Nuclear Medicine Technique I

RAD 355

Lecture’s Title: INTRODUCTION TO NUCLEAR MEDICINE

Dr. Mohammed Emam
Overview

- Introduction
- Imaging Principles Radiotherapy
- An Approach to Image Interpretation
- Following chapters Overview

INTRODUCTION

Nuclear medicine encompasses both therapeutic and diagnostic modalities that support practically every field of medical endeavor. Despite changes in referral patterns and the advent of managed care, nuclear medicine studies remain among the most cost-effective for the diagnosis and management of a variety of diseases. Radiographic, ultrasonographic, and MR studies provide high spatial resolution and important anatomic or structural information from which pathologic processes are inferred. On the other hand, nuclear medicine studies provide high functional resolution and provide physiologic and functional information not otherwise available.

Anatomic imaging can measure the dimensions of a spot, but functional imaging can show whether it is active and whether it is malignant or not (Fig. 52.1) With this being the decade for advancing functional imaging, many new, important techniques have become commonplace in the clinical environment.
PET-CT and now SPECT-CT have improved the sensitivity and specificity for neural, cardiac, and oncological imaging. PET-CT has greatly improved patient throughput, tumor staging, and evaluation of tumor response to therapy (Fig. 52.2). Molecular medicine and molecular imaging promise to bring applications of genomics and protein messaging quickly into the clinical arena. We now have the ability to follow gene therapy as well as stem-cell therapy through their introduction into the patient.
Lymphoscintigraphy is helping surgeons to better stage melanoma and breast cancer and has significantly decreased patient morbidity following nodal staging procedures. Hand-held probes allow better localization of sentinel nodes as well as of small difficult lesions identified on PET FDG (fluorodeoxyglucose) scans. New therapies include antibody therapy for lymphoma, and research is being advanced for breast cancer antibody therapy, I-131 MIBG and yttrium (Y-90)-labeled octreotide.
The material in this section is intended to provide an overview of the specialty and at the same time serve as the basis of review for those residents preparing for board examinations. The information should also be useful to those who may not practice nuclear medicine regularly or may not have done so recently.
IMAGING PRINCIPLES

The basic principles of diagnostic nuclear radiology are simple to grasp, yet somehow seem to elude first-year residents as they are overwhelmed with information at the outset of their training. The concept of nuclear imaging is based on the external detection and mapping (emission image) of the biodistribution of radiotracers that have been administered to a patient. The knowledge of the normal patterns of uptake, distribution, and excretion permits us to make decisions concerning the presence or absence of disease.

Sometimes a radionuclide or radioisotope of a naturally occurring element essential to normal biologic function (e.g., Iodine-123) or an analog (e.g., Technetium-99m Pertechnetate, Tc-99m-O₄) is used without additional chemical alteration (Fig. 53.3).
More commonly, a radioactive isotope is combined with a physiologically “active” compound to create a radiopharmaceutical which can be administered intravenously, orally, or via direct injection. Thus Tc-99m-O$_4$ may be combined with a diphosphonate compound for skeletal imaging. If the same radioisotope is combined with an iminodiacetic acid derivative, the biologic distribution reflected by the images will be that of a biliary scan.
This simple concept is the foundation for imaging the biodistribution of radiolabeled blood cells, monoclonal antibodies, peptides, and energy substrates such as glucose and fatty acids. If this unifying principle can be kept in mind while reading the various sections on nuclear imaging, the diverse number and types of studies may seem somewhat less bewildering.
Radiotherapy is an extremely important arm of nuclear medicine and is critical to several areas of clinical medicine. The distinguishing feature of therapeutic radioisotopes and radiopharmaceuticals is that they are particulate emitters, with beta emitters being utilized much more commonly than alpha emitters. Beta particles only travel a short distance through tissues, depositing most of their energy within a couple of millimeters.

I-131 is utilized for benign thyroid conditions such as Graves’ disease, toxic adenoma, and Plummer disease or toxic multimodular goiter (Fig. 52.3). I-131 is also the primary treatment of choice for thyroid remnant ablation and metastatic thyroid cancer. I-131 MIBG and Y⁹⁰ octreotide are under evaluation for treatment of metastatic neuroendocrine tumors as well.
P-32 can be given intravenously for hematological disorders such as essential thrombocytosis, or in colloidal form for localized installation in arthritic joints for radiosynovectomy, in cystic tumors or into malignant fluid collections. Strontium-89 and Samarium-153 have proven effective in palliative pain management for patients with osteoblastic bone metastases. Radioimmunotherapy (RIT) with monoclonal antibodies is now being utilized for refractory lymphoma treatment with ibritumomab tiuxetan (Yttrium-90 Zevalin®) and tositumomab (I-131 Bexxar®) (Fig. 52.4).

