Editorial

PET-CT, an advanced non-invasive imaging tool, gives complementary information on the metabolic and anatomic processes. Installation of Siemens Biograph 40 True Point PET-CT in the Institute is a milestone of the year 2008, which would help in better management of cancer patients. Special Feature highlights the importance of PET-CT in clinical oncology.

Stereotactic Radiosurgery covered in "Perspective" is a highly precise form of Radiation Therapy which now can be used to treat lesions anywhere in the body. "In Focus" highlights breast ultrasound technologies with a revolutionary elastography breast imaging technology, which identifies cancers and may reduce unnecessary breast biopsies. The Cancer Institute (WIA), Chennai, was established with a mission to provide state-of-the-art treatment to all types of cancer patients. This issue sketches the profile of this Institute as a tribute to the outstanding work carried out by it since its inception. A sincere and special thanks to Dr V Shanta, Chairman, for providing us with a write-up on the Institute.

Dr Christopher Amies, Vice-President - R&D, Siemens OCSG, USA delivered a technical presentation on Image Guided Radiotherapy, a new paradigm in cancer treatment. This informative presentation as well as a DNB Symposium on Lung Cancer have been covered under "Activities of RGCI&RC". Other regular features covered in this issue are: Research and Development, New Technologies, Cancer Control, Watch-Out, Clinical Trials and Globe Scan.

Siemens Medical Solutions is one of the world's largest suppliers of the healthcare industry. The company is known for bringing together innovative medical technologies, healthcare information system, management consulting and sport services, to help physicians achieve tangible, sustainable, clinical and financial outcomes. A special thanks to Siemens Medical Solutions for supporting this issue of Cancer News.

RGCON-2008, an Annual International Conference, is being organized by the Institute from 7th to 9th March 2008. Special theme this year will be on Colorectal Cancer. A message from Dr Kapil Kumar, Organizing Secretary, has been included in this issue.

The Institute gratefully acknowledges the contributions made by Dr P S Choudhury, Prof P S Negi, Dr (Col) R Ranga Rao, Dr S Avinash Rao, Mr S N Sinha and Dr Chidambara Jha and providing the technical inputs. Views and suggestions on Cancer News from readers are welcome.

Wishing a Happy New Year and Seasons Greetings to our readers.

Dr. (Mrs.) Ira Ray
Director Research

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RESEARCH & ANALYSIS TEAM

Ms Rupal Sinha *Research Officer*

Mrs Swarnima Jaitley *Research Officer*

Dr (Mrs) Nimmi Kansal *Research Officer*

Dr (Mrs) Harsh *Research Officer*

Editor : Dr (Mrs) Ira Ray
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SPECIAL FEATURE

PET-CT IN CLINICAL ONCOLOGY

Introduction

Morphological imaging techniques, such as X-Ray Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), have been in use in clinical oncology since long. The emergence of Positron Emission Tomography (PET) more than a decade ago promised a major breakthrough in the early diagnosis of malignant lesions being based on tumor metabolism and not on morphology. PET and CT give complementary information and together increase the probability of lesion localization and reduce the artefacts of interpretation. This was the principle of new hybrid gamma cameras and PET-CT. It is now commercially available since the last few years. PET-CT has made this technology the most important tool in the management of cancer patients. With such a device, anatomic and functional images can be acquired for each patient in a single scanning session and accurately co-registered. It reduces the image acquisition time, improves tumor localization and calculates more accurately the target tumor volume for radiotherapy planning.

Mode of Action

When PET is used to image cancer, a radiopharmaceutical, such as fluorodeoxyglucose (FDG) labelled with ^{18}F is injected into a patient. Cancer cells metabolize sugar at higher rates than the normal cells and the radiopharmaceutical is drawn in higher concentrations to the cancerous areas. The highly sensitive PET scan picks up the metabolic signal of actively growing cancer cells. The CT scan generates a detailed picture of the internal anatomy, locating and revealing the size and shape of the abnormal cancer growths. When these two results are compiled together with an integrated PET/CT scanner, a co-registered image gives information on both morphology and function. Such a device has the capability to acquire accurately aligned anatomic and functional images of a patient from a single scanning session.

Additionally, since the patient remains positioned on the same bed for both the imaging modalities, temporal and spatial differences between the two sets of images are minimized. Spatial differences include not only an overall patient positioning and movement but also the involuntary and uncontrollable motion of the internal organs. Thus, by eliminating the need for labor-intensive software fusion, registered anatomy and function can be acquired routinely for every patient, with the images available for viewing while the patient is still in the scanner.

Radiotracers for Clinical Use

The most widely available radiotracer is ^{18}F-FDG. However, many more tracers are being evaluated with success.

Metabolism: The increased level of glycolysis within the tumor cells led to the discovery that glucose could be used as a possible tracer for identification of tumor cells within the body. Cells take up FDG by means of glucose transporter (GLUT-1) and phosphorylate to FDG-6 phosphate. With the increased number of glucose transporters on the malignant cells, there is an increased FDG-uptake and trapping of FDG-6 phosphate and a gradual accumulation of FDG in these malignant cells, allowing a three-dimensional image of the tumor to be visualized.

Hypoxia: Use of nitroimidazoles to image regions of tumor hypoxia is under investigation. Knowledge of tumor hypoxia is useful for prognostic information and may help identify regions within tumor that can be targeted with higher dose of external radiotherapy. ^{18}F-fluoromisonidazole (18-FMISO) is a lipophillic compound that enters cells by passive diffusion. In hypoxic cells, it is reduced and binds covalently to the intracellular macromolecules trapping the FMISO. In nontoxic cells, reduction does not take place and the compound moves freely out of the cells.

Cellular Proliferation: 3 deoxy-3-(^{18}F) fluorothymidine (FLT) is a thymidine analogue. It is taken into cells and undergoes phosphorylation by thymidine kinase-1. Once phosphorylated, it becomes trapped intracellularly but not incorporated into the DNA. It is thought to reflect cellular proliferation because thymidine kinase-1 level increases ten-fold during DNA synthesis. FLT uptake correlates with the proliferation markers in colorectal cancer, small cell lung cancer and other malignancies.

Endocrine Markers: ^{18}F-fluorodihydrotestosterone (FDHT) is a radiolabelled ligand of the prostate androgen receptor. This receptor is involved in the growth and

proliferation of prostate cancer cells. It is accumulated by most prostate cancer metastatic cells. ^{18}F-fluoroestradiol (FES) has been used for imaging estrogen receptor positive breast cancers.

Apoptosis: Phosphotidyl serine is externalized during apoptosis. Annexin V binds to phosphotidyl serine with a very high affinity. Labelling of annexin with a positron emitter allows PET to give high resolution image.

***Generator Based Positron Emitters*:** Ga^{68} is a positron emitter which can be eluted from a Ge^{68}–Ga^{68} generator daily. These can be labeled with different radiopharmaceuticals for different clinical indications, especially in neuroendocrine tumors. One generator can be used for around one year.

Advantages of Integrated PET/CT

- Integrated PET-CT allows a comprehensive metabolic and morphological evaluation in a single session.
- The synergistic advantage of adding CT is that the attenuation correction needed for PET can also be derived from the CT data, an advantage not obtainable by integrating PET and magnetic resonance imaging. This makes PET-CT 25% - 30% faster than PET alone with the standard attenuation-correction methods, leading to higher patient throughput and a more comfortable examination, which typically lasts less than 30 minutes.
- It improves tumor localization, which at times is difficult with PET alone, increasing accuracy.
- PET-CT adds complementary information in staging, restaging and followup in oncology patients, leading to changes in the management plans many times.
- The dual modality PET-CT imaging system has added unprecedented diagnostic capability by revealing the precise anatomic localization of metabolic information and metabolic characterization of the normal and abnormal structures.
- Introduction of combined PET-CT scanners enables the almost simultaneous acquisition of transmission and emission images, thus obtaining optimal fusion images in a very short time.
- Some limitations, such as low FDG uptake in some cancers, substantial FDG uptake in the inflammatory cells and the lack of anatomical details in PET have been overcome by PET-CT.
- PET-CT using FDG is clinically useful in the detection of cancer staging and the assessment of response to therapy as well as detecting the recurrence of most cancers. PET-CT has become the new standard approach to imaging in the diagnosis and management of many cancer patients.
- It has the potential to significantly affect treatment planning by guiding biopsies and surgical interventions and defining target volume for radiation therapy fields.

