## **C**ontents

Editorial	
Radiology education & practice- mapping the road to professional excellence Brigadier C Mohan, Surg Cdr IK Indrajit	1
Communication skills in clinical radiology: "Radiologists are bright people in dark rooms" Dandu Ravi Varma	4
Commentaries	
A basic review of nuclear medicine Lt Col Harkirat Singh, Brigadier SS Anand	6
Displaced proximal humeral fractures Mallinath.G	16
Necrotizing soft tissue infections P.Sampath Kumar	18
Down syndrome – screening and diagnosis P. Reddi Rani	22
Review articles	
Basics of multislice CT Namita Singh Saini, RP Tripathi, Lt Col Giriraj Singh	26
Basics of CT perfusion imaging Uday D Patil	32
PET/CT - a new imaging modality Venkatesh Rangarajan, Sneha Shah, Nilendu Purandare Anshu Rajnish	36
Interventional radiology-a basic introduction Surg Cdr R Pant	42
Fetal MRI : a clinical review Sona Pungavkar	48

Lesion localization on plain chest radiographs Sanjay Jain	57
Role of multislice CT in colonic lesions and CT colonoscopy Rajul Rastogi	62
Imaging in head trauma - a review Surg Cdr IK Indrajit, Brigadier C Mohan	67
Correspondence	
Surgical experience of well differentiated papillary carcinoma Thyroid with involvement of Larynx Satish Jain, Sandeep Jhanjee T. Singh, Saurabh, Sumit Jain	73
Spring-water cyst in an atypical location in the mediastinum Rajul Rastogi, Satish Kumar Bhargava Anupama Tandon, Sumeet Bhargava	75
Pulmonary arteriovenous malformation in a child-a case report Rajul Rastogi, Aatish Kumar Bhargava Gopesh Mehrotra, Sumeet Bhargava	77
Multi organ involvement and regional nerve block: anesthetic technique for above knee amputation in ASA III – ASA IV risk patients D. A Karthiraj, S Vasishta	79
Recent advances	
Melatonin – a mystery Rakesh Chandra Chaurasia	82
Osteoarthritis and stem cell Latika Arora	85
Metastatic spinal cord compression: current concepts in management Shyama Prem S, Gopalakrishnan K Sathyanarayana Reddy	93

**Editorial** 

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adiology and Imaging constitutes an integral part in today's world of medicine. This speciality plays an important role in clinical management of patients from almost all other specialities. Over the last few decades staggering advances have occurred in Radiology and Imaging, mostly technology driven, resulting in newer modalities, novel imaging applications and powerful utilites. As much as this has been globally accepted and universally appreciated, few challenges in radiology education and practice have emerged. For students of Radiology, these dilemma occur at two specific time points. The first is at the very start, which is experienced during handling the speciality while studying for the post graduation course. Here the issues include the vastness of the subject, the excessive amount of information available in Radiology literature that continuously reaches out to all other specialites, the apprehension in handling theory and viva exams. The second arises after obtaining the necessary professional degrees in Radiology and commencing practice. The issues that dominate around this time in ones career includes where to practice, which modality to practice, how to keep pace with the ongoing technology advancement, how to stabilise ones career and what are the means of learning in the desired profes-

sional field. Set against this background, this material outlines an achievable method in mapping the road of professional excellence in Radiology Education & Practice, under the framework of National Board of Examinations<sup>1</sup>, Medical Council of India<sup>2</sup> and various deemed and other Indian universities.

Professionalism in Radiology Education-When approached from an exam point of view, Radiology as a subject comprises of the following broad systems: Radiophysics, Radiation, Modalities, Brain, Head and Neck, Chest, Cardiovascular, Abdomen, Hepatobilairy, Genitourinary, Gynecology and Female Pelvis, Obstetrics and Fetal Imaging Musculoskeletal and Vascular Systems. These system forms the basic foundation for preparing the curriculum and syllabi, as well as in preparing the sets of question papers during the time of examination. Such a convenient division of the entire subject can serve as a broad template in making a timetable for revision, over a course of 3 years of the post graduation course. All students of Radiology need to understand and possess a working knowledge of the basics, The basics of anatomy, the fundamental principles of radiography, the nittygritties of radiographic contrast as well as radiation are to be well understood 3. One successful method is to write down the text or book material, making some sort of notes; drawing diagrams is another method to understand topics better, since they would always come in handy during the theory segment of exams. As regards to viva, the whole issue is one of answering as correctly and confidently as possible. A cool countenance with intelligent answers, an unruffled approach with self-assured expression of common entities and practical issues in radiology, an ability to answer all questions nonstop as accurately as possible will be the surest way to crack the examination successfully. Never enter into academic differences of opinion, not at least at the exam table, and remember the age old adage: Common conditions are commoner than uncommon conditions; likewise atypical presentation of common conditions are commoner than typical presentations of uncommon conditions. Clearly, viva voce requires total knowledge, fluent verbal expression, anticipatory performance and communication skills. One way to prepare for an viva voce is to read and listen to your own voice speak. This is similar to a practice session, wherein one is prepared, reflecting the famous "Repetition is the mother of learning". During the formative years in Radiology courses, few measures help in a long way to become a successful professional. These would include maintaining a log book regularly, working with a positive attitude and a pleasant personality, having an overall bearing and dressing sense, observing polite courtesy to one and all, following ethical practices, showing respect for seniors and juniors alike, possessing good communication skills with patients and skills with peers.

Professionalism in Radiology Practice-The transition from a student in Radiology to a practicing Radiologist is essentially a shift in direction. The focus ironically shifts from books, journals and patients to a reverse order of patients, journals and books. The all-important role played by Radiology comes in here, which when spelt in a nutshell, essentially provides imaging answers to clinical questions. However, it must be remembered that when one launches into practice in modality or modalities, there are four key areas that needs attention and eventual mastery. Firstly one should be well conversant with the clinical aspects of a given case, even before the case is worked up on the modality; Secondly a technical knowledge of the modality equipment should be mastered, be it Ultrasonography or Color Doppler, CT or MRI. Attention must be given to its abilities and capabilities, upgradeability and emerging newer premium features; Thirdly the technique of image acquisition, processing and post-processing has to be constantly fine tuned hands-on. Clearly, this would include patient handling from start to finish. Fourthly and importantly the quality of the generated investigation report. It should reflect the meticulousness and thoroughness of the work done in previously described three areas, and answer the clinical referral as closely as possible to the truth.

Radiology Education and Practice in the immediate future - Over the years, few changes have occurred in Radiology practice. An awareness of this is a must for students, since these will have a direct impact on Radiology practice in the years ahead. There are important professional bodies which enhance radiological skills. These bodies, comprising radiology experts from our country, are an opportunity to sustain the professional momentum which is triggered initially during post graduation. These bodies include Indian Radiological & Imaging Association (IRIA)<sup>4</sup>, Indian Journal of Radiology and Imaging (IJRI) 5, Indian College of Radiology (ICRI)6, Indian Society of Neuroradiology (ISNR)<sup>7</sup>, Indian Vascular Society of Interventional Radiology (ISVIR)8 and Refindia (Radiology Education Foundation) 9, to name a few. Computers and Internet have entered into the daily practice of Radiology, and occupies a central position in areas like patient flow, billing, records, equipment, report generation, image archiving and image transfer. Digital Imaging and Communications in Medicine (DICOM) is a "cooperative standard" that allows compatibility between imaging systems, by connectivity of imaging and associated medical equipments of different vendors<sup>10</sup>. It enables integration of scanners, servers, workstations, printers, and network hardware from multiple vendors into a picture archiving and communication system. It promotes the development of PACS and Image Networking in a LAN and WAN scenario. PACS (Picture Archiving and Communication Systems) is a network system that integrates all modalities equipments and its accessories into a 100% digital environment. This "streamlines workflow, reduces operating expenses, and improves patient care". Legal awareness in professional practice is important with the central theme being exercise of reasonable skill and professional care. The PNDT act and its impact on Ultrasonography is to be understood clearly. Another area needing attention is writing ethics, especially issues like plagiarism. Plagiarism simply denotes literary theft. Common deviations that constitute plagiarism includes "a) downloading a free research paper; b) copying an article from the web or an online electronic database; c) copying material from a local source; d) cutting and pasting to create a paper from several sources; e) quoting less than all the words copied; and g) faking a citation<sup>11</sup>.

To steer clear of unethical scientific writing, a small but valuable set of guidelines comprises the following:

 At all times acknowledge the contribution of original authors, even if their written ideas are paraphrased. Remember paraphrase involves

- restating author's ideas, in your own words<sup>12</sup>
- Cite the source of material written, as fittingly and as correctly as possible, when preparing a written document or a slide presentation.
- Use inverted quotes suitably, if material from citation or article is inserted unchanged. Furthermore, inverted quotes should be used mandatorily for all direct quotations, including occasional phrases.
- Be aware of Ingelfinger rule, (named after Franz J. Ingelfinger, editor of New England Journal of Medicine in 1969)13, which denotes a "policy of considering a manuscript for publication only if its substance has not been submitted or reported elsewhere<sup>14</sup>, essentially "to protect the Journal from publishing material that had already been published and thus had lost its originality". Rarely at times, for reasons of dissemination of vital information for improving health care, this rule has been relaxed.
- Exercise caution while referring, analyzing and incorporating scientific material available on the Internet. There are several instances of incomplete, misleading, inaccurate, disparate medical information available on the Internet<sup>15</sup>
- Always encourage yourself to think and write on original and new ideas.

Conclusion-Radiology is an ever expanding speciality, at the cross-roads of all medical disciplines. Professional excellence in Radiology Education & Practice is an important issue in Radiology. Today's Radiology students are tomorrow's practioners, reflecting the continuum of Radiology education into Radiology practice. Few implementable methods in harnessing the full potential of professional skills the speciality has been outlined in this article.

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### **Editorial**

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adiology has always been on the cutting edge of medical science. Especially, the last three-and-a-half decades have seen several advances in the field of radiology, that have brought in revolutionary changes in the screening, diagnosis and management of disease<sup>1</sup>. In today's medical practice, radiological investigations form an integral part of strategies to screen for disease, to confirm suspected disease, to delineate the extent of disease, to guide biopsies and to monitor the efficacy of treatment. These advances have readily and consistently translated into progresses in other fields of medicine and have made large contributions to the growth of specialties such as gastroenterology, urology, neurology and neurosurgery. Thus, it would not be an exaggeration to say that radiology has now assumed a central role in today's medical practice. The progress in medical imaging technology has brought in newer, more complex equipment into the radiologist's armamentarium. As radiologists became more and more preoccupied with their 'new toys', they began to forget the very basis of their identity as a medical expert - patient care<sup>2</sup>. The separation of radiology into diagnostic radiology and radiation therapy has further widened the gap between the radiologist and the patient. The entry of technology such as Picture Archiving and Communication System (PACS) and teleradiology has improved the

workflow for the radiologist, but has further widened the chasm between the radiologist and the patient. Today, except for a select few practicing interventional radiologists, most radiologists choose to shy away from directly dealing with patients – except for limited contact during diagnostic procedures<sup>3</sup>.

Even worse is the tendency for most radiologists to avoid interaction with the referring consultant. The busy consultant rarely finds time to come to the radiology department and the radiologist rarely tries to actually ask the consultant for relevant clinical details. As a result, when a referring physician sends a patient for a radiological investigation, he receives a report that is as ambiguous and confusing as the radiograph itself. The report usually contains what the radiologist can see in the image - and not what the physician wants the radiologist to look for. Consequently, the radiologist has become a behind-the-scenes player in current medical practice. It is immediately apparent to the lay public, what a surgeon or a dermatologist does, but not many patients appreciate the role of the radiologist in today's healthcare. A radiological procedure essentially starts with a review of the patient's history and physical findings, and defining the questions that need to be answered for appropriate clinical management. Interacting with the referring physician provides vital information that would ensure that

the study is properly performed and interpreted. The radiologist has to remember that though for him, it may be just one more procedure to be done; it may be the first ever for the patient. Often the patient is wheeled in early in the morning from the warmth of his bed, to the cold and impersonal radiology department; where the radiologist would seem more interested in looking at the monitor of an ultrasound scanner than look at him. One can only imagine the plight of the sick and confused patient, who is sent into a bore of an MR unit, without being properly counseled. It is basic courtesy to inform the patient what procedure is being performed, why it is being performed, and to explain what the instructions he is expected to follow during it.

Paying attention to these principles prior to starting the investigation helps to ensure that the appropriate radiological investigation is performed and that it is customized to the specific requirement of the patient. In this endeavor, the radiologist should not shy away from visiting the patient in his ward, introducing himself and eliciting the clinical information he needs. The patient would feel more comfortable with a radiologist who introduces himself in the ward, a day prior to the procedure, rather than in the cold confines of the radiology department. This goes a long way in reducing the number of the so called 'un-cooperative' patients. Effective communication is a means by which the radiologist can instill confidence and trust in the patient's mind. It is surprising how many children consent to painful procedures such as biopsies, simply by augmenting the effects of local anesthesia with 'vocal anesthesia'.

The most important means of communication between the radiologist and the referring consultant is through the requisition form and the radiological report. The requisition form should not be interpreted as an order for a radiological investigation, but should be perceived as a request for a radiological consultation. Every attempt should be made to integrate the clinical skills of the referring physician and experience of the radiologist, so as to meet the needs of the patient. The radiological report not only documents and provides an interpretation of the radiological findings, but also forms an important part of the patient's medical records. The American College of Radiology has recognized that effective communication is a critical component of diagnostic imaging and spells the essential components of a radiological report<sup>4</sup>.

Radiological investigations seldom give Aunt Minnie like pictures where imaging findings alone can provide a diagnosis. In the real life, most often, the key pieces in a diagnostic puzzle are not in the image but in the medical history and findings of clinical examination. Accurate clinical history makes the difference between a vague report that just describes the imaging features and gives a long list of differential diagnoses; and a crisp report that offers clinically relevant information and suggests appropriate follow up studies. For example, presence of a lower zone opacity in a chest radiograph would have different implications depending on whether the subject is an asymptomatic athlete, a comatose patient with fever, or a patient with a known malignancy. The requisition form rarely contains this information and a personal interview of the patient by the radiologist is the only effective means to elicit this information.

Considering that the average radiologist has undergone all basic training as a medical doctor and that the referring colleague has barely any structured training in radiological sciences, it is only natural that the radiologist has a better chance of assimilating clinical and radiological findings and coming to an accurate diagnosis than the referring doctor. This is if and only if the radiologist believes that he can make a difference, and is willing to put in the effort.

We need to come out of our dark rooms. In this era where it is possible to visualize every nook and corner of the body using radiological techniques, the need of the hour is to improve the visibility of the radiologist. Radiologists should make attempts to initiate meaningful dialogue with both the patient and the referring physician, and use his skills to play an active role in the clinical management of the patient. If radiology is to retain its identity as a specialty, communication skills must be made a part of the radiology curriculum and attempts should be made to convert the radiology training into a more clinical radiology training. Radiology trainees should devote as much attention to the clinical details and appropriateness of the investigation, as to lesion de-

tection and differential diagnosis<sup>5</sup>. Considering that the field of radiology attracts the cream of medical graduates into its fold, we should strive to bring the specialty back to its rightful place – Radiologists should become the bright people under the spotlight. Acknowledgement-The Author wishes to acknowledge the contribution of Prof.A.K.Gupta, Professor and Head, Department of Imaging Sciences and Interventional Radiology, Sri Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, who has always stressed the importance of a more clinical approach to radiology and made efforts to inculcate this habit in all his students.

#### Further reading

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# Commentary

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uclear Medicine is a branch of medicine that involves the use of radionuclides for diagnosis and therapy. Its clinical applications include 'In vitro' applications like Radio-immuno-assay (used in assay of hormones/drugs/ tumor markers etc) and 'In vivo' applications that include Radionuclide scintigraphic (Imaging) studies and Radionuclide therapy. Medical imaging is based on the interaction of energy with biological tissues. In Nuclear Medicine, Gamma ray emitting isotopes are tagged with certain biologically active pharmaceuticals to form tracers called radiopharmaceuticals (RP). The radioactive component of the RP permits external detection and the biologically active moiety determines the biodistribution of the RP. Diagnostic inference is gained by recording the distribution of RPs, both spatially and temporally. Tracer pharmaco-kinetics and selective tissue uptake form the basis of diagnostic utility. The unique strength of Nuclear medicine imaging lies in its ability to assess the organ function along with the structure. For studying different organ systems, radiotracers are selected based on their pharmaco-kinetics and biodistribution characteristics. The RP is either injected, ingested, or inhaled. The radioactive isotope decays, resulting in the emission of gamma rays. Radiation detection & instru-

detection devices called 'gamma cameras' are used to record the temporal and spatial distribution of the radioactivity in the subject. The components making up the gamma camera are- the collimator, detector crystal, photomultiplier tube array, the position logic circuits, and the data analysis computer.

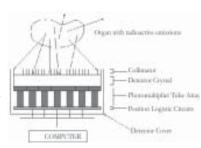


Figure 1, Layout of a gamma camera

### Image acquisition

Planar imaging-The simplest acquisition protocol is the planar image in which the detector array is stationary over the patient, and acquires data from one angle only. The two-dimensional image created with this type of acquisition is similar to an X-ray radiograph. Bone scans are done primarily in this fashion.

Planar dynamic imaging-Since the camera remains at a fixed position in a planar study, it is possible to observe the transit of a radiotracer through the body by acquiring a series of planar images of the patient over time. Each image is a result of summing data over a short time interval, typically 1-10 seconds. If many projections are taken over a long time, then an animation of the tracer movement can be viewed (in a cine mode) and data analysis can be performed. The most common dynamic planar scan is done to measure glomerular filtration rate in the kidneys

lar filtration rate in the kidneys. SPECT imaging -Conventionally used planar radionuclide imaging suffered from an inherent drawback of reduced object contrast as a result of the background activity. This was overcome by incorporation of tomographic or "cut section" imaging technique similar to that used in X-ray computed tomography (CT). Tomographic imaging improves object definition and aids in more accurate depiction of the distribution of radio-activity. Single Photon Emission Computed Tomography (SPECT) systems consist of gamma camera heads mounted on a rotating gantry. As its name suggests, single photon gamma ray emissions (vs dual photon coincidence imaging in PET), are the source of information, rather than X-ray transmissions as used in conventional Computed Tomography. In SPECT imaging the camera rotates around the patient, and acquires views of the tracer distribution at multiple angles. After the data has been acquired from different angles, it is possible to reconstruct a three dimensional view of the radiotracer distribution within the body. The number of detector heads may vary from one to four. Multiple heads

mentation-Specialised radiation

are desirable as they allow more data collection in a given time period, reducing the imaging time while retaining the image quality. Gated SPECT imaging-As the heart is a moving object, by performing a regular SPECT of the heart, the end image obtained will represent the average position of the heart over the time the scan was taken. It is possible to view the heart at various stages of its contraction cycle however, by subdividing each SPECT projection view into a series of subviews, each depicting the heart at a different stage of its cycle. In order to do this, the SPECT camera must be connected to machine which ECG

synchronises the data acquisition with the cardiac cycle.

Clinical applications

Nuclear medicine has vast applications covering almost all the organ systems of the body.

Cardiovascular system-Scintigraphic evaluation of myocardial perfusion called Myocardial perfusion imaging (MPI), is a valuable noninvasive diagnostic technique for the diagnosis of coronary artery disease. MPI is classically performed as a combination of post-stress and rest studies to detect reversible myocardial ischemia. Thallium-201 (201Tl) introduced as a myocardial perfusion imaging agent in the early 1970s remained in

common use until the mid-1980s, when 99m Tc-labeled radiopharmaceuticals were developed and, for the most part, replaced thallium for evaluating myocardial perfusion abnormalities. MPI depicts two physiological events. First, the radiopharmaceutical must be delivered to the myocardium. Second, a viable, metabolically active myocardial cell must be present to extract the radiotracer. Other scintigraphic cardiac studies include Infarct avid imaging (to detect myocardial infarction), Radionuclide ventriculography multigated acquisition (MUGA) & study of adrenergic status of the heart (Table-1).

Table-1, Common Nuclear Medical Applications in Heart				
Type of scan	Indication	RP used	Biological Behaviour/ Mechanism	
Myocardial Perfusion	Diagnosis of coronary artery disease.	Thallium-201	Behaves like Potassium ion.	
Imaging(MPI)	Evaluation of known coronary disease, its		Extracted in proportion to blood	
	location and extent of ischaemia		flow.	
	Evaluating the effectiveness of medical			
	treatment.			
	Risk stratification, post MI			
	Determine the cause for change in	99m–Tc Isonitriles	Myocardial uptake of cationic	
	symptom pattern in patients with	(Sestamibi/	complexes, proportional to blood	
	known CAD	Tetrofosmin/	flow.	
	Pre operative evaluation of major non	Teboroxime).		
	cardiac surgery in patients with known			
	coronary disease			
	Assessment of Haemodynamic			
	Significance of lesion seen on			
	Coronary Angiography.			
	Post Infarction - Assessment of			
	Myocardial perfusion and reserve.			
	Post revascularization – graft			
	patency after CABG or Stent			
	stenosis after PTCA			
	Cardiomyopathy – Ischemic vs.			
	Nonischemic			
Radionuclide	Accurate assessment of ventricular function	99m -Tc labeled	Labeled RBCs serve as blood pool	
venticulography	(ejection fraction, stroke volume, cardiac	RBCs	agents to assess Cardiac chamber	
(MUGA Scan)	output, ventricular filling and emptying		motion	
	rates), wall motion abnormalities and cardiac			
	shunt quantification.			

Genito-urinary system -Renal scintigraphic studies are used for assessment and quantification of renal function, differentiating obstructive from non obstructive hydronephrosis, confirming urinary leaks, evaluation of blood flow and viability in native and transplant kidney, and diagnosing acute pyelonephritis (Table-2). Over 50% of renal function may be lost before a rise in serum creatinine occurs. Therefore it is important to apply more sensi-

tive techniques to detect early impairment of renal function. Wellestablished imaging and non-imaging techniques are available to measure glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) using radionuclide agents. In acute renal failure, radionuclide imaging has a diagnostic and prognostic role. 99m Tc-mercaptoacetyltriglycine (MAG3) is now established as the renal tracer of choice. MAG3 excretion occurs mainly via tubu-

lar secretion at the distal part of the proximal tubule. Dimercaptoacetyl succininic acid (DMSA), used for renal cortical imaging localizes in the renal cortex by binding to the proximal tubules, and provides primarily morphologic information. Acute bacterial infection of the kidney may appear as focal, photon-deficient areas in the renal cortex, which can be best seen with <sup>99m</sup>Tc-DMSA.

Radionuclide   Renogram   Renal Function assessment (especially in children & diabetics).   Quantifying Function of Each Kidney – split renal function.   Non visualization of Kidney on IVP.   Renal Transplant   Evaluation   Post-op Leaks   Ectopic Kidney   Diagnosis of Renovascular   Hypertension (RVH)   -Uncontrolled BP on drugs -Young hypertensive   -Unilareal small kidney -Abdominal Bruit   -Occlusive Arterial Disease elsewhere in the Body -Worsening Renal Function   Decision regarding necessity of Surgical Intervention   Post Intervention Follow up.   Localisation of Ectopic Kidney   Surgical Intervention Follow up.   Decetion of Follow ip.   Active Pyelonchritis   Detection of Scars in VUR.   Pynamic Radionuclide   Vesico-uretral Relax (VUR)   - Pynamic Reintigraphy   Torsion, epididymo-orchitis   Pym Tc- Pertechnetate   Intravascular localisation.   Pym Tc- Pertechnetate   Pym Tc- Pertechnetate   Pym Tc- Pym	Tabl	Table-2, Common Nuclear Medical Applications in GUT				
Renal Function assessment (especially in children & diabetics). Quantifying Function of Each Kidney – split renal function. Non visualization of Kidney on IVP. Renal Transplant Evaluation Post-op Leaks Ectopic Kidney ACE inhibitor (Captopril) Renography  ACE inhibitor (Captopril) Renography  ACE inhibitor (Captopril) Renography  Diagnosis of Renovascular Hypertensive - Unitareal small kidney - Abdominal Bruit - Occlusive Arterial Disease elsewhere in the Body - Worsening Renal Function with ACE Inhibitors.  Diuretic Renography  Districtive Uropathy. Differentiate between functional and mechanical obstruction Decision regarding necessity of Surgical Intervention Follow up.  Renal Cortical Scan  Localisation of Ectopic kidney. Acute Pyelonehritis. Detection of Scars in VUR.  Dynamic Radionuclide Cystography (DRCG)  Renal Function assessment (especially inclided a diabetics). Quantification of transl function. Allow assessment and quantification of renal function.  Pown To DTPA/ (MAG-3)  Drop in renal function.  Pown To DTPA/ (MAG-3)  Addition of diuretic helps to differentiate between functional and mechanical obstruction.  Addition of diuretic helps to differentiate between functional and mechanical obstruction.  Pown To DMSA/GHA  Cortical binding in proximal tubules.  Compartmental localisation.  Drop and transplant Evaluation of direction of detecting VUR, with low radiation burden.	Type of scan	Indication	Radionuclide Biological behaviour/			
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Testicular scintigraphy Torsion, epididymo-orchitis 99m Tc- Pertechnetate Intravascular localisation.						
	Testicular scintigraphy	Torsion, epididymo-orchitis	99m Tc- Pertechnetate	Intravascular localisation.		

Pulmonary system-Ventilationperfusion (V/Q) lung scanning is a non-invasive method of evaluating patients for pulmonary embolism. When pulmonary embolism is suspected the goal of diagnostic imaging is to direct and validate treatment, be it anticoagulation or thrombolysis. Accurate interpretation of V/Q scan requires comparison with a chest radiograph taken within 24 hours. Ventilation images are acquired using xenon-133, krypton-81m, radiolabelled aerosols (DTPA);

perfusion images are obtained using 99mTc macroaggregated albumin (MAA) (Table 3). Lung scans are typically interpreted as being normal or having low probability, intermediate (indeterminate) probability, or high probability for pulmonary embolism. Interpretation criteria for these are complex and require integrating clinical, radiological, and physiological data. A normal lung scan excludes clinically important pulmonary embolism, whereas a scintigraphic study showing multiple, wedge shaped perfusion defects with normal ventilation and a chest radiograph that is clear in the corresponding areas suggest high probability for pulmonary embolism. Patients with normal or very low probability scans do not require treatment for pulmonary embolism, whereas those with a high probability scan do. Interpretation of intermediate probability scans requires more expertise, and consultation with the specialist in nuclear medicine is essential.

Table-3,	Table-3, Common Nuclear Medical Applications in Pulmonary System			
Type of scan	Indication	Radionuclide	Biological behaviour/	
		used	Mechanism	
Lung Perfusion scan.	Pulmonary Embolism (PE)	99m Tc– Macro-aggregated albumin (MAA)	Capillary blockade	
Lung Ventilation scan.	Pulmonary Embolism (PE)	99m Tc – DTPA (aerosolized) 133 Xe / 81 Kr gas	Distribution in lung airspace.	
DTPA Aerosol Clearance Study	Interstial Lung Disease	99m Tc - Aerosolized DTPA	Ventilation study of lung	
Gallium Scan	Sarcoidosis, Interstitial lung disease.	Gallium-67	Binds to lactoferrin & ferritin.Concentrates in inflammatory cells. Uptake indicates active disease.	

Skeletal system-The availability of technetium labeled bone seeking radiopharmaceuticals with improved soft tissue clearance has paved way for sensitive, high resolution images which accounts for the widespread use of these agents in bone scanning. Radionuclide bone scanning is commonly performed using radiolabelled diphosphonates such as 99mTc methylene diphosphonate (99mTc-MDP) (Table-4) and is commonly used to detect skeletal metastases. The bone scan often provides an earlier diagnosis and demonstrates more lesions than can be found by radiographic procedures. The technique is sensitive and allows visualization of the whole skeleton in a short time. Bone scintigraphy is used to stage the disease and to evaluate the efficacy of treatment. Bone scans are more sensitive than Radiographs, since lesions generally cannot be seen on radiographs until 30%-50% of bone mineral matrix has been lost. In primary bone tumors, the major roles of bone scintigraphy are to detect distal bone metastases, evaluate the response to neoadjuvant chemotherapy, and restage the dis-

ease. In benign bone disease, bone scintigraphy is used to diagnose athletic injuries (such as stress fractures and shin splints), show avascular necrosis of the hips and knees, differentiate between loosening and infection of joint prostheses, diagnose metabolic bone disease, perform a joint survey in arthritis, and investigate patients with bone pain of unknown origin. Tomographic imaging, with its improved sensitivity over planar imaging, is particularly beneficial in the investigation of low back pain.

Table-	Table-4, Common Nuclear Medical Applications in Skeletal System			
Type of scan	Indication	Radionuclide used	Biological behaviour/ Mechanism	
Cortical Bone Scan	Metastases work Up Stress Fracture Avascular necrosis of bone Backache Metabolic Bone Disease Post Joint Replacement – Loosing vs. Infection	99m Tc- Polyphosphate compounds. Methyl diphosphonate (MDP) is most commonly used .  F-18 PET bone Scan.	MDP is a phosphate analogue and concentrates in the mineral matrix (hydroxy-apatite) of the bone.  Fluoride ions behave as	
	Paget's Disease Fibrous Dysplasia Viability of Bone Graft Osteoid Osteoma Scaphoid Fracture		analogues of hydroxyl ions and localize in hydroxy-apatite mineral matrix.	
Bone Marrow scan	For marrow disease -marrow infarction, metastases, infiltration.	99m –Tc Colloid scan.	Localise in reticuloendothelial cells by phagocytosis.	
		18 F-FDG PET	Metabolism in marrow: native cells and tumors.	
Bone infection scan	Osteomyelitis	<sup>111</sup> Indium Leukocyte <sup>67</sup> Gallium Scan	Cellular diapedesis	

Gastro-intestinal & hepatobiliary system-Motility tests can assess oesophageal, gastric, and small and large bowel motility. Gastric emptying is one of the more common tests and is used investigate suspected gastroparesis in diabetic patients and patients after gastric surgery or when taking medication which affects gastric motility. In vitro tests include the carbon-14 urea breath test for Helicobacter pylori infection, the modified Schilling test to differentiate between vitamin B-12 malabsorption secondary to intrinsic factor deficiency (pernicious anaemia)

and ileal malabsorption, and the selenium-75 homotaurocholate (SEHCAT) test, which is used to detect malabsorption of bile acid. Although endoscopy is often used to detect gastrointestinal bleeding, it can be unhelpful, particularly if the bleeding is intermittent or very heavy and the mucosa is obscured. In such cases, imaging of radiolabelled autologous red blood cells may be of help. Bleeding can be detected for 24 hours after radiotracer is given, and positive results may obviate the need for angiography. Red blood cell imaging is well tolerated, is easy to perform in acutely ill patients, and has a high sensitivity, even at low bleeding rates (0.5-1.25 ml/ minute). Where Meckel's diverticulum is suspected, 99mTcpertechnetate should be used, and scintigraphy has a sensitivity of greater than 80% for detecting ectopic gastric mucosa. Biliary scintigraphy using 99mTciminodiacetic acid derivatives (Table-5) is used to assess hepatobiliary function. Iminodiacetates are taken up the hepatocytes and excreted in the bile, with accumulation in the gall bladder and excretion into the small bowel.

Table-5, Commo	Table-5, Common Nuclear Medical Applications in GIT and Hepatobilairy System			
Type of scan	Indication	Radionuclide used	Biological behaviour/ Mechanism	
Hepatobiliary scan	Acute cholecystitis, Biliary atresia, Biliary Leaks, Enterogastric Reflux, Sphincter of Oddi dysfunction, Cystic Duct Syndrome, Ectopic Gallbladder.	99m Tc- Imino-diacetates ( HIDA/ Mebrofenin )	Active uptake by hepatocytes and secretion into bile. Follow bilirubin excretion pathway.	
Liver- spleen Colloid scan	Hepatic Cirrhosis, S.O.Ls of Liver/ spleen, Ectopic spleen, Splenenculi, RES function.	99m Tc- Sulfur colloid	Localise in reticuloendothelial cells by phagocytosis.	
GI bleed scan	Detection of G.I. Bleed- Useful for detecting intermittent GI bleed. Can detect bleed as small as 0.05 ml/min.	99m Tc- RBC/ Sulfur Colloid	Extravasation in bowel.	
RBC liver scan	Hepatic Hemangioma- Multi headed SPECT can detect all hemangiomas larger than 2 cm and may show lesions as small as 0.5 cm.	99m Tc- RBC	Red cell pooling	
Sulfur colloid-Milk Scan	Detection of Gastro-esophageal Reflux	99m Tc- Sulfur colloid	Compartment localisation & tracer transit	
Gastric Emptying Study	Diabetic Gasteroparesis	99m Tc- Sulfur colloid	Tracer transit	
Meckles' Scan	Detection of Meckles' Diverticulum containing ectopic gastric mucosa	99m Tc- Pertechnetate	Uptake by gastric mucosa	
Salivary glands scan	Gland function and duct patency assessment.	99m Tc- Pertechnetate	Active uptake and secretion.	

Endocrine system- In thyroid disease, the most common reason for scintigraphy, which can be performed with either <sup>99m</sup>Tc-pertechnetate or Iodine (123/131), is to determine which nodules require needle biopsy. Functional nodules are unlikely to be malignant, whereas "cold" nodules either solitary or those that are a dominant part of a multinodular goiter require biopsy. Thyroid scintigraphy is also used to differentiate between Graves' disease and Plummer's disease, in-

vestigate patients with suspected thyroiditis (particularly Hashimoto's thyroiditis) and to calculate the optimal therapeutic dose of radioactive iodine. In young patients, scintigraphy is used for the differential diagnosis of anterior neck masses: apart from sublingual thyroid tissue, all anterior neck masses, including thyroglossal cysts, do not appear as functional tissue on scintigraphy. Metaiodobenzylguanidine (MIBG) is an analogue of guanethidine which

concentrates in sympathoadrenal tissue. Its radiolabelled form has high sensitivity for neural crest (88% tumours phaeochromocytoma, 89% for paraganglioma, 92% for neuroblastoma, 71% for carcinoid, and 35% for medullary thyroid cancer) and is complementary to structural imaging in detection, staging, and follow up (Table 6). Scintigraphic evaluation is an integral part of assessment for possible treatment with 131 I-MIBG for these tumors.

Table-6,	Table-6, Common Nuclear Medical Applications in GIT and Hepatobiliary System				
Organ	Indication	Type of scan	Radionuclide used	Biological behaviour/ Mechanism	
Thyroid	Evaluation of gland size and uptake Solitary Thyroid Nodule. Ectopic thyroid/ Lingual thyroid Thyroiditis Thyrotoxicosis – Autonomous nodules, thyroiditis,preradioiodine therapy Thyroid Cancer – detection of metastases, follow up after radioiodine Therapy	Thyroid Scan: Distinguishes between hot and cold nodules.	99mTc- pertechnetate or Iodine (I-131, I123)	Active uptake. (Iodine also undergoes organification).	
Parathyroid	To detect / rule out parathyroid adenoma/ hyperplasia	Parathyroid Imaging	Tc-99m labeled Sestamibi/ Tetrofosmin.	Cationic complexes concentrate in mitochondria.	
Adrenal	Neuroendocrine tumors (Pheochromocytoma, Paragangliomas)	Meta-iodo-benzyl- guanidine (MIBG) Scan	I-123/ I131- MIBG	MIBG is a guanethidine analog similar to epinephrine. It is taken up by chromaffin cells. useful for imaging sympathetic adrenergic tissue.	
Neuroendocrine tumors	Somatostatin receptor positive tumors (Carcinoids, insulinoma etc)	Somatostatin receptor imaging	111 In - Octreotide	Somatostatin analogue.	
Whole body Scan	Thyroid Cancer	Whole body Iodine scan	(I-131, I123)	Concentration in thyroid tissue- native and metastatic	

Oncology- It was only after introduction of gallium 67 citrate that the non invasive localization of primary and metastatic neoplasms using nuclear medicine techniques was realized. In lymphoma, <sup>67</sup>Ga-citrate imaging is superior to both computed tomography and magnetic resonance imaging in the evaluation of mediastinal masses after radio-

therapy. High dose <sup>67</sup>Ga-citrate tomography has a sensitivity of 82-92% for residual tumour. The interpretation of gallium scan images is complicated by poor anatomic resolution and by interfering activity in the bowel. Nowadays PET (positron emission tomography), has become the main clinical imaging tool for evaluation of neoplasms. The

most commonly performed nuclear medicine investigation in patients with malignancy is a bone scan for tumour staging. A broad range of techniques is used to detect primary tumours and recurrences, and after treatment to differentiate residual viable tumour from fibrosis (Table-7).

