**Vol. III. No.2** **Editor : G.A. Rama Rao** **April 2004**

**Editorial**

*Living things have evolved in an environment, which has significant levels of ionising radiation. Furthermore, many of us owe our lives and health to such radiation produced artificially. Radiation is used to diagnose ailments, and some people are treated with radiation to cure diseases. We all benefit from a multitude of products and services made possible by the careful use of radiation.*

*Medical physicists have made many important contributions to biomedical research. In medical imaging physics, important contributions include the development of advanced imaging methods in such areas as functional MRI, proton and phosphorus spectroscopy, diffusion tensor imaging, optical imaging, digital radiography, and near-infrared spectroscopy. The radiation imaging techniques have received significant contributions from computer scientists, biomedical or electrical engineers, chemists, physicists, and nuclear engineers.*

*Radiation imaging techniques can be broadly grouped into those which use ionizing radiation and those that do not. The ionizing radiation group consists of those images created by the use of x-rays or gamma rays. Both x-rays and gamma rays are high energy, short wavelength (less than an angstrom) electromagnetic radiation that is capable of penetrating and passing through most tissues. Gamma rays arise from the nuclear decays of radioactive tracers introduced into the body, while x-rays arise from an x-ray tube where high speed electrons bombard a small spot on a tungsten anode target.*

*Non-ionizing radiation techniques mainly use either acoustic pulses (ultrasound) for echo-ranging imaging (somewhat like radar) or radio-waves combined with high-field magnets, in the case of magnetic resonance imaging.*

*IANCAS gratefully acknowledges the exemplary job that Dr.(Mrs.) Meera Venkatesh, the Guest Editor, who has been active in the field of Radiopharmaceuticals used in nuclear medicine, has done for this bulletin and all the authors for contributing the articles despite their busy schedule.*

***G.A. Rama Rao***

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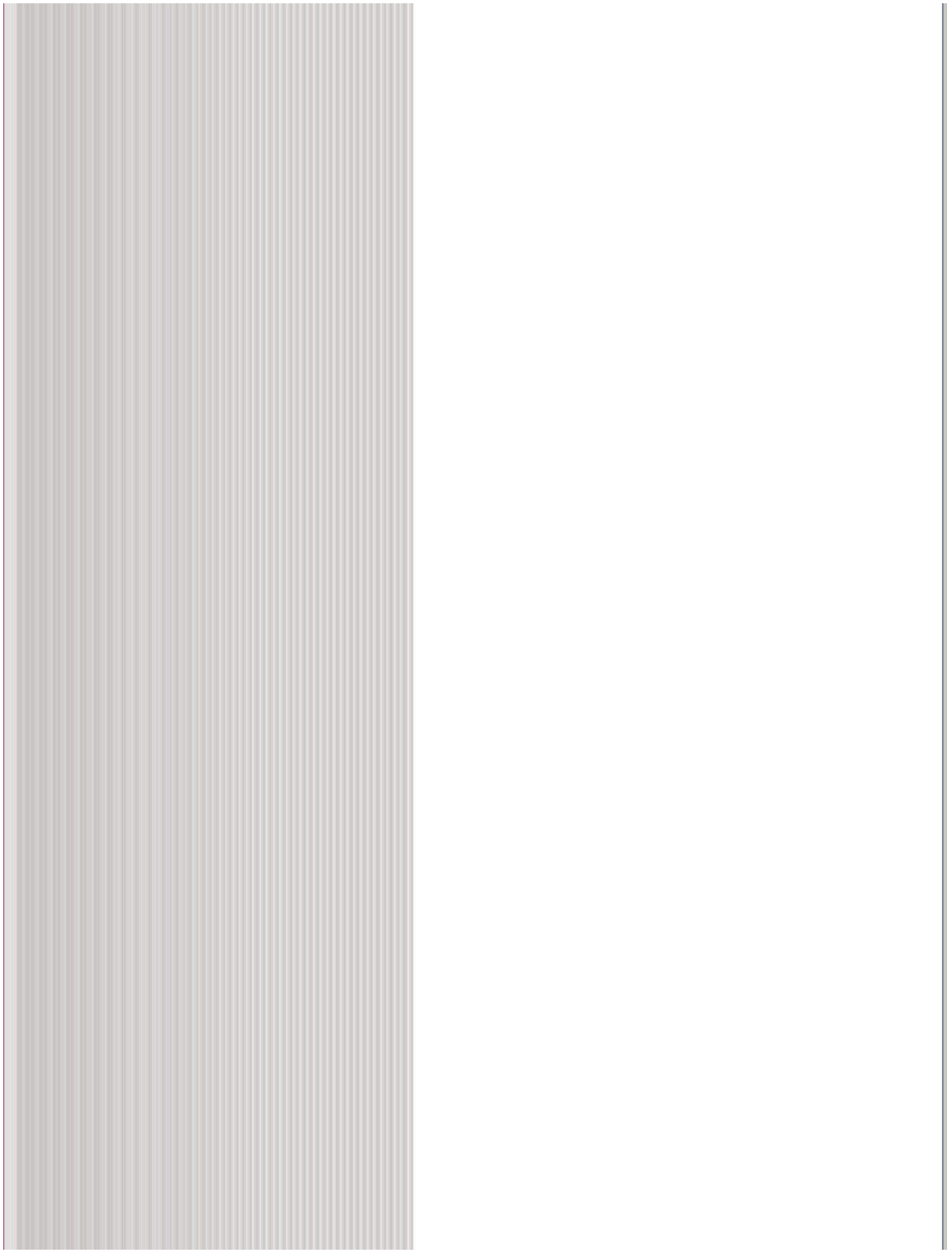

## IANCAS Dr. Tarun Datta Memorial Award to

## Dr. Raghunath Acharya

**INDIAN ASSOCIATION OF NUCLEAR CHEMISTS AND ALLIED SCIENTISTS (IANCAS)**

is happy to bestow

**IANCAS Dr. Tarun Datta Memorial Award**

on

**Dr. Raghunath Acharya**

Radiochemistry Division
Bhabha Atomic Research Centre
Mumbai, India

For his outstanding contributions in the field of Nuclear Analytical Chemistry relating to Research and Development work on the $k_o$-methodologies in conventional, prompt gamma ray and internal monostandard neutron activation analysis (NAA) for multielement determination in a variety of matrices. Dr. Acharya has been instrumental in developing these methods for the first time in India. These methods have been applied to non-destructive analysis of various samples of geological, biological and environmental origin including reference materials. A standard-less approach of NAA has been applied to analyze high purity metals like aluminium and metallic alloys like Zircaloys and Stainless Steels (SS), which is an important contribution to the field of analytical sciences. The prompt gamma ray NAA (PGNAA) method has been developed especially for low Z elements not amenable by conventional NAA. In addition, Dr. Acharya is actively engaged in R&D work on chemical separations of trace elements and speciation of important elements like arsenic.

February 16, 2003

**(V. Venugopal)**
President, IANCAS

## IANCAS Prof. H.J. Arnikar Best Thesis Award to

## Dr. K. Ananthasivan

**INDIAN ASSOCIATION OF NUCLEAR CHEMISTS AND ALLIED SCIENTISTS (IANCAS)**

is happy to bestow

**IANCAS Prof. Arnikar Best Thesis Award**

on

**Dr. K. Ananthasivan**

Fuel Chemistry Division
Chemical Group, Indira Gandhi Centre for Atomic Research
Kalpakkam, India

For his important contributions in the field of synthesis and thermodynamics of nuclear materials. Dr. Ananthasivan made original contributions to the thermal analyses of actinide bearing alloys by way of devising two new experimental methods viz., the "illuminated-spot technique" and the "spot-DTA". His work amply demonstrates the utility and wide applicability of these methods that are valuable tools for establishing phase diagrams at relatively low temperatures. In addition, he introduced the "de-agglomeration technique" - a novel and ingenious procedure for the synthesis of sinteractive thoria, which is very useful for fabricating thoria bodies with high densities, at lower sintering temperatures.

February 16, 2003

**(V. Venugopal)**
President, IANCAS

# Imaging Diagnostics using Radiation

*Guest Editor*

**Dr. (Mrs.) Meera Venkatesh**

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Mumbai 400 085

# Focus

Dr. (Mrs.) A.M. Samuel

*The technologic revolution that is being fueled by the development of increasingly powerful computers and rapid telecommunications is currently affecting all branches of medicine, but none more than diagnostic imaging. Getting pictures of body organs is now in vogue since a hundred years, ever since the discovery of X-rays by Roentgen in 1896. Everyone is familiar with this imaging method. Doctors often tell patients to take an X-ray of the chest or head, or for suspected fractures after injuries. In fact often patients ask the doctor if they should get an X ray of the chest done if they have a cough that has been troubling them for several weeks. X rays provide an easy method to detect abnormalities that cause changes in the density, such as a fracture or lung filled with fluids as in the case pneumonia/tuberculosis etc.*

*So in this ingenious way, medicine has utilized the properties of physics to develop techniques to look inside the body, without opening up the patient. X rays have served as excellent tool for diagnosis over a century now and the technique has undergone several improvements for optimal use. Tissues with poor density are studied with the aid of contrast agents.*

*However there are some limitations imposed in X ray images. It is a flat or 2 dimensional picture of a three dimensional object. Hence any changes that might be present in the depth of the organs will be missed and diagnosis will be missed. Years later, two very ingenious British scientists discovered the CT or computerized scanning technique. With the advances of computer hardware with large storage capacities and using software that was adapted (from the reconstruction of images obtained from objects in space used by NASA for identifying stellar objects from data received by powerful telescopes, used initially for reconstruction of images in CT and extended to Single Photon Emission Tomography and Positron Emission Tomography in Nuclear Medicine) the same principles were used to reconstruct images obtained by the CT scan. Although CT works on the principles as do Xrays and depends on the attenuation of the radiation depending on the tissue attenuation it is more sensitive to minor differences in tissue absorption (ie., exhibits greater tissue contrast) than ordinary radiography.*

*In addition, CT can "peel away" superimposed layers of tissue that may obscure detail on ordinary radiographs of the head, chest, abdomen, and extremities, revealing the anatomy of a single layer or section of tissue. The significant improvement was that Xrays were used in a circular ring form and the detector was placed opposite. In this way with one ring which could rotate rapidly over large regions of the body or several rings covering the region, one could now look in the third dimension that is the depth of the organ. This "cutting the organ into slices" without even putting a knife into the patient was called tomography. That is how the CAT or CT (Computerised Axial Tomography ) was given. The present generation of machines have more rapid data acquisition times and better resolutions such that even small tumors up-to 1-1.5 mm can be seen in the pictures. Malignant tumors or cancers often alter the normal spatial relationships in tissues, and radiological imaging is critical not only for diagnosing cancer but also for staging tumors and monitoring patients after they have received treatment. In the future, it is expected that technologic advances related to imaging may assist clinicians in evaluating functional parameters in tumors and in assessing the effects of treatment. A CT scan can help the doctor to localize the tumor, see whether it has spread, whether it is growing rapidly, whether it is pressing on some vital regions of the brain, its size and other information required to decide about the treatment.*

*Discovery of radiation and artificial radioactivity led to their applications in a various fields and diagnostic medicine has been one of the very successful application among these. Although the world of science lost no time in exploring the possibility of using radioactive isotopes as tracers in various fields including medicine, it was during the 1950s when artificially produced radionuclides were available commercially in adequate quantities that this modality grew in leaps and bounds.*

*From simple studies using radioiodine I-131 as sodium iodide in the initial days the field of Nuclear Medicine has come a long way. The brilliant concept of using radionuclides as tracers which can be detected by scintillation detectors has opened new field of "functional imaging". The added information which helps the physician to study disease processes by not only demonstrating anatomical changes but physiological or functional changes in organs and tissues of the body helps in better patient care and treatment. As a simple example when radioiodinated sodium iodide is given in trace amounts, the thyroid gland in the body concentrates sodium iodide for its function of hormone synthesis, if there is a disease of the gland not only will one be able to show whether there is a abnormal growth or tumor in the gland but its capability to concentrate radioiodine and thereby its function.*

*On one hand, the availability of radioisotopes from reactors and cyclotrons, invention and availability of radionuclide generators (for important nuclides such as $^{99m}$Tc - the work horse of diagnostic nuclear medicine) and the availability of "cold kits" to produce radiopharmaceuticals accelerated the growth of this modality. Radiopharmaceuticals are compounds which are tailored to target to special organs of the body and when radiolabeled will identify structural and functional changes in the organ. The immense potential this capability of radiopharmaceuticals is a gift to the medical fraternity. Imagine "tailoring" your needs to patients.*

*On the other hand, the phenomenal exponential growth in the development of electronic and computer technology has aided in fast data acquisition and collection of large volumes of data which with the ever-growing sophistication of software for processing data has improved imaging techniques and further speeded up the growth of nuclear medicine. From hand held probes for counting the activity inside a body the changes have been very quick leading to the use of multi head gamma cameras or PET cameras through the path of the scintillation camera, the rectilinear scanner, gamma camera and so on.*

*In addition the ability to use the same radionuclides fro diagnosis and treatment of certain cancers has no parallel in medicine. Its like using drugs which in right doses can be used for curing diseases but overdoses are like poisons. So larger quantities of the radionuclides like radioiodine can be used to treat cancers of the thyroid.*

*Another new development in imaging methods is MRI (Magnetic Resonance Imaging) in which a powerful unidirectional magnetic field is used to orient or polarize hydrogen atoms within tissue in the direction of the magnetic field. Short pulses of radiowaves are then sent into the body at a frequency that resonates with the polarized hydrogen atoms. The polarized hydrogen atoms are deflected momentarily from their axes by these radiowave pulses, and subsequently, they emit radiowaves at their resonant frequency. An external radio wave detector can pick up these emissions. With a powerful computer, the radio wave emission patterns from the resonant hydrogen atoms can then be used to synthesize a three-dimensional volume image (or multiple adjacent planar images) of the specific region under study. MR images, therefore, represent a computer-generated map of the hydrogen atom radio wave emitters in a single body region. Our body tissues have water as the major constituent and hence ability to map the concentration of H or water by MRI would in turn mean mapping tissues with respect to their water content. As most of the lesions such as a clot or cancerous mass differ in their density and water content, this technique is very effective in picking up small lesions in organs such as brain, spinal cord etc. MRI, as also X-radiography or CT images, cannot give information of the viability of tissues. However, with the advent of functional MRI, this short coming is addressed to an extent.*

*Ultrasonography is yet another imaging technique that uses sound waves of very high frequency above the audible range. These ultrasound waves come in contact with tissues when the transducer which produces*

*the waves is placed in close contact with the skin. The waves get reflected in the interfaces of the body tissues and returns back to the detector that is the transducer. The signals are converted by software and computers into images. This is a very safe technique as not many effects of ultrasound on the body have been reported. As a result this method is used extensively in women who are pregnant and infants and children. USG studies can be very useful in detecting defects even before the birth of the child that helps in taking corrective action as early as possible. Doppler ultrasound [US] methods can also demonstrate blood flow in tumor vessels non-invasively and may have future applications in clinical cancer diagnosis.*

*Each of the imaging modalities has its special features and capabilities and advantages. With the possibility of merging two images obtained from different machines like CT, MRI PET, SPECT of the same organ, we now have "fusion images" or overlaying images so that there is a good comparison of the same abnormal tumor or mass .whereby the advantages of two different modalities can be added together! Fusion of MR image with NM image has shown excellent pictures for delineating minute defects in brain scans. The availability of these multiple tools enables the physician to choose the best option for a particular situation. The need for sensitivity and clarity of image is one consideration while the cost becomes the other consideration while treating patients and a good physician weighs all the aspects and chooses the right modality.*

*This issue of IANCAS gives a broad idea of the imaging modalities using radiation. The introduction of the reader to the ongoing progress in medical sciences will bring about a better awareness about technologies using various physics principles and the use of electronics, computers, data processing, mathematical models in the development of software and imaging. No longer do the barriers exist between medicine, physics, chemistry and biology. The trend is for a holistic approach and the isolation of the basic sciences from applications is blurring rapidly.*

# Guest Editorial

Dr. (Mrs.) Meera Venkatesh

*Our human body is a great wonder and the greatest is perhaps the brain. Human brain with the billions of neurons is ever active exploring new ways to make the life better and easier. We are lucky to be in this period to enjoy the fruits of labour of our forefathers who invented all the luxuries that have become part of our life-style without which we cannot imagine our life! Among these luxuries are the medical facilities that help alleviate the sufferings of humans, some of which have become common tools today. For example, even an illiterate person knows that if he has had a bad fall with suspicion of bone fracture, he would need to take an X-ray picture. Today, apart from the X-radiograph, we are all very familiar with the terms CT scan, Ultrasound picture, MR scan and to some extent with Nuclear medicine scans. Presently, even a layperson is aware that an accidental fall with head injury would need a CT scan, a persistent severe headache could need a MR imaging, the growth of a fetus is monitored by an US imaging and a cancer patient may be tested for recurrence by NM imaging.*

*X-rays, or rather Roentgen rays, revolutionized the field of medical diagnosis within a short span of few months since its discovery in December 1895 by the great physicist Prof. Wilhelm Conrad Roentgen. The X-radiography was soon employed to "see" a variety of disorders – from minor fractures to blocked blood vessels! With the advent of computers and computational methods (it is interesting to note that David Kuhl developed 'emission reconstruction tomography' in nuclear medicine imaging in 1962 which was extended later for 'transmission reconstruction tomography' in X-radiography) X rays could be used to get 3D images and "Computerized Axial Tomography" or CT/CAT was born in 1972. Around the same time Magnetic Resonance Imaging was also introduced in the medical field. Although the phenomenon of Nuclear magnetic Resonance was understood in 1946 and developed into an analytical tool in 1950s (but modifications to improve were continuously on during 1960's and 1970's), it was waiting for the acceptance by the medical world for such an expensive hardware! Being an expensive tool, it was dear in the early days. But it's importance and versatility as a diagnostic tool was realised soon and it is reported that in 2003, 75 million scans have been performed using the 10,000 MRI units installed worldwide! The advent of functional-MRI in 1993 has increased the scope of studies even further. Ultrasonogrphy, which was conceived in 1953, could be demonstrated for its benefits in imaging heart disorders by 1955 and has grown into a very important diagnostic tool. Nuclear medicine, which deals with utility of radioisotopes in medicine, could be considered to have begun in early years of last century, soon after the discovery of radioactivity. But, in a true sense, such utility developed after the accelerators and nuclear reactors that were used for artificial production of radionuclides, were invented. While initial uses of radionuclides were for therapy rather than diagnosis (after invention of cyclotron, P-32, Na-24 etc. were used since 1930's and in 1946, $^{131}I$ was used for treatment of thyroid cancers), diagnostic nuclear medicine emerged with force during 1950's (during 1940's studies using radiotracers were reported, but only after the nuclear reactors were available for production of radionuclides, the utility could be seen). With advent of $^{99m}Tc$ generator in the 1960's and the introduction of "instant kits" for $^{99m}Tc$ radiopharmaceuticals in the 1970's, the range grew very quickly and over 100 imaging procedures were established in short period. The development of PET technique and wide availability of medical cyclotrons boosted the growth of PET radiopharmaceuticals in the 1980's and 1990's. The world of diagnostic medicine has come a long way with multiple modalities with huge potential.*

*As physicists and chemists, we are often fascinated by the great things that little waves can do! The whole span of electromagnetic spectrum is used in scientific measurements, aiding in qualitative and quantitative analyses. Based on the laboratory observations, human ingenuity could succeed in using the properties of the electromagnetic and sound waves to device excellent mechanisms for medical diagnosis.*

*This bulletin of IANCAS dwells on the established diagnostic imaging tools based on various types of radiations. In order to appreciate the true value of the techniques, actively practicing medical specialists were requested to contribute in the areas of their specialization. With a view to get an overall feeling for the topic, an attempt has been made to give glimpses of history, principle involved and typical examples in the diagnostic modality being discussed.*

*However, techniques under clinical trials such as "Computerized Thermal Imaging" wherein IR rays are imaged to detect tumours are not addressed here, as their value is yet to be established. "Thermal Imaging" was not accepted by the medical community although the technique got approval by FDA in the US. Similarly, techniques that are just out of research stage and need to establish utility are also not dwelt upon here. One such is "Synchronization Tomography", a new brain imaging method pioneered by a German research group from several institutions, which involves mapping the fluctuating magnetic fields produced by tiny electrical currents in the brain, and determining which brain regions are synchronized with an activity. Imaging techniques such as "Electrical Impedance Scanning" which do not involve radiations have also not been addressed.*

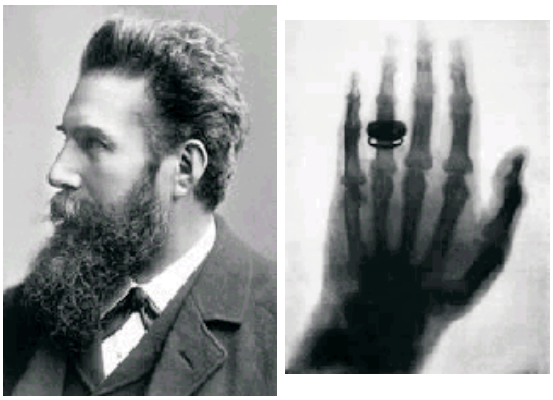
*I hope the information in this bulletin will make interesting reading to all our readers and I welcome comments and suggestions from the readers.*

# X-Rays/Roentgen Rays : as a Diagnostic Tool

***Dr. Ravi Ramakantan**, M.D. (Radiology), is the Head and Professor of Radiology at the Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital, Mumbai, from where he had his entire medical education with brilliant academic record. Dr. Ravi Ramakantan is contributing to the growth and understanding of radiology which is evident from his active participation in the academics. He is a member of the editorial board of the journals 'Indian Journal of Radiology and Imaging', 'Postgraduate Journal of Medicine' and 'Asian Oceanian Journal of Radiology'. Dr. Ravi is the founder secretary of the 'Society of Academic Radiologists of Bombay', founder trustee of the 'Radiology Education Foundation', founder president and executive committee member of the 'Indian Society of Neuroradiology'. Dr.Ravi has delivered prestigeous orations such as N.G. Gadekar Memorial Oration, Dr. Kurulkar Memorial Oration and 'Claris Annual Oration' and has severd as a faculty member at conferences both in India and abroad. He has also been contributing to the 'World federation of Neuroradiological Societies' as a member of its education council since 2000 and has about 60 publications in reputed journals.*

**Introduction**

The term 'X-rays' are so familiar to even the common public that perhaps they do not need an introduction. However, perhaps not many are aware of the situations under which these rays were discovered. Wilhelm Conrad Roentgen (1845-1923) who was professor of physics and the director of the Physical Institute of the University of Wurburg, was fascinated Cathode rays and started working with them around end 1895. On November 8, 1895, while Roentgen was working alone with a Crookes tube in his laboratory late in the evening, he suddenly noticed a shimmering light on a screen of fluorescent material lying on the table top few feet away from the tube. He was astounded and repeated the experiment moving the screen away. To his astonishment the results were the same. The tube was covered with a light-proof cardboard jacket and there was no chance of the cathode rays penetrating the wall of the tube and visible light penetrating the jacket. Greatly excited he hypothesized that a new form of radiation was being produced and he experimented for the next two months studying its properties. When he tried its penetration through matter holding various materials in its path, he found that the screen still fluoresced but with different intensities depending on the material being used. When he placed a lead disk, which he was holding, in the cathode ray path he was astonished to find the shadow of the round circle appeared on the screen along with the outline of his thumb and forefinger and within them the bones of his hand! He replaced the screen with a photographic plate and employed his wife Bertha (Frau Röntgen) to place her hand on the photographic plate while he directed the rays at it for fifteen minutes. The image that emerged is the famous first radiograph!



*Roentgen and the radiograph of his wife's hand.*

Roentgen used the term "X-Rays" as he did not know what these rays were and published the results in the Proceedings of the Physical Medical Society of Wurburg in December 1895. He was awarded the Rumford gold medal of the Royal Society in 1896 and the Nobel Prize for physics in 1901, the money of which he bequeathed to scientific research at Wurzburg. There was a great awe at this discovery and the medical world immediately recognized the extraordinary import of the discovery. Within months of the announcement, a multitude of foreign

bodies, fractures, and calculi had been radiographed. But "bullets, bones, and kidney stones" were not the only uses medical observers envisioned. The first angiography, moving-picture X-rays, and military radiology were performed in early 1896. Dr. Edwin Frost (1866-1935) is credited with making the first diagnostic radiograph in the U.S. in February 1896. Angiographic work began in January of 1896 with the post-mortem injection of mercury compounds.

