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From the desk of the editor

Prof. Dr.Arun Chougule

I happy to bring out the AFOMP newsletter issue and present before you. Looking to the challenging and multidimensional profession of medical physics, which has potential to contribute to every aspect of healthcare and shape the future of healthcare, this issue of the newsletter focuses on the non-traditional roles of medical physics. The article by Dr. K. Murlidhar titled "The future of Physics in Medicine and its Role in Genomics" covers the role of genomics in cancer management. The article titled "Physics of Cancer" by Prof. Arun Chougule focuses on the application of physics for the diagnosis of cancer. The article by Dr. Nand Relan titled "Hybrid Imaging Technology– Application of Positron Imaging Tomography-Magnetic Resonance Imaging [PET-MRI] in the Cinical Management of Lymphoma" speaks about molecular imaging. I hope the readers of the newsletter will appreciate the efforts of Editorial Board for thinking out of box.

Further I take this opportunity to request the office bearers of the NMOs of AFOMP to be proactive to make the national medical physicist organization in their respective country to be more vibrant for propagating knowledge, and improving the status of medical physicist and the profession. As you know, this year's IDMP theme is "Medical Physics: Providing a Holistic Approach to Women Patients and Women Staff Safety in Radiation Medicine ". Kindly celebrate IDMP in various parts of your country to make the presence of medical physicists felt and showcase the contribution of medical physics to healthcare.

Looking forward to see you all in Jaipur for AOCMP-AMPICON 2017 meeting during 4th-7th November 2017.(www.aocmp-ampicon2017.org)

With good wishes to all

Prof. Arun Chougule
Editor, AFOMP Newsletter
Vice President, AFOMP

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WELCOME TO PINK CITY JAIPUR

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In conjunction with
38th Annual Conference of Association of Medical Physicists of India "AMPICON - 2017"

4th - 7th November 2017
Jaipur, India

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Hybrid Imaging Technology: Application of Positron Emission Tomography - Magnetic Resonance Imaging (PET-MRI) in the Clinical Management of Lymphoma

Nand K Relan, PhD and Robert Matthews, MD
Department of Radiology
Stony Brook University Medical Center, Stony Brook, NY

Lymphomas are a heterogeneous group of neoplasms originating from the transformation of lymphocytes during various stages of lymphocyte ontogeny. There are more than 50 distinct types of lymphomas with a variety of different pathophysiology, clinical history, prognosis, and treatment. The World Health Organization (WHO) broadly classifies lymphomas as mature B-cell neoplasms, Hodgkin's lymphoma, mature T-cell neoplasms, and post-transplantation lymphoproliferative disorders. The most common types of lymphoma are diffuse large B-cell lymphoma and follicular lymphoma accounting for half of all cases (1).

Initial diagnosis of lymphoma depends on pathological evaluation of tissue specimen usually involving surgical resection of a lymph node because a large sample is needed for morphologic, immunophenotypic, and cytogenetic analysis. After confirming the pathology by biopsy, initial staging of lymphoma comprises clinical examination, various laboratory studies, bone marrow biopsy, computed tomography (CT), and fluorodeoxyglucose (FDG) positron emission tomography (PET) (2). Other than staging purposes, FDG PET imaging may be used in the early stage of diagnosis in order to distinguish indolent lymphomas from aggressive lymphomas using the standardized uptake value (SUV). The SUV can guide appropriate biopsy site based on the metabolic activity, and determine if transformation of indolent lymphoma to a more malignant form has occurred. PET imaging alone is not sufficient. An abnormal PET scan with areas of increased FDG uptake still necessitates a biopsy for confirmation (3).

Until two decades ago imaging techniques routinely used in the detection of different types of cancers were CT scans and MRI giving structural information used in radiology and single photon emission computer tomography (SPECT) and PET imaging giving functional detail used in nuclear medicine as stand-alone techniques. Soon thereafter in the late 1990's, advances in the computer technology led to the development of fusion software. This allowed the reader to superimpose images from two different modalities providing structural with functional imaging. In applying this to clinical applications, the fusion software gave the interpreting physician increased lesion detection rate accompanied with an increased level of confidence in the image interpretation (4). Eventually in early 2000s this fusion software led to hardware development of the first hybrid camera where structural imaging using CT scanner and functional study using PET scanner merged into PET-CT camera with a single machine for clinical imaging (5).

Like the previous fusion software, the hybrid technology of PET-CT gave a greater ability and confidence in the detection of cancer superior to fusion software alone. In addition, the CT component provided attenuation correction allowing for better images resolution and quantification of data such as standardized uptake value (SUV) used in FDG imaging. Combined PET-CT camera provided an even higher sensitivity and specificity than fusion software alone and allowed target specific radiotracers to be used according to pathology being studied with CT providing anatomical or structural information. The combination of PET and CT can provide an early diagnosis of occult cancer, stage the spread of cancer, monitor treatment response, and detect tumor recurrence (6). But this development came with a price of increased radiation dose to the patients with radiation dose from the radiotracer used in PET imaging as well as radiation from CT. The radiation from the CT is often two or three times the radiation from the radiotracer. In particular, the radiation dose is excessive in pediatric patient population and for adults who need multiple scans for staging and restaging cancer during their treatment of cancer (7).

In 2010s a new hybrid camera PET-MRI was introduced for the use of clinical oncology and neurology applications. CT in the hybrid imaging was replaced with a MRI scanner. The development of PET-MRI systems has triggered a great awareness of the full capabilities of hybrid imaging and that provides an entirely different set of challenges when compared to PET -CT. Siemens Medical Systems was the first to develop the simultaneous PET-MRI machine that was considered a major advancement in pre-clinical and clinical imaging. Authors of this article acquired Siemens' PET-MRI called Biograph mMR at their institution (8).

Siemens Biograph mMR consists of a PET ring detector that fits in 3T magnet of MRI and is housed in one device as an integral unit. This is a whole body integrated PET-MRI scanner, acquires simultaneous PET-MRI scans which reduces imaging time as well as less radiation dose to the patients. Siemens used unique PET block detector architecture that included integrated cooling features to provide optimal PET performance and a specialized shielding to eliminate magnetic field interference in the PET data acquisition. The photomultiplier tubes (PMT) used in the transfer of data from the crystal detector into a computerized signal consisted of a newly developed PMT that silicon based avalanche photo-diodes (APD) (9).

Biograph mMR has the limitation of attenuation correction since conventional transmission scan as used in CT is not possible. Therefore, derivation of attenuation data from MRI is different and is not correlated with material density as measured on CT. MRI data cannot be linearly transferred to CT and MR based attenuation correction provides a biased

information in comparison to CT based attenuation. This uses a sophisticated approach of attenuation correction ATLAS based approach where dedicated MRI sequences generate rich signals and predict a pseudo CT patterns called “μ-maps” used for attenuation correction (10).

Compared to CT, MRI has more sensitive detection and better characterization of lesions of soft tissue as well as marrow infiltrating osseous lesions. MRI is excellent at evaluating abnormalities of the brain. It is superior to CT in looking at abdominal organs including liver, biliary tract, kidneys, spleen, and pancreas (11). It also provides excellent soft tissue contrast within the organs of the pelvis such as the prostate gland, uterus, and rectum. MRI can detect many musculoskeletal pathology including metastatic lesions. What MRI is less useful in evaluating is lung metastases and certain osseous lesions (12).

The most common imaging finding of lymphoma is lymphadenopathy. Lymph node evaluation is determined by short and long axis dimensions, morphology including the presence of a fatty hilum and bean shaped lymph node, number of lymph nodes, location, enhancement following intravenous contrast, and FDG activity (13). Abnormal lymph nodes may be a single lymph node, multiple scattered lymph nodes, clusters and conglomerates, and large bulky masses. The lymph nodes may be surrounded by adipose tissue or may involve neighboring organs including soft tissue and bone. Both PET-CT and PET-MRI are useful for imaging single and multiple metastatic lymph nodes. PET-CT is favorable to determine cortical bone destruction, while PET-MRI would better characterize soft tissue involvement (14) (Figure 1).

Although CT is superior to MRI in the evaluation of lung nodules and metastatic disease, primary lymphoma of the lungs is rare. Pulmonary involvement of lymphoma has been reported to be as high as 24% of non-Hodgkin’s lymphoma cases and 38% of Hodgkin's lymphoma cases, although these high numbers are not routinely seen in the clinical setting. When there is lymphoma involvement of the lungs, it is usually easily detected by both FDG PET-CT and PET-MRI (15). More subtle cases of ground glass opacities and interlobular septal thickening indicating lymphoma cannot be detected by MRI, but this represents a mild version of tumor involvement with more extensive disease elsewhere.

Lymphoma of the spleen is more readily detected by MRI than CT imaging. Lymphomatous lesions have mild T2 hyperintense signal and T1 mildly hypointense to hyperintense signal on MRI. They may be single, multiple, small or large. The lesions are typically hypovascular and therefore do not enhance. There is accompanied intense FDG activity within the splenic lesions on PET imaging. Splenomegaly is common with lymphoma patients, but is

neither specific nor sensitive for tumor involvement. Microscopic diffuse lymphoma involvement of the spleen is more difficult to detect on both FDG PET-CT and PET-MRI (16).

Lymphoma of the gastrointestinal tract including the stomach and small intestines can often be overlooked or confused with physiological uptake on PET imaging if the reader is not attentive to the clinical history. Lymphoma of the gastrointestinal tract is usually part of mucosa associated lymphoid tissue (MALT) lymphoma, an uncommon form of non-Hodgkin's lymphoma (17). On MRI lymphomatous involvement of stomach and small intestines is more easily detected since MRI shows better depiction of the gastric and intestinal wall layers. Tumor extension from peritoneal lymph nodes into the intestines can also be easily seen by PET-MRI.

Lymphoma uncommonly involves the skeletal system. Primary lymphoma has a variable appearance on PET-MRI. It may be sclerotic, lytic or have a mixed appearance with the sclerotic appearance most commonly developing after chemotherapy or radiation therapy. FDG uptake is usually intense in lymphoma involvement of the bone. Compared to CT, MRI better delineated osseous lesions (18). With more advanced cases of lymphoma, bone marrow involvement can occur. This may be focal or diffuse in appearance and typically requires a bone marrow biopsy for diagnosis. Increased FDG uptake is usually seen on PET imaging, but its finding is not specific for marrow involvement. PET-MRI better detects lymphomatous infiltration of the bone marrow compared to PET-CT demonstrating low T1 weighted signal and mildly hypointense to hyperintense signal on T2 weighted images (19) (Figure 2).

Hybrid imaging technology consisting of PET-MRI is an excellent diagnostic tool that uses low radiation and provides more sensitive detection and better characterization of lesions of soft tissue in comparison to PET-CT. However, the role of PET-MRI still needs to be defined for all types of lymphomas.