RIT is also being studied for refractory metastatic breast cancer. A new form of radioembolotherapy (RET) is being utilized in conjunction with interventional radiology. After careful planning and dosimetry calculations, Y-90 microspheres are injected directly into selected hepatic arteries for treatment of unresectable hepatocellular or for metastatic liver disease.
FIGURE 52.1. PET-CT Scan of Brain. PET scan of the brain with FDG is fused onto CT scan and shows increased FDG metabolic activity (arrow), confirming the recurrence of glioblastoma after previous surgery and radiotherapy.
FIGURE 52.2. Maximum Intensity Projection (MIP) Image From Whole-Body PET FDG Scan. Whole-body PET CT scan was done for initial staging in breast cancer patient and demonstrates multiple areas of abnormal hypermetabolic foci, consistent with diffuse metastatic breast cancer.
FIGURE 52.3. Iodine-123 Thyroid Scan. The patient presented with symptoms and laboratory findings of hyperthyroidism. The scan shows diffuse, homogeneous enlargement and an increased uptake of 77%, consistent with Graves’ disease. She was then successfully treated with oral Iodine-131.
FIGURE 52.4. Indium-111 Zevalin ©Antibody Diagnostic Scan. Whole-body scan demonstrates normal biodistribution of the antibody agent and multiple foci of increased uptake, consistent with known B-cell lymphoma. The patient was then successfully treated with Y-90 Zevalin © radioimmunotherapy with good clinical and CT response.
AN APPROACH TO IMAGE INTERPRETATION

Obviously, a basic fund of anatomic, physiologic, and nuclear imaging knowledge is necessary in order to make intelligent diagnoses and differential diagnoses, based on nuclear medicine images. The suggested approach to image interpretation provided here will make more sense after reading the remainder of the nuclear medicine section, and for the resident will be of greater value after the second or third nuclear medicine rotation.
When preparing to discuss a case, it is first important to determine the radiopharmaceutical and therefore the type of study which may be as simple as reviewing the film margins or paperwork for textual information. It is poor form to ask, “What type of study is this?” when the information is readily at hand. At the same time, one may also glean important information about the age and sex of the patient, the site of injection, the temporal sequence when multiple images are present, the type of images (planar or tomographic, static, or dynamic), and patient orientation during imaging (right/left, oblique, posterior, upright/supine, etc.).
If the radiopharmaceutical information is not known, then the first step in analysis is based on determining the relative count density of the images. Typically, images of Tc-99m-O₄-labeled radiopharmaceuticals have relatively high count density. Many medium- and high-energy isotopes (Indium-111, Gallium-67, Iodine-131, etc.) have lower count density based on longer half lives and therefore lower administered dose.

This often results in relatively noisy images. A notable exception to this generalization is arterial flow studies performed with Tc-99m-labeled radiopharmaceuticals. Because these studies are performed as dynamic acquisitions at a typical rate of 1 to 5 seconds/frame, they too will have a low count density.
The number and type of images presented and the type of acquisition (e.g., PET, SPECT or planar) should be noted. If a series of frames are provided, the study is either a dynamic acquisition with the typical timing of seconds or minutes per frame, or possibly a series of SPECT image slices that will usually have more counts and appear somewhat smoothed because of the processing algorithms employed.

Next, study the biodistribution of activity and anatomy in the images: Is there evidence of cardiac or great vessel blood pool activity? Is skeletal activity present? What organs or structures are visualized? Are there obvious focal abnormalities? From a knowledge of the biodistribution evident on the images and a reasonable assumption about the likely radioisotope, one may make some conjecture as to the most likely radiopharmaceutical in use.
After determining the radiopharmaceutical and the type of study, proceeding with the rest of the analysis is fairly straightforward. Again, a basic knowledge of the normal biodistribution of the radiopharmaceutical and the usual indications for performing the study is required. Given these, plus a relatively rudimentary understanding of anatomy and physiology, one can “make the finding(s)” with relative certainty. A word of caution is in order. There are two common errors that continue to cause problems for each new generation of residents.

First, it is extremely difficult to “see what is not there.” Always “take attendance” and be certain that all organs and structures that should be “present” on a given study are visualized with their normal pattern and relative uptake of radiopharmaceutical. Next, frequently more than one finding of importance will exist. It is easy to suffer from “search satisfaction” and quit looking for additional abnormalities after one is found. A rigid approach to image analysis is required to prevent both of these errors.