Tab	Table-7, Common Nuclear Medical Applications in Oncology			
Type of scan	Indication	Radionuclide used	Biological behaviour/ Mechanism	
Bone Scans	Bone Metastasis	Tc- 99m MDP	MDP localizes in the hydroxy-apatite mineral matrix.	
Whole Body Iodine-131 scan	Papillary and Follicular Thyroid  Cancer: for follow up and ruling out residual disease / distant metastases.	Iodine-131/ 123	Concentration in functioning metastatic thyroid tissue.	
Whole body scan	Lymphomas	Gallium-67	Taken up by cancer cells. Binds to lactoferrin & ferritin.	
Whole body Antibody Imaging	Colorectal & ovarian Cancer, B-cell Lymphomas	99m Tc/111 In labeled antibodies	Antigen- antibody recognition	
Whole body receptor imaging	Neuroendocrine Tumors	I131-MIBG, 111In- Octreotide	Receptor binding.	
Whole body PET Imaging	Lymphomas, lung, breast, colon, head & neck, thyroid, esophagus, cervical and ovarian Cancer, Brain Tumors	F18 – Flouro deoxy glucose (FDG)	Asessment of Glucose metabolism.	
Thallium Scans	Brain Tumors (Necrosis vs. residual tumor)	201 Thallium.	Following disruption of blood- brain barrier (BBB), concentrates in tumor cells.	
Scintimammography	Detection of Primary Breast Lesion in Patients with dense breast tissue.  Suspected recurrence over operated scar or silicon implant or post radiation setting.	99m Tc - Tetrofosmin	Cationic compound that concentrates in mitochondria of cells.	

Central nervous system -The most common forms of radionuclide brain imaging are cerebral blood flow studies with <sup>99m</sup>Tc-HMPAO/ ECD and positron emission tomography studies with fluorine-18-fluorodeoxyglucose (<sup>18</sup>F-FDG). Both techniques can be used to locate the focus of the seizure before surgery in patients with intractable temporal lobe epilepsy. In HIV positive

patients, nuclear medicine studies can help to determine whether space occupying lesions are due to Toxoplasma gondii, abscess or lymphoma. Finally, radionuclide cerebral blood flow studies are a useful adjunct in the differential diagnosis of dementia (Table 8). Infection & inflammation -In many patients with fever, a diagnosis of active infection is obvious from clinical history and physical examination in

conjunction with structural imaging techniques. However, after surgery or the insertion of a joint prosthesis, diagnosing active infection using structural imaging techniques may be difficult because of distorted anatomy. By contrast, nuclear medicine techniques image inflammatory activity, irrespective of the causative factor, and can be used to identify active infection even where anatomy is distorted.

	Table-8, Common Nuclear Medical Applications in CNS				
Type of scan	Indication	Radionuclide	Biological behaviour/		
		used	Mechanism		
Brain perfusion scan	Cerebrovascular Disease – Assessment of Cerebral Vascular Reserve in Post Cerebral Infarct or in Carotid Artery occlusion Refractory Epilepsy- Demonstration	99m- Tc labeled Hexa-methyl propylamine oxime (HMPAO), Ethylcysteine dimer (ECD).	Diffusion through BBB and extraction by neural tissue.		
	of Epileptic focus  Dementia- Alzheimer's vs. Multi Infarct Dementia	- do-			
BBB integrity scan	Brain tumors- Diagnosis of tumor. Radiation Necrosis vs. Recurrence	99m- Tc labeled GHA, Thallium 201	Concentrates in tumor cells, following disruption of bloodbrain barrier (BBB).		

Table-9, Common Nuclear Medical Applications in Infection work up			
Type of scan	Indication	Radionuclide used	Biological behaviour/ Mechanism
Diagnobact scan (Ciproflox scan)	P.U.O, Post-op Infection in Orthopedic Cases.	99m Tc - Ciprofloxacin	Binds to the bacterial cell membrane.
Immunoglobulin scan	Infection & Inflammation	99m Tc –Immunoglobulins/ Igranulocyte antibodies	Target the receptors on cells of inflammation.
18F-FDG PET scan	P.U.O.	18 F-FDG	Uptake in activated macrophages.
Leukocyte scan	P.U.O, Post-op Infection in Orthopaedic Surgery, Inflammatory Bowel Disease.	Indium-111 labeled leucocytes, 99m Tc - HMPAO labeled leucocytes	Cellular diapedesis
Gallium scan	Sarcoidosis, Tuberculosis	Gallium-67	Concentrates in inflammatory cells. Uptake indicates active disease.

**PET**: Clinical applications PET and PET-CT have taken the centre stage in oncologic imaging of late in medical practice. F-18 fluorodeoxyglucose (FDG), an analog of glucose, is the most commonly used PET radiopharmaceutical, which allows assessment of glucose metabolism in various body tissues. FDG enters cells by the same transport mechanism as glucose and is intracellularly phosphorylated by hexokinase to FDG-6-phosphate (FDG-6-P). Intracellularly FDG-6-P does not get metabolised further and accumulates in proportion to the glycolytic rate of the cells. Most malignant cells have higher rate of glycolysis & higher levels of glucose transporter proteins (GLUT) than do normal cells and therefore accumulate FDG-6-P to higher levels than do the normal tissues (1). Therefore cancer at any site (primary or metastatic) is likely to exhibit intense FDG uptake vis-à-vis the background tissues. Few

common indications of PET today are given in Table-9.

	Table-10, Common PET Applications				
Type of scan	Indication	Radionuclide used	Biological behaviour/ Mechanism		
PET myocardial perfusion scan	CAD	13N-Ammonia, 82 Rubidium.	Perfusion of myocardium, proportional to the flow rate. Glucose metabolism.		
PET viability scan	Myocardial Viability	18 F-FDG			
Brain PET scan	Identifying brain metastases, epileptic focus, primary brain tumors, Dementias	18F- FDG, 11C-Methionine, 18F-Fluorodopa.	Glucose metabolism Amino-acid metabolism Dopaminergic receptor imaging		
Metabolic Imaging for	Lymphomas	18F – (FDG)	Glucose metabolism		
Staging-	Lung Cancer	101 – (1100)	Glacose metabolism		
Assessment of Response to Therapy	Breast Cancer Brain Tumors	11C-Methionine,	Amino-acid metabolism		
Detection of recurrence.	G.I. Cancers  Cancers of Reproductive  System (cervix, ovary	18F-Fluorothymidine (FLT),	Cell turnover		
	testis) Head & Neck Cancer Melanoma Prostate Cancer Hepatoma Soft tissue Sarcomas Neuroendocrine tumors.	18F- Fluoro-ethyl-tyrosine (FET).	Amino-acid metabolism		

#### Radionuclide Therapy

Most therapeutic applications involve use of radionuclides that decay by beta emission. Advantage of the cytocidal effect and reasonable penetration power of beta rays is taken to ablate the tumor cells by selective irradiation (Table-12).

Conclusion- Nuclear medicine as a discipline has made giant strides in the recent years. As of today, it has vast clinical applications which include imaging and non-imaging diagnostic studies covering almost all the organ systems of the body, in addition to various therapeautic applications. In most instances, the functional information provided by Nuclear imaging studies is complementary to that available from morphological imaging techniques like radiographs, CT and MRI.

The availability of metabolic functional imaging in the form of Positron Emission Tomography (PET) has greatly enhanced our understanding of various pathologic processes like cancers and neuro-psychiatric disorders and opened newer options for incorporation of this information into patient management protocols. Recently, integration of Computed Tomography (CT) with PET into a composite PET/CT scanner has led to creation of a powerful imaging tool that combines functional information of PET with the anatomic information provided by the CT. In the future there is likely to be further amalgamation of morphological and functional imaging techniques, necessitating close cooperation between the Radiologists and Nuclear medicine physicians. Thus it is essential for all Radiologists to have a basic knowledge of the basic principles and common applications of Nuclear Medicine techniques.

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Table-12, Common indications of Radionuclide therapy					
Type of scan	Indication	Radionuclide used	Biological behaviour/ Mechanism		
Radioiodine (I-131) therapy I-131MIBG therapy	Thyroid cancer (Papillary, Follicular), Thyrotoxicosis Neuroblastoma, Malignant Pheochromocytoma	I-131 I-131MIBG	Uptake in functional thyroid tissue. Uptake in functional adrenergic tissue		
Strontium-89 or Phosphorous -32 Radiation Synovectomy I-131 Lipiodol therapy	Medullary Thyroid Cancer Palliation of Bone Pain in Metastases Rheumatoid Arthritis, Heamophilia Hepatocellular Carcinoma	Strontium-89 or Phosphorous -32 90Yttrium I-131 Lipiodol	Concentrate in mineral matrix and ablate the tumor tissue.  Ablation of inflamed synovium.  Selective irradiation of tumor tissue.		
Yttrium -90 Radioimmuno Therapy (Zevalin therapy)	B-cell Lymphoma	Yttrium -90	Selective irradiation of tumor tissue by targeting antigens on tumor cells.		
Isotope labeled Octreotide Therapy	Metastatic Carcinoid Tumors	I-131or Yitrium-90 octreotride	Selective irradiation of tumor tissue by targeting somatostatin receptors on tumor cells.		

## Displaced Proximal Humeral Fractures

## Commentary

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 ↑ he proximal humerus becomes more susceptible to fracture with age because of the structural changes that occur with age. The majority of patients who sustain proximal humeral fractures are in the middle and older age groups. In younger patients these fractures are often the result of high-energy injuries. Osteoporosis plays a significant role in the older sedentary patient. Eighty-five percent of proximal humeral fractures are minimally displaced or nondisplaced8.

Surgical Anatomy-The proximal humerus consists of four well-defined parts: the humeral head, the lesser and greater tuberosities, and the proximal humeral shaft. Neck- angle measures an average of 145 degrees in relation to the shaft and is retroverted an average of 30 degrees. The rotator cuff and shoulder girdle muscles create equilibrium force when the proximal humerus is intact. There are three main arterial contributions to the proximal humerus. The major arterial contribution to the humeral head segment is the anterior humeral circumflex artery<sup>2</sup>.

General Classification-In 1970, Neer1 devised a classification scheme based on the displacement of the four proximal humeral segments<sup>7</sup>. In this system, a segment is considered to be displaced if it is separated from its neighboring segment by more than 1cm or is angled more than 45 degrees from its anatomic position. The fracture pattern refers to the number of displaced segments (i.e., two-part, three-part or four-part). The AO group has proposed an alternative classification scheme, which emphasizes the vascular supply to the articular segment<sup>3</sup>.

Radiographic Evaluation-Anteroposterior, lateral scapular, lateral axillary views are required in most cases to ensure consistent identification of fracture type. If only two views can be obtained, true anteroposterior and axillary would be ideal for classification<sup>1</sup>. Axillary view provides information about the fracture configuration, detects a locked posterior dislocation with an impression fracture, and provides an assessment of the glenoid margin. Computed tomography (CT) is helpful in defining the magnitude of humeral-head defects in headsplitting fractures, impression fractures, and chronic fracturedislocations.

Treatment-Many methods of treatment of proximal humeral fractures have been proposed. Fortunately, the majority (85%) of proximal humeral fractures are minimally displaced or nondisplaced and therefore can be treated nonoperatively with a sling. Success in treating these injuries is related to an accurate diagnosis, realistic patient expectations, and the skill of the surgeon.

Displaced two-Part Anatomic-Neck Fractures-The two-part anatomic-neck fracture is extremely rare. Closed reduction is difficult because the articular-head segment is usually angulated or rotated. Open reduction and internal fixation with interfragmentary screws is an option in younger patient. Prosthetic hemiarthroplasty through deltopectoral approach provides the most predictable result.

Displaced Two-Part Greater-Tuberosity Fractures-They are often associated with an anterior glenohumeral dislocation. After closed reduction, residual displacement of the greater tuberosity is common. Displacement of the fragment by more than 1 cm was pathgnomonic of a longitudinal tear of the rotator cuff. In most cases, the greater tuberosity is displaced superiorly and posteriorly by the unopposed pull of the rotator cuff. If the fracture heals in this displaced position, it will cause impingement under the acromion, limiting forward elevation and external rotation. Closed reduction and percutaneous pinning of the fracture fragment can be attempted with longitudinal traction, flexion, and adduction of the arm to the neutral position.

Displaced Two-Part Surgical-Neck Fractures-Because both tuberosities are attached to the head, it often remains in a neutral position. A posterior hinge is frequently present, which con-

tributes to the apical anterior angulation of the fracture. Most displaced two-part surgical neck fractures are unimpacted, and the shaft is displaced anteromedially by the pull of the pectoralis major. Reduction may be prevented by interposition of the periosteum, biceps tendon, or deltoid muscle or by buttonholing of the shaft through the deltoid, pectoralis major, or fascia. The technique of closed reduction involves distal traction and lateral displacement with simultaneous flexion of the shaft. Traction is then released to lock the fragments together. If an acceptable reduction is achieved, sling immobilization for 3 to 4 weeks is adequate. In unstable fractures percuataneius pinning is required. Irreducible fractures require open and internal fixation.

Displaced Three-Part Fractures-Closed reduction and percutaneous pinning achieves acceptable results with minimal disruption of the surrounding blood supply and soft tissues, provided an acceptable reduction can be obtained. Open reduction and internal fixation with a buttress T plate was once popular, but several studies have reported inferior results<sup>5</sup>.

Displaced Four-Part Fractures-In the four-part valgus impacted fracture closed reduction or limited open reduction and minimal internal fixation can produce satisfactory results<sup>4</sup>. In classically described four-part humeral fractures immediate hemiarthroplasty has become the accepted method of treatment in elderly patients.

**Fracture-Dislocations-**Fracture-dislocations require reduction of the humeral head and are

usually managed according to the fracture pattern. Management can often be complicated by associated neurologic compromise, such as axillary or brachial nerve injury. Angiography should be performed without delay in suspected cases, since early diagnosis and repair are crucial to outcome.

the shoulder with the use of
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Acute injury, < 20% impression fracture	Closed reduction, immobilization in external for 6weeks.
>6m, 20% to 45% defect	McLaughlin procedure or Neer's modification of the McLaughlin transfer
>6m, 45% impression defect	Hemiarthroplasty

Articular-Surface Fractures-Impression defects or head-splitting fractures may result when the humeral head has been severely impacted against the glenoid rim. Management is determined by the size of the impression defect and the time the locked posterior dislocation has been present<sup>6</sup>.

Rehabilitation- The rehabilitation program must be individualized to optimize the recovery of shoulder function. The postoperative management program has three well-defined phases: phase I consists of passive or assisted range-of-motion exercises; phase II consists of active range-ofmotion exercises with terminal stretching; phase III is a resisted program with ongoing active motion and terminal stretching. Complications- Infection, neurovascular injury, malunion, nonunion, hardware failure, joint stiffness, avascular necrosis, and heterotopic ossification can result after the treatment

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# **Commentary**

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ecrotizing soft tissue infections represent a group of diseases involving skin, subcutaneous tissue and muscles. The common superficial pyodermas do not extend beyond the skin (epidermis and dermis), and include erysipelas, impetigo, folliculitis, furunculosis, and carbuncle. Cellulitis is a deeper skin infection than erysipelas, involving also the superficial part of subcutaneous tissue. Necrotizing fasciitis primarily involves superficial fascia, subcutaneous fat and deep fascia. Necrotizing fasciitis is an uncommon soft-tissue infection usually caused by toxinproducing, virulent bacteria characterized by widespread fascial necrosis with the relative sparing of the skin and underlying muscle. The other necrotizing soft tissue infections include anaerobic cellulitis and necrotizing myositis (both clostridial and non-clostridial). However distinction between these various necrotizing soft tissue infections is not that important as their prognosis and treatment are the same.All these three necrotizing infections differ from cellulitis in having widespread necrosis of tissues and are associated with severe toxicity and high mortality. It's of utmost importance to recognize early these virulent infections and only an early and aggressive surgical treatment can save the lives. Historical background-Necrotizing fasciitis was known to

Hippocrates, who discussed it as a complication of erysipelas. In the early 19th century, necrotizing fasciitis was known as gangrenous ulcer, putrid ulcer and phagedenic ulcer. During the US civil war this entity was called as hospital gangrene. A variant of the disease has come to be known as Fournier's Gangrene, after a necrotizing infection of the perineum was described by Fournier in 1884. Meleney in 1924 described the synergistic associa-tion of anaerobic streptococci and staphylococci causing Postoperative synergistic gangrene of abdominal wall. Wilson (1952) coined the term Necrotizing Fasciitis finding fascial necrosis to be the most consistent manifestation of the disease.

Causative organisms - No single organism is responsible for the ne-crosis and systemic toxicity seen in necrotizing fasciitis. In fact, the synergistic action of facultative aerobic and anaerobic bacteria could be responsible for the often fulminant course of the disease. Necrotizing fasciitis Type I is polymicrobial. The predominant organisms in these polymicrobial infec-tions are aerobic and anaerobic Gram-negative enteric bacilli, enterococci, and, less commonly, staphylococ-cal and streptococcal (b haemolytic, non-group A streptococci) species. The anaerobes include Bacteroides and clostridial species. Facultative organisms lower

the oxidation-reduction potential of the wound microenvironment, and promote favourable conditions for the growth of anaerobes. In Type 2, also known as hemolytic streptococcal ganpathogen grene, the **b**-haemolytic, group strepto-cocci, either alone or in combination with staphylococci. The type of organisms present in necrotizing fasciitis tend to depend on the site of infection. Abdominal and perineal infections, particu-larly postoperative cases, tend to be polymicrobial. Extremity lesions more commonly monomicro-bial, predominantly Streptococcus caused by pyogenes.

Pathophysiology-Organisms spread from the subcutaneous tissue along the superficial and deep fascial planes, facilitated by bacterial enzymes and toxins. This infection causes vascular occlusion, ischemia, and tissue necrosis. Superficial nerves are damaged, producing the characteristic localized anaesthesia. Septicemia ensues with systemic toxicity. Histological sections show fascial necrosis along with blood vessels occluded by thrombi. A dense infiltration of neutrophils may be observed in deeper parts of the subcutaneous tissue and fascia. Subcutaneous fat necrosis and vasculitis are also evident. Types of necrotizing fasciitis-

Types of necrotizing fasciitis-Giuliano et al (1977) divided necrotizing fasciitis into two distinct

Type I or polymicrobial necrotizing fasciitis, usually occurs after trauma or surgery. This form is likely to be seen in Abdominal and perineal infections.

Type II or group A streptococcal necrotizing fasciitis, is the socalled flesh-eating bacterial infection. Extremity lesions are more likely to be monomicro-bial.

Clinical presentation -Factors that may predispose the patients to develop necrotizing fasciitis include chronic disease states such as diabetes mellitus, pe-ripheral vascular disease, intravenous drug abuse, alcoholism, malnutrition, and AIDS. The pamay also immunocompromised by malignancy or the administration of chemotherapy, resulting in granulocytopenia. The steroid-dependent as well as the transplant recipient, are also at risk. Patients who have suffered severe injury have an increased incidence of infection secondary to breaks in the skin bar-rier, presence of a foreign body, devitalized tissue, or a fluid collection especially blood. Necrotizing fasciitis usually begins with the development of characteristic skin changes. An erythematous, tender, swollen, hot area of cellulitis, accompanied with local pain and fever, is commonly the first sign. Early necrotizing fasclitis is very painful. Pain out of proportion to physical findings in a patient who appears to have cellulitis and systemic toxic condition should raise the suspicion of necrotizing fasciitis. Following the initial cellulitic skin changes, the skin becomes smooth, shiny, and tense. In a few days, the skin darkens to patchy, dusky blue areas while blisters and bullae develop. Initially, the bullae are filled with serous fluid, which later becomes hemor-rhagic. Crepitus may appear indicating presence of gas in subcutaneous plane. Necrosis of the superficial fascia and fat takes place, producing a watery, thin, foul-smelling fluid known as "Dishwater pus". Normal looking skin is undermined while un-derlying muscle usually remains intact. The extent of fascial necrosis is more widespread than changes in the overlying skin suggest. The subcutaneous nerves are then destroyed and the previously tender skin becomes anesthetic. Thrombosis of the skin's nutrient arteries causes focal areas of necrosis, appearing as deep thermal burns. Purplish skin becomes frankly gangrenous. Hypocal-cemia can develop from extensive fat necrosis. Some patients present with malaise, chills, fever, nausea, vomiting, and diarrhea. There may be even loss of consciousness. Untreated. the disease is almost invariably fatal. As organisms and toxins are liberated into the bloodstream, the patient devel-ops signs and symptoms of sepsis syndrome. Progression to septic shock, multiple organ failure, and death ensues.

Differentiation from Cellulitis -Cellulitis is a more superficial infection affecting the deeper layers of dermis and superficial part of subcutaneous tissues. In contrast necrotizing fasciitis affects deeper layers of subcutaneous tissue and deep fascia. In early stages of necrotizing fasciitis, skin is relatively spared. Necrosis of fascia extends far wider than the skin changes indicate. In

necrotizing fasciitis pain and tenderness are far more severe than in cellulitis. Blisters and bullae are often seen in necrotizing fasciitis. Presence of subcutaneous gas (crepitus) favours necrotizing fasciitis. Anaesthetic patches of skin indicate necrotizing fasciitis with ischaemia of cutaneous nerves. Gangrenous skin patches appear subsequently in necrotizing fasciitis. Finally "easy passage" of probe or gloved finger beneath skin in subcutaneous plane indicates tissue necrosis, hallmark of necrotizing fasciitis. Frozen section biopsies have also been used in doubtful situations to diagnose necrotizing fasciitis. Contributing factors to increased mortality -Necrotizing fasciitis is a serious life threatening condition. McHenry and colleagues (1995) in a large series, reported a mortality rate of 29%. There are several factors that contribute to such a high mortality: Delay in diagnosis and treatment (particu-larly adequate surgical debridement and fasciotomy) correlates with poor outcome. Other risk factors that have been shown to correlate with increased mortality include age over 50 years, diabetes mellitus, peripheral vascular disease, poor nutritional status, and anatomic site of infection in-volving the trunk and chest wall involvement. The cause of death in patients with necrotizing fasclitis is usually either overwhelming sepsis or multiple organ system failure with or without ARDS. McHenry and colleagues (1995) found that early deaths (within the first 10 days after initial debridement) were due to the conse-quences of sepsis syndrome, whereas late deaths were

attributable to multiple organ system failure.

Investigations in a suspected case of necrotizing fasciitis-The WBC count may be elevated. Leukocytosis is usually present. It may be more than 14,000 cells per ml.The blood urea nitrogen level may be elevated. The serum sodium level may be reduced. The level may be less than 135 mmol/L. Elevated serum CPK levels indicate associated myonecrosis, an uncommon feature in necrotizing fasciitis. Hypocalcaemia indicates widespread fat necrosis. Gram staining of the exudate may provide a clue as to whether a type I or type II infection is present. Cultures (both aerobic and anaerobic) from the discharge or affected tissue obtained at initial debridement should help in identifying the organisms and their susceptibility pattern. Excisional deep skin biopsy with frozen section may be helpful in diagnosing necrotizing fasciitis.

Imaging Studies-X-Ray of the part may show subcutaneous gas. Detection of soft-tissue gas by plain radiograph is more sensitive than by physical examination. CT scans, ultrasonography and MRI have also been used in diagnosing necrotizing fasciitis. Soft tissue gas, detected clinically or radiologically, is a classic sign, but its absence does not exclude necrotizing infection. CT scanning is more accurate in detecting softtissue gas and in de-lineating the extent of spread of the infection, espe-cially in cervical necrotizing fasciitis. Ultrasonog-raphy has been used to aid in delineating the extent of Fournier's gangrene and to differentiate it from other

causes of "acute scrotum." MRI is useful to detect soft-tissue fluid and fascial necrosis. However the main use of CT Scan and MRI is in detecting the spread of necrotizing fasciitis to inaccessible ares like mediastinum and retroperitonium. They are also useful in deciding whether a reexploration is required after initial debridement.

Management -The following principles are essential:

Resuscitation- A patient who is in shock will need adequate intravenous fluids, ionotropic support, blood transfusion. Metabolic acidosis will need to be corrected. The patient should be adequately resuscitated to permit surgery at the earliest.

Antibiotics-Which antibiotics to be given will be known from culture and sensitivity reports, which however will take time. Until such reports are available, empirical antibiotic therapy should be initiated targeted at Gram +ve, Gram-ve and anaerobic organisms. It is recommended that a beta lactam antibiotic in combination with aminoglycoside (Penicillin or Ampicillin and Amikacin) will cover adequately both gram +ve and -ve organisms. Either Clindamycin or Metronidazole will take care of anaerobic organisms. Others have reported a III generation Cepalosporin with Clindamycin or Metronidazole as being equally effective until the culture reports are available.

Surgery -This is the single most important factor in treatment. Certain points here need to be emphasized. Once a diagnosis of necrotizing fasciitis is made or even suspected, surgery should be done at the earliest. Best survival results are obtained when surgery is undertaken within 12 hrs after the onset of the disease. Under adequate anaesthesia, liberal incisions should be made and all the infected and necrotic tissues should be excised. The incisions should extend beyond the necrotic tissues into normal tissues. Undermined and devitalised skin will need to be excised. No attempt should be made to suture or close the wounds. After thorough debridement, wound should be irrigated with saline and left open with dressing. It's possible that subsequently more tissues may become necrotic. Hence after 24 hrs, the wounds need to be inspected, reexplored and excision repeated until no further progression is noticed. It should be very clear that ordinary "Incision and drainage" approach will not be adequate and surgery should be "Excisional debridement". Only an early and aggressive surgery will save the life of the patient.

Other supportive treatment-Postoperatively patient will need supportive treatment depending on the general condition. These patients often require ICU care so that cardiac, pulmonary, renal, and metabolic systems can be monitored. Antibiotics should be continued till all evidence of sepsis subsides. Nutritional support should be instituted if needed. Two other modalities of treatment have been mentioned in the literature

 Immunoglobulins; Use of intravenous immunoglobulins has been described as being effective, but there are no

- controlled trials showing increased survival benefit.
- Use of Hyperbaric Oxygen also has been described, especially in hastening wound healing. However again there are no controlled trials showing increased survival benefit. It's again emphasized that aggressive surgery is more important that hyperbaric oxygen therapy. If facilities are there in the same hospital, it may be tried but that should not delay surgery.

Special varieties of necrotizing fasciitis

Fournier's idiopathic gangrene of scrotum-This condition is defined as a polymicrobial necrotizing fasciitis of the perineal, perianal, or genital areas. Patients with diabetes mellitus or immunocompromised state are more prone to this condition. Fournier's gangrene is always due to mixed aerobic and anaerobic bacteria. The classical triad of pain, swelling and systemic sepsis is very commonly noticed. Presence of bullae filled with serous fluid is an important diagnostic clue and should raise the suspicion of this condition. This condition progresses very rapidly. It may extend beyond the genitalia onto anterior abdominal wall. Skin soon shows features of necrosis and gangrene, discharging "dish water pus". Crepitus may be elicited in subcutaneous plane. Patient can go into sepsis and multi organ failure. Broadly speaking the principles of management are similar to that of necrotizing fasciitis in the form of resuscitation, combination antibiotics and surgical debridement of all necrotic tissues. Surprisingly, the testes usually escape

any harm probably because of separate blood supply from the aorta. The reported mortality rates vary from 3 -40%. Poor Prognostic factors include:

Increasing Age; Female gender; Anorectal causes; Number of organs failed at admission; Delay in presentation and treatment; Associated Diabetes or HIV

Aeromonas hydrophilia- It is a facultative anaerobic, Gramnegative bacillus, which causes a fulminant myonecrosis. The rapidity of the infectious process is similar to that of clostridial myonecrosis, but gas production is not a consistent feature. The infection usually occurs in the setting of penetrating freshwater trauma. Aggressive surgical debridement and antibiotic coverage for Gram-negative rods are the essential features of treatment.

Clostridial cellulites- It is a necrotizing soft tissue infection that clinically resembles necrotizing fasciitis, but the infection is more superficial. It usually occurs in the setting of surgery or trauma (Clostridium perfringens), but it can occur spontaneously in association with malignancy (Clostridium septicum). The skin and subcutaneous fat are involved. Gas production is a prominent feature. Since the infection is more superficial than clostridial myonecrosis, the associated toxicity is usually not as severe. Surgical exploration reveals viable fascia and muscle. This distinguishes clostridial cellulitis from necrotizing fasciitis and gas gangrene. The differentiation is obviously important. Clostridial cellulitis requires debridement of skin and subcutaneous fat, but more aggressive and extensive surgical therapy is not needed. A very similar superficial necrotizing infection can also be caused by a variety of anaerobic bacteria, either alone or as a mixed infection. This is termed nonclostridial anaerobic cellulitis, or synergistic necrotizing cellulitis. Diabetes mellitus is often a predisposing factor. The treatment approach is the same as for clostridial cellulitis.

Necrotizing fasciitis is caused by the marine vibrios (Gramnegative rods), particularly Vibrio vulniftcus, Vibrio parahemolyticus, Vibrio dam-sela and Vibrio alginolyticus. Vibrio vulniftcus is believed to be the most virulent. The usual portal of entry is a puncture wound caused by a fish, or a cut or insect bite exposed to sea water, shellfish, or fish in tropical waters. The pathogenic vibrios are be-lieved to synthesize an extracellular toxin that mediates much of the soft-tissue damage in necrotizing fascii-tis.

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## Down Syndrome - Screening and Diagnosis

## Commentary

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own syndrome or Trisomy-21 is a genetic disorder caused by the presence of all or part of an extra 21st chromosome. It is named after John Langdon Down, the British doctor who described it in 1866. It is characterized by a combination of major and minor differences in body structure associated with some impairment of cognitive ability and physical growth as well as facial appearance. It is the most commonly recognized genetic cause of mental retardation with an estimate prevalence of 912 cases per 10,000 live births<sup>1</sup>. Because of the morbidity associated with Down syndrome, screening and diagnostic testing for this condition are offered as optional component of prenatal care. Prenatal diagnosis of Trisomy-21 allows parents the choice of continuing or terminating an affected pregnancy. The incidence of Down syndrome is estimated at 1 per 800 to 1 per 1000 births. In 2006 the center for disease control estimated the rate as 1 per 733 live births in the United States<sup>2</sup>.

Causes and risk factors-95% of observed Down syndrome are Trisomy-21 caused by a meiotic non-disjunction with 88% coming from non-disjunction in the maternal gamete and 8% coming from non-disjunction in the paternal gamete.3-4% is due to Robertsonian translocation

1-3% is due to Mosaicism, usually milder. There is a mitotic error in embryo.

Likely risk factors-Previous child with Trisomy-21 (1-2% risk). Advanced maternal age. The risk of having a child with Down syndrome increases in a gradual, linear fashion until about age 30 and increases exponentially thereafter. Increasing number of prior spontaneous abortions is associated with increased risk of fetal aneuploidy. At maternal age 20 to 24 the risk is 1 in 1490, at age 35 the risk increases to 1 in 365 and at age 45 the risk of having a child with Down syndrome increases to 1 in 303. Although the risk increases with maternal age, 80% of children with Down syndrome are born to women under age 35 reflecting the overall fertility of that age group. There is no paternal age effect.

Screening tests- Over the last 20 years new technology has improved the methods of detection of fetal abnormalities including Down syndrome. Procedures like chorionic villus biopsy or amniocentesis though useful for diagnosis is associated with increased cost and slight amount of risk to the fetus. So screening tests have been developed to try to identify those pregnancies at high risk in whom these procedures can be done diagnose. Historically, maternal age can be viewed as the first

screening test. At age 35 years the second trimester prevalence of Trisomy-21 (1/270) approaches the estimated risk of fetal loss due to amniocentesis (1/200). Therefore the age 35 was chosen as the screening cut off the risk threshold at which diagnostic testing is offered4.With the introduction of a screening test for Down syndrome, genetic screening has been broadened to include women who have not had access to it. Various guidelines were developed to review and evaluate the best available evidence for the use of ultrasound and serum markers for screening. Serum screening has reduced the number of diagnostic tests performed and therefore the resulting fetal losses.

First trimester screening-First trimester screening using both nuchal translucency measurement and biochemical markers is an effective screening test for Down syndrome in general population and results in a higher detection rates than does the second trimester triple test and a comparable rate to the quadruple screen with the same false positive rates. Estimates are that first trimester screening by means of maternal age and measurement of Nuchal translucency could provide a trisomy detection rate of 63% with a 5% false positive rate. Combining this procedure with the measurement of maternal serum beta-hCG sub unit

and pregnancy associated plasma protein A (PAPP-A) could increase the detection rate to 80% at the same false positive rate<sup>5</sup>. Screening in the first trimester, gives the option of termination of pregnancy early if it is confirmed by diagnostic test and reassurance if the results are normal. Improvements in ultrasound imaging made even in early pregnancy it were possible to observe fetal abnormalities like cystic hygroma and anencephaly. Nuchal translucency (NT) should be preformed only by standardized conditions by a trained clinician using appropriate ultra-

sound equipment. Women with NT of 3.5 mm or more in first trimester should be offered a targeted fetal USG, fetal echocardiogram or both.Genetic counseling and option of chorionic villus sampling midtrimester amniocentesis should be offered to women with increased risk of baby with Down syndrome on first trimester screening<sup>6</sup>.

Second trimester screening-This is of following types Maternal serum screening-Maternal multiple – marker serum screening can allow detection of Trisomy-21 pregnancies in women in younger age group also.

**Triple test -** Alpha-fetoprotein (AF), unconjugated estriol(uE<sub>3</sub>)

and human chorionic gonadotropin (hCG) are the serum markers most widely used to screen for Down syndrome as triple test. It is usually performed at 15 to 18 weeks of gestation and the level of each serum marker is measured and reported as a multiple of the median (MOM) for women with pregnancies of the same gestational age as that of the patients. The triple test can detect 60% of the Trisomy-21 pregnancies with a false +ve rate of 5%. A normal result reduces the likelihood of Trisomy-21 but does not exclude it7. A positive test is an indication for

gestation and maternal age. The four serum markers are alpha-fetoprotein human chorionic gonadotropin (hCG or b-hCG), unconjugated estriol (uE<sub>3</sub>) and inhibin A. Addition of inhibin A improved the detection rates. Integrated and serum integrated tests are now being field tested as they have high detection rate with less false positives.

Ultrasound screening-Continued improvements with ultrasound technology have allowed the identification of increasing number of soft markers. It also helps in more accurate assess-

A comparison of Down's screening tests at a fixed 85% detection rate <sup>9</sup>				
Tests (including maternal age)	Measurements	False +ve rate % for an 85% detection rate		
Nuchal Translucency measurement (NT)	NT at 12-13 weeks	20.0		
Double test Triple test Quadruple test	AFP and free β-hCG at 14-20 weeks AFP, uE3, free β-hCG at 14-20 weeks AFP, uE3, free β-hCG and inhibin-A at 14-20 weeks	13.1 9.3 6.2		
Combined test	NT, free β-HCG and PAPP-A at 10 weeks	6.1		
Serum- Integrated test	PAPP-A at 10 weeks, AFP, uE3, free β-hCG and inhibin-A at 14-20 weeks	2.7		
Integrated test	NT, PAPP-A at 10 weeks, AFP, uE3, free ß-hCG and inhibin-A at 14-20weeks	1.2		

amniocentesis.In women older than 35 years the triple test fails to detect 10 to 15% of pregnancies affected by Trisomy-21<sup>8</sup>. In these women maternal serum screening should not be offered as an equivalent alternative to amniocentesis or chorionic villus sampling.

Quadruple test-It uses four serum markers at 14-22 weeks of

ment of gestational age than the patients last menstrual period.

