and breast tumour models using ^{99m}Tc labelled and ^{131}I labelled monoclonal antibodies.

Department of Tumour Microbiology

Thrust has been on hazard assessment and standardization of short term tests for carcinogenicity and mutagenicity screening. We address environmental risk factors and molecular mechanism of DNA instability vis-à-vis tumor progression. Focus is again on long term studies backed up by nuclear magnetic resonance spectroscopy and histopathology to elicit structure activity relationship.

We have established by critical analysis of the carcinogen molecular adducts, mutations and cytogenetic changes in the target epithelial cells viable prognostic indices. Transfer of technology for the evaluation of biomarkers in the management of tumors as well as in biomonitoring high risk groups has been beneficial, to put in use on routine basis, newer techniques such as single cell gel electrophoresis,

HPLC, NMR, flow cytometry, oxidative damage and adducts in DNA Immuno cytochemistry and polymerase chain reaction based technology.

Recent studies address the risk of dietary factors such as deep fried and charred food in gastric carcinogenesis and intervention with flavanoids and triterpenes.

Another epithelial tumor of common incidence is cervical carcinoma. We look at the differential level of cytokine production and quantify by Polymerase Chain Reaction to identify and manage high risk cervical carcinoma patients. This ongoing collaborative research with a French laboratory is funded by the Indo French Centre for the Promotion of Advanced Research.

Bio-Medical Research

The Bio-Medical Engineering Dept. of the Institute has been involved in the designing and fabrication of Radiotherapy related equipments saving precious Foreign Exchange. As early as 1962, the Cesium Tele-curie therapy Unit, followed in 1968 by the radiotherapy simulator were designed and installed by our Physicists. In 1971, Manual afterloading applicators were designed, fabricated and developed for clinical use. Using an IBM 370 computer, our Physicists computerised Intracavitary dosimetry. In 1980, the Institute designed and developed a Styrofoam block cutting machine and identified a low melting point alloy for use in specialised Radiation fields. In addition, Indigenous tissue equivalent rubber was developed in collaboration with Rubber Research Board, Kerala which replaced the imported rubber sheets for radiation dosimetry.

In 1997 a rotating platform for Total Skin Electron Therapy was designed and developed and used. The most recent accomplishment has been the designing, fabrication and installation of a remote afterloading Brachytherapy Unit (CITRON) in 2000, which costs only around Rs.800,000 (single patient treatment system) compared to the cost of an imported unit at Rs.8 million (2 patient treatment system).

College of Oncologic Sciences

Dr.Muthulakshmi College of Oncologic Sciences was established at the Cancer Institute in March 1984, the first such college in the country, to offer speciality training in surgical and medical oncology. It took almost 13 years of persistent effort and lobbying with the Medical Council of India before the speciality training could be introduced. So far over 100 specialists have been trained and our alumni are heading various new oncology centers and oncology wings of medical colleges all over the country. The college in addition runs the Master's training courses for medical physicists (the only one in the country) and registers students for doctoral and post doctoral research.

Preventive Oncology & Registries

The centre for preventive oncology is more a network of programmes rather than a physical entity. It consists of

two main components –

1. Cancer prevention and early detection
2. The Registries – Demographic & Hospital

The preventive program is essentially educational at the public and professional level. Since 75% of the India population is rural the educational programmes are mainly rural based. It also includes the training of village health nurses (VHN) and multi purpose workers in the detection of an abnormal cervix, abnormal changes in the mouth and the female breast. Over 750 VHNs & 250 rural medical practitioners have been trained in early detection and for taking Pap smears. Rural training centers and cytology laboratories for negative screening have been established. The main problem that one faces in the Population Screening Programme is compliance, both by the target population and the VHN.

Registries: Demographic & Hospital:

The fully computerized hospital and demographic registries at the Institute are rated highly. The hospital registry has good documentation and the follow-up division has over 80% life time follow up of patients treated. The data from the registry are accepted without any reservation by the International agency for Cancer Research in all its publications.

The demographic registry has provided the lead for cancer control activity in our area. The rising trend in lung cancer incidence in men and breast cancer incidence in women is ominous.

The registry is collaborating in a number of epidemiologic studies with Japan. A major tobacco survey and impact of tobacco on mortality is ongoing with support of World Bank, Clinical Trial Service Unit of Oxford and W.H.O.

Some “Firsts” To Our Credit

- It was the first comprehensive cancer center in South India and the second one in the country.
- It was the first center to install a Cobalt 60 Teletherapy unit in Asia in 1956. This ushered in the Super Voltage Therapy era in Asia.
- It was the first center in India to establish a department of Nuclear Medical Oncology in 1956, 6 years before the DAE established its Isotope Division.
- The first indigenous therapy simulator was designed by us in 1965 and fabricated by the I.G.E. and installed in 1968.
- “Pediatric Oncology” as a speciality was introduced by us in the country in 1960.
- The Institute introduced the technique of Lymphangiography in the diagnosis of lymphoid tumours in 1960 and the technique of Mammography in the diagnosis of occult breast tumours in 1965 for the first time in India.
- The Institute is a world pioneer in the combination

therapies of oral cancer with radiation, surgery, chemical sensitisers and cytotoxic drugs, raising the cure rate from 19% to 60%

- The first Linear Accelerator in India was installed at the Institute in 1976. The Institute introduced for the first time in the country, Hyperbaric Oxygen Therapy in the treatment of Cancer in 1978, and is at present the only place where this facility is available.
- Blood Component Therapy using the blood cell separator, in the supportive treatment of high dose Chemotherapy, was introduced into India by us for the first time in 1978.
- The Institute established the first PEPA programme in the country in the Chemotherapy of cancer.
- We were the first to institute Post Graduate courses leading to M.Ch in Surgical Oncology, D.M. in Medical Oncology and M.Sc., in Physics as applied to Medicine.
- We were the first and at present the only center in India to introduce Hyperthermia in the treatment of Cancer (1984)
- The first ND-YAG Surgical LASER in the country was installed at the Institute in 1985 and we were the first to perform Endoscopic LASER Surgery.
- The first (1992) and at present the only center in the country where Intra-Operative Electron Therapy in the treatment of cancer is available.
- A fully indigenous Brachytherapy unit for intracavitary treatment of cancer designed and fabricated. (1995)
- The first conformational therapy unit Linear Accelerator Clinac 2300 C/D was installed (1999).