Ionizing radiations are playing an increasingly significant role in medical diagnosis and therapy. To encourage safety culture in every group of professionals handling radiation and radioactive materials, “Special Feature” highlights ‘Radiation Protection in Hospitals’. The Institute is highly obliged to Dr KS Parthasarathy, Raja Ramanna Fellow, Department of Atomic Energy for providing “Guest Article” on ‘Radiation Protection: An Overview’.

An unusual enzyme called telomerase acts on parts of chromosomes known as telomeres and is being eyed as new target for cancer diagnosis and therapy. A special thanks to Dr Showket Hussain and Dr Mausumi Bharadwaj, Institute of Cytology and Preventive Oncology, Noida, for reviewing “Perspective” on ‘Telomeres, Telomerase and Cancer’.

ARA Healthcare Pvt Ltd has set up a state-of-the-art molecular biology and tissue culture laboratory facility at RGCI&RC. A brief introduction to ARAHC is covered under “Molecular Biology Laboratory at RGCI&RC”.

Physiotherapy has a key role to play in the management of patients throughout their cancer journey. An overview of “Physiotherapy in Cancer” has been portrayed in this issue. Tobacco use, the most widespread addiction, is one of the biggest public health threats the world has ever faced. This issue profiles ‘Tobacco Epidemic – File Facts’ under "In-Focus".

Our special gratitude is due to Punjab National Bank for supporting this issue of Cancer News. We also gratefully acknowledge the contributions made by clinicians and scientists of the Institute. Views and suggestions from readers on the Cancer News are welcome.
RADIATION PROTECTION IN HOSPITALS

Introduction

Ionizing radiation consists of subatomic particles or electromagnetic waves that are energetic enough to detach electrons from atoms or molecules, ionizing them. The largest use of ionizing radiation in medicine is in medical radiography, using X-rays, to treat diseases in radiation therapy. Tracer methods are used in nuclear medicine to diagnose diseases and are widely used in biological research. It has been recognized since early studies on X-rays and radioactive minerals that exposure to high levels of radiation can cause clinical damage to the tissues of the human body. The acceptance by society of risks associated with radiation is conditional on the benefits to be gained from the use made of radiation.

Radiation Sources in Hospitals

Sources of radiation in hospitals include X-ray machines and radioactive materials used in the diagnosis and treatment of diseases.

Diagnostic Uses

- X-ray machines, including mobile (portable) units, fluoroscopes (C-arms) and CT scanners.
- Radioactive materials (capsules, liquids or gases) used in nuclear medicine for diagnostic procedures.
- Radioactive materials used in the laboratory for the diagnosis of diseases.

Therapeutic Uses

- Linear accelerators or teletherapy machines used in radiation therapy for the treatment of cancer and other diseases.
- Radioactive sources in small, sealed containers used for patient implants for treatment of cancer.
- Radioactive drugs used to treat patients.
- Gamma irradiators for post bone marrow transplant.

Radiation Effects

Exposure to radiation at high doses can cause such effects as nausea, reddening of the skin or, in severe cases, more acute syndromes that are clinically expressed in exposed individuals within a short period of time after the exposure. Such effects are termed ‘deterministic effects’ because they are certain to occur if the dose exceeds a threshold level. Deterministic effects are the result of various processes, mainly cell death and delayed cell division, caused by exposure to high levels of radiation. If extensive enough, these can impair the function of the exposed tissue.

Radiation exposure can also induce somatic effects, such as malignancies which are expressed after a latency period and may be epidemiologically detectable in a population; this induction is assumed to take place over the entire range of doses without a threshold level. Also, hereditary effects due to radiation exposure have been statistically detected in other mammalian populations and are presumed to occur in human populations also. These epidemiologically detectable effects—malignancies and hereditary effects—are termed ‘stochastic effects’ because of their random nature.

Other health effects may occur in infants due to exposure of the embryo or foetus to radiation. These effects include a greater likelihood of leukaemia and, for exposure above various threshold dose values during certain periods of pregnancy, severe mental retardation and congenital malformations.

Since a small likelihood of occurrence of stochastic effects at even the lowest doses is assumed, the standards cover the entire range of doses with the aim of constraining any radiation detriment that may arise.

Radiation Protection & Safety

The most effective methods of radiation protection and safety are to Minimize Time, Maximize Distance and Maximize Shielding. Summary of the principles of radiation protection and safety is as follows:

- Practice that entails or that could entail exposure to radiation should only be adopted if it yields sufficient benefit to the exposed individuals or to society to outweigh the radiation detriment it causes or could cause;
- Individual doses due to the combination of exposures from all relevant practices should not exceed specified dose limits;
- Radiation sources and installations should be provided with the best available protection and safety measures under the prevailing circumstances, so that the magnitudes and likelihood of exposures and the numbers of individuals exposed be as low as reasonably achievable, economic and social factors being taken into account;
Radiation exposure due to sources of radiation that are not part of a practice should be reduced by intervention when this is justified, the legal person authorized to engage in a practice involving a source of radiation should bear the primary responsibility for protection and safety;

Safety culture should be inculcated that governs the attitudes and behavior in relation to protection and safety of all individuals and organizations dealing with sources of radiation;

Protection and safety should be ensured by sound management and good engineering, quality assurance, training and qualification of personnel, comprehensive safety assessments and attention to lessons learned from experience and research; and

Any over-exposure of radiation worker and patient must be reported to Atomic Energy Regulatory Board (AERB) so that it becomes a knowledge base like "Radiotherapy Risk Profile (WHO-2008)" and "Preventive Accidental Exposures from New External Beam Radiation Therapy Technologies(ICRP-2009)".

**Radiation Protection Procedures at RGCI&RC**

**Procurement of Radiation Generating Equipment:**
One has to verify from the supplier that the unit (which is either radiation generating equipment, such as Medical Accelerator/ Simulator, or houses sealed radioactive material, such as Telecobalt/ Gamma Knife/ Brachytherapy unit) to be installed is either type approved by AERB or a NOC is issued by AERB to the local supplier of the unit. The copy of type approval certificate or NOC issued by AERB will be furnished by the local supplier on demand. The next step would be to get approval of Room Layout Plan of Radiation Therapy Installation. The Medical Physicist in consultation with the architect of the supplier of the unit should prepare the room layout drawings and submit along with application form to the Head, Radiological Safety Division (RSD), AERB. Construction of the Radiation Therapy facility should be started only after receiving the approved plan from AERB.

The location of the teletherapy installation should be so chosen that it is away from unconnected facilities and is close to the associated facilities. The associated facilities include Simulator room, Minor Operation Theatre (for Brachytherapy), Mould room, Treatment Planning System room, Physicist(s) room, Radiation Oncologist(s) room, patient waiting area etc. During such process one has to appoint adequate number of full time Medical Physicists, Radiation Oncologists and Radiation Therapy Technologists as per the qualification and experience stipulated in AERB Safety Code SC/MED- 1 and 3. In case of appointment of Medical Physicists, it is to be ensured that at least one of them is eligible to work as Radiological Safety Officer (RSO-III).

Further, it is mandatory to procure Personnel Monitoring Badges from the agency recognized by AERB for all the radiation workers so that they are available during installation of the unit and procure appropriate measuring instruments for measurement of output and other dosimetric parameters (Thimble Ionisation Chamber, Parallel Plate Ionisation Chamber, Well Type Ionization Chamber, Electrometer, Radiation Field Analyser etc.) and appropriate monitoring instruments for area monitoring (Survey Meters, Contamination Monitors, Gamma Zone Monitors etc.). It may be noted that Gamma Zone Monitor for Telecobalt unit and Remote after loading Brachytherapy unit should be of auto-reset type, whereas that for manual Brachytherapy, must have manual-reset button.

To procure Radiation Sources, obtain authorisation from RSD, AERB by sending the filled up form AERB/ RSD/RT/ATH along with all the necessary documents mentioned therein for procurement of sources to be used in Radiotherapy (which includes sealed Radioactive sources, depleted uranium and radiation generating equipments such as Medical Accelerator and Simulator). The form must be filled in properly to avoid undue delay. Obtain road transport permission from RSD, AERB for transporting the radioactive source from the airport/ port to the institution (not required in case of Accelerator and Simulator).