When studying dynamic series such as arterial flow studies, Tc-99m-labeled red blood cell studies for GI hemorrhage localization, renal function images, and so forth, it is important to note the time per frame because you will need to make comments concerning the timing of the arrival of the radiopharmaceutical in various structures.
This information may be critical to image interpretation and is frequently overlooked by neophytes. Identifying changes from one frame to the next may be difficult. One approach to enhance and speed detection of abnormalities and asymmetries is to study the first frame or two relatively closely and then move directly to the last frame. Direct comparison of early and late images will demonstrate changes between the two most dramatically and will allow you to direct your attention to the appropriate areas on the intervening images and define the correct timing of events.

It is helpful to “back through” the images from last to first after identifying any abnormalities on the later images. This approach will rapidly identify with great temporal and anatomic accuracy the exact time of appearance and location of GI hemorrhage, for example.

An orderly approach to image analysis for static images is also required, but will vary based on the type of study in question. Here are specific techniques for some common studies that may be helpful.
**Skeletal Imaging.** Review the images provided with a “top–down” approach, addressing skeletal structures, first on the anterior view, then on the posterior view (Fig. 52.5). Note areas of increased or decreased activity without attaching strong clinical significance to them initially. Always comment on the renal activity that should normally be present and use this as a reminder to evaluate soft tissue activity for abnormal increases, decreases, and asymmetry. This type of approach works well with many of the whole-body imaging studies, although the biodistribution will vary.
**SPECT Myocardial Perfusion Imaging.** Always view the raw data images first, if available, and evaluate for quality control issues, artifacts, and ancillary or incidental findings (breast attenuation, motion, pacemaker artifact, pulmonary uptake, breast tumor, etc.). Always review the exercise data to confirm adequacy of stress or determine what, if any, pharmacologic agent was employed. Next review the short-axis slices, then the vertical long-axis slices, and finally the horizontal long-axis slices. Note the presence or absence of areas of decreased perfusion and whether they appear fixed or seem to change between stress and rest images.

Note the chamber size and whether or not it is more dilated at stress than rest. Attempt to confirm the presence of any defects in two planes. Then evaluate the wall motion, brightening, and thickening. Check the end diastolic and end systolic volumes. Evaluate the stress and rest data including the ejection fractions. Is the study normal or does it demonstrate reversible changes of ischemia? Does it demonstrate a fixed defect consistent with infarction or hibernating myocardium? Does it demonstrate poststress dilatation or decreased LVEF after stress?
**Ventilation–Perfusion Imaging for Pulmonary Embolus.** Always review the chest radiograph or chest CT first, if provided. If not initially available, comment that review of the radiograph is essential prior to making a definitive statement about the likelihood of pulmonary embolus. Review the perfusion study in its entirety first. Note the presence of any defects, their relative sizes (lobar, segmental, and subsegmental), and their locations. Attempt to confirm the findings in more than one view.

Once the number and location of the defects are known, attempt to match these defects in the corresponding areas on the ventilation study. Summarize the findings and segmental anatomy, verbally reciting the number and size of matched and mismatched defects. State that there is no evidence of pulmonary embolism (normal study) or offer a probability of pulmonary embolus based on the findings. Then determine if another study such as CT angiography may be needed.
**Hepatobiliary Imaging.** For this and any other study where flow studies and dynamic imaging are performed, studying the images in the order in which they were acquired is best: flow study first, then dynamic images using the approach outlined previously, and finally static images (right lateral or left anterior oblique views would be typical) if any. Note the temporal sequence of the arrival of the arterial bolus in the kidneys, spleen, and finally liver if an arterial flow study of the abdomen is provided.

With approximately 80% of hepatic blood flow arriving via the portal system, the liver should appear later than the other organs—if it does not, portal hypertension may be present.
Early flow to the gallbladder fossa implies significant inflammation. On the dynamic series, note the appearance of the early images, then study the later images: Are gallbladder activity and bowel activity present? If so, “back through” the images and note their first appearance.

Is activity visualized in the normal sequence of intrahepatic ducts, common hepatic duct, gallbladder, common bile duct, and duodenum? Is there activity in any areas other than expected—stomach, esophagus, or free spill into the peritoneum? Are there any focal accumulations of labeled bile in the liver, gallbladder fossa, or elsewhere?
For a situation in which a finding has been made but no explanation is readily apparent, it is helpful to contemplate the finding while considering a standard list of generic causes as well as mechanisms that might lead to the finding.