Dr. Edwin Frost's laboratory, the first medical radiograph of a fracture and an early angiograph are seen here above. The X-rays or 'Roentgen rays' as it was called in Germany, soon found multiple applications from medical to military. The contribution of X-rays in the world of medical diagnosis is enormous resulting in immense benefit to millions of people. The detrimental effects of ionising radiation were recognised early on, with the result that the history of radiation hazards and protection is nearly as long as that of X rays itself.

**Principle**

X-rays are electromagnetic rays which on passage through matter interact with the atoms of the matter and lose their energy. The extent of attenuation of their energy will depend on the density of matter. An image of the rays emanating after passage through an object will have intensities distributed as per the density distribution in the object. The medical radiograph, a photograph taken of an organ or tissue after passage of X-radiation is used to visualize defects such as fractures, blockages, abnormal tissues etc.

***Chest Radiography***

Chest X-ray are the most frequent of all plain X-rays. They are used to visualize the lungs, the hear and boney thorax. A variety of diseases – both common and uncommon can be diuagnosed by the ubiquitous chest radiograph. In our country tuberculosis is an obvious example. At the other extreme – the uncommon interstitial lung diseases can also be diagnosed. Though less often performed for cardiac problems, every patient with such diseases will have at least one or perhaps more x rays done, either as a base line study as some common reasons for chest x rays include:

(a) Pulmonary disorders such as pneumonia, emphysema (or pneumothorax – presence of air or gas in the chest cavity outside the lungs)

(b) Diseases such as tuberculosis

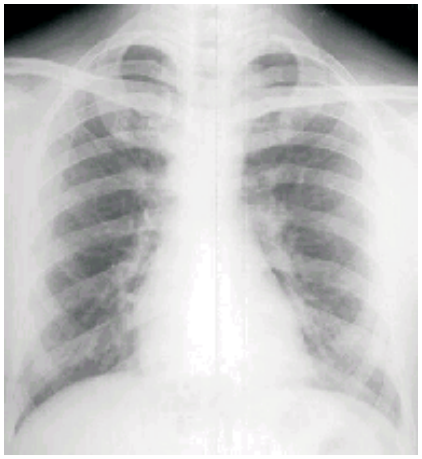
(c) Cancer: to check for tumours in lungs, thyroid, lymphoid tissue, bones of thorax

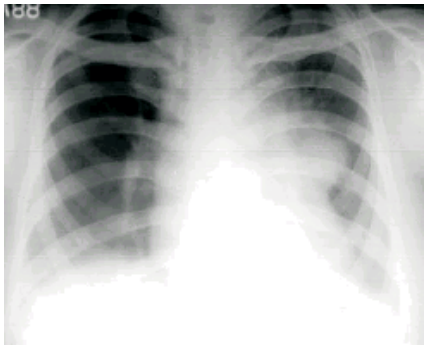
(d) Cardiac disorders such as pulmonary edema or congestive heart failure (though echocardiography is more sensitive for these purposes)

(e) Verification of correct placement of catheters, chest tubes etc.

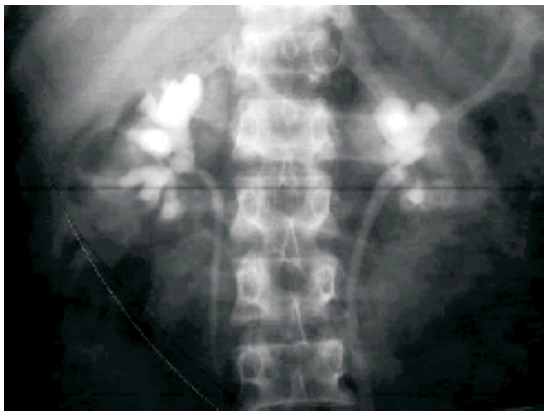
(f) Identification of foreign bodies inhaled or swallowed

A radiograph of normal lungs which perhaps is quite familiar to many of us and a radiograph of lungs with a mediastinal mass (growth on the central chest bone) are shown below.





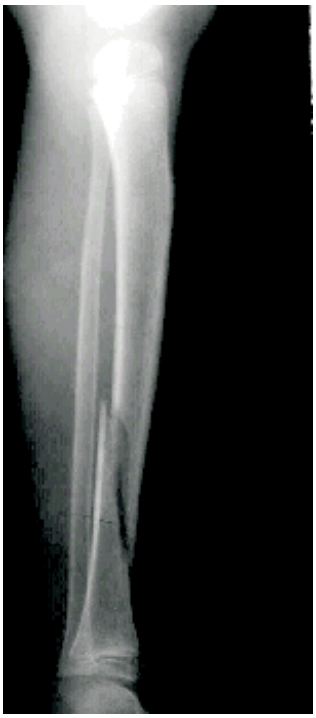
An image of tuberculosis infected kidney is seen below.

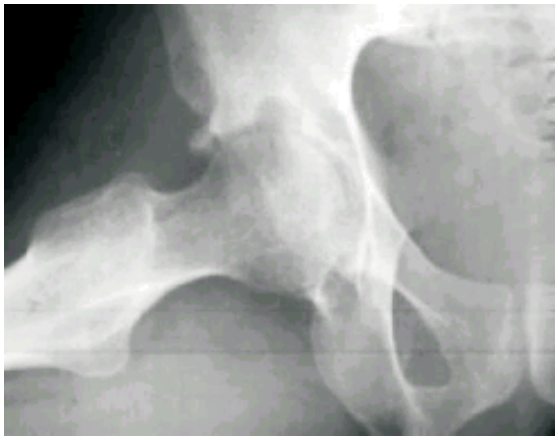


***Bones and Fractures***

As mentioned earlier, the utility of X-rays in fractures or disorders related to bones is a very established fact. Orthopedic surgeons rely heavily on the radiographs for diagnosis and follow up of treatment. These serve as permanent records in a variety of bone related disorders and help physicians take crucial decisions. A radiograph of a joint affected by osteoarthritis is given below. Situations such as extra growth of a bone are best detected by radiography. Bone radiographs are also useful in the diagnosis of generalized diseases such as metabolic bones diseases (rickets, scurvy etc), diagnosis of skeletal dysphasia's (developmental defects) as also for primary and secondary tumors.

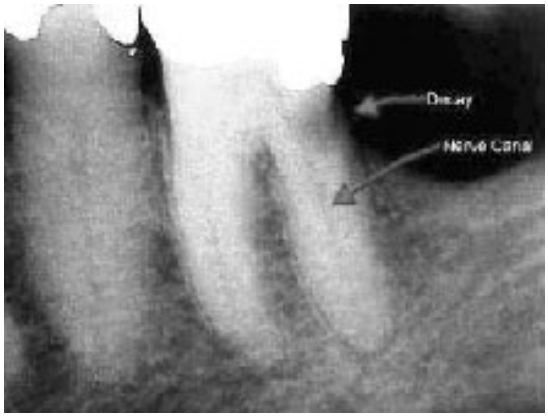
X-radiographs of a fractured bone of the leg and osteoarthritis affected knee joint are seen below.





***Dental X radiography***

To see into the teeth and its parts not visible to clinical examination dental radiography is essential It allows diagnosis of diseases of the crown as well as the roots and also of the surrounding bones. Orthodontic treatments rely heavily on radiographic evaluation.



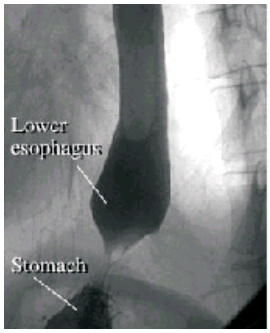

Although the bones could be clearly visualized in the background of soft tissues and air filled lungs, the radiographs lacked clarity when organs such as stomach etc. were imaged. In the due course of time researchers in this field found out ways and means of overcoming such impediments by ingenious means. An attempt to describe the various limbs of X-radiography as practiced to day is attempted here.

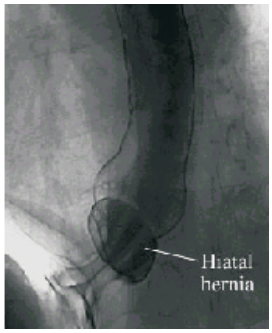
***Radiographic Contrast (Dye) Materials/Injections***

These are substances that are used by the radiologist during the course of certain radiological investigations to obtain clearer view of the various structures in the body. These contrast media which are popularly known as "dyes" are of various types and are used in standard radiological examinations, in CT scans and during MRI.

Among the various contrast media used in radiology, 'Barium' is one of the most well known. Basically, it is a barium sulphate powder of various consistencies in liquid form, which is administered, for investigations of the gastro-intestinal tract (gullet, stomach, small and large intestines). These agents are harmless; most patients find the flavour acceptable; at worst, some patients may feel slightly nauseated on drinking the barium suspension. The barium is passed out of the body in the stools in a day or two; thus the stools may be of unusual color or consistency after a barium examination. This is normal and should not cause any anxiety. Barium liquid is also used an enema for the study of the large intestine. For all practical purposes, there are no side effects of these procedures and in most cases; the patient can resume normal activity and resume normal diet immediately after these investigations. The following are the investigations performed using X-rays with barium as the contrast agent.

Barium swallow, also known as an esophagogram is done for the evaluation of the esophagus (gullet). This is a short, painless procedure, which takes 10-15 minutes to perform. The patient may be asked to starve overnight for the procedure. The patient will be asked to swallow the barium liquid several times as the radiologists observes its flow under fluoroscopy (x ray screening). He will also take x rays as required in different positions. Typical X-rays of Esophagus are seen below.




In some cases an intravenous injection may be given to relax the muscles of the esophagus to obtain good quality pictures.

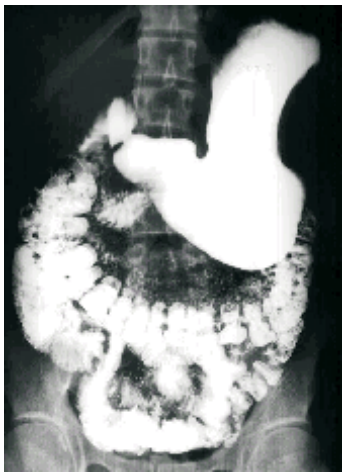
Barium Stomach duodenum (SD) also known as the "Upper GI series" is carried out for the investigation of the stomach and the upper part of small intestine. This procedure is also similar to the barium swallow. The patient will be asked to report on empty stomach after overnight starvation. It is painless and takes up to 20 -30 minutes to perform, In addition to the barium the patient will be asked to swallow a gas producing powder which will give better quality X-ray pictures. In some cases an

intravenous injection may be given to relax the muscles of the stomach to obtain good quality pictures. X-ray pictures will be taken in different positions to visualize the various parts of the stomach and the duodenum.

Barium follow through (FT) also known as the "small bowel series" helps in evaluating the small intestine. In addition to overnight starvation and reporting on empty stomach, often the patient will be asked to take laxative tablets on the night before the examination. The patient will be given one or more glassfuls of barium to drink and x ray pictures will be taken at periodic interval (hourly or so). Towards the end, fluoroscopy (screening) is done and more pictures taken. At this time, a enema tube may be passed and air instilled into the patient large intestine (this part of the procedure tends to be a little unpleasant though is essentially painless. The patient may even feel a very strong urge to pass stools). The whole examination may take anywhere between an hour and 4- 6 hours (typically about 2 hours) depending on how soon the barium passes through the small intestine. Though not painful, the waiting may be a little boring. In some cases the patient may be asked to report for a "24 hour" film on the following morning.

Small bowel enema is used for selective and specialized visualization of small intestine When detailed information on the small intestine is required and especially when it is not available even after the barium follow through examination described above. For this procedure again, the patient will have to report on empty stomach after overnight starvation. The patient may be asked to take laxative tablets on the night preceding the examination to clean the bowels. For this procedure a long rubber tube is passed through the patient's mouth (or sometimes through the nostril) and is guided by the radiologist into the small bowel under screening control. This part of the procedure takes about 10 minutes and can be unpleasant - especially when the tube is being passed through the gullet. In spite of this, the procedure is essentially painless. Once the tube is in place, the radiologist will inject barium and some other liquid through this tube and x ray pictures of the small intestine are obtained. The whole procedure lasts about 30-45 minutes.

A X-radiograph picture showing tuberculosis infected small intestine is depicted below.



Barium enema is used for the visualization of the large intestine. For two or more days before the procedure, the patient will be asked to take purgative tablets to clean the large intestine. Some radiologists insist that on the day prior to the investigation, the patient take only light food or sometimes only liquids. All this is quite inconvenient but is essential to the performance of a good study and the more the patient cooperate the better the quality of the examination. On the morning of the procedure, most radiologists will allow their patients to drink fluid. For the procedure itself, a thin suspension of barium is prepared and is then introduced into the large bowel through an enema tube. Following this, air is pushed through the tube with the help of a pump. During this time, there is no real pain but patients experience varying degrees of discomfort and urge to pass stools. Serial x-ray pictures are obtained under fluoroscopy to depict the various parts of the large intestine. After the procedure, the patient will be allowed to pass stools and can resume a normal diet immediately.

Apart from barium, various organic compounds of Iodine are used for a number of radiological investigations such as intravenous pyelography (IVP), angiographies, CT scans etc. These are mostly injected intravenously (for IVPs and CT scans) or intra arterially (for angiographies). Though these contrast agents are by and large very safe, occasionally, mild or rarely, serious side effects

could occur following the injection of these contrast agents. Although, these side effects are unpredictable (no reliable pre-testing is possible), fortunately they are uncommon and should not put the patient off from undergoing these investigations when a doctor advises them. However if one is allergic to any drug or suffer from asthma or are an uncontrolled diabetic, the chances of developing a reaction are more. The radiologist will carefully question the patient for these conditions and will then take adequate precautions to "minimize" the chances of a reaction occurring or treat it should one occur. It is usual to have a feeling of warmth and a metallic taste in the mouth when these agents are being injected. However, if there is any other symptom such as nausea, vomiting, itching, or breathlessness, the patient should immediately be requested to bring this to the attention of the radiologist. The iodine based contrast agents are broadly divided into two categories: older "Ionic" variety and the newer "Non ionic" variety. The main difference is that the incidence of adverse reactions is vastly less with the newer "Non ionic" agents as compared to the older "Ionic" agents. The only reason the newer and safer "Non ionic" contrast agents are not universally used is that they are up to three times more expensive than the older "ionic" contrast agents.

Intravenous Pyelography/Urogram (IVP,IVU) is done to evaluate the kidney, the ureter (the tubes that connect the kidney to the urinary bladder) and the urinary bladder. It is essential to have a clear picture of the abdomen before this procedure is done. Therefore most radiologists will prescribe that the patient takes laxative tablets for two nights prior to the procedure. Also tablets to reduce the gas in the abdomen are also prescribed for 2-3 days prior to the investigation. This may be quite inconvenient but is essential to the performance of a good study and the more the patient cooperate the better the quality of the examination. The patient will be asked to starve overnight and report on empty stomach. At first a "plain" x-ray of the abdomen is obtained. Amongst other things, this is to ensure that the abdomen is clean. At times, when this is not so, the procedure will be delayed after another day's abdomen cleansing. Once the plain x ray film of the abdomen is satisfactory, an intravenous iodinated contrast injection will be given after which 8-10 x rays of the abdomen will be obtained for up to 1-2 hours. After the procedure is over, the patient can take normal diet and resume normal activities immediately.

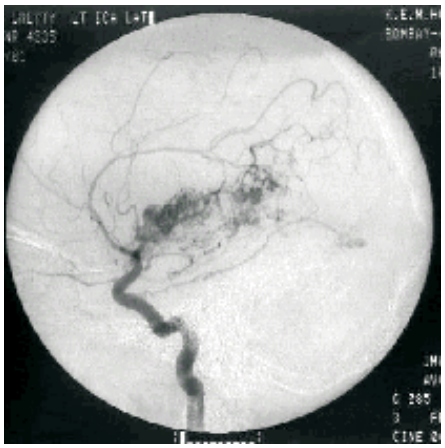
Micturating cystourethrogram (MCU) is almost always performed in men to study the urinary bladder and the urethra (the passage through which urine is passed). Patients are asked to refrain from drinking water for several hours before the procedure. A catheter (a thin hollow tube) is passed through the urethra into the urinary bladder. This is done under local anesthesia and may be mildly painful. Then the urinary bladder is filled with contrast medium and x ray films are obtained. One of the films may be done while the patient is actually passing urine on a special x-ray table. The procedure lasts about 30 minutes and the patient can resume normal activities immediately after the procedure.

Dynamic retrograde urethrogram (DRU) is done in males to look for narrowing of the urethra (the passage through which urine is passed). No prior preparation is required. Iodinated contrast injection is made into the urethra after application of local anesthesia and X rays are obtained at this time. The procedure lasts around 10 minutes. No significant pain or only mild pain is associated with this procedure. The patient can resume normal activity immediately after the procedure.

Computed Tomography is essentially a modification of the conventional X-radiography as this is also based on attenuation of X rays. With the advent of CT scanning and MR imaging, tests such as myelography and cisternography are seldom carried out these days using plain x-radiography. Both Myelography and cisternography are generally indicated for diagnosis of the compression of nerve roots and spinal cord or for cases of cerebrospinal fluid (CSF) leak. For both these procedures, non-ionic, iodinated contrast medium is injected by a lumbar puncture. A lumbar puncture is done by inserting a needle under local anesthesia between the bones in the low back. It is a moderately painful procedure and may take up to 15 minutes. The patient has to starve for about 4 hours prior to the procedure. After the lumbar puncture is done, the contrast is injected into the fluid casing around the spinal cord. Once this is done, the patient will be examined in the scanner for about 15-30 minutes. Once this is done, the patient will be examined on an

X-ray table in varying positions (including a "head low position"). This takes an additional 15-30 minutes. After the procedure is over, the patient will have to take complete bed rest for up to 24 hours. Many patients experience varying degrees of headaches and backache for a day or two after this investigation. In spite of the pain and discomfort, the procedure is, by and large, safe.

Angiography is a procedure to the study of blood vessels (arteries and veins) in the body. When, as is the most common case, arteries are studied it is called an arteriogram, (most of the time, the word angiogram is used synonymously with an arteriogram) and when the veins are studied it is called a venogram. Depending upon which particular artery is examined, these procedures have special names such as carotid angiograms - when vessels of the brain are investigated, coronary angiogram when the arteries supplying the heart are studied or a renal angiogram when the arteries of the kidney are looked at. In the current practice of angiography, small tubes called catheters (about the diameter of a ball pen refill) are introduced into various blood vessels through a small puncture of the artery in the groin. Sometimes, the entry point may be through blood vessels in the upper limb (axilla, elbow or wrist). Through this tube, iodinated medium is injected and x rays are obtained. These x rays show up the state of the patient's blood vessels. Typically, a few days before the angiogram, blood tests are done to make sure that the clotting parameters of the blood are normal and that the kidneys are functioning normally. To avoid infection, hair in and around the patient's groins is shaved before the procedure. The patient is admitted in a hospital on the night before or on the morning of the angiogram and is advised to take nothing by mouth for 4-6 hours before the procedure. In most situations, angiograms are done under local anesthesia. However, in cases of small children or adults who are unable to cooperate or in altered sate of consciousness, the procedure may be done under deep sedation or even general anesthesia. The moment the patient enters an angiogram room, the patient will see a bewildering array of equipment. There will also a be 5-6 persons including nurses, technicians, orderlies and of course the radiologist. To avoid infection, the angiogram is performed with care as in an operation theater. The patient is made to lie down on the x-ray table and an intravenous saline infusion is started. The radiologist then anesthetizes the area, often groin, through which the angiogram is to be done (mostly on the right side; sometimes the left and occasionally both sides). The local anesthetic is injected with a very fine needle following which the blood vessel in the groin is punctured and a catheter inserted. Guided by x ray control, the catheter is then nudged into the desired blood vessel and a suitable contrast medium injected. X radiographs are taken to picture the path of the contrast medium. During the actual injection of the contrast medium, for 5-10 seconds, the patient will feel varying degrees of warmth in the area being injected and rarely even mild pain. If non-ionic contrast media are injected, there is no warmth or pain. An average angiogram lasts between 30 and 90 minutes. After the angiogram is finished, the catheter will be taken out and pressure will be applied on the puncture site to stop bleeding. This will last 5-10 minutes and is mildly painful. The patient will then be sent back to the hospital room. The patient should not move from bed or move the limb through which the angiogram has been done for at least 6 hours. Some radiologists may recommend bed rest for up to 24 hours. Rare instances of bleeding from the puncture site are stopped by application of firm pressure and further medical attention. The patient will be allowed to take fluids after about 2 hours of the angiogram and then solids a couple of hours later. Thus an angiogram is a minor procedure, entails hospitalisation for 12-24 hours, and is mildly painful and generally risk-free. The array of equipment and clutter of the instruments in the room where angiogram is done, may unnerve a patient and hence care is usually taken to reassure the patient. A venogram is a much simpler procedure, usually done without catheterization. Normally it is done for lower limb varicose veins and an intravenous injection of contrast medium is made in the foot and multiple x rays are obtained. The procedure is minimally painful. The procedure lasts about 15 minutes and the patient can resume normal activities immediately thereafter.



A brain angiogram is seen above.

Interventional radiology are procedures where X- ray guidance is used not just for diagnosis but also for treatment. Some examples are:

***Ángioplasty , Stenting, Embolisation***

Angioplasty is a procedure in which blocked blood vessels are opened up using catheters. In balloon angioplasty, this is achieved by expanding a balloon attached to the end of the catheter after localizing it at the right place where the block is present. Stenting is a step further to balloon angioplasty and is done to prevent the vessel from collapsing/getting blocked again after the balloon is withdrawn. A metallic stent is placed at the blocked site to hold the vessel in open position. Embolisation is entirely different and here, abnormal or leaking blood vessels are closed with substances introduced through catheters. These and similar procedures where the radiologist treats diseases of blood vessels and other organs is known as interventional radiology and are generally performed as an alternative to surgery or in some cases as the only form of treatment where no surgery is possible. These procedures are similar to an angiogram in most respects. The main difference is - whereas an angiogram is used to diagnose blood vessel disease, angioplasty and embolisation are used to treat diseases of blood vessels or the organ that these blood vessels supply (brain, kidney, liver etc). In these procedures, catheterization is similar to that of angiography. However, depending upon the specific area being treated and the specific condition for which the procedure is done, there will be variation in the technique, procedure time and complications. As the indications and the scope of these procedures are very vast, it is very difficult to generalize.

Hysterosalpingography (HSG) is done to visualize the female reproductive system, namely, uterus & fallopian tubes usually in infertility. The procedure is usually done on the $9^{th}$ or $10^{th}$ day of the menstrual cycle when the chances that the patient may have conceived are the least. The procedure is done without anesthesia; some patients may need some pain killers during the procedure as some may experience moderate pain. The procedure involves cannulation of the cervix under direct vision with a cervical cannula & injection of radio-opaque contrast media into the uterus. Then multiple x-rays are taken to record the flow of contrast into the uterus and the tubes. The procedure lasts about 30 minutes; patients may have some pain for a few hours after the procedure; but usually resume normal activities immediately thereafter. Patients may be asked to take a course of oral antibiotics after the procedure.

X-ray mammography is another procedure commonly used since the early 1970s. It is considered the gold standard in screening and breast cancer diagnosis. Mammography can detect approximately 85% of breast cancers and is the only FDA approved screening tool to help detect cancer in women with no signs or symptoms of the disease. However, mammography can miss up to 15% of breast cancers. A number of adjunctive tools including ultrasound, magnetic resonance and nuclear medicine have been developed to assist in determining when a breast biopsy may be used in conjunction with mammography. T-scan breast imaging is a promising new development in breast cancer diagnosis. T-scan imaging, used in conjunction with mammography, may be more sensitive than mammography alone.

*Safety Aspects*

Medical irradiation is by far the largest man-made contribution to the radiation burden of the population; for example, a study of the average annual dose to the UK population reveals over 90% of radiation dose from artificial sources is due to medical examination.