**Equipments in RGCI&RC:** The Institute has four Linear Accelerators, two of them were installed in the year 1996, one in Physical Intensity Modulated Radiotherapy was implemented in Feb 2002. An IMRT Linac with 58 leaves MLC’s was installed in 2004 and IGRT Linac with 160 MLC leaves installed in 2009. Phoenix Teletherapy Cobalt-60 unit was installed in 1996 which was dismantled in 2004. Remote Brachytherapy installed in 1996 contained Iridium-192 radioactive source in Radiation Oncology Department and Iodine-131 sources in Nuclear Medicine Department for thyroid treatment. Radiation waste is drained to associated delay tank duly monitored before being
disposed to municipal drainage. Besides Phosphorous-32, Samarium-153 and Strontium-89 are used for palliative bone metastasis. Institute has Fluorine-18 in the form of Fludeoxyglucose (FDG) for PET/CT diagnosis, Technetium-99m, Thallium-201 for nuclear medicine imaging.

**Waste Disposal Procedures:** Institute has remote after loading Brachytherapy where the Iridium-192 source, which is attached on a steel wire is kept inside a shielded container. For disposal of the source the machine is programmed by the engineer to remove the source along with the steel wire inside a transport flask. For disposal of Brachytherapy sources, the original supplier of the existing decayed source is contacted to obtain their concurrence for accepting the decayed source for disposal.

Sources are to be checked for contamination. In case the sources are found to be contaminated, Radiological Safety Division is contacted for specific advice for packing the sources. Sources are unloaded by AERB certified company engineers under the supervision of hospital RSO Level III to ensure the radiation safety levels during the procedure. In case the sources are free from contamination, they are to be packed, marked and labelled properly as per the transport regulation. The unloaded source container is monitored by Radiation Survey Meter.

In Nuclear Medicine Department, all syringes, vials and unused radioisotopes containing radioactive materials are put in Blue plastic bag and placed in storage room for decaying of the activity (for more than 3 months). After the disposable limits are achieved (5 MBq per cu.m.), waste is sent as municipal garbage.

For Iodine-131 therapy linen, clothes used by patients are also put in plastic bags and kept in storage room for decay. Patients fecal matter and urine is stored in delay tank for radioactive decay and monitored regularly. It is passed to the sewage system when disposable limit is achieved [75 MBq (2 mCi) in any one month].

**Decommissioning of Teletherapy Cobalt-60 Unit:** Consent for decommissioning of Phoenix Teletherapy Cobalt unit was obtained from AERB vide letter No. AERB/RSD/RT/DL-069/2007/11888 dated November 19, 2007 and authorization to retain the dismantled unit was also obtained. After obtaining necessary approval for source transfer and disposal at Board of Radiation and Isotope Technology (BRIT), the job of source transfer and dismantling and transport of source to BRIT was assigned to M/s Kirloskar Theratronics Ltd (KTL). The source transfer procedure in the source transfer flask F-147 #81 was carried out by the AERB approved engineers under the supervision of RSO. The source was transported to BRIT after obtaining necessary NOC for transport vide No. AERB/RSD/TR/5/2008/CT-253 dated January 2009 on an identified carrier/truck arranged by M/s KTL as per AERB guidelines. Further, AERB acknowledged after receiving the source at their end.

**Key Points for Radiation Protection**

- The main responsibility for radiation protection and to oversee radiation protection matter in the Institute has been assigned to Radiation Safety Officer to ensure that radiation sources are used only by competent persons. He should have knowledge of properties and hazards of ionizing radiation, protection, knowledge of appropriate legislation and codes of practice relating to uses of ionizing radiation in relevant medical areas.
- Ensuring that appropriate measures are taken to control the exposure of pregnant employee.
- Assess potential hazards from foreseeable incidents and drafting contingency plane.
- Ensuring that necessary leak testing of sealed sources is performed.
- Decontamination procedures should be supervised.
- Waste disposal procedures to be adopted as specified by the regulatory authority.
- Required records should be maintained and comprehensive annual report to be made (including any over-exposure, accidents, radiation sources).
- There should be arrangement for monitoring workers and the workplace, including the acquisition and maintenance of radiation protection instruments.
- System for calibration of sources and clinical dosimetry.
- The system for constraining the exposures of comforters, carers and volunteers.
- Need for assurance of quality and process improvements.
- Education, training and continuous professional development are key to the effective radiation protection of patients and the overall quality management system in radiology, nuclear medicine and radiation oncology.

(Reviewed by Prof P S Negi, Advisor Radiation; Mr S N Sinha, Chief Medical Physicist, Medical Physics Division)
GUEST ARTICLE

RADIATION PROTECTION: AN OVERVIEW

Introduction

Recent radiation incident in Mayapuri, Delhi, reminded the stakeholders to be ever more vigilant in handling radioactive substances. Misunderstanding about the concept of half life and the potential hazard of an intense source of Cobalt-60 as it decayed, led to the first radiation death in India. “Back to basics” is the need of the hour. Ionising radiation is a double edged sword. Modern medical radiation sources deliver high radiation doses. Accidental exposures will be disastrous. We must follow Atomic Energy (Radiation Protection) Rules 2004 and codes and standards and inculcate safety culture in every group of professionals handling radiation and radioactive materials.

Radiological Safety

The US Department of Health and Human Services, (USDHHS) in its 11th edition of the Report on Carcinogens (ROC), released in January 2005, has added X-rays and gamma rays to the list of ‘known human carcinogens’. The need to exercise greater caution in the use of X-rays and gamma rays in medical procedures is obvious. This may not be news to radiation protection specialists, but is a universally accepted affirmation for others. Radiation protection specialists unanimously agree that radiation at high dose levels causes cancer. At low dose levels there are doubts.

Challenge to LNT Concept

Specialists believe in Linear-No-Threshold (LNT) dose-effect relationship. That means that the dose-effect relation is linear without a threshold; any dose however small will have some deleterious effect. It is a practical necessity. They should account for hormesis, adaptive response, bystander effects and genomic instability. The French Academy of Sciences and the French Academy of Medicine published a report in March 2005. The American National Academy of Sciences’ Committee on Biological Effects of Ionizing Radiation (BEIR) published its BEIRVII – phase 2 report in July 2005. These report can be accessed from the following URLs:


The reports have arrived at different conclusions on the LNT concept, seemingly using the same set of peer-reviewed papers on the topic. I brought the dilemma to the notice of Dr Richard Monson, Chairman BEIR-VII while seeking his reaction to the report from the French Academy.

Dr Ian Douple responded thus: “As director of the Board on Radiation Effects Research that provided oversight to the BEIR-VII report, I received a copy of your email message from Dr Monson and he asked me to respond to you. You raise an important point in that when two learned academies come to opposite conclusions on an important scientific issue, it is often difficult to decide which is the most prudent decision or conclusion to accept. This is especially difficult for the non-scientific public and the news media. Analyses of the risks associated with the exposures to low-dose ionizing radiation are an example of this and a clear indication that this is an especially difficult and highly technical issue to resolve”. He clarified that there could be several reasons why the two reports might have led to different conclusions. He gave three possible reasons.

1. Approach Used by the Committee: The BEIR-VII committee recognized that the world’s most important epidemiological study of radiation exposures in humans is the study of the A-bomb survivors being conducted by the Radiation Effects Research Foundation (RERF) in Hiroshima and Nagasaki—which includes a significant low-dose (<100 mSv) population in the cohort—and developed a risk model using the RERF data and the latest appropriate medical and occupational data. I don’t think the French report developed their own risk model or developed quantitative risk models.