Clinical Indications

Cancer Staging: Integrated PET-CT offers incremental diagnostic advantages over PET-CT alone for the major cancers. It is increasingly being used for staging, restaging and treatment monitoring for the cancer patients worldwide. At many institutions, integrated PET-CT has replaced separately acquired PET and CT examination for many oncologic indications, despite the fact that only a relatively small number of well designed prospective studies have verified the imaging findings against the gold standards of histopathological tissue evaluation. However, a large number of studies have used acceptable reference standards, such as pathology imaging and other clinical follow up findings for validating the PET-CT findings.

Early Detection of Cancer Recurrences: Early detection of recurrences is clinically important and can improve the prognosis and survival of patients with cancer. In addition to the accurate diagnosis and definition of the whole extent of recurrent cancer, PET-CT has an impact on patient management because it can assist in defining potential candidates for surgery for cure, planning the appropriate surgical or radiotherapy approach and referring patients with unresectable disease to the other therapeutic options.

Screening: The clinical and statistical relevance of occasionally detected cancers is likely to be too low to justify population wide screening efforts with these two imaging modalities. Researchers may investigate the utility of whole-body PET-CT for the surveillance of selected groups of patients who have cancer, who have completed curative treatment, but who remain at high risk for the disease to recur.

Radiotherapy Planning: PET-CT could be used as the prime tool in the delineation of tumor volumes and the preparation of patient treatment plans, especially when integrated with virtual simulation. PET imaging, using

^{18}F-FDG can provide data on metabolically active tumor volumes. These functional data have the potential to modify treatment volumes and guide treatment delivery to cells with particular metabolic characteristics. The introduction of functional data into the radiotherapy treatment planning process is currently the focus of significant commercial, technical, scientific and clinical development. Novel markers of tumor hypoxia or proliferation have the potential to modify the delineation of target volumes, allowing for dose planning in selected sub-volumes. Variations in tumor volume and viability during radiotherapy are under intense investigation, potentially paving the way for adoptive dose distribution during treatment.

Pediatric Oncology: ^{18}F-FDG PET-CT is becoming increasingly important as an imaging tool in the non-invasive evaluation and monitoring of children with known or suspected malignant diseases. Most tumors in children accumulate and retain FDG, allowing high-quality images of their distribution and pathophysiology. PET is emerging as an important diagnostic imaging tool in the evaluation of pediatric cancers. Dual modality PET/CT imaging system has added unprecedented diagnostic capability by revealing the precise anatomical localization of metabolic information and metabolic characterization of normal and abnormal structures. The use of CT transmission scanning for attenuation correction has shortened the total acquisition time, a desirable attribute in pediatric imaging.

***Some Specific Indications*:**

(i) PET scanning is useful for staging intermediate and high grade Non-Hodgkin's lymphoma and is predictive of the treatment response.
(ii) In Hodgkin's disease, addition of PET with conventional imaging can result in a change of management in upto 25% of the patients. There is some evidence that obtaining a PET scan during treatment can predict outcome.
(iii) PET can be useful for the diagnosis, staging, prognosis and radiotherapy planning of non-small cell lung carcinoma (NSCLC). PET-CT is a promising tool in planning radiotherapy in NSCLC.
(iv) Restaging of head and neck cancer with possibilities of curative treatment.
(v) PET has shown promise in the diagnosis of primary and recurrent disease, staging, prognosis and therapy response in breast cancer.
(vi) Very useful tool for the diagnosis of recurrent colon cancer, when rise in carcinoembryonic antigen is observed but conventional imaging is negative.
(vii) It can be of great help in the detection of recurrent or metastatic disease in melanoma.
(viii) In the context of a rising serum thyroglobulin and a negative radioiodine scan, PET can detect metastasis not seen on MRI or CT in thyroid carcinoma.
(ix) Differential diagnosis between recurrent tumor and scar or radionecrosis in brain tumor.
(x) Characterization of residual masses post treatment.
(xi) PET-CT imaging is becoming a standard of care in radiation oncology where utilizing conventional imaging techniques results in either over or under treatment of patients with cancer.

Challenges

Stringent protocols used to be standardized from the patient protection point of view, especially in young and potentially curable malignancies. It must be noted that when integrating full dose CT in PET-CT, the radiation dose from CT may amount to approximately 15-20mSv for a scan from the head to upper thighs. If CT is performed in a low dose manner, the radiation burden is reduced 5-fold to 3-4mSv. Proper disease specific standardized protocols need to be ensured. Newer pharmaceuticals depicting the other metabolic aspects of tumor biology also need to be explored.

Future Perspective

PET-CT has become the new standard approach to imaging in the diagnosis and management of many cancer patients. It is the most advanced method for metabolic imaging and is capable of precisely localizing and assessing tumors. It is an emerging imaging technology and standardization of imaging protocols is increasingly important for establishing the efficacy of PET-CT for specific clinical applications. Continuous dialogue between Nuclear Medicine specialists, Diagnostic Radiologists and Clinical Oncologists would be essential for continued development of PET-CT protocols and maximizing the benefit of combined PET-CT studies.

(The Institute appreciates Dr P S Choudhury for his contribution to the Special Feature on PET-CT in Clinical Oncology.)

PERSPECTIVE

STEREOTACTIC RADIOSURGERY

Introduction

Stereotactic Radiosurgery (SRS) is a highly precise technique used to treat brain tumors and other intracranial disorders. SRS involves a single, high dose application of radiation to the tumor, instead of the many smaller doses given in standard radiation treatment. This technique is accurate to one millimetre or less and does not require surgery. SRS includes the participation of Radiation Oncology, Radiology and Surgical teams who work together to evaluate and treat each patient.

Mode of Action

SRS works in the same way as all other forms of radiation treatment. It does not remove the tumor or lesion, but it distorts the DNA of the tumor cells. In lesions, such as AVMs (a tangle of blood vessels in the brain), radiosurgery causes the blood vessels to thicken and close off. For benign tumors and vessels, this will usually be 6 months to 18 months. For malignant or metastatic tumors, results may be seen in a few months.

SRS is limited to the head and neck because these areas can be immobilized with skeletal fixation devices permitting the most precise and accurate treatment without damage to healthy brain tissues, cranial nerves and the brain stem.

Stereotactic radiotherapy (SRT) delivers lower doses of radiation over a series of treatment sessions. Patients who have larger lesions that are not appropriate for radiosurgery, may benefit from the precision and focal radiation applied with SRT. It is also convenient in that it is usually delivered in one to five treatment sessions.

Indications

SRS may be used as the primary treatment or be recommended in addition to other treatments that are needed. Some of the most common indications for treatment are:

- Arteriovenous Malformations
- All benign brain tumors, including Acoustic Neuromas, Meningiomas, Pineal and Pituitary Tumors
- All Malignant Brain Tumors including Glial Tumors, Astrocytomas and Low Grade Tumors
- Metastatic Brain Tumors
- Functional disorders including Trigeminal Neuralgia, Essential Tremor, Parkinson's Tremor/Rigidity
- Current research areas include epilepsy, headaches and neuro-psychiatric conditions.