The scientific unit of measurement for radiation dose, commonly referred to as effective dose, is the . Other radiation dose measurement units include rad, rem, roentgen, and sievert.

Because different tissues and organs have varying sensitivity to radiation exposure, the actual dose to different parts of the body from an x-ray procedure varies. The term effective dose is used when referring to the dose averaged over the entire body.

The effective dose accounts for the relative sensitivities of the different tissues exposed. More importantly, it allows for quantification of risk and comparison to more familiar sources of exposure that range from natural background radiation to radiographic medical procedures

As practiced today, X-ray examinations are very safe. With improvement in the quality of the equipment used and radiation protection standards, no patient (with the exceptions described below) should avoid having a radiological examination for fear of harm by radiation. There are however, a few situations where X-ray examinations may be more harmful. For example - in young patients - whether they are boys or girls, additional protective measures will be taken by the patient's radiologist to protect their reproductive organs. X-ray examinations performed during pregnancy may have adverse effects on the unborn child. This includes malformations of the fetus and increasing chances of childhood leukemia. These risks are maximal in the first three months of pregnancy and decrease substantially during late pregnancy. Therefore, in pregnancy, an X-ray examination will not be advised unless it is absolutely essential. Radiation produced by CT scans is the same as for x-rays and rules are essentially the same as mentioned above for X-rays.

# Principles of Imaging using X-ray Computed Tomography and the salient features in Diagnosis

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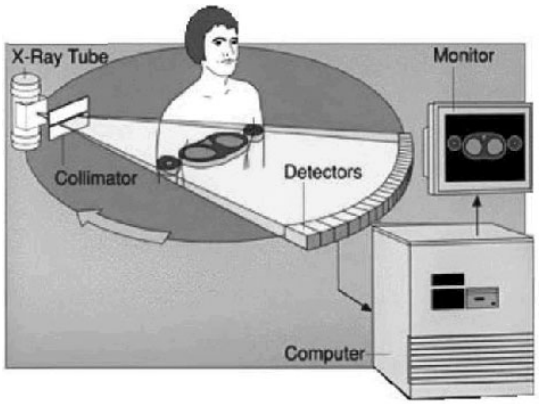
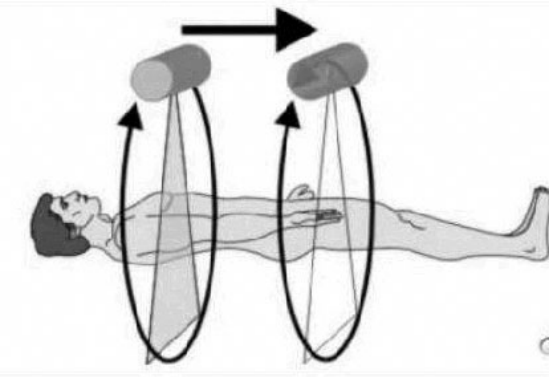
Computed tomography (CT) is a medical imaging technique that uses x-rays to produce images of thin slices of any part of the body.

**Data Acquisition**

The patient lies on a motorized table that positions the patient within the CT gantry. The gantry is a large ring surrounding the patient. It contains the x-ray tube and the x-ray detectors. During a CT scan the x-ray tube makes a complete rotation around the patient, typically in 1 to 2 seconds. The x-ray beam is restricted (or collimated) to the slice of the body being imaged and fans out over a wide enough angle to encompass the entire width of the body. At any instant of time during the scan, this flat beam of x-rays is attenuated by the



*Principle of conventional CT scan*

body: different parts of the beam are attenuated by varying amounts, depending on the types and amounts of tissues the x-rays pass through. Bone, for example, attenuates the x-rays more than does soft tissue like fat or muscle. Once the different parts of the x-ray beam pass through the patient, their remaining intensity is measured by an arc of about 500 x-ray detectors. These x-ray measurements by the detectors are repeated hundreds of times during the scan as the x-ray tube shoots x-rays through the patient at different angles. The x-ray detectors produce electronic pulses proportional to the x-ray intensity they receive. These hundreds of thousands of data pulses, from different detectors and at different positions of the x-ray tube, are fed into a computer which uses them to form a digital image of the slice of the patient through which the x-rays passed.

To obtain images of successive slices of the body, the patient table is moved through the gantry as the x-ray tube makes successive rotations around the body. In this way an entire volume of the body can be imaged as a series of slices.

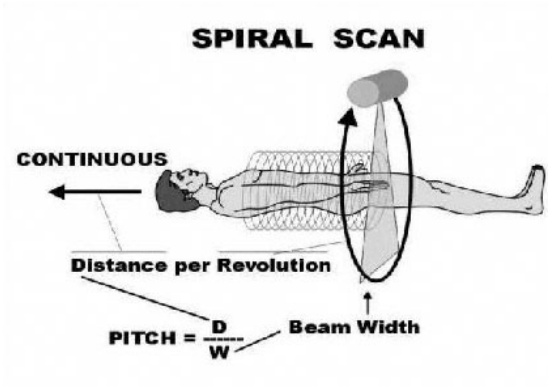
***The Evolution of Computed Tomography***

In April 1972 G. N. HOUNSFIELD, a senior research scientist at EMI Limited in Middlesex, England announced the invention of a revolutionary new imaging technique called COMPUTERIZED AXIAL TRANSVERSE SCANNING, now referred to as COMPUTED TOMOGRAPHY (CT).

Modern CT scanners fall into two basic types. With both types the tube rotates around the patient as x-ray data is collected. However, in a "rotate-rotate" or "third generation" CT scanner the detectors also rotate around the patient. The detectors subtend an arc sufficient to intercept all x-rays which pass through the patient, and about 500 detectors are required for a quality image.

In a "rotate-stationary" or "fourth generation" CT scanner the detectors are stationary and totally surround the patient. Only a fraction of the detectors see the attenuated x-rays that pass through the patient at any tube position; at least 4000 detectors are required in this case for a quality image at reasonable patient dose. Both third and fourth generation scanners are now being manufactured as state-of-the-art machines with comparable quality. Earlier, more primitive, CT scanners designs, the first and second generation types, have not been commercially produced for several years.

When computed tomography (CT) was first used in the mid-1970s, scan time was about 1 to 2 minutes and reconstruction time per slice (ie, per

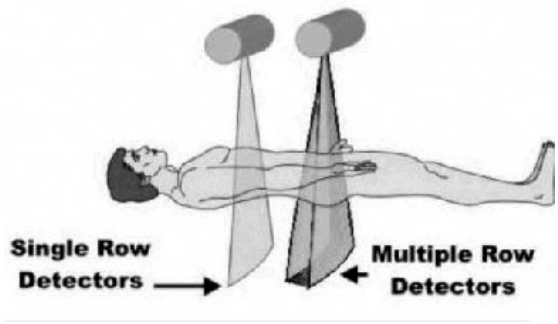



*Principle of helical CT scan*

cross-sectional image) was 1 to 5 minutes and resolution was limited. The 1990s have brought helical (spiral) scanning, another leap in CT technology. Conventional CT involved an x-ray source that was enclosed in a doughnut-shaped gantry, rotating clockwise around the patient in order to obtain a single transverse image. It then "unwinds" i.e. rotates anticlockwise to its starting position to prepare for another rotation and another scan. The patient was required to suspend respiration for each scan. Then, patient and operator had to wait for realignment of the table before the next scan could begin.

The advent of slip-ring technology in the 1990s enabled the x-ray source to rotate around the patient without having to unwind. In addition, more powerful computers and higher- energy x-ray tubes allowed a process known as helical CT, which consists of continuous activation of the x-ray source and continuous movement of the tabletop through the gantry, resulting in volumetric acquisition. In other words, whereas conventional CT required a stop-start maneuver to acquire a single slice, helical CT uses similar, but much faster and nonstop, technology to acquire multiple transverse slices and volumetric results.

These advances have revolutionized CT scanning. Thinner slices can be obtained, organs can be scanned in a single breath-holding period, and intravenous contrast agents can be used more appropriately.




***Features and Advantages of Helical CT***

Pitch is a new factor introduced with helical CT. It is defined as table speed (in mm/sec) divided by slice collimation (in mm) multiplied by the gantry rotation period. In other words, the rate of coverage over the long axis of the patient is directly related to table speed.

The major advantages of helical CT over conventional CT include a higher degree of lesion detection, better lesion characterization, reduction in volume of i. v. contrast material used as well as minimization of respiratory misregistration. The device's ability to scan the entire liver or thorax in a single breath-holding period prevents overlooking small lesions because of changes in their level between slice acquisitions due to respiratory movements. The radiation dose used is similar to or less than that used in conventional CT.

*Multislice CT*

The introduction of this new CT technique in 1998 was as revolutionary for the field of radiology as its original introduction in 1972. Multiple rows of detectors in Multislice CT allow very fast image acquisition with total body scanning times reduced to less than 30 seconds. This speed is beneficial when large segments of the body have to be scanned or image acquisition has to be fast to catch a dynamic event such as brain perfusion or CT angiography or cardiac CT. MSCT allows scanning with sub millimeter slice thickness producing ultra high resolution images, thereby allowing different types of post processing such as multiplanar reformats, volume rendering and surface shaded display of 3-D images.

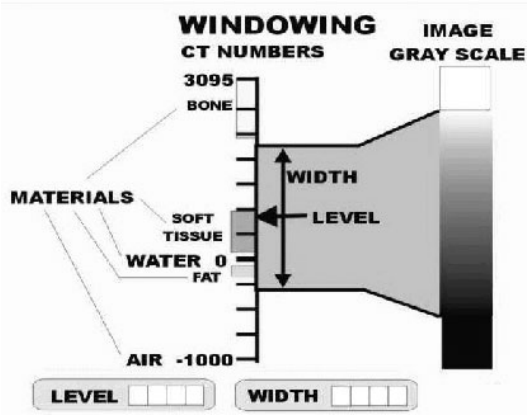



***Image Reconstruction***

The CT image is a cross-section of the body in which tissues which attenuate (absorb) the x-rays more strongly appear lighter (whiter) and tissues which are less attenuating appear darker (blacker). Since the following list is in order of increasing attenuation, it is also in order of increasing brightness in the CT image: bowel gas (black), lung tissue, fat, muscle, bone (whitest). The CT image is actually composed of a number of small boxes called pixels (short for "picture elements"). This "image matrix" usually has 512 pixels across and 512 pixels down. In creating the image, the computer assigns each pixel a number between -1000 and about +3000. This is called the pixel's CT number.

The CT numbers for various elements in the human body are:

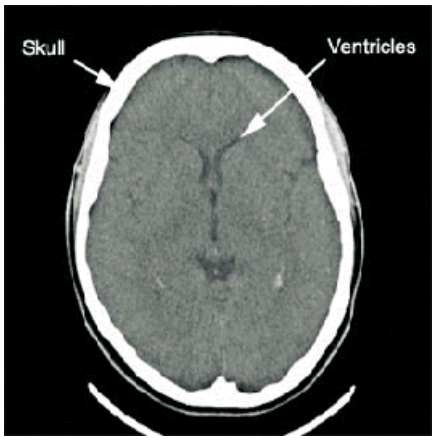
- Air (-1000)
- Water (0)
- Fat (-20 to -100)
- Muscle (+40 to +60)
- Dense bone (+1000)

The larger the CT number the greater the attenuation of the tissue represented within that pixel and the brighter that pixel will appear in the image. By definition, the CT operator can control the precise manner in which the image matrix of CT numbers is displayed by adjusting the image display window settings, thus making the image brighter or darker with greater or lesser contrast. During the imaging process the patient can be intravenously injected with an organic substance containing iodine that strongly attenuates x-rays. Blood vessels containing this "contrast material", and tissues that take it up, become more attenuating and will appear brighter (whiter) in the CT image. This technique is often used to visualize tumors which are more vascular than normal tissue. A similar type of contrast material can be given to the patient orally to better define the esophagus, stomach, small bowel, and colon. As the internal surfaces of these hollow organs become coated with the contrast material, or these organs become filled with the material, they will appear brighter (whiter) in the CT image.

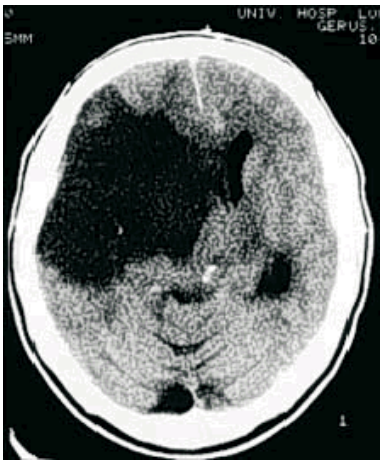
**Clinical Applications of CT scan**

CT morphology and identification of attenuation values (CT numbers) within an organ or mass may determine diagnosis, while CT guidance is widely used for needle biopsy of solid masses as well as aspiration and drainage of fluid collections or abscesses. In the staging of malignant disease, CT provides important information for the surgeon, oncologist and is routinely used in the planning of radiotherapy treatment. A single CT examination can provide information vital for diagnosis and staging of cancer, such as:

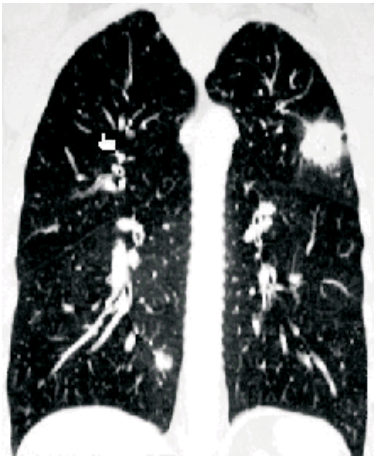
- Size and extent of primary tumour
- Direct invasion of adjacent organs by the tumour
- Spread of cancer to distant sites-lymph nodes, lungs, liver, bone, etc. through the lymphatics or blood stream..




*CT scan of normal brain.*




*CT scan of a brain infarct*



*Bronchogenic carcinoma in upper lobe of left lung*

***Scanning the Head and Neck***

CT of the brain can assist in locating skull fractures and brain damage in patients with head injuries, detecting an infarct or bleed within the brain shortly after a patient exhibits symptoms of a stroke, detecting brain tumors and planning radiation therapy in malignant neoplams, detecting congenital diseases or malformations of the brain and skull as well as evaluating parenchymal and meningeal infections. It is also useful in guiding the passage of a needle used to obtain a tissue sample (biopsy) from the brain.

CT also helps in diagnosing diseases of the temporal bone and inner ear structures, orbits, paranasal sinuses, larynx and soft tissues of the neck. The information obtained by scanning these organs is often vitally important for planning surgery.

**Scanning the Thorax**

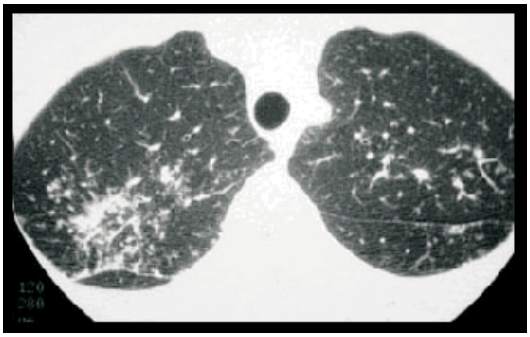
Cross sectional imaging of the thorax using CT provides a simple, non invasive demonstration of all the structures of the thorax. It can often identify confusing superimposed shadows seen on the plain film chest radiograph. It is recognized primarily as an accepted technique to provide diagnosis, differentiation and staging of pulmonary, pleural and mediastinal disease.

Helical CT's ability to scan the thorax during a single breath-holding period has improved quantification of metastatic nodules, characterization of solitary pulmonary nodules, and densitometric assessment of nodules for subtle calcification or fat (which indicates a benign process). Scanning the thorax during peak pulmonary arterial enhancement via injection of contrast material in the peripheral venous system allows direct assessment for pulmonary emboli in a relatively noninvasive manner. CT scans have been shown to pick up small lung cancers and pulmonary metastatic nodules even when they are not visible on the conventional chest X-ray, and hence is often used to look for lung disease even when the chest X-ray is normal, whenever there is high clinical index of suspicion for lung disease, or to conclusively rule out pulmonary metastases in cancer patients.

Another application of helical CT in the thorax is 3-D visualization of the airways. After rapid data acquisition through the region of the major airways, computer post-processing is used to produce a 3-D surface display of the trachea and bronchi. "Virtual bronchoscopy," is a noninvasive form of endoscopy in which strictures and other anomalies can be visualized in a video format.

In practice, although helical scanning has become routine for CT imaging of thorax, there are a few instances where conventional CT may still be preferred and these are listed below:

- High Resolution CT (HRCT) for detailed imaging of lung parenchyma (interstitial lung



*High resolution CT of the chest in interstitial lung disease*

disease, bronchiectasis, airway disease) and differentiation of pulmonary nodules and focal lung disease, using very thin 1 mm sections with a high resolution algorithm for reconstruction of images

- Biopsy, aspiration and drainage of lung nodules and pleural fluid collections
- Radiotherapy planning

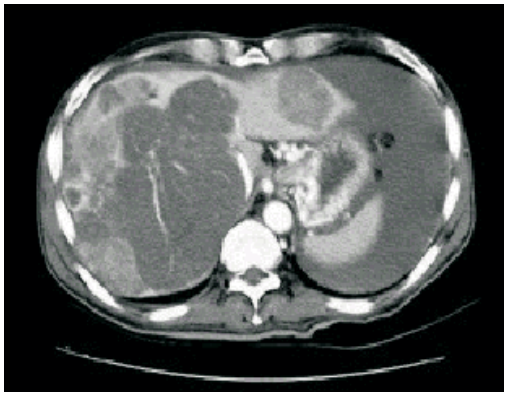
**Scanning the Abdomen and Pelvis**

***Hepatobiliary System***

The hepatobiliary system is well evaluated on CT. Primary and metastatic disease, infective processes, hematomas, cysts in the liver as well as gall bladder pathologies are well depicted.

The ability of helical CT to scan rapidly allows it to obtain thinner slices and acquire images of the liver during appropriate phases of contrast injection. Whereas conventional scanners required 1.5 to 2.5 minutes to scan the entire liver, helical scanners routinely do so in 15 to 25 seconds.

An initial helical acquisition through the liver is obtained during the arterial phase at 20 to 25 seconds and the second helical acquisition during the portal venous phase at 60 to 70 seconds after intravenous contrast injection. Since 70% to 80% of the blood supply to the liver is through the portal venous blood flow, scanning during the arterial phase enables selective enhancement of vascular tumors which are fed by the hepatic artery. For example, adding arterial-phase CT to routine portal



*CT scan of abdomen in a case of hepatocellular carcinoma*

venous-phase CT in imaging of hepatocellular carcinoma has significantly increased detection and conspicuity of tumor foci. Arterial-phase enhancement of liver lesions also improves specificity by differentiating malignant from benign liver nodules in the cirrhotic liver.

***Pancreas, Spleen and adrenals***

CT is useful in evaluating acute and chronic pancreatitis and its complications as well as in diagnosis and staging of pancreatic tumours. It is the modality of choice in splenic trauma. CT assists in diagnosis of adenomas, metastasis and infections in the spleen and adrenals.

***Urinary Tract***

Indications include assessment of renal masses and differentiation of solid and cystic lesions, tumor staging and surgical planning, renal trauma and renal infections.

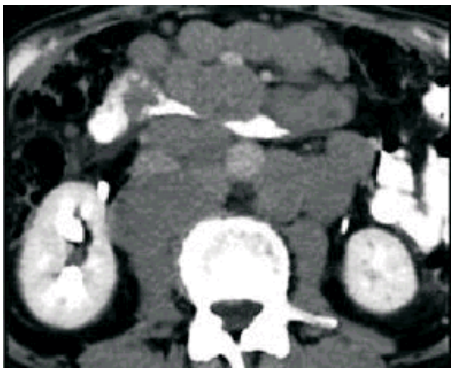
An exciting recent development in helical CT is establishment of protocols for investigating renal colic. Unenhanced CT scanning can be performed quickly (30 to 40 seconds) and is highly accurate in identifying stones in the kidneys or ureters, perhaps more so than the intravenous pyelogram, traditionally considered the "gold standard" for this indication. In addition, unenhanced helical CT requires no contrast material and therefore avoids the remote yet potential risk of allergic reaction to contrast material carried by the standard intravenous pyelogram.

***Pelvis***

CT is useful in staging and diagnosing pelvic carcinomas, vascular pathologies, fluid collections, abscesses and evaluating the bony pelvis.

***Lymph Nodes***

CT is an ideal modality in evaluating lymphadenopathy. Lymph nodal enlargement can be due to metastatic carcinoma, malignant lymphoma, sarcoidosis, tuberculosis or fungal infection.



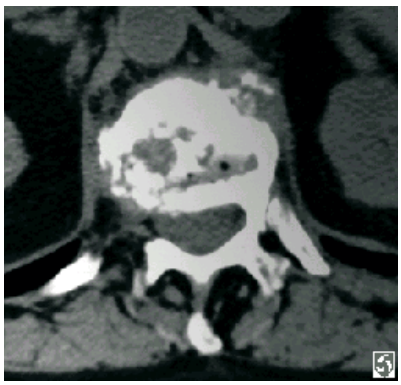
*CT scan in a case of malignant lymphoma*

***Gastrointestinal Tract***

Helical CT can visualize intraluminal, intramural and extra luminal components of the gastrointestinal tract and allows accurate diagnosis of appendicitis, diverticulitis and helps in staging neoplasms. Normally, these conditions can be diagnosed on clinical grounds, but when findings are unclear or complications (eg, abscess, free bowel perforation) are suspected, CT might be indicated. Meticulous attention to technique is required for CT diagnosis of appendicitis and diverticulitis using oral, rectal and intravenous contrast material. CT can establish or rule out other causes of pelvic pain. Compared with barium enema evaluation, CT has the distinct advantage of enabling visualization of intramural and extramural extent of disease.

***Scanning the Spine***

The imaging modality of choice for majority of spinal conditions is Magnetic Resonance Imaging or MRI. However CT is still preferred for patients who cannot tolerate the narrow tunnel found in most MRI scanners, those who are just too large to fit into the MR scanner or those who have implanted metallic prosthesis or cardiac pacemakers in which cases MR is contraindicated. CT is essential for imaging of bones in cases of spinal fractures due to trauma, for visualization of foraminal stenosis, particularly in the cervical region. Spinal biopsy and preoperative spinal marking are some other indications for CT.

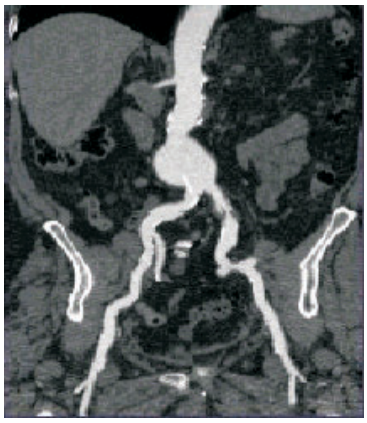


*Vertebral body destruction on CT scan of spine*

**Scanning the Vascular System**

CT angiography is a revolutionary non-invasive method to assess the arteries and veins in the vascular tree. This study can be performed with helical scanners by injecting 100 to 150 ml of contrast material into the peripheral venous system and rapidly scanning the area of interest during the arterial phase. Computer manipulation and editing of the data set produce a 3-D angiographic display. The 3-D model can display maximum pixel values (intravascular contrast agents and bone), known as maximum intensity projections, or it can display the external contour (ie, the shaded surface display) of the structure in question. In video format, models can be rotated 360°; by means of computer manipulation using a mouse, real-time interaction is possible.