2. Timing of the Report Release and the Information Available or Used by the Committee: The BEIR VII committee had direct access to the very latest RERF data, including cancer incidence data, with the new dosimetry (DS02), and actually developed its own risk model. The French report issued this year was issued before the release of the 15-country nuclear workers study (by France’s IARC) which actually is quite consistent with the BEIR-VII report, but it was released while BEIR-VII was already in the Academies’ review process and the committee had completed its draft. Furthermore, BEIR-VII did look at all of the latest biological data that might have some impact on the mechanisms of radiation-induced carcinogenesis. An earlier French report had concluded that those biological
phenomena (bystander effects, genomic instability, adaptive responses, hormesis, etc.) must be operative in humans and they concluded that they must result in lowering risks of health effects at low doses. The BEIR-VII committee has been following closely the work in this area and did not assume that those phenomenological observations in cell systems under defined experimental conditions necessarily were operative in humans or translated into animals or people at relevant environmental doses and under realistic scenarios. The BEIR-VII report contains a detailed description of the phenomena and points out why at this time one should not extrapolate directly from those data to human health effects.

3. Composition of the Committee and Charge to the Committee: The BEIR-VII committee was charged specifically to develop a recommended risk model using the latest appropriate available data. Great care was taken by the US National Academies to appoint a balanced and non-conflicted membership with the charge to develop a consensus report. Committee members were chosen with the areas of expertise required for the task and members were appointed who did not have a prior reputation of being outspoken or having taken a position on low-level radiation effects. The charge to the BEIR-VII committee was not to validate or test LNT—it was to develop a model that fitted best the data available to the committee. BEIR-VII had European and Canadian expertise represented, including Dr Elisabeth Cardis from IARC in France. The committee members were distinguished scientists who have been experimenting in radiation physics, biology, epidemiology, and medicine.

“.....While the French report says that one should use the LNT concept with caution at low doses, the more recent US report said that it examined all of the data available since BEIR-V and sees no reason to use a threshold or supra-linear model in preference to LNT and therefore LNT is the best model to use at this time.... Ultimately, a policy decision must be made by regulatory and governing bodies and persons such as yourself must make those decisions based on levels of risk that your government is willing to accept”, Dr Douple deftly threw the ball back in to the regulator’s court!

The French report targeted the paper titled “Cancer risks attributable to low doses of ionizing radiation: Assessing what we really know” in the Proceedings of the National Academy of Sciences (PNAS, 25 November 2003). It’s authors include all the famous ones across the world.

I sent the extracts of the French criticism to the lead author David J Brenner, Center for Radiological Research, Columbia University, USA. Rather than replying to all points, he chose to address one major point. Evidently, it appears that there is no agreement when they deal with biological effects at a few to few tens of mSv, the region of interest in radiation protection. I sent Brenner’s views to Prof Tubiana who chaired the French committee. He promised to address the issues in some reports later.

Those interested in the subject must read the following:

The regulatory agencies will stick to LNT as it is a practical model. LNT-baiters are not able to give precise threshold doses for various effects nor do they recommend any dose limits.

Modern Developments

Quibbling on radiation protection principles continues. Specialists can now measure a single Double Strand Break (DSB), an event which is likely to have profound influence in carcinogenesis. Kufner, Schwab and colleagues, researchers from Germany, demonstrated Double Strand Breaks (DSBs) of DNA in the white blood cells of patients undergoing cardiac CT and angiography examinations by sampling blood from the patients before and after the tests (European Congress of Radiology, 2009). Unparalleled technological advances in the study of cells do not in any way diminish the potential use of computed tomography or conventional angiography in clinically indicated instances.

For insights into the developments in radiation protection, one may access the interviews with Dr Roger Clarke, former Chairman, ICRP, and Dr Jack Valentin, Scientific Secretary, ICRP:
In India, newspapers started advertising CT screening of symptomless patients. The day is not far off when a tennis/cricket player or a film star in India would be endorsing and advising his/her fans to undergo CT scans.

The International Atomic Energy Agency makes pioneering efforts in popularising radiation protection. Well scripted material on all topics is available at rpop.iaea.org. Every professional involved in radiotherapy must read the IAEA Safety Report No 17 on “Lessons learnt from accidental exposures in radiotherapy”.

The safety report will help to ensure that “Mayapuri” is not repeated in radiation therapy.

(Dr K S Parthasarathy, Raja Ramanna Fellow, Department of Atomic Energy)

MOLECULAR BIOLOGY LABORATORY AT RGCI&RC

Rajiv Gandhi Cancer Institute and Research Centre (RGCI&RC) has a well equipped laboratory to offer diagnosis, monitor response to therapy and provide prognostic information. However, there was a shortfall on certain information of contemporary value required for cancer patient care.

ARA Healthcare Pvt. Ltd (ARAHC) has set up a Molecular Biology and Tissue Culture laboratory facility at RGCI&RC to provide the most advanced laboratory support in the management and care of cancer patients in the hospital.

ARAHC is a biotech research and development company established with the mission to develop biological molecules and stem cells for therapy. ARAHC aims to set-up state-of-the-art molecular diagnostic & research services and other contract research services, which include screening and development of molecules, recombinant protein development and biomarker validation. It plans to develop world class research and development facilities in the areas of Translational Medicine, Stem Cell Research, Target Validation and Herbal Medicines. Its scientific team has several years of experience and expertise in the related research fields and has strong capability to develop bio-therapeutic drugs. The company has strengths and accomplishments in the area of intellectual property management, regulatory processes and quality assurance processes.

This molecular biology laboratory set up at RGCI&RC is equipped with End Point PCR, Real Time PCR, Flowcytometry, Cytogenetic work-station, Fluorescence In-Situ Hybridization and Biobanking facility. It is also equipped with Class 100 CO2 Incubator, Biosafety cabinet level 2 laminar flow for ex-vivo studies, and facilities for development of novel primary human cancer cell lines. ARAHC will assist oncologists in understanding the molecular pathology of the disease and response to chemotherapy and designing alternative personalized therapy. It will provide in-vitro molecular assays which are sensitive, specific and accurate for diagnosis, therapy selection and monitoring of difficult cancers. Scientists at ARAHC, in collaboration with the researchers and oncologists at RGCI&RC, will carry out molecular studies of biomarkers, cancer phenotypes, signal transductions and genetic functions.
TELOMERES, TELOMERASE AND CANCER

Background

Cancer includes a diverse set of diseases which originate from almost every tissue and display a remarkable heterogeneity in presentation and prognosis. Despite immense range of clinical characteristics, all human tumors share a limited set of behaviors that define the malignant state. Among these hallmarks, unlimited replicative potential and widespread genomic disarray are among the most common characteristics exhibited by human cancer cells. Although several distinct molecular pathways regulate specific aspects of each of these phenotypes, emerging evidence now implicates the maintenance and function of the specialized chromosomal terminal structures, termed telomeres, as essential regulators of both cell life span and chromosomal integrity.

The Nobel Prize in Physiology or Medicine for the year 2009 has been awarded to three scientists - Elizabeth H. Blackburn, Carol W. Greider and Jack Szostak, who have solved a major problem in biology: how the chromosomes can be copied in a complete way during cell divisions and how they are protected against degradation. The Nobel Laureates have demonstrated that the solution lies in the ends of the chromosomes, the telomeres, and in an enzyme that forms them, ie, telomerase. By ingenious genetic experiments, they demonstrated that chromosomal termini have an evolutionarily conserved structure and function. The discovery of telomerase has deeply influenced biomedical research and led to the development of cancer therapies that are presently under evaluation.

Telomeres and Telomerase

Human telomeres are non-coding DNA-sequences at the end of chromosomes, which are composed of (TTAGGG)n hexanucleotide repeats. During each cell division, telomeric DNA (30-100 bp) is lost because of the end-replication problem. Telomeres maintain chromosomal integrity and prevent replication of defective genes. When normal cells reach a critical telomere length, they exit the cell cycle, enter into M2 (mortality stage 2) crisis and thereby undergo senescence. This mechanism is thought to be the biological clock that determines human life span.

Different cell types have different telomere dynamics. The average available telomere length in normal somatic cells is 10 kilobases (kb), their telomeres erode resulting in senescence. The average telomere length of cancer cells, however, is only 5 kb (range ~ 2-9 kb). Among cancers, it has been shown that telomere content (TC), a proxy for telomere length, has prognostic relevance. In prostate carcinomas, low TC predicts for metastasis and recurrence; in breast cancers low TC predicts for poor clinical outcome and a reduced 5-year breast cancer-free survival interval.