Types of Stereotactic Radiosurgery

Particle Beam (Proton) Based SRS: The particle beam exists in a handful of centres in the world. In addition to brain tumors, it treats body cancers in a fractionated manner. The proton facility offers advantages for the treatment of unusually shaped brain tumors and arteriovenous malformations. It is the ideal post-resection therapy for many chordomas and certain chondrosarcomas of spine and skull base as well as for many other types of tumors.

Cobalt-60 (Photon) Based SRS : The cobalt-60 based machines provide extremely accurate targeting and precise treatment for brain cancers. They are dedicated to treating only small brain tumors (< 3 cm) and dysfunctions in a one-day treatment. The most well-known machine is the Gamma Knife®.The Gamma Knife® does not move during treatment, thus providing a high degree of precision within the brain.

Linear Accelerator (Linac) Based SRS : The linear accelerator based radiosurgery machines are also prevalent throughout the world which are preferred to benefit tumor volumes (> 3 cm) treated over several sessions. The machines are made by a number of manufacturers with common brand names: X-Knife®, Axess®, Trilogy®, Novalis®, CyberKnife® and others.

The cyberknife system uses the combination of robotics and image guidance to deliver concentrated and accurate beams of radiation to intracranial and extracranial targets, many of which are inoperable and are at difficult-to-reach locations.

Conclusion

Radiosurgery in the past was essentially restricted to the treatment of lesions within the skull. Now this technology can be used to treat lesions anywhere in the body. The ability to treat intra- and extra-cranial lesions with radiosurgical precision and to hypofractionate the treatments are not only remarkable innovations in the radiosurgical field, but may lead to an epochal change in the treatment of cancer and other lesions, replacing or complementing invasive surgical procedures or aggressive chemotherapies with focused non-invasive radiosurgical treatments.

(The Institute appreciates Prof P S Negi for reviewing write-up on Stereotactic Radiosurgery)

RESEARCH AND DEVELOPMENT

Cancer Resistant Mice

Prostate apoptosis response-4 (Par4), a tumor suppressor gene was discovered in 1993 by Dr Vivek M Rangnekar from University of Mumbai, India, now settled as Professor of Radiation Medicine at the University of Kentucky in the USA. Par4 selectively induces apoptosis in the cancer cells and can shrink solid tumors in animals. It is being developed as a molecular therapy for cancer. This breakthrough gives hope that one day scientists could use this gene to make cancer resistant humans.

Researchers have created transgenic mice, expressing the SAC module of Par4 that are resistant to the growth of spontaneous and oncogene induced tumors. These mice displayed normal development and life span. Researchers found that the gene offered a potential way, unlike most other cancer treatments, of destroying cancer cells without harming the normal cells. The gene is expressed in every cell type. Researchers are now planning to breed these supermice with other types of animals that are prone to cancers of the lung, breast and colon to see if pups become resistant to these cancers. The implications for humans could be that through bone marrow transplantation, the Par4 molecule could potentially be used to fight cancer cells in patients, without the toxic and damaging side effects of chemotherapy and radiation therapy.

(Cancer Research, Oct 1, 2007)

Epothilones New Class of Agents

Scientists at Helmholtz Centre for Infection Research (HZI) have discovered epithilone, a class of natural substance that is produced by soil bacteria, and prevent somatic cells from dividing. In future, epothilone could help many patients overcome cancer.

The US pharmaceuticals company Bristol-Myers Squibb (BMS) acquired the licence for the substance known as epothilone B from the HZI and developed it so that it could be launched in the market. Starting immediately, medical practitioners in the US can prescribe it under the trade name Ixempra to treat metastatic breast cancers that have proven resistant to other medications. It is expected to be approved for use in Europe next year.

(Hemholtz - Gemeins Chaff, Nov 27, 2007)

Gene Expression Profiling

Gene expression profiling explores the patterns of genes that are active in tumor cells. A study conducted by researchers in Europe showed that gene expression profiling may help physicians select the most appropriate neoadjuvant (before surgery) chemotherapy regimens among women with estrogen receptor-negative, operable breast cancer.

Women received neoadjuvant chemotherapy with either fluorouracil, epirubicin, and cyclophosphamide (FEC) or docetaxel followed by epirubicin plus docetaxel (TET). The researchers were able to confirm that gene signatures that they had identified previously did in fact predict response to each of these chemotherapy regimens. Various women had gene signatures predictive of response to FEC or TET and some had gene signatures that predicted that neither regimens would be effective. This information may help physicians select the most appropriate chemotherapy regimen leading to more individualized and ultimately more effective treatment.

(Lancet Oncology, Nov 14, 2007)

microRNAs in Prostate Cancer

Researchers from U.C. Davis Cancer Centre have specifically looked at the functional effects of microRNAs on the progression of prostate cancer. The identification of cellular pathway that makes prostate cancer fatal is the first discovery and is an important link to find new treatments targeting this cellular function and reducing cancer deaths.

Research team used high resolution analysis techniques to identify microRNAs that were differentially expressed. Of five that were distinct, one-miR-125b was present at high levels in both androgen-dependent and androgen independent prostate cancer cells.

After a period of success with androgen suppression therapy, the cancer starts to thrive again and the disease becomes fatal. This particular microRNA supports the ability of prostate cancer cells to exist and grow in its androgen – independent state. There is currently no effective treatment for the androgen – independent state of the disease. miR-125b screening would at some point become standard diagnostic tool and that genetic and chemotherapy treatments can be developed that remove this essential survival mechanism for cancer cells.

(UC Davis Cancer Center, Nov 22, 2007)

NEW TECHNOLOGIES

DIAGNOSTICS

Cancer Blood Test

Scientists at Massachusetts General Hospital Cancer Center have developed a new blood test that uses microchip technology to sift blood to search for the circulating tumor cellls (CTCs) coming from tumors. The test is termed as a "new and effective tool", having "broad implications" for cancer research, early detection, diagnosis and management while monitoring tumor response to treatment.

The scientists have developed a counter intutive approach, using a tiny chip with critical geometrical features to process large volumes of blood in a very gentle and uniform manner – almost like putting a "hose" through a microchip. They used the CTC blood test on 116 cancer patients. The test spotted CTCs in the blood samples from 99% of the cancer patients. The test detected CTCs even when there were only 5 CTCs in a millilitre of a patient's blood. The test found no CTCs in blood samples from healthy people. The researchers also used the blood test to monitor changes in CTC levels in cancer patients undergoing treatment.

(WebMD,Inc, Dec 20, 2007)

Early Detection of Viruses

Iowa State University researchers have developed a single molecule spectroscopy technique that detects a single molecule of the human papilloma virus (HPV) associated with cervical cancer in women. Current test involving polymerase chain reaction technique requires 10 to 15 virus molecules for detection. Detecting lower levels means earlier diagnosis. HPV is the most common sexually transmitted infection and vaccines administered after early detection could still have time to stop the virus.

Single molecule spectroscopy technique involves creating chemical reagents that recognize and fluorescently tag the genetic sequence of the human papilloma virus. Test samples pass through a laser beam that lights the tags. Cameras capture the images for computer analysis. The research team tested the technique using samples from normal pap smears. They also spiked some of those samples with the virus to make sure that the tests picked up known amounts of the virus.

(Biocompare News, Oct 30, 2007)

New Biomarker for Breast Cancer

Researchers at the University of Cincinnati have identified a molecule that may be more accurate than existing biological signposts used to predict breast cancers that would develop into advanced forms.