Clinical applications for CT angiography include preoperative planning in potential renal donors, preoperative assessment of aortic and other aneurysms for both surgery and stent insertion, diagnosis and follow-up of aortic dissections, screening for and diagnosis of renal artery stenosis, and use in many other areas that have traditionally been the domain of standard angiography. CT is



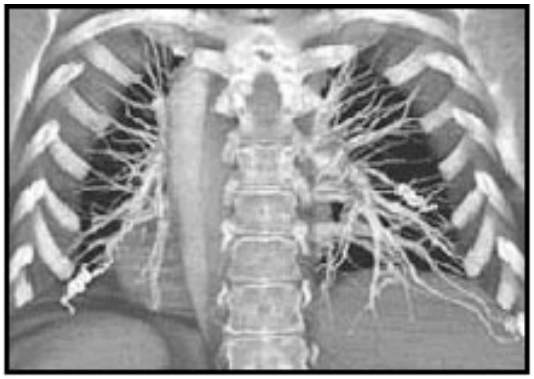
*CT angiography demonstrating an aortic aneurysm*

ideally suited for the postoperative evaluation of aortic stents, assessing both patency and any extravasations of contrast into the aneurysm sac. It is less invasive and more accurate at predicting aneurysm size and better at demonstrating thrombosis, inflammatory aneurysms and retroperitoneal bleeding or coexistent pathology.

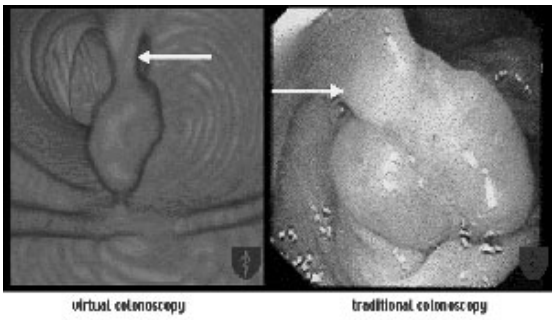
**Newer Advances**

Rapid advances in technology are enabling dozens of newer clinical applications, including:

- CT imaging of the heart and coronary arteries to screen for signs of early heart disease
- CT-PET hybrid combining positron emission tomography with CT scan
- Blood flow imaging (CT Perfusion) in the brain to diagnose stroke or brain tumours
- Sophisticated 3-D volume rendering of the bones and soft-tissue organs
- 3-D and virtual reality imaging of the interior of the colon and the lung (virtual colonoscopy and bronchoscopy )



*Surface shaded display of the thorax*




*A benign polyp detected on CT colonscopy*

**Conclusion**

In the last several years, CT has evolved rapidly into an important tool in evaluation of complex disease processes, while use of intravenous pyelography, barium studies, invasive diagnostic angiography, and some plain-film radiography has undergone a corresponding decline. The inherent high sensitivity of optimal-quality CT and widespread availability of the technique probably account for much of the increase in use.

The relationship between clinicians and radiologists also has experienced dramatic changes in recent years. In today's healthcare climate, referring physicians probably should make better use of radiologists' triage skills early in the consultation process, in addition to seeking their expertise in interpreting the final images. Nurturing a team approach between radiologist and primary care physician by increasing communication is sure to enhance patient care.

# Diagnostic Nuclear Medicine

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**Introduction**

This nascent branch of medicine had its origin around 50 years ago and is now a vibrant medical specialty for both diagnosis and therapy of various disorders.

The origin of nuclear medicine stems from many scientific discoveries, most notably the discovery of x-rays in 1895 and the discovery of "artificial radioactivity" in the mid-1930s. A landmark event for nuclear medicine occurred in 1946 when a thyroid cancer patient's treatment with radioactive iodine led to complete disappearance of the patient's cancer. Wide-spread clinical use of nuclear medicine, started in the early 1950s as its use increased to measure the function of the thyroid and to diagnose thyroid disease and for the treatment of patients with hyperthyroidism.

During the mid 1960s, the use of nuclear medicine as a specialty discipline began to see exciting growth with significant advances in nuclear medicine technology. The 1970s brought the visualization of additional organs (besides the thyroid) with nuclear medicine, including liver and spleen scanning, brain tumor localization, and studies of the gastrointestinal tract. The 1980s saw the use of nuclear medicine for diagnosing heart disease as well as the integration of digital computers to add additional power to the technique. Today, there are approximately 100 different nuclear medicine imaging procedures which provide information about nearly every organ system. Nuclear medicine is now an integral part of patient care and is extremely valuable in the early diagnosis, treatment and prevention of numerous medical conditions. The other major event was introduction of FDG-PET in the routine clinical management which made a revolutionary impact in all systems in general and oncology in particular.

Nuclear medicine imaging mainly focuses on the organ function. This information provides insight into the organ dysfunction. This is due to the fact that the radionuclides are absorbed by or taken up at varying rates by different tissue types. For instance, the thyroid gland specifically takes up radioactive iodine because of the presence sodium iodide symporters on thyroid follicular cells and this has been successfully exploited in diagnosis as well as targeted treatment of various thyroid disorders with $^{131}I$ e.g. thyrotoxicosis and carcinoma thyroid. Nuclear medicine uses unsealed radioactive substances for in vitro and in vivo diagnosis.

While nuclear medicine images may show less detail (spatial resolution) than other types of imaging, the functional information they provide can be valuable (and in some cases, may not be available from other types of imaging. A diseased or poorly functioning tissue will emit a different signal than healthy tissue, thus giving the physician an indication of how the tissue or organ is functioning. For example, infection of bone results in increased cellular activity of bone tissue, causing radionuclides to be taken up in greater amounts by diseased bone. Thus the functional image of the bone may show the disease sooner than the anatomic image provided by an x-ray or CT scan.

Organ specific radiopharmaceuticals can be labelled with suitable radionuclides for imaging eg diphosphonates can be tagged with $^{99m}Tc$ for

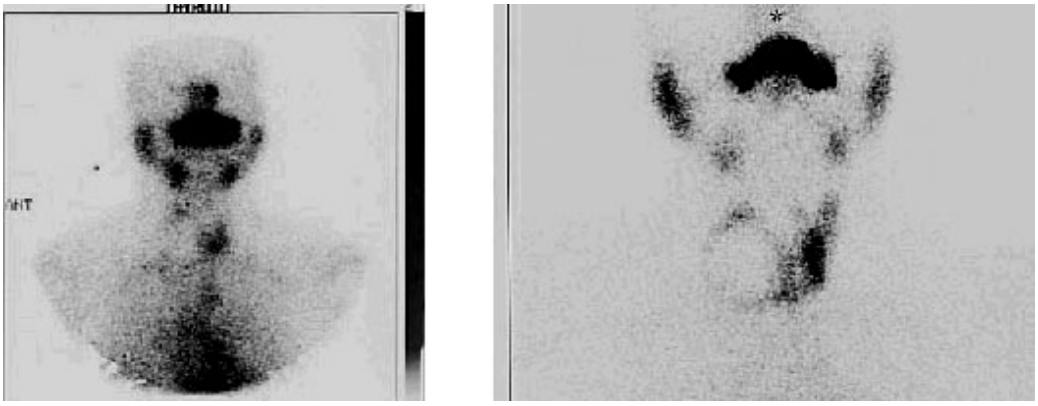


*Fig. 1* *$^{99m}TcO_4$ thyroid scan showing cold right solitory thyroid nodule*

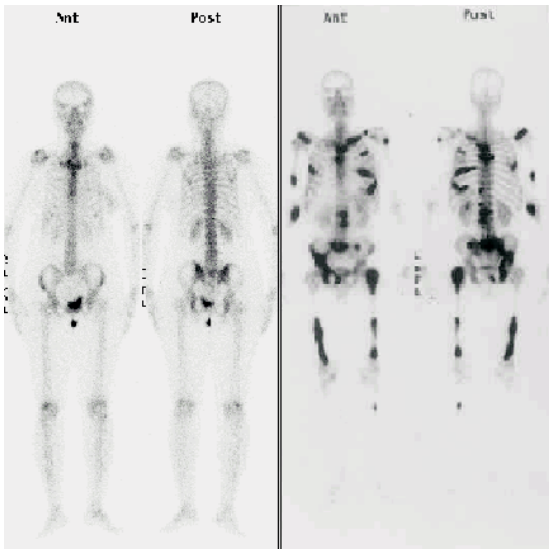



*Fig. 2* *Showing normal bone scan on left side and abnormal (multiple skeletal metastasis) bone scan on right side*

imaging skeleton. A single injection of $^{99m}$Tc-MDP can give us the image of the whole of skeleton as seen in Fig. 2. In whole body bone scan areas of increased activity (called "hotspots") represent disease or injury (pathology). Skeletal metastasis can be identified at very early stage compared to anatomical imaging modalities.

$^{99m}$Tc is the radionuclide of choice in the field of diagnostic nuclear medicine because most of the organ specific radiopharmaceuticals can be tagged with it for imaging. Examples of radiopharmaceuticals which can be labelled with $^{99m}$Tc are MIBI, tetrofosmin (for myocardial perfusion), RBC's (for MUGA, hamengioma in the liver and GI bleeding), mebrofenin (for hepatobiliary function), DTPA (for renal perfusion, cortical function and drainage), DMSA (for renal cortical defects and medullary carcinoma), sulphur colloid (for RE cells function in liver), ECD and HMPAO (for cerebral perfusion), and macroaggregated albumin (for lung perfusion) etc.

Coronary artery disease (CAD) is a major disease in today's world and there is a need to know the impact of CAD on myocardial perfusion and function because of its high mortality. By nuclear medicine techniques myocardial perfusion and function can be assessed using $^{201}$Tl or $^{99m}$Tc-MIBI, $^{99m}$Tc-tetrofosmin (Fig.3). This study gives us the information on myocardial perfusion, wall motion (Fig.4), wall thickening, global and regional LV function. This information is utilised by the cardiologist for the management of patients with heart disease. The commonest conditions for which this test is done are

- To improve the sensitivity and specificity of exercise stress testing combined with electrocardiography.
- To assess myocardial ischemia in-patients who are unable to exercise.
- To evaluate the physiologic significance of anatomic lesions detected on coronary angiography.

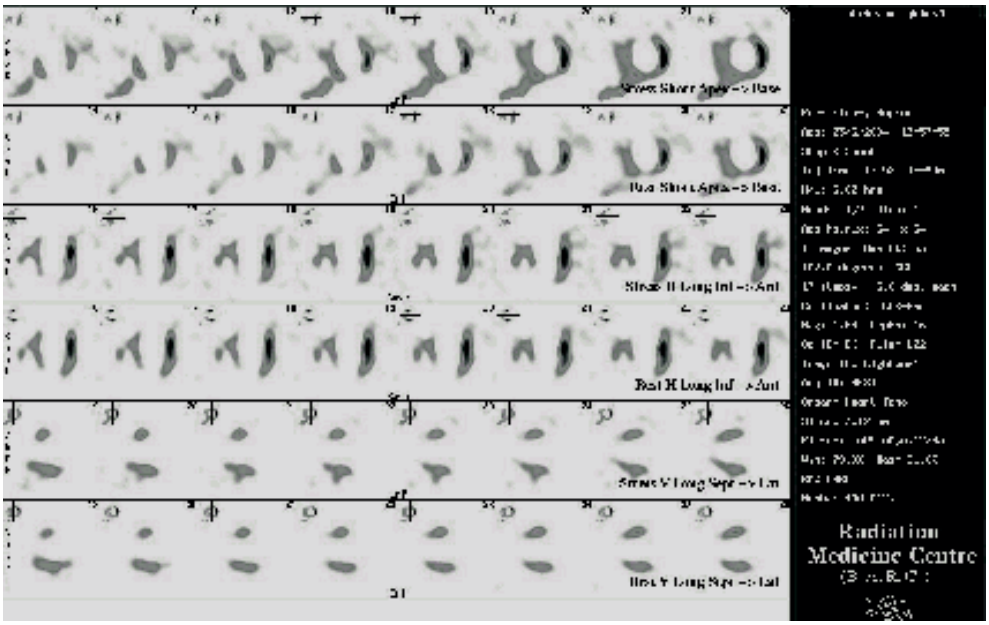



*Fig. 3 Showing dilated left ventricle with extensive infarction in apex, anterior, septal and infero-apical segments of the myocardium without any significant peri- infarct ischemia.*

- To evaluate patients after revascularization, especially those with recurrent chest pain
- To evaluate patients with chest pain who are stable
- To risk stratify patients with known coronary artery disease, especially post-infarction patients or those in the stable phases.

The central nervous system imaging has evolved in the last 1-2 decades. Earlier the blood brain barrier abnormalities was the basis of conventional brain scanning as most intracranial lesions will alter the blood-brain barrier, and the radiopharmaceutical will leak from the capillaries into or around the lesion. The lesion appears as a "hot spot" in the normal low background of the brain (Fig. 5). A conventional brain scan includes a dynamic flow scan, followed by immediate static images and after a 4-hour delay in images in anterior, posterior, and both lateral projections.

In recent times cerebral perfusion can be imaged using $^{99m}$Tc-HMPAO and $^{99m}$Tc-ECD which are newer lipophilic chelate radiopharmaceuticals. They have a high extraction fraction and are taken up by the brain proportionally to perfusion. There is a very stable pattern of uptake within a few minutes and slow or no washout from the brain overtime (Fig. 6).

Cerebral uptake of $^{99m}$Tc-HMPAO correlates well with cerebral perfusion measured with labeled microspheres up to 200 ml / 100 g / min. cerebrovascular reserve can be assessed in both pre and post actezolamide conditions which is important in patients with carotid stenosis who are at risk of developing cerebral ischemic events. Another area in which cerebral perfusion imaging can play a role is in epilepsy where in a focus of epilepsy can be identified by ictal scan (hyperperfusion) or interictal scan (hypoperfusion). In the field of psychiatry pattern of cerebral perfusion can tell us the cause of dementias which will guide the psychiatrist for management.

There are diverse radionuclide imaging procedures available for studying the morphology and function of the gastrointestinal (GI) tract.

Although the details of anatomic alterations are demonstrated more reliably by conventional radiographic techniques such as computed

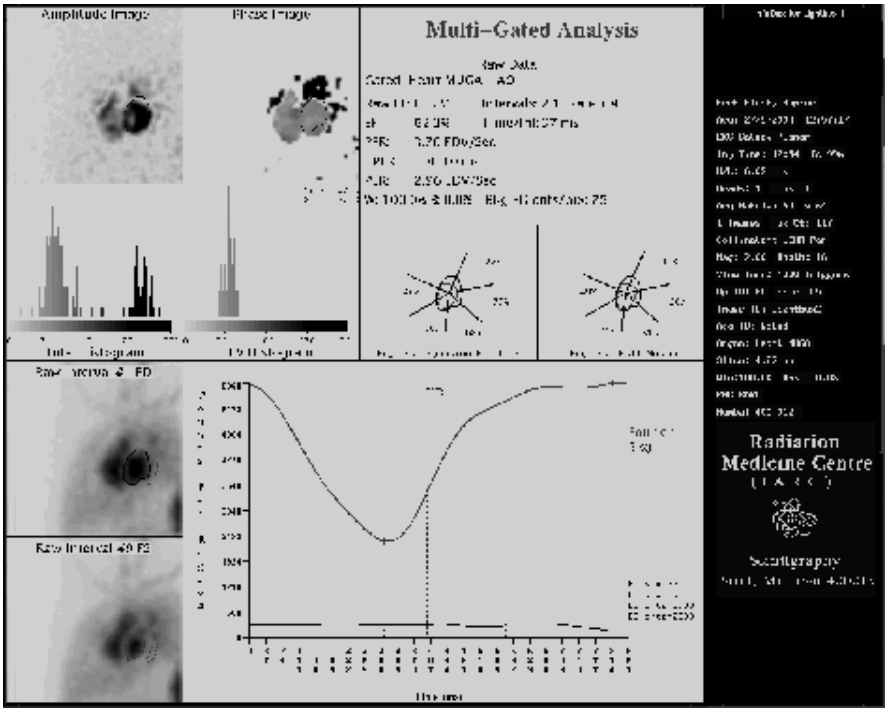



*Fig. 4* $^{99m}$*Tc-RBC scan showing normal LVEF and myocardial wall motion*

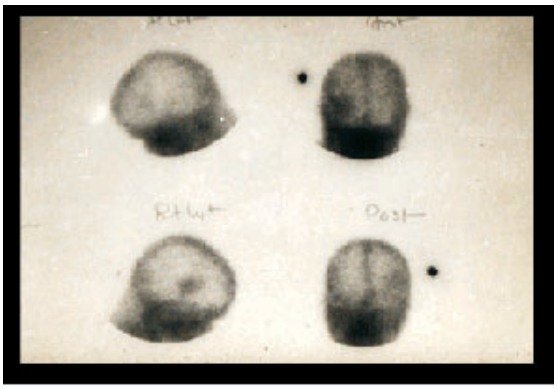


*Fig. 5 Conventional brain scan using* $^{99m}TcO_4$ *shows metastasis in the right parietal region*

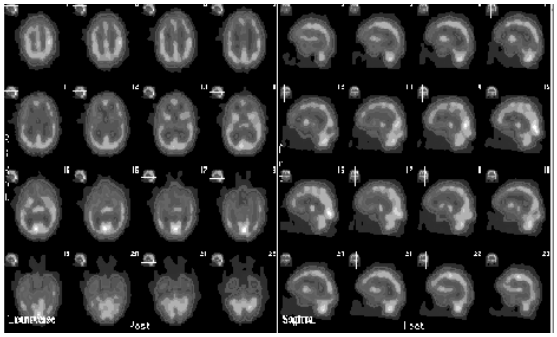


*Fig. 6* $^{99m}$*Tc-ECD scan showing normal cerebral perfusion*

tomography (CT), ultrasound, and magnetic resonance imaging (MRI). Radionuclide scintigraphy remains a unique and noninvasive modality with quantitative capabilities for the evaluation of equally important functional disorders of the GI tract.

Hepatic scintigraphy using different radiopharmaceuticals is based on different physiologic mechanisms that provide information about morphology and function. There are different types of radionuclide hepatic imaging techniques currently in use.

Patients with biliary dyskinesis usually present with right upper quadrant discomfort. The

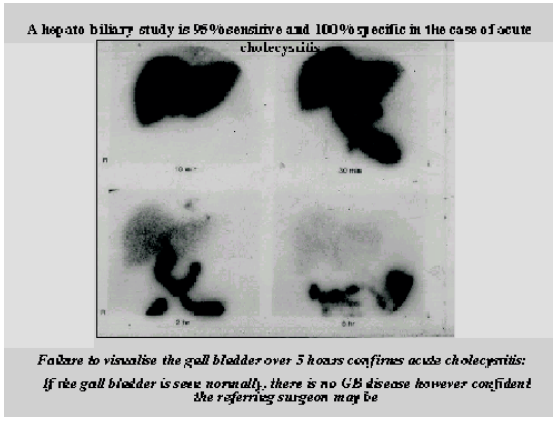



*Fig. 7 Hepatobiliary scan confirming the diagnosis of acute cholecystitis*

differentiation of acute cholycystitis from other gastric disorders can easily be done with $^{99m}$Tc-mebrofenin hepatobiliary scan. On injection of $^{99m}$Tc- mebrofenin intravenously is quickly taken up by hepatocytes, which then rapidly excrete it without conjugation into the bile canaliculi and subsequently in to the gut and gall bladder within 30-45 minutes (Fig. 7). Visualisation of gall bladder within 1 hour of injection rules out acute cholycystitis. In such patients, scintigraphy provides valuable diagnostic information, which aids in the management of patients.

Other conditions where in mebrofenin scan is commonly used, is the pediatric nuclear medicine for confirming the diagnosis of biliary atresia.

The best methos to evaluate reticuloendothelial cells noninvasively is by intravenous injection of $^{99m}$Tc-sulfur colloid; the colloid particles are phagocytized by the reticuloendothelial cells normally distributed in the liver (Kupffer's cells, 85%), spleen (10%) and bone marrow (5%). In the case of diffuse liver disease most of the RE cells of liver are damaged and hence there is a colloid shift to spleen and bone marrow which not only confirms the diagnosis of chronic diffuse liver disease but can also help in prognostication (Fig. 8,9).

Esophageal transit scintigraphy is an easily performed procedure for the evaluation of esophageal dysmotility. The test is useful in evaluating dysphagia and atypical chest pain and

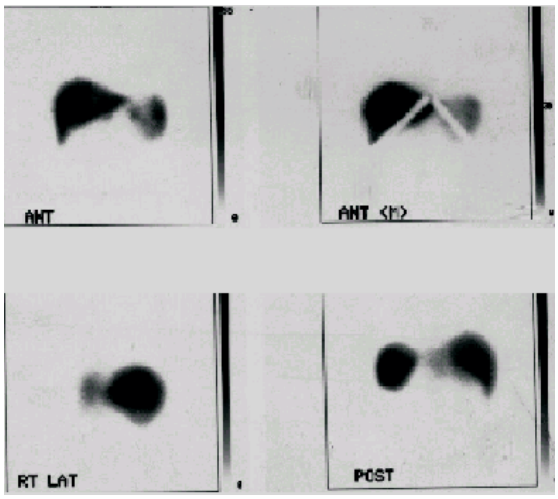



*Fig. 8 Colloid scan normally functioning RE cells of the liver (normal liver scan)*

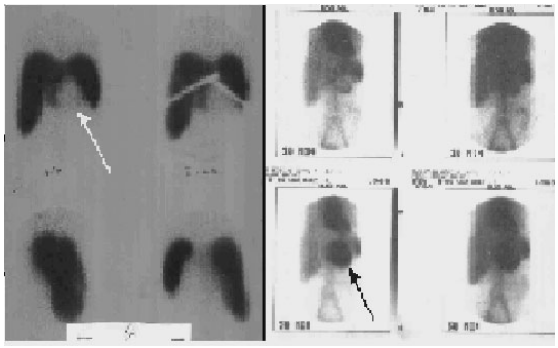


*Fig. 9 On the left is the colloid scan showing a large cold area in the left lobe of the liver and on the right is the $^{99m}$Tc-RBC scan showing gradually filling and retaining the tracer confirming the diagnosis of haemengioma*

assessing the response to medical or surgical treatment of achalasis and scleroderma (Fig.10).

Gastrointestinal reflux scintigraphy is a physiologic noninvasive procedure for the detection and quantification of reflux in infants and adults.

Gastric emptying scintigraphy is a well-established procedure for the assessment of gastric motility disorders.

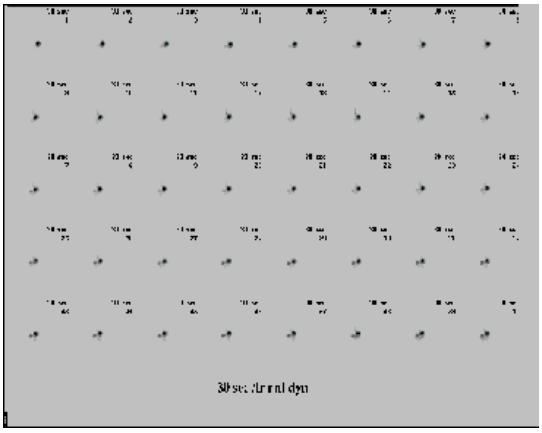


*Fig. 10 Milk scan positive for gastro-esophageal reflux*

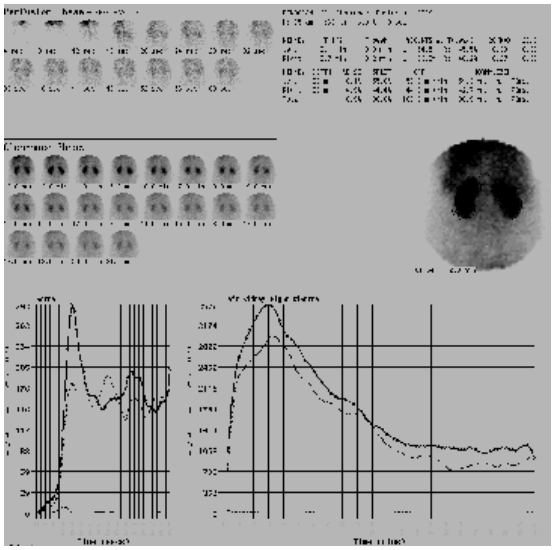


*Fig. 11 Normal $^{99m}$Tc-DTPA renogram showing normal perfusion, cortical function and drainage*

Scintigraphy of the abdominal blood pool following IV injection of the patient's RBCs tagged with $^{99m}$Tc is an established diagnostic and complementary technique to endoscopy and angiographhy for the detection of GI bleeding.