Telomerase is a ribonucleoprotein reverse transcriptase. It is composed of two essential subunits human telomerase RNA component (hTERC), which acts as a template for addition of new telomeric repeats, and a catalytic subunit human telomerase reverse transcriptase (hTERT). Telomerase permits cells to overcome one of the fundamental limitations to mammalian cell immortality, the progressive loss of telomeric DNA. Cell populations that continue dividing throughout life, such as germ and stem cells require the addition of new telomeres to their chromosomes to compensate for sequences lost during cell division. The latter and cancer cells, which have acquired a high proliferative potential, bypass replicative senescence by activation of the enzyme telomerase. As telomerase is reactivated, it can de novo synthesize TTAGGG hexanucleotide repeats onto shortened telomeres, thus maintaining them at stable length. Virtually, all human tumor cell lines and approximately 85% of human cancer tissues have been shown to possess telomerase activity. By contrast, normal tissues adjacent to tumor and human somatic tissues, other than stem cells, do not possess detectable levels of telomerase.

Relevance in Diagnostics

Many studies have described the use of telomerase assays and the in situ expression of hTERT as diagnostic tools. One potential use for such assays is to improve the sensitivity and specificity of detecting malignant cells in cytology specimens. Particularly in urine, pleural and peritoneal effusions and bronchial alveolar lavage, some studies have shown promise in improving sensitivity of cytologic examination. However, because some normal, differentiated cell types express telomerase, the specificity of these types of tests must be evaluated closely.

Initial surveys of human cell lines and tissue with a sensitive biochemical assay for telomerase activity

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Initial surveys of human cell lines and tissue with a sensitive biochemical assay for telomerase activity
telomere repeat amplification protocol [TRAP] demonstrated readily detectable telomerase activity in the majority of cancer cell lines and tumors. In contrast, most normal human cells lacked telomerase activity. During the early stages of cell transformation, telomere attrition suppresses malignant transformation by limiting cell life span; whereas, telomere maintenance by telomerase or alternative lengthening of telomeres in later stages of cancer development facilitates oncogenesis.

Although recent methods, demonstrating the detection of telomere length in tissue sections, will aid in determining how to best use telomerase expression in diagnosis of cancer, additional work is required to validate hTERT as a diagnostic marker. Studies that simultaneously compare histologic evaluation, telomerase activity, hTERT protein expression, and telomere length, are required to elucidate the relationships among these parameters and to define what role telomeres and telomerase play at each stage of cancer development.

**Therapeutic Target**

It is believed that targeting telomerase is a novel approach to targeted cancer therapeutics. There are three general classes of agents that have been developed to target telomerase biology. These are:

**Gene Therapy:** There are two general types of telomerase gene therapy - suicide gene therapy and oncolytic viral therapy. As a whole, the preclinical studies of telomerase gene therapy have shown a remarkable attention to specificity and efficacy using normal cells strains and an extensive array of cancer models. Ad-hTR-NTR is a telomerase-targeted adenoviral suicide gene therapy vector whose phase-I study of intraperitoneal Ad-hTR-NTR in patients with advanced inoperable intra-abdominal cancer has started in 2008. Telomerase-specific oncolytic virus utilizes adenoviruses that have been manipulated or engineered to have oncolytic or cancer killing properties, enabling them to selectively target and destroy cancer cells that express telomerase.

**Telomerase (hTERT) Immunotherapy:** Telomerase may be a promising universal tumor antigen with broad immunotherapeutic applicability to a wider range of distinct cancers. There are two general approaches that have advanced to clinical trials. One is the dendritic cell presentation approach such as the telomerase cancer vaccine GRNVAC 1 which is being developed to help extend the remission of acute myelogenous leukemia, while the other is the peptide vaccine approach e.g. GV 1001 which is a therapeutic vaccine for treatment of advanced pancreatic cancer and vaccination against hepatocellular carcinoma.

**Telomerase Template Antagonists:** These small molecular oligonucleotides target the RNA component of telomerase. GRN163L is a short chain oligonucleotide that is unique in its resistance to nuclease digestion in blood and tissues and its very high affinity and specificity for telomerase. On the basis of broad in vitro and in vivo proof of concept for efficacy of telomerase inhibition in many major cancer types tested, good safety profile and excellent pharmacokinetics and biodistribution, GRN163L has entered clinical trials in patients with refractory or relapsed chronic lymphocytic leukemia, advanced solid tumors, stage III B and IV non small cell lung cancer in combination with chemotherapy.

**Telomerase and Cancer Stem Cells**

Similar to normal stem cells, cancer stem cells also have the ability to self-renew as well as undergo differentiation to give rise to the phenotypically diverse types of cancer cells. There are emerging data that suggest that normal stem cells may have longer telomeres compared with cancer stem cells and thus there may be a window of opportunity to target cancer stem cells by inhibiting telomerase and driving telomeres short and cells into apoptotic cell death, hopefully without irreversible damage to normal stem cells.

**Conclusion**

Telomere biology is important in human cancers. Cancer cells need a mechanism to maintain telomeres if they are going to divide indefinitely, and telomerase solves this problem. It is encouraging to see that since the first demonstration of widespread telomerase activity in tumors 13 years ago, drug development has been rapid, with several clinical trials planned, in progress and completed with scope for innovative clinical trial design and application. The challenge is to intervene and exploit our increasing knowledge of telomere biology for the diagnosis and treatment of malignancies.

(Reviewed by Dr Showket Hussain, Research Associate; Dr Mausumi Bharadwaj, Assistant Director/Scientist D & Chief, Division of Molecular Genetics & Biochemistry, Institute of Cytology & Preventive Oncology (ICMR), Noida)
Diabetes and Colon Cancer

Older women with diabetes face a more than double risk for some types of colorectal cancer, according to results presented at the annual meeting of the American Gastroenterological Association. For this population based cohort study, researchers examined data from 37,695 participants of the Iowa Women’s Health Study which enrolled women in the age group of 55-69 years in 1986 and remains ongoing. Of these women, 2,361 reported a diagnosis of Type 2 diabetes and 1,200 developed colorectal cancer. They found that diabetes was strongly associated with the microsatellite instability-high, CpG island methylation-positive and BRAF gene mutation cancer subtypes in this group of older women. Diabetes appeared to confer a greater than twofold increase in risk for these molecularly-defined tumors, compared to women without diabetes. These findings may lead to new strategies for colon cancer screening, chemotherapy and chemoprevention in women with diabetes. The researchers aim to understand more about the biology of colorectal cancer and its link with diabetes.

(Reprinted from Mayo Clinic News, May 2, 2010)

Leukemia Relapse

According to the researchers at Perth’s Telethon Institute for Child Health Research, 80% of children with T-cell acute lymphoblastic leukemia (T-ALL) achieve complete remission while around 20% relapse and their prognosis can be very poor. The research team analysed bone marrow samples from children treated under the International Children’s Oncology Group (COG) protocols and identified a consistent pattern in the expression of five genes in patients that relapse. Importantly, this pattern was found to hold true across multiple patient cohorts, the first time that such a robust gene signature of this kind has been found for T-ALL.

This discovery has significant potential to improve outcomes for patients at high risk of relapse. Patients identified using these markers could potentially be treated with more aggressive therapies from the outset to give them the best hope of achieving complete remission. The prognostic potential of the gene markers identified from this research would now be investigated as a part of large COG study of T-ALL patients undergoing the latest therapy.