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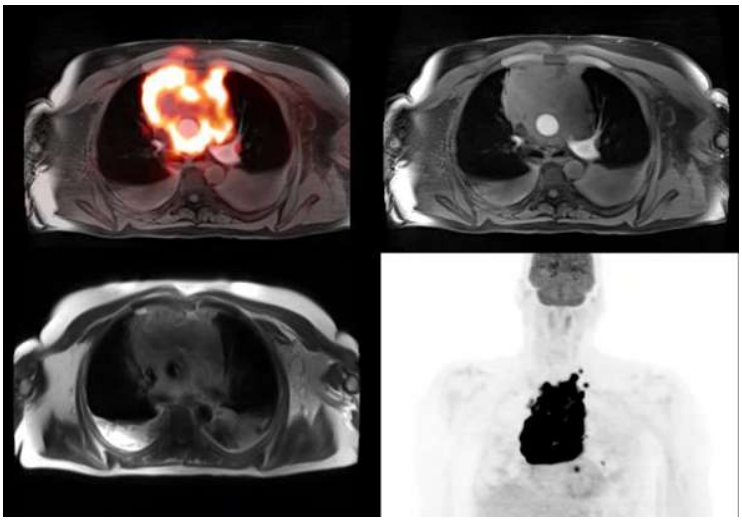


Figure:1

Figure 1. 51 year old male with newly diagnosed diffuse large B-cell lymphoma and left vocal cord paralysis. PET-MRI demonstrates a large hyper metabolic mass in the anterior mediastinum encasing the great vessels (top left). The mass is iso intense on T1 radial VIBE (top right) and hyper intense on T2 weighted images (bottom left). PET MIP image shows the large mass with multiple small lymph nodes and lung nodules in the chest (bottom right).

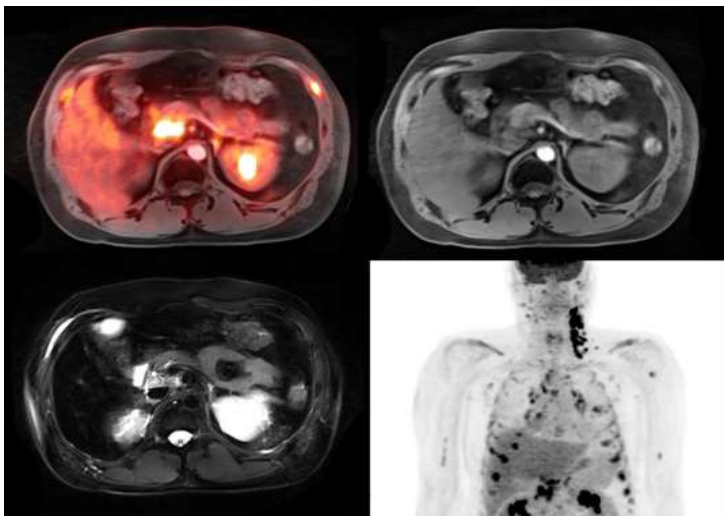


Figure:2

Figure 2. 48 year old male with recurrent T-cell lymphoma. PET-MRI demonstrates a small cluster of hyper metabolic lymph nodes in the precaval region of the upper abdomen (top left). The lymph nodes are mildly hypo intense on T1 radial VIBE (top right) and hyper intense on T2 blade with fat suppression (bottom left). PET MIP image shows multiple hyper metabolic left neck lymph nodes in addition to the upper abdominal lymph nodes. There is bone marrow involvement that is best seen within the ribs (bottom right).

The Future of Physics in Medicine and its Role in Genomics.

Dr K R Muralidhar, Chief Medical Physicist and RSO.

American Oncology Institute, Hyderabad, India

It is a wonderful and nature that our genes help us for various purposes. For this we need to find how we can alter the gene activity in a positive direction. The aim of this study is to know how to make our genes help us with integrated teams of physicists, cancer biologists, mathematicians and engineers.

Introduction New genetic technologies have transformed health care especially on the practice of medicine in cancer therapy. The current existing imaging technology is limited from 0.1 mm to 10 mm range which has its own drawbacks. Whereas genomic study is in the micro meter to picometer range which can give us enough data for diagnosis and treatment. Today, it is well-known that DNA is the molecule containing our genetic code. Genome is made up of DNA and with special proteins. The genome is found within an organelle called the nucleus.

The genome is packaged into structures called "chromosomes." There are 23 pairs of chromosomes. Each chromosome is a length of DNA coiled up tightly to create structures called "chromatin loops." When we look closer at these loops, we can see that DNA is wrapped around proteins known as histones to form structures called nucleosomes. DNA itself is a double helix, like a twisted ladder. It is made up of four letters, or bases, called adenine, cytosine, guanine, and thymine-- A, C, G, and T. A always pairs with T, and C always pairs with G. The order or sequence of these letters of DNA carry the instructions for how a cell behaves and functions. Specific sections of the DNA, called genes, carry the instructions for producing molecules. Like other emergent phenomena, cancer cannot be readily understood by merely characterizing all its components. Developing a fundamental understanding of cancer that recognizes and embraces the great heterogeneity of tumors and their emergent properties may benefit from integrated teams of physicists, cancer biologists, mathematicians and engineers.

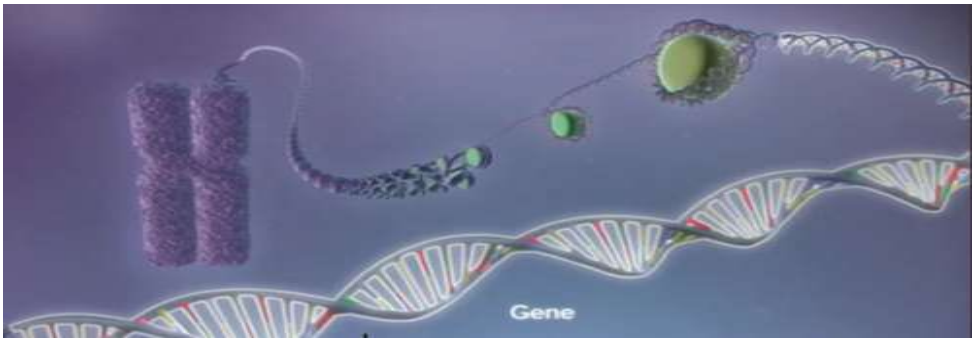


Figure : Gene (Courtesy to University of Bath)

Materials and Methods: (Physics in Genomics)

Structure of DNA: X-ray diffraction was a tool that allowed scientists to determine the structure of DNA by Franklin in Cambridge. The double helix structure of DNA was probably the most important biological work of the last century and it forms the basis for the evolving field of genetics and genomics got noble prize for this invention in 1962.

Translate in to Treatment: Large-scale cancer genomics, proteomics and RNA-sequencing efforts are currently mapping in fine detail the genetic and biochemical alterations that occur in cancer. However, it is becoming clear that it is difficult to integrate and interpret these data and to translate them into treatments. This difficulty is compounded by the recognition that cancer cells evolve, and that initiation, progression and metastasis are influenced by a wide variety of factors. To help tackle this challenge physics should work with oncology centers to bring together physicists, cancer biologists, chemists, mathematicians and engineers

Physics in Chemotherapy: Max Delbrück, a physicist, was one of the pioneers of molecular genet-ics. In collaboration with the biologist Salvador Luria, he showed that phage resistance in a population of bacteria is caused by random mutations. The equa-tions they developed to model this process are still used to predict how cancers gradually become resistant to chemotherapy. Treatments have also been influenced by the physi-cal sciences. Chemotherapy began in chemistry labo-ratories, in which chemists sought to develop new dye molecules.

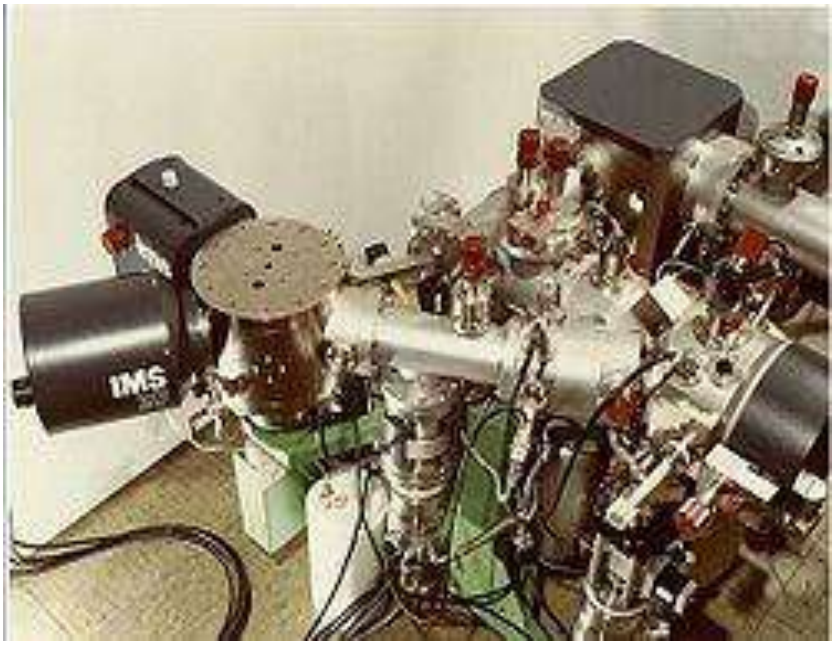
Monte carlo Method: This new vista of cancer in all its heterogeneity and complexity suggests additional ways in which the physical sciences can assist cancer researchers and clinicians. Entire scientific fields, such as the study of superconductivity and the fractional quantum hall effect, are devoted to understanding the unexpected things that can happen when large numbers of simple pieces interact. It is very difficult, or it may even be impossible, to predict the aggregate behavior of these systems even if all the laws that are relevant to each constituent are known. Ultimately, physical scientists were forced to invent a completely new set of theoretical and computational tools, such as the Monte-Carlo method, to explore and to simulate systems with many coupled degrees of freedom.

Cancer mechanics or Mechanobiology: The connections between tissue mechanics, cancer progression and patient outcomes are established. Much of what we know about the role of mechanics in biological function (and dysfunction) comes from studies of organ development and the investigation of clinical specimens with new tools such as magnetic resonance electrography. Tensile forces within developing organs are master regulators of cell sorting and packing, thereby specifying overall tissue architecture

Cancer evolution: Viewing neoplasms as a result of evolutionary forces operating on tissues within multicellular organisms provides physicists, mathematicians and population geneticists with an opportunity to use their tools to describe the evolution and ecology of cancer cells with mathematical constructs. Such theoretical modelling, together with the principles of evolutionary biology, has been successfully used to study the mechanisms and dynamics of tumor initiation and progression.