Abdominal scintigraphy with $^{99m}TcO_4$ is the technique of choice for the detection of ectopic gastricmucosa as the cause of GI bleeding. The most

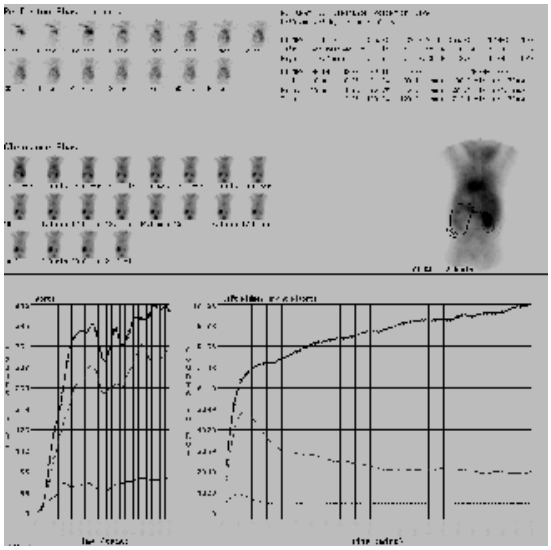


*Fig. 12 Abnormal $^{99m}$Tc-DTPA renogram showing left PUJ obsrtuction with retained cortical function.*

common site of ectopic mucosa is in a Meckel's diversification.

There are many radiopharmaceuticals available for renal scintigraphy. Selection of the radiopharmaceutical depends on the specific clinical question that is asked. Based on the mechanism of uptake, renal radiopharmaceuticals can be divided into three categories: glomerular, tubular, and cortical agents (Fig. 11,12). Commonly used radiopharmaceuticals in renal scintigraphy are DTPA, DMSA and EC labelled with $^{99m}$Tc.

Renal scintigraphy has been used in clinical nephrourology since the early 1960s. It provides functional and anatomic information, both closely related. Structural information, however, is limited. Functional information is quite unique. For example, a radionuclide study can separately measure renal function on each side (Fig.13).

Common indications of renal scintigraphy are assessment of renal perfusion, quantitation of renal function, haemodynamically significantly renovascular hypertension, pyelonephritis, urinary tract obstruction, renal transplantation, and acute renal failure. Also, radionuclide cystogram and scrotal scintigram have a well-established place in

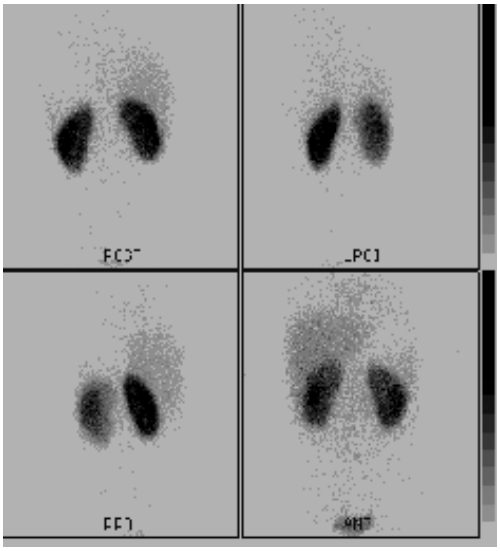


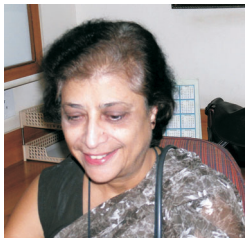
*Fig. 13* *$^{99m}$Tc DMSA renal scan showing normal renal cotrex (no cortical defects)*

detecting vesicoureteral reflux (VUR) and torsion Vs Epididymoorchitis, respectively.

**Conclusion**

From the above deliberations it can be seen that Nuclear Medicine, which use radiopharmaceuticals, is an excellent example of peaceful applications of radioisotopes and radiations. Diagnostic nuclear medicine has the special distinction of being able to give information both on the physiology as well as the function of the organ. This is possible because the accumulation of radiopharmaceuticals in the target organ depends on the function of the organ. Moreover, the possibility of carrying out imaging at various time points enable information on the dynamic functioning of organs such as liver, heart, kidneys etc. In some situations, nuclear medicine gives unequivocal information and this makes it an important tool in such situations.

# Diagnostic Nuclear Medicine : Basic principles and Applications of Positron Emission Tomography



*Dr.(Mrs.) Aban Samuel joined the Radiation Medicine Centre of BARC in 1966 and since then, served in the field of nuclear medicine till 2002. Dr.(Mrs.) Samuel was an outstanding scientist who headed the Radiation Medicine Centre from 1990 and became the Director of Bio-Medical Group from 1998. Dr.(Mrs.) Samuel has served as an IAEA expert in the field of Nuclear Medicine in many countries and has to her credit more than 250 papers in International and National journals. Dr.(Mrs.) Samuel is currently the Chairperson of decision making bodies such as the Radiopharmaceuticals Committee, Safety Committee for Nuclear Medicine Facilities. She also continues to be a senior member of several advisory committees. After a meritorious full term service in BARC, Dr. Mrs. Samuel continues to serve the society with her experience and knowledge as the consultant Nuclear Medicine Specialist at the Mandakini Imaging Centre, Chembur, Mumbai.*

**Introduction**

Nuclear medicine is a special branch of medicine where radiolabeled molecules are used for either diagnosis or therapy of diseases. Soon after the discovery of radioactivity around the end of last century, the radioactive elements were put to a variety of uses. Among these, the use of radioactive tracer by Dr. George de Hevesey could be considered to mark the beginning of Diagnostic Nuclear Medicine. However, only after the production of radionuclides artificially using charged particles as in cyclotrons or using neutrons as in nuclear reactors, this branch got the impetus to bloom into a speciality. The advances in counting systems, computing systems and the availability of a variety of radionuclides have aided the phenomenal growth of nuclear medicine in the past 50-60 years. A major milestone has been the advent of Positron Emission Tomography or popularly known as PET around 1980, where positron emitting radionuclides are employed to obtain tomographic pictures of the organs. In the past 2 decades, PET has been employed in a very large number of studies and has provided a vast knowledge that would otherwise have not been possible.

Radioisotopes being unstable isotopes of elements, transmute to emit radiations such as alpha, beta and gamma rays, of which the gamma rays are electromagnetic rays similar to Xrays in their properties. Just as X-rays, these too get attenuated depending on the density of the matter in its path. However, gamma ray emitting radionuclide can be tagged to a suitable molecule, introduced in the body and allowed to localize in an organ of interest before an image of that organ is taken. The significant difference between Radiography and use of radioisotopes known as Nuclear Medicine is that while the X-rays are produced in an X-ray machine and made to pass through the body from outside the patient, radioisotopes are given to the patient internally and detected by a gamma camera. It is called as a gamma camera because it can take pictures, like an ordinary camera, of the gamma rays that are coming out of the patient's body. Another very important difference is that the radioisotopes can be tagged on to a vast variety of chemicals. These can be selected so that the chemical is targeted to the organ, which is to be studied. Since the chemical is localized in the target organ it depends for localization on the special function of the organ and the amount of blood flowing to the organ. In this way not only is the anatomy or structure of the organ evaluated but also the function or physiology of the system. If there is a defect in the function or physiology this will be shown by the radiopharmaceutical (Radioisotope which is tagged on the special chemical). If there is an anatomical defect this too will be shown. Hence nuclear medicine works as a double-edged knife. It can show

an abnormal function and an anatomical defect of an organ. The other modalities such as CT, MRI, US etc. detect structural or anatomical defects. A combination of two –three or more tests may at times be needed to evaluate the problems in the patient.

**Trends in Nuclear Medicine**

Nuclear medicine, a unique discipline in medicine has evolved over the last 4 decades so rapidly that it has become a difficult task to keep abreast of the advances that are taking place at an exponential growth rate. Despite its great potential and useful applications in the diagnosis and management of patients it is still a relatively unknown entity. The unique contribution of this speciality is the ability to examine the dynamic state of body constituents as reflected in every organ of the body. The emissions of gamma photons, which can be measured by radiation detectors outside of the human body has enabled the study of regional function and its underlying biochemistry. In fact, the advances in this field are such that it may be necessary to change the term "Nuclear Medicine" to a more appropriate term, which will indicate the true potential of the discipline to "Molecular Medicine".

In future, measurement of 'in-vivo' chemistry will become commonplace. Molecules will be the targets of detection instead of cells, tissues and organs, in other words we will start looking inside the cells rather than at the cells. The use of radioactive tracers in medicine is comparable to the invention of the chemical balance and the discovery of X-rays. The tracer principle, that is, the monitoring of molecules that participate in the dynamic state of body constituents, led to a whole new approach to biology and medicine, characterizing the chemistry of growth, development, and maintenance of life in experimental animals and human beings. No other techniques have the sensitivity, specificity, and quantifiability in the study of in situ chemistry. No other field of medicine has a greater ability to define disease as a problem in coordinating and balancing the billions of chemical reactions involved in the normal function of cells and tissues in the body.

An important disease to be understood at the molecular level is cancer. The definition is wide ranging depending on which aspect of cancer one looks at. Whether it is the unruly and autonomous growth of the cells or the function and many other cellular and molecular aspects of the disease. However one such definition is the view that cancer is a communication disorder. Life is maintained because atoms and molecules can recognize each other. Radioactive tracers can be "molecules with messages" such as mRNA, then as hormones and neurotransmitters and message signals, information transfers, recognition of molecules by receptors, transporters of molecules, all of which has evolved from unicellular organisms as a means of facilitating intercellular molecular communication.

The expression of receptors on plasma membranes such as VIP {vasocative intestinal peptide} or somatostatin {SS}, and others can detect many types of cancers. Metabolic changes in cancers occur usually by virtue of up regulation of glycolytic pathway and increased expression of glucose transporter proteins allowing the study of this pathway by $^{18}$F-flurodeoxyglucose and PET imaging. Intensive studies on the GLUT 1-6 transporters and the inhibitors is under way so that appropriate compounds can be synthesised and used to detect the receptors on the plasma membrane of various cancers

Some other areas where nuclear medicine studies would help are in the differential diagnosis of certain disorders such as Parkinson's disease, myocardial infarction etc. In classical Parkinson's disease there is a deficiency of the dopaminergic presynaptic neurons, while in idiopathic Parkinson's disease the D1 and D2 receptors are normal and in striatonigral there is degeneration of postsynaptic neurons. This indicates that the drug therapy is to be tailored to the biochemical changes occurring in the diseases. Since the clinical manifestations of Parkinson's is related to the degree of the receptor deficiency, monoxidase inhibitors can be useful in the early stages of the disease. The availability of positron and single photon emitting radiotracers to study dopamine transporters can be helpful in the study of environmental and genetic factors associated with movement disorders. This is only an example of how nuclear medicine or Molecular Medicine has changed the world of physicians in understanding the very basis of diseases which were considered as black boxes and treatment was based

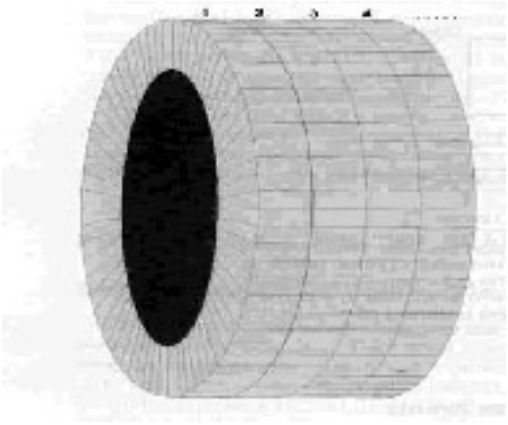


*Fig. 1 Shows a full ring scanner. Rings of detectors enclose cylindrical field of view*

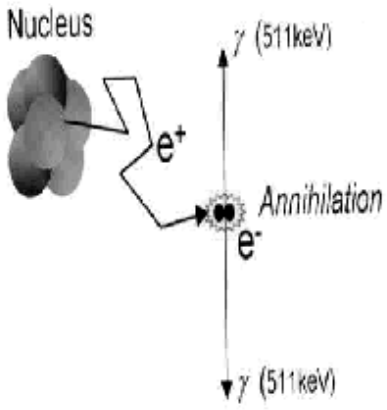



*Fig. 2 Shows physics used in imaging Positron and electron annihilation into 511 keV photons at 180 degrees*

on a hit and miss strategy. This regional molecular approach to diagnosis can be applied in several neuropsychiatric disorders, cognitive disorders, depression, and many others.

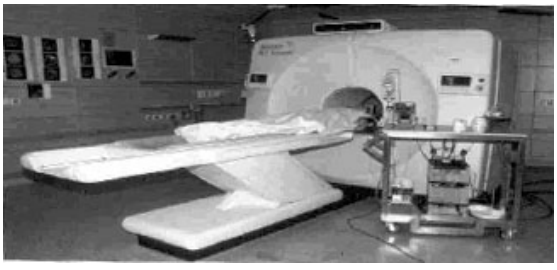
The assessment of myocardial viability is an important criterion in revascularisation procedures. In patients with chronic ischaemia the myocardium adapts to the reduced energy demand as a result to reduced blood flow by reducing its contractility. The hibernating myocardium can be revived by revascularisaton of the viable and live myocardium. PET has been an important method for identifying hibernating but live viable myocardium. $^{18}$FDG is taken up by a poorly perfused but viable myocardium, which utilizes glucose as a substrate for energy production. This flow-metabolism mismatch is indicative of viability of the muscle. A match of flow-metabolism image is evidence of scar.

**Principles of a PET Scanner**

PET tracers are positron emitting radionuclides. These radionuclides are proton rich and hence unstable. They reach a stable state by emission of positron decay, that is conversion of the extra positron into a neutron, a neutrino and a positron. This positron is emitted from the nucleus of the atom. During interactions with matter it is slowed down and finally interacts with an electron, its antiparticle. This phenomenon is called annihilation. The positron and electron after annihilation are converted into two photons of 511 keV energy each. They travel in opposite direction at $180^0$.

The PET scanner can detect the photon pair by a process of coincidence detection. The detectors are scintillation crystals made of BGO (Bismuth Germanium Oxide). Interaction of the gamma rays in the crystal results in transfer of energy to the crystal, which gets excited, and on returning to the ground state emits light photons. The number of light photons is proportional to the incident energy. The adjacent photomultiplier tube converts the light to current after amplification and feeds it into a processing device. The localization of the radionuclide is dependent on the site of annihilation. The detectors register the photons after annihilation at 180 degrees apart, at the same time.

Fig 3 shows the PET scanner with a set-up for $H_2{}^{15}O$ study.



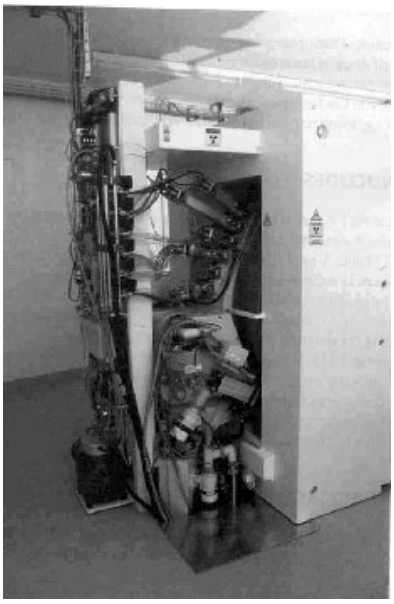


*Fig. 4 Compact Cyclotron for the production of positron emitters*

**PET Radionuclides**

A PET center is equipped with an in-house cyclotron to provide the common positron emitting isotopes, $^{11}C$, $^{13}N$, $^{15}O$, and $^{18}F$. The present generation cyclotrons are small, compact, computer driven and negative ion type. Hydrogen or deuterium is accelerated as negative ions and negatively passing the beam through a carbon foil, which diverts the particles to the target, strips charge electrons.

The inherent importance of these positrons is that they are constituent elements of biomolecules enabling them to probe biochemical processes in the living state. $^{18}F$ can often replace hydrogen or hydroxyl groups without modifying essential biological properties. With automated synthesis modules for radiolabelling positron radionuclides to suitable substrates under optimized conditions, production is easy, safe, quick and efficient. The synthesis strategies are different for ultra-short half-life isotopes.

Fig 4 shows a compact cyclotron for the production of positron emitters.

Whereas complicated $^{11}C$ products can be produced batch wise for in house use, $^{13}N$, $^{15}O$, because of their ultra-short half-lives are produced as simple molecules. $^{15}O$ water is produced on line when needed. Some common positron isotopes and their uses are shown in Table 1.

**Applications of PET in Oncology**

Pet scanning has an important role to play and is used in difficult situations and where other investigative modalities offer unequivocal information. PET studies are mostly carried out in the field of oncology. Some of the common situations where PET studies help are listed below.

- In diagnosis of unknown primary malignancy and the patient presents with metastatic disease.
- To stage the disease for subsequent management
- To detect early recurrence.
- In focal pulmonary lesions to differentiate benign from malignant tumors. The higher the

**TABLE 1. Radionuclides produced by ultra compact cyclotrons**

| Nuclide | Properties | | Reaction | Target | Yield (GBq) |
|---|---|---|---|---|---|
| | Half-life | decay | | | |
| $^{11}C$ | 20min | $\beta^+$ | $^{14}N\ (p, \alpha)^{11}C$ | Nitrogen gas | 0 |
| $^{13}N$ | 10min | $\beta^+$ | $^{16}O\ (p, \alpha)^{13}N$ | Water liquid | 8 |
| $^{15}O$ | 122sec | $\beta^+$ | $^{14}N\ (d,n)^{15}O$ | Nitrogen gas | 10 |
| $^{18}F$ | 110min | $\beta^+$ | $^{18}O\ (p,n)^{18}F$ | $^{18}O$ water | 50 |
| | | | $^{20}Ne\ (d, \alpha)^{18}F$ | Neon gas | 20 |

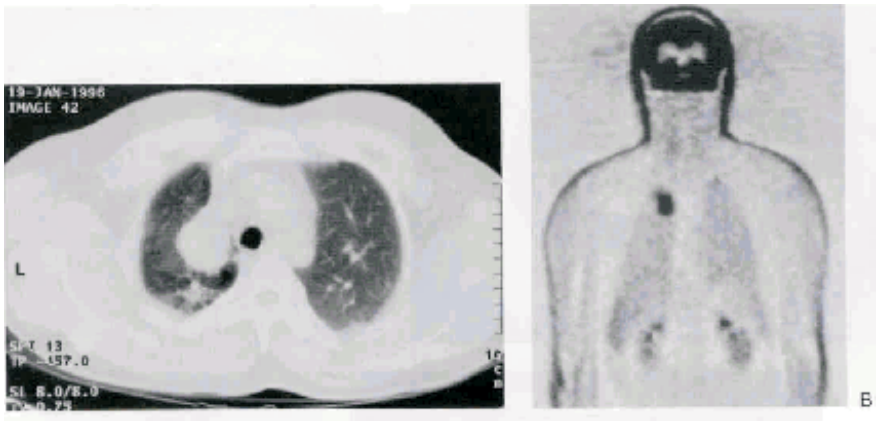



*Fig. 5 Increased uptake of $^{18}$FDG in a lung cancer.*

uptake of $^{18}$FDG in the lesion, the greater is the chance of it being a malignant lesion.

- In lung cancers especially non-small cell cancers accurate staging of mediastinal nodes is needed before considering surgery. PET is more sensitive than CT or MRI in identifying involved but normal sized nodes. A combination of CT and PET is advocated for benefiting from the advantages of both modalities.

Fig 5 shows an increased uptake of $^{18}$FDG in a lung cancer.

Whole body $^{18}$FDG is a sensitive method of identifying distant metastasis and saves the need for performing a battery of tests to exclude distant metastasis.

Fig 6 shows a whole body scan of $^{18}$FDG. Metabolically active cells take up glucose and appear as dark areas. The whole body can be screened for looking for the spread of the cancer as well as to locate the primary cancer disease. Extensive nodal disease is seen in the left upper chest. No other abnormalities are seen.

- Study of drugs and the planning and monitoring of drug treatment.
- Homeostatic processes characterized by radiotracers will make it possible to examine the genetics of homeostasis, repair processes and other functions.

*Fig. 6 Whole body scan of $^{18}$FDG*

- Gene mutations associated with diseases and the way the abnormal gene functions.
- Study of breakdown of feedback processes and the resultant disease manifestations can be evaluated.

- Targeting of specific drugs to specific cancer causing genes and cancer causing mutations can be studied with tracers.

**Clinical PET Imaging of the Brain**

PET tracers and technology have been instrumental in understanding the mechanisms of action of brain. Disorders of brain – both physiological and psychological have been shown to exhibit differences in the uptake of molecules such as $^{18}$F-FDG leading to abundant research in these areas. Several $^{11}$C labeled drugs and small molecules have been employed by researchers to understand the mechanism of drug action.

In regular practice, the application PET for brain imaging is seen in the following conditions.

- Brain tumors and inflammation
- Epilepsy
- Cerebrovascular disease
- Dementias

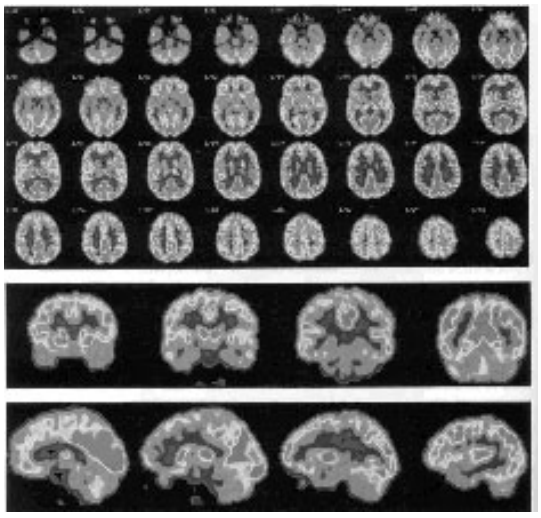


*Fig. 7 Shows normal concentration in the brain. In the axial views prominent activity is seen in cortex, cerebellum, basal ganglia and thalamus. Other views are coronal and sagittal covering all the regions of the brain.*

- Movement disorders

The indications for FDG scan in brain tumor patients are as follows

- Determination of the grade of malignancy
- Determination of regional differences of uptake before biopsy
- Establishing prognostic criteria
- Therapy monitoring
- Diagnosis of grade change
- Differential diagnosis of recurrence and radiation necrosis.

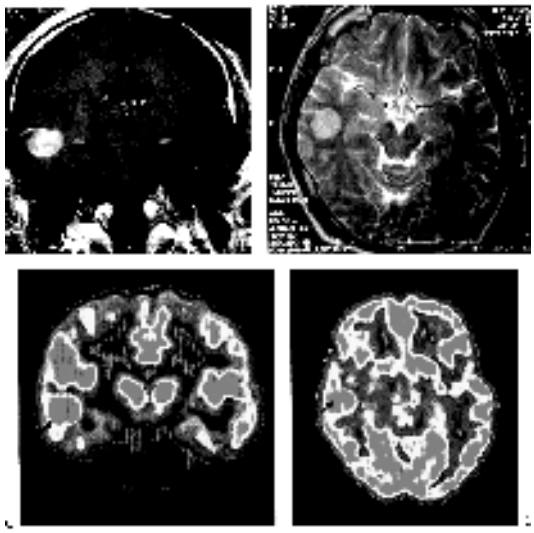


*Fig. 8 Shows a right temporal glioma $^{18}$FDG shows increased uptake in the lesion seen in MRI images.*

The potential of PET tracers in diagnosis is enormous which has been understood by the medical community and is being exploited. In fact, the number of PET studies carried out in the past 2 decades has been continuously increasing and the use of $^{18}$F-FDG has overwhelming earning it the name "Molecule of the Millennium". With the commissioning of a medical cyclotron in India and the opening of PET facilities in many hospitals, we are entering into a new phase of development in our country.