 Ultrasound measurement of Nuchal translucency in first trimester has been studied alone and in combination with biochemical markers as a potentially useful test for the prediction of Trisomy-21.
 NT refers to the fluid filled space between the fetal skin

- and soft tissue overlying the cervical spine.
- Second trimester ultrasound measurement helps to detect

the various congenital anomalies associated with Trisomy-21.

#### USG findings associated with fetal Down syndrome are 10

Intrauterine growth restriction
Mild cerebral ventriculomegaly
Choroid plexus cysts
Increased nuchal fold thickness
Cystic hygromas
Echogenic intracardiac foci
Congenital heart defects
Increased intestinal echogenicity

Duodenal atresia (Double bubble sign)
Renal pelvis dilation
Shortened humerus and femur
Increased iliac wing angle
Incurving and hypoplasia of the fifth finger
Increased space between first and second toes
Two vessel umbilical cord

Routine karyotyping of all pregnancies with these markers would have major implications both in terms of miscarriage and financial cost. It is best to counsel them on an individual estimated risk for chromosomal abnormality. It is important to keep in mind that even the best combination of ultrasound findings and other variables is only predictive and not diagnostic. For diagnosis the chromosomes of the fetus must be examined. Future developments

et al<sup>11</sup> reported that fetuses with Down's syndrome could potentially be detected in the first trimester because of the ultrasound findings of absent nasal bones. They reported a detection rate of 73% for a false +ve rate of 0.5% use of nasal bones together with integrated approach gives a detection rate of 95% with a false +ve rate of 1%. Fur-

ther work is required in this area as preliminary results seem promising.

Doppler ultrasound of the ductus venosus showed abnormal ductus venous flow in 59-93% of aneuploid fetuses but similar findings were noted in 2-21% of normal fetuses also suggesting that this should be used as a complement to existing nuchal translucency screening programmes which may improve the detection rate with reduction in false positive rate<sup>12</sup>.

Diagnostic tests for Down Syndrome- Women who are at high risk for Down's syndrome by screening tests should be offered diagnostic tests to confirm prenatal diagnosis of Trisomy-21 by cytogenetic analysis of cells obtained by one of three invasive procedures which include

1. Chorionic villus sampling (CVS)

- 10 to 12 weeks

Early

2. Amniocentesis

Late

- 16 to 20 weeks

3. Percutaneous Umbilical Blood Sampling

3. Percutaneous Umbilical Blood Sampling (PUBS)

18 to 22 weeks

CVS and early amniocentesis offer the opportunity for first trimester diagnosis when elective pregnancy termination carries the lowest risk of maternal morbidity as compared to risks in second trimester. CVS is associated with fetal loss rate of 0.5 to 1.5%, early amniocentesis with 1 to 2% and second trimester amniocentesis with 0.5 to 1%4. PUBS carries the greatest risk of miscarriage. Karyotype analysis usually requires 7 to 10 days. A recently developed assay that uses fluorescent in situ hybridization can allow rapid diagnosis of Trisomy-21 after amniocentesis<sup>13</sup>.

Recurrence risk-If there is a past history of Trisomy-21 in the past pregnancy, the risk of recurrence in the subsequent pregnancy increases approximately 1% above the baseline risk determined by maternal age. Karyotype analysis of both parents should be done if fetus has chromosome 21 translocation. If both parents have normal karyotypes, the recurrence risk is 2 to 3%<sup>14</sup>.

Counseling-Assessment of the risk of Down syndrome begins with the first prenatal visit and it should be voluntary. Consultation with a genetic counselor should be sought if the previous pregnancy was complicated by a chromosomal abnormality or if either parent is known to carry a balanced translocation. Women who will be 35 years or older on their due date should be offered maternal serum screening and ultrasound evaluation before they make a decision about having amniocentesis informing them of

limited sensitivity of non invasive testing. If diagnostic tests reveal fetal Trisomy-21, consultation with a medical geneticist, genetic counselor and with the pediatrician should be done to decide on course of action which may be continuing the pregnancy and raising the child, or termination of pregnancy. Regardless of which screening or diagnostic test, information about the detection and false +ve rates, advantages, disadvantages, limitations, risks and benefits of procedures should be available to patients so that they can make an informed decision.Screening for Trisomy-21 should be offered to all women as part of routine antenatal care and it should be voluntary. The aim is to achieve high detection rate with a low false positive rate. Integrated test is the most reliable test available at present to achieve this.

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### Basics of Multislice CT

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# Review Article

linical Computed Tomography came into being with the development of the CT scanner in 1972 by Sir Godfrey Hounsfield for which he received the Noble Prize in Medicine in 1979. The first Brain Scanner took four minutes to complete a single rotation, 40 minutes to cover 10 cm of the head, showed 8 grey levels and image reconstruction took overnight. CT uses X rays to obtain cross sectional images of the human body by means of rapid rotation of the X ray Tube around the patient placed in the CT gantry. The internal structure of the object is reconstructed through multiple projections of that object. Early scanners acquired one image with one gantry rotation (sequential mode). Advances in the slip ring technology during the 1980s ushered in the era of the spiral CT with volumetric data acquisition

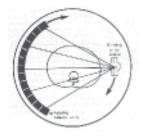


Fig-1, Shows the CT gantry with the X ray tube detector assembly rotating around the patient (Earnest J Wisen & Floro Miraldi in Computed Tomography and Magnetic Resonance Imaging John R Haaga, Charles F Lanzieri, David J Sartorius, Ellas A Zerhouni)

The introduction of spiral CT in 1985 demonstrated continuous scanning in a single breath hold. This was a major leap in imaging as it reduced the respiratory misregistration caused by inconsistent levels of inspiration. This also initiated the development of three dimensional image processing techniques as there was a continuous spiral acquisition of data resulting in a volumetric scan. This enabled processing of data to generate multi planar reformations (MPR) and maximum intensity projections (MIP) and surface shaded displays (SSDs).In spiral CT the X ray tube rotates continuously. The table on which the patient is lying moves mechanically through X ray beam . The transmitted radiation thus takes the form of a helix or spiral to give a continuous volume of contiguous slices.

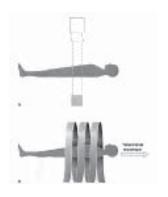


Fig-2, Depicts volumetric acquisition of data in a spiral scan (Image courtesy intl.elsevierhealth.com/ebooks/pdf/aw.pdf)

Spiral CT enabled larger areas of the body to be covered in a single breath hold. Not only did this reduce the incidence of motion artifacts in uncooperative patients but it also increased patient throughput. As a larger area was covered in a single breath hold this removed artifacts due to respiratory misregistration. In a conventional CT due to different levels of breath hold amongst consecutive sections, respiratory misregistration would often result in loss of data from the intervening areas between scans. The introduction of the two slice CT in 1992(Elscint Twin) heralded the dawn of the era of Multi slice CT. In 1998 the four slice CT was launched. It had a rapid gantry rotation, as fast as 0.5 secs which resulted in fast scan speeds, improved utilization of tube output and improved transverse resolution<sup>2</sup>. Speed of acquisition is a cornerstone of Multi slice CT which also helps capture dynamic events such as CT perfusion and CT angiography. Speed of scanning has made non invasive cardiac imaging a reality and also has helped develop CT fluoroscopy. High tube currents can be achieved because of improvements in tube design and tube heating capacity and faster scan times. This enables scanning through dense bone such as shoulder and facilitates visualization of orthopaedic hardware.

Technological advances such as high power X ray tubes, magnificent computing power, multi channel detectors have thus resulted in acquisition of sub millimeter slices with wider scan coverage and faster rotation times. This has allowed CT to step into the realm of diagnostic cardiology, 3 D musculoskeletal anatomical imaging, vascular imaging, Perfusion Imaging and CT fluoroscopy.

detector assembly consists of more than a single row of detectors. The detector arc and x ray tube rotate together. All MDCT scanners use a slip ring technology. Gantry rotation speeds as fast as 0.33 seconds for a full rotation of 360° enables larger anatomical coverage in a shorter time. These scanners, scan, more

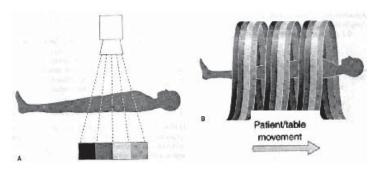


Fig-3, A 4 slice CT with 4 detector rows; B Helical acquisition with 4 detector rows (Image Courtesy: intl.elsevierhealth.com/ebooks/pdf/awpdf)

Multi detector CT – It is also called multi slice CT. In this CT, there is simultaneous but independent measurement referred to as the number of slices. The technical capability of the system ( eg 40 slice, 64 slice MDCT) is determined by the number detector rows in the detector assembly. Unlike a single slice CT a four slice CT acquires data of four slices in one gantry rotation. When the gantry rotation is reduced to 0.5 secs then a four slice CT will acquire 8 slices in a second; unlike a single slice CT which acquires 1 slice per sec as it has a gantry rotation time of 1 sec. Similarly a 16 slice scanner with a gantry rotation time of 0.5 secs will acquire 32 slices per second. Thus as the number of channels (detector rows) increase in a CT scanner, it covers a greater volume per unit time. The

than a single slice simultaneously. Thus there is more efficient utilization of radiation. The time to scan a volume of tissue is considerably reduced. Specific anatomic volume can be covered with thinner slices. This improves

the spatial resolution in the longitudinal direction and is helpful achieving multi-planar reformations &3D reconstructions.Cornerstone for MDCT is very fast image acquisition. Speed is beneficial as large egments of body can be scanned Speed is essential to catch a dynamic event such as Brain perfusion, CT angiography, Cardiac CT imaging. MDCT can also produce high milli amperes due to improvement in tube designs. This allows scanning through dense areas such as the shoulder and through orthopaedic hardware.

Detector Configuration-The width of the detectors can be of equal or unequal size. Depending on the adjacent detector array sizes there are three configurations available in Multi slice CT matrix, progressive and hybrid configurations. In Matrix configuration the detector arrays are of the same size. In the progressive type the detector arrays are of unequal sizes. In the hybrid type the detector rows in the centre are thinner while those in the periphery are thicker.



Fig-4A, is showing the matrix configuration of detector assembly

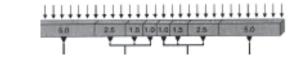


Fig-4B, shows the progressive design



Fig-4C, shows the Hybrid configuration of the detector assembly

Depending on the number of detectors in a scanner, each gantry rotation acquires that many channels of raw data. The raw data can later be reconstructed into thinner and thicker channels. Hence after a single acquisition of the chest. Thin HRCT slices using high definition algorithms, can be reconstructed from the raw data without requiring the patient to be rescanned, leading to tremendous dose reduction for the patient. The slice widths to be acquired can thus be selected either before or after scanning the patient. The collimation however has to be selected before scanning the patient.

Isotropic Imaging- One of the major advances of multi slice CT technology. When slice thickness approaches the in plane details one gets isoptropic images. Here each voxel is cuboidal in shape unlike earlier CT data where the voxels were non cuboidal. As resolution is the same in all the three orthogonal planes, with isotropic imaging, one can reconstruct in any of the orthogonal as well as oblique planes. This technique thus supports multi planar reformation, volume rendering and surface shaded displays. This also obviates the need for patient positioning as after acquiring the raw data in the axial plane one can reconstruct thin or thick slices in any plane of ones choosing. Hence like MRI CT too can produce images in multiple planes.

Limitation of the 4 slice scanners-Transverse resolution of 1 mm did not match the in plane resolution of 0.5 mm so isotropic resolution was not possible with these scanners. For long range studies eg CTA peripheral arteries-thicker slices of 2.5 mm had to be chosen for acceptable scan times. While doing a cardiac CT, stents and severely calcified arteries showed blooming as a result of partial volume effects and because of insufficient transverse resolution. Larger scan times of 40 secs to cover the heart with a 4 x 1 mm collimation resulted in poorer image quality. Thus more than 4 simultaneously acquired slices were needed for true isotropic scanning. To improve resolution of cardiac imaging gantry rotation times had to be reduced to 0.42 secs

Pitch- Pitch is the table translation per gantry rotation divided by the slice thickness Increasing the pitch, by increasing table speed, results in reduction of radiation dose delivered to the patient. It also reduces scanning time but at the cost of image resolution as the spiral helix gets stretched. Decreasing pitch results in increased dose delivered to the patient as the scanning is done with over lapping slices. This however gives better resolution. A pitch of 1 results in contiguous scan with no overlap/ gap, a pitch <1 -overlapping scans, a pitch > 1 - scan with a gap

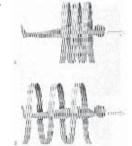


Fig-5A,-The pitch is low. The table moves less for each rotation The image is sharper B-Pitch is high The table moves further per gantry rotation The image is blurred The helix is stretched (Image Courtesy: intl.elsevierhealth.com/ebooks/pdf/aw.pdf)

The total detector assembly width for a 16 slice scanner varies between 20 to 24 mm between different vendors. Hence in each gantry rotation this much of anatomy gets covered. With the newer scanners, the gantry rotation times decreasing to 0.33 seconds. This allows a larger area of the human body to be covered in 1 second. The earlier single slice scanner could cover at the most 10 mm in 1 second gantry rotation. This has distinct advantages. The patient's scanning is faster as there is greater area covered per second. This allows scanning without motion blur in critically ill patients and also reduces tube heating, reduces the dose of contrast needed in angiography. In single channel scanners tube heating prevented scanning long regions with thin slices as in peripheral angiography. This is no longer the limitation with multi slice scanners because raw data can be acquired using a wider collimation and thinner slices reconstructed to get high resolution images in peripheral angiographies. Use of wider collimation allows higher tube currents. The tube in multi slice scanners are heavy duty and have better tube cooling capacity.

Image reconstruction-More complicated on MDCT than in a single slice CT. As detector width increase, the X ray beam diverges along the Z axis to irradiate the wide detector assembly. This results in an X ray beam which is equivalent of multiple fan beams along Z axis. This scanning geometry is called cone beam scanning. In MDCT spiral projections are sampled by multiple detectors. The image that is formed

involves spiral interpolation between adjacent scan paths. This is called Z axis interpolation<sup>3</sup>



Fig-6, Multipoint interpolation scheme (Z filtering) for a four slice scanner where all data points falling inside a predetermined filter width are used (courtesy HD Nagel PhD, Clinical Science CT, Philips Medical Systems, Hamburg, Germany)

After acquisition of volumetric data, the image post processing must be done in ways appropriate to the clinical situation. In Multiplanar reformation, (MPR), a section through the three dimensional array of contiguous CT is taken in the sagittal, coronal and oblique planes. With three dimensional Imaging- reconstructed computer data enables the external and internal structure of organs to be viewed. The data can be projected as a three dimensional model to display spatial information, surface characteristics (volume and surface rendering). This is becoming increasingly useful for patients unable to have invasive endoscopy Two dimensional image reconstruction approaches used in single slice scanners required measurement rays contributing to an image to run in a plane perpendicular to the patient. In Multi slice CT this condition is violated. The measurement rays are tilted by an angle relative to the plane perpendicular to the Z axis-the cone angle. The cone angle is largest for slices at the outer edge of the detector rows

Cone angle- signifies the divergence of radiation beam along the z axis. With increasing number of slices the cone angle in-This results creases. misregistration of diagnostically important information. For upto 6 slices this can be neglected Bevond 6 slices cone beam artifacts become obvious. They are most pronounced for lesions located most distant from the central rows of detectors. These artifacts can be corrected with 2D fan beam or 3D cone beam algorithms

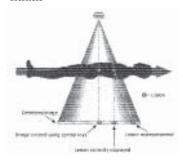


Fig-7, (courtesy HD Nagel PhD, Clinical Science CT, Philips Medical Systems, Hamburg, Germany)

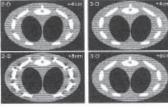
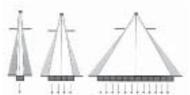


Fig-8, (courtesy HD Nagel PhD, Clinical Science CT, Philips Medical Systems, Hamburg, Germany)

Contrast Enhancement -Maximum contrast enhancement is determined by the amount of iodine injected per second. Flow rates between 3 and 5ml/s are generally recommended Data acquisition should be obtained during the plateau phase of sufficient contrast enhancement.

This phase becomes shorter when a higher flow rate is used. A large amount of contrast medium allows longer scanning time. But in MDCT scanning time has reduced necessitating the use of smaller volumes of contrast.

Radiation Dose Issues-Initial reports after introduction of MDCT indicated increased pt dose. More recent report-indicate comparable/lower doses. The dose efficiency is actually becoming superior in Multi slice CT. A scanners dose efficiency depends upon geometric efficiency, detector sensitivity and the Z axis efficiency. Z axis efficiency is the ratio of the umbra width to the umbra plus penumbra<sup>4</sup>



SDCT 4 channel CT 16 Channel CT

Umbra increase as the collimation is widened

Z efficiency of dose used = ratio of umbra to the umbra plus penumbra

MDCT Specific Dose advantages-There are two conditions where patient dose decreases acquiring a single data set by scanning thin slices which enables the acquisition of high resolution images. Thicker slices can be reconstructed from the same data set. Secondary reformations are also possible without requiring further scanning as raw data with thin slice scanning is available for MPRs. Secondly increasing the scan speed allows the entire scan

to be over in a single breath hold. Dose delivered to the patient is reduced as there is no requirement now to overlap as required in case of multiple breath holds with earlier single channel scanners. A quicker scan reduces artifacts due to motion therefore decreases the requirement to repeat the CT scan.

Specific Dose penalties-Due to inherent technique of multi slice scanning there are specific dose penalties. As technologists and physicians have reduced experience with this new technique, they are unable to optimally utilize the technique. The dose needs to be adapted to the patient size. Rule of thumb: The dose necessary to maintain a constant image noise has to be decreased by a factor of 4 when the patients diameter decreases by 8 cm in pediatric protocols. In CT Angiographies, contrast to noise ratio for a fixed patient dose increases with decreasing X ray tube voltage. Pt dose can be reduced by using lower kV settings. Each dtector is separated by septae which are not sensitive to radiation. So no detector signal is obtained from these inactive zones. With increasing number of slices, the number of inactive zones thus increase. Large no of inactive zones results in minor/major geometrical losses. Further there is decreased sensitivity of the edge of each row of detectors and the edges of each row are located within the beam unlike in a SDCT.

Over beaming- MDCT the primary collimation must be made wider than selected slice thickness to avoid penumbral effects. This is more serious for smaller slice collimations

Over beaming becomes less serious in large channel detectors. Use of cone beams instead of fan beams increases scatter. This requires more dose to improve SNR

Over ranging -To provide data points for interpolation at the beginning and end of the scan . Put for detector assembly width up to 32 mm it isn't a major issue.

In applications like CT Angiography of coronary arteries, retrospective ECG gating is sometimes employed. In retrospective gating, only selected intervals of cardiac cycle are used, but patient is exposed throughout the cardiac cycle. In prospective ECG gating, the patient is imaged during the diastole. The tube current is stepped down to 20% in systole. Thereby decreasing the overall dose administered to the patient. Driven by technology most clinicians are ordering MDCT scans without adequate scrutiny of the clinical indications. Over lapping sections are ordered, with frequent repeat studies on the same patient contributing to unnecessary increase in patient dose.

Technical factors to reduce CT dose-CT Manufacturers have developed systems for automatic dose control. These adjust mAs product to individual patient size so thicker patients get more dose in comparison to thinner patients. Dose modulating technologies adjusts dose factors according to the body contour by stepping up the dose while scanning thicker

areas as the shoulders and hips and stepping down the dose while scanning in the antero-posterior/ postero-anterior planes. Improvements in detectors designs, filters and tracking tube detector alignment have further reduced the delivered dose to the patient. Using organ shielding, selecting slice thickness and utilizing the appropriate pitch (Pitch less than 1 for high resolution examinations such as coronary angiographies and a pitch of more than 1 for routine scanning of the patient)

Other technical challenges-There is a dramatic increase in data due to increased number of slices, volume imaging, reduced rotation speed. Data rates of > 1000 M bits/s handled in A/D conversion. Data transfer from gantry to console requires improved hardware such as dedicated application specific integrated circuits (ASIC), optical slip rings and high speed data buses. With the introduction of the 16 slice scanner, CT has become a virtual volumetric data acquisition tool. It is no longer sufficient to view only axial slices. Workstations are provided with advanced viewing tools which allow image assessment rapidly in any orthogonal/oblique planes.

Future trends-16 slice scanner allows truly isotropic imaging in virtually any application. Hence traditional axial slice is loosing its clinical predominance, replaced by interactive viewing and manipulation of isotropic volumes. Only key slices/views in arbitrary directions are used in films. Newer clinical applications have

become possible, in view of tremendous increase in scanning speed such as CT angiographic examination in pure arterial phase. It is now possible to acquire the Circle of Willis in 3.5 s, and to complete thorax abdominal CTA in 17 s. With a spatial resolution of .5x.5x.6mm3 16 slice CT sets today's benchmark in spatial resolution for non invasive coronary angiography. In Cardiac Imaging, beta blockers are currently used to help achieve images of improved diagnostic quality by reducing the heart rate. But it is desirable to avoid patient preparation. Increasing the temporal resolution will have a greater impact on Cardiac CT than further increases in the number of slices. Mechanical forces in gantry rotation- The tube detector assembly, experiences a mechanical force of 17 G for 0.42 sec rotation. It increases to more than 33G for 0.3 s rotation. Temporal resolution of 100ms is required to freeze heart motion. Rotation times of 0.2 sec (>75G mechanical force) for 100ms which is beyond the realms of current research in quantum physics. Another alternative is to reconsider a scanner concept with multiple tubes and multiple detectors.

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## Basics of CT Perfusion Imaging

# Review Article

adiological imaging has always been targeted at anatomic imaging. Physiologic imaging has been the focus of Nuclear Imaging. With advances in imaging technology, the focus is shifting towards obtaining physiologic information, while maintaining excellent anatomical detail. Mainstay of physiologic imaging, Nuclear imaging, has always lacked anatomical details. Blood flow is essential for survival by all organs. The brain is highly susceptible to ischemia and anoxia. Hence, understandably, stroke was the first target for the application of perfusion studies. Until recently, options for cerebral blood flow measurements were restricted to SPECT, PET or Xenon CT that applied freely diffusible tracers for perfusion assessment and tracer kinetic modeling. Limited availability and time consuming procedures limit their use in acute situation. CT perfusion can be performed non-invasively on a standard CT scanner in a very short time. Resulting quantitative information on cerebral blood flow could have tremendous implications for the management not only of acute stroke patients, but also of patients with chronic steno-occlusive vascular disease. Performance of perfusion CT

Performance of perfusion CT
-The main principle of perfusion imaging is based on the analysis of plain and contrast-enhanced CT scans obtained at dif-

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ferent times. Most important is a sharp bolus of contrast medium resulting from rapid injection of contrast media through a large bore, over 20G, cannula placed in a large(typically antecubital) vein. Initially, very high injection rates to the tune of 10-20 ml/ sec were required1. However, further work has made it possible to use more practical contrast injection rates or 4ml/sec<sup>2</sup>. This method is based on the central volume principle of cerebral hemodynamics and a mathematic operation called deconvolution is used.Initial noncontrast CT of the brain is obtained to rule out hemorrhage. Then the plane passing through the basal ganglia is determined. 40 ml of iodinated, non ionic contrast media is then injected at the rate of 4ml/sec and cine CT scans using multislice CT are taken at gantry rotation speed of 0.5 sec rotation per second. Scanning commences 5 sec after the beginning of injection and is continued for 50 seconds. For single slice CT scanners, the rotation speed is one rotation per second and images are reconstructed at 0.5 second intervals. The images are then transferred to the workstation for further analysis. Following the administration of an intravenous contrast medium bolus the X-ray density of the brain temporarily increases. The artery and vein in the image are identified. The software then generates

the time-density curves in these regions (arterial and venous input function). It also generates the time-density curve in each pixel of the image. (Fig 1) Conclusions about cerebral blood flow can be drawn from the extent and course over time of this increase in density. Using various mathematical algorithms parameters denoting cerebral perfusion are calculated and represented in the form of colour-coded parameter images. The exact mathematical basis of these is beyond the scope of this article, but is based on the Fick Principle.

The formula used for calculating the perfusion parameters using the deconvolution method is:

 $Q(t) = F \cdot C_a(t) R(t)$  where, \* is the convolution operator.

Q(t) is tissue concentrations of contrast media.

 $C_{a}(t)$  is arterial concentrations of contrast media.

R(t) is the deconvolution between the above two curves then gives  $F \cdot R(t)$ . The initial height of this corresponds to CBF, and the area under the curve corresponds to CBV.

MTT (Mean transit time) is calculated as CBV / CBF which is based on the Central volume principle. (Fig 2)

Stroke perfusion imaging (Fig 3)-The usual analysis parameters used in acute stroke imaging are as follows:

Cerebral blood flow (CBF)-Cerebral blood flow is the most important parameter. It indicates how much blood is flowing through the brain tissues, and it is measured in ml blood/100 g brain tissue/min. Normal CBF is between 50 and 80 ml of blood/ 100 g of brain tissue/ minute. Gary matter has CBF values which are 2-3 times higher than those for white matter. Cerebral blood flow is controlled by continual changes in the diameter of the vessels and is kept relatively constant (auto-regulation). If the perfusion pressure decreases due to increase in systemic blood pressure or vascular stenosis, there is vasodilatation, if the pressure increases, there is vasoconstriction. The CBF will decrease only when maximal vasodilatation has occurred in the region which can not compensate for the further fall in the perfusion pressure. Below a CBF of 20 ml/ 100 g/min, the synaptic function of the nerve cells is retarded due to the lack of energy and there is neurological failure. This may be completely reversible if blood flow is normalized again. Below a CBF of 10-15 ml/100g/min the metabolism of the nerve cells can no longer be maintained. If CBF remains below the threshold for 2-10 minutes, there is irreversible cell damage. In infarcts around the infarct core with CBF values below 10-15 ml/100 g/ min, there is a margin of brain tissue in which the CBF is maintained by collateral vessels at 10 to 20 ml/100 g/min. The cells of this infarct penumbra are not yet irreversibly damaged. Structural damage does not occur until hypoperfusion has been maintained in the penumbra for a longer time. This period, which may be many hours, cannot be predicted in individual cases. The treatment of ischaemic cerebral infarcts is not directed on the already irreversibly damaged infarct core, but on the tissue in the penumbra that may recover after perfusion rates have been brought back to normal (salvageable tissue, tissue-at-risk). In interpreting perfusion scans the above detail about the amount of CBF must be considered only as approximate standard values. The local CBF calculated can depend on cardiac function and blood pressure, as well as severe upstream stenosis. Also the CBF values of white matter are considerably lower than those of grey matter and partial volume effects are unavoidable.

Cerebral blood volume (CBV)-Cerebral blood volume (CBV) is defined as the percentage of blood vessels in a specific volume of tissue. Highly vascularised areas of the brain such as gray matter have higher CBV than cerebral white matter. The CBV is also a functional parameter and alters if vessel size changes in the due to vascular auto-regulation. Unlike CBF, which is reduced both in the infarct core and in the penumbra, the CBV in infracted tissue is reduced and in the penumbra, CBV usually increases. This is caused by cerebral autoregulation causing vasodilatation. This is very helpful in diagnosing strokes: areas showing reduced CBV in the acute stage of ischaemia are, as a rule irreversibly damaged. The CBV, however could be unreliable in the presence of severe stenosis upstream

as well as poor cardiac function. All the calculations are on the basis that the contrast remains intravascular and there is no leak in the interstitium. Since there is breakdown of the blood brain barrier in the acute infarct, which increases with time as vascular intimal damage occurs, there is contrast extravasation into the interstitial fluid. In the presence of such a leak, there is increase in the tissue density due to the contrast accumulation. In such a situation, the CBV may be erroneously calculated as higher than the actual CBV. In addition, using the arterial input function from a non stenosed or a stenosed artery (e.g. right and left MCA when there is unilateral ICA stenosis) could lead to varying values of CBV.

Time to peak and mean transit time (TTP, MTT)-The most common of the parameters indicating retarded perfusion or delay in perfusion are MTT and TTP. There is a direct correlation between them and cerebral perfusion pressure. Even slight disturbances to the blood supply can lead to the MTT and TTP being extended5. In clinical studies on strokes the MTT and TTP were found to be very sensitive to disruption in regional perfusion of the brain. Indeed this is not specific to ischaemia. Pathological MTT and TTP values are found both in the infarct core and in the penumbra, but may also be caused by the feeding vessel stenosis (e.g. in the internal carotid artery) or vasospasm.

The clinical application of CT perfusion imaging in acute stroke is based on the understanding that the penumbra shows

- An increase of the mean transit time with moderate decrease of the cerebral blood flow (>60%) and normal or increased cerebral blood volume (80%–100% or higher) secondary to autoregulatory mechanisms.
- Increased mean transit time with marked reduction of cerebral blood flow (>30%) and moderate reduction of cerebral blood volume (>60%).
- Infarcted tissue shows severely decreased cerebral blood flow (<30%) (Figure 4) and cerebral blood volume (<40%) with increased mean transit time<sup>5</sup>

In patients with known chronic cerebral ischemia related to stenotic lesions, it is necessary to distinguish tissue in need of increased blood flow (tissue under hemodynamic stress) from tissue with decreased CBF due to decreased metabolic demand. Hemodynamic stress can be evaluated by using a tolerance test such as acetazolamide administration in conjunction with quantitative measurement of CBF. Acetazolamide administration causes vasodilatation of cerebral arterioles and an increase in CBF. Patients with hemodynamic stress are already maximally vasodilated due to the utilization of cerebral autoregulatory mechanisms in response to decreased perfusion pressure and cannot respond further to acetazolamide. These patients are considered to be at increased risk of stroke and may benefit from interventions to increase CBF. Perfusion CT has been used to monitor cerebral perfusion after SAH. Minimal CBF and CBV values occur both, 1–3 and 10–17 days after SAH, and mean CBF and CBV are significantly lower in patients with moderate to severe vasospasm, compared with those with absent to mild vasospasm.

Tumor perfusion Imaging-In recent years, interest has extended to perfusion imaging of tumors6.The purpose is visualizing angiogenesis (or its modification by therapy) before changes become morphologically evident. Most tumors have higher vessel density, resulting in an increased blood volume (BV) within the tumor bed. The tumor vessels also have loose endothelial junctions at the capillary level. Hence, they often exhibit increased permeability (P) resulting in increased extravascular leakage of blood into interstitial spaces. Tumors enhance more and stay enhanced longer than normal tissue. The capability to quantify these changes of vascularity and permeability would be highly valuable to differentiate between different tumor types. Permeability or Capillary Permeability Surface Area Product is measured in ml/ min/100g. Initially, the technique was used for brain tumors, astrocytoma. Higher grade astrocytomas showed high CBV as well as higher permeability. Low grade astrocytoma shows low CBV and no evidence of contrast leak. Another utility was to differentiate between recurrent GBM and post radiation necrosis. There GBM shows high CBV due to neoangiogenesis. Radiation necrosis does not neoangiogenesis and hence shows low CBV. Recent advances have permitted imaging of neoangiogenesis in the body including lung, liver, pancreas, kidneys, rectum, etc. The advantages of CT perfusion over MRI are the easy availability and robust technique. It is quick and a complete study including processing and analysis can be completed in 5 minutes. The disadvantage is limited coverage. In spite of recent 64 slice CT scanners, the coverage is limited to 40cm. This can be increased by the toggling table technique to 80 cm. but with loss of temporal resolution. The other disadvantage is the use of ionizing radiation.In summary, perfusion CT is fast and available for most standard spiral CT scanners equipped with the appropriate software. Perfusion CT can be used to assess not only patients with acute stroke but also patients with other cerebrovascular diseases. It may also be helpful in the diagnosis and subsequent treatment response in patients with a variety of tumors.

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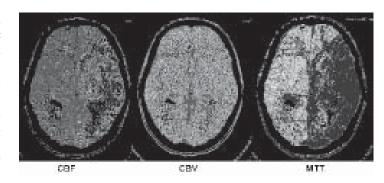


Fig-3, Perfusion maps in a large area of decreased CBV in left hemispheres. The CBV in this area is not decreased. The MTT map shows a larger area of increase transit time. This indicates significant left carotid stenosis without infarction.

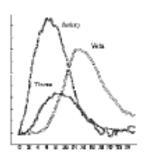


Fig-1, Time density curves from CT perfusion data

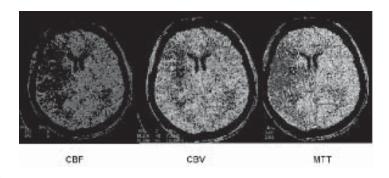


Fig-4, Perfusion maps in a large area of decreased CBV in left hemispheres. The CBV is decreased in a smaller area. The MTT map shows a larger area of increased transit time. This indicates significant left carotid stenosis with infarction. The mismatch between the infracted area as seen on the CBV map and the larger areas in the CBF and MTT maps is the penumbra and is salvageable brain parenchyma.

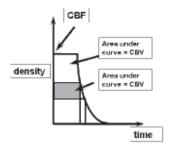


Fig-2, Graphical representation of perfusion parameters

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Review Article

Nuclear Medicine is an imaging modality which utilizes in vivo isotopes for imaging cellular function. It uses tracer compounds that are called as radiopharmaceuticals (RP's), which is made up of a radioisotope tagged to a biological carrier or a pharmaceutical. Each radiopharmaceutical has a characteristic biodistribution, normal physiological uptake, retention and degradation. Based on the distribution of the radiopharmaceutical in the body, a direct assessment of the physiology or pathophysiology of tissues/organs can be assessed. The term functional imaging is also used as the function of the tissue or organ is manifested in the image. The prime difference between xray based imaging and nuclear medicine study is that radiation is transmitted in an xray technique while it is an emission in nuclear imaging. The patient is the source of radiation unlike radiological procedures where the machine is the source of radiation.

Positron Emission Tomography (PET)-The radioisotope used in these form of scans decay by positron emission. Routine nuclear medicine procedures use gamma emitters that have single photon or multiple photons. Table 1summarizes the main Positron emitting radioisotopes available for scanning. 18F-Flourine and Gallium (Ga) 68 are

the popular isotopes that are in use.

which annihilates (conversion of mass to energy) to release 2 pho-

Table- 1, Common isotopes used

Isotope	Half life (T1/2)	Beta Energy (MeV)
C-11	20.4 min	0.385 (99.8%)
N-13	9.97 min	0.492 (99.8%)
O-15	122 sec	0.735 (99.9%)
F-18	110 min	0.250 (100%)
K-38	7.64 min	1.216 (99.3%)
Cu-62	9.74 min	1.315 (97.6%)
Cu-64	12.7 hrs	0.278 (17.9%)
Ga-68	68.1 hrs	0.836 (8.79%), 0.352 (1.12%)
Rb-82	75 sec	1.523 (83.3%), 1.157 (10.2%)
I-124	4.18 day	0.686 (11.3%), 0.974 (11.3%)

The machine for this imaging technique is a PET scanner. It is made up of a ring gantry made up of multiple blocks of detector crystals arranged either in a circular, hexagonal or circular fashion. Each block of crystal has a collection of many smaller crystals. The detectors materials are BGO (Bismuth Germanate), LSO, GSO or LySO. Each crystal material has its own advantages and disadvantages but the manufacturer use them in such a way that all the detectors are comparable in their final performance

Mechanism of interaction and image formation-The radiopharmaceutical injected into the patient emits positrons, which interacts with the electron of adjacent cells and form a positronium (for a fraction of a second)

tons of equal energy in 180 degree. The photons penetrate the tissues and exit from the patient body. Ideally these would move in 180 degrees, hence the electronics of the machine are adjusted so as to detect the simultaneous interaction of 2 photons in detectors placed at 180 degree as a single event. This is called a true event. When photons are detected otherwise, they are called random. There is no physical collimation required in this form of imaging, only those events occurring in the specified time frame simultaneously at 180 degree are considered. This term called electronic collimation. The scintillation created by the photon on the detector is converted to electrical units by the PMT and multiplied many fold in a ratio proportional to the energy deposited in the detector. The line formed connecting the 2 detectors which have received the opposite released photons to extrapolate the source of the photons is called the line of response (LOR). These lines would have a specific length depending on the distance of source from the detectors. Multiple LOR in all angles in the entire ring gantries will help in locating the distance of the source of emission. The statistics collected from tens-of-thousands of coincidence events, a set of simultaneous equations for the total activity of each parcel of tissue along many LORs can be solved by a number of techniques, and thus a map of radioactivities as a function of location for parcels or bits of tissue ("voxels"), may be constructed and plotted. The resulting map shows the tissues in which the molecular probe has become concentrated.