(Reprinted from ScienceDaily, May 12, 2010)

New ‘Microbead’ Radiotherapy

According to a study reported at the Society of Nuclear Medicine’s 57th Annual Meeting, radiomicrtrack therapy guided by molecular imaging is an emerging area of radiotherapy and has the potential to target treatments for cancer patients. This technique provides the most effective and individualized therapy with minimal complications for the patient. It involves the injection of tiny highly radioactive beads that “nestle up” with cancerous tumors and destroy them with precision. Radiomicrtrack therapy can lead to unwanted damage to healthy tissues, so technologists and physicians must work together to carefully plan each patient’s treatment using molecular imaging to ensure that the beads are going to travel and potentially destroy normal tissue and do not wander off into other areas of the body. According to the study, molecular imaging called SPECT/CT technology makes radiomicrtrack therapy a more powerful and safer tool for cancer therapy. This technology provides the essential information interventional radiologists need to then block blood vessels surrounding the targeted organ with small metal coils, effectively isolating the microbeads during therapy.

(Society of Nuclear Medicine, June 7, 2010)

Ultrasensitive PSA Test

New research from Northwestern University Feinberg School of Medicine and the University International Institute for Nanotechnology showed that an ultrasensitive prostate-specific antigen (PSA) test using nanoparticle-based technology may be able to definitively predict after surgery if the cancer is cured long term or if it will recur. It detects PSA at levels in the blood that cannot be detected by conventional tests. The new test is 300 times more sensitive than the currently available commercial tests and can detect a very low level of PSA that indicates the cancer has spread beyond the prostate. Scientists found that the low and non-rising PSA levels of patients meant that the prostate cancer was effectively cured and did not return over a period of at least 10 years. The test also may pick up cancer recurrence at a much earlier stage, when secondary treatment is most effective for a patient’s survival. These studies suggest that the nanotechnology PSA test might become the preferred postoperative PSA test for men who have been treated with radical prostatectomy. It should be especially useful in the early identification of men who would benefit from adjuvant postoperative radiation therapy and those who need postoperative salvage radiation therapy for recurrence.

(Northwestern University, June 2, 2010)
**NEW TECHNOLOGIES**

**DIAGNOSTICS**

**Innovative Imaging Techniques**

To streamline and improve medical imaging, researchers at University College London, King’s College London and Imperial College would investigate innovative medical scanning techniques concentrating on magnetic resonance imaging and computerized tomography scanning. The research team plans to create computer models of anatomy, motion and micro-structures that can be used directly with raw sensor data to extract information about disease progression or response to therapy. Clinicians could use this information to diagnose cancer and plan and monitor appropriate therapies. This could noticeably cut the time imaging takes, potentially increase the accuracy of scanning moving structures and decrease the costs of the scanning process. It would decrease the exposure to harmful radiation as imaging could be quicker and fewer images would be required to gather the same amount of information. The researchers predict that the new technology would be able to better detect a range of lethal cancers such as of lung and liver.

*(Institute of Cancer Research, May 3, 2010)*

**New Ovarian Cancer Test**

The US Food and Drug Administration has cleared Abbott’s new ARCHITECT HE4 (human epididymis protein 4) assay for ovarian cancer, the first automated diagnostic test of its kind available in the United States. It is a chemiluminescent microparticle immunoassay for the quantitative determination of HE4 antigen in human serum. The assay is designed to be used as an aid in monitoring recurrence or disease progress in patients with epithelial ovarian cancer. The current test, CA125, is most widely used for monitoring ovarian cancer. While 80% of ovarian cancers express CA125, 20% of all ovarian cancers do not. HE4 is an excellent marker for monitoring ovarian cancer patients, especially in those where CA125 is not a marker for their disease. By using Abbott’s new HE4 test in conjunction with other clinical methods, including CA125, physicians can get a more comprehensive clinical picture when monitoring ovarian cancer patients. This assay is also approved for use in Europe, Asia Pacific and Latin America.

*(Abbott Diagnostics, June 4, 2010)*

**Simple Gene Test**

A simple genetic test that uses only three genes, ie, ESR1, ERBB2 and AURKA, is among the most effective means of classifying breast cancer into subtypes for more personalized treatment, that was reported by researchers from Dana-Farber Cancer Institute in Boston at the IMPAKT Breast Cancer Conference in Brussels, Belgium. They performed the largest comparative study to date of breast cancer subtypes, analyzing 32 publicly available gene expression data sets, including more than 4600 breast cancer patients and six different classification models. They found that subtype classification model (SCM) yielded stronger concordance than single sample predictor (SSP). They observed that SCMs, including a simple model that uses only three genes, were significantly more robust than SSps. The robustness of SCMs makes them promising candidates for an implementation into the clinic, especially in the simplest form, that is, a model using only three genes.

*(European Society for Med Oncol, May 9, 2010)*

**Stool DNA Testing**

Results of pilot studies presented at Digestive Disease Week 2010, the annual meeting of the American Gastroentrological Association, demonstrated that sensitive non-invasive stool DNA test developed at Mayo Clinic may be useful for detection of premalignant dysplasia in patients with inflammatory bowel disease (IBD) and of an important type of colorectal pre-cancer called serrated polyps. Compared to widely used fecal blood tests, stool DNA testing has higher detection rates for curable stage colorectal cancer and for common pre-cancerous polyps. The first study involved identifying both cancer and a pre-cancerous lesion called dysplasia, in people who suffer from IBD. Researchers found that stool DNA testing was positive in 5 of 5 with cancer and 4 of 5 with dysplasia. Given the limitations of colonoscopies in detecting these lesions, stool DNA testing could play a complementary role to improve the effectiveness of cancer surveillance. For the 2nd study, the researchers identified mutant BRAF and methylated vimentin genes that were present in serrated polyps but not in normal colon. They observed a 71% detection rate with stool DNA testing. This was significantly higher than the 7% rate with conventional fecal blood tests. Detection of these two types of pre-cancer by stool DNA testing offers promise in efforts to more effectively and affordably prevent colorectal cancer.

*(Mayo Clinic News, May 4, 2010)*
DRUGS

Multikine

Multikine, a patented defined mixture of naturally derived cytokines, is the first immunotherapeutic agent in a new class of drugs called “Immune SIMULATORS”. They are multitargeted, simultaneously cause a direct and targeted killing of specific tumor cells, and activate the immune system to produce a stronger anti-tumor attack. It is the first immunotherapeutic agent being developed as first line standard of care treatment for cancer. It is administered prior to any other cancer therapy because that is the period when anti-tumor immune response can still be fully activated. In phase 2 clinical trial, it was shown to be safe and well tolerated and eliminated tumor in 12% of patients after only 3 weeks of treatment. This patient response preceded commencement of the current treatment regimen and followup showed an improvement in overall survival by 33% at a median of three and a half years following surgery. The US Food and Drug Administration gave the go ahead for phase 3 clinical trial and granted orphan drug status to Multikine in neoadjuvant therapy of patients having squamous cell carcinoma of head & neck.

(CEL-SCI Corporation, May 7, 2010)

Onsolis for Breakthrough Pain

Onsolis (fentanyl buccal soluble film), a new and patented product, is an oral transmucosal form of the potent opioid analgesic, fentanyl citrate, a pure opioid agonist, whose principal therapeutic action is analgesia and its unique delivery system gives rapid and reliable delivery of fentanyl. It is specially indicated for the management of breakthrough pain in patients with cancer, 18 years of age and older, who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. This product must not be used in opioid non-tolerant patients. It is supplied as film (200, 400, 600, 800, or 1200 mcg) intended for application to the buccal mucosa. The FDA approval of onsolis was based on results of a double-blind, placebo-controlled, cross over study. The primary outcome measure, the mean sum of pain intensity differences at 30 minutes for onsolis treated episodes was statistically significantly higher than for placebo-treated episodes. The New Drug Submission for onsolis has been approved by the Canadian regulatory authority, Health Canada also.

(Meda AB, May 11, 2010)

TECHNIQUES

Breast Tomosynthesis

According to the study conducted by Fornik et al from Malmo University Hospital, Malmo, Sweden, breast tomosynthesis (BT) is superior to digital mammography (DM) in the assessment of breast tumor size and stage. BT, a 3D X-ray imaging technique, is a promising mammography screening technology, in which low dose images are acquired over a limited angular range at a total dose comparable to DM. These low dose images are used to mathematically reconstruct a 3D image volume of the breast, thus reducing the problem of superimpose. Tumor size measurements can be difficult with 2D plane mammography because the breast structures are superimposed. The researchers investigated whether breast tumor size can be more accurately assessed with BT than with DM and ultrasound (US), by reducing the disturbance effect of the projected anatomy. The results showed that tumor outline could be determined in significantly more cases with BT and US than DM. BT and US size correlated well with pathology and significantly better than DM size. Accordingly, staging was significantly more accurate with BT than with DM.