Three standard molecules, estrogen receptor (ER), progesterone receptor (PR) and HER 2, are used as biomarkers for diagnosis and individually to detect only a fraction of breast cancers. They are not a good predictor of tumor metastasis. Researchers have identified a molecule, osteopontin -c, that is absent from the normal breast and appears to more accurately predict breast cancer that will become metastatic. They found in a study that osteopontine-c was present in 78% of cancers and in 36% of the surrounding tissues. It was present in a substantially higher number of breast cancers than the three traditional biomarkers used to diagnose breast cancer. Moreover, it was correlated with a higher tumor grade. If it is known that the patients have this molecule early in their diagnosis, they can be treated more aggressively because of the invasive nature of cancer.

(Int. J of Cancer, Oct 24, 2007)

Stereoscopic Digital Mammography

BBN Technologies, Cambridge, Massachusetts, has developed stereoscopic digital mammography, a 3-D breast imaging technology that may give a more accurate method of detecting breast cancers. It may cut false-positive results to half.

A stereoscopic mammogram image works on the principles similar to the old view-master slide viewers. The viewing monitor for stereomammography merges two distinct images to create a 3-D look at tissue. By giving radiologist a view of slices through the breast, 3-D tomography would allow them to see lesions that are missed on standard mammography and otherwise obscured by being superimposed on the normal breast tissue. Most of these may turn out to be benign, but some additional cancers would be found.

Another advantage of the stereoscopic digital mammography is that it is much better at picking up cluster calcifications that can be associated with malignancy. Being able to cut that number by half would reduce both patient anxieties and cost. This new promising technology would make mammography much better.

(Medlineplus, Nov 28, 2007)

DRUGS

Hope for CML Patients

Chronic myeloid leukemia (CML) is a cancer that originates in the immune cells. These leukemia cells crowd the bone marrow and blood, suppressing formation and function of other blood cells normally present in these areas.

The US Food and Drug Administration has approved the targeted agent Tasigna® (nilotinib) for the treatment of chronic and accelerated phase CML for patients who are not able to tolerate or who have stopped responding to Gleevec® (imatinib). Gleevee is a biological agent that binds to and slows or stops the uncontrolled growth of cancer cells with the Philadelphia chromosome genetic mutation. Some patients stop responding to Gleevec or are not able to tolerate it.

Tasigna is an agent that also targets the same protein as Gleevec but through a different mechanism. Some trials have indicated that Tasigna is more potent than Gleevec. Patients treated with Tasigna had improvements in their blood cell levels while tolerating therapy well. For clinical benefits and survival of patients, further followup of the trial is required.

(Novartis Pharma, Oct 20, 2007)

Light Powered Platinum

Researchers from the Universities of Warwick ,Edinburgh, Dundee and the Czech Republic's Institute of Biophysics have discovered a new light-activated platinum-based compound known as "trans, trans, trans – [Pt (N3) 2 (OH) 2 (NH3) (py)]" or a light activated Pt IV complex. It is highly stable and non-toxic if left in the dark, but if light falls upon it, it becomes much less stable and highly toxic to cancer cells. It is between 13 and 80 times more toxic to the cancer cells than the current platinum-based anti-cancer drug Cisplatin. It kills the cells by a different mechanism of action, so it can also kill Cisplatin-resistant cells.

The compound could be used in particular to treat surface cancers. It is more efficient in its toxic action on cancer cells that it does not require the presence of significant amount of oxygen within a cancer cell to become toxic. The researchers are hopeful that in a few years time, the new platinum compound could be used in a new type of photoactivated chemotherapy for cancer.

(Warwick University$_2$, Dec 23, 2007)

EQUIPMENTS

Revolutionary Scanner

Royal Philips Electronics of the Netherlands, a global leader in healthcare, lifestyle and technology has unveiled the latest 256-slice Brilliant iCT scanner. It is so powerful that it can produce stunning 3-D images of an entire organ, including the heart and brain. Philips has showcased five research projects at the 93rd annual meeting of the Radiological Society of North America (RASNA) in Chicago demonstrating where radiological technology for diagnosing and treating heart disease and cancer is heading.

Brilliant iCT features Philips Essence technology, consisting of new X-ray tubes, detectors and construction design elements. It allows the radiologist to produce high quality images with exceptional acquisition speed while reducing patient's exposure to X-rays. The scan is much quicker as the machine's X-ray emitting gantry can rotate four times in a single second, which is 22 percent faster than the current system. Moreover, it has reduced radiation doses by upto 80 percent. This innovative technology would make the job of the clinicians easier. To date, more than 30 CT systems with Essence Technology have been shipped.

(www.medical.philips.com, Nov 25, 2007)

Robotic Device

Radical Tonsillectomy, using new transoral robotic surgery (TORS), offers excellent access for resection of carcinomas of the tonsil with acceptable acute morbidity. The surgical system consists of a console, where the surgeon sits at a distance from the patient; a surgical cart; the instrument-holding arms and a central arm with an endoscope. This lighted optical instrument with two video cameras offers a three-dimensional view of the inside of body. Surgical arms are controlled by the surgeon's movement of handles in the console. In TORS, the mouth is held open and incisions are made in the gums, soft palate, tongue and throat muscles to reach and remove the tonsils and any surrounding cancerous tissue.

The surgeons from the University of Pennsylvania, Philadelphia, have evaluated the feasibility of TORS. They were able to remove all cancerous tissues with no complications like death, pneumonia or fistula that are usually reported during other types of procedures.

(Medical News Today, Dec 18, 2007)

IN FOCUS

ULTRASOUND BREAST ELASTOGRAPHY

Introduction

Siemens Medical Solutions offers a breakthrough in breast ultrasound technology with a revolutionary elastography breast imaging technology package. The technology, known as eSie Touch™ Elasticity Imaging, is a new, real time, qualitative imaging technique that displays the relative stiffness or hardness of tissues to provide further insight into potential pathology. Elasticity imaging is a byproduct of a standard ultrasound exam and may reduce reliance on invasive breast biopsy procedures and provide a clinically relevant differentiation of the benign and malignant tissues.

This technology can be integrated into selected systems to deliver a complete solution for breast imaging, diagnosis and followup. It improves lesion detection sensitivity, increases exam specificity and enhances exam efficiency, workflow and patient throughput. The software for this diagnostic advance is offered with the 5.0 release of the Acuson Antares Ultrasound System.

It is expected to enable physicians to accurately distinguish characteristics of breast lesions by more clearly demonstrating relative tissue stiffness or hardness, infiltration and cystic regions.

Elastogram

Principle: Elastography looks at only the elastic properties of tissues by applying a slight compression to the tissue and comparing an image obtained before and after compression. Some newer techniques utilize heart pulsations and breathing movements instead of compression and relaxation. The data collected before and after compression are compared using a cross-correlation technique to determine the amount of displacement each small portion of tissue undergoes, in response to the compression applied by the ultrasound transducer. The compression is very small, usually only 0.2 to 0.6 mm. The rate of change of displacement of the breast tissue as a function of distance from the transducer causing the compression is called a strain image and constitutes the elastogram. Initial evaluation suggests that elastography can correctly classify most benign and malignant masses.

Interpretation: Three different patterns have been identified in elastograms of cancers: a well-defined, very hard (dark) mass or nodule; a moderately hard mass or nodule containing much harder (darker) foci within it ;and a very dark or hard central core surrounded by a somewhat softer or less dark peripheral component.

One area where elastography may be of great benefit is in distinguishing fibrosis of the breast from cancer. In elastography, fibrosis generally shows as a uniform, moderately hard region with no distinct foci of increased hardness, whereas a cancer usually stands out as a well-defined though irregular region of increased hardness. Malignant masses appear darker or harder and in the transverse dimension than benign masses would appear. They appear larger because of the surrounding desmoplastic reaction, which produces a zone of increased hardness surrounding the actual cancer. Benign masses, however, frequently measure either smaller or the same size as their sonographic image.