One such generic list uses the mnemonic, VINDICATE as follows: Vascular (any cause of increased/decreased blood flow, collagen vascular diseases); Infectious (always include TB, Fungal, HIV); Neoplastic (benign or malignant, primary or metastatic); Drug-induced (radiopharmaceutical preparation and QC, recent prior radiopharmaceutical administration or contrast study, thyroid hormone ingestion), Idiopathic (sarcoidosis, amyloidosis); Congenital, Artifact (related to patient, clothing, imaging equipment, computer processing, or film processing); Trauma; or Endocrine/metabolic (Paget disease, hyperparathyroidism, etc.).
If the physiologic mechanisms of radiopharmaceutical localization are understood, then mechanistic explanations for findings allow another route to a solution. Thus, from a mechanistic standpoint, increased activity on a bone scan is caused by either increased delivery of radiopharmaceutical to the bone or increased incorporation due to either increased osteoblastic activity or increased dwell time for extraction by normally functioning osteoblasts.

Reasons for increased delivery include the following: arterial injection, arteriovenous malformation, infection, tumor, localized inflammation due to trauma, increased use of a limb, neurologic reflex increased flow, and apparent increased uptake with actual reduced uptake in the contralateral body part. Reasons for increased osteoblastic activity include the following: normal growth in epiphyseal bone and enhanced repair in response to fracture, infection, and benign or malignant tumors. Increased dwell time may be caused by constricting clothing, tourniquets, venous obstruction, and lymphatic obstruction.
When analyzing a case it is best to follow your initial comments concerning the findings with a final image review as you verbally summarize what you believe to be pertinent to the diagnosis. It is not uncommon to realize only as the summary is presented aloud that a specific diagnosis is indicated or that the findings significantly limit the differential diagnosis.

The foregoing discussion is not meant to be all-encompassing and does not do justice to the entire spectrum of studies and diseases that will be encountered. However, it should provide a starting point for development of one’s own approach to image analysis and case-discussion skills. Consider using the images in each of the subsequent chapters as sample unknown cases and attempt to analyze them before reading the captions. This sort of practice will undoubtedly enhance one’s ability to take unknown cases with greater confidence and accuracy.
FIGURE 52.5. Whole-Body Bone Scan With Tc-99m methylene diphosphonate (MDP). The scan demonstrates multiple areas of increased uptake due to diffuse bony metastatic disease in this patient with prostate cancer.
FIGURE 52.6. Response to Therapy Demonstrated on Whole-Body PET FDG Maximum Intensity Projection Scans. A. Baseline scan shows extensive and metastatic disease in a patient with inflammatory breast cancer. B. Follow-up scan after two cycles of chemotherapy shows excellent early response to therapy which is a predictor of how the patient will ultimately respond.
As you will see in the following chapters, nuclear medicine offers several distinct advantages over traditional anatomically oriented imaging techniques. There is whole-body detection of disease with bone scans, WBC scans, I-131 metascan, I-123 MIBG, Ind-111 octreotide, and PET-CT. It can provide functional evaluation with computer analysis such as with radionuclide ventriculography, gated cardiac SPECT, renal scintigraphy, gallbladder ejection fraction, gastric emptying, esophageal transit, and thyroid uptake. Split function analysis can be done for kidneys, lung, and brain. Diagnostic evaluation is done with I-123 for thyroid nodules, PET FDG for pulmonary nodules, diuretic renography for ureteral obstruction, Tc-RBC for hepatic hemangioma, and Tc-SC for hepatic focal nodular hyperplasia.
Response to therapy is judged with octreotide, MIBG, I-131, and bone scan, but for early response to therapy, PET FDG has been shown to be the best and can be predictive of outcome (Fig. 52.6). Molecular processes can now be evaluated with molecular imaging techniques such as PET FDG, C-11 choline, F-18 fluorothymidine, and F-18 dopamine. Radiotracer techniques are commonly utilized for stem-cell tracking and in studying genomics and proteomics. Targeted radiotherapy techniques utilize many new forms of molecular targeting and more individualized therapies in the near future.
For this edition of the text, the nuclear medicine section has been thoroughly revised and updated with multiple new images and current references as needed. The inflammation and infection chapter has been completely rewritten. The oncology chapter has been completely rewritten to incorporate new molecular imaging information. A separate chapter on the rapidly expanding area of PET and PET-CT has been added. In every case, the authors have attempted to provide clear, concise, current, and useful information. I have no doubt that you will find that they have succeeded.
Floor is open for Questions and Discussion

Thank you