(Acta Radiol, April 2010)

Revolutionary Ablative Therapy

Specialist Microwave Technology Company Acculis of England has got regulatory clearance under the European CE Mark system of its revolutionary new device for destroying unwanted tissues, such as liver tumors. The device is a single high power high frequency, 2.45 GHz, microwave needle that burns a 5 cm sphere of tissue in just 5 minutes, 3-10 times faster than old school radiofrequency based systems or lower frequency 915 MHz microwave systems. This system gives surgeons and interventionalists the ability to treat previously inoperable patients. Early data shows promising clinical outcomes for tumor control when compared to current ablative therapies, such as radiofrequency ablation and cryotherapy. This device is the latest in a series of product innovations from Acculis. Its sheer speed and power allows decisive new therapy for patients for whom there was previously little hope. The new device makes the technology available to whole interventional radiology community throughout Europe and elsewhere where CE Mark system is recognized.

(Acculis, March 2, 2009)
CLINICAL TRIALS

Acute Myeloid Leukemia

According to a multicenter trial, more individualized therapy and better supportive care helped push survival of children with acute myeloid leukemia to 71%, three years after diagnosis, which is 20% better than previously reported US rates. Researchers focused on getting maximum benefit from existing therapies and applying lesson learnt from earlier studies to identify and treat patients who faced highest risk of relapse. This study featured the first use of minimal residual disease (MRD) to guide timing and makeup of later chemotherapy and the first time all patients received antibiotics to prevent bacterial and fungal infections. Patients initially received 3 drug combination therapy, including either high or low-dose cytarabine. After first and second course of chemotherapy, investigators used genetic factors including chromosomal rearrangements & gene mutations and MRD measures to determine additional care a patient received, including whether patients were referred for a transplant to replace diseased blood producing stem cells with cells from a healthy donor. (Lancet Oncology, June 2010)

Evolution of Hyperthermia

A phase 3 randomized trial provides first evidence that regional hyperthermia (HT), using BSD-2000 hyperthermia system, added to preoperative and postoperative chemotherapy [etoposide, ifosfamide and doxorubicin (EIA)] is clinically more effective than chemotherapy alone in locally advanced soft tissue sarcoma patients who are at high risk of recurrence and disease spread. Combination of HT & EIA demonstrated improved overall survival, tumor reduction, disease-free survival and time to disease progression. Addition of regional hyperthermia to chemotherapy resulted in a significant reduction in disease progression or death with a median disease-free survival of greater than 120 months for the HT+EIA group, as compared to 75 months in the EIA only group. Local tumor progression at 2 years was 19% for the HT+EIA group, compared with 30% in the EIA only group. The addition of HT also more than doubled the proportion of patients whose tumor responded to chemotherapy. It is a significant event in the evolution of hyperthermia. (BSD Medical Corporation, April 30, 2010)

OncoVAX® for Colon Cancer

A randomized Phase 3a clinical trial for OncoVAX® for the adjuvant treatment, covering 250 stage II colon cancer patients, has been successfully completed at twelve sites in the Netherlands. OncoVAX® has been granted Special Protocol Assessment and Fast Track Status by the FDA. Vaccinogen, the producer of OncoVAX®, has selected Clinipace Worldwide, a global clinical research organization to manage global pivotal Phase 3b confirmatory clinical trial for OncoVAX® in the treatment of stage II colon cancer. OncoVAX® is an autologous immunotherapy vaccine which is administered to the patient by three weekly injections one month after surgery. A fourth “booster” is administered six months later. In a previous Phase 3 study, the vaccine reduced tumor recurrence or death due to disease progression by over 50%. The treatment has been shown to be safe and well tolerated in three randomized, multicentre studies. (Clinipace Worldwide, May 7, 2010)

Tarceva® for Non-Small Cell Lung Cancer

Roche has received approval from the European Commission for Tarceva® (erlotinib) as a monotherapy maintenance treatment in patients with advanced non-small cell lung cancer (NSCLC) whose disease remains largely unchanged after platinum-based initial chemotherapy. The European Union approval was based on data from the pivotal Phase III SATURN study, an international, placebo controlled, randomized, double-blinded study that enrolled patients with advanced NSCLC. Patients were treated with four cycles of standard first-line platinum-based chemotherapy and then randomized to Tarceva® or placebo if the cancer did not progress. The study showed that Tarceva® given as a maintenance therapy immediately after first-line chemotherapy, significantly extended overall survival and greatly improved the time people with advanced NSCLC lived without the disease getting worse. Tarceva® inhibits the tyrosine kinase activity of the epidermal growth factor receptor (EGFR) signaling pathway inside the cancer cell. OSI Pharmaceuticals, along with its partner Roche, is looking forward to advance Tarceva® life cycle program, which includes evaluating Tarceva® in the adjuvant setting and as a first-line treatment for advanced NSCLC patients with an activating EGFR mutation as well as branching into other disease settings. (OSI Pharmaceuticals, April 30, 2010)
**WATCH-OUT**

**Breakthrough 3-D Breast Ultrasound**

TechniScan Inc, USA has developed a revolutionary non-invasive imaging tool to provide an automated 3D ultrasound images of physical structures within human breast, using a process called Warm Bath Ultrasound. TechniScan Inc has announced the grant of US Patent No 7,684,846, entitled "Apparatus and Method for Imaging Objects with Wave Fields", which provides methods in creating diagnostic images from complex wavefields. The patent algorithms outlines how algorithms are translated into a high resolution, 3D ultrasound images of human breast. It also includes recursive methods for increasing speed at which images are processed and can deliver faster clinical outcomes for women awaiting breast imaging results. Images are captured using a comfortable, radiation free method as a woman lies prone on examination table and ultrasound is directed, using warm water as a coupling medium, through her breast tissue. This imaging device is limited by US law to investigational use, unless and until, cleared by the FDA. (TechniScan Inc, May 6, 2010)

**Cancer Stem Cells**

The inventors Hansford Leon M (CA) et al have been assigned Patent No US2010105574 (A1), entitled “Cancer Stem Cells and Uses Thereof” on April 29, 2010. The invention relates to preparation of stem cells, particularly cancer stem cells derived from neural crest tissue. It also relates to methods of isolating and using them in diagnostic, therapeutic and other clinical and non-clinical applications. Disclosed are enriched preparations of neuroblastoma tumor initiating cells (NB TICs). Methods are also disclosed for preparing enriched preparations of NB TICs, such as from neuroblastoma tumor tissue and metastasized bone marrow and for screening candidate substances to identify therapeutic agents for treatment of neuroblastoma. Methods are also provided for screening a sample for neuroblastoma and to identify its stage. Kits are provided for selecting appropriate anti-neuroblastoma compounds for a patient, and to utilize isolated compositions of the patients’ neuroblastoma tumor initiating cells. A customized medicinal profile for the patient may thus be devised. (www.patentlens.net, May 18, 2010)

**Head and Neck Cancer**

University of Southern California (US) has been issued Patent, No US2010099102 (A1), entitled “Development of Diagnostic Markers from the Saliva of Head and Neck Cancer Patients” on April 22, 2010. The invention relates to biomarkers useful for cancer detection, and to biomarkers and methods of using biomarkers for early detection of head and neck cancer. Microarray data shows elevation of IL-8, IL-6, VEGF, MMP-9, TGF-B, MMP-7, plasminogen activated (PA), uPA, IGF and INF-2 proteins in head and neck squamous cell carcinoma (unpublished data). To practice methods relating to the early detection of cancer, biomarker expression levels of sample biopsies from persons believed to be at risk for developing cancer are compared to the expression levels of control biopsies and advanced stage cancer biopsies. If sample biomarker expression levels are higher than normal control biomarker expression levels, but less than cancer biopsies, then cancer has been detected early.