Information coding and decoding: Complex systems represent major areas of study for physical scientists. Fundamental insights from areas such as thermodynamics, fluid and classical mechanics, in combination with advanced computational visualization and simulation, could potentially aid in understanding cancer. Genomic instability is a fundamental characteristic of cancer, inherently variable between patients even with nominally the same disease and during cancer progression within the same patient

Transport and delivery in cancer: To verify or disprove the Transport Onco Physics approach, several concurrent, novel investigational modalities and tools are required, which are based on mathematics and the physical sciences: a multiscale mathematical theory of mass and momentum transport through the body; multiscale imaging that enables the tracking of mass transport in living organisms, with integrated resolution from subcellular to full body levels; and multiscale probes, in conjunction with imaging techniques, to determine the transport properties at various levels. Once the physical laws of transport are determined, their parameters for individual lesions can be obtained from direct observation through suitable imaging techniques.



Information to support the scope of research work in physics in biology

1. Every cell in our body is talking to many other cells via genetic messages.
2. 90% of the genetic information in our body is bacterial. Our ancestors were microbes and they are in many ways still present in the structure our cells.
3. Only four letters are dectacting the total life in the universe.
4. Genes are having backup copies.
5. Genes can be switched on and off by

epigenes.

6. Microbiomes are 90% of our body cells.

Challenges:

We have 3.2 billion bytes of information in one cell. Is it possible to read them? Can we get some treatment solution through physics in biology? Are we going in positive direction ?

Personalized treatments:

Most recently, the availabil-ity of fairly inexpensive high-throughput sequencing is making it possible to contemplate highly personalized cancer therapies, in which patients are treated with drug regimens that are specifically tailored to their disease.

In addition to laying the foundation for new, personal-ized treatments, these large-scale sequencing efforts have also helped scientists to delineate the enormous com-plexity of the disease and the degree to which signaling, drug resistance and genomic alterations vary from patient to patient and even within one patient.

Conclusion:

The physical laws and principles that define the behavior of matter are essential for developing an understanding of the initiation and progression of cancer at all length scales. In reality our body is not constant so the problems. The physics aspects can reach a size of atom level. Even microbes are in size more than atoms. Hence there is every chance that we can reach microbe or protein level to control cancer in gene level. Therapeutics to the core of a tumor, as well as its distant metastases, will all benefit from an application of physical science approaches to oncology; from mechanics to evolution, chemistry and nanotechnology. Thus, the successful integration of approaches from mathematics, physics and engineering with cancer biology may be our best hope to understand complex systems of cancer and to develop effective strategies for a cure.

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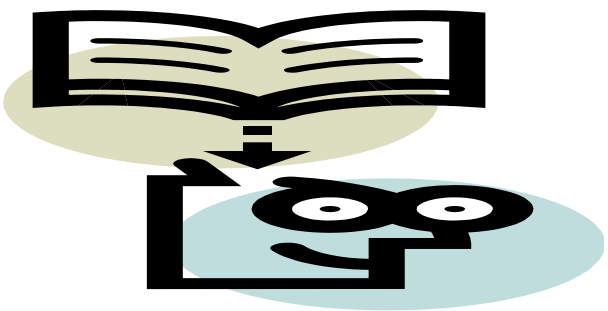
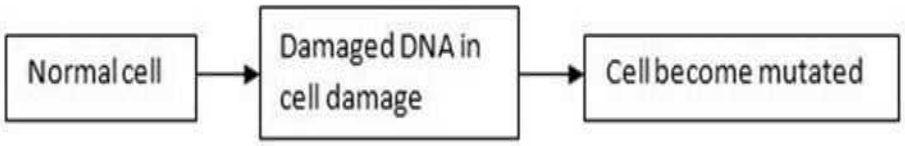


Physics of Cancer

Prof. Arun Chougule , Ms. Gomati
Department of Radiological Physics
S.M.S. medical college & Hospitals, JAIPUR, INDIA
arunchougule11@gmail.com

Cancer is not a new disease and is as old as human civilisation however the incidence of cancer is increasing rapidly. **Hippocrates [400BC]** reported to have distinguished benign from malignant growths. He introduced the term "**karkinos**", from which the word "carcinoma" is derived. Cancer is a complex family of diseases, and carcinogenesis – the turning of a normal cell into a cancer cell – is a complex multi-step process.



1.1 Cancer cells are different to normal cells in various ways.

1. Cancer cells don't stop growing and dividing

Cancer cells don't stop growing and dividing when there are enough of them. So the cells keep doubling, forming a lump (tumour) that grows in size. Cancers of blood cells (leukaemia) don't form tumours but they make many abnormal blood cells build up in the blood.

2. Cancer cells ignore signals from other cells

Cells send chemical signals to each other all the time. Normal cells obey signals that tell them when they have reached their limit and will cause damage if they grow any further. But something in cancer cells overrides the normal signalling system.

3. Cancer cells don't stick together

Cancer cells can lose the molecules on their surface that keep normal cells in the right place. So they can become detached from their neighbours

4. Cancer cells don't specialise

Cancer cells are not mature, they are not able to work properly. And because they are dividing more quickly than usual, there's a higher chance that they will pick up more mistakes in their genes. This can make them become even more immature, so that they divide and grow even more quickly and haphazardly.

5.Cancer cells don't repair themselves or die

In Cancer cell, the molecules that decide whether a cell should repair itself are faulty. For example, a protein called p53 normally checks to see if the genes can be repaired or if the cell should die. But many cancers have a faulty version of p53, so they don't repair themselves properly.

6.Cancer cells look different

Under a microscope cancer cells may look very different from normal cells. The cells are often very different sizes and some may be larger than normal while others are smaller. Cancer cells are often abnormally shaped and the control centre of the cell (the nucleus) may have an abnormal appearance.

2.1 Biopsy

For confirmation of malignancy and cancer typing based on tissue, tissue biopsy is the gold standard. A biopsy is the removal of tissue from suspicious area in order to examine it for disease. The tissue samples can be taken from any part of the body. Biopsies are performed in several different ways. Some biopsies involve removing a small amount of tissue with a needle while others involve surgically removing an entire lump, or nodule, that is suspicious. Often, the tissue is removed by placing a needle through the skin (percutaneous) to the area of abnormality. Biopsies can be safely performed with imaging guidance such as ultrasound, x-ray, computed tomography (CT), or magnetic resonance imaging (MRI). These types of imaging are used to determine exactly where to place the needle and perform the biopsy.

2.2 Limitations of biopsy

Due to the invasive procedure and many times difficult to reach the tumour site because of critical organs around it turns to be risky. Further the procedure of biopsy diagnosis takes time and is not instantaneous. In some cases, the amount of tissue obtained from a needle biopsy may not be sufficient and the biopsy may have to be repeated. This may be particularly true with trying to make a diagnosis of lymphoma.

Rarely, less invasive breast biopsy procedures may be unable to detect some lesions or determine the extent of disease present. If the diagnosis remains uncertain after a technically successful procedure, surgical biopsy will usually be necessary.

Any imaging-guided procedure will not be able to be used unless the area of abnormality can be seen. Some lesions, such as clustered calcifications on mammography are not as clearly shown with ultrasound as they are with mammography. Therefore, stereotactic biopsy is usually used in breast imaging to biopsy calcifications. Fluoroscopy sometimes will not be able

to locate chest nodules, and CT will be used for guidance. And all such invasive approaches carry the risk of infection or other complications for the patient

2.3 Liquid biopsy:

To overcome these difficulties NCI (National Cancer Institute) developed the **tracking cancer -liquid Biopsy**.[1]

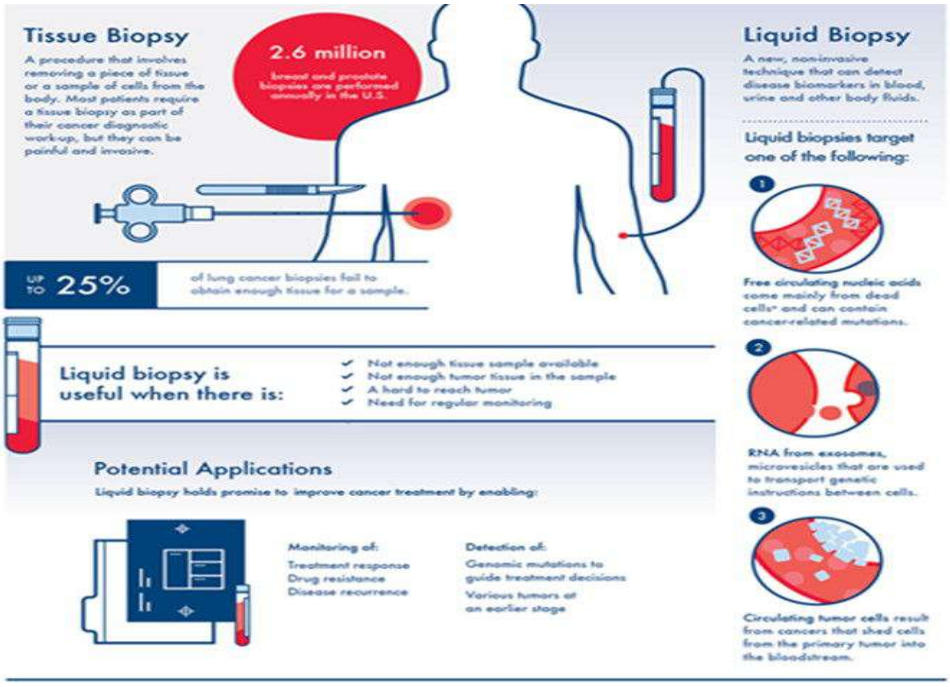


Figure:1- Solid and Liquid biopsy procedure

3.1 Physical properties of the tissue

Over the past two decades, however, the field has begun to appreciate that an important part of this cancer growth involves changes in the *mechanical* phenotype .The cell and tissue, as reflected both in intrinsic changes in cell and tissue structure and mechanics and in the bi-ophysical properties of the cell's microenvironment, such as the mechanics, geometry, and to-pology of the Extracellular Matrix (ECM).

The interplay between the biophysical properties of the cell and ECM establishes a dynamic, mechanical reciprocity between the cell and the ECM in which the cell's ability to exert contractile stresses against the extracellular environment balances the elastic resistance of the ECM to that deformation (i.e., ECM rigidity or elasticity) [2]. It has now become clear that this force balance can regulate a surprisingly wide range of cellular properties that are all critical to tumourogenesis, including structure, motility, proliferation, and differentiation might be use to detect cancer .