Study Results

In a recently published study, 80 patients with a total of 123 suspicious lesions were examined. Using elasticity measurements from the eSie Touch Elasticity Imaging application, 18 lesions were classified as malignant, which was confirmed in17 cases by a needle-guided biopsy. Of the 105 lesions predicted as benign, all were biopsy-proven benign. “Elasticity imaging has a high specificity,” confirms Richard G. Barr, Professor of Radiology at the Northeastern Ohio University College of Medicine and Radiology, Ohio, USA. Barr hopes that the use of elasticity imaging will help to reduce the number of breast biopsies for many patients. The results of the Barr study are presently being validated in comprehensive studies in Europe and the United States.

Future Perspective

Over the past year, elastographic image quality has improved, along with the sharpness of margins and the resolution within the interior of hard lesions. If further evaluations prove the initial observation of this technique then it may prove to be a very valuable adjunct to screening as present methods of screening (mammography, ultraound or MRI) are less effective at distinguishing benign from malignant lesions, resulting in a high number of invasive biopsies. As per the American Cancer Society reports nearly 80% of biopsies following a screening examination are negative for malignancy. This may obviate many biopsies of benign lesions and reduce the cost and discomfort of diagnosing breast cancer.

CANCER CONTROL

Cervical Cancer Survivors Screening

The long term increase in cancer risk that follows cervical cancer – particularly that treated with radiation therapy – highlights the importance of cancer screening in this group of women.

To explore the long term cancer risk of cervical cancer survivors, researchers have evaluated data from cancer registries in Denmark, Finland, Norway, Sweden and the United States. They found that second cancer risk in cancer survivors is 30% higher than risk in the general population. Cancer survivors had increased risk of both HPV-related cancers (such as cancers of the oropharynx, female genital sites and rectum/anus) as well as smoking-related cancers (such as lung, pancreas and bladder). Women who had received radiation therapy for cervical cancer had increased risk of second cancers in organs close to the cervix (colon, rectum, bladder, ovary and female genital sites). This risk persisted for more than 40 years after the initial radiation therapy.

(UFSCC, Nov 1, 2007)

Global Cancer Toll

According to a report of the American Cancer Society, cancer would claim 7.6 million lives world wide in the year 2007. Cancer burden is increasing in the developing countries, with infection playing a greater role in shaping cancer incidence, three times higher than in developed nations. Infection with Helicobacter pylori is linked to stomach cancer; infection by the human papillomavirus (HPV) is a strong risk factor for cervical cancer; and liver cancer is linked to hepatitis B and C infections. Lower surgical rates in less developed parts of the world reflect a lack of prevention, early detection and treatment resources.

Data on increasing tobacco use in developing countries indicated that 84% of the 1.3 billion smokers worldwide live in developing countries. In 2000, 1.42 million people died from cancer related to smoking. Cancer burden is increasing as people in the developing countries adopt western lifestyles, such as cigarette smoking, higher consumption of saturated fat and calorie- dense foods, and reduced physical activity.

(ACS, Dec 17, 2007)

Grapes and Colon Cancer

A study conducted by the University of California – Irvine researchers showed that a diet rich in grapes may help prevent the third most common form of cancer, that is, colon cancer that kills more than half a million people worldwide each year.

Resveratrol, a nutritional supplement derived from grape extract, blocks a cellular signaling pathway known as the Wnt pathway linked to more than 85% of sporadic colon cancers. The study showed that the supplements did not have an impact on existing tumors. Biopsied colon tissue showed that Wnt signaling in the patients taking 80 grams of grape powder was significantly reduced. Similar changes were not seen in patients taking higher doses of grape powder or resveratrol pills.

The resveratrol chemical is found naturally in grape skins, wine and also in peanuts. Eighty grams of grape powder equals half a glass of wine or one pound of grapes, which is equivalent to three dietary servings of grapes. Researchers are designing a clinical cancer prevention study to see how daily diet of grapes affects Wnt signaling.

(Science Daily, Nov 15, 2007)

Nicotine-Reduced Cigarettes

The study conducted by researchers at the University of California, San Francisco and San Francisco General Hospital Medical Center showed that providing smokers with cigarettes of gradually decreasing levels of nicotine over a number of weeks could help cut their nicotine addiction. They also noted that about 25 percent of the smokers quitted smoking entirely during the study.

The study included 25 adult smokers. They puffed on their usual brand for the first week of the study and then began a six week program where they smoked cigarettes with steadily decreasing amounts of nicotine. At the end of six weeks, the smokers were free to start using their regular cigarette brands again. After one month, they were found smoking about 40 percent fewer cigarettes a day compared to when the study began. Reducing the levels of nicotine in cigarette tobacco could spare millions of people from the severe health affects of long-term smoking.

(Health Day News, Nov 14, 2007)

INSTITUTE
Cancer Institute (WIA)

Introduction

The Cancer Institute (WIA), Chennai, was established more than 50 years ago as a mission to provide scientific treatment and to promote health education amongst all sections of society without regard to social or economic considerations. It was a period when there was no concept of oncology, and minimal facilities for cancer care.

The Institute was established by public donations as a voluntary charitable non-profit cancer centre. It consisted of a single building, minimal diagnostic and therapeutic facilities and a cluster of huts to house patients. Finances were meagre and daily existence was a struggle. The Christmas Eve 1956 was their tryst with destiny. A cable received on that day from the AECL, Canada announced the gift of a Cobalt-60 unit to the Institute, the first one of its kind in Asia, ushering in the super voltage era in the country. The Institute had not only come to stay but had assumed the mantle of a national pioneer. The next few decades witnessed a continuous flow of international aid from philanthropic agencies in Canada, Germany, the Netherlands, Denmark and Japan in the form of Co-60 units, diagnostic imaging equipments, linear accelerators and several other ancillaries to build a state-of-the-art centre.

The Cancer Institute today is a comprehensive cancer centre, comprising of a hospital of 428 beds, a Research Centre and a Muthulakshmi College of Oncologic Sciences and a Division of Preventive Oncology.

Annually, over 120,000 patients from all over the country pass through the portals of the Institute; two-thirds of them are indigent with fewer than 1% covered by health insurance. These patients are treated either totally free or at a highly subsidized cost.

In 1969, WHO in conjunction with the Cancer Institute established the first International Cancer Control Programme in the developing world at Kanchipuram near Madras.

The Hospital

The Division of Radiation Oncology has an array of 4 linear accelerators, 2 cobalt-60 units, 3 remote after loading brachytherapy units and supporting ancillary facilities like treatment planning system, interfaced CT scanner, simulator etc. 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.

Surgical oncology is still the solid foundation on which the cure of many cancers depends. All major surgical procedures, including state-of-the-art surgery like limb conservation in malignant tumours of bone, skull base surgery, laparoscopic surgery are practised. The Institute has modern state-of-the-art operating rooms with intensive care facilities.

The Institute pioneered as early as 1958 the multimodal approach to the management of cancer. It introduced it in locally advanced oral, cervical and breast cancers, using a combination of radiotherapy and surgery in the early years. With the advent of chemotherapy, the Institute started using a combination of radiotherapy, surgery and chemotherapy. The concept of multimodal therapy in cancer was introduced for the first time at the Institute in 1963 (British Medical Journal) and this was referred to as "Innovative Technics" in the Year book of Cancer 1964. Today, multimodal therapy is considered state-of-the-art the world over.

Medical oncology introduced as a distinct specialty for the first time in the country in 1970 enhanced the scope of cure in many cancers that were earlier considered beyond the scope of treatment. An intensive protocol for pediatric ALL evolved in collaboration with the National Cancer Institute changed the outlook to leukemia children with almost 50% returning to normal health.