(esp@cenet.com, May 11, 2010)

**Radiosurgery for Ocular Disorders**

United States Patent Office has assigned Patent No 7,697,663 to Oraya Therapeutics, Inc.(CA) entitled “Orthovoltage Radiotherapy” on April 13, 2010. This radiotherapy relates to treatment of ocular disorders using targeted photon energy and particularly to apparatus, systems and methods for image-guided low energy x-ray therapy of ocular structures. A radiosurgery system delivers a therapeutic dose of radiation to a target structure in a patient. In some embodiments, inflammatory ocular disorders are treated, specifically macular degeneration, and in some others, ocular structures are placed in a global coordinate system, based on ocular imaging, which leads to direction of an automated positioning system. In some others embodiments, the position of an ocular structure is tracked and related to a radiosurgery system and yetin some others, a treatment plan is utilized for a specific disease to be treated and/or structures to be avoided. In some embodiments, a fiducial aids in positioning the system. In some embodiments, a reflection of the eye is used to aid in positioning. In some embodiments, radiodynamic therapy is described in which, radiosurgery is used in combination with other treatments and can be delivered concomitant with, prior to, or following other treatments. (USPTO, May 13, 2010)
GLOBE SCAN

Most Deadly Cancer

Pancreatic cancer claims five Australian lives every day and is one of the nation’s most lethal diseases. Yet it has remained off the health radar in part, because of the grim prognosis of sufferers and no significant development in treatment. The report providing a snapshot of pancreatic cancer in Australia states that Australians have a greater chance of dying from pancreatic cancer than in a car accident. A recent report states that 2244 new cases of pancreatic cancer were diagnosed in Australia in 2006 while 2076 people died of the disease in the same year. Despite considerable research efforts into pancreatic cancer over the past decade, very little progress has been made in the treatment of this disease. Global understanding of pancreatic cancer is still equivalent to where bowel cancer was about five to ten years ago. The challenge is to find better treatments for this most deadly cancer.

(Australia: UICC Cancer News, April 2010)

Revolutionary TrueBeam™ System

The University Hospital of Zurich has become the first medical center in the world to commence treating cancer patients with the revolutionary TrueBeam™ system from Varian Medical Systems. It is a new platform for image-guided radiotherapy and radiosurgery that was designed from the ground up to treat a moving target with unprecedented speed and precision. Doctors have delivered treatments for prostate and lung cancer, as well as schwannomas, brain and spinal metastases. This system gives dose distributions that are slightly superior to Intensity Modulated Radiotherapy from a conventional system, with lower doses to surrounding healthy tissues. At the highest dose delivery rate available on the system, it took just over 1.6 minutes to deliver treatments that would require 6-8 minutes at conventional dose delivery rates. In addition, these treatments took advantage of system’s ability to deliver RapidArc treatments from a flexible range of angles to maximize the dose to targeted tumor and avoid important nearby critical structures.

(Switzerland: Varian Med Systems, April 20, 2010)

New Quick Screening Exam

A five-minute, one-off screening test could prevent thousands of people dying from bowel cancer every year. Screening with flexible sigmoidoscopy (named the Flexi-Scope Test) works by detecting and removing growths on the bowel wall, known as polyps, which can become cancerous, if left untreated. The new 16-year study led by Imperial College London showed that a single Flexi-Scope test in men and women aged between 55 and 64 reduced the incidence of bowel cancer by a third compared with a control group which had usual care. Over the course of the study, bowel cancer mortality was reduced by 43 percent in the group that had the Flexi-Scope test compared with the control group. The study showed for the first time that incidence of bowel cancer and the number of people dying from the disease, by using this one-off test, could be dramatically reduced. According to the researchers, no other bowel cancer screening technique has ever been shown to prevent the disease. In addition to saving lives, a screening programme using Flexi-Scope could also reduce the costs associated with treating people with bowel cancer. Cancer Research UK is calling on its government to add the test to the existing national bowel screening programme, as one of its first priority.

(UK: ScienceDaily, April 29, 2010)

Provenge for Prostate Cancer

Provenge (sipuleucel-T), an autologous cellular immunotherapy, the first of its kind, manufactured by Dendreon Corp. has been approved by the US Food and Drug Administration for the treatment of certain men with advanced prostate cancer, who currently have limited effective therapies available. It is indicated for treatment of asymptomatic or minimally symptomatic prostate cancer that has spread to other parts of body and is resistant to standard hormone treatment. Effectiveness of provenge was studied in 512 patients with metastatic hormone treatment refractory prostate cancer in a randomized, double-blind, placebo controlled multicentre trial, which showed an increase in overall survival of 4.1 months. Provenge is designed to stimulate a patient’s own immune system to respond against the cancer. It is manufactured by obtaining a patient’s immune cells from the blood, using leukapheresis. To enhance their response against cancer, immune cells are exposed to specific proteins found in prostate cancer, linked to an immune stimulating substance. The patient’s own cells are then returned to the patient to treat the prostate cancer. Provenge is administered intravenously in a three dose schedule given at about two-week interval.

(USA: US FDA News, April 30, 2010)
**Introduction**

Physiotherapy is a branch of modern science which provides therapeutic services where movement and functioning of the body are threatened by aging, injury, disease or environmental factors. It aims to optimize the patient’s level of physical function and takes into consideration the interplay between the physical, psychological, social and vocational domains of function. Physicians like Hippocrates and Hector are believed to have been the first practitioners of primitive Physical Therapy advocating hydrotherapy and manipulations to treat people in 460 BC. The earliest documented origin of actual physical therapy as a professional group dates back to 1894 when four healthcare professionals in Great Britain formed the Chartered Society of Physiotherapy. Over the years, physiotherapy has gained vast acceptance in healthcare.

**Role of Physiotherapy**

Physiotherapy has a key role in the management of patients throughout the cancer journey, from diagnosis to the end stages of the disease. The aim of the physiotherapist working with cancer patients is to minimize some of the effects which the disease or its treatment has on them. It is often possible to improve their quality of life regardless of their prognosis by helping them to achieve maximum functional ability and independence or gain relief from distressing symptoms. Physiotherapists conduct ongoing assessment of the needs of the patient and the caregivers in order to apply skilled interventions which are vital for patient’s independence, functional capacity and quality of life.

Restorative services are provided to cancer patients in all stages of treatments, as these may have lasting effects on physical and cognitive functions resulting in impaired functional ability. Clinically effective therapeutic modules are tailored and implemented to take quality care of special needs of cancer patients. A few conditions are listed below.

**Lymphedema Programmes**

Patients who undergo breast or pelvic surgeries with lymphnode removal are given an overview of lymphedema prevention. In this programme proper positioning, precautions and life style modifications are advised along with the standard exercise regimen. These measures help in collateral channel formation and thereby promote lymphatic drainage. In already established lymphedema cases assessment is done for treatment planning. The treatment depends on the grade, and may include compression garment, self lymphatic drainage, manual lymphatic drainage along with skin care, precautions and life style modifications.

**Head & Neck Cancer**

The common challenges faced after surgery or radiation in head and neck cancer patients are: (i) Dysfunction of stomatognathic system—mucositis dysphagia, trismus, xerostomia, muscle imbalance, pain etc. which further leads to generalised weakness and fatigue; (ii) Impaired neck movements leading to muscular pains, postural changes etc; and (iii) Shoulder joint dysfunction which affects activities of daily living. The aim is to achieve optimum mobility with minimum residual dysfunction. The effective therapeutic tools in the above mentioned cases may include Laser, Transcutaneous Electrical Nerve Stimulation (TENS), Cryotherapy, strengthening and stretching etc. along with postural strategies.

**Neurological and Musculoskeletal Cancers**

In musculoskeletal tumor cases, post surgery/radiation patients need training to alleviate muscular imbalance, sensory deficits, gait deviations etc. With advancement in skills and technology, limb sparing surgeries are preferred over amputation, which need extensive physical therapy. Physiotherapy ranging from use of electrotherapy modalities to retrain/reeducate a muscle and nerve via TENS to strengthen and proprioception training is given. Enhancing endurance and gait training helps further in achieving optimum balance and independence. Primary tumors of brain, spinal cord or peripheral nerve involvement may lead to physical disability as well as balance and coordination dysfunction. Specific exercise programmes to regain balance and coordination along with motivation and encouragement may yield miraculous results. In patients who are subjected to amputation of upper/lower limbs at various levels, physiotherapy and gait training are vital in hastening the patients recovery and return to normal life and occupation.