Image reconstruction-Coincidence events can be grouped into projections images, called sinograms. The sinograms are sorted by the angle of each view and tilt, the latter in 3D case images. The sinogram images are analogous to the projections captured by computed tomography (CT) scanners, and can be reconstructed

Attenuation-As different LORs traverse different thicknesses of tissue, the photons are attenuated differentially. This result in structures deeply located in the body as having falsely low tracer uptake. This is achieved by attenuation correction. For this a correction map is required that is ob-

tained from a transmission image. This was conventionally obtained by a radioactive source Germanium 68. This transmission data for the whole body would take almost the same time as obtained the study data or the emission data. The transmission source was later replaced by CT and the xray photons from the CT were used for the correction. This lead to an overall reduction in the time of the scan as CT data was obtained in a fraction of the time compared to radioactive source based transmission data. CT also provided the necessary data for anatomical localization and for fusion.





Figure-1A &B, 1A: Non attenuated image. Note that the deep structures are hazy and not well perceived. In Figure 1B following attenuation correction, the deep structures are well defined.

Current hardware-PET/CT scanner has a CT scanner and PET scanner gantries placed together one after the other with a common tunnel. The fusion of the PET and CT could be a software fusion while some manufacturers have made true hardware fusion with sharing of certain electronics and controls. The CT component in a PET/CT is typically a state of art multislice CT, currently up to 64 slices CT scanner can be fused with a PET scanner can be fused with a PET scanner.

ner. The CT in a PET/CT scanning technique is a low voltage CT image. The voltage could range between 80 to 140 mA. The images of these CT scan are used only for attenuation mapping and help in localizing the sites of abnormal tracer concentration. The CT component can be variable 1) Low voltage/current CT and a no contrast injection, most commonly used mode, Autocurrent mode; a diagnostic quality CT image without contrast or 3) diagnostic contrast enhanced CT mode.

Figure 2 shows a typical PET/CT reporting section: similar axial cuts of CT and PET along with a Fusion image of fused PET/CT data set and a MIP image( maximum Intensity projection)

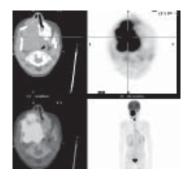


Figure-2, A typical PET/CT

Mechanism of localization of FDG-FDG is analogous to the glucose molecule. It enters the cell like glucose through the GLUT receptors. There is conversion of the glucose and deoxyglucose molecule in the cytoplasm to glucose 6 phosphate or fluorodeoxyglucose 6 phosphate. The further conversion of flurodeoxyglucose is not possible due to inability of the glucose 6 phosphatase

enzyme to act on this molecule, leading to its accumulation in the cell. This forms the principle of FDG PET/CT. Figure 3 is a schematic diagram explaining this mechanism.

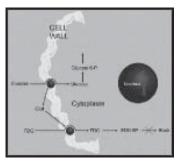


Figure-3, FDG uptake mechanism

Preparation for FDG PET/CT study-Patient needs to be fasting for 6 hours prior to the study. Care is taken that the patient does not have a high intake of carbohydrate even a day before the study. Diabetic patients are refrained from taking their oral antidiabetics or insulin dose in the morning of the scheduled date of appointment. The cut off value for the fasting blood glucose levels is ideally less than 160 mg %. Patients are advised not to undergo strenuous muscular exercise on the day of the appointment. Medications for other ailments like hypertension, cardiac ailments etc can be continued as regular.

Procedure-The patient receives an intravenous injection of the radioisotope and is kept in an isolation room for approximately 45 min to an hour for maximum uptake. The patient is then moved to the scanner room after voiding and the scan last for approximately 15-20 min for a whole

body study. As described earlier the scan consists of 2 parts, CT and PET component. The CT scout is obtained first and the CT attenuation map is taken followed by the PET scan.

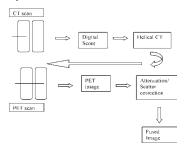


Figure-4, Schematic diagram to show the protocol of PET/CT

PET/CT scans are acquired with patients breathing normally. In cases requiring lung evaluation to identify nodules or smaller pathologies, a breath hold CT is obtained separately after the completion of the study. Special care for pediatric patients is needed. Most of the studies can be performed with the help of hypnosedatives. Low voltage CT component is used with 10 - 40mA, so as to reduce the radiation burden to the child. A typical PET/CT study would take 15-20 minutes for a whole body study that includes from the base of skull to mid third of thigh. This protocol is ideal for most oncological indications.

Information derived from a PET/CT study-Information related to size, location can be obtained from the CT data. Enhancement characteristics are not detailed on the CT component of PET/CT as contrast is not given routinely. The images can also be viewed at different density windows to assess lung parenchymal and bone lesions. PET data of-

fers metabolic information of the region under scrutiny. These are in two forms -Qualitative with visual description. This is with relation to the uptake in the brain (which is considered as the organ with maximum uptake of tracer) and location described in a similar fashion as the diagnostic CT. The uptake pattern could vary in cases of necrosis wherein this would be heterogeneous and Semi – quantitative with Standard uptake values (SUV).

Standardized Uptake Value - Although qualitative interpretations of FDG-PET scans are often sufficient, standardized uptake values (SUVs), are often used in FDG-PET reports in order to impart some semi-quantitative measurement of the degree of FDG accumulation. The SUV is a ratio that can be understood as the concentration of FDG within a lesion divided by the concentration of radiotracer distributed throughout the body. Mathematically, it can be expressed as follows:

SUV = C (T)/ (dose injected/body weight)

where C is the tissue concentration of FDG at time T. SUV method is preferred in practice than the visual scoring as it is a definitive number allowing a better comparison for follow up evaluation.

Clinical applications of PET/CT technology-Table 2 enumerates the various radiopharmaceuticals that have been used clinically and some which are commercially available for use. The principle of its utilization is mentioned alongside.

Table- 2, Radiopharmaceuticals in PET/CT

Radiopharmaceuticals	Parameter Measured in the body	
FDG – Fluorodeoxyglucose (F18)	Glucose metabolism	
FDOPA- Dopamine (F18)	Amino acid metabolism	
FCH - Fluorocholine (F18)	Chlorine cell membrane synthesis	
FLT - Fluorothymidine (F18)	Thymidine DNA synthesis	
FES - Fluorestradiol (F18)	Estradiol Estrogen receptor	
NaF – Sodium Fluoride (F 18)	Bone formation	
Ammonia (N13)	Tissue perfusion	
Methionine (C11)	Amino acid metabolism	

The commonest radioisotope available for PET imaging is the 18F Fluro–deoxyglucose (FDG). All the data which has received approval of these studies is in relation to the utilization of this isotope [Figure 5].

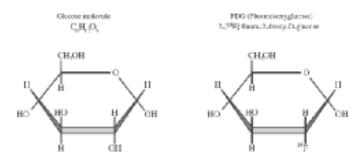
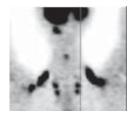


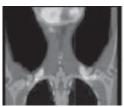
Figure-5, Note the similarity between Glucose and Fluro deoxy glucose structure.

Normal FDG Distribution-FDG-PET maps the distribution of glucose metabolism in the human body. Intense physiologic uptake is seen in the brain, an obligate user of glucose. Myocardial uptake is variable and depends on the fasting status. Activity is seen in the bladder if the patient has not voided between the time of injection and imaging, as well as varying degree of accumulation in the upper urinary tract. FDG uptake is variable in the alimentary tract with activity seen in the region of the stomach and colon. Low-level FDG

uptake outlines the liver, spleen, kidneys, and marrow-containing bones such as vertebral bodies and the pelvis. Prominent uptake in the parapharyngeal/tonsillar lymphoid tissue is present. Lowgrade FDG uptake is commonly observed in the laryngeal musculature. Variable muscular uptake is seen in the upper extremities. Brown fat is the fat responsible for the production of the extra energy required in catabolic states and during increased demand for keeping the body warm. The show increased FDG accumulation in the head and neck, supraclavicular, posterior triangle, anterior mediastinum, axillary and paravertebral regions [Figure 6]. It is usually symmetrical on either sides and hence can be easily differentiated from abnormal site of tracer. But often a unilateral area of brown fat could mimic a pathological lesion and needs a confirmatory correlation on the corresponding CT images.







Cardiac PET/CT Studies-This investigation is considered as the gold standard for myocardial viability. Unlike whole body scan, the patient is loaded with glucose (either orally or using an insulin glucose pump) to saturate the glucose receptors in the body creating a state of increased blood glucose. In these conditions the myocardium shifts its energy supplementation from fatty acid synthesis to energy produced

from glucose metabolism. Infarcted areas would not show glucose metabolism and hence be easily identified on the reconstructed images as a defect where normal myocardium would show increased FDG concentration. Rubidium 82 and 13N as Ammonia are used to study PET myocardial perfusion. They provide excellent resolution and there are no attenuation related artifacts commonly seen in myocardial

perfusion SPECT (single Photon Emission Tomography) study.

Neurological Indication-The majority of the studies from the conception of the PET scanner to its present day evolution have been done on the brain. Perfusion of the brain parenchyma in different physical conditions, pathologies has been done. Interictal brain perfusion studies have been done to identify the areas of hypometabolism which along

with an ictal brain SPECT study localizes the focus of ictus. Neurodegenerative states have been studied to identify the region of the parenchyma showing hypo metabolism e.g Alzheimer's shows a reduced metabolism in the temporo-parietal regions.

Oncological application-More than 90% of all studies in any PET/CT department are of oncological indication. [Table 3].

## Table-3, Oncologic PET/CT Applications

#### Role

Differentiation of benign from malignant nodules

Diagnosis, staging, and restaging Diagnosis, staging, and restaging

Initial staging of patients with distant metastases

Restaging of patients with locoregional recurrence or distant metastases Monitoring response to therapy in patients with locally advanced and metastatic breast cancer when a change in therapy is contemplated Restaging of recurrent or residual thyroid cancers of follicular origin, pre viously treated with thyroidectomy and radioiodine ablation, raised thyro globulin > 10 ng/mL and negative whole-body I-131 scan

Colorectal cancer

**Clinical Conditions** 

Solitary pulmonary nodules

Lung cancer (non-small-cell)

Lymphoma Esophageal cancer

Melanoma\*

Head and neck cancer\*\*

Breast cancer\*\*\*

Thyroid cancer

Important clinical information to be made available before interpreting a PET/CT scan, to provide the highest accuracy are:

- Timing of latest surgery or intervention
- Timing of last chemotherapy
- Timing of last radiotherapy and portals included
- Histopathology of tumor when available
- History of infection and granulomatous diseases
- Immune status
- Injection of Granulocyte colony stimulating factor

Surgical findings when available

PET/CT directed biopsy has added a new dimension; it identifies focus of metabolic activity in a large dormant mass which is otherwise unremarkable on CT. This also adds clinical value of PET/CT study in the overall clinical picture. PET/CT fusion image is also used to redirect the Radiation Oncologist to replan his radiation fields as it would delineate metabolically active lesions from dormant ones, thereby increasing radiation to

the diseases focus and decreasing dose to other areas.

Conclusion-PET/CT has come a long way from merely being a PET study. Today its valuable role in mapping anatomy with functional data, makes it a powerful tool. CT provides attenuation correction and localization, while PET provides quantitative and qualitative functional inforamtion. In years ahead newer PET radiopharmaceutical will increase the accuracy of this powerful modality further.

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Radiology officially traces its beginning to Wilhelm Conrad Roentgen's discovery (and naming) of x-rays in 1895.

Experiments conducted prior to this official beginning – one as early as 1785 by Welsh mathematician William Morgan – actually were the field's first steps. Scientists had experimented with cathode rays during the 1850s. But Roentgen's work was carefully and scholastically presented to the scientific community and then quickly replicated by others.

As with any advance in a scientific field, getting the word out and having others reproduce the work with the same result pushes the discovery toward usefulness. Fortunately, the equipment was easily replicated. Within a year of Roentgen's work there were nearly 1,000 scientific papers published about x-rays! While there was much interest in the diagnostic use, the therapeutic use was also quickly explored. In 1896, JAMA carried an article theorizing the therapeutic use of x-rays.

However, some of the early work resulted in harm and death. Early x-ray tubes lacked protection and there were no standards for exposure. Operators tended to use their own hands to teat the apparatus. From 1896 to 1903, 14 British operators died from over exposure. Protection and standards for exposure were gradually introduced, and professional associations for operators formed to provide training.





## Interventional Radiology-a Basic Introduction

# Review Article

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n January of 1964, an 82 year old diabetic lady was in the hospital with a cold pulseless left foot with gangrene. Her name was Laura Shaw, and an angiogram showed that her condition was due to a narrowing in her superficial femoral artery. She was advised an amputation, which she refused. An alternative was offered by an unlikely person. Charles T Dotter was the chief of radiology in the University of Oregon, the youngest ever head of department appointed, at the age of 32 years. In 1963 he had given a landmark lecture in the Czechoslovak Radiological Congress in Karlovy Vary where he had pointed out the therapeutic potential of the angiographic catheter, which was till then considered a purely diagnostic device1. Charles Dotter decided to carry out a procedure that he had been planning for some time. Using a technique he had developed with his resident Melvin P Judkins, he dilated the stenosis using serially larger catheters. The artery remained open, improving the blood flow to the leg and foot. The ulcers healed, and Laura walked home2. This was the beginning of angioplasty, and the technique of using catheters to dilate a stenosis is now called "Dottering" after Charles T Dotter. For his many contributions and original work, Charles T Dotter is regarded as the father interventional radiology (IR).

The term "Interventional Radiology" (IR) was used by Alexander Margulis to describe procedures of a therapeutic nature, carried out under imaging guidance<sup>3</sup>. Further developments included procedures for controlling haemorrhage [4], removing retained gallstones through T-Tube track 5, percutaneous nephrostomy and nephrolithotomy, and many many others. The past two decades have seen a rapid expansion in techniques and indications for IR procedures. The recent advances in IR have resulted from two different directions of evolution. The development of new devices that can achieve results not achievable by earlier devices. An example of this is the development of Guglielmi Detachable Coil (GDC) that has revolutionized therapy of intracranial aneurysms<sup>6</sup>. This technique is now replacing the classical approach of clip placement in therapy of subarachnoid aneurysms. The application of existing techniques to new areas so that clinical outcomes achieved by other means can now be achieved by interventional techniques. This is demonstrated by the popularity of Uterine Fibroid Embolisation (UFE) which achieves the clinical outcome of rendering symptomatic fibroids asymptomatic using a classical technique of particulate embolisation to reduce the blood supply of uterine fi-

broids. Evidence has shown that the minimally invasive procedure is equivalent to hysterectomy<sup>7</sup>. Interventional techniques have been adopted by almost all specialties and branches of medicine. An example would be the procedure of Percutaneous Dilatational Tracheostomy (PDT) where a needle puncture of the trachea with a guidewire insertion and dilatation is used to insert a tracheostomy tube, which is a classic Seldinger technique<sup>8</sup>

Techniques & terminology-IR is based on two fundamental skills acquired by all radiologists in the past. A thorough understanding of anatomy and its representation on radiologic images, fluoroscopic, US, CT or MR based. Some skill in the use of catheters, guidewires and needles. Interventional techniques can be grouped into the following basic steps or techniques:

- Access-This is essentially the placement of a needle in a desired anatomical region. This may be space or an anatomical location or structure, as for Vascular Access or for Needle placement under guidance
- Catheter / guidewire manipulation- This step follows the first step, but may be done without using needles through natural body orifices, as in the oesophagus, or fallopian tubes etc. This is

- the process of inserting a catheter that is manipulated into a desired location.
- Implants/ Prosthesis use-Many devices are deployed in interventional procedures. These may be coils, used for blocking a channel, or stents, used for opening a channel. The use of these requires additional skill sin the manipulation of these devices.

Interventional procedures can be fundamentally divided into two different classes in terms of required skills and procedure design:

- Needle procedures-These are procedures where needles are placed in specific locations under imaging guidance (Fluoroscopy/ CT/ US/ MR). These needles may be used to carry out biopsy, ablative procedures (RF/ Laser/ Chemical injections), or aspirations (diagnostic/therapeutic). A list of needle based procedures is listed in Table 1.
- Catheter procedures-This is a step ahead of simple needle insertion. The needle is introduced into a space and then used to insert a catheter. This employs of the Seldinger technique, or a Trocar mounted catheter insertion.
- Seldinger technique -The Seldinger technique, so named after Sven Ivar Seldinger 9 is a series of steps using a needle, guide wire and catheter to place a catheter in any duct, vessel or space. The

- Seldinger technique is made up of steps as below:
- First, needle insertion into a space (artery/ vein/ abscess)
- Insertion of a guidewire through the needle
- Removal of needle
- Insertion of catheter over the guide wire. An intermediate step of dilatation may be necessary to allow a catheter of required size to be inserted.

The trocar-catheter system uses a catheter mounted over a trocar/ needle. After puncturing the required cavity/ channel, the needle is removed and catheter is left in place. This is identical to how a venous cannula ( IV catheter) is inserted in a peripheral vein. After placement of catheter into a ductal system, the catheter/guidewire combination is advanced to a desired location. For example, from the common femoral artery into the carotid artery, or from the intrahepatic biliary radical into the duodenum etc. On reaching a desired site, the catheter and / or guidewire may be used to carry out many procedures, for example balloon angioplasty, embolisation etc. The basic procedures recanalisation, occlusion, drainage and drug or device delivery. These can be carried out in many different areas as given in Table2.

What is a catheter -A catheter is described in terms of tip shape, size and function. Catheter sizes are measured in the French Scale

(1 mm = approx 3 F) Catheters are available in two basic types:

- Drainage Catheters: Used for drainage of collections. These are larger bore and shorter length catheters, usually with multiple holes. They are usually stiffer than angiographic catheters. Usual calibres range from 6 – 12 F. Most drainages are done with 8 F catheters.
- Diagnostic Angiographic Catheters: These are longer (60 to 100 cm) and usually smaller in calibre (4- 6 F)

Properties of catheters-The basic skill of manipulation requires an understanding of the behavior of endovascular devices (catheters and guidewires). This is described in terms of

- Trackability: This is the ability of a catheter to follow complex curves. It depends on the degree of flexibility and the amount of friction between the catheter and tissue. Ideal catheter can go across any number of curves and still advance.
- Pushability: Force can only be applied on the part of the catheter outside the body.
   How well the force applied on the part is transferred to the tip of the catheter is the pushability. An ideal catheter moves forward in proportion to the force applied at the hub.
- Torquability: The tip of the catheter will rotate as the hub is rotated. This movement may not be equal at both

ends. Due to friction and deformability (softness) of the intervening portions of the catheter, the tip does not rotate as much as the hub does. Ideal catheters approach a 1:1 response, a 45deg rotation of the hub leads to a 45 deg rotation of the tip.

In the real world, there are no ideal devices. Furthermore, there is an inverse relationship between different properties. A trackable catheter is softer, but will therefore have less pushability, and torquability, while a stiff catheter will be less trackable. To some extent, the mutual conflicts can be resolved by having a graded stiffness along the length of the catheter, such that a soft tip is followed by stiffer section down the length to the hub. The same can be done with a guide wire. The varying stiffness is achieved by the changing the wall thickness, and the wire braiding in catheter. The shaft thickness and material can be varied in guide wires. These properties are balanced in different ways to give products with characteristics that make them suitable for differing purposes. This is why a typical interventional lab will contain products of many confusingly different shapes sizes and names, so that a variety of procedures may be carried out safely. A list of common devices (hardware) is mentioned in Table 3.

Clinical Aspects-A surgeon approaches the disease processes through surgical exposure and employs operative techniques,

either minimally invasive or open, to achieve therapeutic goals in consonance with accepted principles of therapy and available evidence. An interventional radiologist differs only in the tools and techniques used. An IR specialist needs all the clinical abilities and approach of a surgeon, and must have the ability to clinically evaluate the situation and manage the patient as a whole, using of drugs as necessary. Interventional radiology requires not only manipulative skills and a thorough understanding of anatomy but also a commitment to the understanding of disease processes and therapeutic options available for any given situation. It is a clinical specialty and demands a clinical approach to not the image but the patient as a whole. Disease pathogenesis, natural history and available therapeutic strategies are all an essential fundamental on which therapeutic decisions and choice of therapy are based. From this point of view, many conflicting opinions about the training of future interventional specialists have emerged. The lack of a clinical rotation in basic radiology training is a big hindrance in the development of interventional radiology. All IR practitioners have to understand the basics of patient management. From this point of view, all IR practitioners should probably undergo a clinical rotation and sub-specialty rotation depending on area of subspecialisation (e.g, vascular surgery, neurology/ neurosurgery etc.) so that there is a base of shared knowledge and patient management protocols. The performance of a procedure is in itself only a portion of the tasks of an interventional radiologist. To achieve good results and maintain a clinical practice, the essential clinical tasks of pre- and post-procedure evaluation, "Rounds" to see patients in the wards as well as referral protocols as in any other clinical specialty, are imperative. An interventional radiologist who performs a procedure and then forgets the patient is unlikely to achieve a sound and long lasting professional existence. IR has to examine, admit, manage and treat patients, referring to other specialties as required.

Conclusion-IR is prominent in the field of emerging specialties. The future of IR is expanding and bright. The promising field of stem cell therapy and genetic therapy includes a large group of procedures that require the targeted placement of therapeutic agents and vectors in specific areas through vascular channels (arteries and veins). The field of organ transplant is poised for a revolution with the development of pancreatic islet cell transplant, carried out through a portal venous access, and many more promising developments are nigh. The future is bright and unlimited. The basic skills in IR can be learnt by most radiologists and will serve them well in expanding their skills and practice. Whether or not a radiologist specializes in IR, acquisition of basic IR skills and an understanding of image guided procedures is likely to immensely improve standard of care provided. Involvement in the care of patients and therapy is deeply rewarding and of immense benefit to patients. The need for IR exists, and interventional procedures are here to stay. We can be involved and participate in the revolution, or be left behind.

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Table 1,Needle placement procedures		
Needle Procedure Guided Biopsies Fine needle	Clinical Indications	
Trucut Tumour Ablative Procedures RF Ablation Laser ablation	For Solid Tumours in Liver, kidney, lung etc.	
Chemical Ablation (Alcohol/ acetic Acid) Cementoplasty Vertebroplasty Other sites	For Osteoporosis/ Neoplastic Lesions with Pain	
Pain Management Alcohol Ablation RF Ablation	Neural ablation of coeliac/ other areas	
Non Ablative Interventions for pain relief	Steroid/ anaesthetic injections Epidural Facetal Transforaminal Joint Space	
Percutaneous Sclerotherapy	Vascular Malformations	

Table- 2, Catheter based procedures		
Body Region VASCULAR	Procedure Type	Procedure
VISCOLIN	Revascularization	Balloon Angioplasty Stent Placement Thrombolysis/ Thrombus extraction (Pharmacological/ Pharmacomechanical)
	Aneurysm Exclusion	Coil Embolisation (Detachable/ Pushable) Stent Graft Placement
	Embolisation	Coil Embolisation Particulate Embolisation Liquid Embolics
	Sclerotherapy	Sclerotherapy of Vascular Malformations
	Venous Ablation	RF/ Laser Ablation of Saphenous Vein
	Venous Access	Central Venous Catheter Placement
	Porto-Systemic Shunt Creation	TIPS
	Venous Recanalisation	DVT Thromboysis Venous Angioplasty and Stent placement
	Transvenous Biopsies	Transjugular Biopsy of Liver/ kidney
NON VASCULAR Liver	Biliary Drainage	Percutaneous Transhepatic Biliary Drainage (PTBD) Biliary Stent Placement
GUT	Urinary Drainage	Percutaneous Nephrostomy (PCN) Ureteric Stent Placement
	Recanalisation	Fallopian Tube Recanalisation (FTR)
Abscess/ Collection	Abscess/ Collection Drainage	Intraperitoneal, Pelvic, Retroperitoneal, Pleural Collections, Pseudocysts etc
Bronchial Tree	Recanalisation	Tracheal Stent Placement
GIT	Recanalisation	Balloon Dilatation (Oesophageal)
	Stoma Creation	Stent Placement (Oesophagus, Duodenum, Colon) Percutaneous Gastrostomy , Jejunostomy, Caecostomy
Stent-graft	Fistula Closure	Tracheo-oesophageal fistula exclusion by
Miscellaneous	Nasolacrimal Duct Recanalisation	Nasolacrimal Duct Stent placement

	Table- 3, Commonly used devices (hardware)
Device	Purpose
Needles Arterial Puncture Needle	Short bevel needle, usually 18 G , used for arterial and venous Punctures. Hub is designed to facilitate guide-wire insertion.
Chiba Needle	A thin flexible needle, 21 or 22 G. Very safe due to small size. Does not cause laceration as is flexible during respiratory motion. May be used for biopsy or ablative injections. Available in varying lengths from 10 cm to 60 cm. Echotip versions are easier to see on US. Most are designed with a hub that can be used to insert a guide wire.
Initial Puncture needle	A needle with a trocar, outer blunt cannula and sharp needle. Used for puncture into a non-vascular system like biliary or pelvicalyceal system. Usually larger calibre (16G- 18 G). Designed for guidewire insertion
Spinal Needle	Standard Lumbar Puncture needle. 19-24G. Used for spinal interventions, biopsies etc. Designed to be relatively rigid and has a stillete. This needle is not designed for guide wire insertion
Tru-cut needles	These are designed for core biopsy. They may be manual or automatic. Size ranges from 21 G to 14 G.
Drainage Catheters Pigtail drainage catheter Malecot Catheter Straight Dranage Catheter Dilators	
Vascular dilators	These are meant for dilating the passage before inserting catheters into vascular structures. Non –radio-opaque and softer
Fascial Dilators Diagnostic Catheters Forward curve Reverse curve Flush Catheters Guidewires	For dilating passages in drainage procedures. Radio-opaque
Teflon or PTFE coated	J curve or straight tip shape. Diameter 0.018" to 0.042". Length 80 to 260 cm. Used for all basic procedures.
Hydrophilic	Angled, straight or J tip. Coated with hydrophilic substances to reduce friction with tissue. 0.018" to 0.038" diameter. Length 150 to 260 cm. Usually used for crossing obstructions or catheterizing tortuous anatomy.

## Fetal MRI: a Clinical Review

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## Review Article

 ↑ he principal purpose of antenatal screening programs is to identify disease and then to give the parents the option of termination of pregnancy. Till now, ultrasound has been the major contributor for early diagnosis. There was a lack of non-ionizing imaging modality which could provide the gap left by ultrasound. Fetal motion has always precluded the advent of a cross-sectional imaging modality. However, technical advances in full form MRI now allow imaging inspite of fetal motion. In this chapter, the author presents a spectrum of fetal abnormalities diagnosed using MRI. Although high resolution ultrasonography permits the detection of many anomalies, it does have limitations. Poor views due to maternal obesity oligohydramnions can be surmounted by ultrafast fetal magnetic resonance imaging. Faster imaging sequences now permit a single slice to be obtained in less than 400 ms, thereby eliminating most fetal motion artifacts. Besides, identifying the abnormality, MRI has been found to have more applications than considered previously, such as volume assessment, spectroscopy etc. As the use of MRI is increasing, newer applications are being

Safety considerations -There are no known hazards to the fetus due to MRI <sup>1-5</sup>. No delayed

sequelae from MRI examination have been encountered and hence, MRI is thought to be safe for the fetus. According to the Safety Committee of the Society for Magnetic Resonance Imaging<sup>6</sup>, MRI procedures are indicated for use in pregnant women if other forms of nonionising imaging are insufficient or if the examination provides important information that would otherwise require exposure to ionizing radiation. Different types of physical agents are known to cause damage to the fetal cells in the first trimester. Hence, it is prudent to limit the fetal examination to the second and third trimester. All patients should be informed regarding the risks and benefits of MR imaging. Older MRI techniques met with limited success7. Now, with ultrafast imaging, superior quality, fetal imaging is possible without the need for maternal or fetal sedation8.

Ultra-fast MR imaging -A higher gradient strength is required to obtain shorter scan times so as to allow performance of ultrafast imaging. The ultrafast sequences such as respiratorygated single shot fast spin echo (ssFSE) and breath-hold spoiled gradient (SPGR) sequences allow superb anatomic delineation of the fetus. ssFSE is a variation of fast spin echo (FSE). In FSE, the complete image data is acquired over a number of TRs. The total acquisition time for a FSE se-

quence can stretch from one to 3 – 4 minutes. In ssFSE, all the data acquired for a complete image is acquired in a single TR. Thus, the total acquisition time for a typical ssFSE is 300 to 1000 ms, essentially less than 1 second. A one-second delay between the image acquisition minimizes the specific absorption rate. As this is a slice acquisition technique, it is relatively immune to motion artifacts and susceptibility artifacts which degrade EPI images and is easily repeatable.

# Patient preparation and technique

Counseling - Knowledge of presence of some abnormality in the fetus is a significant stress factor to an expectant mother. Before taking the patient for the study, it is worthwhile to spend a few minutes with her and to prepare her mentally for the study, explaining to her what to expect. This eases the anxiety and provides better co-operation.

Previous imaging -Ideally, an ultrasound scan must be performed immediately before the MR examination. This is important so as to allow placement of the surface coil over the region of interest in fetus, with respect to the maternal body. Also, there may have been some variation in the disease process, since the last ultrasound, such as increase in the ventricular dimensions or decrease in the size of the lesion such as a haematoma.

Patient positioning - The patient is positioned supine with feet first into the magnet to avoid claustrophobia. A rest may be provided below the patient's knees to reduce backache. If the supine position is uncomfortable, as it is encountered in late pregnancy, the patient may be imaged in the left decubitus position.

Technique- Fetal MRI was performed on a 1.5 T system (GE Echospeed, Signa, Milwaukee, USA), at Dr. Balabhai Nanavati Hospital. A three-plane T1weighted scout, followed by T2 weighted imaging of the entire gravid uterus is initially done in axial, coronal and sagittal planes using an ssFSE sequence. This allows for preliminary assessment of the fetal and placental positions as well as the uterine wall. The cervix and adnexal regions can also be simultaneously evaluated. Depending on the indication of the study, images are obtained in orthogonal planes with respect to the targetted fetal anatomy. Imaging in additional planes, such as oblique axial, coronal and sagittal is then performed with reduced slice thickness and/or higher matrix to acquire detailed information of the anatomy or an abnormality. One breath-hold, T1-weighted sequence is usually sufficient to assess for blood products / haemorrhage or confirm presence of fluid as in a cyst.

#### Clinical fetal MRI

Central nervous system - The commonest request for fetal imaging is to evaluate the central nervous system. The cerebral ventricles are large in fetuses aged 20 to 25 weeks, corresponding to the normal so-called fetal hydro-

cephalus, especially at the level of the posterior horns (Fig 1 A). In young fetuses, the ventricular size at the atria level does not exceed 10 mm. However, the ventricles appear large due to inadequate development of the cerebral mantle. Later on, the ventricles become smaller and are too subtle to be seen by week 35 (Fig. 1 B). The subarachnoid spaces are also prominent in young fetuses. From 20 weeks onwards, there is formation of the primary and secondary sulci. This development extends upto term. The corpus callosum can be seen on sagittal images as early as 20 weeks. However, it is very thin in young fetuses and not very well depicted.

Indications for fetal brain MR imaging: Ventricular dilatation and suspected partial or complete agenesis of the corpus callosum are the most frequent abnormalities which are referred for MR evaluation. Other indications are as follows:

- A pregnancy with potentially destructive brain lesion related to maternal hypoxia, maternal trauma, multifetal pregnancies with or without death of the co-twin, vaginal bleeding, and premature labor.
- Maternal infection with potential fetal brain involvement, in cases of toxoplasmosis seroconversion, cytomegalovirus infection, and less commonly, HIV, chickenpox, measles, and hepatitis infections.
- Fetuses presenting with extracerebral multiple malformations as some of these can

- be associated with brain lesions
- Known CNS malformation or chromosomal aberration in the siblings.
- A family history of genetic disorders involving the CNS (e.g. tuberous sclerosis, and neurofibromatosis type 1).

Rarely is MR imaging performed to evaluate extracerebral, cervico-facial masses, or because the sonographic examination is technically difficult, especially when oligohydramnios is present <sup>7</sup>.

Corpus callosal agenesis-Agenesis of the corpus callosum is easily depicted by MR imaging in utero. The associated abnormalities include ventricular dilatation with a colpocephalic appearance, parallel alignment of the lateral ventricles. Partial agenesis may be related to an interhemispheric cyst. Girard et al have found MR imaging useful in demonstrating associated neuronal migration disorders such as heterotopia as well as in the diagnosis of septo-optic dysplasia. These conditions are difficult to diagnose on ultrasound 7,9,10.

Neural tube defects- Malformations such as anencephaly (Fig. iniencephaly, myelomeningoceles, and Chiari type III malformations are well depicted by prenatal US, but may need confirmation or a detailed look for other associated abnormalities. In cases of iniencephaly, the abnormalities include a short or absent neck with a star-gazing appearance of the fetus (Fig 2 B). Most abnormalities involve the posterior fossa and the cervical cord and are not easily depicted on ultrasound. MR imaging is occasionally performed to evaluate anatomical parts that have herniated into the meningo-encephalocele, to describe brain changes in myelomeningocele by showing the Chiari type II malformation and hydrocephalus (Fig 3 A), and to plan neonatal surgery when the pregnancy is continued. In cases of encephalocele, the subcutaneous fat is absent, while in cases with meningocele, fat is present<sup>7</sup>. At times, ultrasound is unable to differentiate between a thickened nuchal fold and a meningoencephalocele and MRI may be useful (Fig 3B). Diverticulation disorders-MR imaging is performed in alobar or semi-lobar holoprosencephaly, when the abnormality is depicted late in pregnancy during the third trimester, to rule out other malformation presenting with ventricular dilatation. MR imaging is adequate in demonstrating lobar holoprosencephaly, which can be missed on US7.

Posterior fossa cystic malformations- Ultrasonography is accurate in demonstrating severe forms of Dandy-Walker malformation consisting of posterior fossa cyst in combination with vermian agensis and hydrocephalus. However, MR imaging may provide information about the position of the dural structures like tentorium (Fig 4 A,B)<sup>7</sup>.

Destructive lesions- Parenchymal damage can occur due to vascular or infective insult, leading to leukomalacia and/or atrophy. The primary abnormality depicted by ultrasonography is ventricular dilatation, which may be symmetric or asymmetric. Parenchymal lesions may or may

not be well depicted on Ultrasonography, which on MRI is seen as lack of symmetry, presence of abnormal signal or absence of normal signal. Prenatal MR imaging identifies subtle parenchymal lesions (Fig 5 A,B) and may predict occurrence of cerebral palsy or epilepsy in the postnatal life<sup>7</sup>.

Hemorrhage- Hemorrhage is seen as an area of increased echogenicity on ultrasound11. MRI shows hemorrhagic lesions as high-signal intensity areas on T1 and low-signal intensity on T2 weighted images within the parenchyma, the ventricles and the germinal matrix. MRI is superior in detection of subdural, subarachnoid and intraventricular hemorrhage. Intracranial hemorrhage in the fetus is thought to be a result of several causes such as sudden change in blood pressure or asphyxia 12. Zanders et al have suggested consideration of fetal MRI in evaluating intracranial echogenicity detected on sonography in fetuses at high risk of developing hypoxia 13.

Maternal infections- Infection can cause destructive lesions or neuronal migration disorders depending on the time of occurrence during pregnancy. Intracranial calcifications are difficult to detect by fetal MRI as the technique is inherently insensitive to calcification. The presence of calcification can be susepcted, especially when there is presence of leukomalacia (Fig 5 A,B).