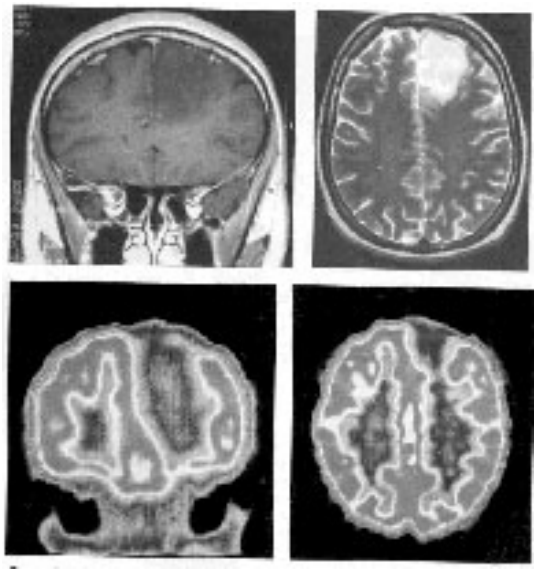


*Fig. 9 Shows a reduced uptake of $^{18}$FDG in the lesion seen on MRI images*

Modern diagnostic imaging techniques have not only improved care and decreased patient suffering, they may also have reduced overall medical expenditure and loss of income to patients by simplifying diagnostic procedures, shortening the time to diagnosis, decreasing the need for hospitalization, and helping to tailor therapeutic approaches to individual patient

Hence it is seen that the advances in technology have been tremendous in the past 3 decades. The line between pure physics, chemistry and biology has blurred and all these disciplines have come together to help understand disease processes at the molecular level and also produce fantastic images to help in disease management.

# Magnetic Resonance Imaging (MRI)

***Dr. Omprakash Tavri*** *is the Professor in radiology at Lokmanya Tilak Medical College and Hospital, Mumbai since the past 25 years. He is also the Director of Insight Imaging Centre and the Chief Consultant at Magnum MRI Center and Diamond Imagine Center, Mumbai. Dr. Tavri had been very active practicing MRI since the past several years and was responsible for the MRI clinic at Breach Candy Hospital and Lilawati Hospital & Research Centre, Mumbai. Dr. Tavri has also been contributing to the education and research in this field as the convenor for M.D. and D.M.R.D. examinations of many universities such as Mumbai, Pune and Manipal. Dr. Tavri served as the president of Indian Radiology and Imaging Association in 2003 and was the Editor-in-Chief of Indian Journal of Radiology and Imaging for seven years from 1995. Dr. Tavri has been the recipient of several fellowships to work at various centres in the USA, such as Chicago, Cleveland, Texas, Maryland, San Francisco, Boston, Los Angeles, New York, Kansas in the area of MRI and CT. Dr. Omprakash Tavri has authored the 'Text Book on Radiology and Imaging by ICR' (Ed. Prof. K. Subbarao), a chapter on "MRI in Spine" in the text book of Neurosurgery and several research papers.*

**Introduction**

In 1946, Felix Bloch and Edward Purcell independently discovered that a magnetically energized substance bombarded with RF emitted a "tune" similar to a tuning fork. They found that the nuclei of different atoms absorbed radio waves at different frequencies. In 1952, Bloch and Purcell received the Nobel Prize for their discovery of what was referred to as Nuclear Magnetic Resonance (NMR), eventually to be known as Magnetic Resonance (MR). In 1970, the medical imaging world significantly changed with the contributions of Dr. Raymond Damidian. Dr. Damidian discovered that the structure and abundance of water in the human body was the key to MR imaging, and that the water (hydrogen) emitted a signal that was both detectable and recordable. Dr. Damidian and his team spent the next seven years diligently designing and creating the first MRI scanner for medical imaging of the human body. It was Paul Lauterbur, however, who implemented the concept of tri-plane gradients used for exciting selective areas of the body ($G_{x,}$ $G_{y,\ and}$ $G_{z.}$).

MR was earlier referred to and is based on the physics of nuclear magnetic resonance (NMR). MRI is a second generation term for this imaging modality.

**Basic Principles of MRI**

In order to understand MRI, it is necessary to understand the properties of atoms. Atoms consist of a dense nucleus surrounded by orbiting electrons. The nucleus of most atoms is made up of positively charged particles called protons, and neutrally charged particles called neutrons. The electrons orbiting around the nucleus are extremely small negatively charged particles which balance the positive charge of the nucleus.

The simple nucleus of the hydrogen atom consists of one proton, and no neutrons. The hydrogen atom has a positive charge and an atomic number of 1 due to the presence of only one proton in its nucleus. For the purposes of MR, the hydrogen atom is referred to as a proton. The abundance of the hydrogen atoms in the human body, and the large magnetic moment (discussed below) created by the single proton in the nucleus of the atom, make hydrogen atoms extremely sensitive to magnetic resonance. Approximately 70% of the body is made up of water which contains two hydrogen atoms and one oxygen atom. It is the hydrogen atom that is focused on to produce an MR image.

Based on the laws of electromagnetism, any electrically charged particle which moves creates a magnetic field called a magnetic moment. This is the

property that allows protons to behave predictably within an external magnetic field. The moving (spinning) protons create a magnetic field, and thus perform as a tiny magnet with a north and a south pole.

Hydrogen atoms rotate randomly outside the presence of a magnetic field and are considered to have a net magnetization of zero. When in the presence of an external magnetic field, the atoms align either with or opposed to the main magnetic field. The parallel and anti-parallel protons cancel each other out, leaving a relatively small number of protons aligned with the main magnetic field.

***Precession and Resonance***

Hydrogen atoms do not actually align directly with the direction of the magnetic field, but rather rotate or wobble around the axis of the magnetic field. The term to describe this secondary spin is precession. Protons actually precess at an angle spinning a cone-shape fashion to the direction of the magnetic field. This action is similar to the action of a spinning top rotating around a vertical axis. The speed at which the protons or the net magnetic vector (NMV) precesses is referred to as the precessional frequency and is measured in megahertz (MHz). The stronger the magnetic field, the higher the precessional frequency.

Larmor frequency is the frequency at which the nucleus will absorb energy. The absorption of that energy will cause the proton to alter its alignment. In MR imaging, the energy that is transferred is radio frequency waves (RF) and ranges from 1-100 MHz. If an RF pulse at the Larmor frequency is applied to the nucleus of an atom, the protons will alter their alignment from the direction of the main magnetic field to the direction opposite the main magnetic field. As the proton tries to realign with the main magnetic field, it will emit energy at the frequency of the Larmor frequency.

Resonance is referred to as the property of an atom to absorb energy only at the Larmor frequency. This is the basis of MR. An atom will only absorb external energy if that energy is delivered at precisely its resonant frequency. The energy must also be delivered at 90° to the NMV and main magnetic field ($B_0$). Otherwise, no energy will be absorbed. The deflection of the magnetization or total angle created after the end of the RF pulse is referred to as the flip angle.

Depending on the strength of the applied energy, the protons will flip into the X-Y plane (transverse magnetization), or exactly the opposite direction of the main magnetic field. The transverse magnetization induces a voltage in an antenna or receiver coil, which will be eventually become the MR signal. As the RF is turned off, the protons dephase and lose their coherence as they try to realign with $B_0$. Two phenomenons occur simultaneously. Transverse magnetization decreases (T2 decay), while longitudinal magnetization increases (T1 recovery).

As the hydrogen atoms release their energy that they previously absorbed in the surrounding tissue (lattice), in their attempt to realign with the main magnetic field, T1 relaxation or T1 recovery occurs. This phenomenon is sometimes referred to as "spin-lattice" relaxation. T1 recovery is the time it takes for 63% of the longitudinal magnetization to "regrow" or recover in the tissue.

Unlike longitudinal relaxation, transverse relaxation is not a process of dissipation or absorption of energy into tissue. The nuclei which began spinning "in-phase", lose their phase coherence or dephase over time and spin in a random fashion. This process results in an exponential decrease or decay in transverse magnetization and MR signal dies out.

***Tissue Contrast***

Due to the T1 and T2 relaxation properties, we can differentiate between various tissues in the body. As well as T1 and T2 contrast in tissues, proton density can also be measured. Proton density is measured by the number of protons per unit of tissue. Various tissues have different T1 and T2 values. These T1 and T2 values significantly influence the type of signal generated during MRI and thus contribute greatly to the MR image.

For e.g.; due to the slow molecular motion of fat nuclei, longitudinal relaxation occurs rather rapidly and longitudinal magnetization is regained quickly. The net magnetic vector realigns with $B_0$ leading to a short T1 time for fat. Water is not as

efficient as fat in T1 recovery due to the high mobility of the water molecules and therefore take longer to regain longitudinal magnetization resulting in a long T1 time. As we know, T2 decay is dependent on the interaction of nuclei and the exchanging of energy with near by nuclei. Fat has a very efficient energy exchange and therefore has a relatively short T2. Water is less efficient than fat in the exchange of energy, and therefore has a long T2.

### *T1 and T2 Weighting*

Nearly all MR images are weighted to enhance the contrast and obtain better quality images for better diagnosis. Among these, weighting for T1 and T2 effects are most common. T1-weighted images are obtained to compare the T1 differences in tissues or to compare the relaxation rates of the tissue being examined. T2-weighted images are obtained to compare the T2 contrast in tissues and compare the transverse relaxation rates.

Parameters such as TR and TE, which are controlled by the operator, are manipulated by the user to obtain the type of image contrast desired.

- TR stands for repetition time, or the elapsed time between successive RF excitation pulses, in milliseconds.
- TE stands for echo delay time, or the time interval between the RF pulse and the measurement of the first echo, in milliseconds.

| | TR | TE |
|---|---|---|
| Tl Weighting | Short | Short |
| Proton Density Weighting | Long | Short |
| T2 Weighting | Long | Long |

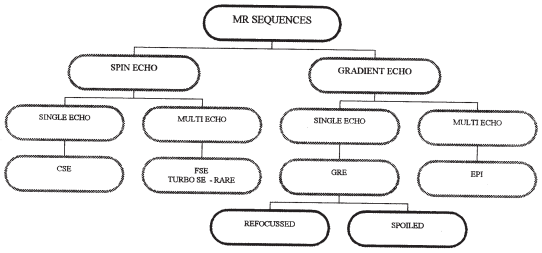
### Magnets Used in MRI

There are three types of magnets used commercially in medical imaging, all of which provide homogenous large magnetic fields. The main differences are the strengths, energy requirements, production costs, and the magnetic field direction.

- Permanent Magnets
- Resistive Magnets
- Superconductive Magnets

### *Various MR Sequences and their Applications*

The various sequences of the magnetic resonance applied are schematically shown below.




SPIN ECHO technique comprises of standard 90 and 180 degree pulses for excitation and rephasing respectively.for e.g T1 and T2 sequences.

GRADIENT ECHO refers to reversing the polarity of frequency encoded gradient instead of using 180 degree refocusing pulse.

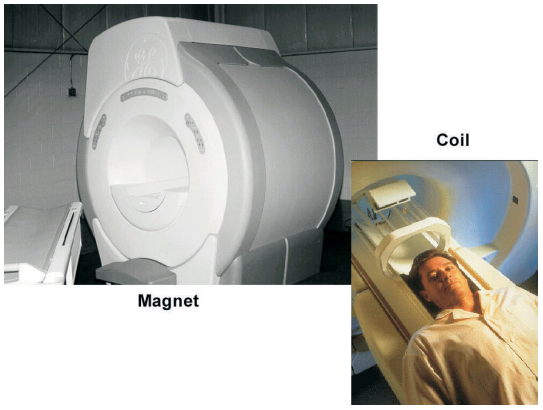
SINGLE ECHO refers to repeated excitation followed by only one reading frequency encoded echo where as MULTI ECHO refers to repeated excitations followed by different frequency encodings.

SINGLE ECHO SE sequences comprise of conventional spin echo sequences.

MULTI ECHO SE sequences comprise of FSE (fast spin echo) and TURBO spin echo techniques. FSE has replaced SE in brain and spine imaging due to reduction in scanning time and better resolution. In addition, it provides excellent sequence for MRCP techniques i.e.RARE and HASTE.

SINGLE ECHO GRE sequences comprise of spoiled gradients like FLASH and SPGR which are used to obtain good T1 wted images, 2D and 3D acquisitions like in MRA and CEMRA. Refocused GRE sequences like GRASS and FISP are used to obtain good T2wted images of brain and joints.

MULTIECHO SINGLE SHOT (i.e. single excitation followed by multiple frequency encoding gradients) GRE comprises of EPI i.e. echoplanar imaging.It is used in diffusion,perfusion imaging,



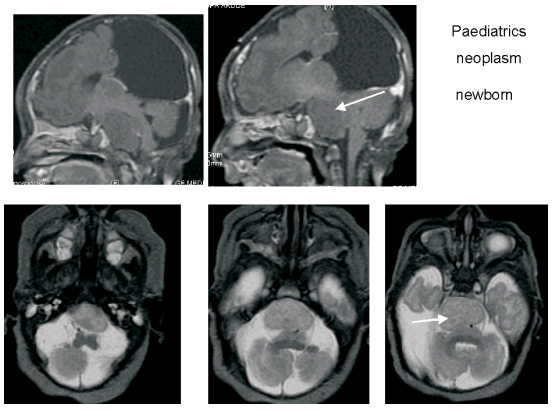

neuron activation studies, breath hold techniques for body imaging and in cardiac imaging.

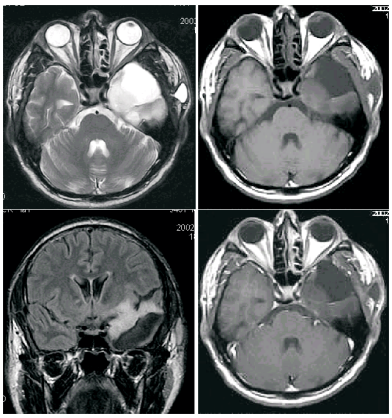
Sequences where previously prepared longitudinal magnetization is used are called magnetization prepared sequences. These are used for fat and fluid suppression imaging for e.g. IR and FLAIR sequences.

**Clinical Applications of MRI**

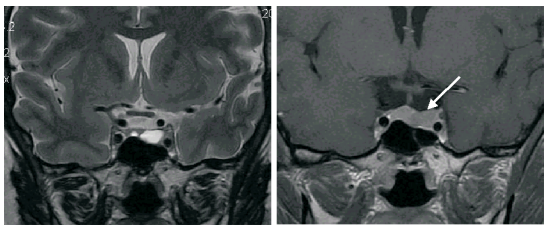
***Brain***

Typical indications for a MRI of the brain include headaches, dizziness, visual changes, hearing loss, seizures, nausea, history of cancer, auto-immune disease, and tingling or numbness in extremities. MRI of the brain can help detect tumors, infections, metabolic, congenital disorders and demyelinating diseases like multiple sclerosis etc. It functions as a very important diagnostic tool in epilepsy and cranial nerve disorders.

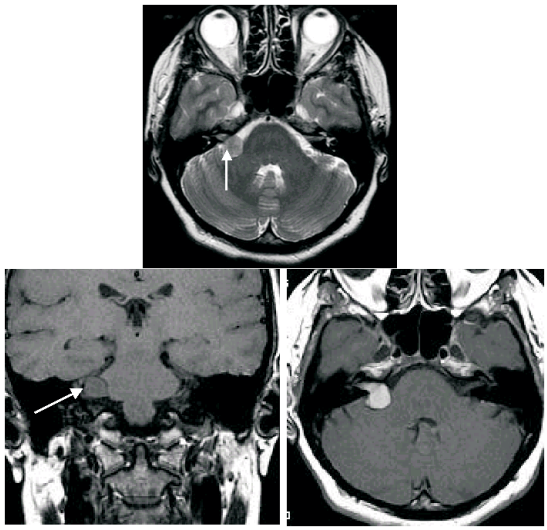


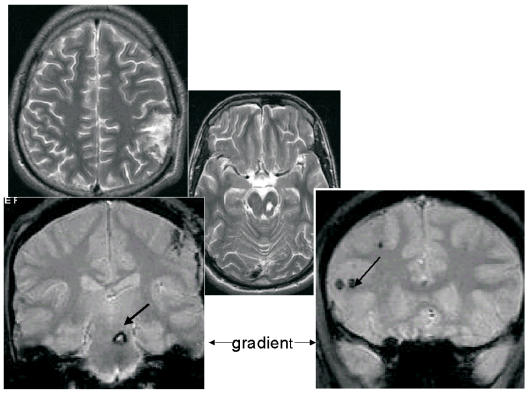
*Post OP/RT evaluation glioma*



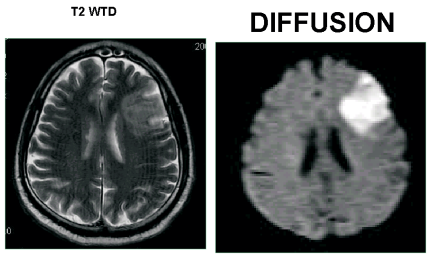
*Pituitary Macroadenoma - Dynamic contrast enhanced imaging for microadenoma*



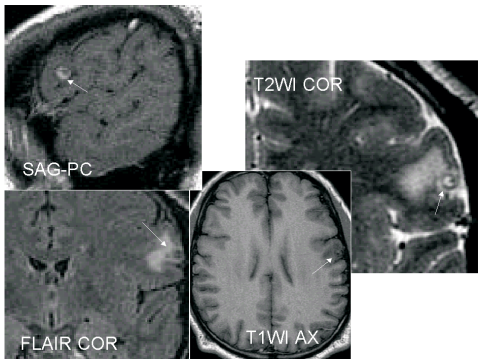
*Acoustic Schwannoma*



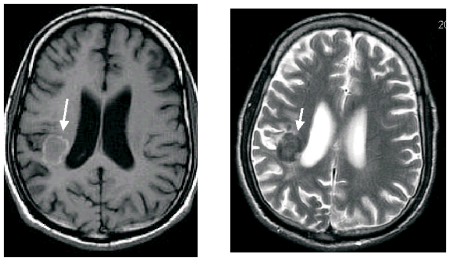

*Trauma-diffuse axonal injury*




*Detection of infarct within 3 hrs of onset of symptoms.*



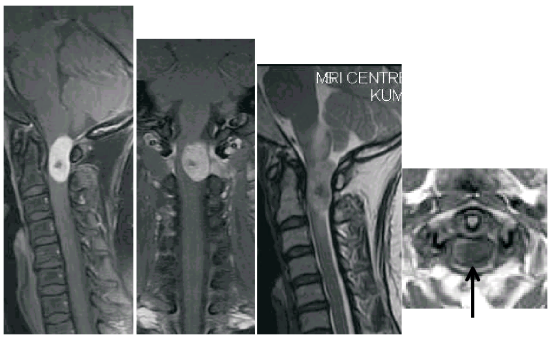

*Cysticercosis*



*Giant tuberculoma*

***Neck***

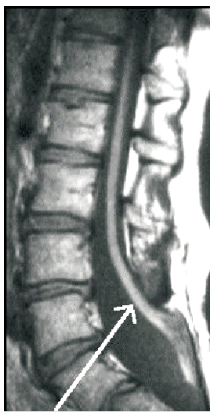
MRI helps distinguish differences between lymph nodes and blood vessels. Typical indications for a MRI of the neck include enlarged lymph nodes or a palpable mass. MRI of the neck can help detect tumors and other lesions, vascular abnormalities, and structural abnormalities.



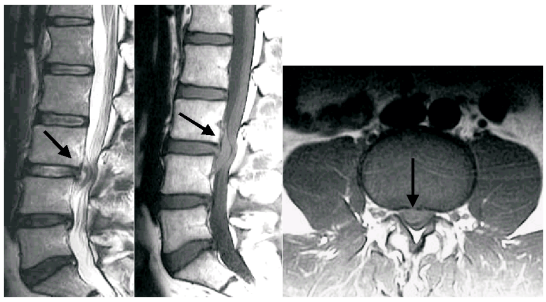
*Meningioma*

***Spine***

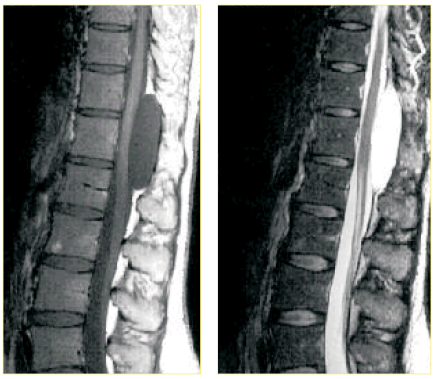
Typical indications for a MRI of the spine include back pain, numbness or tingling in extremities, history of cancer, and loss of bladder or bowel control. MRI of the spine can help detect disc degeneration, arthritic changes, tumors and demyelinating lesions. It also functions as a very important post operative investigation to determine differences between a post operative scar or recurrent disc.



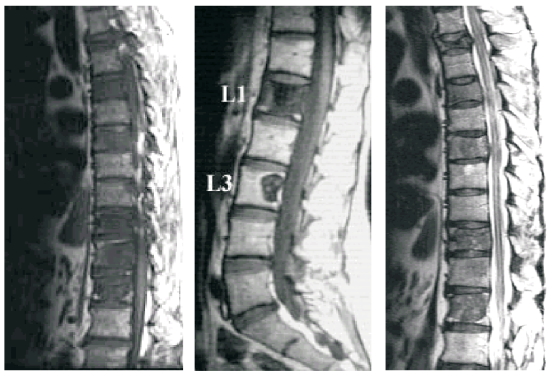
*Tethered Cord and Tight filum syndromes - congenital anomalies*



*Degenerative diseases of spine - Extrusion*



*Extradural Archnoid Cyst - Tumors*



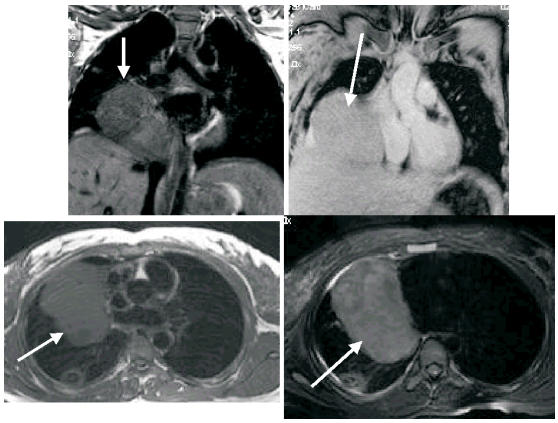

*Extradural tumors - Metastasis*

***Thorax (Chest)***

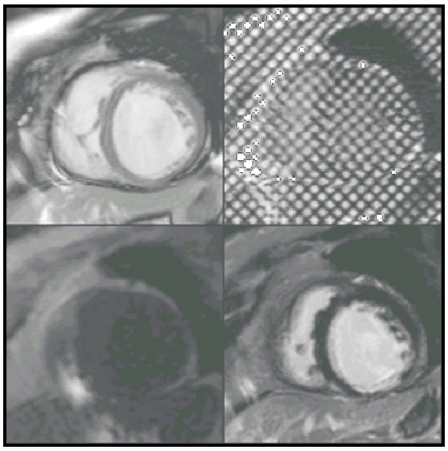
In the past, it was difficult to obtain diagnostic pictures of the thorax with MRI due to heart and breathing motion. However, MRI has improved its capability to take pictures by using a set of cardiac leads to monitor heart rhythms and acquire pictures with a "snapshot" eliminating heart motion. Breath-hold imaging utilizes ultrafast techniques while a patient holds his/her breath to acquire motion free pictures. Typical indications for a MRI of the Thorax include history of cancer and a questionable mass. MRI of the Thorax can help detect metastatic disease, aortic aneurysms, and aortic dissections.

***Cardiac (Heart)***

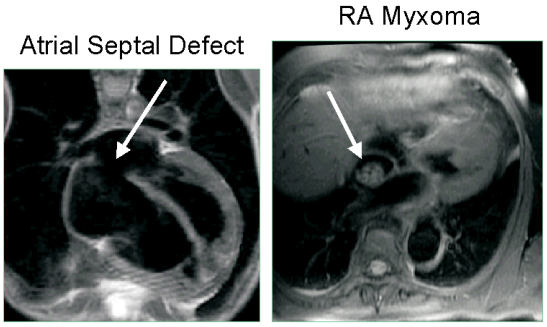
MRI is currently improving methods for evaluating the heart. Cardiac Gating reduces heart motion and allows visualization of heart structures, but coronary arteries are still difficult to evaluate. Typical indications for a MRI of the heart include congenital and acquired heart disease.