**Cardio-Respiratory Care**

Major concerns in intensive care unit and post operation unit etc are reduced lung volumes; retention of
secretion; increased work of breathing; poor breathing pattern; ineffective cough; pain etc. Physical therapy along with the medical treatment proves to be very effective. The techniques used vary from percussion, postural drainage, airway clearance techniques, manual hyperinflation, etc. Sputum clearance techniques add to patient’s comfort in such cases. Post surgery, such patients require extensive physical therapy before resuming normal daily routine. The aim of the intervention is to achieve cardiovascular fitness, shoulder and chest wall movement restoration, enhanced strength and endurance to regain functional mobility.

**Bone Marrow Transplant/High Dose Chemotherapy**

These treatments may cause muscle and nerve damage, balance and coordination disorders, cardiopulmonary compromise and general deconditioning. Specific exercises are tailored according to individual needs, keeping in view the other health related issues. The psychological support, motivation and encouragement combined with exercises gives optimum outcomes.

**Pain Management**

Pain may surface as tumor may be compressing the nerve/muscle or secondary to cancer treatment. Physical modalities like cold packs, TENS, exercises or myofascial release techniques can help to relieve the pain.

**Palliative/Supportive Care**

The stage where cancer cannot be cured or patient is in terminal stage, then the pain relieving modalities, general exercises, proper joint positioning, chest clearance techniques etc. may prove beneficial for patient’s comfort.

**Rehabilitation Aids**

Various prosthetic and orthotic devices are made available like spinal supports (cervical collar, Taylor’s brace), walking aids etc.

**Holistic Wellness Programme**

Taking care of the patient’s physical, emotional, social and vocational needs by counseling about their limitations guiding them about alternatives and solutions. The programme actually ‘bridges the gap’ between being a patient and returning to usual or new activity.

**Services in RGCI&RC**

Physiotherapy Department at Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC) has the latest equipments which are indicated in the conditions mentioned in the Table.

<table>
<thead>
<tr>
<th>Services</th>
<th>Indications</th>
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<tbody>
<tr>
<td>Lymphapress Unit</td>
<td>Lymphedema - arm &amp; leg</td>
</tr>
<tr>
<td>Cryotherapy Unit</td>
<td>Cellulitis, acute lymphedema</td>
</tr>
<tr>
<td>Electrotherapy Unit</td>
<td>Pain relief, muscle strengthening</td>
</tr>
<tr>
<td>Transcutaneous</td>
<td>Pain relief, muscle strengthening</td>
</tr>
<tr>
<td>Stimulation (TENS)</td>
<td>Neuromuscular reduction</td>
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<tr>
<td>Electric and Muscle Stimulator</td>
<td>Chest physiotherapy</td>
</tr>
<tr>
<td>Laser</td>
<td>Nerve &amp; muscle reduction, mucositis, tendinitis, etc.</td>
</tr>
<tr>
<td>Breast Prosthesis Unit</td>
<td>As per patient’s requirement</td>
</tr>
</tbody>
</table>

**Lymphapress Unit:** An electronic, pneumatic pump which causes sequential lymphatic drainage. It creates controlled pressure in different segments of a sleeve which is applied to lymphedemous arm/leg. It assists in increasing return of blood, excess fluid, improves venous stasis and encourages absorption of waste products.

**Cryotherapy Unit:** It is also called ‘Cold Compression Unit’ and has analgesic, anti-inflammatory and muscle relaxing effects.

**Electrotherapy Unit:** The unit offers low and medium frequency current forms which are indicated in a variety of conditions.

**TENS:** It works on ‘pain-gate’ mechanism primarily to relieve pain.

**Electronic Nerve & Muscle Stimulator:** The equipment can provide interrupted galvanic and surge faradic currents useful in neuromuscular re-education.

**Electronic Precursor:** The frequency of the device is tuned to mobilize deep seated secretions in chest wall.

**Laser (Light Amplification Stimulated Emission of Radiation):** Low power diode laser delivers specific dosage of radiation energy to the affected tissues.

**Breast Prosthesis Unit:** Breast prosthesis and surgical braces of various sizes are made available as per patient’s requirement.

**Conclusion**

In addition to providing individualized programmes to help cancer patients recover from their illness, it provides psychological support as well. Physiotherapists often work very closely with their patients and develop a bond with them, which gives them hope, encouragement and strength. Physiotherapy plays a vital role in their recovery.

(Dr Vandana Bhardwaj, Sr Physiotherapist, Dept of Physiotherapy; Reviewed by Dr Akshay Tiwari, Assoc Consultant; Dept of Surgical Oncology)
**TOBACCO EPIDEMIC - FILE FACTS**

Tobacco use is one of the biggest public health hazards the world has ever faced and is the most widespread addiction in the world.

1. There are nearly 1.3 billion smokers in the world, 80% of them are in the developing countries.

2. India has more than 300 million smokers, more than 5 million child smokers, with 55000 children taking up tobacco use every year. The global rates of smoking among men have peaked while rates among women are rising.

3. Women are a major target for the tobacco industry, which needs to recruit new users to replace smokers who will die prematurely (almost 50 percent of current users) from tobacco-related diseases. Data from 151 countries show that about 7 percent of adolescent girls smoke cigarettes as opposed to 12 percent of adolescent boys. In some countries, almost as many girls smoke as boys.

4. Tobacco use kills 5.4 million people a year - an average of one person every six seconds - and accounts for one in 10 adult deaths worldwide. Tobacco killed 100 million people in the 20th century. If current trends continue, there would be up to one billion deaths in the 21st century. Unchecked, tobacco-related deaths will increase to more than eight million a year by 2020, and 80% of those deaths will occur in the developing world. In India, total number of tobacco related deaths are likely to be between 800,000 to 900,000 per year. There is ‘one’ tobacco related death every eight seconds, four million unnecessary deaths per year, 11,000 every day. About half of the teenagers who use tobacco will eventually be killed by it (about a quarter in middle age and a quarter in old age). It is estimated that India as compared to any other country will have the fastest rise in tobacco related deaths each year.

5. In India, beedi smoking is the most popular form of tobacco smoking (54%), followed by cigarette smoking (16%); while tobacco chewing accounts for 30% of the total consumption. Paan with tobacco is the major chewing form of tobacco. Dry tobacco, areca nut preparations such as paan masala, gutka, khaini and mawa are also popular and highly addictive.

6. In India tobacco contributes to 56.4% and 44.9% of cancers in men and women, respectively. Smokers/tobacco consumers are 2 to 3 times more likely to develop heart disease and paralysis than non-smokers.

7. Smoking/tobacco consumption is a cause of impotence in men and decreases estrogen levels in women. Menopause occurs earlier, decreases ability of physical activity and decreases physical endurance.

8. Pregnant women, who smoke, have a greater chance of losing the baby, or having a baby with a low birth weight, or babies with developmental problems, or sudden infant deaths (sudden unexplained cot deaths). It has also been found that smoking/tobacco consumption increases the risk of diabetes and lowers the good cholesterol in the blood.

9. Smoking/tobacco suddenly raises the blood pressure and reduces the blood flow to the heart. It also decreases the flow of blood to the feet and can cause gangrene of the legs. Smoking causes health problems for children and other family members (due to second hand smoke). It has also been found that smoking/tobacco consumption increases the risk of diabetes and lowers the good cholesterol in the blood.

10. A non-smoker living with two packs per day smoker, smokes passively equivalent of three cigarettes per day according to urine nicotine levels.

Knowing file facts of tobacco epidemic - Are you prepared to quit tobacco just now and for ever???

(Reviewed by Dr A K Dewan, Sr Consultant, Department of Surgical Oncology)