3.2 Characterizing the mechanical phenotype

- **Stress**
- **Strain**
- **Elasticity (Young's Modulus)**
- **Viscoelasticity**

* **Mechanical stress** is the force applied per unit area to an object (e.g., a cell), and strain is that object's deformation normalized by its initial size. Thus, mechanical stress is expressed in units of force/area (e.g., N/m2 or Pascals (Pa)).Strain is a dimensionless quantity.
* The mechanical properties associated with the ability of a material to internally store mechanical energy and is therefore independent of the rate of deformation Pascals (Pa)
* The Young's Modulus offers a way to quantify mechanical differences between tissues, and indeed the measured bulk elasticity of human tissues span some five orders of magnitude. e.g., fat (17 Pa), mammary gland (160 Pa), brain (260–490kPa), liver (640 Pa), kidney (2.5 kPa), skeletal muscle (50 kPa), cartilage (950 kPa)

  Critical to capture both the elastic, or "storage" properties and the viscous, or "loss" properties.
* Viscoelastic materials and the aggregate viscous and elastic response of a material to mechanical deformation
* **Interstitial forces** Tumour cell involves its ability to withstand nonspecific mechanical forces that arise from the growth of the tumour itself, tissue homeostasis, and transport in the lymphatic system and bloodstream. Even before the initiation of invasion and metastasis, tumour expansion compresses the surrounding ECM, which in turn constricts flow in the vasculature, lymphatic system, and interstitial space. Compression forces can also shrink the interstitial space surrounding the ductal structures, which can in turn concentrate growth factors and cytokines to facilitate autocrine and paracrine signalling and promote tumour growth. Tumour-associated changes in interstitial pressure and compressive stress also present significant challenges for drug delivery to solid tumours. These pressures may be compounded by tumour-induced stromal stiffening, which forces the tumour to exert even higher stresses to expand than would be needed in normal tissue. [3]
* **Shear forces** If a tumour cell successfully escapes the confines of its primary tissue of presentation and arrives at the vasculature or lymphatic system en route to metastasis, it must deal with an entirely new set of mechanical forces, in particular those associated with fluid flow and shear .Even if the primary tumour is successfully excised, surgical

manipulations such as irrigation and suction may subject tumour cells to substantial shear forces or altered patterns of flow .Exposure to shear can activate specific signalling pathways in tumour cells that can in turn induce dramatic reorganization of the cytoskeleton and adhesive machinery and ultimately facilitate reinforcement of cell structure and attachment to the vascular wall.

4. <u>The location of metastatic sites</u>

4.1 Tumor invades into the bloodstream and develops metastasis at new location

If cells break away from such a tumour, they can travel through the blood stream or the lymph system to other areas of the body and establish new tumours. They continue to grow in new locations. The spread of a tumour to a new site is called metastasis.

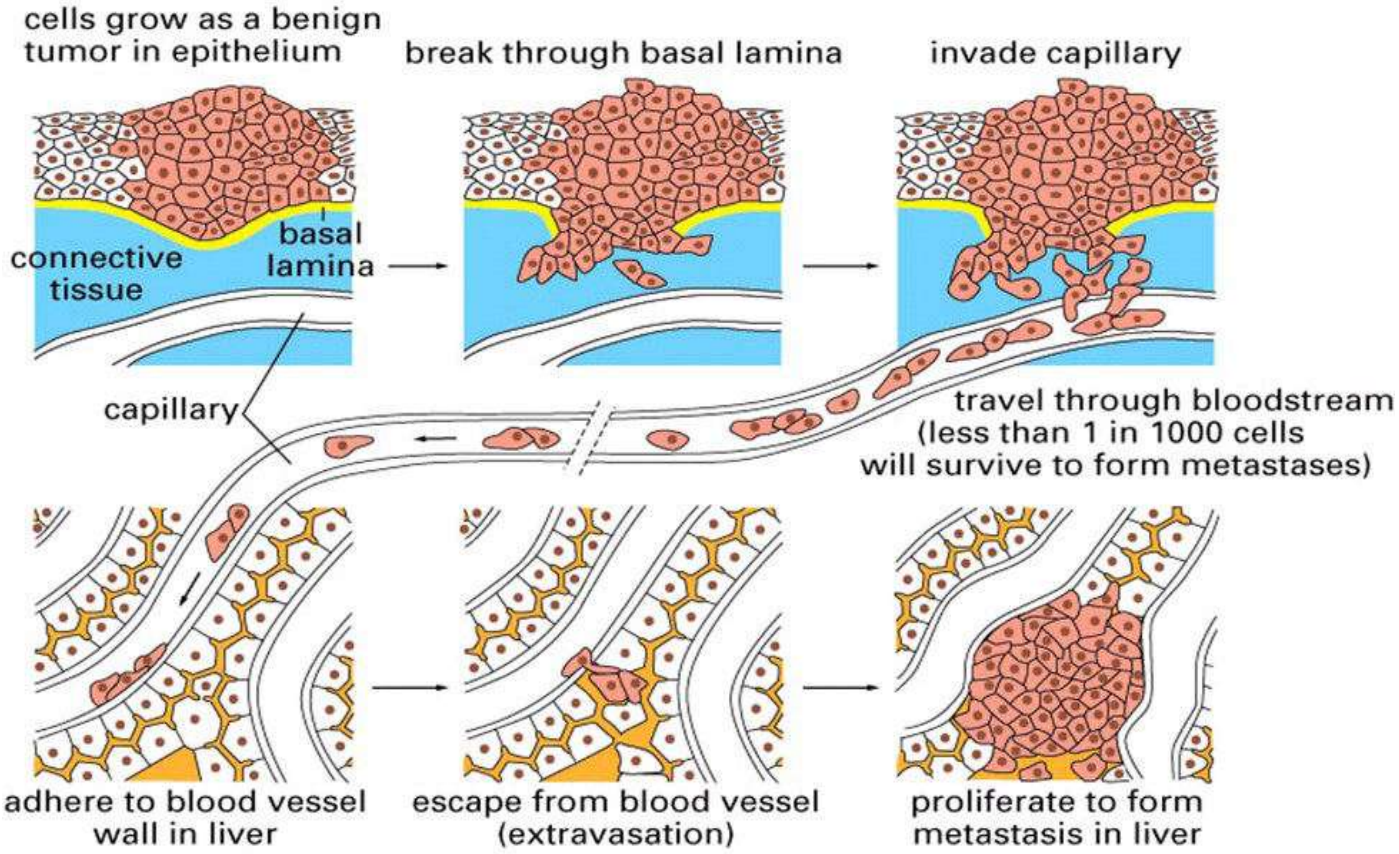


Fig: 2- Showing the tumour Invasion

4.2 The organ capillary bed are characterized by a network of small blood vessels.

- If a tumour cell encounters a capillary of diameter smaller than the size of the cell dcell > dvessel then the probability of cell trapping by physical occlusion at that site is very high.
- For a metastasis to occur, the tumour cell must still extravagate and colonize the local tissue.

- Every collision between a circulating tumour cell and a blood vessel wall, where dcell < dvessel, has the potential to result in adhesion.

5. Imaging modalities available

(diagnosis, staging and treatment of human cancers)

⇒ X-ray - plain film and fluoroscopy

⇒ Computed tomography [CT])

⇒ Ultrasound (US)

⇒ Magnetic resonance imaging (MRI)

⇒ Single-photon emission computed tomography (SPECT)

⇒ Positron emission tomography (PET)

⇒ Optical imaging

Out of these, only four (CT, MRI, SPECT, and PET) are capable of three-dimensional (3-D) detection of cancer anywhere in the human body.

MODALITY	TYPICAL VOXEL/PIXEL DIMENSION	MAX NO OF CELLS PER VOXEL/ PIXEL	LIMITATIONS
US	1micro L (1x1x1mm)	10^6	Micro bubbles remain intravascular in most tissue
CT	1micro L (1x1x1mm)	10^6	requirement for molar concentrations precludes targeted imaging
MRI	1micro L (1x1x1mm)	10^6	would require >10^7 gb^{3+} atoms per cell for detectability
SPECT	1.7cm^3 (12x12x12mm)	1.7x10^9	on average approximation 0.01 radio atoms per cell
PET	0.5cm^3 (8x8x8mm)	5x10^8	on average approximately 0.01 radio atoms per cell
OPTICAL (2D)	0.01mm^2 (0.1x0.1mm)	10^3	surface only NIR fluorescence requires approximately 10^4-10^5 fluorophores per cell for detectability
OPTICAL (3D)	1cm^3(1x1x1cm)	10^9	NIR tomography based requires approximately 10^4-10^5 fluorophores per cell for detectability

Table: 1- Sensitivity and resolution of cancer cell imaging modalities

5.1 Vibrational spectroscopy

One of the big advantages of vibrational spectroscopy, especially IR, is that it is not limited to a particular state of the sample. Spectra can be obtained from liquids, solids (pellets, powders, films, tissues), slurries and suspensions. In principle, Raman has an intrinsic advantage over IR for liquid biological samples, due mostly to the weak scattering of water [4]. To that effect, a significant proportion of IR applications to-date have concentrated on the in-vitro studies of

tissues and cells, whereas in Raman spectroscopy the big push is toward the in-vivo diagnostics.

5.1.1 Raman spectroscopy

Raman spectroscopy is a scattering technique. It is based on Raman Effect, i.e., frequency of a small fraction of scattered radiation is different from frequency of monochromatic incident radiation. It is based on the inelastic scattering of incident radiation through its interaction with vibrating molecules. It probes the molecular vibrations. [5]

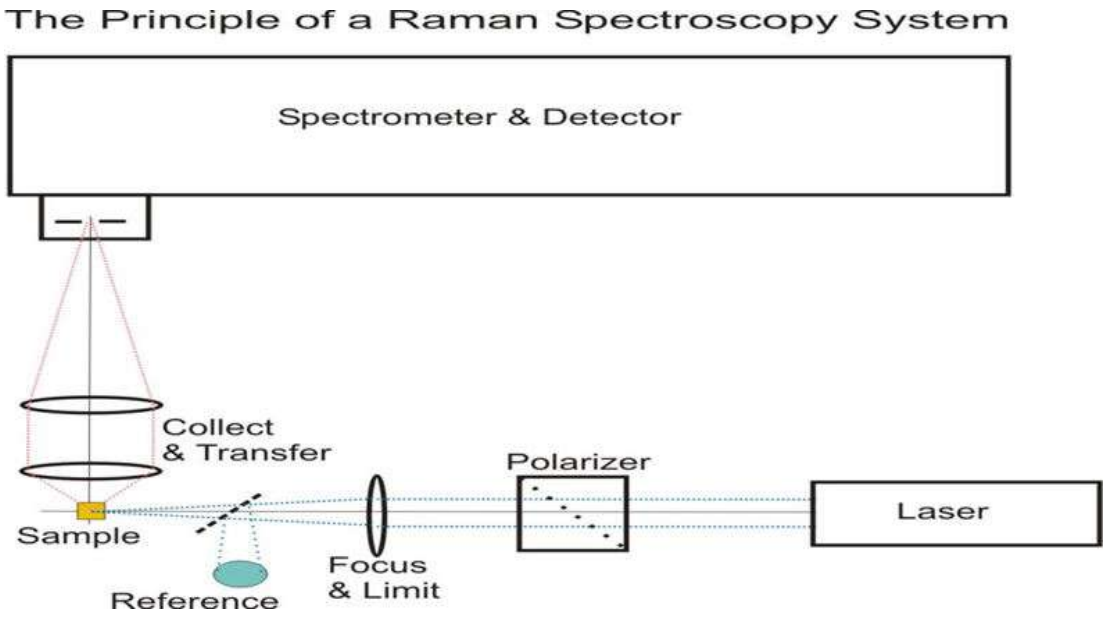


Fig. 3 – Schematic diagram of Raman spectroscopy

Raman spectroscopy can measure both morphological and chemical information in samples and multivariate classification models can be developed to provide objective diagnosis of independent tissue samples obtained from new patients. Raman spectroscopy techniques rely on established optical technologies and offer cost-effective approaches when compared to conventional medical imaging techniques, such as MRI, CT or ultrasound.