These three main clinical divisions are supported by state-of-the-art imaging services (Radiology, Ultrasonography, Nuclear Imaging), Hematology (including blood component therapy), Pathology, Cytology, Cytogenetics, Medical Physics, a prosthetic laboratory and a rehabilitation and counselling service.

Preventive Oncology

One of the vital activities of the Institute is the preventive programme which is educational at both the public and professional levels. Rural-based educational programmes include the training of village health nurses (VHN) and multi-purpose workers in the early detection of cancers of the cervix, oral cavity and female breast. The WHO sponsored tobacco cessation clinic at the

Institute is actively involved in de-addiction and tobacco control activities.

College of Oncologic Sciences

As early as 1970s, it was realized that specialized and trained oncologic personnel were essential for excellence in oncologic care and research. After 10 years of struggle, the Institute was able to introduce the concept of oncology as a speciality and the Medical Council of India recognized its superspeciality courses of MCh (Surgical Oncology) & DM (Medical Oncology).

The Institute has till date trained over 150 superspecialists who occupy senior positions in almost every state of India. It is the only centre in the country which trains medical physicists. Their trainees man all the major radiation centres in the country. It was the first center (1981) to award the MSc degree in Medical Physics of the Anna University of Technology. It also offers DMRT and MD courses in Radiation Oncology. The college is permanently affiliated to the University of Madras and the Tamil Nadu Dr M G R Medical University.

Research

Organising oncologic research in the early 60s was certainly not an easy task. Governmental support was minimal. The major problem was to find qualified staff. Physicians and surgeons were reluctant to even enter the portals of a laboratory when clinical practice was so rewarding. Attempts to recruit staff and send them abroad for training, most often resulted in the staff member continuing comfortably in the laboratory where they were trained.

Despite various obstacles and hurdles, the Institute has set up a well establish research section. The Molecular Oncology Division at the Institute is designated as a "Centre of Excellence" by the Department of Science and Technology. The hereditary cancer detection and prevention programme of the Cancer Institute (WIA) is the only one of its kind in India. Apart from this, the division is also involved in sub-classification of cervical and breast cancer by gene profiling, using microarray techniques, identification of genes in drug resistance and many others.

Some "Firsts"

- The Cancer Institute was the first comprehensive cancer centre in south India and the second one in the country.
- It was the first centre 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 centre in India to establish a Department of Nuclear Medical Oncology in 1956, 6 years before the DAE established its Isotope Division.
- "Pediatric Oncology" as a speciality was introduced by the Institute in the country in 1960.
- The first indigenous therapy simulator was designed by the Institute in 1965 and fabricated by the I.G.E. and installed in 1968.
- 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 the Institute for the first time in 1978.
- The Institute established the first "PEPA" programme in the country in the chemotherapy of cancer.
- This Cancer Centre was the first in India to institute Postgraduate courses leading to MCh in Surgical Oncology, DM in Medical Oncology and MSc in Physics as applied to medicine in 1981 & 1984.
- Establishment of a Demographic Tumour Registry (1981).
- The Institute was the first and at present the only centre in India to introduce Hyperthermia in the treatment of cancer (1984).
- The first (1992) and at present the only centre 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 was designed and fabricated (1995).
- The first conformational therapy unit Linear Accelerator Clinac 2300 C/D was installed (1999).
- Tobacco Cessation Clinic (2002).
- The first Hereditary Cancer Clinic (2002).
- Development of Dendritic Cell Vaccine for treatment of cervical cancer (2003).
- Establishment of a National Tumor Bank (2006).

CLINICAL TRIALS

Brain Cancer Trial

The survival advantage conferred by the addition of temozolomide to radiation therapy in glioblastoma multiforme brain cancer remains highly significant with a longer followup. This is what the researchers concluded from a phase III clinical trial involving more than 500 European and Canadian patients.

The updated results showed that 12.9% of patients who received temozolomide during and after radiation treatment lived for 4 years compared with 3.8 % of those who received radiation alone and also lived for 4 years. Patients who survived for 4 years after diagnosis, were mostly younger than 50 and in otherwise good health without any prior major medical condition. Approximately 28 % of these patients who were treated with temozolomide and radiation lived for 4 years versus only 7 % of patients who received radiation therapy only.

Two years ago, researchers had reported that survival benefit with this drug was 2.5 months. Now additional follow-up has shown that some patients have survived for several years beyond the 6 to 12 months that is typical for this deadly disease.

(NCI Cancer Bulletin, Nov 6, 2007)

Early Stage Hodgkin's Disease

According to the researchers from France, chemotherapy plus involved-field radiation should become the standard of care for early-stage Hodgkin's disease. Early-stage is classified as favorable or unfavorable, based on the prognostic factors. Involved-field radiation therapy is administered to all lymph node regions known to contain cancers.

Researchers conducted two clinical trials to evaluate different treatment options for patients with either favorable or unfavorable early stage Hodgkin's lymphoma. The trials included 1,538 patients who had not received prior therapy, median followup for both trials was 92 months. Chemotherapy used in these trials was MOPP(mechlorethamine, vincristine, procarbazine and prednisolon) plus ABV (doxorubicin, bleomycin and vinblastin). Results of first trial indicated that survival at 10 years was 97% for those treated with chemotherapy plus radiation therapy versus 92% for those treated with radiation therapy only. They concluded that chemotherapy plus involved field radiotherapy should be the standard treatment for Hodgkin's disease with favorable prognostic feature. The second trial included patients with early stage unfavorable Hodgkin's. The researchers concluded that in patients with unfavorable features, four courses of chemotherapy plus involved-field radiotherapy should be the standard treatment.

(NEJM, Nov 2007)

New Drug Combo for SCLC

Researchers in Europe conducted a Phase III clinical trial, which showed that chemotherapy with Camptosar® (irinotecan) and paraplatin ® (Carboplatin) may result in better survival than chemotherapy with VePesid ® (etoposide) and Paraplatin among patients with small cell lung cancer (SCLC).

Due to suboptimal long-term outcome for patients with SCLC, researchers continue to evaluate alternative chemotherapy combinations to the standard therapy. Under this trial, researchers compared camptosar and paraplatin to chemotherapy with VePesid and Paraplatin among 210 patients with extensive SCLC. The results showed that one year survival was 35% among patients treated with camptosar and Paraplatin compared with 28% among patients treated with VePesid and Paraplatin. A complete response was observed in 18 patients treated with Camptosar and Paraplatin and 7 patients treated with VePesid and Paraplatin. The overall quality of life was similar in the two treatment groups.

(Cancer Consultants.com, Nov 7, 2007)

Revlimid Improves Survival

Researchers from the Abramson Cancer Center of the University of Pennsylvania announced that findings from two large international clinical trials showed that patients with relapsed or refractory multiple myeloma, who were treated with Revlimid (lenalidomide) and dexamethasone significantly improved by all measures including a median survival of nearly three years, the longest median survival known for this difficult to treat patient group. Revlimid from Celgene, an oral medication which treats without the ravages of chemotherapy is the first in a new class of medication called immunomodulatory drugs (IMiDs).

Some positive patient response suggests that treatment with Revlimid early in the course of the disease may be beneficial. These findings have caused a change in the official physician guidelines for multiple myeloma which were recently updated to add Revlimid as an initial treatment, instead of waiting until other treatments have failed.

(NEJM, Nov 22, 2007)

WATCH-OUT

Ablation of Tumor Cells

Cao Densen and Jensen Steven of the United States have been awarded a US patent under Patent No. US 2007265607 entitled 'Cancer treatment using low-energy lasers', published on Nov 15, 2007. It relates to a method and apparatus for destroying cancerous cells or tumors, including placing fibre needles into the human body adjacent to cancerous cells or tumors that have been biologically dyed and exposing them to low-energy laser to destroy the cancer cells or tumors through ablation without destruction of surrounding healthy tissue.