 Toxoplasmosis is a common in-utero infection. It can cause necrotizing meningoencephalitis, with consequent hydranencephaly. Sub-

ependymal cysts, ventricular dilatation, and brain destruction can be seen in some cases. Cytomegalovirus (CMV) infection manifest as micrencephaly, meningoencephalitis, periventricular or cortical calcifications, lissencephaly, cerebellar hypoplasia. periventricular leukomalacia ventriculomegaly, which are seen on MRI. Girard et al also have found MRI to be an efficient technique in demonstrating brain damage and white matter abnormalities in materno-fetal infections7.

Ventriculomegaly - Ventriculomegaly is defined as ventricular size greater than 10 mm at the level of atria. It can be caused by a tumor, a malformation or a destructive lesion<sup>7</sup>. The ventricular dilatation can be isolated and without a detectable cause in some cases. In few cases, when ultrasound demonstrates only mild ventricular dilatation, MR may depict parenchymal destruction, hemorrhage or associated malformation, a situation leading to a change in management.

Tumors- Congenital brain tumors are rare with the incidence ranging from 0.5 % to 1.5 % of all pediatric CNS tumors. Teratomas represent one-third of congenital tumors, gliomas (astrocytomas, glioblastomas, ependymomas, and papillomas of the choroid plexus) represent another one-third, and others (primitive neuroectodermal tumors, meningiomas, craniopharygiomas, lipomas, and hamartomas) represent the last one-third. The detection of hamartomas can have genetic

implications, such as in tuberous sclerosis or Bourneville's disease, in hypothalamic hamartoma. The commonest tumors include teratomas and choroid plexus papillomas (Fig 5 C), mostly presenting with fetal hydrocephalus<sup>14</sup>. Intracranial cysts- Most intracranial cysts are isolated, single and stable in size. These fluid collections on ultrasound can be mistaken for a dilated ventricle and if large in size, their extent may not be easily delineated. These fetuses usually have a favorable postnatal outcome or the clinical outcome is not related to the cyst volume and location, but upon the integrity of the brain parenchyma<sup>15</sup>. It is also superior in demonstrating lack or presence of associated abnormalities of the parenchyma. Rarely, surgery is needed for the treatment of an evolving hydrocephalus or an expanding cyst.

Vascular malformations - Intracranial arteriovenous shunts detected during the in-utero life consist of a vein of Galen aneurysmal malformation (VGAM) or a dural sinus malformation (DSM). VGAM is now a well recognized as an embryonic vascular malformation and is seen as a large signal void area on T2 weighted images along the expected course of the vein of Galen (Fig 5 D).

Fetal thorax -The fetal lungs because of their fluid content are seen as high-intensity areas on T2 weighted images. These bright areas are well delineated against the low-intensity thoracic wall and the signal void of the heart. The bronchovascular tree is visualized as linear signal void (vessels) and fluid intensity (bronchi)

areas with a branching pattern against the hyperintense lung tissue. The left dome of the diaphragm is seen as isointense curvilinear stripe and is well visualized on the sagittal and coronal planes, contrasting against the spleen and other abdominal organs against the fluid-filled hyperintense lung. On the right side, the dome merges with the superior margin of the liver.It may be visualized only when there is fluid interposition due to ascites or effusion (Fig 6D). In cases with congenital diaphragmatic hernia, the prognosis depends on presence of hepatic tissue as part of the herniated contents. This is difficult on ultrasound, at times, unlike coronal MR images (Fig 6 A-C). Meconium-filled bowel loops appear hyperintense on T1 weighted images and are found in the thorax in almost all cases of diaphragmatic hernia (Fig 6 A). MRI allows accurate delineation of the ipsilateral lung and also assessment of the extent of mass effect on the contralateral lung (Fig 6 B). This condition leads to pulmonary hypoplasia, the severity of which determines the prognosis. Determination of lung volumes using computer planimetry of echoplanar MR images is possible. There is an exponential increase in the lung volume from 21 ml at 23 weeks to a maximum of 94 ml at term (Fig 6C) 16.

Other thoracic abnormalities which have been assessed using MRI include congenital cystic adenomatoid lung malformation (CCAM), bronchogenic cyst, sequestration of the lung and esophageal atresia. The signal in-

tensity of the CCAM and sequestrated lung is higher than the normal lung<sup>17</sup>.

Fetal urogenital system -\_On T2 weighted images, the renal cortex appears as high-signal area in the retroperitroneum adjoining the vertebral column. The appearance of fetal urine in the genitourinary system is bright on T2 weighted images. Hence, the pelvicalyceal system is seen as linear, branching hyperintensities near the hilum. The ureters are not visualized in the normal physiological condition. The urinary bladder is easily detected in the pelvis as an oval hyperintense structure with a thin hypointense wall<sup>18</sup>. The delineation of the genitals is also satisfactory on MRI<sup>19</sup>. This allows assessment of the fetal perineum in cases where it is an important consideration for diagnosis, such as posterior urethral valves. It is essential to locate both kidneys in the same section in all orthogonal planes with respect to the kidney, to confirm their presence or absence and to rule ectopia. These are then assessed for size, symmetry and signal intensity. MRI of common cases include unilateral and bilateral renal agenesis, multicystic dysplastic kidneys (Fig 7A), crossed fused ectopia (Fig 7B), unilateral pelviureteric junction obstruction (Fig 7C), horse-shoe kidney, and obstruction due to posterior urethral valves (Fig 7D). Other conditions which have been assessed on MRI include ureter duplication with ectopic ureterocele, prunebelly syndrome and megacystis microcolon intestinal hypoperistalsis syndrome<sup>20</sup>. Chen et al have reported MRI findings in a case of congenital mesoblastic nephroma, associated with fetal hydrops and polyhydramnios <sup>21</sup>.

Fetal musculosketal system -Ultrafast MR imaging allows excellent delineation of the extremities, including the digits in most fetuses in the late second and third trimester, using T2 weighted sequences. It is possible to identify the bony components including the cortical bone, marrow and epiphyseal cartilage. It's use to confirm presence of talipes equinovarus deformity (Fig 8A), and entites like complete unilateral phocomelia and associated contralateral pelvic dysplasia (Fig 8 B,C) is well established. Multifetal pregnancies-The prevalence of congenital structural anomalies is higher in twin pregnancies, more commonly monozygotic twins, than in single gestations <sup>22,23</sup>. Structural defects in twins can be conjoined twins, acardiac twin and co-twin demise which are unique to monozygotic gestation<sup>24</sup>. Increased incidence of conditions like neural tube defects, hydrocephalus, congenital heart disease, congenital hip dislocation and clubfoot may be found. MRI analysis of conioined twins including craniothoracoabdominopagus (Fig 9A,B) is well established. Associated abnormalities, included omphalocele with polysplenia in one twin. In complicated multifetal pregnancies (Fig 9C), such as acardia, MRI is useful in depicting the complex anatomy of the anomalous fetus as well as in delineating the normal appearance of the co-twin (Fig 9D) 25.

Placenta and uterus -Placenta previa is not a common indication for MRI, but can be used as an useful adjunct to ultrasound, when there is uncertainty as regards the placental edge or the when the cervix is not well visualized. In these cases of placenta previa, a sagittal T2 weighted sequence along the long axis of the cervix is used to assess the lower margin of placenta and it's relationship to the internal os<sup>26,27</sup>. MRI is particularly useful in cases of complications such as increased placental volume (Fig 10A) due to transfusion incompatibility, maternal diabetes and anemia<sup>28</sup>. On ultrasound, the portion of the placenta away from the transducer may be difficult to evaluate because of the enlarged size.

MR is also useful for assessment of uncommon conditions like placenta increta, percreta and accreta (Fig 10B) or amniotic band (Fig 10C). These cause intrapartum haemorrhage with a high risk of surgical intervention and mortality<sup>29</sup>. This is a condition where the myometrium is invaded by the placenta to a varying extent and occurs in patients with multiple casearean sections or myomectomies<sup>30</sup>. Levine et al have found that when the placenta is posteriorly located, MRI may help more than ultrasound. Hence, for patients with history of previous surgery and posteriorly located placenta, they suggest evaluation by MRI 8.

Artifacts -Fetal MRI is distinct for the reasons that the fetus as well it's surrounding environment (liquor) are mobile. Also, imaging of the fetus is affected by maternal factors. The artifacts encountered are frequently related to motion and the technique, and uncommonly to the equipment. Motion artifacts affect anterior longitudinal ligament fetal examinations. However, as the images are obtained in 300 to 400 milliseconds, ssFSE allows for diagnostic quality imaging despite motion. However, it is essential to understand / recognize motion artifacts in order to avoid diagnostic errors. There is resultant increase in noise and edge blurring due to motion. Streak artifacts are also seen at times. They are attributable to fetal motion, fluid motion and maternal motion. Technique related artifacts include aliasing and partial volume averaging. The equipment related artifacts are related to inhomogeneous radiofrequency signal reception and radiofrequency interference artifact.

Contraindications & limitations of fetal MRI-Some absolute contraindications to the MR technique include presence of a ferro-magnetic aneurysmal clip, pacemaker etc. Patients suffering from claustrophobia may not be willing to undergo the exam. They may also experience difficulty in lying on their backs, especially in the third trimester. Excessive fetal motion may limit the quality of images, not providing diagnostic value. Also, small fetal structures may be difficult to evaluate due to small signalto-noise ratio. Calcification is per se is not well seen on MRI and in the fetus, these may be very small. Thin structures surrounded by fluid can be difficult to assess as a result of partial volume averaging. Thinner sections may be required, which in turn compromises the signal-to-noise ratio. Conclusion - Although obstetric imaging will continue to be dominated by ultrasound because of its easy availability, low cost and easier performance, MRI is an invaluable complementary investigation to ultrasound. It may detect additional findings that may alter patient counselling and case management. This is especially important when in-utero or immediate post-natal intervention is an option.

However, high cost continues to be a limiting factor for wide usage.

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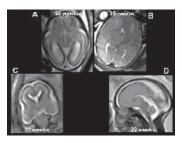


Figure-1 A&B, Normal MRI appearance of atria in 25 and 35 week fetus. The ventricles, generally, appear large as compared to the cerebral mantle due to incomplete development. The atria in the later pregnancy gradual reduction in size and appear very small near term. Figure 1 C&D: Normal appearance of the corpus callosum in 22 week fetus. Coronal section shows integrity of the normal midline anatomy. Sagital section shows corpus callosum as a subtle hypointensity in the midline.



Figure-2 A&B, 2A: Anencephaly seen on MRI as a midline sagital section with absence of bony calvarium and the brain parenchyma exposed to the CSF. The eyeball appears relatively large. Figure 2 B shows Iniencephaly featured by a midline split of medulla and cervical cord into equal halves.

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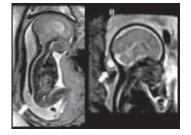


Figure-3 A&B, Meningomyelocele seen on Fetal MRI as a midline defect in lower spine. A thin-walled fluid-filled sac is detected in relation to the defect. The thin wall suggests a non-skin covered back mass. Figure 3 B demonstrates Occipital meningocele with a rounded fluid-filled sac in the occipital region. No contents are seen within it ruling out an encephalocele. The outer wall covering is thick and double layered suggesting a skin covering.

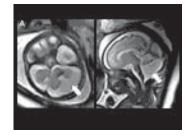


Figure-4 A&B, Fetal MRI of Dandy-Walker malformation. Axial MRI section shows fourth ventricle communicating with cisterna magna, and the cerebellar hemispheres appear hypoplastic. Sagital section reveals enlarged posterior fossa. The vermis is hypoplastic and is seen only in superior aspect in this midline section.

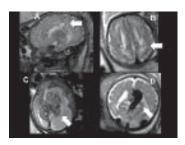


Figure-5 A-D, Fetal MRI of cerebral infection and tumor. A shows toxoplasmosis infection related periventricular calcification and subependymal cysts, while B demonstrates ventriculomegaly with parenchymal damage and calcification. The size of the lateral ventricles is increased. The calcifications are better appreciated on this axial image. Figure C is a fetal MRI image of Choroid plexus papilloma. There is severe hydrocephalus. A large isoechoic mass with lobulated margins and multiple small cystic components is seen in the ventricle. The fetus was delivered after repeated cephalocentensis. Histopathology confirmed choroids plexus papilloma. Figure D depicts Vein of Galen aneurysm seen as a large flow void in midline with no evidence of intraluminal thrombus

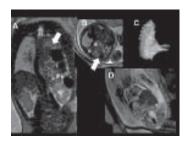


Figure-6 A-D, Fetal MRI of Thorax. A, B, C Congenital diaphragmatic hernia indicated by right hemithorax occupied by bowel loops, some fluid-filled. The right lung is markedly compressed and is seen as

a sliver of hyperintensity in the contralateral thorax. The heart is seen as a signal void and is displaced intralaterally. The left lung is also compressed. 3D reconstruction and volume assessment demonstrates volume of contralateral lung is significantly reduced, probably hypoplastic. The lung on the involved side measured about 2 to 3 cc. Figure 6D shows bilateral pleural effusion with fluid seen along edges of both lungs in a case of hydrops

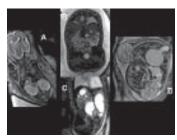


Figure-7 A-D, Fetal MRI of Urogenital System. A is a case of Multicystic kidneys with coronal section showing both kidneys enlarged and markedly hyperintense due to presence of multiple small cysts. There is associated oligohydramnios. Figure 7 B is a fetus with crossed fused ectopia. The coronal section demonstrates fusion of lower pole of one kidney and the superior pole of the other kidney. The fused kidneys are located in the pelvis. Figure-7 C, a case of Unilateral pelviureteric junction obstruction with coronal image depicting a large septated thin walled fluid-intensity lesion in the left retroperitoneum representing a dilated pelvicalyceal system secondary to a pelviureteric obstruction. Figure 7 D is a case of posterior urethral valves in Twin gestation. The sagital section shows urinary bladder and posterior urethra dilated in the twin on the left side of the maternal abdomen. The urinary bladder in the other twin is normal in size.

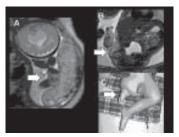


Figure-8 A-C, Fetal MR in musculoskeletal imaging. Figure 8A is a case of club foot. Tracing the limb on contiguous images for assessing alignment shows an inwardly rotated foot. The fetal brain is included in this section and reveals dilatation of the frontal horns. The septum pellucidum is not visualized suggestive of septal agenesis. B, C in a case of Unilateral complete phocomelia shows foot attached to hip. The joint is associated with abnormal soft tissue. The femur, tibia and fibula are absent. C. Photograph after birth confirms MRI findings.

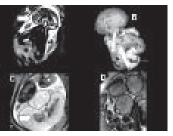


Figure-9 A-D, Fetal MRI in multifetal pregnancy. A, B. Craniothoracoabdominopagus is a rare complex type of conjoining with fusion of the head, neck, thorax and abdomen. Coronal MRI shows fusion of the calvarium, soft tissues of the neck, thorax and abdomen. The brain parenchyma and spines are unfused. Surface rendering 3D reconstruction allow visualization of the fetus as a whole. C. Triplet pregnancy seen on oblique sagital section demonstrating the three heads of a thirty-four week triplet gestation, simultaneously. D. Acardiac twin pregnancy seen as thin-walled fluid-filled sac, posteriorly. A fetal kidney and a part of the upper limb are visualized within the acardiac fetal sac. The normal twin is seen anteriorly.

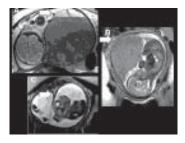


Figure-10 A-C, Fetal MRI and Placental pathologies. Placental hemorrhage showing placenta enlarged with mass effect on fetal head and limbs. An ill-defined hyperintensity detected in the central portion of the placenta represents hemorrhage. A fluid-fluid level is detected in the anterior aspect of the placenta and is probably secondary to the hemorrhage. 10 B, sagital MRI demonstrates Placenta increta covering the internal os. The margins are irregular. Heterogeneity detected within the placenta is likely to represent intraplacental hemorrhage. There is invasion of the uterine myometrium. Figure 10 C is a case of amniotic band seen within the superior portion of the sac, extending from the anterior to posterior walls.

# Antoine-Henri Becquerel (1852 - 1908)



French physicist who discovered radioactivity through his investigations of uranium and other substances. In 1903 he shared the Nobel Prize for Physics with Pierre and Marie Curie.He was a member of a scientific family extending through several generations, the most notable being his grandfather Antoine-Cesar Becquerel (1788-1878), his father, Alexandre-Edmond Becquerel (1820-91), and his son Jean Becquerel (1878-1953). After his early schooling at the Lycee Louis-le-Grand, Henri received his formal scientific education at the Ecole Polytechnique (1872-74) and engineering training at the Ecole des Ponts et Chaussees (Bridges and Highways School; 1874-77). In addition to his teaching and research posts, Becquerel was for many years an engineer in the Department

of Bridges and Highways, being appointed chief engineer in 1894. His first academic situation was in 1876 as assistant teacher at the Ecole Polytechnique, where in 1895 he succeeded to the chair of physics. Concurrently, he was assistant naturalist to his father at the museum, where he also assumed the physics professorship upon his father's death. Electricity, magnetism, optical phenomena, and energy were major areas of physical investigation during the 19th century. For several years the young man's research was concerned with the rotation of plane-polarized light by magnetic fields, a subject opened by Michael Faraday and to which Henri's father had also contributed. Henri then concerned himself with infrared radiation, examining, among other things, the spectra of different phosphorescent crystals under infrared stimulation. Of particular significance, he extended the work of his father by studying the relation between absorption of light and emission of phosphorescence in some uranium compounds. By 1896 Henri was an accomplished and respected physicist—a member of the Academie des Sciences since 1889—but more important than his research thus far were his expertise with phosphorescent materials, his familiarity with uranium compounds, and his general skill in laboratory techniques, including photography. Together, these were to place the discovery of radioactivity within his reach. At the end of 1895, Wilhelm Rontgen discovered X rays. Becquerel learned that the X rays issued from the area of a glass vacuum tube made fluorescent when struck by a beam of cathode rays. He undertook to investigate whether there was some fundamental connection between this invisible radiation and visible light such that all luminescent materials, however stimulated, would also yield X rays. To test this hypothesis, he placed phosphorescent crystals upon a photographic plate that had been wrapped in opaque paper so that only a penetrating radiation could reach the emulsion. He exposed his experimental arrangement to sunlight for several hours, thereby exciting the crystals in the customary manner. Upon development, the photographic plate revealed silhouettes of the mineral samples, and, in subsequent experiments, the image of a coin or metal cutout interposed between the crystal and paper wrapping. Becquerel reported this discovery to the Academie des Sciences at its session on February 24, 1896, noting that certain salts of uranium were particularly active. He thus confirmed his view that something very similar to X rays was emitted by this luminescent substance at the same time it threw off visible radiation. But the following week Becquerel learned that his uranium salts continued to eject penetrating radiation

even when they were not made to phosphoresce by the ultraviolet in sunlight. To account for this novelty he postulated a long-lived form of invisible phosphorescence; when he shortly traced the activity to uranium metal, he interpreted it as a unique case of metallic phosphorescence. During 1896 Becquerel published seven papers on radioactivity, as Marie Curie later named the phenomenon; in 1897, only two papers; and in 1898, none. This was an index of both his and the scientific world's interest in the subject, for the period saw studies of numerous radiations (e.g., cathode rays, X rays, Becquerel rays, "discharge rays," canal rays, radio waves, the visible spectrum, rays from glowworms, fireflies, and other luminescent materials), and Becquerel rays seemed not especially significant. The far more popular X rays could take sharper shadow photographs and faster. It required the extension in 1898 of radioactivity to another known element, thorium (by Gerhard Carl Schmidt and independently by Marie Curie), and the discovery of new radioactive materials, polonium and radium (by Pierre and Marie Curie and their colleague, Gustave Bemont), to awaken the world and Becquerel to the significance of his discovery. Returning to the field he had created, Becquerel made three more important contributions. One was to measure, in 1899 and 1900, the deflection of beta

particles, which are a constituent of the radiation in both electric and magnetic fields. From the charge to mass value thus obtained, he showed that the beta particle was the same as Joseph John Thomson's recently identified electron. Another discovery was the circumstance that the allegedly active substance in uranium, uranium X, lost its radiating ability in time, while the uranium, though inactive when freshly prepared, eventually regained its lost radioactivity. When Ernest Rutherford and Frederick Soddy found similar decay and regeneration in thorium X and thorium, they were led to the transformation theory of radioactivity, which explained the phenomenon as a subatomic chemical change in which one element spontaneously transmutes into another. Becquerel's last major achievement concerned the physiological effect of the radiation. Others may have noticed this before him, but his report in 1901 of the burn caused when he carried an active sample of the Curies' radium in his vest pocket inspired investigation by physicians, leading ultimately to medical use. For his discovery of radioactivity, Becquerel shared the 1903 Nobel Prize for Physics with the Curies; he was also honoured with other medals and memberships in foreign societies. His own Academy of Sciences elected him its president and one of its permanent secretaries.

## Lesion Localization on Plain Chest Radiographs

# Review Article

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Chest radiographs are commonly performed in radiology practice, allover the world. They are routinely analysed for identifying the presence or absence of a lesion. Once a chest lesion is identified, it is further localized to parenchymal or mediastinal or pleural or extrapleural location on plain chest radiographs in most cases. This article is a basic overview of methods used in localizing a lesion on a chest radiograph.

Views-At the outset it is important to understand that for ideally localizing a lesion, few basic chest radiograph views are required. These includes PA view, the Lateral view, Special views like lordotic view and apicogram and penetrated or high kV view.

Broad Localization strategies-During analysis of a lesion on a chest radiograph, it is important to classify whether a given lesion is pulmonary parenchymal or mediastinum or pleural or extra pleural. By using basic roentgen principles, especially by lines, stripes and Silhouette Sign [1], it is possible to differentiate the four, to a large extent. Fundamentally, the radiographic densities discernible on radiographs include air, water, fat, metal and calcium. In chest radiographs, the heart and aorta contains blood which represents water density, while the lung contains air density

Anatomy of Lines and Stripes-Familiarity with appearances of normal parenchymal and mediastinal structures on chest radiography is important in identifying a chest abnormality (Figure 1 A&B). The anterior and posterior junction lines are normal mediastinal structures, when present can be helpful in determining an abnormality [2]. The anterior junction line, courses obliquely from the upper right to lower left behind the retromanubrial region toward the heart [3]. It is formed by a close apposition of lungs and pleura anterior to ascending aorta and right ventricular outflow tract. The posterior junction line, coursing vertically from the lung apices to the top of the aortic arch, is formed by a close apposition of lungs and pleura posterior to esophagus and anterior to spine [4]. Both these lines are smooth and concave. Absence of these landmarks usually indicates no abnormality. However its displacement or bulge may be an indicator of a possible mediastinal abnormality. The right paratracheal stripe is seen as a thin, soft tissue density structure located between the tracheal air column and the right lung. It is vertically undersurface of clavicles to azygos arch. It ranges in width from 4 mm [5]. azygoesophageal recess is an interface formed by the apposition of the right lung and pleura and

the right lateral margin of the azygos vein and esophagus. It should be smooth without focal bulges or extreme deviation from the midline. The left paraspinal interface is formed where the left lung and pleura abut the left lateral margin of the vertebral bodies and paravertebral soft tissues. Silhouette Sign-Propounded by Felson in 1950's, this useful sign states that 'an intra-thoracic radio-opacity, if in anatomic contact with a border of heart or aorta, will obscure that border'. It also implies that 'an intra-thoracic lesion not anatomically contiguous with a border or a normal structure will not obliterate that border' [1]. Therefore, when two structures of similar radiographic densities come in anatomic contact, the interface between these two structures is obliterated. When a mass abuts a normal mediastinal structure of similar radiodensity, the margins of the two structures will be obliterated. Commonly, it indicates air space disease.

This sign is called as the "silhouette sign," even though in reality there is de-silhouetting of the normal structure by the lesion. The loss of margins of normal structure is used to localize a mediastinal mass to the same compartment as that of normal structure. In practice, the obscuration is usually analysed at a normally seen border as in diaphragm or heart. As a rule, a loss

of the contour of the heart or diaphragm is used to localize a parenchymal process. Therefore a lesion involving the medial segment of the right middle lobe obscures the right heart border; Similarly, a lesion involving the a lingual obscures the left heart border; whereas a basilar segmental lower lobe lesion obscures the diaphragm. However, in few instances, pleural and mediastinal disease can also obliterate silhouettes[6].

Few common applications of Silhouette Sign are enumerated in Table 1.

	Table-1, Common applications of Silhouette Sign			
S	ilhouette Location	Adjacent Lobe / Segment		
1.	Right diaphragm	RLL/ Basal segments (Fig 2)		
2.	Right heart margin	RML/ Medial segment (Fig 3)		
3.	Ascending aorta	RUL/ Anterior segment (Fig 4)		
4.	Aortic Knob	LUL/ Posterior segment (Fig 5)		
5.	Left heart margin	Lingula/ Inferior segment (Fig 6)		
6.	Descending aorta	LLL/ Superior & medial segments (Fig 7)		
7.	Left diaphagram	LLL/ Basal segments		

Cervicothoracic sign-This special silhouette sign is used to determine the location of a mediastinal lesion in the upper chest (Fig 8) . The uppermost border of the anterior mediastinum ends at the level of the clavicles. However, the medial and posterior mediastinum extends above the clavicles. It is based on the tenet that if a thoracic lesion is in anatomic contact with the soft tissues of the neck, its contiguous border will be lost. As a result, a lesion clearly visible above the clavicles on the frontal view, must lie posteriorly and be entirely with in the thorax. Conversely, when the cephalic border of a shadow disappears as it approaches the clavicles, it is cervicothoracic i.e. partly in the anterior portion of the mediastinum and partly in the

Hilum overlay sign-The hilar overlay sign is useful in distinguishing an anterior mediastinal mass from a prominent cardiac silhouette (Fig 9). It is based on the normal apposition of the main pulmonary arteries to the lateral edges of cardiopericardial silhouette. If the bifurcation of the main pulmonary artery is >1 cm medial to the lateral border of the cardiac silhouette, it is strongly suggestive of a mediastinal mass. If the pulmonary artery arises from the lateral heart border, this favors an enlarged heart. Pulmonary arteries arise from the heart, and therefore when the heart enlarges, the pulmonary arteries must move laterally with the heart border. An anterior mediastinal mass that appears as an enlarged cardiac silhouette will not cause displacement of the pulmonary arteries.

Hilum convergence sign-The hilar convergence sign distinguishes a prominent hilum from an enlarged pulmonary artery (Fig 9). If the pulmonary arteries converge into the lateral bor-

der of a hilar mass, the mass represents an enlarged pulmonary artery. If the convergence appears behind the abnormality or arises from the heart, a mediastinal mass is more likely. Pulmonary artery branches arise from the main pulmonary artery trunk, and therefore an enlarged pulmonary artery will have branches that arise from its outer margin (the vessels converge toward the main pulmonary artery). A hilar mass will show the vessels not arising from the margin; they pass through the margins to converge on artery.

Thoracoabdominal sign-A silhouette sign on its lowermost margin indicates that the mass ends at the diaphragm or extends below it (Fig 10). Convergence of the lower lateral margin towards the spine indicates that the lesion is probably entirely intrathoracic. Conversely lack of convergence or actual divergence of the lower border indicates an iceberg con-

figuration, with a segment hidden below in the water density of the abdomen. The thoracoabdominal sign seen in aneurysm, neoplasm and azygous continuation of the inferior vena cava. The abdominal structures are mainly of water density, a sharply marginated mediastinal mass seen through the diaphragm on either a chest or an abdominal film must lie in the thorax

Thymic sail sign-It is used to differentiate right upper lobe consolidation from Thymic shadow (Fig 11) [7].

Other Miscellaneous Imaging Parameters-It includes margins, presence or absence of air bronchogram, uni/bilaterality, multiplicity, calcification/fat, and bone involvement. In practice, presence of an air bronchogram confirms pulmonary lesion. The margins of the lesion can additionally help. A pleural/extra pleural lesion will have sharp outline. It subtends an obtuse angle with the chest wall, which is referred to as 'the pregnant lady' sign (Fig 12 A,B). A pulmonary parenchymal lesion will have an unsharp outline, and often subtends an acute angle with the thoracic wall (Fig 13).

## **Avoidable Errors**

Few areas which can give rise to errors in interpretation include

- Wrong patient or wrong date
- Small apical pneumothorax may be overlooked
- Callus around old rib fracture can be misdiagnosed as pulmonary or pleural mass or rib tumour

- Medial part of scapula may overlie lung field and be mistaken for a pneumothorax or pleural mass
- Skin lesions (for example a lipoma or sebaceous cyst) may be mistaken for an intrathoracic lesion
- Prominent pulmonary arteries in emphysematous patients (due to pulmonary hypertension) may be mistaken for Hilar tumour or nodes
- Extraneous objects such as buttons or contents of pockets may be mistaken for intrathoracic lesions
- Scoliosis or kyphosis, commonly cause rotation and distortion of other chest structures
- Costotransverse articulations (especially of upper ribs) may be mistaken or a fracture of the posterior rib
- Lytic or sclerotic lesions of ribs are commonly overlooked
- Large peripheral bullae may be mistaken for a pneumothorax
- Scarring form old pleurisy or from thoracic surgery may cause blunting of the costophrenic angles and may be mistaken for an effusion
- Mastectomy appearances can make a lung field apparaently hypertranslucent.

Conclusion-Chest radiographs are routinely used for identifying the presence or absence of a lesion. A systematic approach may further localize the lesion as parenchymal or mediastinal or pleural or extrapleural location on plain chest radiographs in most cases. To this end a knowledge of stripes and lines, an insight into mediastinal and lung anatomy and correct application of silhouette sign may be immensely useful in practice. This article is a basic overview of methods used in localizing a lesion on a chest radiograph.

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Figure-1 A & B, Normal lung parenchymal and mediastinal structures on Chest PA and Lateral Radiographs



Figure-2, Silhouette of right hemidiaphragm obscured by lesion at Basal segment of right lower lobe

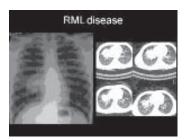


Figure-3, Silhouette of right heart margin obscured by lesion at medial segment of right middle lobe



Figure-4, Silhouette of Ascending aorta obscured by lesion at anterior segment of right upper lobe

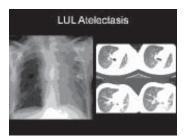


Figure-5, Silhouette of Aortic Knob obscured by lesion at posterior segment of left upper lobe



Figure-6, Silhouette of left heart margin obscured by lesion at segments of lingula

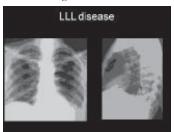


Figure-7, Silhouette of descending aorta obscured by lesion at superior and medial segments of left lower lobe



Figure-8, Cervicothoracic sign for determining the location of a mediastinal lesion in the upper chest



Figure-9, The hilar overlay sign (left) is useful in distinguishing an anterior mediastinal mass from a prominent cardiac silhouette, while hilar convergence sign (right) distinguishes a prominent hilum from an enlarged pulmonary artery

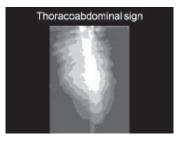


Figure-10, Thoracoabdominal sign with a silhouette sign on its lower-most margin indicates that the mass ends at the diaphragm or extends below it

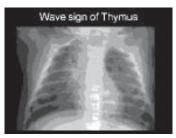


Figure-11, Thymic sail sign is used to differentiate right upper lobe consolidation from Thymic shadow



Figure -12 A,B, A pleural/extra pleural lesion has sharp outline, subtending an obtuse angle with the chest wall.



Figure-13, A pulmonary parenchymal lesion has an unsharp outline, often subtending an acute angle with the thoracic wall

## Key Advances and Special Awards in Radiology

1896 - Henri Becquerel discovers radioactivity and nuclear medicine is born.

1901 – W.C. Roentgen receives the Nobel in Physics for the discovery of x-rays.

1905 - The first English book on Chest Radiography is published.

1910 - Köhler publishes the first edition of his classic book on normal variants, providing the needed anatomical knowledge required and the identification of normal variants so physicians could distinguish calcified lymph glands, gallstones, kidney and bladder stones and other shadows on an abdominal radiograph.

1913 –Coolidge hot cathode tube is introduced, simplifying the work of technicians and allowing more uniform results.

1914 – M. von Laue receives the Nobel in Physics for x-ray diffraction from crystals.

1915 – W.H. Bragg and W. L. Bragg receives the Nobel in Physics for crystal structure derived from x-ray diffraction.

1917 – C.G. Barkla receives the Nobel in Physics for characteristic radiation of elements.

1918 – Eastman introduces film. Until then, radiographs were made onto glass photographic plates.

1920 - Society of Radiographers forms. 1924 - K.M.G. Siegbahn receives the Nobel in Physics for x-ray spectroscopy.

1927 – A. H. Compton receives the Nobel in Physics for scattering of x-rays by electrons.

1930s – From this point, doctors are appointed with specific interests in diagnosis or therapy.

1931 - Ernerst 0. Lawrence developes the cyclotron and paves the way for major experiments later conducted at the Radium Institute in Paris.

1936 – P. Debye receives the Nobel in Chemistry for diffraction of x-rays and electrons in gases.

1937 -The first clinical use of "artificial radioactivity" is carried out for the treatment of a patient with leukemia at the University of California at Berkeley.

1946 -A landmark nuclear medicine advance. A thyroid cancer patient's treatment with radioactive iodine causes the complete disappearance of the spread of the patient's cancer. This is considered by some as the true beginning of nuclear medicine. Wide-spread clinical use of nuclear medicine does not start until the early 1950s.

1950s - Development of the image intensifier and X-ray television.

1955 - First use of a radioactive tracer in the lungs with the introduction of inhaled xenon-133 and external counting.

1956 - The medical use of Ultrasound starts in Glasgow. Professor Ian Donald M.D. and his colleagues, working at the University of Glasgow's Department of Midwifery are the first to apply ultrasound as a diagnostic modality in the fields of obstetrics and gynaecology.

1962 - M. Perutz and J. Kendrew receive the Nobel in Chemistry for the structure of hemoglobin. J. Watson, M. Wilkins, and F. Crick receive the Nobel in Medicine for the structure of DNA.

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# Review Article

olorectal cancer is one of the most common causes of cancer deaths. Colorectal cancer is one of the most successfully treated cancer, if detected at an early stage. It is well known that there is a low patient acceptance for conventional colonoscopy as most patients are apprehensive about related risks. Against this background, let us examine the role of CT and CT Colonscopy. Computed tomography (CT) is a technique of acquiring the cross sectional data of an object by utilizing the x-rays followed by reconstruction of an image based on the differences in attenuation of x-rays. Single slice CT (SSCT) refers to a helical CT with a single row of detectors capable of acquiring one slice per rotation of the tube. On the other hand, multislice CT (MSCT) is a helical CT with multiple rows of detectors in the z-axis with capability of acquiring two or more slices per rotation. First MSCT with 4-slices per rotation was launched in 1998 with a tube rotation time of 0.5 sec. Since the year 2000, MSCT with 8, 16, 32, 64 slices per rotation has been launched with a tube rotation time of as low as 0.33 sec.

Indications of MSCT in colonic disease-The common indications for evaluation of colonic disease by MSCT are-Diverticular disease of colon, Inflammatory bowel disease,

Screening for polyps and Colorectal cancer.

Diverticular disease of colon-It primarily involves the sigmoid colon. The middle aged and elderly individuals are most susceptible. MSCT is the modality of choice, which reveals in uncomplicated cases the following key findings: presence of diverticula which is seen as an outpouching from the serosal surface of the bowel wall; diverticulum may be filled with air, fluid or admixture of both (Figure 1A) and Mural thickening is associated with diverticulitis. In mildly complicated cases findings include pericolonic inflammation seen as soft tissue attenuation fat stranding in the mesocolic or omental fat surrounding the inflamed, thick walled diverticula. In extreme cases there are inflammatory changes in the mesocolon with dilated vasculature and colonic perforation at the site of inflamed diverticula (Figure 1B). The signs of colonic perforation include focal wall thickening, extraluminal gas and fluid adjacent to bowel wall and free intraperitoneal air.