5.2 PET (Positron emission tomography)

Positron emission tomography (**PET**) is a nuclear medicine, functional imaging technique that is used to observe metabolic processes in the body. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer-fludeoxyglucose (FDG), which is introduced into the body on a biologically active molecule. Use of this tracer to explore the possibility of cancer metastasis (i.e., spreading to other sites) is the most common type of PET scan in standard medical care (90% of current scans). However, although on a

minority basis, many other radioactive tracers are used in PET to image the tissue concentration of other types of molecules of interest. One of the **disadvantages of PET scanners is their operating cost.**

PET-CT is the fusion of functional and anatomic information acquired almost simultaneously that lets us see the body and disease in a way that is diagnostically very powerful. By combing the structural anatomic information with functional data, we are able to visualize form and function. An understanding of the normal and benign as well as the pitfalls and artifacts is essential to accurate interpretation

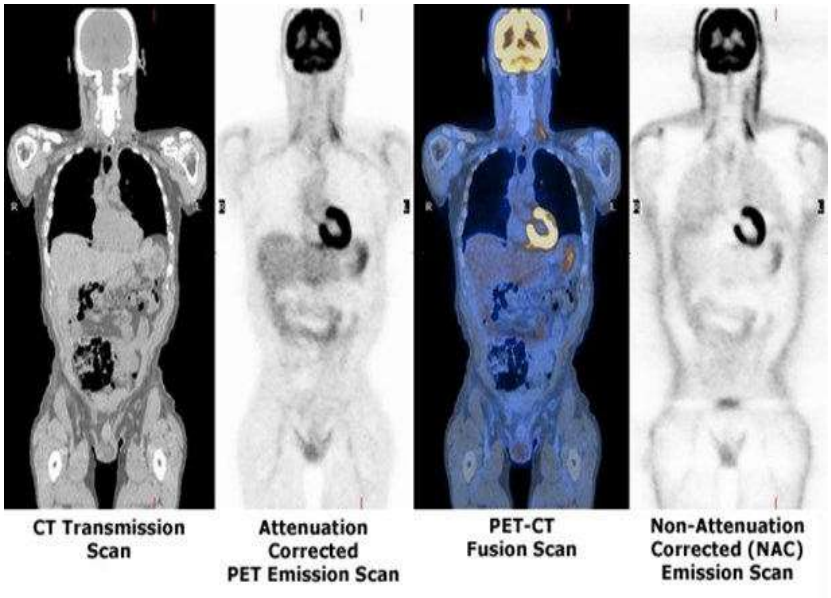


Fig. 4 PET- CT images

The majority of patients still need to undergo an invasive biopsy in order to make and/or to confirm the diagnosis in vitro. Observations regarding the response of glioma cells to substrate stiffness change the increased local stiffness might contribute to increased tension, motility, and proliferation of the tumour cells. Imaging tests can find large groups of cancer cells, but no imaging test can show a single cancer cell. Sometimes Imaging tests can show something that looks like cancer.

6. Future prospects: Towards molecular mechanisms

6.1 Theranostic nanoparticles:

The last two decades various nano particles (NPs) have been described and few of them have been suggested for their use in nanodiagnostics and/or nanotherapeutics. Recently, there is a growing interest for **theranostic NPs**, which combine therapy and diagnosis in a single bio-

compatible and biodegradable nanosystem. However, none of the so far described nanosystems are incorporated in clinical practice, except for iron oxide NPs (IONPs), particularly due to the lack of reproducibility, suitable bio distribution and pharmacokinetics

Several NPs have been successfully combined with **imaging modalities**, because of their beneficial properties as fluorescent probes (controllable emission wavelengths, sharp emission profiles, robust signal strength and the use of a single excitation source) and their potential for fictionalization with peptides, antibodies and various drugs such as chemotherapeutics. Most studies suggest that NPs systems based on passive targeting of tumour sites, can be more effective for targeting solid, primary tumours with fairly large size (at least 2mm) and well developed vasculatory system. However, early stage primary tumours and micro-metastases do not demand robust blood supply and are not detectable via passive targeting. Therefore, tumour-specific detection via active targeting is still a challenge of great significance. The combination of the existing imaging technology with theranostic NPs, gives a great advantage for high resolution in vivo cancer imaging, drug monitoring and drug delivery in a specific mode of action. So far, FDA has approved 35 imaging or/ and therapeutic NPs for clinical trials among them, IONPs, gold nanocages and nanoshells, biodegraded polymeric NPs, silica and silica-gold NPs. However, the incorporation of NPs in molecular imaging still needs a lot of progress since such nanomaterials are characterized by pharmacokinetic properties that cannot be easily controlled.

6.2 Genomics

Genomics is the study of the sequence of these letters in your DNA and how each string of letters passes information to help each cell in your body work properly. In **cancer** cells, small changes in the genetic letters can change what a **genomic** word or sentence means. Over the past decade, large-scale research projects have begun to survey and catalogue the genomic changes associated with a number of types of cancer. These efforts have revealed unexpected genetic similarities across different types of tumours. **[6]**

Genomics is an interdisciplinary field of science focusing on genomes. A genome is a complete set of DNA within a single cell of an organism, and as such genomics is a branch of molecular biology concerned with the structure, function, evolution, and mapping of genomes.

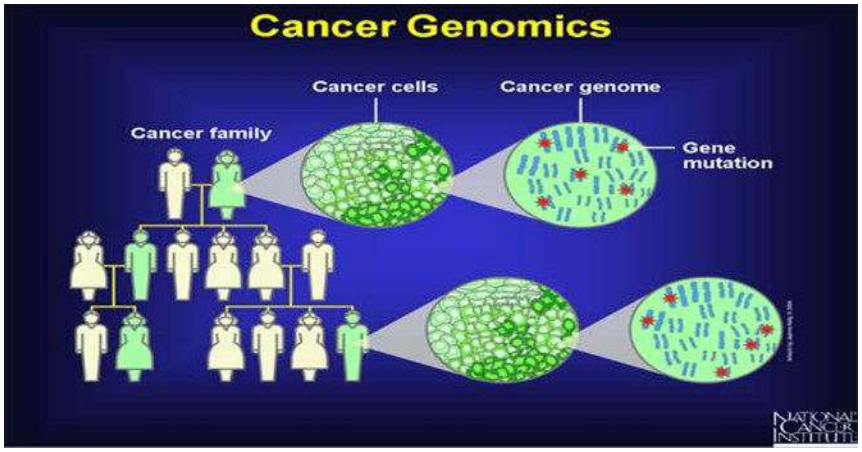


Fig. 5- Cancer Genomics

6.3 Radiomics

Radiomics is a field of medical study that aims to extract large amount of quantitative features from medical images using data-characterisation algorithms. These features, termed radiomic features, have the potential to uncover disease characteristics that fail to be appreciated by the naked eye. The hypothesis of radiomics is that the distinctive imaging features between disease forms may be useful for predicting prognosis and therapeutic response for various conditions, thus providing valuable information for personalised therapy. Radiomics emerged from the medical field of oncology and is the most advanced in applications within that field.

In the same way that genomics describes the characterization of tumour phenotype using a wide and diverse array of genetic alterations (copy number, gene expression, methylation etc.), the term 'radiomics' refers to the characterization of tumour phenotypes based on a diverse array of image-derived, quantitative measurements (shape, morphology, intensity histogram, texture etc.). The image analysis tools used in radiomics build on those developed over the past decades for tasks such as computer-aided diagnosis of lung nodules and breast lesion. [7]

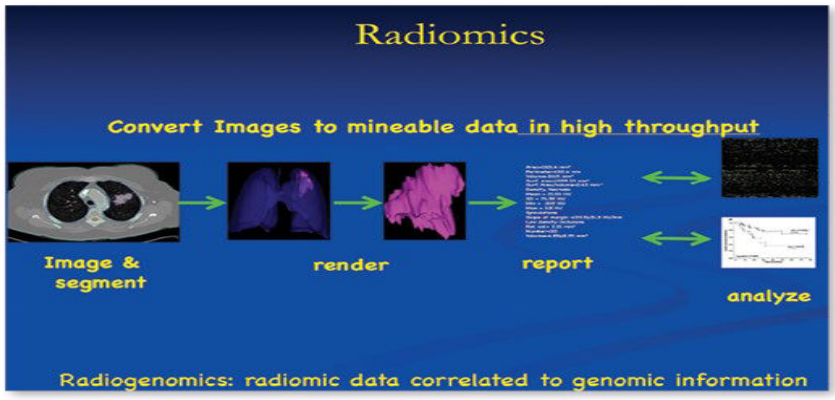


Fig. 6 – Radio-genomics

Solid cancers are spatially and temporally heterogeneous. This limits the use of invasive biopsy based molecular assays but gives huge potential for medical imaging, which has the ability to capture intra-tumoural heterogeneity in a non-invasive way. During the past decades, medical imaging innovations with new hardware, new imaging agents and standardised protocols, allows the field to move towards quantitative imaging. Therefore, also the development of automated and reproducible analysis methodologies to extract more information from image-based features is a requirement. Radiomics – the high-throughput extraction of large amounts of image features from radiographic images – addresses this problem and is one of the approaches that hold great promises but need further validation in multi-centric settings and in the laboratory.

7. Conclusion

One of the central challenges in understanding the role of the mechanical phenotype in cancer is elucidation of the molecular mechanisms that enable tumour cells to modulate their mechanical responses and phenotype and their ability to sense and actively direct the biophysical properties of the ECM. This problem is particularly daunting because it requires facility with **cell biology, biophysics, materials science, and imaging**. It also requires a willingness to integrate new knowledge about mechanics and mechanobiology into our existing understanding of the molecular and cellular biology of cancer. The field has made tremendous strides over the past decade towards identifying key molecules and signalling pathways relevant to cellular mechanobiology in cancer.

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Report from IOMP-AFOMP travel Awardee on ICMP-2016, Bangkok

Matrika Adhikari, Nepal

It was great pleasure to receive the IOMP-AFOMP travel award of $500 and additional $400(arranged by IOMP President) to participate the "International conference on Medical Physics" 9-12 Dec. 2016, Bangkok, Thailand.