*Pericardial neoplasm*



*Mycardial viability examination*

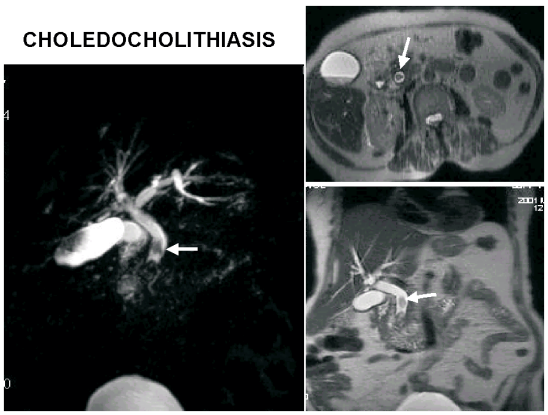


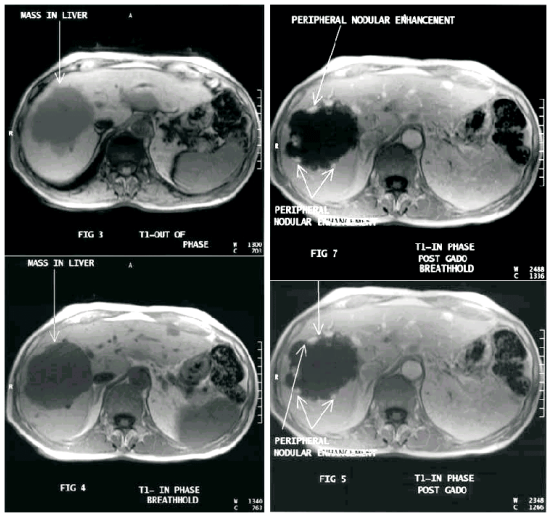

### *Breast*

MRI's ability to differentiate water, fat, and silicone makes it the procedure of choice for evaluating silicone breast implants or residual silicone from removed implants. MRI of the breast for cancer detection or screening is currently being developed, but not yet accepted as the procedure of choice.

### *Abdomen*

With the advent of breath-hold imaging techniques and new equipment (coils), MRI is increasingly used to evaluate the liver, spleen, kidneys, and pancreas. Typical indications for a MRI of the abdomen include history of cancer, pain, loss of organ function, bleeding, cirrhosis of the liver, and hepatitis. MRI of the abdomen can help detect enlarged lymph nodes, metastatic disease, tumors and other lesions, aneurysms, and structural abnormalities.

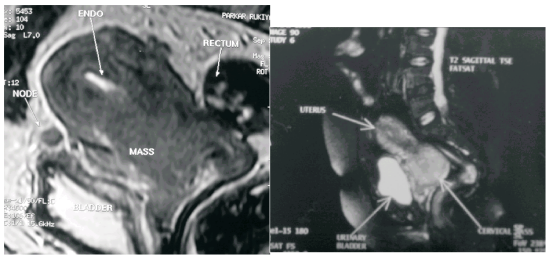



*Hepatoma*

### *Pelvis*

New equipment (coils) now available greatly improves imaging in the pelvis. In women, MRI of the pelvis is increasingly used to evaluate the uterus, cervix, ovaries, bladder, fetus, and placenta. In men, MRI of the pelvis is increasingly used to evaluate the prostate, bladder, penis, and scrotum. Typical indications for a MRI of the pelvis include cancer staging, pain, palpable masses, and pregnancy complications. MRI of the pelvis can help detect enlarged lymph nodes, fibroids, ovarian masses, prostate cancer staging, metastatic disease, testicular cancer, and structural abnormalities.

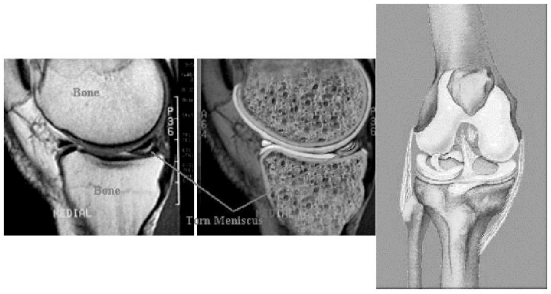



*CA cervix*

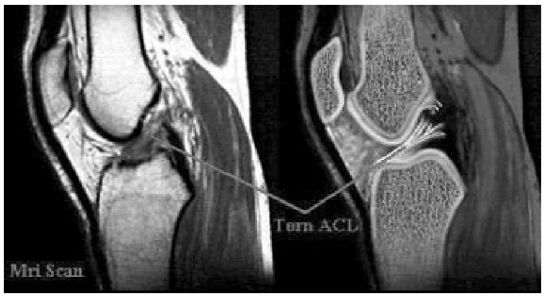
### *Musculoskeletal*

MRI is able to evaluate the shoulder, wrist, knee, ankle, and feet with exquisite detail. Typical

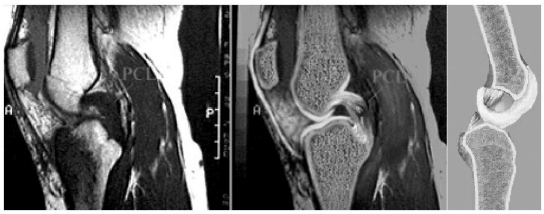
indications for a MRI of a joint or soft tissue include pain, swelling, weakness, palpable mass, or decrease in range in motion. MRI of the joints and soft tissue can help detect torn ligaments, torn cartilage, edema (swelling), arthritic changes, tumors, lesions, osteomyelitis, and structuralchanges.



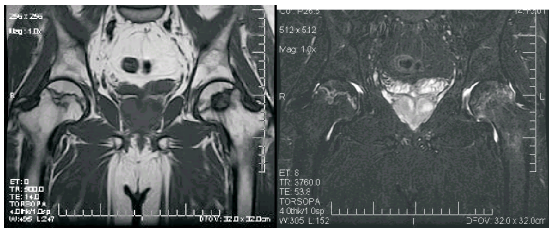

*Meniscal Tears*




*ACL tear*



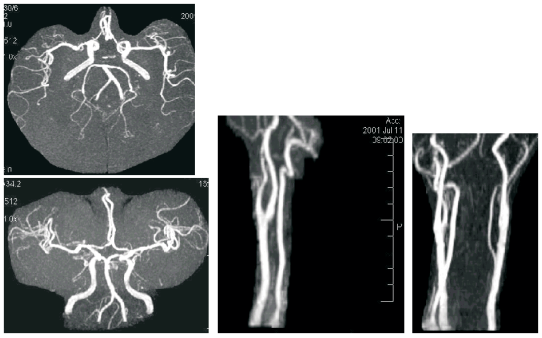

*PCL tear*



*Hip joints - AVN with transient osteoporosis*

***MR Angiography (MRA)***

MRI is now able to utilize the blood as its own contrast agent to evaluate the blood vessels of the head and neck. This technique is known as MR angiography (MRA). MRA can evaluate blood vessels of the head and neck without injecting the patient with a contrast agent. This non-invasive technique requires only one additional set of pictures taken in addition with a standard MRI exam. MRA of the head and neck can help detect vessel narrowing (stenosis), blood vessel blockage, cerebral aneurysm, arteriovenous malformation (AVM), and blood vessel dissection. Peripheral and renal MRA have also come up a big way.



*Normal angio*

***Contrast Enhanced MRA***

Contrast enhanced MRA is a relatively new technique utilizing an injected MRI contrast media (Gd-DTPA) into the blood stream while simultaneously acquiring MRA pictures. Contrast enhanced MRA is now utilized for the evaluation of blood vessels in the thorax, abdomen, pelvis, and legs.

***Advantages of MRI***

- No ionizing radiations
- Inherent excellent tissue contrast
- Intravenous iodinated contrast agents have no application, hence no fear of contrast reactions. Gadolinium used in CEMRA has minimal side effects.
- Non invasive angiography can be performed.

***Disadvantages of MRI***

- Time consuming technique
- Artifacts due to foreign bodies and implants make it unacceptable for diagnostic evaluation.
- Claustrophobic patients, patients with pacemaker, aneurysmal clips cannot be evaluated.
- Calcium cannot be effectively detected.

***Advances in MRI***

These include:

- Functional MR comprising of diffusion, perfusion and BOLD techniques. These are very useful in evaluation and prognostication of early stroke.
- MR spectroscopy which involves imaging of the physiological parameters of the various tissues and serves as a problem solving tool in differentiating one pathology from the other. It is particularly useful in differentiating tumor and demyelinating diseases of the brain from infections. It also plays an important role in diagnosis of dementic diseases.
- Time resolved MRA is coming up a big way in dynamic evaluation of blood vessels thus aiding in flow studies.
- Cardiac MRI is also not limited purely to functional evaluation. MR coronary angiography is also evolving rapidly.

Finally MRI is a wide angled camera which has the capability of shooting every part of the body in a fine, harmless and gentle manner.

# Ultrasonography: A diagnostic tool, Principles and Practice

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**Introduction**

'Ultrasonography', a technique to image organs using sound waves of high frequency, is a very familiar term to all of us. Its use is so common that a facility to perform ultrasonographs exists in nearly every suburb of town. Perhaps most of us undergo an ultrasound scan at some stage in life.

A large spectrum of electromagnetic waves has been used as sources for imaging leading to a variety of imaging techniques. Ultrasound imaging (also called ultrasound scanning or sonography) is a relatively inexpensive, fast and radiation-free imaging modality. Ultrasound is excellent for non-invasively imaging a number of organs and diagnosing various conditions, without radiation.

Ultrasound imaging and ultrasound angiography are finding a greater role in the detection, diagnosis and treatment of heart disease, heart attack, acute stroke and vascular disease which can lead to stroke. Ultrasound is also being used more and more and to . Diagnostic ultrasound is the most innovative sector of the diagnostic imaging market today and constitutes the largest imaging modality worldwide.

**Principle**

In the 1960's the principles of sonar (developed extensively by the Defense Department during the second world war) were applied to medical diagnostic imaging. Sound and ultrasound waves consist of a mechanical disturbance of a medium such as air. The disturbance passes through the medium at a fixed speed causing vibration. The rate at which the particles vibrate is the frequency, measured in cycles of sound waves per second or hertz (Hz). Sound becomes inaudible to the human ear above about 20 kHz and is then known as ultrasound.

Speed of sound through a medium is dependant on the density and compressibility of the medium. As such materials with increasing density and compressibility will increase the speed of sound transmission. A fixed relationship between acoustic speed, wavelength and frequency exists as follows:

$$V = F \lambda$$

Where V: Speed of sound in conducting material,
F: Frequency in Hertz and
$\lambda$ : Wavelength in metres

Ultrasound can be produced by passing AC to a Piezo Electric substance. Alternately when a Piezo crystal is compressed eletric voltage is generated. The ultrasound waves were produced using naturally occurring crystals such as Quartz. However, other advanced ceramic crystals with better mechanical properties and ease of fabrication replaced quartz progressively.

This process involves placing a small device called a transducer, against the skin of the patient near the region of interest, for example, against the back to image the kidneys. The ultrasound functions as both a loudspeaker (to transmit the sounds) and a microphone (to record them).

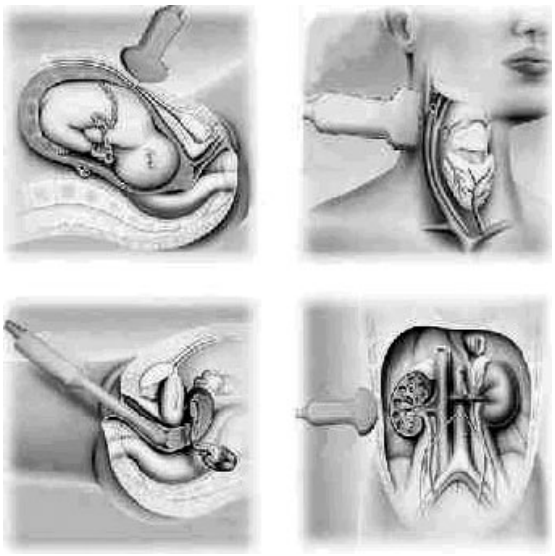


*Fig. 1 View of the transducer for imaging various organs*

When the transducer is pressed against the skin, it directs a stream of inaudible, high-frequency sound waves into the body. As the sound waves echo back from the body's fluids and tissues, the sensitive microphone in the transducer records the strength and character of the reflected waves. With Doppler ultrasound, the microphone captures and records tiny changes in the sound wave's pitch and direction. These signature waves are instantly measured and displayed by a computer, which in turn creates a real-time dynamic picture on the monitor. The live images of the examination can be recorded on videotape or on a disk. In addition, still frames of the moving picture are usually "frozen" to capture a series of images. These "frozen" images are used to obtain measurements and to document the essential positions of the examination.

Diagnostic imaging uses much higher frequencies, in the order of megahertz (MHz). The higher the frequency used, the better the resolution (the ability to distinguish two adjacent objects). However, as the frequency increases, more of the ultrasound beam is absorbed by the medium and the beam cannot penetrate very far. For this reason, higher frequencies (for example, 7.5 MHz) are used to image superficial organs such as the thyroid gland, testes, and breast in detail while lower frequencies (for example, 3.5 MHz) are used for examination of deep-seated organs such as the abdomen.

**Probes for Producing the Image**

Ultrasound probes are made from a piezoelectric ceramic substance that vibrates at a resonant frequency when an alternating electric current is applied across it. The resulting vibration is transmitted into the tissue in short bursts. The speed of transmission within most soft tissues is 1540 m/s, producing a transit time of 6.5 micro seconds/cm. When the waves encounter a boundary between two tissues of different density (such as soft tissue and bone) some will be reflected and return to the probe. The probe then acts as a receiver, converting mechanical energy back into an electric signal, which is used to display an image on a video monitor. Because the velocity of ultrasound waves is constant the time taken for the wave to return to the probe can be used to determine the depth of the object causing the reflection. The object can then be displayed at an appropriate place on the monitor.

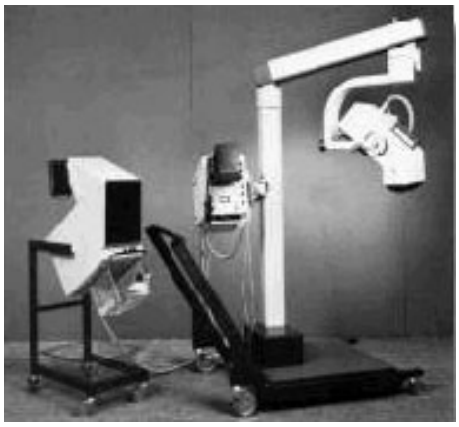
If the ultrasound beam meets a rough surface or small object the beam is scattered in all directions and only a small amount will be received by the probe. Air within the bowel also scatters ultrasound, and this is one of the main causes of non-diagnostic scans of the abdomen.

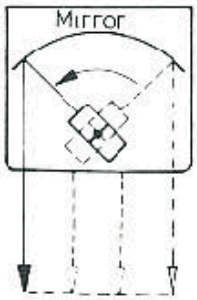
Continuous improvements in technology are leading to higher resolution images and thus to new applications, which is also an important contribution to cost reduction by replacing more expensive and harmful diagnostics.

This article attempts to review how modern instrumentation has changed the scope and confidence in diagnostic accuracy.

**Ultrosonography - Progress in Modern Diagnostics**

Ultrosonography, as a tool, was first used in the seventies and the earliest equipment used were static scanners with images in shades of gray. They attempted to differentiate solid masses from cystic i.e. water containing lesions which are generally accepted as more harmless and benign. A refined imaging mode was introduced in 1972, called gray-scale display. This was a huge step forward because the internal texture of many organs became





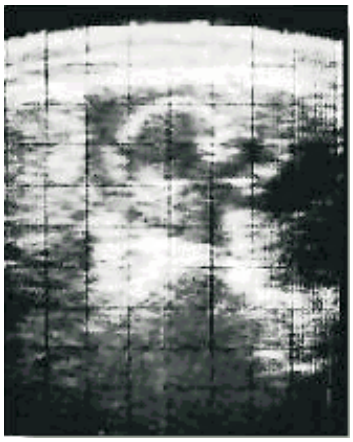
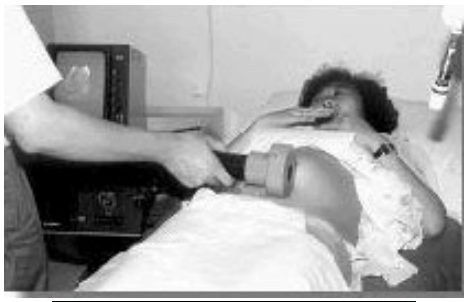



*Fig. 2 The image with basic gray scaling using rotating transducers*

visible. In gray-scale display, low-level echoes are amplified and recorded, giving many degrees of brightness. Because of this, ultrasound (along with radionuclide scans) is now the most useful method of imaging the liver.

The innovation, which had soon completely changed the practice of ultrasound scanning, was



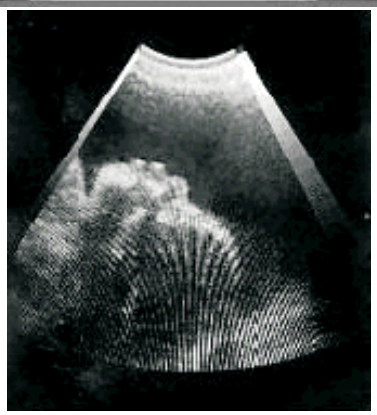


*Fig. 3 The large hand-held circular rotating transducer and the resultant sector image.*

due to the advent of the Real-time scanners. The first real-time scanner, better known as fast B-scanners at that time, was developed in Germany in 1965. It's first use in Obstetrics and Gynecology was published in 1966 in the German language. The paper in 1968 on "Intrauterine diagnosis of hydrops fetus using ultrasound" also in German, is probably the first paper in the medical literature describing formally the diagnosis of a fetal malformation using ultrasound.

They used 3 rotating transducer housed in front of a parabolic mirror in a water coupling system and produced 15 images per second. The image was made up of 120 lines and basic gray-scaling. The use of fixed focus large face transducers produced a narrow beam to ensure good resolutions and image. Fetal life and motions could clearly be demonstrated.

Although these have relatively heavy probes they produced outstanding real time resolution in the near and far field (because of highly focused beams resulting from the relatively large curvatured transducers and the lens apparatus) and with much

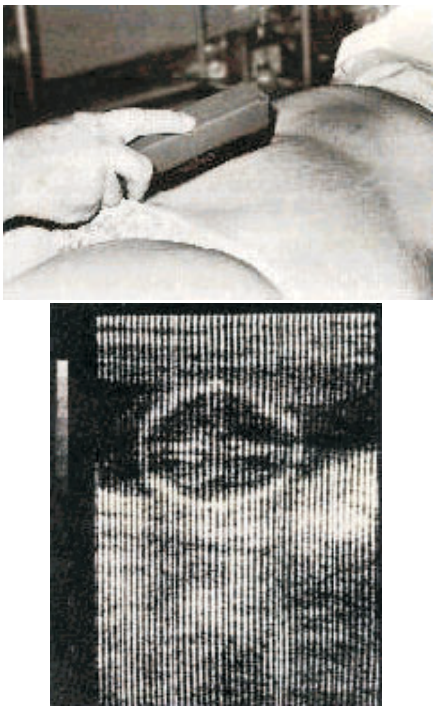


*Fig. 4 Early scans with obtrusive lines with less clarity*

less image-degrading electronic noise that was associated with electronic scanners that soon became available at around the same time.

The transducer is connected to the main console by a flexible cable. Early scanner probe was bulky to fit on the abdomen. Images from early real-time scanners had obtrusive scan lines, low dynamic range and resolution.

Prior to the 1990s, B-scan ultrasound images made steady progress in resolution and quality, but the improvements were not dramatic and except for a few really top-end brands, most had felt that images in the late 1980s did not have significant improvements over those in the early 80s.

It was only in late 1990's when excellent beeam linearity and super sensitive detection could be achieved, that 'harmonic imaging' could be developed. The harmonic signals which are far lesser in amplitude than the original fundametal signal, provide valuable information, particularly in obese patients. It is expected that the harmonic imaging

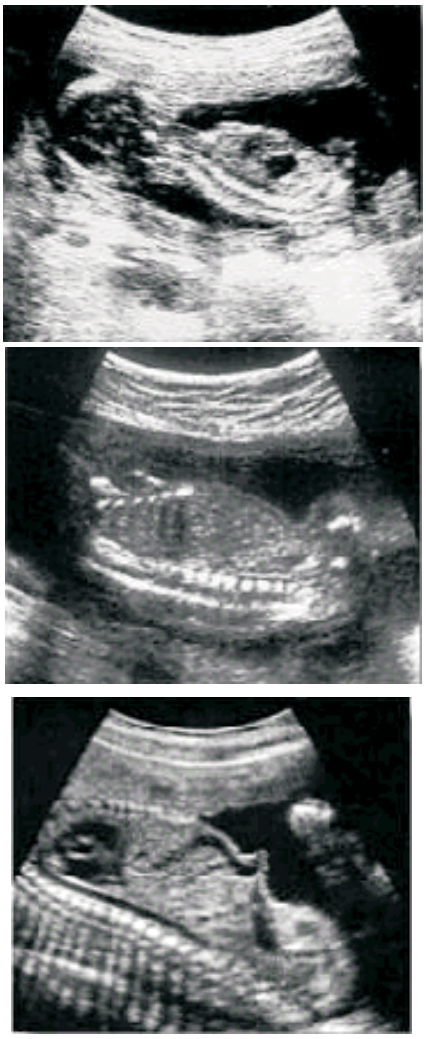


*Fig. 5 Changes in quality of image over the years during 1985-1995*

technique would improve further and become less expensive, in the near future.

From top: Changes in image quality from 1985, 1990 to 1995 respectively. There were improvements in spatial and contrast resolution, background noise reduction, dynamic range, and near and far field visualization.

With the revolution in computers and advent of better software the application of Doppler, colour and Power Doppler techniques have added depth for sonography diagnostics. This technique has enabled

not only imaging the physiological dimensions but also parameters such as blood flow, volume flow and also the nature of vessels involved in pathological conditions. Research is already going on in employing contrast injections to highlight the vessel flow better, particularly in smaller blood vessels.

Tissue and contrast Harmonics have been able to indicate better outline and borders between hazy areas thereby exactly localizing abnormal tissue and defining its borders, outlines and nodularity.

**Doppler Imaging Techniques**

Real time scanners sweep the ultrasound beam rapidly through the region of interest. The image is updated with each sweep so that you can see movement (for example, of a heart valve).

Doppler imaging depends on the fact that if the reflecting surface is moving in relation to the probe (for example, blood flowing in a vessel) the frequency of the received ultrasound wave will be different from that of the transmitted wave. If the reflector is moving towards the transmitting probe, the frequency will be increased and vice versa. There is a constant relation between this change in frequency and the velocity of the moving reflector, and this can be used to calculate the velocity of flow within vessels. For example, in carotid arteries the velocity of flow increases with the severity of stenosis. Ultrasonography can therefore pick up critical stenoses, which require surgery and display the site of the stenosis at the same time.

Conventional Doppler imaging produces a wave form that can be used to calculate the actual flow rate in a vessel, whereas colour flow Doppler displays the same information by superimposing the image of moving blood in colour on the usual real time image. The colour flow immediately draws the operator's attention to areas of high flow or disturbed flow, which can then be examined more thoroughly and quantitatively with conventional Doppler imaging.

The Doppler effect has been used not only to study the images but to generate ideas about velocity and directional flow in blood vessels. This has immensely helped in the study of major blood vessels, clot formation and assessment of turbulent flow if any. With steady progress in the instrumentation, smaller vessels can be studied in greater detail.

Power Doppler sonography is an option in colour Doppler sonography as just as in colour Doppler, the signal is sampled at multiple locations along each scan line. In addition, ultrasound contrast agents are being tested for intravenous injections, which can accentuate the colour flows in such areas where gas tends to prevent direct vision. This is seen in the blood flow to the kidneys and bowel walls.

**Preparation of the Patient**

For ultrasonography, very little patient preparation is required, but it is important to get it right. Patients must fast before examination of the abdomen to ensure that the gall bladder is full and therefore visible. A full bladder is required for examination of the pelvis in females. This pushes small bowel loops out of the pelvis, allowing the uterus and ovaries to be seen.

Another barrier to sound is the air layer between the patient's skin and the transducer. In order to overcome the reflections at this level, the sonographer liberally smears mineral oil (or a suitable lubricant) on the patient's skin before she begins the scanning. The sonographer asks the patient to take a deep breath and hold it. This brings the top of the liver out from under the ribs.