Ulcerative colitis-In Ulcerative colitis the rectum is invariably involved. There is contiguous involvement of colon and sometimes distal ileum. Mural thickening is typically in the range of 6-10 mm. There is characteristic thickening of submucosa with relatively thin and enhancing

mucosa & serosa. The sign of pericolonic inflammation may be seen in the mesenteric fat. The rectum shows a characteristic target appearance (Figure 2A) and the entire colon may be involved in severe cases

Crohn's disease-The hallmark of Crohns disease is non-contiguous involvement of the colon with skip (uninvolved, normal) areas is characteristic and differentiates it from the ulcerative colitis. Mural thickening is typically greater than 10 mm in most of the cases at the time of diagnosis (Figure 3A). Inflammation of the pericolonic fat with fibrofatty proliferation in mesentery may occur (Figure 3B). Pericolonic abscess formation is common. Fistulas and sinuses may be seen as soft tissue tracts (Figure 3C)

Colorectal carcinoma-Role of MSCT in Colorectal Carcinoma comprises of staging in a proven case of carcinoma; preoperative diagnosis in a symptomatic patient and screening to detect precancerous and early stages. The important findings include asymmetric mural thickening is typical, but sometimes symmetric thickening may be seen (Figure 2B), focal mural thickening more than or equal to 6 mm (Figure 4A), polypoidal or sessile intraluminal mass, abrupt transition between normal and abnormal zone is seen and moderate to intense, heterogeneous postcontrast en-

hancement is seen. Extension into adjacent fat is seen as soft tissue infiltration, which may also be seen due to reactive inflammation (Figure 4B). There may be regional / distant lymphadenopathy, invasion of the adjacent structures is seen as loss of fat plane between the apposing surfaces with irregular interface, hepatic metastases or signs of perforation / obstruction may be seen. A criterion for CT staging of primary colorectal tumors is as follows: Stage I – Intraluminal mass without thickening of wall; Stage II - Thickened wall (> 0.6 cm) or pelvic mass, no invasion or extension to sidewalls; Stage III a – Thickened wall or pelvic mass with invasion of adjacent structures but not to pelvic sidewalls or abdominal wall; Stage III b - Thickened wall or pelvic mass with extension to pelvic sidewalls and / or abdominal wall without distant metastases and Stage IV - Distant metastases with or without local abnormality. The above-mentioned criterion of CT staging correlates very well with the following surgico-pathologic staging system which represents the Astler-Coller version of the Dukes classification, as modified by Turnbull : Stage A – Limited to mucosa; Stage B1 - Extension into, but not through, the muscularis propria; Stage B2 - Extension through muscularis, no nodes; Stage C1 - Limited to bowel wall, positive nodes; Stage C2 - Extension through bowel wall, positive nodes and Stage D - Distant metastases.

CT colonoscopy-It refers to the technique that allows the intralu-

minal evaluation of the colon by means of MSCT, similar to that achieved by the use of the actual endoscope; hence it is also termed as 'virtual CT colonoscopy'. The clinical indications of CT Colonoscopy comprises

- Symptoms of colorectal cancer
- Obstructing carcinoma
- Poor clinical status (severe cardiopulmonary disease, elderly frail patient)
- Follow up after polpectomy
- Screening for colorectal cancer (after the age of 50 years at every 7-10 years and in high risk patients every 5 years)
- Incomplete or failed conventional colonoscopy

Technique for CT colonoscopy - It involves the following steps: Bowel Preparation, Bowel Distension, Scanning protocol and Image Display & Interpretation.

Preparation for CT colonoscopy - The aim of bowel preparation is to achieve a thoroughly clean colon as far as free from fecal & fluid matter as possible.

First method: A low residue diet for 48-72 hours prior to evaluation is recommended. Thorough bowel catharsis using magnesium citrate / phosphosoda / polyethylene glycol preparations. The latter are prone to leave some fecal and fluid residue in the lumen but are useful in renal and cardiac patients as they are relatively free from electrolytes disturbances. Rectal suppository can be used to cleanse the residual fecal matter. Midnight fasting before the day of examination is

- needed. The disadvantages are inconvenience & discomfort to patient and relative noncompliance in elderly
- Second method: Low residue diet for 48-72 hours prior to evaluation with mild bowel catharsis, dietary fecal tagging and midnight fasting before the day of examination are the salient features. The advantages include improved patient tolerance & compliance and Improved diagnostic accuracy

Need for fecal tagging-Fecal residue often mimics tumor especially small polyps and results in false positive and negative diagnosis. Fecal tagging is achieved by oral administration of the dilute positive contrast agent that is impregnated in to the residual stool (stool tagging) and also mixes with the intraluminal fluid (fluid tagging). The different protocols used to achieve this are: a) 250 ml of 1-2% barium sulfate is given three times a day for 48 hrs before exam; b) Single dose of 200 - 250 ml of 1-2 % iodinated contrast media is given 30-45 min before the scanning or c) Combination of both

Bowel distension for CT colonoscopy-The role of intravenous Buscopan prior to CT colonoscopy is debatable. But many authors have experiences that suggest better distension of the colon. Colonic distension can be achieved by rectal insufflations of air or carbon dioxide through a rectal tube or Foley's catheter in the left lateral decubitus position using patient comfort as a guide. Air is preferred because it

is easily available, inexpensive and does not require high-tech apparatus. 30-40 puffs are considered adequate but right iliac fossa palpation to judge optimal cecal distension is a better guiding tool. Air insufflation is associated with post-procedural abdominal discomfort. On the other hand, though carbon dioxide is more comfortable for the patient as it is rapidly absorbed in to the bloodstream and hence stays for less time after the procedure but it has to be continuously insufflated during the procedure and is expensive. Normally, 1.5-2.0 L of CO<sub>2</sub> is insufflated in to the rectum at a controlled rate and pressure followed by slow rate of insufflation during the procedure. Scanning protocol for CT colonoscopy-Four slice to 64slice MSCT can be used for evaluation. Scout film / AP topogram in the supine position is the first step as it helps in determining the optimal distension

of the entire colon. Noncontrast scanning is done in prone position followed by postcontrast scanning in supine position. Some amount of additional insufflation is required before scanning in done in supine position. Although use of IV contrast injection increases the time and cost of the examination but it makes the polyps more identifiable and also allows evaluation of extracolonic component of the disease and hepatic metastases. Scanning is done from pubes to the domes of the diaphragm. Supine scanning is done at 1-1.25 mm detector collimation and routine mAs & kV (160-200 mAs and 140 kV) while prone scanning is done at similar collimation but low mAs (10-30 mAs) and minimum FOV for optimal image quality and minimal radiation doses. Reconstruction interval of 1 – 3 mm is optimal

val of 1-3 mm is optimal display Image in CTcolonoscopy-2D axial images in both supine and prone positions are mainstay for evaluation with colon tracking from rectum to cecum or vice versa. Both lung window and soft tissue settings are used for evaluation (Figure 5A,B). 2D multiplanar reconstruction images are used as problem solving images. Other types of image display used as problem solving tools in CT Colonoscopy are

- Tissue transition projection (Figure 6A)
- Panoramic display (also known as virtual dissection) allows for complete evaluation of undersurface of the haustral folds (Figure 5 C)
- Surface rendering (Figure 6B)
- Volume rendering
- Perspective rendering (Figure 5D)
- Fly-through / navigation —
   Although these images appear like true endoscopic images, but they have multiple limitations including the blind spots at the site of turns and flexures in colon (Figure 6D). Hence, optimal visualization of colon by this method only, requires at least four passes in supine and prone position and antegrade and retrograde direction, which it time intensive.

Image interpretation in CT colonoscopy-Normal colonic mucosa has a smooth surface

without discontinuous elevation. Haustral folds have concave edges as they run from one wall to another. Polyps and tumors are seen as focal round or lobulated elevations on 2D axial images or protuberances on the mucosal surface on endoscopic views.

Differentiating polyp from stool-The following features aid in differentiating polyps form stool.

- Shape Polyps are well defined while fecal matter is polymorphic
- Density Polyps are of soft tissue attenuation while fecal matter is low in attenuation with presence of air pockets
- Homogeneity Polyps are usually homogeneous but fecal matter is a heterogeneous admixture of stool and air
- Enhancement Polyps show mild to moderate postcontrast enhancement
- Feeding vessel Feeding arteries can sometimes be recognized supplying the polyp especially in the pedunculated ones at the site of attachment to the bowel wall. Clear cut attachment to the bowel wall is lacking in the fecal matter.
- Mobility Polyps have no or limited mobility while fecal matter is freely mobile

Advantages of CT colonoscopy - The technique has higher acceptability rates (day procedure, minimal complications and post-procedural effects), high accuracy, higher safety and comfort due to noninvasive nature and no need for sedation and a higher rates of complete examination  $\simeq 95\%$  against 65–90% in

conventional. It can be done even in the elderly / frail patients and those on anticoagulant therapy. In 5-10% cases; it detects other unsuspected extracolonic lesions Accuracy of CT colonoscopy-The comparable results of CT colonoscopy in high risk population in several series are given in undermentioned Table.

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Size of polyp	Sensitivity	Specificity
> 10 mm	70 – 100 %	90 – 96 %
6 – 9 mm	47 – 82 %	63 – 96 %
< 6 mm	26 – 59 %	80 – 92 %

Limitations of CT colonoscopy-It includes a higher cost, a lower sensitivity and specificity for < 6 mm and sessile polyps an is non-therapeutic nature. The procedure can not be performed in patients with hip prosthesis, active inflammatory disease, history of previous perforation, diverticulitis and severe abdominal pain or severely obese patients who do not fit in the CT gantry. In cases of occlusive growth, inadequate preparation is encountered and air insufflation may lead to perforation. The radiation exposure in this technique performed with routine dose is 7.5 - 11.4 mGy, while using low dose it is 3.9 - 5.7 mGy.

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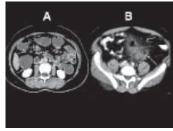


Figure-1A,B: Transaxial CECT image at left panel (A) shows diverticula filled with fluid and air (arrows); At right panel (B) diverticulitis with pericolonic inflammation (arrows) is shown.

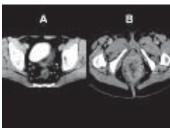


Figure -2 A,B, Transaxial CECT image in left panel (A) shows a characteristic target appearance of rectum in a case of ulcerative colitis; Right panel (B) displays an asymmetric and heterogeneously enhancing mural thickening of the rectum with aeroceles in wall reaching up to the serosa (arrows) s/o impending perforation in a case of rectal carcinoma

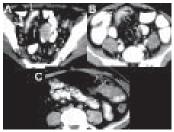


Figure-3 A,B and C, Spectrum of Transaxial CECT findings in Crohn's disease. A shows mural thickening of the sigmoid colon with pericolic adenopathy; B shows mural thickening of the sigmoid colon with fibrofatty proliferation in the sigmoid mesocolon (arrows); C shows a sinus tract extending from the small bowel to the anterior abdominal wall

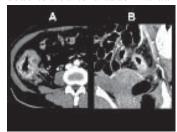


Figure-4 A,B, Transaxial CECT findings in carcinoma colon. A shows asymmetric mural thickening with heterogeneous enhancement in the ascending colon with pericolic adenopathy; B delineates extension of tumor in to the pericolic fat

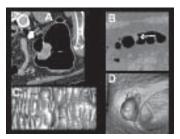


Figure-5 A-D, CT delineation of polyps. Transaxial NECT image in soft tissue window settings (A) shows a sessile polyp in the left colon (arrow); Image in lung window settings (B) shows a small sessile polyp; Panoramic display image (C)showing two sessile polyps; Perspective image (D) showing a large polyp on the endoluminal image

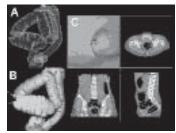


Figure-6, A-C, Tissue transition projection (A) similar to double contrast enema in a case of carcinoma of ascending colon (arrows); Surface shaded projection (B) in a case of carcinoma of ascending colon (arrows); Fly through / navigation view (C) shows image in 3 planes along with the endoluminal image

Max Theodor Felix Von Laue (1879 - 1960)



German recipient of the

Nobel Prize for Physics in 1914 for his discovery of the diffraction of X rays in crystals. This enabled scientists to study the structure of crystals and hence marked the origin of solid-state physics, an important field in the development of modern electronics.

Laue became professor of physics at the University of Zurich in 1912. Laue was the first to suggest the use of a crystal to act as a grating for the diffraction of X rays, showing that if a beam of X rays passed through a crystal, diffraction would take place and a pattern would be formed on a photographic plate placed at a right angle to the direction of the rays. The pattern would mark out the symmetrical arrangements of the atoms in the crystal. (See Laue diffraction pattern.) This was verified experimentally in 1912 by two of Laue's students working under his direction. This success demonstrated that X rays are electromagnetic radiations similar to light and also provided experimental proof that the atomic structure of crystals is a regularly repeating arrangement.

Laue championed Albert Einstein's theory of relativity, did research on the quantum theory, the Compton effect (change of wavelength in light under certain conditions), and the disintegration of atoms. He became director of the Institute for Theoretical Physics at the University of Berlin in 1919 and director of the Max Planck Institute for Research in Physical Chemistry, Berlin, in 1951.

## Imaging in Head Trauma - a Review

# Review Article

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n today's world, trauma constitutes one of the most important causes of morbidity and mortality in human beings. Patient presentation after head injury is influenced by many factors, which is an interplay between head, force, and protection given to the head. More importantly, factors like direction and nature of force producing the injury, position of head at time of injury, density of ossification of calvarium and the protection afforded to the head at the time of injury are highly significant. Holbourn's early pioneering work concerning the mechanisms of head injury has served as a fundamental basis for understanding cerebral injury 1,2. Using a gelatin model of the brain, he concluded that injury to the brain occurred through two major mechanisms: direct injuries due to skull distortion (contact phenomenon) and(b) indirect injuries that arise irrespective of skull deformation. Direct injuries due to skull distortion are produced by localized fracture or inbending of the skull with neural damage, typically superficial and localized to immediate vicinity. Examples of lesions caused by this mechanism are cortical lacerations due to depressed fracture fragments and epidural hematomas secondary to lacerations of meningeal arteries. Lesions occurring irrespective of skull deformation may produce extensive neural

damage, through two types of structural deformations. Compression-rarefaction strain is characterized by a change in cell volume without a change in shape and is of minimal importance in the production of cerebral injury. Shear-strain deformation is characterized by a change in shape without a change in volume and is responsible for the vast majority of mechanically induced lesions. Shear-strain forces are greatest at the junction of tissues of different density and rigidity (CSF/ brain, gray/white matter, brain/ pia-arachnoid, pia-arachnoid/ dura, skull/dura). Rotationally induced shear-strain injury typically produces lesions at one of four levels: cortical surface of brain (contusions), cerebral white matter (diffuse axonal injury), brainstem, and penetrating blood vessels (arteries or veins).

Gamut of lesions- Most authors are in agreement that two basic types of traumatic lesions exist (Table-1)<sup>3,4</sup>. Primary lesions are those that arise as a direct result of the initial traumatic force. Secondary lesions are those that develop subsequent to initial impact. The latter either arise from sequelae of primary lesions or from the neurologic effects of systemic injuries.

Table 1. Classification of traumatic intracranial lesions Adapted from Reference <sup>3</sup> Primary lesions Primary neuronal injuries

- Diffuse axonal injury
- Cortical contusion
- Subcortical gray matter injury
- Primary brainstem injury

## Primary hemorrhages

- Epidural hematoma-Arterial origin, Venous origin
- Subdural hematoma
- Intracerebral hematoma
- Intraventricular hemorrhage
- Subarachnoid hemorrhage
   Primary vascular injuries
- Carotid-cavernous fistula
- Arterial pseudoaneurysm
- Arterial dissection/laceration/occlusion
- · Carotid sheath hematoma
- Dural sinus laceration/occlusion

Traumatic pia-arachnoid injuries

- Post-traumatic arachnoid cyst
- Subdural hygromas

## Secondary lesions

- Territorial arterial infarction
- Boundary and terminal zone infarction
- Diffuse hypoxic injury
- Diffuse brain swelling/edema
- Pressure necrosis (due to brain herniation)
- Secondary brainstem injury
- Secondary hemorrhage
- Other (fatty embolism, infection)

The distinction between primary and secondary lesions is not merely an academic one but one that has great therapeutic ramifications. Secondary lesions, by definition, are potentially preventable, provided that causative factors are quickly recognized

and appropriate treatment promptly instituted. CT and MRI distinction between primary and secondary lesions can generally be made on the basis of lesion size, shape, location, and distribution, and in conjunction with the timing of when the lesions first appeared. Virtually all primary traumatic intraaxial lesions arise as a result of shear-strain deformation of either neurons or blood vessels produced by rotational acceleration of the head. Primary intraaxial lesions clearly fit into four anatomically welldefined categories: (a) diffuse axonal injury, (b) cortical contusion, (c) subcortical gray matter injury, and (d) brainstem injury. This method of classification is applicable to both radiologic imaging and pathologic analysis and avoids imprecise nomenclature<sup>3</sup> Clinicoimaging Features in **Common Entities** 

Diffuse axonal injury - Diffuse axonal injury (DAI) is a type of primary injury found in patients with severe head trauma. DAI is characterized by multiple, small, focal traumatic lesions scattered throughout the white matter. Most lesions spare the overlying cortex, frequently being located at the gray-white matter interface. Occasionally, the cortex may be secondarily involved by larger lesions. DAI lesions are usually (80%) nonhemorrhagic in nature. Lesions range in size from 5 to 15 mm, with peripheral lesions tending to be smaller than more central ones. Lesions are usually ovoid to elliptical in shape (Figure-1), with the long axis parallel to the direction of the axonal tracts that are involved. Classically, patients with DAI present

with severe loss of consciousness starting at the moment of impact. Patients with DAI usually have significantly greater impairment of consciousness than do patients with many other primary lesions, such as cortical contusions, intracerebral hematomas, and extraaxial hematomas. DAI tends to occur in three fundamental anatomical areas: lobar white matter, corpus callosum, and the dorsolateral aspect of the upper brainstem<sup>3</sup>

Cortical contusion -Cortical contusions are the second frequently encountered group of primary intraaxial lesions. Cortical contusions, by definition, primarily involves the superficial gray matter of the brain. The underlying white matter is usually spared unless the contusion is extremely large. Due to gray matter being more vascular than white matter, contusions are much more likely to be hemorrhagic than are DAI lesions.

Subcortical gray matter injury -This is an uncommon diffuse type of injury characterized by multiple petechial hemorrhages primarily localized to the upper brainstem, basal ganglia, thalamus, and regions around the third ventricle. These lesions are most commonly seen in severely injured patients who die shortly after trauma.

Brainstem injury - Brainstem injury are separated into primary and secondary forms, depending on when the injury occurs [Table 2]. Primary lesions are those that result from the initial traumatic force, while secondary ones are those that develop subsequent to initial trauma. CT is not sensitive to allow detection and character-

ization of most types of Brainstem injury, unlike MRI which effectively evaluates and characterizes Brainstem injury in nonfatally injured patients. Secondary Brainstem injury arises from two general mechanisms: systemic factors (anoxia, hypotension, ischemia), and severe mechanical compression or displacement of the upper brainstem<sup>4</sup>. Intrinsic secondary lesions within the brainstem includes Duret hemorrhages. These consist of centrally placed, generally midline, collections of blood in the tegmentum of the rostral pons and midbrain (Figure-2)5. These hemorrhages may vary from numerous petechia to massive central tegmental hemorrhages involving the entire upper brainstem. They are usually located in the ventral and paramedian aspects of the midbrain and upper pons, with relative sparing of the dorsolateral aspects of the brainstem. Duret hemorrhages are not limited to head injury patients but also occur following transtentorial herniation from other causes.

Table -2,Classification of traumatic brainstem injury Adapted from Reference <sup>4</sup>

Primary brainstem injury

- Direct superficial laceration or contusion
- Diffuse axonal injury
- Multiple primary petechial hemorrhages
- Pontomedullary rent or separation

Secondary brainstem injury

- Secondary (Duret) hemorrhages
- Focal brainstem infarcts from vascular compromise

- Compression, displacement, and deformity
- Pressure necrosis from transtentorial herniation
- Diffuse hypoxic/anoxic/ischemic injury

Combined primary and secondary brainstem injury Epidural hematoma - Epidural hematomas are most commonly of arterial origin. They usually arise from direct laceration or tearing of meningeal arteries (typically the middle meningeal artery) by skull fractures. Occasionally they may occur from stretching and tearing of meningeal arteries in the absence of fractures, as in children and is usually due to transient deformation and depression of the calvarial vault. The dura is displaced away from the inner table of the skull and is seen as a thin line of low signal intensity between brain and lenticular-shaped hematoma (Figure -3)<sup>3</sup>. Venous epidural hematomas are much less common than those of arterial origin and are usually due to laceration of a dural sinus by occipital, parietal, or sphenoid bone fractures. The most common locations of venous epidurals are - the posterior fossa from laceration of the transverse or sigmoid sinus; - the middle fossa from injury to the sphenoparietal sinus; and - the parasagittal area from a tear of the superior sagittal sinus.

Subdural hematoma - Subdural hematomas (SDH) are typically caused by stretching and tearing of bridging veins that traverse the subdural space as they leave the cortical surface of the brain to drain into the dural sinuses [Figure 3]. Displacement

of cortical veins away from the skull, crescentic shape, and extensive spread of the lesion over the whole hemisphere indicates a subdural hematoma. SDH are usually found along supratentorial convexity posterior fossa, along falx and adjacent to tentorium. Interhemispheric and tentorial leaf subdural hematomas are commonly found in children who are victims of nonaccidental injury3. Those subdurals that are missed with CT, but identified on MRI are almost always only 1-2 mm in thickness and of no clinical significance. Chronic Subdural Hematomas arise from slow effusion of venous blood into the subdural space and, in contrast to acute subdural hematomas, usually are not accompanied by focal cerebral parenchymal injury. Thick membrane develops on the more vascular dural side of the clot and a thinner membrane on the arachnoid side.

Intracerebral hematoma -These are focal collections of blood that most commonly arise from rotationally induced shearstrain injury to intraparenchymal arteries or veins. They may occasionally result from penetrating injury to a vessel. Intracerebral hematomas (ICH) may vary in size. Differentiation from hemorrhagic contusions or DAI is often difficult. The distinction rests primarily with the fact that ICH primarily expand between relatively normal neurons Figure-4, while the hemorrhage within contusions is interspersed in areas of simultaneously injured and edematous brain. Intracerebral hematomas are usually located in the frontotemporal white matter or basal ganglia.

Intraventricular hemorrhage-Intraventricular hemorrhage is a common entity [Figure 4], and is caused by a variety of traumatic lesions like DAI, intracerebral hematoma or large contusions. The etiology of IVH in most cases, is due to rotationally induced tearing of subependymal veins on the ventral surface of the corpus callosum and along fornix septum the and pellucidum.

Subarachnoid hemorrhage-Subarachnoid blood loses its density over the ensuing days, with the breakdown of the globin molecule. As a complication of subarachnoid hemorrhage, fibroblastic proliferation in the subarachnoid space and arachnoid villi may lead to the production of a communicating hydrocephalus. Subarachnoid hemorrhage is considerably difficult to detect with MRI than with CT. While CT detects it easily as hyperdense blood distributed in subarachnoid spaces ,Figure- 5, it should be clearly understood that MRI is not sensitive to the presence of acute subarachnoid hemorrhage. Skull Fractures - A fracture of the calvarium represents objective evidence of bony injury from trauma. If it is associated with brain damage is considered significant. The types of fracture includes linear, stellate and depressed fractures. Linear fractures appear more lucent than vascular grooves or closed cranial sutures. They are wider in their midportion and narrower at either end. They are usually less than 3 mm in overall width. In the young child with a thin calvarium, and in thin portions of the calvarium in the adult, such as the

temporal squama, linear fractures are more difficult to visualize. Continued enlargement of a fracture line indicates formation of a leptomeningeal cyst or brain hernia<sup>6</sup>. Depressed Fracture occurs due to failure of bone to rebound or locking after fracture edge has been pushed under the adjacent calvarial margin results in a depressed fracture (Figure-6). Depressed fractures are often comminuted and most common in the parietal and frontal regions. Depressed fractures are considered significant when the they overly a major dural venous sinus or motor cortex or associated with dural tears, penetration of the cerebral parenchyma by a foreign object, or the presence of underlying parenchymal injury. Basilar Skull Fracture is suspected when otorrhea or rhinorrhea occurs after trauma. Sutural Diastasis is the traumatic separation of the sutures and may be recognized when the width of the sutures is greater than 3 mm (Figure- 7).

Cerebrospinal Fluid Leaks and Pneumocephalus -This occurs in a compound depressed fracture of the calvarium or skull base, with an external communication that causes CSF to leak out or air to enter the intracranial space. Pneumocephalus can occur with or without evidence of CSF leakage. Resolution of the CSF leak occurs within 1 week of injury in 70% of patients and within 6 weeks of injury in over 99%3. With pneumocephalus, air can lie within the epidural, subdural, subarachnoid, intraparenchymal space. Air within the epidural space is

bound down by the attachments of the dura at the sutures. Air within the subdural space usually gravitates to the most superior portion of the subdural space overlying the frontal lobes. With subdural air, the sulci are not be filled. Subarachnoid air shows filling of the cerebral sulci, cisterns, and fissures. Subarachnoid pneumocephalus can also change with alteration in patient position. Intraventricular air usually gravitates to the most superior portion of the ventricular system with which it is in contact, most often the frontal horn of the lateral ventricles. Intraparenchymal air dissects within the brain parenchyma, usually gaining entrance at the site of contusion<sup>7</sup>.

Special Considerations in Imaging of Head Trauma

Neurotrauma Triage and Imaging Study Selection -Neurotrauma patients are usually categorized into three clinical groups, depending on the degree of impairment of the admission GCS score: 1. mild (GCS = 13-15), 2. moderate (GCS = 8-12), and 3. severe (GCS <8). Mild acute head injury patients generally present after head trauma with headaches, slight transient disorientation, or confusion. By definition, these patients have little or no persistent impairment of consciousness11. CT is the most efficacious method for evaluating the lesions most commonly found in this group of patients. The moderate and severe head injury categories share many clinical features and management concerns. Neurologically unstable patients in these two categories should be initially studied with CT. Moderate and severe head injury patients who are initially stable can be primarily evaluated by MR. All moderate to severe head injury patients should be evaluated with MR at some point in time during the first 2 weeks after injury.

Relative and Comparative Roles of Imaging Studies- CT provides a rapid method for detecting most treatable forms of head injury. CT scanners have advantages of fast examination time, wide availability, lack of contraindications, and high accuracy for detecting hemorrhage. This has made CT the diagnostic study of choice for initial evaluation of head injury patients. However, it must be remembered that CT has never been particularly useful for classification and staging of injury. Its low sensitivity for nonhemorrhagic lesions and the difficulty of obtaining multiplanar images has severely limited its usefulness 9. MRI has a supplementary role limited by issues of greater cost, lesser availability, slightly longer examination time, greater difficulty of patient monitoring and lower accuracy for detecting fractures. Nevertheless, MRI offers distinct advantages over CT for classification of traumatic cerebral lesions. Firstly, more lesions can be classified with MRI than with CT because of its much higher sensitivity. Also, the ability of MRI to obtain images in multiple planes is particularly beneficial since this allows more reliable localization and classification of the lesions10.

Infants and Head Trauma-Infants have greater calvarial flexibility and cerebral plasticity that allows absorption of impact effectively. Moreover, young infants have open sutures, thin calvarium. The greater plasticity has been attributed to poor myelination of white matter. However. these attributes also cause severe distortion between skull and dura, as well as on the cerebral vessels. It permits distraction between the brain and its coverings, with forces tending to tear bridging veins and dural attachment, producing interhemispheric subdural haematomas and dural venous sinus tears, lesions that are rarely seen in adults<sup>11</sup>.

Importance of assessment of Cervical Spine -The optimal mode of radiological evaluation of the head injury patient commences mandatorily with a preliminary assessment of cervical spine. To mobilize the patient for head trauma imaging, fracture and dislocation of the cervical spine must first be excluded. An adequate cervical spine clinical examination in emergency department often detects evidence of spinal injuries. Minimal radiological examination is a single, lateral radiograph that demonstrates the spine from the cranial base to the bottom of the seventh cervical vertebral body.

Conclusion-In current practice, standard skull X-rays have been superseded by craniofacial (bony windows) and brain CT scan (parenchymal windows). Furthermore, multi-detector CT has supplanted plain X-ray films of the skull as the initial imaging study of choice. Brain MRI is less accessible in the emergency setting but is feasible in some centers. It is the best choice in the first

weeks following mild brain injury but may be normal. Functional imaging techniques (SPECT, fMRI, PET-scan) are optionally needed to show axonal damage or brain atrophy. MR Spectroscopy is a promising research tool<sup>12</sup>. MRI, including fluid-attenuated inversion recovery, gradient echo T2\* and diffusionweighted sequences, is useful in determining the severity of acute brain tissue injury and may help to predict outcome<sup>13</sup>. Craniocerebral trauma remains a major cause of death among adolescents and young adults. Imaging plays an important role not only in identifying intracranial injury, but also in characterising and prognosticating the given case of head injury. Preliminary evaluation with CT is the established form of practice, with MR of late playing an increasingly important role.

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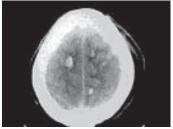


Figure-1, CT Brain in a case of head injury with Diffuse Axonal Injury showing multiple lesions ovoid to elliptical in shape, ranging in size from 5 to 15 mm. They are usually nonhemorrhagic in nature.

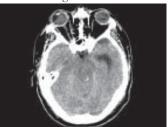


Figure-2: Duret Hemorrhages is essentially a secondary brainstem injury developing subsequent to initial trauma. A CT Brain at level of brainstem shows punctate petechial haemorrhages, central and midline at tegmentum of rostral pons.

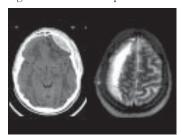


Figure- 3, The fundamental imaging differences between extradural (shown at left) and subdural hematoma (shown at right). Extradural hematoma are Biconvex, located between skull and dura, crosses dura but not sutures and are associated with fracture in 90 % cases. Subdural hematoma are concavoconvex or crescentic, located between dura and arachnoid, crosses sutures but not dural attachments with a rarer association with fractures.



Figure-4, CT Brain showing Intraceberal Hematoma (left panel) seen as a large hyperdense area at right side, which primarily expands between relatively normal neurons. The CT at right panel shows Intraventricular Hemorrhage, which is seen as hyperdense material within the frontal horn of lateral ventricle, attributable to rotationally induced tearing of subependymal veins.



Figure-5, CT Brain showing Subarachnoid Haemorrhage seen as hyperdense smear bilaterally spreading along subarachnoid spaces of the tentorial leaf. It is considerably difficult to detect with MRI than with CT, though FLAIR MRI sequences may be helpful

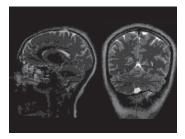


Figure-6, MRI Brain showing a Depressed fracture of occipital bone. They are Linear, Stellate or

Depressed. Depressed Fracture occurs due to failure of bone to rebound after fracture and are often comminuted. They are considered significant because they overly major dural venous sinus or cortex, are associated with dural tears and can cause penetration with underlying parenchymal injury.



Figure-7, Volume Rendered Multidetector CT Skull in a case of head trauma shows the key differences between fractures and sutures. Fractures have a width greater than 3 mm, is widest at center and narrow at ends, runs through both outer and the inner lamina of bone, usually runs in a straight line with angular turns. Sutures have a width less than 2 mm, possess same width throughout, appears lighter on x-rays compared with fracture lines, occur at specific anatomic sites, do not run in a straight line and are curvaceous.

Surgical Experience of Well Differentiated Papillary Carcinoma Thyroid with Involvement of Larynx

45-year of male presented with right neck swelling, progressively increasing in size over last 6 years and hoarseness of voice since past one year. Patient underwent a neck surgery four years back (details of surgery and HPR not available), but the swelling again started increasing in size after sometime. Local examination revealed a 15 x 6 cm nodular swelling a rising from thyroid extending from lower border of mandible up to supraclavicular fossa. Inferior border was palpable and there was no cervical lymphadenopathy. Trachea was shifted to left.IDL revealed right vocal cord palsy. Haematological, biochemical parameters including X-ray chest were normal. FNAC was suggestive of papillary carcinoma thyroid.CT scan neck showed huge mass arising from right lobe of thyroid & measuring 12.6 x 9.5 x 2.3 cm, there was evidence of destruction of right lamina of thyroid & cricoid cartilage, also evidence of destruction of hyoid bone, Mass was reaching up to right angle of mandible, there was no evidence of lymphadenopathy. Fig (1). Exploration of the neck revealed huge thyroid tumor invading strap muscles, right IJV, Right RLN & adherent to laryngeal cartilages. Patient underwent Thyroidectomy, Laryngectomy with permanent Trachestomy & Central compartment lymphnode dissection. Post op recovery was uneventful.

HPR revealed 14 x 10 x 8 cm papillary Ca Thyroid, Left lobe normal, tissue over tracheal wall showed presence of tumor infiltrating the tracheal cartilage. Laryngectomy specimen showed presence of tumor (fig 2) in the soft tissue adherent to the larynx with infiltration into the laryngeal cartilage, all 6 lymph node dissected were free of tumor. Final diagnosis Papillary carcinoma thyroid T<sub>4a</sub> N<sub>0</sub> M<sub>0</sub>-Post op patient received 44 Gy EBRT & also Radio iodine therapy. Patient is well and on regular Follow up & using electro larynx for phonation.

Discussion-The most common site of aerodigestive involvement in carcinoma of thyroid were the trachea (64%), larynx (43%), cricoid cartilage (39%) followed by esophagus/ hypopharynx (25%)².Although Ultrasound is the gold standard for imaging thyroid masses, it is of limited use in the evaluation of upper aerodigestive tract invasion by thyroid carcinoma. Subtle signs of invasion can be detected by

computed tomography (CT) and MRI can detect both.

Management upper aerodigestive tract invasion-Shave excision is defined as removal of all gross tumors by resection of a partial thickness of the aerodigestive tract wall; however, an assumption is made that microscopic foci of tumor remain. "Shaving" is affectively used in those early cases of aerodigestive tract involvement where there is obvious cartilage invasion but no direct intraluminal involvement. This approach has been shown in many studies to be as effective, in locoregional control and survival, as complete resection without the morbidity of extensive procedures that affect swallow, speech and voice<sup>5,6</sup>. A study of 292 patients with invasive well-differentiated thyroid carcinoma retrospectively evaluated over a 40-year period. Comparison was made among complete excision, shave excision and incomplete excision showed a statistically significant difference in survival of all patients. Similarly, when types of surgical excision were compared in patients with laryngotracheal invasion alone, there was a statistically significant difference in survival. However, comparison between complete excision and shave excision demonstrated no difference<sup>7</sup>. From these studies it may be concluded that survival rate of patients undergoing shave exci-

sion were no different from those of pt undergoing radical tumor resection if gross tumor did not remain8. Shave excision is generally not appropriate in cases of direct intraluminal invasion, removal of the disease adherent to the airway that leaves residual gross intraluminal tumor is ineffective treatment that leads to death by local disease recurrence in many cases9. Complete resection of gross intraluminal tumor violating the aerodigestive tract is necessary in cases of direct intraluminal invasion to improve locoregional control and survival. However once the decision to open the aerodigestive tract is made, strong consideration should be given to partial procedures that can preserve function. That it is acceptable to leave presumed positive microscopic margins with the shave excision for early cases of invasive thyroid carcinoma is in direct contradiction to the management of upper aerodigestive tract squamous cell carcinoma. However, adjuvant treatment with I 131 or external beam radiotherapy can be used to effectively control microscopic disease and is far more acceptable in most cases than the morbidity associated with a large procedure that offers a little survival advantage10

Adjuvant therapy for invasive thyroid carcinoma-All patients with invasive thyroid carcinoma are in a poor prognostic category for survival &, as such, require adjuvant postoperative therapy with either I<sup>131</sup> or external beam radiotherapy for adequate

locoregional control. In cases of gross residual disease where the morbidity of the procedure required to remove all disease is not acceptable to the patient or the patient is not a surgical candidate, external beam radiotherapy can be effective in controlling locoregional disease. External beam radiotherapy should be considered as an option when surgical and radioactive iodine interventions are exhausted. Suppression with L thyroxin should also be done routinely because prolonged elevation of TSH in cases of thyroid carcinoma is associated with a high incidence of tumor recurrence in many cases. Thyroglobulin leaves and I131 scanning may be used to determine tumor recurrence and spread and should be included in surgeon's algorithm for the long team follows up of patients with thyroid carcinoma.