I would like to express my sincere gratitude to the Nepalese Association of Medical Physicist (NAMP), IOMP and AFOMP for selecting me for the award. My special thanks goes to IOMP president Prof. Dr. Slavik Tabakov, Dr. Howell Round and Prof. Anchali Krisanachinda for the support they provided me to make my participation possible in the conference. The effort and initiation made by IOMP to support the Medical physicist from developing world is appreciable indeed.

I had two papers accepted for presentation in the conference. The first was "Errors in Radiotherapy: Experiences and issues in Nepal" which was presented in 10th Dec. and another was "Status of Medical Physics Service and Professional Development in Nepal" which was presented on 11th Dec.

It was great honor to represent Nepal on the prestigious International forum and present scientific paper in it. It was great platform to share experience and learn various aspects of Medical Physics such as Dosimetry, Radiotherapy Planning, Radiation Protection, Brachytherapy and new development in this field from the Medical Physics experts and various companies as well.

I expect to share the knowledge, technology, innovations learned in this field amongst the Medical Physics professionals, Oncologist and radiotherapy technologists in my country and apply it to improve the radiotherapy of Cancer patient, improve the Radiotherapy facilities, educate the students and professionals etc.

Similarly I was impressed to know the activities conducted by various national, international and regional organizations such as IOMP, IAEA, AFOMP, SEAFOMP, EFOMP, IUPAP, IPEM, MEFOMP, TCEB, JSRT etc for the betterment of Medical physics profession and professionals.

And last but not the least I was very much delighted to be familiar with the Thai Culture, society, magnificent places and Buddha stupas in Bangkok.

Report of the International Symposium on "Physical, Biological and Clinical aspects of Hypofractionated Radiotherapy"

Prof Arun Chougule

The International Symposium on "Physical, Biological and Clinical aspects of Hypofractionated Radiotherapy" was hosted and organized by the Department of Radiological Physics, SMS Medical College & hospital, Jaipur in collaboration with the Rajasthan university of Health sciences (RUHS), Jaipur on April 2nd, 2017. This international symposium was jointly the part of the 70th year celebration of the SMS Medical College, Jaipur. The aim of organizing this international symposium was to simulate knowledge and to promote hypofractionated radiotherapy. The main aim was to promote the interdisciplinary research. Around 200 participants including doctors, scientists, faculty, residents, research students and graduate students had attended the symposium.

The program started with a inaugural function which was presided over by honored guests Dr. Digamber Singh, Vice Chairman, 20 Point Programme, Government of Rajasthan and our guest of honor and special international guest speaker Prof Carlo Greco, Director, Champalimaud Foundation, Lisbon, Portugal. He elaborated the role of SBRT in management of oligometastatic disease. He has also explained about his institutional experience with ultra high-dose single fractionation. He briefly discussed about the various trails and clinical practice in the institute. He also motivated the participants to practice hypofractionated radiotherapy with emphasizing on robust quality assurance prior to treatment. Both the talks by Prof. Carlo Greco were of significant interest by the participants and very much appreciated by the chairpersons in the end. Invited talks by Dr. D. N. Sharma, Professor, Department of Radiation Oncology, AIIMS, Delhi described about the importance and challenges in SBRT in Gynecological malignancies. In the end of his talk, he emphasized on the advantages of SBRT. According to him the use of hypofractionated radiotherapy effective, efficient and reliable treatment option with more patient throughput. Dr. J. K. Bhagat, Head, Department of Nuclear Medicine, Bhagawan Mahaveer Cancer Hospital & Research Center, Jaipur talked about the potential role of the molecular imaging in cancer diagnosis, planning and treatment. He stressed upon the importance of the molecular imaging in countering and treatment planning decisions in radiotherapy. Other speaker Dr. V. Subramani, Head, Department of Medical Physics, AIIMS, New Delhi who discussed about the clinical implementation of 4D ultrasound-based image-guided SBRT with VMAT. He also touched upon the recent advances and developments in field of hypofractionated radiotherapy.

All the sessions were quite interactive and the participants were involved in the presentations which was obvious from the level of questions asked by them. The symposium was concluded by a valedictory session. In the valedictory function, Prof. Arun Chougule, Chairman Organizing Committee, thanked all the participants for attending the symposium. The session came to a conclusion with feedbacks from the participants. One of the participants Prof. N. K. Lohiya, Sr. Professor, University of Rajasthan, Jaipur expressed his thanks the organizers for successfully organizing the symposium with a great success. Participants were grateful to all the speakers. There was a special thanks to our guest of honor Prof. Carlo Greco who shared his experiences.

Glimpses

Report of International Conference on Medical Physics (ICMP 2016), Bangkok, Thailand

Gourav Kumar Jain, India, AFOMP Travel Award 2016

It was a great experience for me attending the "International Conference on Medical Physics" (ICMP 2016) along with 16th Asia Oceania Congress of Medical Physics (AOCMP) & 14th South East Asia Congress of Medical Physics (SEACOMP) themed "Medical Physics Propelling Global Health" organised by Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand under the auspices of International Organisation for Medical Physics (IOMP) and International Union of Pure and Applied Physics (IUPAP) during December 9-12, 2016 held at Shangri La Hotel, Bangkok, Thailand.

The conference's stellar scientific program well comprised of a number of educational and scientific sessions. It was indeed a true platform for the participants where eminent speakers from all around the world shared their knowledge and wisdom in the diverse field of diagnostic radiology, nuclear medicine and radiotherapy. About 500 delegates attended the conference and certainly benefitted from a well organised scientific sessions in form of several educational mini symposia, invited talks, oral and poster sessions. I am one of them who really benefitted from attending the ICMP 2016.

It was a great international scientific platform for me to gain knowledge and sharing my research work in form of two oral talks which were delivered during the ICMP 2016. The title of my first presentations was "Measurement of eye lens doses received by occupational staff for various cardiac interventional procedures" in interventional radiology session on December 11, 2016 which focused on the various aspects of machine parameters and assessment of eye lens doses of occupational staff performing/involved in cardiology procedures. The title of my second presentations was "A comprehensive intercomparison study of thermoluminescent and optically stimulated dosimeters for in vivo dosimetry" in clinical dosimetry session on December 12, 2016. During this talk, the dosimetric characteristics of thermoluminiscent and optically stimulated dosimeters were discussed broadly with their clinical implication in radiotherapy. Both the presentations were followed by questions and answers and well appreciated by the chair of scientific session. Overall, it was a great opportunity for me to enhance my professional and research skills by gaining knowledge through several highly informative and educational mini symposia organised during ICMP 2016 and sharing outcomes of my studies and knowledge to others by research work.

I have learnt about the various aspects of radiation protection, radiation dosimetry, diagnostic imaging, treatment planning, quality assurance, radiobiology and heavy ion therapy

in scientific sessions during ICMP 2016. A mini symposium of IOMP Grand Lecture on "Pioneering, Development and Future of e-Learning in Medical Physics" provided information about online available e-Learning material in Medical Physics like EMERALD and EMITEL. I communicated the information to my colleagues and other professionals to access these online e-learning materials and asked them to provide contribution to refine and expand content of this e-learning material. I continue to contribute to advanced cancer research and treatment to deliver best cancer diagnosis and treatment in my country in better and upgraded manner what I learnt in John Cameron Memorial Lecture, clinical dosimetry, treatment planning and diagnostic radiology sessions. A variety of activities designed to ensure the safe use of both ionising and non ionising radiation for a wide variety of applications in medicine during the sessions on radiation protection and IOMP Schools in ICMP 2016. It added knowledge to use the medical equipment in justified and optimized way with proper safety precautions to patient and occupational workers during its use. A healthy interaction with invited guest speakers and delegates during the ICMP 2016 helped me a lot to enhance my analytical approach towards my research aptitude and implementing ideas. Certainly, attending the ICMP 2016 helped me to enhance my academic, teaching and professional skills. I transfer the gained knowledge and skills through my academics to students, professionals and service of patients in the country. In addition to scientific programme the trade exhibition was of much help for me to know recent developments and availability of various dosimetry, QA and treatment equipment/ accessories. I learned a lot by visiting the trade stalls and interacting with the product specialists about various radiation related gadgets available for dosimetry, diagnosis and treatment.

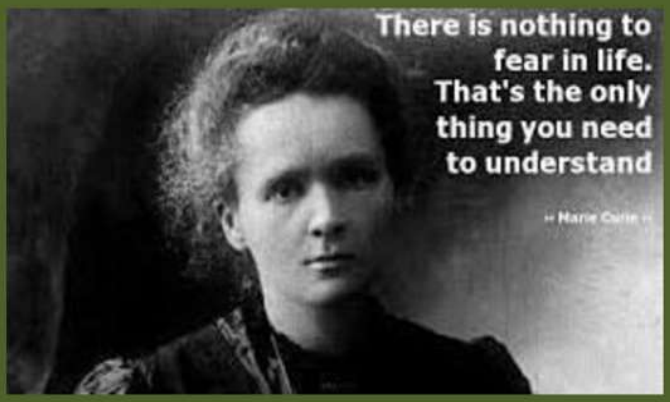
Many thanks to organising team of ICMP 2016 for providing a well planned and executed scientific program and I congratulate them for organising a successful ICMP 2016. My special thanks to IOMP and AFOMP for providing me opportunity to attend this scientific event in form of AFOMP Travel Award.