A region within the human body that contains a cancer tumor or cells is located using conventional steps such as laser scanning, magnetic resonance imaging, X-ray imaging or CT scans. The tumor cells are then injected or painted with a biological dye material. The fibre needle is inserted with its end in close proximity to the tumor cells. Laser light from the laser system is applied through the fibre needle to the tumor cells and is continued for effective duration in order to destroy at least a portion of the tumor cells through ablation of the tumor cells.

(esp@cenet.com, Nov 26, 2007)

Laser Imaging Apparatus

Imaging Diagnostic Systems Inc has developed a revolutionary new imaging device to aid in the detection and management of breast cancer. The company is a pioneer in laser optical breast cancer imaging systems and has been awarded a Chinese patent Z L 99816608.1 entitled "Laser Imaging Using Biomedical Markers That Bind to Cancer Cells" by the Chinese government, thus extending its protection in another important market. With this patent comes additional hope that breast cancer may some day be imaged and treated with light-activated compounds. The company's current proprietary CT Laser Mammography System (CTLM®) is uniquely capable in these applications. CTLM® is designed to be used in conjunction with mammography to visualize the process of angiogenesis which usually accompanies tumor growth.

The Chinese patent is in addition to the Australian patent 775069, European patent EP01181511, Hong Kong patent HK 1043480 and German patent DE 69925869, which protect the concept of imaging and activating a photodynamic therapy agent in an optical CT scanner, a combined diagnostic and therapeutic system.

(Imaging Diagnostic System Inc, Nov 6, 2007)

Ovarian Cancer Diagnostic

HealthLinx Limited specialises in ovarian cancer biomarker diagnostics to detect cancer at early stage. It has reached an agreement with the University of Liverpool (UK) to in-license additional patented biomarker technology and antibodies that have shown efficacy in detecting grade I & II ovarian cancer.

HealthLinx and the University of Liverpool have been jointly developing this technology which has the potential to be the world's first commercially available multi-marker early stage ovarian cancer diagnostic. Preliminary studies indicate the detection of early stage ovarian cancer (grade I & II) and discrimination between the mucinous and serous tumours. At present no product with either of these benefits is available in the world. HealthLinx has announced the phase II biomarker results for its first generation OvPlex panel with an increase in diagnostic efficiency of ovarian cancer by greater than 15% compared to CA125. Once this panel has been designated and validated, the company would aim to introduce the product into the market through its partners as a community based screening test to boost survival rates.

(HealthLinx Limited, Nov 26, 2007)

Small Molecule Id-Inhibitors

AngioGenex Inc. is actively engaged in the discovery, acquisition and development of anti-cancer molecules that act by inhibiting either the Id genes or proteins to prevent angiogenesis. It has identified and filed a patent application on small molecules that are potent inhibitors of the Id proteins. It is a major milestone in the company's goal to develop orally active anti-cancer drugs. The work establishes the drug ability of the Id proteins as targets, allowing the company to move forward with the preclinical work.

AngioGenex is currently testing a companion diagnostic that detects low levels of the Id proteins in serum. Preliminary results suggest that it has the potential to detect presence of Id proteins at an early stage of tumor development allowing early medical intervention; it may also be useful to follow the course of therapy and determine whether there is a recurrence of disease.

(AngioGenex Inc, Oct 16, 2007)

GLOBE SCAN

Cancer Feeder

The researchers at the Queensland Institute of Medical Research and Flinders Medical Centre in Adelaide, Australia have discovered that cells in the human body once believed to be "innocent bystanders" in cancer may actually be recruited by the disease to feed tumors and help them spread. This finding may one day open the way for new therapies to slow down tumor growth or even stop it "dead in its tracks".

The researchers made the observation in female bone marrow transplantation patients who went on to develop secondary cancers including skin, cervical and gastric cancer. In gastric cancer patients, they found that the cells had migrated in from the bone marrow, which looked like fibroblasts and were likely to be contributing to the growth and regulation of the cancer. The finding was significant because it opened up the possibilities of controlling or regulating the mechanism.

*(*Australia *: The Age.com, Nov18, 2007)*

Light Activated Vaccines

According to the researchers based at the British Columbia Cancer Agency in Vancouver, Canada, tumor cells could be used to develop personalized light-activated cancer vaccines using photodynamic therapy which acts by activating a light sensitive drug as well as stimulates an immune response against a tumor. The researchers performed photodynamic therapy on mouse tumor cells in the laboratory and injected them back into the same mice. This new technique was as effective as using cancer cells grown in the laboratory in the vaccine, but cut out the time-consuming process of culturing cells and allowed the treatment to home-in the unique characteristics of the individual's tumor.

The prospect of using samples from a patient's own tumor to treat him is really exciting. Using targeted treatments with better delivery and manipulating the body's own immune system to fight the disease means patients would experience a fewer side effects.

*(*Canada *: British Journal of Cancer, Nov 13, 2007)*

Promising Research

Ireland Cancer Center of University Hospitals Case Medical Center has recently made great strides in stem cell gene therapy research by transferring a new gene to the cancer patients via their own stem cells, with the ultimate goal of being able to use stronger chemotherapy treatment with less severe side effects. Under this protocol, MGMT, a drug resistance gene, is added into purified hematopoietic stem cells to protect these cells from the damage of chemotherapy regimens.

Eight patients were enrolled in the trial and six were infused with their own stem cells which were engineered to carry the MGMT gene. In three patients, stem cells carrying the gene were identified in their blood or bone marrow. In one patient, stem cells carrying the gene were detected up to 28 weeks after their administration. This significant finding has never been reported before with this gene and drug combination.

*(*Ireland : *Biocompare News, Dec 12, 2007)*

Cancer Care Advances of 2007

The 21-member oncologists editorial board of the American Society of Clinical Oncology (ASCO) has identified a number of significant cancer advances 2007. Some of these advances are:

1. *First systemic treatment for primary liver cancer*: A large study found that patients who took the targeted therapy sorafenib (Nexavar) for advanced liver cancer lived about 44% longer than the patients who did not.

2.*Treatments for advanced kidney cancer continued to expand*: Adding becacizumab (Avastin) to the standard kidney cancer treatment nearly doubled the progression free survival.

3. *MRI better for screening women at high risk of breast cancer*: This year, new guidelines based on the findings from several studies showed for the first time that MRI can be effectively used in women at high risk of developing cancer.

4. *HPV linked to head and neck cancer* : Two studies showed that the human papilloma virus (HPV) was found in 72% of the several types of head and neck cancers, suggesting a possible role for the new HPV vaccines in preventing head and neck cancers.

5. Drop in breast cancer cases linked to declining use of hormone replacement therapy.

6.Preventive radiation therapy to whole brain can stop the spread of advanced lung cancer while cutting the risk that the cancer would spread to the brain by about two thirds and as a result double the one-year survival rates.

(US : Medical News Today, Dec 19, 2007)

ACTIVITIES OF RGCI&RC

PRESENTATION ON IMAGE GUIDED RADIOTHERAPY

A technical presentation on 'Image Guided Radiotherapy (IGRT)' was made by Dr Christopher Amies, Vice President- R&D, Siemens OCSG, USA, on December 10, 2007 in the conference hall of Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC). It was attended by Mr K K Mehta (Hony Secretary), Mr D S Negi (CEO), Dr A K Chaturvedi (Medical Director), senior consultants of radiation oncology, medical physicists, resident doctors and research officers of RGCI&RC. Mr Vijay Kumar and Mr Vivek, representatives from Siemens, were also present.