Conclusion-Though rare, invasive well-differentiated carcinoma is associated with a high incidence of morbidity and mortality. Structures commonly invaded by thyroid carcinoma include the strap muscle, larynx, trachea, esophagus and recurrent laryngeal nerve. Symptoms that are often life threatening include stridor, hoarsenss, homptysis and dysphagia & occur in mose cases in patients with a previous history of treated thyroid malignancy. The goal in treating this disease is to provide adequate locoregional control while minimizing not only the morbidity of the tumor, but also the morbidof ity the surgical

treatmentAlthough there is no consensus on extent of surgery when the aerodigestive tract is invaded by thyroid carcinoma, we strongly believe that successful treatment requires radical excision of the tumor along with the involved part of the aerodigestive tract. Appropriate reconstruction of the resected part of the aerodigestive tract should be done if required. It is very important to note that morbidity of aerodigestive resection upon voice, respiration, and swallowing is often significant and should be an important consideration while developing a treatment plan.Aggressive management of thyroid carcinoma invading the aerodigestive tract at the time of initial surgical resection may offer improved local control and possibly prolonged survival.

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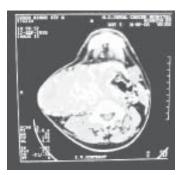


Fig.-1, CT scan image of the disease - CT scan neck showed huge mass arising from right lobe of thyroid & measuring 12.6 x 9.5 x 2.3 cm, there was evidence of destruction of right lamina of thyroid & cricoid cartilage, also evidence of destruction of hyoid bone

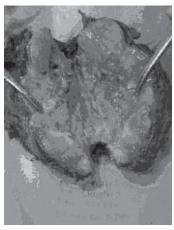


Fig.-2, Specimen cut open – Thyroid specimen showing presence of tumor with infiltration into the laryngeal cartilage



Fig.-3, Post op during follow up

# Spring-Water Cyst in an Atypical Location in The Mediastinum

Spring-water cyst, also known as pleuropericardial cyst or pericardial cyst or pericardial celomic cyst, is a relatively rare and the only benign tumor of the pericardium. Pericardial cysts arise from the persistent portions of the pericardial celomic ventral parietal recesses that fail to fuse with the pericardial cavity.1 It usually presents as a anterior or middle mediastinal mass. They are most commonly located the right pericardiophrenic angle (approximately 70%)2. We are presenting a case of pericardial cyst located in an atypical location in the mediastinum.

Case Report -A 30 years old male came to the outpatient department of medicine with nonspecific complaint of cough since 2-3 weeks. The patient denied history of fever. Clinical examination of the patient revealed wheezes all over the chest. Laboratory examination was unremarkable except for mild increase in ESR. The patient was advised a chest radiograph to rule out the possibility of any low-grade infectious etiology especially tuberculosis. Chest radiograph revealed a soft tissue dense, homogeneous opacity along the right cardiac border causing widening of the cardiac shadow and superior mediastinum. Since the nature of the lesion was undetermined, the patient was advised to undergo computed tomography (CT) of the thorax.CT thorax revealed a nonenhancing, homogeneously water dense, smooth and thin walled lesion intimately related to the right cardiac border extending in to the anterior and middle mediastinum (figure 1a and 1b). The lesion was elliptical in shape and the epicenter was the region of right atrium and the lesion was extending in to the superior mediastinum as well. There was mild compression atelectasis of the adjacent portion of the right lung. The pericardiophrenic angle was normal on both sides. Based on the above findings, the diagnosis of the spring water cyst of the pericardium on the right side was made. The lesion remain unchanged during the six months period following treatment during which the patient was asymptomatic.

Discussion-Pericardial cysts are unilocular & thin walled lesions lined by mesothelium and attached to the pericardium either intimately or by a pedicle, and are in some ways similar to the pericardial diverticula, except that these do not communicate with the pericardial cavity.3 They are most frequently seen in the right pericardiophrenic angle but may be located adjacent to any portion of the pericardium.<sup>4,5</sup> It usually presents as an anterior or middle mediastinal mass. Most are asymptomatic but may present with pain, cough or dyspnea.2The smaller cysts may take up a 'tear-drop' shape and lie in an elongated fashion in the lower end of the oblique fissure, though the large ones are almost spherical.3 Occasionally, they may be seen as lobulated masses attached to the pericardium. In the majority of cases, the diagnosis

is obvious on the plain radiograph, where they appear as rounded, cystic shadows anteriorly in the pericardiophrenic angle.3 They are sharply marginated but may have a pointed lateral margin, secondary to the cyst entering the lower portion of the major fissure.7,8 In the right pericardiophrenic angle, the cyst has to be differentiated from a Morgagni hernia; barium study distinguishes the two. On fluoroscopy, they may change shape with respiration and with position indicating its pliable nature.7CT shows a nonenhancing, water density, round to oval mass adjacent to the pericardium, which may occasionally have attenuation values if the fluid is viscous.8 The cyst wall may show calcification.2 MRI shows the typical fluid signal i.e. hypointense on T1WI and hyperintense on T2WI.

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Figure-1a and 1b, Coronal and sagittal MPR CT scans show a large, elliptical pericardial cyst along the right cardiac border



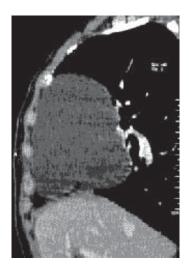


Figure - 1b

# Pulmonary Arteriovenous Malformation in a Child-a Case Report

ulmonary arteriovenous malformations (PAVM) are abnormal congenital connections between a pulmonary artery and a pulmonary vein. Majority is solitary, unilateral and seen in the lower lobes of the lungs. Very few among them are diagnosed in the childhood. Hence, we are presenting a case of PAVM involving the upper lobes of the lungs detected in childhood, for the reason of the rarity of this type of presentation of the PAVM and review the diagnosis of such lesions.

Case Report-A 7 years old female child presented to the pediatric department of our hospital with the history of mild hemoptysis off and on since 2-3 months. There was additional complaints of early fatigue, weakness, dyspnea on exertion and lack of gain in weight. History of fever,

trauma & surgery and family history of tuberculosis was denied. Clinical examination of the child revealed mild cyanosis and clubbing of the nails. The chest examination was however, unremarkable. Laboratory tests revealed mild increase in hematocrit with normal hemoglobin. Chest radiograph was advised to look for any chronic pulmonary pathology. Chest radiograph revealed multiple soft tissue density, nodular lesions in bilateral upper lobes of the lungs. The size of the nodules was larger on left side. Few soft tissue densities were elongated or club-shaped resembling the vessels and were radiating from the hilum towards the upper lobe in the left lung. The main pulmonary artery and its left branch appear mildly enlarged. Based on these clinical and radiographic findings, the diagnosis of PAVM was suggested and computed tomography (CT) of the thorax was advised for confirmation. C T thorax confirmed the findings of the chest radiograph (figure 1a, 1b, 1c). There was a large PAVM involving the left pulmonary artery and left superior pulmonary vein in the upper lobe of the left lung. In addition, multiple, tortuous, ectatic vascular channels of varying sizes were seen in the adjacent pulmonary parenchyma as well as in the upper lobe of the right lung. The main pulmonary artery and the left pulmonary artery were enlarged. Based on the above findings, the diagnosis of the multiple PAVM was made involving the bilateral upper lobes of the lungs with pulmonary arterial hypertension.

Discussion-Congenital communications between the pulmonary arteries and veins without an intervening capillary bed are termed as PAVM whilst the term pulmonary arteriovenous fistula (PAVF) is preferred for acquired lesions. The latter are rare and secondary to surgery, trauma, pulmonary infections, metastatic carcinoma and hepatic cirrhosis1. The malformation may be single or multiple and discrete or may present as a nodule or a mass lesion, or may be tiny and diffuse (telangiectatic). They occur in the lower lobes in approximately 60%, are solitary in 65% and are unilateral in approximately 75% of patients. The diagnosis is made in childhood in only 4-6% of patients.2, 3About 30-40% of patients with pulmonary telangiectasia have Rendu-Osler-Weber disease; AVM are found in skin, mucous membranes and the lungs. This condition, also known as hereditary hemorrhagic telangiectasia (HHT), is transmitted as an autosomal dominant trait2, 4 and at least 15% of patients with HHT have PAVM.5Patients may be asymptomatic or may have dyspnea on exertion, fatigue, hemoptysis and cerebrovascular complications. Clubbing and cyanosis may be seen as a result of the right to left shunt. Chest radiographic findings range from completely normal to the presence of one or more, soft tissue dense nodular lesions of variable sizes, especially if the lesions are large and have led to sufficient dilatation of the peripheral artery and vein. A change in size of these lesions may be appreciated if they are studied fluoroscopi-

cally during extremes of respiration.2,6When the diagnosis is suspected on chest radiograph, CT and MRI are useful to establish the definitive diagnosis. On CT and MRI, AVMs appear as rounded or lobular masses with rapid enhancement and washout after intravenous contrast medium administration. Enhancement typically occurs after enhancement of the right ventricle and before enhancement of the left atrium and left ventricle.7 There is no enlargement of the main pulmonary artery in uncomplicated AVMs.6 MRI may be useful in differentiating a solid mass and an AVM, especially using flow sensitive techniques.8Contrast GRE echocardiography is sensitive for the detection of the associated right to left shunt9, but pulmonary angiography is required if surgery or embolisation procedures are contemplated to demonstrate the precise vascular anatomy of complex malformation or the presence of multiple tiny AVM's that may not be visible on CT and MRI.7,9The prevention of the paradoxical embolism, which leads to the transient ischemic attacks, strokes and cerebral abscesses, is the real reason for treating PAVM.<sup>1</sup> The only safe agents used for embolisation of the PAVM are detachable balloon catheters or steel coils.10

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Aatish Kumar Bhargava Gopesh Mehrotra Sumeet Bhargava Department of Radiology & Imaging University College of Medical Sciences, Delhi Figure-1a, 1b and 1c, Contrast enhanced axial (1a), delayed axial (1b) and coronal MIP CT (1c) images show a large PAVM in the left upper lobe with multiple smaller but similar lesions in the bilateral upper lobes of both lungs. Direct communication between a left pulmonary artery and left superior pulmonary vein is well demonstrated in the larger

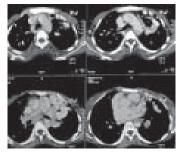


Figure-1a,

PAVM

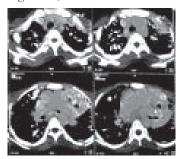
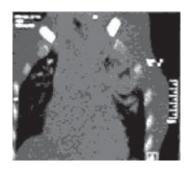


Figure- 1b



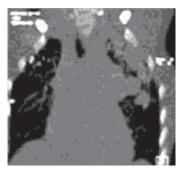


Figure -1c

Multi organ Involvement and Regional Nerve Block: Anesthetic Technique for Above Knee Amputation in ASA III – ASA IV Risk Patients

egional nerve blocks are extremely useful in surgeries for patients who pose high risk for either general anesthesia or central neuraxial blockade. There is no hemodynamic disturbance in the regional nerve block and if done methodically, using a nerve locator, chances of failure is rare and extremely beneficial to the patient. Very poor risk patients respond well to peripheral nerve blocks of 3 - 6hours duration. For major upper and lower limb surgeries effective analgesia for 12 hours or

more is possible when the brachial plexus or sciatic or femoral nerves are blocked with bupivacaine 0.5% or 0.25%. Bupivacaine of 0.75% can produce analgesia for more than 24 hours. Continuous peripheral nerve block with indwelling cannulae produce longer duration of analgesia and is beneficial for postoperative period. The ischemic pain can have major impact on patient well being and can be difficult to treat effectively because very many times the pain will be opioid resistant. Many patient with ischemic limb have associated diabetes mellitus and the stress will destabilize the insulin regimen. We present two cases of above knee amputation, who were classified as belonging to ASA III and ASA IV risk categories, under lower limb nerve blocks.

Case-1,

58 years old male patient was admitted and treated in July this year for non healing diabetic ulcer right foot. He was hospitalized for 3 weeks; had wound suturing and split skin graft of the raw area for the right foot ulcer sedation and supplemental local anesthesia. Discharged in that condition with advise for regular follow up. Readmitted within a week for recurring pain and the wound was debrided under local anesthesia. Doppler study showed posterior tibial artery occlusion and was posted for AK amputation. Uncontrolled diabetic status; dilated cardiomyopathy with very poor LV ejection fraction (30%); cardiologist felt he was at high cardiac risk for the procedure; he was also in renal failure and was treated by the nephrologists.

Clinical findings-Toxic looking 60 kg weighing male patient; Pulse 108/mt; BP 125/77 (88); conscious, well oriented, painful lower limb because of ischemia, already sutured and skin grafted wound. Tachypnoeic (resp rate 28/mt) probably because of pain. Echocardiography revealed dilated cardiomyopathy with EF of 30%. Diagnosis of vascular occlusion done by Doppler studyposterior tibial artery occlusion. Decision: surgical management by above knee amputation- since the patient was toxic, had poor ejection fraction because of dilated cardiomyopathy, regional nerve block - sciatic, femoral and lateral cutaneous n of thigh- is contemplated.

Anesthetic procedure-After explaining the procedure to the patient an informed consent was obtained. Anesthetic machine check done, good i.v. access obtained in the patient, monitors connected – ECG, NIBP, SpO2. All resuscitative equipment including a defibrillator kept ready. Emergency drug trolley checked. In lateral position with the affected side uppermost, with the use of nerve locator sciatic nerve identified- 20 ml of 0.25% preservative free bupivacaine given. The patient then turned supine and under strict aseptic precaution femorla N block done with 15 ml 0.25% preservative free bupivacaine and lateral cutaneous N of thigh blocked with 8 ml of the same bupivacaine solution. (the total dose given is well within safe limits the bupivacaine). The conduct of surgery and anesthesia was smooth

without any critical incident. The patient and the surgeon were very comfortable and appreciative. The postoperative analgesia lasted for 8 hours and patient needed supplementary analgesia with pethidine for the night.

## Case 2

A female patient of 63years was admitted with h/o trauma in the right foot - had metatarsal #; was referred to our hospital from outside because she had elevated renal parameters; She is a known case of HT, DM and under treatment for over 15 years. She had GA twice - once for total abdominal hysterectomy 25 yrs back, and for CABG 12 years back; both anesthesiae were uneventful. She has no h/o any known drug allergy. Her investigation charts are attached. She was initially posted for i&d of the cellulitis of the right foot and was done under GA with 40 mics of fentanyl i.v and o2 sevoflurane under spontaneous respiration and the decision was to manage her medically. A Doppler study showed narrowing of major vessels to the lower limb and block of posterior tibial artery on the right side. She was posted for above knee amputation.She was planned for regional peripheral nerve block technique and after connecting her to the monitors sciatic, femoral and lateral cutaneous nerve of thigh were blocked using total volume of 40 ml of 0.25% preservative bupivacaine. The operative and postoperative period were uneventful. The anesthetic charts for both cases are attached separately. It was quite heartening to see the peripheral nerve blocks

in these two ASA IV risk patients helped to treat them and relieve their pain. There was no hemodynamic instability.

Discussion-It is obvious that if these three nerves are blocked it will be comfortable to do above knee amputation. The Sciatic Nerve can be approached by posterior route, the lateral approach, the supine lithotomy approach or anterior approach. We preferred the lateral approach because we were familiar and comfortable. Patient in lateral position with the affected side upper, the landmarks - posterior superior iliac spine, the greater trochanter and the sacral hiatus are marked after thorough preparation of the skin with antiseptics and alcohol sprays (the marking can be done by sterile marker available). The technique should be performed under strict aseptic precautions. The anesthesiologist after scrubbing, gowning and gloving, loads and local anesthetic solution (the required quantity of preservative free solution). A line is drawn connecting posterior superior iliac spine, greater trochanter. From the midpoint of this line a perpendicular is dropped to meet another line joining the greater trochanter and the sacral hiatus as shown in the diagram. Having located the point of entry of needle, the 10 cm needle (we used stimuplex needle by B BRAUN) is connected to the nerve locator and after local infiltration of the site the needle is advanced with the stimulation at 2mA till a twitch is elicited in the muscles supplied by sciatic N. Through the cannula at the side the local anesthetic is injected. Then the

patient is turned supine and Femoral Nerve Block done. Blockade of the femoral nerve provides sensory anesthesia of the anterior thigh, keen, and medial aspect of the calf, ankle and foot. The femoral nerve block should be distinguished from the "three-in-one" block, the technique of lumbar plexus anesthesia that achieves anesthesia of the lateral femoral cutaneous and obturator as well as the femoral nerves. The femoral nerve lies below two facial planes: the fascia lata and the fascia iliacus. Simply feeling two successive "pops" as a short bevel regional anesthesia needle passes through these fascial layers indicates placement of the needle in the perineural space. The structures used to locate the femoral nerve are the inguinal ligament, and the femoral artery. A line representing the inguinal ligament is drawn between the anterior superior iliac spine and the public tubercle. The pulsations of the femoral artery are palpated and the artery is marked distal to the ligament. The femoral nerve lies lateral to the artery. Think of the mnemonic "NAVELS" to remember the relationship between the femoral nerve and the femoral artery (structures ordered laterally to medially: Nerve, Artery, Vein, Empty space, Lymphatics, public Symphysis). The point of needle insertion is marked 1.5 cm lateral and the 1.5 cm distal to the intersection of the inguinal ligament and the femoral artery.

Technique-The groin is prepared sterile with preps and alcohol spray. In the awake patient, cutaneous anesthesia at the point

of needle insertion is obtained with a skin wheal of local anesthetic. A 10 cm STIMUPLEX NEEDLE is inserted through the skin at a 45 degree angle to the skin and directed cephalad and slightly medically toward the umbilicus.Once the needle is through the skin, the nerve stimulator output is adjusted to 1.5-2.0 mA with a frequency of 1.0 Hz.An evoked response of the rectus femoris is sought as the needle is carefully advanced. Movement of the patella indicates stimulation of the femoral nerve: . If this motion is not found, the needle is brought back to the skin and advanced after redirecting the needle in a more lateral or medical direction. The needle should be systematically redirected in a "fan" across the expected path of the femoral nerve if the nerve is not easily located. Once the nerve is located the needle position optimized and the stimulus intensity is adjusted downward until a patellar twitch remains present at an output of 0.3 to 0.4 mA. Aspiration is performed to rule-out intravascular placement as the needle is held immobile. An epinephrine test dose is also administered to rule-out intravascular placement. Injection of a small amount of local anesthetic should abolish the evoked motor response. Persistence of the twitch may indicate that the nerve is separated from the needle by a thin tissue membrane that conducts current easily but prevents local anesthetic from reaching the nerve. The needle should be advanced further and the test dose repeated. Following a negative

test dose, local anesthetic is injected in divided doses while watching for signs of systemic local anesthetic toxicity). The lateral cutaneous nerve of thigh can be approached 2 cm medical and caudal to the anterior superior iliac spine With the help of nerve locator within 3 cms depth the nerve can be reached and blocked with the local anesthetic.

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## Neuroimaging

History of neuroimaging-The history of neuroimaging, began in the early 1900s with a technique called pneumoencephalography. This process involved draining the cerebrospinal fluid from around the brain and replacing it with air, altering the relative density of the brain and its surroundings, to cause it to show up better on an x-ray. It was considered to be incredibly unsafe for patients. A form of magnetic resonance imaging (MRI) and computed tomography (CT) were developed in the 1970s and 1980s. The new MRI and CT technologies were considerably less harmful and are explained in greater detail below. Next came SPECT and PET scans, which allowed scientists to map brain function because, unlike MRI and CT, these scans could create more than just static images of the brain's structure. Learning from MRI, PET and SPECT scanning, scientists were able to develop functional MRI (fMRI) with abilities that opened the door to direct observation of cognitive activities.

Early uses of brain imaging-The desire to understand the human mind has been one of the main desires of philosophers throughout the ages. Questions about thoughts, desires, etcetera have drawn psychologists, computer scientists, philosophers, sociologists and the like together into the new discipline of cognitive science. Non-invasive imaging of the human brain has proven invaluable in context.Structural imaging began with early radiographic techniques to image the human brain. Unfortunately, because the brain is almost entirely composed of soft tissue that is not radio-opaque, it remains essentially invisible to ordinary or plain x-ray examination. This is also true of most brain abnormalities, though there are exceptions such as a calcified tumour (e.g.meningioma, craniopharyngioma, some types of glioma); whilst calcification in such normal structures as the pineal body, the choroid plexuses, or large brain arteries may indirectly give important clues to the presence of structural disease in the brain itself.In 1918 the American neurosurgeon Walter Dandy introduced the technique of ventriculography whereby images of the ventricular system within the brain were obtained by injection of filtered air directly into one or both lateral ventricles of the brain via one or more small trephine holes drilled in the skull under local anaesthesia.

# Melatonin – a Mystery

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Recent Advances

elatonin is something of a mystery. It is synthesized exclusively in the pineal gland, that plays a role in establishing circadian rhythms. The pineal gland believed by Rane Descartes as "the seas of the soul". It may be said to constitute a pigment of the imagination. Now, it is well known that melatonin may function as a timing device to keep internal events synchronized with the light dark cycle in the environment.

Pineal Gland-The pineal gland arises from the roof of the third ventricle under the posterior end of the corpus callosum and is connected by a stalk to the posterior commissure and habenular commissure. There are nerve fibres in the stalk, but they apparently do not reach the gland. It has highly permeable fenestrated capillaries. The pineal stroma contains neuroglia and parenchymal cells with features suggesting that they have a secretory nature. Small concretions of calcium phosphate and carbonate (pineal sand) appear in the tissue. In infants, the pineal is large, and the cells tends to be arranged in alveoli. It begins to involute before puberty.

Melatonin-Melatonin is the hormonal product of pineal gland. It is principal indoleamine. Chemically, melatonin is 5-methoxy-N-acetyl-tryptamine.

Synthesis of Melatonin- Melatonin is synthesized by pineal parenchymal cells. extrapineal site of synthesis are retina, iris, ciliary gland and harderian gland etc. The synthesis of melatonin is initiated by tryptophan, an amino acid which get converted into 5-hydroxytryptamine i.e serotonin (an neurotransmitter). Pineal gland contains two important enzymes not found elsewhere. The enzymes are N- acetyl transferase and hydroxy indole -O-methyl-transferase (HIOMT) which covert serotonin by N-acetylation and O-methylation to melatonin. This conversion take place only during the night because the enzymes involved are inactivated by light. Nor-epinephrine is another neurotransmitter which assists in melatonin production. It act as catalyst to metatonin production by stimulating cells in the pineal gland to begin making melatonin even in the absence of light.

Regulation of Secretion-Melatonin is secreted by pineal parenchyma into the blood and the cerebro-spinal fluid. It's synthesis and secretion are increased during the dark period of the day and maintained at a low level during the day light hours. The remarkable diurnal variation in secretion is controlled by input from the retina, via a nor-ad renergic retinohypothalamic fi-

bres that terminates in the suprachiasmatic nucleus (SCN) in the hypothalamus, a structure often termed the "biological clock", which generates the circadian rhythm. From the hypothalamus descending pathways converge on the intermediolateral gray column of the thoracic spinal cord and end on the preganglionic sympathetic neurons that in turn innervate the superior cervical ganglion, the site of origin of the post-ganglionic neuron to the pineal. Therefore SCN controls the pineal, not directly, but via post ganglionic sympathetic fibres i.e. nervi conorii that innervate the gland. The nor-epinephrine acts via beta-adrenergic receptors in the pineal to increase intracellular cAMP. This cAMP in turn produces a marked increase in Nacetyl transferase activity. This results in increased melatonin synthesis and secretion.

Melatonin Receptors-Melatonin receptors are widespread and come in different types. Two main receptors are recogenized as MT<sub>1</sub> and MT<sub>2</sub> found mainly in the brain (SCN) and retina, also in peripheral tissues. Two melatonin-binding sites have been characterized –a high affinity MT<sub>1</sub> and a low affinity MT<sub>2</sub> site. Two subtypes of the MT<sub>1</sub> receptors – a and b have been cloned. All the receptors are coupled to

G protein, with MT<sub>1</sub> receptors inhibiting adenylyl cyclase and MT<sub>2</sub> receptors stimulating phosphoinositide hydrolysis. Apart from melatonin receptors, another type has been identified as "orphan receptors", a member of the retinoic acid intracellular receptor family which regulates gene transcription.

Metabolism - Circulating melatonin is rapidly metabolized in the liver by 6- hydroxylation followed by conjugation, and over 90% of the melatonin that appears in the urine is in the form of 6-hydroxy conjugates and 6-sulfatoxymelatonin.

Physiological role -We currently know very little about the physiological processes that are controlled by melatonin, though there is intense research activity in this area. It is well clear that melatonin secretion is diurnal and controlled by light intensity, being high at night and low by day. This diurnal change in melatonin secretion that functions as some sort of timing signal which co-ordinates internal events with the light dark cycle in the environment. The pineal normally inhibits the onset of puberty, because pineal tumors are sometime associated with sexual precocity but only when they produce hypothalamic damage. However its effect may be facilitated in others. Sometime for one reason or another the body does not produce adequate amount of melatonin for its needs. This can result in insomnia and depression.

Clinical Implications-The use of melatonin for medicinal pur-

pose has become something of an "alternative medicine". Melatonin is well absorbed after oral administration, but quickly metabolized, its plasma half life being a few minutes. It can be used in increasing does without significant adverse impact. Melatonin can be used mainly in the treatment of jet-lag and other circadian sleep disorders. It also has an inhibitory function on CNS activity and can be used in depression and migraine. Melatonin has anti-convulsant potential and can be used in epilepsy and other convulsive disorder. Exogenous administration of melatonin in evening has to be inhibit tumorgenesis in some malignent conditions like breast cancer, prostrate and colorectal carcinoma. Melatonin has anti-oxidant potential and protect the various body systems from free radical induced injuries. Melatonin surve a role in regulating biological rhythms and shows promise in treatment of circadian sleep disorders. The jet-lag syndrome and other sleep scheduling disorders are described in brief.

Jet-lag Syndrome -This rapid time-zone change syndrome isassociated with excessive day-time sleepiness, sleep onset insomnia and frequent arousals from sleep, particularly in the latter half of the night. Gastro-intestinal discomfort is common. The syndrome is transient and observed in air travelers, typically lasting two to fourteen days depending on the number of time zones crossed, the direction of travel as well as traveler's age and phase shifting capacity. Travel-

ers who spend more time outdoors reportedly adapt more quickly than those who remain in hotel rooms, presumably due to bright (outdoor) light exposure. Avoidance of antecedent sleep loss and obtaining nap sleep on the afternoon prior to overnight travel greatly reduces the difficulty of extended wakefalness. Melatonin can enhance sleep efficiency, but only if taken when endogeuous melatonin concentrations are low. Furthermore melatonin may induce phase shifts in human rhythms.

Sleep Scheduling Disorders-These are circadian rhythm disorder in which sleep occurs at the wrong time, i.e., at a time that does not fit with work, social and commitments. family typicalpattern may be a difficulty in initiating sleep for few night due to stress, whereupon once asleep the subject continues sleeping well into the morning to 'catch up' the lost sleep, thereafter the time since last sleep cue for sleep initiation is delayed and the sleep period gradually becomes more delayed until the subject is sleeping in the day instead of at night. A behavioural program with strategic light exposer is appropriate, with pharmacological treatment as an adjunct, e.g. melatonin, to help reset, the sleep wake schedule.

Therapeutic Indications-Melatonin is used to alleviate symptoms of jet-lag and other disorder resulting from delay of sleep. Sedation and drowsiness can result as adverse effects. The usual

single dose is given before bed time. It is available as 3 mg tablet.

Conclusion - Melatonin is produced in the body by the pineal gland in the brain. Photic information from retina is responsible for its release. Melatonin play a important role in establishing circadian rhythms. Sometime body does not produce adequate amounts of melatonin as for needs, this can result circadian sleep disorders. Melatonin resets the biological clock, being used for this purpose to counter jetlag and other sleep disorders.

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## Neuroimaging

Recent Breakthroughs-Recent breakthroughs in non-invasive brain imaging have been somewhat limited because most of them have not been completely novel; rather, they are simply refining existing brain imaging techniques. fMRI is a perfect example of this from the early 1990s, and it still remains the most popular brain imaging technique available today. Advances have been made in a number of ways regarding neuroimaging, and this section will cover some of the more prominent improvements including computational advances, transcranial magnetic stimulation, and nuclear magnetic resonance. To begin with, much of the recent progress has had to do not with the actual brain imaging methods themselves but with our ability to utilize computers in analyzing the data. For example, substantial discoveries in the growth of human brains from age three months to the age of fifteen have been made due to the creation of high-resolution brain maps and computer technology to analyze these maps over various periods of time and growth (Thompson, UCLA). This type of breakthrough represents the nature of most breakthroughs in neuroscience today. With fMRI technology mapping brains beyond what we are already understanding, most innovators time is being spent trying to make sense of the data we already have rather than probing into other realms of brain imaging and mapping. This can be seen more clearly in the fact that brain imaging archives are catching and on neuroinformatics is allowing researchers to examine thousands of brains rather than just a few (Lynch). Also, these archives are universalizing and standardizing formats and descriptions so that they are more searchable for everyone. For the past decade we have been able to get data and now our technology allows us to share findings and research much easier. This has also allowed for "brain atlases" to be made. Brain atlases are simply maps of what normal functioning brains look like (Thompson, Bioinformatics). Transcranial magnetic stimulation (TMS) is a recent innovation in brain imaging. In TMS, a coil is held near a person's head to generate magnetic field impulses that stimulate underlying brain cells to make someone perform a specific action. Using this in combination with MRI, the researcher can generate maps of the brain performing very specific functions.

## Osteoarthritis and Stem Cell

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# Recent Advances

steoarthritis is a degenerative joint disease most commonly affecting elderly people. The etiology of the disease is multifactorial and is still not understood properly, but commonly thought to be due to wear and tear of joints as one ages. Osteoarthritis mostly affects cartilage, which covers the ends of bones where they meet to form joint. The cartilage allows bones to glide over one another and absorbs energy from shock of physical movement. In osteoarthritis, surface layer of cartilage breaks down which allow bones under cartilage to rub together, causing pain, swelling and loss of motion of the joint. Over time joint loses its normal shape, bits of cartilage break off and float inside the joint space, causing more pain and damage.

## Types of osteoarthritis

Primary osteoarthritis -Occurs in a joint de novo; Occurs in old age; Usually affects weight bearing joints (knee and hip); More common than secondary osteoarthritis

Secondary osteoarthritis-Usually there is an underlying primary disease of the joint which leads to degeneration of the joint, often many years later; Occurs at any age after adolescence; Most commonly affects hip joint

Predisposing factors are- Congenital maldevelopment of joint; Any previous trauma of the joint; Previous disease which produced damaged articular surface; Internal derangement of the knee such as loose body; Obesity and excessive weight

Prevalence of osteoarthritis in India -An estimated 78314013 of Indian population suffers from osteoarthritis. Both sexes have the disease, before 45 years of age, more men develop the disease and after 45 years of age, it is more common in women

Pathology -Osteoarthritis causes degeneration of articular cartilage. With age the water content of cartilage increase and proteoglycans are depleted from cartilage matrix. Repeated use of joints initiates inflammation of the joint. Loss of cartilage cushion causes friction between bones (fig1). Inflammation of cartilage can also stimulate new bone outgrowths to form around the joints.

Clinical features-Commonly affects hands, feet, spine and large weight bearing joints such as hips and knees; Pain - chronic pain with loss of mobility and often stiffness and occurs intermittently in the beginning but become constant over months; Crepitus; Swelling; Stiffness; Instability of joint and locking Investigations- Diagnosis is mainly done by X-ray; Radiological features are-Narrowing of joint space, Subchondral sclerosis and cysts, Osteophyte formation; other techniques, such as MRI, arthrocentesis and arthroscopy, diagnosis can be made by careful study of duration, location, character of joint symptoms and appearance of joints themselves; Serological tests and ESR to rule out rheumatoid arthritis; Serum uric acid to rule out gout

Treatment approaches to osteoarthritis

Supportive therapy-Weight control, Exercise, Rest and relief from stress on joints, Heat and cold; heat or cold (or combination of two); Massage

Medical treatment-Topical pain relieving creams; Oral NSAID and corticosteroids; Injectable hylauronic acid substitutes and corticosteroids

Surgical treatment -If medical and supportive treatment is ineffective then doctor resort to surgical treatment. Joint replacement surgery; Osteotomy - high tibial osteotomy osteotomy for knee and intertrochanteric osteotomy for hip has shown good results; Arthroscopic procedures - clean out cartilage debris from joints

Recent advances-Drugs available today can ease symptoms of osteoarthritis but don't halt the underlying destruction of cartilage. Surgical procedures, the most common being Joint replacement surgery eventually fails, if the patient lives long enough. Tissue engineering offers the potential of recreating a "bio-

logical joint replacement" which may last a lifetime.

Stem cells-These cells are basic building blocks of every other cell in the body, which has provided a cure for many degenerative diseases. Stem cell is a cell that has ability to divide for indefinite periods and under right conditions can give rise to many cell types that make up the organism. Scientist have predicted cure for severest form of arthritis by growing human cartilage from patients stem cells. Cartilage is a tissue with limited capacity of blood vessels, nerves and lymphatics, relative lack of undifferentiated progenitor cells, slow matrix turnover and very less highly differentiated cells, thus has limited capacity for repair when damaged. This lack of healing leaves bone exposed in the joint which is a cause of pain. At present in cartilage repair, there are no long term clinical studies as yet. Thus alternative is to asses how closely the histology or mechanics of repair tissue resembles normal tissue. Once cartilage has been injured it never heals back to original type - hyaline or articular. At best it repairs itself to fibrocartilage which is not as good as articular both functionally and biomechanically. In case of cartilage repair it is not merely hyaline cartilage which is the goal, but it is articular cartilage.

Basic histology of cartilage-Cartilage is composed of rich intercellular matrix with thinly dispersed chondrocytes accounting for 1-2% of tissue volume in adult. The matrix is an unhyderated gel of proteoglycans and matrix proteins reinforced by three dimensional network of collagen fibrils. The chondreytes are responsible for slow turnover of matrix components. The biological half life of aggrecan in adult human joint cartilage is measured in months and years, while that for collagen fibrils is measured for years and decades. Normal chondrocytes rarely divide. There are 4 types of cartilage depending on number and variety of fibers in matrix-Articular cartilage; Hyaline cartilage; Fibrocartilage; Elastic cartilage Articular cartilage- This cartilage lines the articular surfaces of most joints. Articular cartilage is not covered by perichondrium and their surface is kept moist by synovial fluid. It is composed of type 2 collagen, proteoglycans and chondreytes forming a complex, partially hydrated compressed matrix structure. It is composed of four layers (fig2) each with different orientations of collagen fiber, varying cell morphology and matrix composition and function. It has no pain fibers or blood vessels. Metabolism is anaerobic and glucose reaches the cell by diffusion from joint surface and underlying

Fibrocartilage - This cartilage has collagen type 1 fibers and on polarized light has no collagen orientation. It contains vessels and nerves and doesn't function well on articular surface. It gives good symptomatic relief to patients if all bone is covered. Contains vessels and nerves and doesn't function well on articular surface.