**Applications**

Ultrasonography has been very popular due to the many advantages such as being safer even in pregnancy, inexpensive, portable, painless, non invasive, devoid of side effects and so on.

Ultrasonography can also be used to guide needle aspiration and biopsy of masses. The biopsy needle is highly echogenic and appears as a bright line entering the mass. The tip of the needle can be guided to avoid necrotic parts-which may not yield diagnostic material as well as adjacent structures such as blood vessels.

The development of higher frequency probes which allow improved resolution has enabled ultrasonography of "small parts" such as the thyroid and parathyroid glands, salivary glands, breasts, testes, and eyes. The 1990s has also seen the

development of tiny probes which can be attached to endoluminal devices to provide high resolution images. Examples include transvaginal ultrasonography of the uterus and Ovaries, transrectal examination of the prostate, and transoesophageal examination of the heart and aorta.

**Ultrasonography in Obstetrics andGynaecology**

In early pregnancy ultrasonography is used to confirm intrauterine and exclude ectopic pregnancy. It can detect a viable fetus from about seven weeks' gestation and transvaginal probes will detect a fetus even earlier, as shown in the figure. Missed abortions and retained products after terminations can be readily identified.

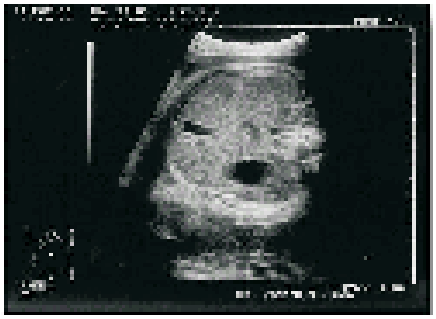
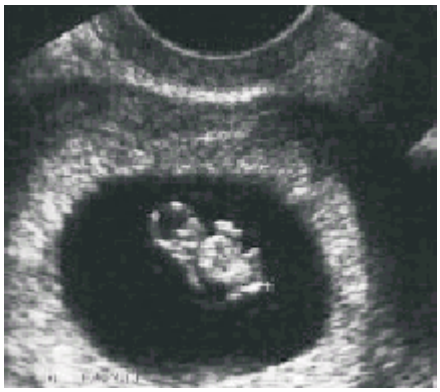


*Fig. 6 Fetus of few weeks*



*Fetus at 9 weeks*

In later pregnancy from 3rd month ultrasonography is used to assess growth and to exclude anomalies. The number of conditions that can be identified antenatally with ultrasonography is continually increasing and includes renal abnormalities, diaphragmatic hernias, neural tube defects, and congenital heart defects.

**Abdominal Ultrasonography**

Ultrasonography is often an initial investigation in patients with abdominal pain or a suspected mass. If ascites is identified it can be tapped, and any mass can be evaluated for biopsy. Ultrasonography can also localise collections in cases of sepsis, and drains can be inserted into subphrenic, subhepatic, and pelvic collections.

Formerly it was almost impossible to view the cervix and lower uterus because they lay under the air-filled intestines which reflect most of the sound. Then doctors discovered that they could create an ideal acoustic window if they had the patient drink 32 ounces of fluid one hour before an ultrasound scan. The distended bladder pushed the air-filled instestines out of the way and permitted sound to reach the reproductive organs in the lower pelvis as shown below.

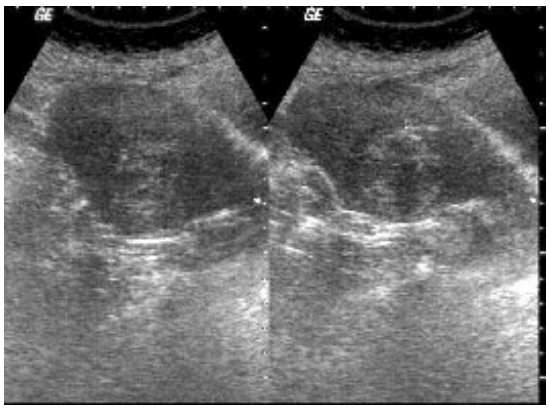


*Fig. 7 Imaging of reproductive organ in the pelvis*

An organ like the liver is ideal for the sonographer to work with. It is a very large homogeneous soft organ that permits sound pulses to move through with only small amounts of reflection so that the spleen, pancreas or kidney which lie beneath the liver can be imaged as well. For this reason, the liver is called an "acoustic window".

The role of ultrasonography in the acute abdomen is less well defined. In equivocal cases of appendicitis, ultrasonography may show an

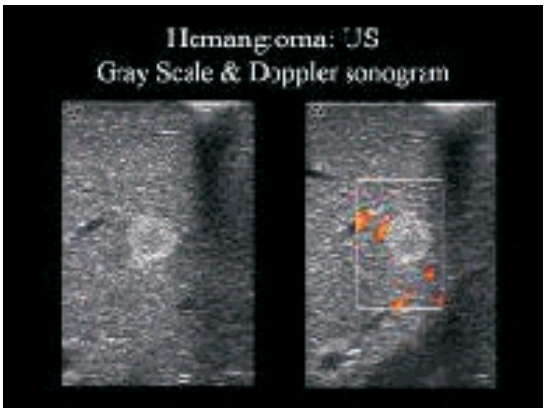



*Fig. 8 Sonography of the liver*

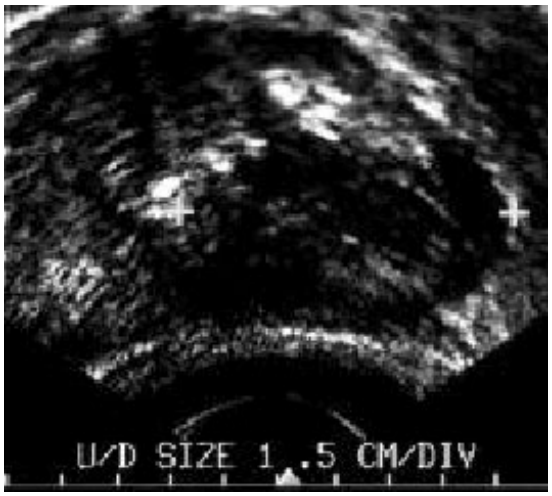



*Fig. 9 Sonography of the malignant prostrate*

appendix mass, stone, or a focal collection of free fluid next to the appendix. Acute cholecystitis and intussusception can also be diagnosed.

***Jaundice***

Ultrasonography is good at detecting gall stones and can determine the level and cause of bile duct obstruction. Cirrhosis of the liver can be identified, as can its complications such as splenomegaly, ascites, varices, and portal hypertension (seen as reversed flow or thrombosis in the portal vein with Doppler ultrasonography).

***Pancreatitis***

Ultrasonography is used to exclude gall stones as a cause of the pancreatitis and to exclude complications such as pancreatic abscess or pseudocyst. Large fluid collections or pseudocysts can be drained at the same time.

***Urinary Tract***

Ultrasonography is the initial investigation of choice in conditions such as haematuria, a possible renal mass, and bladder outflow obstruction due to an enlarged prostate. Transrectal ultrasound (TRUS) of the prostate helps in delineating prostrate enlargements and prostrate cancers. A large hypoechoic area in the left peripheral zone suggestive of prostate cancer is shown in the image.

In haematuria, ultrasonography can identify a tumour in the urinary bladder and exclude a space occupying lesion in the kidney. In a young patient or child with hypertension it will show relative renal size and evidence of parenchymal disease. However, other imaging techniques such as nuclear imaging or MR angiography would be needed to exclude renal artery stenosis.

In renal failure ultrasonography will show the size and morphology of the kidneys and may demonstrate obstruction. The scan can appear normal even if the patient has an obstruction, either because urine output is low or because the obstruction is recent and dilatation has yet to develop.

Transrectal ultrasonography and biopsy are useful for patients with prostatic malignancy. Prostate volume can also be estimated and correlated with serum concentrations of prostate specific antigen to calculate the likelihood of malignant disease.

***Kidneys***

Ultrasonography is an ideal and a very dependable technique in locating the calcium deposits (stones) in the kidneys.

***Chest***

Ultrasonography is not particularly useful in the lungs because air causes a great deal of artefact. It is used, however, to locate and drain small effusions in pleural disease (especially for patients in intensive

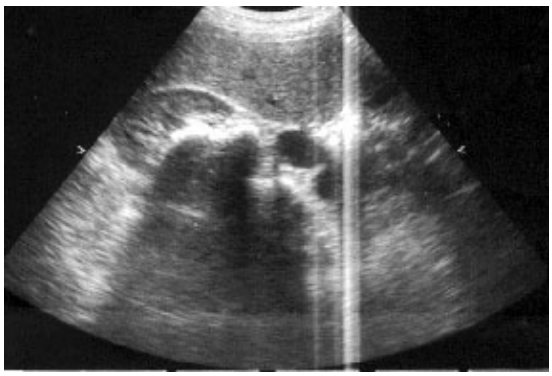


*Fig. 10 Sonography of the kidney stones*

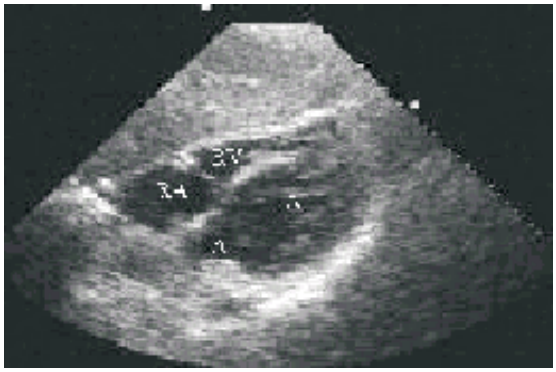


*Fig. 11 Sonography of the heart*

care in whom supine chest radiographs may be difficult to interpret). Solid components within the pleura can be distinguished from loculated fluid and biopsy specimens can be taken under ultrasound guidance.

***Ultrasonography, Cardiac***

This image depicts a normal subcostal view of the heart. The pericardium is a bright reflector surrounding the heart. All 4 chambers of the heart can be seen.

Abdominal aortic aneurysms can be measured and followed up with conventional ultrasonography. The role of Doppler ultrasonography in carotid artery disease has already been mentioned. More recently, it has been used to follow up arterial limb grafts to predict and prevent graft stenosis. Ultrasonography is an effective method of detecting clots and reduced flow in larger vessels of patients with deep vein thrombosis.

***Paediatrics***

Ultrasonography has several specific indications in children. Excellent images of the brain of neonates can be obtained by placing the ultrasound probe on the open fontanelle. This allows identification of haemorrhage in the ventricles or brain substance. Congential anomalies, including the presence and causes of hydrocephalus can also be shown.

In acutely ill infants both intussusception and pyloric stenosis can be identified, avoiding the need for contrast media and ionising radiation. Children with irritable hip can have ultrasonography to identify effusion into the joint and allow aspiration of fluid to exclude septic arthritis. Ultrasonography is now used to screen infants to exclude congenital hip dislocation at an early and treatable stage.

***Mammography***

Colour Doppler ultrasound technique is increasingly used now to differentiate the cyst and the tumour in the breast. X-rays for the soft tissue used in mammography cannot differentiate.

***Small Parts***

*Scrotum*

Ultrasonography is the best investigation for scrotal masses. If a possible malignant lesion is identified ultrasonography of the abdomen should be carried out to exclude para-aortic lymphadenopathy. Epididymitis can also be identified on ultrasonography. Testicular torsion is diagnosed clinically, but ultrasonography may help to show an abnormal lie of the testis or Doppler scanning may reveal absence of perfusion.

*Thyroid*

Ultrasonography is used to guide biopsy of thyroid masses. It will also differentiate between a multinodular goitre and a homogeneously enlarged gland and may confirm retrosternal extension.

*Breast*

Ultrasonography is not sensitive enough to be used to screen for cancer at any age. It is useful, however, in patients with a palpable mass which cannot be seen on mammography, in differentiating a fibroadenoma from a cyst (which look identical on mammography), and in investigating painful lumps such as abscesses, which cannot be compressed for mammography.

*Eye*

Ultrasonography of the eye is quick, painless, and simple. The ultrasound probe is placed directly on the closed eyelid, which is first covered in ultrasound jelly to provide good contact. This technique can show retinal detachments and vitreous haemorrhage and is also useful for detecting foreign bodies such as metal splinters in the eye or the retro-orbital tissues.

**What are the drawbacks to ultrasound?**

Probably the most serious drawback of ultrasonography is the fact that sound is not able to travel through certain organs whose surfaces reflect almost 100% of soundwaves. In such cases the interiors of these organs and those lying directly beneath them cannot be imaged. Organs filled with air such as the lungs, stomach and intestines are opaque to sound as are hard tissues such as bone.

**Conclusion**

Ultrasonography may end up a victim of its own success. The absence of ionising radiation, coupled with the other advantages has led to an overwhelming increase in requests for investigations, and because it is inexpensive and non-invasive, requests are difficult to refuse. Ultrasonography departments are therefore in danger of being overrun with inappropriate requests for an investigation which could have little effect on patient management. Thus a judicious view would be required to employ ultrasonography in the right manner for the benefit of a fitting user. It is also envisaged that ultrasonography could be used for therapy in furture.

High Intensity Focussed Ultrasound (HIFU) is more useful as an advanced therapeutic technique to hit tissues and latest reports suggest the efficacy of the procedure in its use in prostate reduction and also in the reduction of tumour growth.

# IANCAS Roundup

***Dr.(Mrs.) Radha Tomar*** *is Reader in School of Studies in Chemistry, Jiwaji University, Gwalior from 1989 onwards. She obtained M.Sc in Physical Chemistry from University of Mumbai in 1985 and Ph.D from Jiwaji University. Her major fields of interest are Material Synthesis, characterization and sorption studies. She has completed fully funded research project by UGC on "Ionexchange behaviour and catalytic properties of some mica minerals" and a BRNS project on "Sorption of Radionuclides from different aqueous waste solutions using Synthetic Inorganic Ion Exchanger. She is a recognized Research Guide for M.Phil and Ph.D. from Jiwaji University. She is a member of several scientific associations and She has published more than 20 research papers in various journals/symposia.*

A 46th BRNS-IANCAS National Workshop was organized by IANCAS from December 3-11, 2001 at School of Studies in Chemistry, Jiwaji Univeristy, Gwalior. Post Graduate teachers and other staff members of the science college participated in this workshop.

IANCAS donated γ-ray spectrometer and a G.M. Counter to the Nuclear Chemistry laboratory of the college. These equipments have been used by the students doing M.Sc by research under the guidance of Dr.Tomar.

Following the Workshop, a full paper on Nuclear Chemistry under Physical Chemistry (Elective II) was introduced for M.Sc IV Semester students. The topics cover a wide spectrum of the subject ranging from structure of nucleus, Nuclear Reactions, Detection, Measurement and Errors in measurement of radiation, Radiation hazards with safety aspects and Nuclear Reactors. A part of another paper on Computer for Chemists & Nuclear Chemistry also introduces Nuclear chemistry dealing with energetics of nuclear reactions, production and applications of radioisotopes in physico-chemical investigations.

A set of 10 experiments on 'Radiation Measurement' was introduced under Physical Chemistry practicals. In all these experiments sealed radioactive sources are used. A special topic on "Radiation Hazards" covering the various types of radiation, biological effects of radiation, concept of permissible dose and various aspects of shielding was introduced in the special Nuclear Chemistry paper.

The equipment received from IANCAS is being made available for other students in the university.

Dr.(Mrs.) Hemlata Bagla, Reader, Department of Nuclear Chemistry, K.C. College, Mumbai
E-mail:

# NUCLEUS

**Fluorine-18 Radiopharmaceuticals**

Positron Emission tomography (PET) is an imaging modality that is able to detect and quantitate positron-emitting radionuclide localized in the body non-invasively. Probing the intrinsic complexity of living body by imaging physiological, biochemical processes at high sensitivity has become a reality with the advances in PET imaging. Availability of suitable radiopharmaceutical (RPhCs) is the prime requisite for such imaging studies. PET radionuclide can be incorporated into wide range of compounds ranging from simple water to complex organic biomolecules such as drugs, peptides, sugars, amino acids, complex proteins etc. to make potential radiopharmaceutical. 2 Fluro [$^{18}$F]-2-deoxyglucose or $^{18}$F-FDG, is a PET radiopharmaceutical to study Glucose metabolism. $^{18}$F-FDG, like Glucose, is taken up by the cells and converted to 2-Fluoro Glucose-6-Phosphate by the action of hexokinase. However, it does not undergo further metabolism like glucose and hence gets trapped inside the cells. $^{18}$F-FDG is aptly named as the "Molecule of the Millennium" due to its versatility and enormous importance application in oncology, neurology and cardiology. It is the first PET radiopharmaceutical to be included in United States Pharmacopoeia USP 1989. Clinical demand for $^{18}$F-FDG has triggered technological advances in various fields such as accelerator technology, radiochemistry, detector systems and imaging software. Medical cyclotron for isotope production, automated module for radiochemistry and PET camera have become essential features of hospital facility of the modern era.

Among the PET radionuclides [$^{18}$F] is the most attractive candidate for radiopharmaceutical. Its half- life of 110 min. is sufficiently long to allow complex multistep radiosynthesis and utility of the radiopharmaceutical at sites moderately distant from its production. Fluorine due to its sterric size, high C-F bond energies and extremely electronegative nature mimics -OH-group and hence commonly being studied in medicinal chemistry. [$^{18}$F] is produced from both particle accelerators and nuclear reactors by using wide variety of nuclear reactions. The most common ones preferred for large scale routine production are $^{18}$O (p, n) $^{18}$F and $^{20}$Ne (d, $\alpha$) $^{18}$F. [$^{18}$F] decays by emitting positron having maximum energy of 635 MeV and mean range of 2.39 mm in water.

***Design criteria for [$^{18}$F] Radiopharmaceuticals***

The molecular mechanism underlying localization of PET radiopharmaceutical is either receptor binding or metabolic trapping or carrier mediated transport across cell membrane or binding to macromolecules such as DNA, RNA or protein. In the ideal case, radiopharmaceutical should interact only with the target molecule of interest with no non-specific accumulation. However an ideal radiopharmaceutical does not exist. High affinity ($B_{max}/K_d > 4$) and high specificity for target molecule is the main criteria for selection of radiotracer. In-vivo distribution of radiotracer must relate to physiological response to measure biochemical process under investigation. The radiotracer should exhibit adequate lipophilicity (log p>1.5) for optimal passage of lipid bilayer of cell membrane. Tracer should also show adequate in-vivo stability as

**Common PET Radionuclides**

| Radionuclide | $T_{1/2}$ min. | Decay | Max.energy MeV | Max. Specific activity Ci/mmole |
|---|---|---|---|---|
| Fluorine-18 | 109.70 | β+ 97%<br>EC 3% | 0.635 | $1.7\times10^9$ |
| Carbon-11 | 20 | β+ 99% | 0.96 | $9.22\times10^9$ |
| Nitrogen-13 | 9.96 | β+ 100% | 1.19 | $1.89\times10^9$ |

radiolabelled metabolites can bind to other molecules resulting in non-specific accumulation. Ideal pharmacokinetics showing clearance of non-specifically bound radioactivity within the time scale of measurement for PET becomes necessary to discriminate between the target and non- target.

Synthesis of organic compounds labelled with [$^{18}$F] with the goal of use as in-vivo radiopharmaceutical involves many consideration. The most obvious is the yield, specific activity and adequate radionuclidic, chemical, radiochemical and pharmaceutical purity. Short half-life and high radiation field associated with multi curie quantities of PET radionuclides place additional constraints for PET radiopharmaceuticals.

***Radiolabelling: Nucleophilic Fluorination***

Fluorine [$^{18}$F] is unique radionuclide in the sense that radiochemistry for labeling depends on the production route. Irradiation of $^{18}$O enriched water using (p,n) reaction is the most effective and convenient way to produce [$^{18}$F] fluoride in large quantities. After irradiation [$^{18}$F] fluoride is separated from $^{18}$O enriched water. Phase transfer catalyst such as tetraalkylammonium salts or aminopolyethers are used for trapping fluoride ion for nucleophilic substitution reactions. Various aliphatic as well as aromatic substitutions with [$^{18}$F] have been reported. There are two main strategies used. One is direct substitution of an appropriate leaving group by [$^{18}$F] fluoride in the desired molecule followed by hydrolysis of protective groups. Sulfonic acid esters are most effective leaving groups in case of aliphatic nucleophilic substitutions where as nitro or trimethyl ammonium precursors are reported to work well with aromatic ring substitutions. Another approach is preparation of [$^{18}$F] synthon i.e. [$^{18}$F] fluorinated intermediate by nucleophilic substitution followed by its reaction with desired precursor. For example fluoroalkylating agents used in synthesis of [$^{18}$F]Fluorocholine, [$^{18}$F]Fluoroethyltyrosine etc.

***Radiolabelling: Electrophilic Fluorination***

Elemental fluorine $F_2$ as [$^{18}$F] Fluorinating agent has been used from the beginning in PET radiochemistry. $^{20}$Ne containing 0.1-0.3 % fluorine gas when used as the target, fluorination can be performed directly with [$^{18}$F]$_2$ or often by converting into [$^{18}$F]acetylhypofluorite prior to the reaction. The possible reactions that can be performed are addition to double bond or substitutions in aromatic ring. Substitution of trialkyl tin or mercury group is being recently studied. A well-known example is the preparation of L- [$^{18}$F] Fluro-DOPA.

During the last ten years, PET radiochemistry has developed from pioneering position with emphasis on targetry and labeling strategies to a mature field of radiopharmaceuticals. Synthesis modules based on nucleophilic and electrophilic [$^{18}$F] fluorination are now available commercially. Number of drugs and biomolecules are being studied for radiolabeling with [$^{18}$F] in order to achieve target specific radiopharmaceuticals. Increasing specific activity by downscaling the amounts of precursors, developing more precise and quicker purification methods, increasing the yield of radiolabeling are the challenges for radiochemist to scale up research products for routine production.

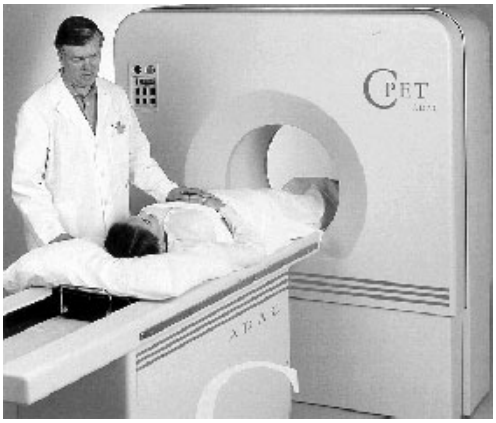
With the availability of first medical cyclotron and radiopharmacy facility at LNMS, (TMH Annexe, Parel) BARC we have entered a new era in nuclear medicine. Radiopharamceutical Programme has taken a first big step by making [$^{18}$F] FDG available routinely for clinical applications to hospitals in Mumbai, but it's just a beginning in an alluring world of PET radiopharmaceuticals.

**References**

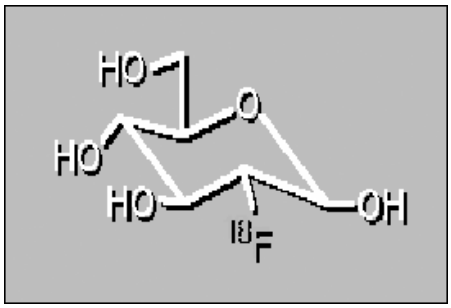

1. PET/CT: a new imaging technology in nuclear medicine, *Eur. J. Nucl. Med. Mol. Imaging,* **30** (2003) 1419.
2. A brief history of positron Emission tomography, Seminars in Nuclear Medicine, 20 (1998) 213.
3. PET radiopharmaceuticals: State of the art and future prospects, Seminars in Nuclear Medicine, 20 (1998) 221.
4. What does positron emission tomography offer oncology? *Eur. J. cancer*, **36** (2000) 2028.
5. $^{18}$F labelled radiopharmaceuticals for PET in oncology excluding FDG, *Nucl. Med. Biol*. **27(2)** (2000) 103.

*Medical Cyclotron and PET Radiopharmacy of BARC at Tata Memorial Centre Basement, Parel, Mumbai*


*Synthesis module for [$^{18}$F] FDG*




*PET imaging*




*[$^{18}$F] FDG*

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