Radiotherapy is identified by 5 major steps: (i) diagnose, (ii) prescribe, (iii) simulate and plan, (iv) setup and (v) treat. In IGRT/VGRT/SGRT/DGRT, the last step of "treat" includes feedback stream of relevant information to setup by sensing 2-D/3-D imaging data or dose data either just before or during radiation treatment. The term 'Image Guidance' (IGRT) is used if the data sensed is 2-dimensional or 'Volume Guidance' (VGRT) if sensed data is 3-D ionic imaging. 'Structure Guidance' (SGRT) refers to an adaptation process in which anatomical organs or symbolic imaging information is sensed while dose guidance (DGRT) requires that dose is measured prior to or during radiation therapy.

The presentation by Dr Chistropher Amies included the capability IGRT and VGRT by Siemens product ARTISTE that covers mechanical accuracy, energies, treatment table, image guidance, gated treatment, 160 MLC, stereotaxy, patient motion monitoring, operative console and connectivity. He informed about MVision-Megavoltage Cone Beam imaging which is in line with KV Cone Beam imaging system enabling patient position verification. He explained the movement of KV source and the movement of the KV detector for inline position for KV CBCT which has space to accommodate attachable MLC's like Moduleaf.

On the current clinical practices, he mentioned that merely taking two dimensional portal images and comparing with digitally reconstructed radiographs from the planning CT to verify patient setup prior to treatment was not sufficient since this process does not make full use of the volumetric information available from treatment planning. This could be overcome by cone beam reconstruction technique that allows to acquire 3-D volume of the patient immediately before delivering the treatment using the treatment beam. The MVision-Megavoltage Cone Beam utilizes the linear accelerator radiation beam and the flat panel detector used for portal imaging to acquire a series of very low dose 2-D projections to reconstruct a 3-D volumetric data set which is compared with the planning CT.

He showed images of prostate and lung taken with MV and KV beams during or prior to treatment. He also mentioned that Respiratory Gating with systems like Anzai belt, RPM (real time position management) and optical imaged based camera systems (rtAlign) can be integrated with ARTISTE. He informed about the ongoing research work on improving the imaging performance of MVCBCT by modifying the beam line in order to slightly increase the low energy component of X-ray beam. Preliminary investigations using low energy beam with no flattening filter and a carbon target, suggest a factor of 3.5 improvements in contrast to noise ratio (CNR), thus allowing a significant reduction of the exposure to obtain a given MVCBCT image quality also called as Diamond View Images. He showed Diamond View Images and hoped that these will replace the current MVCBCT images in future.

He also showed how respiratory gated and non-gated images of lung varied in image quality. The lungs, esophagus, liver, pancreas, breast, prostate and kidneys, among other organs, are known to move with breathing and cause degradation of image quality and subsequent difficulty in radiotherapy dose planning and treatment delivery. He also explained that since patient's breathing patterns can vary in magnitude, period and regularity during imaging and treatment session, gated respiratory treatment is now a challenge for the radiotherapy community.

IGRT treatment modality is time consuming and hence Dr Amies was much concerned on speed vs quality graph and emphasized that to render quality treatment to patients at large, one has to sacrifice speed and obviously that means number. He also highlighted the research work being carried out on Direct Aperture base Optimization (DAO) algorithms for faster treatment delivery.

The queries raised by Dr Chaturvedi, Dr Anand, Prof Negi, Dr Datta and Mr Wadhawan were discussed. This informative presentation ended with thanks by Dr Anand.

Lung Cancer Symposium

Department of Medical Oncology, Rajiv Gandhi Cancer Institute and Research Center (RGCI&RC) had on 20th December 2007 organized the second DNB symposium, an educational debate on the role of adjuvant treatment in early lung cancer. Senior faculty from (RGCI&RC), postgraduates and senior residents from all departments assembled for the event. The programme started with initial comments by Dr Ranga Rao, Senior Consultant, Medical Oncology. He stated how the incidence of lung cancer, the largest killer among all cancers, was steadily rising in the country. Continuous research, however, is coming up with novel therapies and upgrading treatment modalities to improve prognosis.

The first presentation of the evening was on the Role of Molecular Pathology & Markers in Lung Cancer by Dr Chidambara Jha. She outlined the multistep tumorigenesis of lung cancer and the step-wise accumulation of genetic abnormalities. The potential diagnostic markers are tobacco related HYAL2 and FHIT deletions in sputum for early stage lung cancer and telomerase repeat amplification (TRAP) assay in bronchial washings. Poor prognostic markers in non-small cell lung carcinoma (NSCLC) include KRAS activation, HER2 over expression, loss of p53, p16, 3p deletion, Ki67 status, while EGFR mutation predict a favourable outcome. Markers of metastasis such as TIMP indicate poor prognosis. Since small cell lung carcinoma (SCLC) has a much shorter survival, fewer studies have been conclusive. She concluded by stating that DNA microarray and proteomics continue to unravel the molecular mysteries of cancers. Dr D C Doval added that Pharmacogenomics have opened the door for tailor made chemotherapy in lung cancer pateints in the near future. Excision repair cross complementing gene (ERCC-1) has been associated with response to cisplatin based chemotherapy.

Dr Rajesh Jain, while speaking on the role of adjuvant chemotherapy for lung cancer, outlined how adjuvant chemotherapy though advocated, may not be necessary or very useful in completely resected NSCLC, particularly stage IA and IB. He further told that there is little or no data to support adjuvant chemotherapy in patients older than 75 years of age which comprise a sizeable percentage of lung cancer patients. The criteria for considering chemotherapy after complete surgical resection if applied stringently, will rule out the option in many patients, as it requires not just good performance status, adequate renal/hematological, hepatic and bone marrow functions but also absence of co-morbid disease or immunosuppression and absence of stromal / pleural / lymphatic invasion. He summed up his presentation by saying that the way forward, is therefore, targeted and individualized chemotherapy only in specific subgroups rather than blanket therapy in all patients with resected NSCLC.

Dr Pankaj Aggrawal presented data for the role of adjuvant radiotherapy in NSCLC. The role of post-operative radiotherapy (PORT) in lung cancer remains nebulous. The PORT meta- analysis of 9 trials in 1998 concluded that there was no role of adjuvant radiotherapy. Since the publications of past trials, significant advancements have taken place in the quality of radiotherapy & delivery systems. Thus, it may be a serious error to make conclusions about efficacy of PORT based on older trials that used equipment, dose regimens and radiation volumes that are not part of currently accepted practices. He concluded that it would be important to re-evaluate PORT in the modern era of improved radiotherapy technology (Gated Radiation Delivery techniques, Tomotherapy) and improved regimens of adjuvant chemotherapy for patients with resected NSCLC who are at high risk of loco-regional failure.

Dr Ajay Sharma presented the role of adjuvant chemotherapy for (stage I- IIIA) resectable lung cancer. The use of chemotherapy has been extensively studied in both adjuvant and neo-adjuvant settings. He gave an outline of the stage specific guidelines for adjuvant chemotherapy, recommending use in stage II and IIIA but not in stage IA and not routinely in IB. He briefly talked about the molecular markers use to predict response to therapy and concluded that cisplatin based adjuvant chemotherapy offers a definite survival advantage. Its use can save 1 in 15 patients treated over a 5-year period (i.e. the Absolute Risk Ratio).

Dr A K Chaturvedi, Medical Director gave away the prizes for the best presentation and the best questions from the audience to Dr Chidambara Jha and Dr Amal Roy Choudhary respectively. The session concluded with closing comments by Dr S M S Zaidi about adequacy of staging, surgical resection and margins. Dr J B Sharma then shed light on chemotherapy while Dr Rakesh Aggarwal emphasized the role of PORT in N_2 disease.