Hyaline cartilage- This cartilage has histology quite similar to

that of articular cartilage and is better than fibrocartilage, but is not fully normal articular cartilage

Quantification of repair -Absence of repair by fibrous tissue; Absolute measurement of collagen type 2 and type1 as well as proteoglycan; Assessment of collagen orientation

Integration to bone and to adjacent cartilage and overall thickness

Methods of repair- Cartilage doesn't heal if incised or if partial thickness of cartilage is removed. It will, however heal if it is worn down to bone<sup>1</sup> when stem cells from underlying bone emerge through cracks in subchondral bone plate. Partial thickness injuries that don't reach underlying bone have not shown any healing over time. The full thickness of cartilage needs to be removed to allow repair by marrow undifferentiated mesenchymal stem cells as described by Shapiro and coworkers<sup>2</sup>. A good repair response produces fibrocartilage. The authors noted that collagen fibrils of repair tissue were not well integrated with those of surrounding cartilage. Type2 cartilage were present initially, but there were still significant type1 collagen and between 6 and 12 months the matrix and cells become more typical of fibrocartilage. The fibrocartilage formed doesn't display same biochemical composition or mechanical properties of normal articular cartilage and degenerates with use. Exposure of bone has been common theme in range of surgical techniques which have found success in achieving repair.

Drilling of subchondral bone has been used for quite some time for repair of cartilage<sup>3</sup>. More recently the use of microfracture allows easier access to the defect as advocated by Steadman 4. The repair tissue initially had some hyaline like cartilage but becomes more fibrous with time<sup>5</sup> . A useful source of clinical data is found in trials of osteotomy at the knee 6. Generally half of patients need total knee replacement within 5 years following osteotomy. Microfracture or abrasion has been used to improve fibrocartilage formation when there was bone on bone before<sup>7</sup>. The tissue formed when there was significant amount of load applied while the surface heals. The ability to form new tissue under load is important as it opens the way for tissue engineering techniques which depend on tissue growth in active patient.

In case of end stage failure of tissue or organ system prosthetic replacement provide immediate though partial functional restoration in large number of clinical conditions including large bone defects and advanced osteoarthritis. When anatomical damage and functional loss are more limited, as in the case of localized joint tissue, therapeutic goal is to achieve optimal functional and anatomical restoration, thereby preventing possible evolution towards end stage osteoarthritis, ideally with minimal invasive surgery. This is true for young individuals and professional athletes. In these cases repair is sought using biological active device. It is also thought, though not proven with clinical

trials that these treatments would prevent evolution of joint surface lesions towards osteoarthritis. The biological repair of joint surface using cultured cells had been first explored in eighties8. Localized joint surface defects were treated by implantation of autologous, in vitro expanded chondrocytes, injected in suspension under periosteal flap (fig 3). The chondrcytes were obtained with cartilage biopsy from uninvolved area of same joint. The study9 showed symptomatic relief in 14 out of 16 patients with lesions of femoral condyle at 2 year follow up and subsequently follow up to 11 years demonstrated long term efficacy of this procedure in 92% of patients<sup>10</sup>. Despite the proven long term symptomatic efficacy, whether autologous chondrocyte implantation prevent evolution towards osteoarthritis remains to be investigated. Tissue repair is a rapid process that has been evolutionarily selected to allow animal to rapidly escape from danger and consists of scar tissue to join edges of fractured or to fill tissue voids. For skeletal tissue such as cartilage and bone, scars are location of mechanical weakness and thus of future tissue failure under high loads. By comparison regeneration is a slow process which recapitulates many of the steps observed when tissue initially forms in embryo. Based on these observations the key steps or principles that govern embryonic development of bone and cartilage are important components of tissue engineered regeneration of these tissues in adults.

Critical components in tissue engineering of cartilage are - Sufficient cell numbers within the defect such as chondrocytes or multipotent stem cells capable of differentiating into chondrocytes; Access to growth and differentiation factors that modulate these cells to differentiate through the chondrogenic lineage; Cell carrier or matrix that fills the defect and delivers the appropriate cells and supports cell proliferation and differentiation.

The field of tissue engineering has created a need biomaterials which are capable of providing biofunctional and structural support for living cells outside the body. Most of the commonly used biomaterial in tissue engineering are designed, based on their physicochemical properties, thus achieving precise control over mechanical strength, compliance, porosity and degradation kinetics. Biofunctional signals are added to scaffold by tethering, immobilizing or supplementing biofunctional macromolecules such as growth factors, directly to scaffold material. The challenge in tissue engineering remains to find correct balance between biofunctional and physical properties of scaffold material for each application. Cells are often implanted or 'seeded' into an artificial structure capable of supporting three-dimensional tissue formation. These structures, typically called scaffolds. Functional restoration of articular cartilage remains a challenge and none of the existing treatment regimes gives a consistently good outcome. The major sources of

stem cells for tissue engineering are-Embryonic stem cell and adult stem cell

Development of cartilage-In embryogenesis, most of skeletal system is derived from mesoderm germ layer. Cartilage is derived from condensed mesenchyme tissue which differentiates into chondrocytes and begins secreting the materials that form matrix. Early in fetal development, greater part of skeleton is cartilaginous. As the cartilage is afterwards replaced by bone, it is called temporary. In contrast, cartilage in joints remains unossified during whole of life and is called permanent. 2 Genes are of current interest in chodrogenesis; type 2 collagen gene and CD-RAP gene. Type 2 collagen is found in all cartilages and is essentially used to define the phenotype of tissue. A precursor form of cartilage type 2 collagen is type 2 procollagen synthesized by chondroprogenitor cells. This form of type 2 procollagen binds to bone morphogenetic proteins and acts a regulator of cartilage induction in extra cellular matrix. Second gene CD-RAP (cartilage derived retinoic acid sensitive protein) was isolated as major protein influenced by retinoic acid. CD-RAP is very specific to cartilage at all ages. The CD-RAP gene has proven to be very useful for investigation of cartilagespecific gene expression, revealing a number of factors that are important for positive and negative regulation of cartilage genes such as AP-2, Sox 9, def-1 and VSF.

Embryonic stem cell (ES)-Lie inside the inner cell mass of blas-

tocyst, which forms about 2-5 days after fertilization. The cells of inner cell mass are pluripotent and capable of changing into any cell of the body.Pluripotent embryonic stem cells have complete potential for all primary germ layers such as ectoderm, mesoderm and endoderm (Fig-4). Recent developments in human ES have offered a challenge to develop strategies for understanding basic mechanism which play a key role in differentiation of stem cells into specific cell types for their application in regenerative medicine. A micro mass culture system was developed to induce differentiation of ES cells into chondrocytes Toh WS et al 11 compared chondrogenic differentiation of human embryonic stem cells through EB direct plating outgrowth system and EB derived high density micromass systems under defined serum free conditions and demonstrated that cell to cell contact and BMP-2 treatment enhanced chondrocyte differentiation which resulted in formation of cartilaginous matrix rich in collagens and proteoglycans. They provided a 3D model system using human embryonic stem cells to delineate gene function in lineage commitment and restriction of chondrogenesis during embryonic cartilage development. Koay EJ et al <sup>12</sup> chondrogenically differentiated human embryonic stem cells through the use of chondrogenic medium with 2 growth factors TGFâ3 followed by TGFâ1 plus insulin like growth factor. They also extended use chondrogenically differentiated cells for cartilage tissue engineer-

ing through a scaffoldless approach called self assembly which was conducted in two modes with embryoid bodies or suspension of cells enzymatically dissociated from embryoid bodies. Cells in musculoskeletal system can respond to mechanical stimuli, supporting tissue homeostasis and remodeling. Scientist have evaluated the influence of dynamic mechanical compression on chondrogenesis of bone marrow derived mesenchymal stem cell and embryonic stem cell <sup>13</sup> When appropriately directed into chondrgenic lineage, mechanical stimulation is beneficial for further differentiation of cells. Oliver ENet al14defined a method to differentiate human embryonic stem cells into mesenchymal stem cells that don't require the use of feeder layers. The cells obtained were morphologically similar to bone marrow mesenchymal stem cells, were contact inhibited and could be grown in culture for 20-25 passages. Thus the ability to produce mesenchymal stem cells from human embryonic stem cells can prove useful to produce large amounts of genetically identifiable and modifiable mesechymal stem cells which can be used to study biology of mesenchymal stem cells for therapeutic applications. Thus human embryonic stem cells have the potential to self renew and generate multiple cell types, producing critical building blocks for tissue engineering and regenerative medicine.

Advantages of embryonic stem cells-Have unlimited abil-

ity to proliferate in vitro and more likely able to generate broad range of cell types through directed differentiation; Advantageous for transplantation purposes if they don't trigger immune rejection. The immunological status of human ES derived cells has not been studied in detail and it is not known how immunogenic ES derived cells might be. The immunogenicity of cell depend on it's expression of class1 major histocompatibity antigens which allow body to distinguish it's own cells from foreign tissue. Immunological rejection of ES derived cells can be avoided by genetically engineering ES cells to express MHC antigen of transplant recipient or by using somatic cell nuclear transfer technology

Somatic cell nuclear transfer technology (Fig-4)-Nucleus is removed from one of the transplant patient's cell such as skin cell and injected into oocyte. The oocyte thus fertilized can be cultured in vitro into blastocyst stage. ES cells could be subsequently derived from it's inner cell mass and directed to differentiate into desired cell type.

Disadvantages of ES cells -Undifferentiated ES cells can induce teratoma formation and Ethical concerns

Adult stem cells -Adult mesenchymal stem cells have been isolated from several tissue including bone marrow<sup>15</sup>, synovial membrane<sup>16</sup>, perioteum<sup>17</sup> and articular cartilage<sup>18</sup>. These cells can be extensively expanded in culture and effectively cryopreserved, while maintaining their phenotype and multilineage differentiation potential. The

chondrgenic potential mesnchymal stem cell investigated19 being immunomodulatory function of mesenchymal stem cell is being evaluated as possible therapy graft versus disease.Conventional methods for regulating the differentiation of stem cells are largely based on the use of biological agents such as growth factors. A low molecular weight synthetic inhibitor of RAR á and â was able to induce chondrogenic potential of mesenchymal stem cells<sup>20</sup>.Functional suitability and phenotypic stability of ectopic transplants are crucial factors in clinical application of mesenchymal stem cell for articular cartilage repair and might require a stringent control of chondrogenic differentiation<sup>21</sup> Recent reports have shown the superiority of mesenchymal stem cells from synovial membrane for cartilage formation in vitro when compared with mesenchymal stem cells from other sources including bone marrow and periosteum<sup>22</sup>. However it is not known whether this difference is inherent to the cells or due to heterogeneity of the mesenchymal stem cell population with possible contamination by mature or committed cell types like osteoblasts in bone marrow or chondrcytes in synovial membrane. It remains to be investigated whether this superiority in cartilage formation of synovial membrane derived cells is also observed in vivo in appropriate animal models of joint surface repair. Scientists have also used periosteum derived progenitor cells to differentiate into cartilage using atelocollagen as a carrier

and in presence of transforming growth factor  $\hat{a}3^{23}$ .

"Niche" of stem cells-Joint environment may be a source of signaling to prime chondrogenesis in mesenchymal stem cells. This is supported by studies in both animal models and humans<sup>24</sup> in which joint surface repair was obtained by implanting undifferentiated mesenchymal stem cells. Thus adult stem cells could provide a vehicle for gene therapy and genetically engineered human adult stem cells have shown success in treatment of genetic disease.

Advantages of adult stem cell

- No transplant rejection
- More easily differentiated than embryonic stem cells
- Less risk of tumor forma

Disadvantages of adult stem cell

- Adult stem cells not found in all tissues and difficult to isolate from adult tissue
- Limited capacity for proliferation and affected by aging

Umbilical cod blood stem cell-Hopes for treating disease with stem cells from umbilical cord received a major blood has boost, following discovery of primitive cells with clinical potential matching that of embryonic stem cells. The umbilical cord stem cells are not quite as primitive as embryonic stem cells, but more versatile than adult stem cells. Scientists have differentiated mesenchymal progenitor cells into osteogenic lineage and thus provide alternative source for cell based therapies and tissue engineering strategies 25.

Advantages of umbilical cord blood stem cells

- Have higher conc. of blood marrow stem cells, so smaller amount of stem cells needed.
- Less immunogenic-only 3 of 6 loci match of HLA required for cord blood transplant as compared to adult blood stem cells where all 6 HLA matching required

Disadvantages of umbilical cord blood stem cells

- Mother's consent required for allogenic (stem cells from other donor) transplant.
- For autologous (donor and recipient are same) transplant blood banks needed for storing of umbilical cord blood for future therapeutic use.

Conclusions-Management of chondral lesions in osteoarthritis remains a challenge. The study<sup>26</sup> investigated the efficacy of periosteal graft, osteochondral autograft, autologous chondrocyte and mesenchymal stem cell transplants in treatment of chondral lesions in animal models. Results showed that cultured chondrocytes and mesenchymal stem cells had comparable enhancing effects on repair of chondral defects in advanced osteochondritis whereas mosaicoplasty did well initially and periosteal graft did less favorably. Thus stem cells hold great promise for regenerative medicine. Future research will focus on

 Providing adequate source of cells for transplantation and bioartificial tissue construction and to determine ways to prevent these cells from coming under attack by immune system.

- Developing new and better material to build better bionic devices and bioartificial constructs and to stimulate regeneration in vivo.
- Determining how many tissues of the body might contain reserve cells for regeneration in vivo
- Analyzing the molecular differences between cells and environments for regenerating versus non regenerating tissues.
- Understanding the factors and mechanisms involved in proliferation and patterning of regenerating tissues.

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Normal and Arthritic Joints

Figure-1



Figure-2



Figure-3

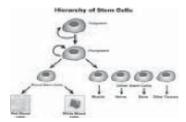


Figure-4

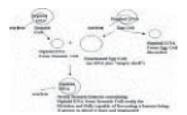


Figure-5

# Neuroimaging

Development of modern techniques-In 1927 Egas Moniz, professor of neurology in Lisbon, introduced cerebral angiography, whereby both normal and abnormal blood vessels in and around the brain could be visualized with great accuracy. In its early days this technique likewise carried both immediate and long-term risks, many of them referable to deleterious effects of the positivecontrast substances that were used for injection into the circulation. Techniques have become very refined in the past few decades, with one in 200 patients or less experiencing ischemic sequelae from the procedure. As a result, cerebral angiography remains an essential part of the neurosurgeon's diagnostic imaging armamentarium and, increasingly, of the therapeutic armamentarium as well, in the neurointerventional management of cerebral aneurysms and other blood-vessel lesions and in some varieties of brain tumor.

Computerized tomography-With the advent of computerized axial tomography (CAT or CT scanning), ever more detailed anatomic images of the brain became available for diagnostic and research purposes. The names of Oldendorf (in 1961) Godfrey Newbold Hounsfield and Allan McLeod Cormack (in 1973) are associated with this revolutionary innovation, which enabled much easier, safer, non-invasive, painless and (to a reasonable extent) repeatable neuro-investigation. Cormack and Housenfield won the Nobel Prize in Physiology or Medicine in 1979 for this work.

Radioactive neuroimaging-Early techniques such as xenon inhalation provided the first blood flow maps of the brain. Developed in the early 1960's by Niels A. Lassen, David H. Ingvar and Erik Skinhøj in southern Scandinavia it used the isotope xenon-133. Later versions would have 254 scintillators so a two-dimensional image could be produced on a color monitor. It allowed them to construct images reflecting brain activation from speaking, reading, visual or auditory perception and voluntary movement.Soon after the invention of CAT, the development of radioligands started the functional imaging revolution. Radioligands either remain within the blood stream or enter the brain and bind to receptors. Radioligands are either single photon or positron emitters. This is how single photon emission computed tomography (SPECT) and positron emission tomography (PET) got their names. Edward J. Hoffman and Michael Phelps developed the first human PET scanner in 1973.Functional imaging took a large step forward with the development of oxygen-15 labelled water (H<sub>2</sub>15O, or H20-15) imaging. H20-15 emits positrons and creates images based on regional blood flow within the brain. Since active neurons recruit a robust blood supply, H20-15 PET allowed investigators to make regional maps of brain activity during various cognitive tasks. Later, a more common sort of functional imaging based on PET scans used FDG, a positronemitting sugar-derivative which is distributed in the brain according to local metabolic activity.

# Metastatic Spinal Cord Compression: and it's Management

# Recent Advances

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etastatic spinal cord compression is a devastating complication occurring in 5-10% of cancer patients.1 Comprehensive evaluation and emergency intervention are imperative to prevent the debilitating consequences of paralysis and loss of sphincter functions. The overall frequency of spinal cord compression in adult patients with history of cancer is roughly 5%.1 At autopsy it has been identified in 5%-10% of the cancer patients. A second episode of malignant spinal cord compression occurs in 7%-16% of the cases. Cord compression is more frequent in males than in females. The comcancers producing cord compression are lung, breast, prostate, colon, renal cell carcinoma, melanoma and sarcoma,<sup>2</sup> In children the frequency of metastatic spinal cord compression is roughly 4%-5.5%. Neuroblastoma, Ewing's sarcoma, rhabdomyosarcoma, osteosarcoma, lymphoma and leukemia are the usual primaries. The vertebra which is most commonly affected is the thoracic vertebra in 60-80% of the cases, followed by the lumbar vertebra in 15-35% and cervical vertebra in 4-15% of the cases. Pathological fracture dislocation is more common in the cervical vertebra. The dependent position of the head, wider range of neck movements, smaller size of the cervical ver-

tebra and the lack of rib cage as a supporting structure render them vulnerable to mechanical disruption. Most patients have disease confined to 1 or 2 adjacent vertebrae, while 30% show evidence of metastasis at a non contiguous site. Multiple sites of involvement are seen in 25 – 50% of the cases.

Classification of spinal metastasis-Spinal metastasis is classified according to anatomic location into extradural (95%) and intradural (5%) metastasis. Intradural metastasis is further classified into extramedullary (4.5%) and intramedullary (0.5%) metastasis.

Pathophysiology-Vertebral body metastasis result from hematogenous dissemination of tumor cells which have tropism for vertebral bone marrow. The metastasis grows more frequently in the more vascularised marrow of the posterior part of the vertebral body. Tumor obliterates the marrow space and expands into the epidural space causing compression of the epidural venous plexus and impinges on the anterior thecal sac. Cord compression can also be caused by destruction of the cortical bone by the tumor, resulting in vertebral body collapse and displacement of the bony fragments against the spinal cord. Less commonly, invasion of the tumor from para-aortic nodes or paraspinous masses through the vertebral foramen can compromise the cord from a postero lateral direction. Posterior thecal sac compression due to metastasis in the posterior neural arch is less common. Blood borne intramedullary metastasis, which is very rare, can cause compression of spinal cord parenchyma from within. (Fig-1)

Stages in spinal cord compression-The first stage in spinal cord compression is extension of the tumor into the epidural space resulting in compression of the epidural venous plexus. This leads to venous outflow obstruction and venous stasis resulting in vasogenic edema. Vasogenic edema coupled with mechanical compression of the cord causes rapid loss of blood flow in the peripheral arterioles and capillaries resulting in ischemic infarction and necrosis of white matter (with relative sparing of grey matter). As a result of ischemia and necrosis, inflammatory mediators like prostaglandins and vascular endothelial growth factors are released, which in turn promote vascular permeability and edema. (Fig-2)

Diagnostic evaluation-Clinical symptoms that most commonly arouse suspicion of possible spinal metastasis is local or radicular distribution of pain (70-95% of patients) followed by weakness, numbness and progressive disturbance in balance. <sup>3</sup> Autonomic symptoms are a late mani-

festation of spinal cord compression. Neurological examination reveals absent or decreased motor, sensory, reflex and autonomic functions below the level of the lesion. Absent perineal and anal reflexes and painless overflow incontinence indicates imminent cord transection.

Plain X-ray-Although plain Xrays are widely used as an initial screening investigation, a radiolucent defect is visualized only when 50% of the vertebral body cortical bone is destroyed. However some abnormality is detected by plain X-ray in up to 90% of symptomatic metastasis.4 Vertebral body collapse or reduction in height of the vertebral body, lytic or sclerotic lesions involving the pedicles (winking owl's sign) and transverse processes, absent visualization of spinous process, paraspinous soft tissue shadow, pathological fracture- dislocation are the characteristic plain X -ray findings. (Fig-3) Posterior or postero-lateral compression due to certain paraspinous masses (as is common in lymphoma and pediatric malignancies) invading vertebral foramen, may not be detected in plain X-ray.

Magnetic resonance imaging-MRI is the gold standard for the diagnosis of spinal cord compression.<sup>5</sup> The location, extent and geometry of cord compression are identified in three planes: coronal, sagittal and transverse. MRI has a sensitivity of 93%, specificity of 97% and diagnostic accuracy of 95%.<sup>6</sup> Tumor appears hypo-intense on T1 weighted images relative to marrow and hyper-intense on T2 weighted images.<sup>7</sup> (Fig-4) MRI

with Gadolinium contrast is required for demonstrating paravertebral tumor, intramedullary metastasis and leptomeningeal involvement.<sup>8</sup> Because of the high probability of multiple non-contiguous lesions, screening of the entire spine, with sagittal sequences, followed by more detailed axial images through areas of abnormality, is desirable.<sup>9</sup>

Computerized Tomography-In the pre MRI era, CT scan with myelography was the investigation of choice for the detection of spinal cord compression. 10 CT is superior to MRI in evaluation of bone destruction and vertebral instability. So CT is mandatory before vertebral body resection or surgical stabilization of vertebral column. In patients with unknown primary, a CT guided FNAC can be performed but misdiagnosis is as high as 20%. CT scan is inferior to MRI in all other aspects.

Myelography-It was the standard method for establishing the level of spinal cord compression prior to the widespread use of MRI. Level of lesion is indicated by blockage of radiographic contrast metrizamide.<sup>5</sup> The need for multiple invasive subarachnoid punctures to demonstrate multiple sites of compression and the possibility of neurological deterioration which can occur in up to 25% of patients are disadvantages.<sup>11</sup>

Bone scan-Bone scan detects unsuspected sub clinical metastasis in the entire skeletal system in a single image. However bone scan is not mandatory before initiating treatment. It lacks specificity and in 30% of the cases

bone scan is positive for benign lesions. <sup>12</sup> Posterior and posterolateral involvement due to neuroforaminal invasion are not identified. Primarily osteolytic lesions as seen in multiple myeloma and lymphoma are also not identified since it depends on radioisotope uptake at sites of osteoblastic reaction at the metastatic foci.

Positron emission tomography-PET scan detects metabolic changes in the spinal cord following spinal cord compression and also differentiates osteoporotic fracture from pathological compression fracture.<sup>13</sup> Its current role in malignant spinal cord compression is yet to be defined. Prognostic factors- The strongest predictor of outcome is the pre-treatment degree of neurological dysfunction.<sup>14</sup>

Pre-treatment statusImprovement
Minimal dysfunction 80 – 100%
Para paresis 30 – 65%
Paraplegia 10 – 15%

The pretreatment neurological status also influences the survival. Patients who were ambulant before treatment had a median survival of 8 months while patients who were nonambulant had a median survival of only 4 months. 15 Ambulation after treatment was also a strong predictor of survival. Patients who were ambulant after treatment had a median survival of 9 months while patients who were nonambulant after treatment had a median survival of 1 month. 15 <sup>16</sup>Histology of primary tumor greatly influenced survival, ambulation after treatment and the degree of neurological recovery. Patients with favourable histologies like breast, prostate and

small cell lung cancer had a better prognosis than patients with unfavorable histologies like non small cell lung cancer, gastrointestinal malignancies and unknown primaries.15 In a prospective study by Marazano et al, the median survival in patients with favorable histologies was 10 months and 3 months in the unfavorable histology group. Also, patients with favorable histology more frequently recovered their gait and bladder dysfunction.<sup>17</sup>The duration of development of neurological deficits was a strong predictor of neurological recovery after treatment. 80% of the patients who were ambulatory after treatment had gradual onset of symptoms (> 14 days) while only 30% of the patients were ambulant after treatment if they had a rapid onset of symptoms (<14 days). A third category of patients who had a very rapid development of neurological symptoms (<48hours) had the worst prognosis. Only 7% of these patients recovered their neurological function. 15

Factors predictive of low recurrence rate were preoperative ambulatory status, favorable tumor histology, tumor in cervical spine, less number of affected vertebral bodies, complete resection and elective surgery.<sup>9</sup>

Treatment -The suspicion of cord compression requires immediate evaluation and treatment. Any delay in initiating treatment is associated with deterioration in motor and autonomic functions. Treatment usually entails a multidisciplinary approach. Corticosteroids-Corticosteroids play a very important role in the

treatment of neurological dysfunction resulting from cord compression. Dexamethasone and methylprednisolone are the commonly used corticosteroids. Dexamethasone is preferred as it has negligible mineralocorticoid activity. The mechanism of action of steroids is that it reduces edema, inhibits prostaglandin E2 and decreases specific gravity of the compressed cord. Dexamethasone down regulates vascular endothelial growth factor [VEGF] expression in smooth muscle cells and prevents cytoskeletal changes associated increased vascu1ar permeability. Although controversial, current recommendation is to give intravenous bolus of 10mg dexamethasone followed by 4mg every 6 hours tapered within three days.18 However, if the patient is ambulant with no signs of cord compression and presents only with pain and radiculopathy, steroids are not indicated. They are also not indicated during radiotherapy unlike its use in brain to prevent acute radiotherapy complications.19 Sorenson et al conducted a prospective randomized trial of high dose dexamethasone versus no corticosteroid therapy.20 81% of the patients in the corticosteroid group and 65% of the patients in the no steroid group were ambulant after treatment. A prospective trial by Vecht et al studied high dose bolus (100mg) versus low dose bolus (10mg) followed by conventional dose of maintenance steroid.21 This trial demonstrated no significant benefit for the high dose bolus. Serious toxicities from high dose dexamethosone have been re-

ported in up to 14% of the patients. Currently there is no role for high dose steroids in the management of spinal cord compression. Maranzano et al demonstrated that the use of steroids can be safely avoided in patients with no neurological dysfunction, or with radiculopathy only. <sup>17</sup> Only patients with demonstrable neurological dysfunction benefit from steroids.

Surgery-Surgery has an evolving role in the treatment of spinal cord compression. The palliative goals of surgery are control of pain, preservation and recovery of neurological functions aiming for restoration of mobility. Indications of surgery are -Spinal instability; radio resistant tumors like melanoma, renal cell carcinoma and sarcomas; Previously irradiated patients with progression of deficits or tumor growth on imaging; Rapidly progressing neurological dysfunction; unknown primary [establishing tissue diagnosis with CT guided FNAC remains an option]. A relative indication is circumferential epidural tumor which is likely to worsen during radiotherapy. The presence of distant metastasis to extra spinal sites and active disease at primary site are not contraindications to spine surgery. Spinal instability has not been clearly defined. Significant kyphosis, subluxation, and retropulsion of bone fragments into the spinal canal causing compression, are indicators of spinal instability. Pathological fracture per se is not an indication for spinal instability. The role of surgery has evolved from the initial indiscriminate use of laminectomy in the 1970s which provided suboptimal decompression of the ventrally and laterally located tumor to more aggressive cytoreduction and decompression via ventral transcavitory and dorsolateral transpedicular approach which are intrinsically combined with newer techniques of spinal stabilization. These techniques have allowed 76-100% improvement in pain, and the percentage of ambulatory patients in modern series is as high as 80%.9Surgical decompression of spinal cord should be approached from the side of the impinging mass. Laminectomy should be reserved for removal of tumors affecting the posterior elements alone and intradural metastasis, both of which are relatively rare. Findlay noted that 25% of the patients with vertebral collapse treated with laminectomy sustained major neurologic deterioration in relation to their surgery.<sup>22</sup> There are several trials comparing surgery and radiotherapy. In a large retrospective study from Memorial Sloan - Kettering, Gilbert et al found no advantage to the addition of laminectomy to radiation in the treatment of cord compression.3 Of the 235 patients evaluated, 46% of the laminectomy group were ambulatory after treatment as compared with 49% in the irradiation alone group. Other trials have also reported that laminectomy adds little to the efficacy of radiotherapy. Young et al reported a small prospective study of laminectomy and radiation versus radiation alone and there was no difference in the outcome.23 Moreover, metastatic disease must be focal since spinal stabilization requires a founda-

tion of solid rather than tumor infiltrated bone at two adjacent spinal levels rostrocaudally. Complication rates from surgery range from 10% to 52% with mortality rates as high as 13% which are related to the medical and oncological conditions.9 There are few data comparing radiation with anterior decompression and this procedure combined with post operative radiotherapy may be superior to radiotherapy alone. Moore and Uttley reported their results with anterior decompression and stabilization in 26 patients with vertebral body collapse.24 Ambulation was achieved in 60% of the patients and pain relief was obtained in 70% of the patients. Patchell et al, in a recent multi-institutional randomized prospective trial of direct decompressive surgical resection plus radiotherapy versus radiotherapy alone [30 Gy delivered in 10 fractions in both groups], reported a statistically significant benefit for the surgery and radiotherapy group compared with the radiotherapy alone group. 25 The post treatment ambulatory rate in the surgery and radiotherapy group was 84% (42/50) compared to 57% (29/ 51) in the radiotherapy alone group (P=0.001). Also post treatment ambulatory patients retained the ability to walk longer in the surgical group (median of 122 vs. 13 days, P=0.003). Moreover, 62% (10/16) of the patients in the surgery group who were non-ambulatory before treatment regained the ability to ambulate compared with only 19% (3/16) in the radiotherapy group (P=0.012). Median survival in the surgery group was 126 days relative to 100 days in the radiotherapy group (P=0.033).

Vertebroplasty and kyphoplasty are minimally invasive techniques of stabilizing compression fractures by direct percutaneous injection of polymethyl methacrylate bone cement [PMMA] via the pedicles. Although epidural compression is a relative contraindication, they are valuable adjuncts along with radiotherapy for rapid control of pain. <sup>26</sup>

Radiation therapy-Radiation plays a pivotal role in the treatment of epidural cord compression. The goals of treatment are cytoreduction of the tumor resulting in decompression of the spinal cord and nerve roots and control of pain. Radiation reduces pain in 70% of the patients, improves motor function in 45-60% and reverses paraplegia in 11% to 21 %.<sup>27</sup>

Target volume-The standard radiation portal encompasses the site of cord compression with a 5cm craniocaudal margin (two vertebral bodies above and below the gross disease). The radiation portal should be centered at the site of epidural compression. Recurrences after irradiation occur in 16% to 25% of the patients and in these patients, 64% of the recurrences are within two vertebral bodies of the site of compression.<sup>28</sup> Accordingly the target volume should encompass these vertebrae. Adjacent sites of paraspinal masses should be encompassed in the treatment port. In the cervical region, opposed lateral fields are appropriate in order to avoid the pharyngeal mucosa. In the thoracic spine single posterior fields are used. Radiation dose is prescribed to a

depth corresponding to the anterior aspect of the vertebral body. Alternatively differentially weighted AP-PA fields can also be used. In the lumbar region AP-PA parallel opposed fields are often used because of the greater depth of cord and cauda equina which makes the entry dose excessively high for single PA fields. The recommended radiation dose for conventional external beam radiotherapy is 30Gy in 10 fractions. There are several trials of various fractionation regimens in spinal cord compression. Greenberg et al reported a 57% ambulation rate in patients treated with 500cGy per fraction x 3days followed by 4 day rest and 300 cGy per fraction x 5days.<sup>29</sup> Maranzano et al conducted a prospective study comparing two fractionation regimens 30Gy/ 10fr or 500cGyX 3, 4-days rest, 300cGy x 5 fractions.<sup>17</sup> Ambulation was attained in 76% of the patients. However complications were less in the smaller fraction size arm. Maranzano et al also studied 800cGy x 2 fractions in patients with ECOG performance status of  $\geq 2$  and short life expectancy.<sup>30</sup> Of the 49 evaluable patients, pain relief was achieved in 67% while motor function improved in 63%. These results were numerically inferior to those achieved with 30Gy in ten fractions. The author concluded that 800cGy x 2 may be appropriate for bed ridden paraplegic hospice patient requiring palliation of pain. Rades et al studied the role of dose escalation (40Gy in 20 fr) .Of the 922 evaluable patients, escalation of dose to greater than

30 Gy did not improve outcome in terms of motor function ,local control or survival and therefore doses greater than 30 Gy are not recommended.<sup>31</sup> Intensity modulated radiotherapy and conformal radiotherapy are increasingly used in the treatment of malignant cord compression in order to reduce late normal tissue toxicity. Intraoperative radiotherapy uses electron beams or high dose rate brachytherapy to treat tumor volume, while lead or gold foil are used to shield the spinal cord. I 125 paraspinal implants after surgical resection of the tumor is also a novel method to reduce normal tissue toxicity. Leland et al found this procedure to be well tolerated with durable control and ambulation.32 Image guided helical tomotherapy is being evaluated in the re-treatment of irradiated spinal cord metastasis.<sup>33</sup> Spinal stereotactic radio surgery involves achieving very high doses of radiation in one or two sessions in a very accurate and highly conformal manner using multiple beams either using a body stereo tactic frame for immobilization or using movement compensating robotic arms as in CyberKnife® (Accuray Incorporated, Sunnyvale, CA). This avoids unnecessary exposure of radiation to normal tissues and hence, does not need fractionation. Although not extensively tested, and still considered experimental by some, it has been shown to achieve durable pain relief and up to 100% tumor control in previously un-irradiated patients.34

Chemotherapy-Most reports on the efficacy of chemotherapy on spinal cord compression are anecdotal. Chemotherapy might be appropriate where radiation related bone growth retardation is an overriding concern as in pediatric spinal cord compression .Chemotherapy can also be used concurrently with radiation. Chemotherapy can be used in adults who are not candidates for surgical or radiation therapy but have chemo-responsive tumors lymphoma, myeloma germ cell tumors.35 Bisphosphonates are used as they significantly reduce the skeletal morbidity associated with other bone metastasis. However bisphosphonates did not reduce the rate of spinal cord compression.36

Conclusion-Radiotherapy currently plays a pivotal role in the management of spinal cord compression. Radical anterior decompressive surgery and reconstructive spinal stabilization and postoperative radiotherapy could be superior to radiotherapy alone, and could become the standard of care in the near future. Early detection and treatment of spinal compression before occurrence of severe neurological deficits is critical in preserving ambulation.

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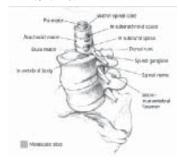


Figure-1, Showing sites of metastatic disease in relation to the cord and dura.

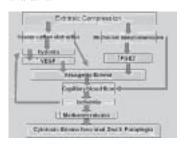


Figure-2, Pathophysiology of metastatic spinal cord compression.



Figure-3, Winking owl sign – destruction of pedicle.



Figure 4, T1Weighted MRI showing vertebral body metastasis causing cord compression.

# Practical achievements of functional brain imaging

In early 2000s the field of brain imaging reached the stage where limited practical applications of functional brain imaging became feasible. The main application area is crude forms of braincomputer interface.

In 1998 scientists in Emory University, Atlanta and University of Tuebingen, Germany implanted a tiny glass electrode into the brain of a 56 year old man parayzsed after a stroke that allowed the patient to control a pointer on computer display.

In 2000 Miguel Nicolelis from Duke University, North Carolina implanted about one hundred electrodes into brains of an owl monkey and used the recorded signals to muscles to control a robot arm. The signals were also transferred over the Internet to control a similar robot hand in MIT, 600 km from the monkey.

In 2001 researchers at the European Commission's Joint Research Centre used Adaptive Brain Interface, the system they developed to interpret the signals from a plastic cap put on the user's head with attached electrodes that picked electromagnetic signals from the brain. The user, Cathal O'Philbin, a 40-year-old paraplegic, was instructed to think about a rotating cube, moving his left arm (which is paralyzed) and relaxing mentally in between. These three distinct patterns were used to control the cursor on the screen. After several hours Mr. O'Philbin trained the system to recognize his mental states and managed to type "Arsenal Football Club" using his brain alone

2002 team a neurosurgeons from Brown University, Rhode Island implanted electrodes in the brains of three macaques. The chips with 7 to 30 electrodes were implanted into the motor cortices. The scientists calibrated the chips when the animals used joysticks to play a computer game, then disconnected the joysticks and used the signals intercepted by the electrodes to control the object on the screen directly.

In 2004 a team of scientists from California Institute of Technology demonstrated decoding of high level cognitive brain signals, when they managed to predict where the monkeys were planning to reach in their visual field and also what reward (water or juice) the monkeys expected to receive. The monkeys were trained to think about the particular point they were planning to reach without looking there during the experiments.