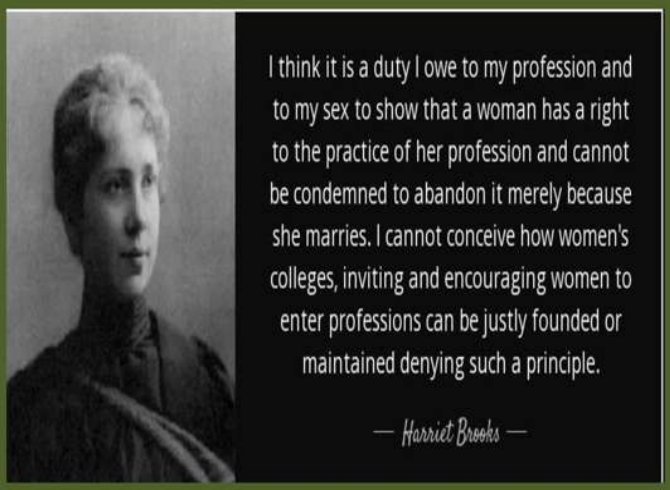
INTERNATIONAL DAY OF MEDICAL PHYSICS

7th November 2017

THEME

Medical Physics: *Providing a holistic approach to women patients and women staff safety in radiation medicine*



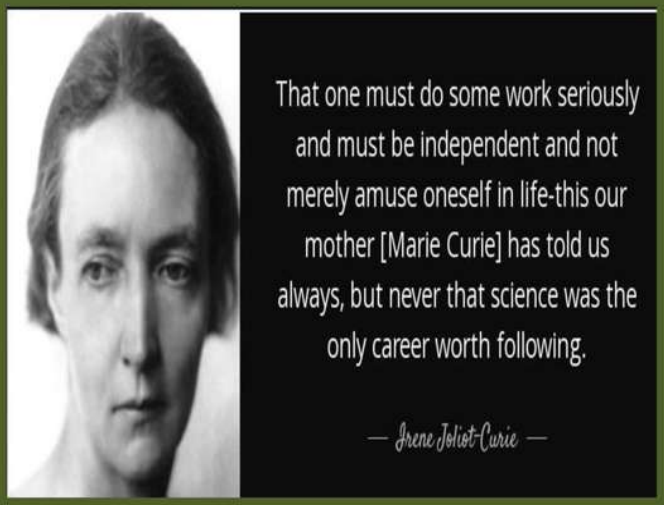


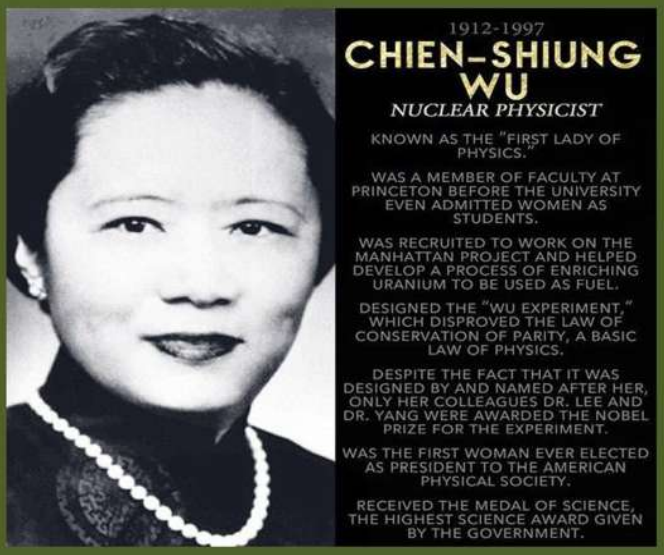
"We must have perseverance and above all confidence in ourselves. We must believe that we are gifted for something and that this thing must be attained."

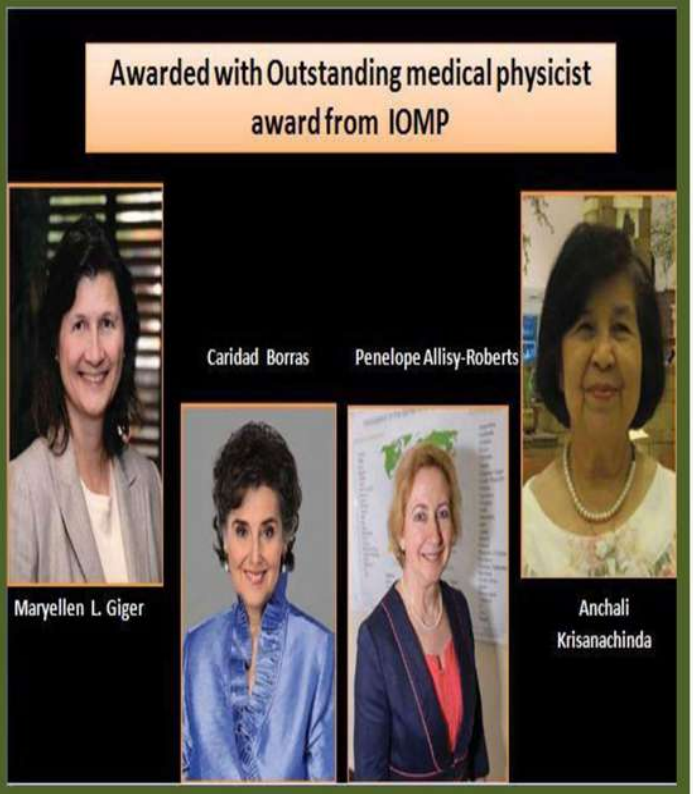
— Marie Curie

*The **I**nternational **O**rganization for **M**edical **P**hysics (**IOMP**) has very appropriately selected 7th November to celebrate the **I**nternational **D**ay of **M**edical **P**hysics (**IDMP**), this day is a testimony of an important date in the history of Medical Physics, as on "7th November" in 1867, great scientist Maria Skłodowska-Curie was born in Poland. She had discovered the phenomena of Radioactivity, which has opened gates of use of radiation for cancer treatment and given new dimension of application of **Physics** to **Medicine** and with this field of **Medical Physics** has **got boost**. Marie Curie was the only scientist to win Nobel Prizes in multiple scientific disciplines (Physics 1903 & Chemistry 1911) in the history of Nobel prizes.*

*IOMP has declared this day 7th November as **I**nternational **D**ay of **M**edical **P**hysics **(IDMP)** to commemorate the contribution of this great scientist in the field of Medical Physics. Since 2013 IDMP is successfully and widely being celebrated worldwide on every 7th November every year. This year, we are celebrating **150th** birth anniversary of Marie Curie. So, this year IOMP has appropriately chosen the theme of IDMP as "**Medical Physics: Providing a holistic approach to women patients and women staff safety in radiation medicine**" to recognize and appreciate the contribution of women in Medical Physicists.*



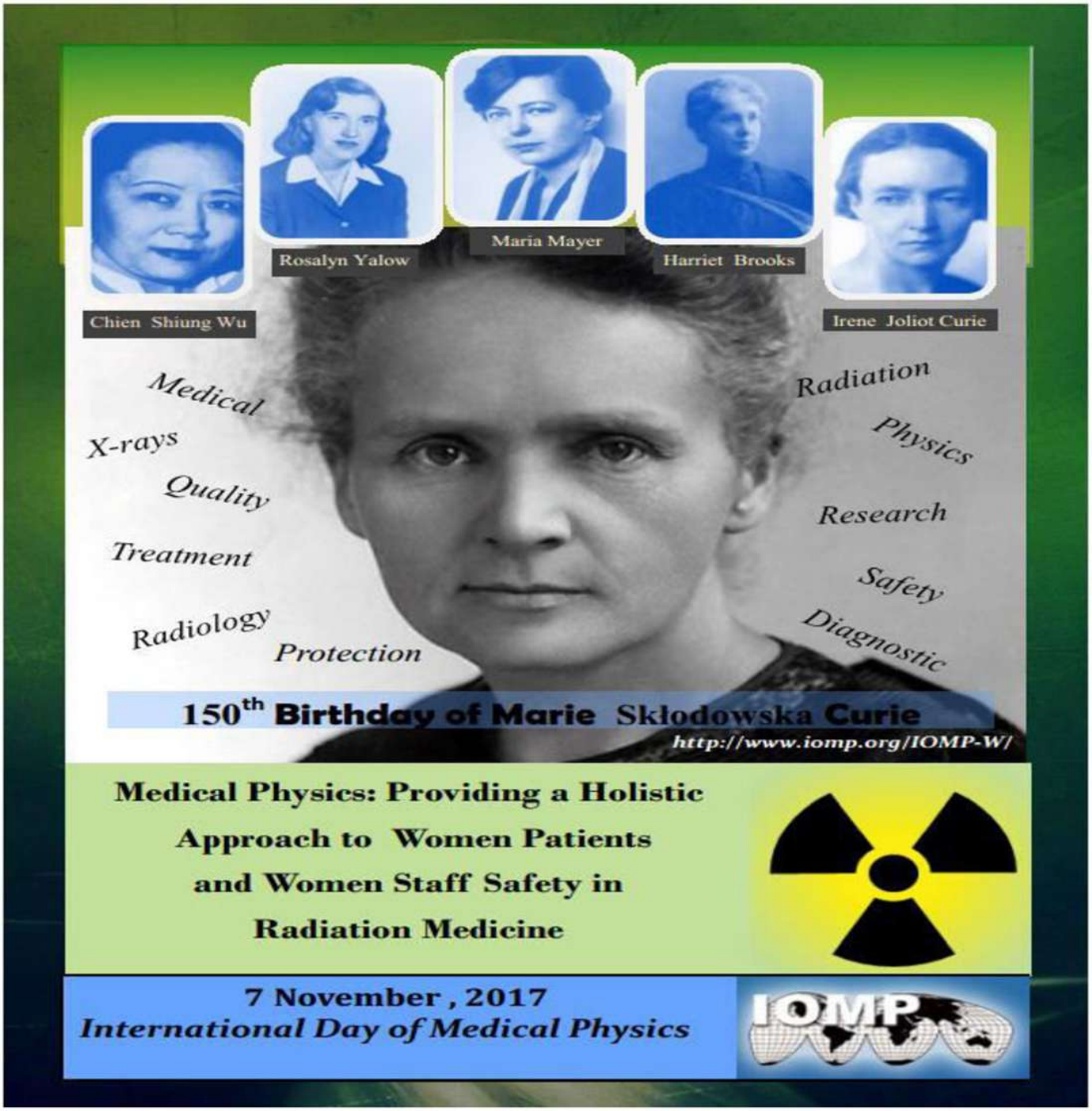




Women have played an important role in every walk of life including creation, advancement and application of Medical Physics. As a frontier science, Medical Physics is less likely to be bound by society's norms and less subjected to be inherent glass ceiling limiting women participation. Women such as ***Marie Curie, Harriet Brook, Maria Mayer, Irene Curie, Chien Shiung Wu*** *and many others helped break through that ceiling and their contribution to Medical Physics and healthcare are noteworthy and appreciated.*

Today, field of Medical physics is touching new horizons in every possible dimension as use of Radiation in Medicine is increasing day by day .Now we cannot imagine field of Medicine without application of Medical Physics. With this, role of women in Medical physics is also increasing as is increasing in every walk of life. But still there is a tremendous scope to enhance the role of women in medical physics and healthcare, as the participation or the number of women Medical physicist is still small. So with this year's theme of IDMP, which is fully based on women, a focus is on for increasing participation of women in Medical Physics and on women radiation safety. Scientific Sessions to discuss and prepare a road map are planned during AOCMP-AMPICON2017 on IDMP at Jaipur. This year's theme is to promote, motivate participation of women in Medical Physics as well as increasing awareness of radiation safety among the women. Special concern and focus is given to women radiation safety at the child bearing age for both women radiation worker and women patients because of potential radiation hazards associated to this particular span of life. There is nothing to be afraid, only right working practices and proper knowledge is required to minimize the radiation risks.

We wish you all, especially women medical physicist a very happy ***International day of Medical Physics.***



To participate or contribute in this IDMP Program please contact us:

IDMP 2017: PROGRAM COODINATORS

Virginia Tsapaki
Secretary-General
International organization of Medical physics
Member IOMP-Women group
virginia@otenet.gr

Rajni Verma
Joint secretary
AOCMP- AMPICON 2017
Member IOMP-Women group
1989vermarajni@gmail.com

Calendar of Events 2017-18

June 2017	**June 20– June 23 , 2017** Second International Conference on Advances in Radiation Oncology (ICARO2) Vienna, Austria, icaro2@iaea.org
July 2017	**July 27 – July 28 ,2017** 4th International Conference and Exhibition on Medical Physics and Biophysics Rome, Italy ,http://medicalphysics.conferenceseries.com/
August 2017	**August 27 – August 30, 2017** 6th International Workshop on Computational Human Phantoms Annapolis, MD, USA, http://www.cpworkshop.org
September 2017	**September 20 – September 22 , 2017** Workshop on the Monte Carlo Radiotherapy System PRIMO - Germany Essen, Germany, http://primoproject.net/workshop/ Marcelino Hermida López: mhermida@VHEBRON.NET **September 24 – September 27,2017** ASTRO Annual Meeting San Diego, CA, USA, https://www.astro.org/2017-ASTRO-Annual-Meeting.aspx
October 2017	**October 15 – October 18 , 2017** International Conference on Monte Carlo Techniques for Medical Applications (MCMA2017) Naples, Metropolitan City of Naples, Italy http://agenda.infn.it/event/MCMA2017
November 2017	**November 4 – November 7 , 2017** 17th Asia-Oceania Congress of Medical Physics "AOCMP – 2017" in conjunction with 38th Annual Conference of Association of Medical Physicists of India "AMPICON – 2017" Jaipur, Rajasthan, India, http://aocmp-ampicon2017.org **November 8 - November 12, 2017** 2nd Indian Cancer Congress – ICC 2017 Bengaluru,http://www.indiancancercongress2017.com/#home **November 26 - December 1,2017** RSNA,Chicago, USA , http://www.rsna.org
December 2017	**December 11- December 15 Dec 2017** Conference on Radiation Protection in Medicine – Achieving Change in Practice IAEA Vienna, https://rpop.iaea.org/RPOP/RPoP/Content/UpcomingEvents/2017-3-international-conference.htm
February 18	**February 10 – February 15, 2018** SPIE Medical Imaging Meeting Houston, TX, http://spie.org/conferences-and-exhibitions/medical-imaging **February 28-March 4,2018** ECR 2018,Vienna,http://www.myesr.org/congress

Officers and Council of AFOMP

President :- Dr. Tae-Suk Suh

Dept. of Biomedical Eng., College of Medicine,
The Catholic University of Korea,
505 Banpo-dong, Seocho-gu, Seoul, 137040, Korea
Telephone: +82-2-2258-7232
Fax: +82-2-2258-7506 E-mail : suhsanta@catholic.ac.kr

Advertising requests should be addressed to:

Dr.Tae-Suk Suh,

E-mail :-
suhsanta@catholic.ac.kr

Dr.Arun Chougule

AFOMP News letter & Event information should be addressed to:

Dr.Arun Chougule

E-mail :-
arunchougule@rediffmail.com

Vice President :- Prof. Dr. Arun Chougule

Dr. Arun Chougule
Dean, Student Welfare, Rajasthan University of Health Sciences,
Sr. Professor & Head, Department of Radiological Physics,
S.M.S. Medical College & Hospitals
Jaipur-302015, India E-mail : arunchougle@rediffmail.com

Secretary General :- Dr Howell Round

Associate Professor, School of Engineering
University of Waikato, Private Bag 3105,
Hamilton 3240,
NEW ZEALAND
Ph +64 7 838 4173, **Mobile** +64 210368549
Email h.round@waikato.ac.nz

AFOMP correspondence should be addressed to:

Dr Howell Round

E-mail :-
h.round@waikto.ac.nz

AFOMP webmaster:

Sunmi Kim

E-mail :-
arcmpsmk@gmail.com

Past President :- Dr. Yimin Hu

(1) Chaoyang Qu Panjiayuan Nanli
No. 17,
Department of Radiation Oncology,
Cancer Institute (Hospital),
Beijing 100021, China

(2) Cancer Research Institute
(Tumor Hospital),
Chinese Academy of Medical Sciences &
Peking Union of Medical College,
Beijing, China

Email: yiminhu888@163.com

Treasurer :- Dr. Kwan-Hoong Ng

Department of Biomedical Imaging
University of Malaya
59100 Kuala Lumpur
Malaysia
Tel: 603 7950 2088 Fax: 603 7958 1973 Email: ngkh@um.edu.my

Committee Chairman's

Education & Training :- Dr. Shigekazu Fukuda

Head of Technical Management Section,
Dept. of Accelerator and Medical Physics,
Research Center for Charged Particle Therapy
National Institute of Radiological Sciences (NIRS),
Japan

Professional Development Committee (PDC) Chair :- Dr. Howell Round

Associate Professor, School of Engineering
University of Waikato,Private Bag 3105,
Hamilton 3240, New Zealand,
Telephone: +64-7-838-4173
Fax: +64-7-838-4835
E-mail : h.round@waikato.ac.nz

Science Committee (SC) Chair :- Dr. Arun Chougule

Dean, Student Welfare, Rajasthan University of Health Sciences
Sr. Professor & Head, Department of Radiological Physics,
S.M.S. Medical College & Hospitals
Jaipur-302015,
India
E-mail : arunchougle@rediffmail.com

Funding Committee (FC) Chair: :- Dr.Young Hi Han

Professor
Sungkyunkwan University School of Medicine
Samsung Medical Center
Department of Radiation Oncology
81 Irwon-Ro Gangnam-gu, Seoul, 06351, Korea
youngyih@skku.edu, youngyihhan@gmail.com

Award and Honor Committee (A&HC) Chair :- Dr. John Drew

Dr. John Drew
Australia
john.drew200@gmail.com

AOCMP – 2017

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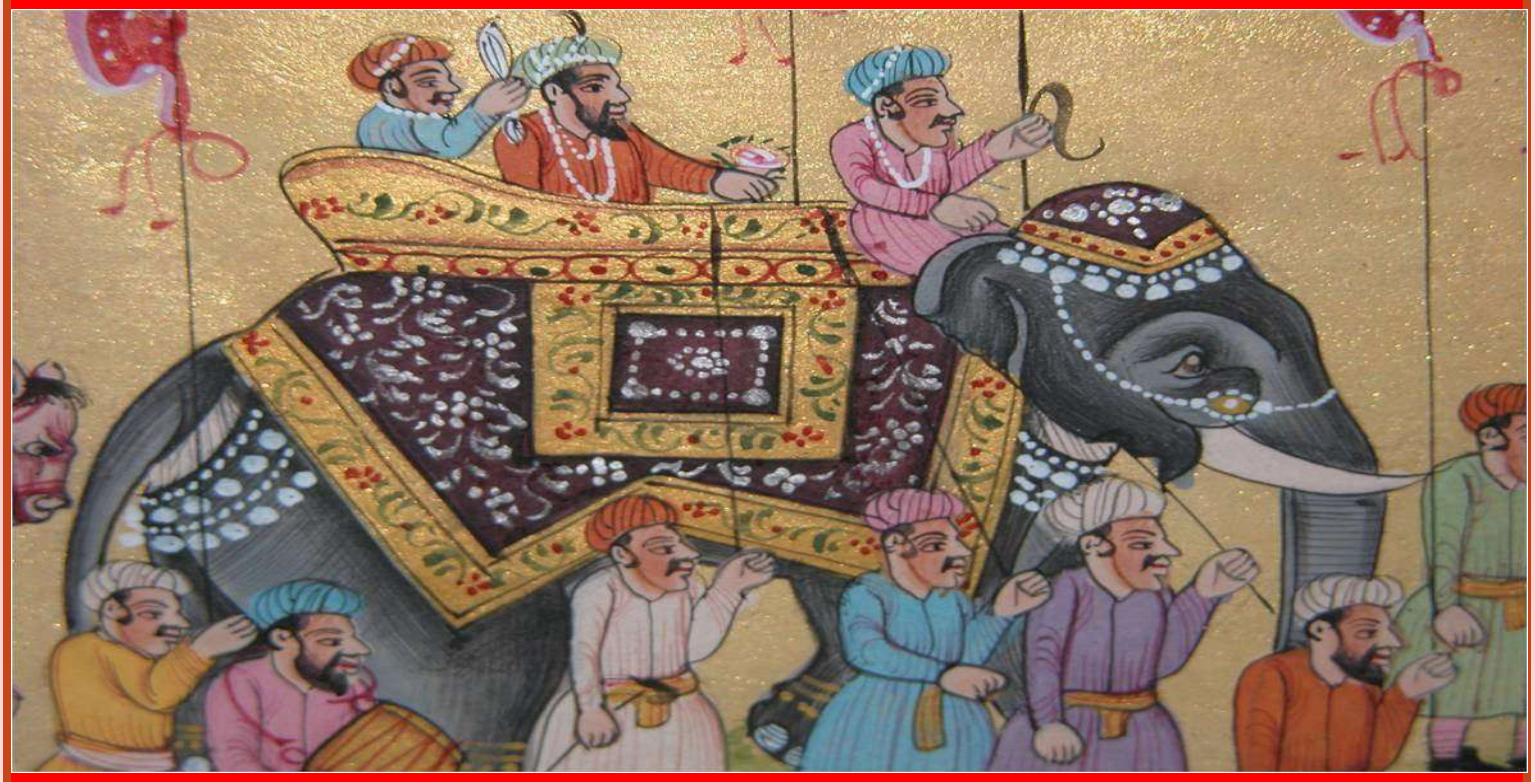
Welcome to land of colours



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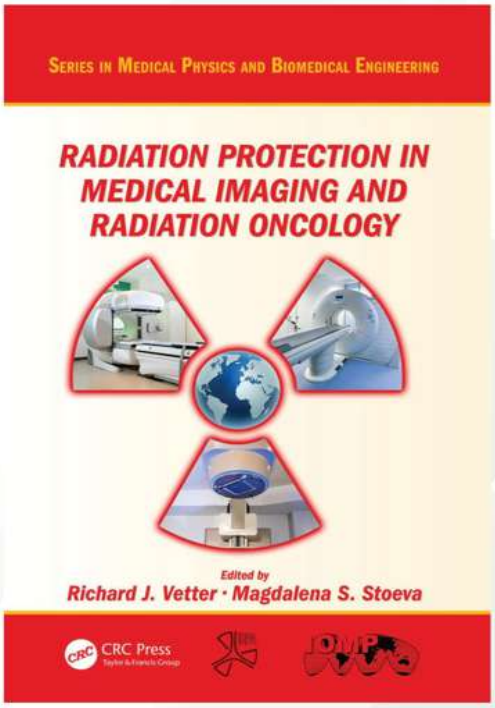

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