Clinical Aspects of General Nuclear Medicine

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Administered Activity and Patient Radiation Exposure (Dose)

In gamma camera nuclear imaging, a patient's radiation exposure depends on:

1. The radionuclide's physical half-life and photon energy(ies)
2. The radiopharmaceutical's biological distribution
3. The kinetics of localization and excretion (half-time)

Calculating the actual radiation exposure for an individual patient is complex and multifactorial, open to uncertainty and not routinely done in the clinical setting. Nonetheless, the simplest approach to reduce patient radiation exposure is three-fold:

1. Reduce the administered activity to the lowest amount possible
2. Employ maneuvers that promote excretion or impact favorably on the biological distribution
3. Judiciously choose and correctly perform the appropriate nuclear medicine imaging examination, including not performing the examination if it is not indicated or not likely to be helpful

Administered Activity and Image Quality

Reducing the administered activity of a radiopharmaceutical will reduce patient radiation exposure, but it will also affect the examination's imaging characteristics and may lower image quality.

In the simplest terms, reducing administered activity will lower the count rate. If the examination's other acquisition parameters are unchanged, this may result in reduced visibility of the organ(s) of interest, increased image noise and limited detection of disease. If imaging times are increased to compensate for lower count rates, then the examination may become more susceptible to patient motion artifacts. The impact of lower administered activities may be greater in certain classes of patients, such as those with large body habitus, in whom count rates are further reduced by soft-tissue attenuation. It must be noted that universally accepted guidelines that optimize imaging by accounting for body habitus, (e.g., employing weight-based administered activities or adjusting gamma camera acquisition parameters according to an individual patient's body type) do not exist; thus, care must be taken in order to maintain sufficient diagnostic image quality when using lower administered activities. The adverse impact of reduced administered activity on image quality can be mitigated by using new camera technologies and software reconstruction algorithms and techniques.[1] See Dedicated Solid State Cardiac Systems for Myocardial Perfusion Imaging.

Appropriateness Criteria, Practice Guidelines and General Nuclear Medicine

The most effective approach to reducing patient radiation exposure is eliminating diagnostic tests that are not likely to benefit the patient. Appropriateness criteria are evidence-based expert recommendations created to optimize imaging algorithms in order to improve patient outcomes, eliminate waste and reduce variations in clinical practice. Many clinical conditions that can be evaluated by general nuclear medicine imaging are included in the American College of Radiology Appropriateness Criteria®.

Overall gamma camera performance must be optimized by applying a rigorous Quality Assurance/Quality Control program. This is especially true when acquiring images from administered activities at the lower end of the recommended range. Nuclear Medicine accreditation programs (e.g., those of the American College of Radiology and the Intersocietal Accreditation Commission) promote proper gamma camera function and, in turn, optimal image quality.

Multiple professional societies have developed practice guidelines that address clinical and technical aspects of general nuclear medicine imaging examinations, including: ACR, Society of Nuclear Medicine and Molecular Imaging, European Association of Nuclear Medicine, American Association of Clinical Endocrinologists and American Thyroid Association.

Patient Radiation Exposure and Choosing the Appropriate Examination

It should be emphasized that when a physician uses diagnostic nuclear medicine imaging, the best strategy is two-fold: first, choose the imaging examination that will appropriately answer the clinical question, and second, perform that examination to the highest technical standards. Nuclear medicine imaging examinations are safe and effective; avoiding these examinations because they use small amounts of radioactivity, or choosing a particular examination solely because it uses less radiation than an alternative examination, can be detrimental to the patient (SNMMI Position Statement on Dose Optimization). Please refer to the physics section of this Image Wisely website for a more technical and detailed discussion of this topic in the article Appropriate Use of Effective Dose and Organ Dose in Nuclear Medicine.

Summary

Taken together, the fundamental Image Wisely goals in general nuclear medicine imaging are:

1. To select the appropriate examination
2. To use the correct radiopharmaceutical in the lowest appropriate administered activity
3. To optimize the imaging parameters, balancing patient radiation exposure against diagnostic effectiveness

Examples of Common General Nuclear Medicine Imaging Examinations and Performance Considerations

Seven common general nuclear medicine imaging examinations are presented below. Each table highlights key performance considerations and emphasizes the use of published practice guidelines and appropriateness criteria. The tables are not comprehensive guidelines, and they only address a limited number of clinical scenarios, but they illustrate how expert consensus opinion can be used to optimize the choice of radiopharmaceutical and imaging protocol.

I. Bone Scintigraphy
II. Parathyroid Scintigraphy
III. Thyroid Scintigraphy and Uptake
IV. Scintigraphy for Differentiated Papillary and Follicular Thyroid Cancer
V. Lung (V/Q) Scintigraphy
VI. Radionuclide Infection Imaging
VII. Hepatobiliary Scintigraphy

I. Bone Scintigraphy

Radiopharmaceuticals	^{99m}Tc diphosphonates (HDP, MDP)
Recommended Adult Administered Activity[1,2]	15-30 mCi (740-1,110 MBq) IV Higher doses may be considered in obese patients
Performance Considerations	Administer lowest activity in prescribed range Balance acquisition duration versus image quality
Maneuvers to Minimize Radiation Dose[1,2]	2 or more 8-oz glasses of water after administration Encourage hydration for 24 hours after the examination
Appropriateness Criteria[3,4]	**Metastatic Disease:** Indications vary based on the type of malignancy, stage of disease and symptoms. **Benign/Traumatic Lesions:** Often radiography is the initial examination of choice; those results determine the next imaging step.

II. Parathyroid Scintigraphy

Radiopharmaceuticals	^{99m}Tc sestamibi ^{99m}Tc sodium pertechnetate ^{123}I sodium iodide
Recommended Adult Administered Activity by Protocol:[5,6] ^{99m}Tc sestamibi Dual Phase ^{99m}Tc sestamibi/^{99m}Tc sodium pertechnetate Dual Tracer** ^{99m} Tc sestamibi/^{123}I sodium iodide** Dual Tracer	 20-30 mCi (740-1,100 MBq) IV 20-30 mCi (740-1,100 MBq) IV/ 1-10 mCi (37-370 MBq) IV 20-30 mCi (740-1,100 MBq) IV/ 0.2-0.6 mCi (7.5-22 MBq) PO
Performance Considerations[5,6,7]	^{99m}Tc sestamibi Dual Phase protocol has a lower radiation exposure than subtraction techniques; it may have a lower sensitivity in "Multiple Parathyroid Gland Disease." Maximize the diagnostic potential of the examination: 1. A combination of planar and/or pinhole imaging, with or without SPECT/CT, may be useful to localize subtle/ectopic disease. 2. The ^{99m} Tc sestamibi/^{123}I sodium iodide Dual Tracer protocol permits simultaneously acquired images, potentially lessening the likelihood of patient motion.
Appropriateness Criteria	Formal appropriateness criteria do not exist. Imaging should be preceded by the clinical diagnosis of hyperparathyroidism, which includes appropriate history and laboratory abnormalities (e.g., abnormal serum calcium and parathyroid hormone levels).

**^{99m}Tc tetrofosmin has been used in place of ^{99m}Tc sestamibi in some protocols, with similar overall results and radiation dosimetry. However, it is less suited to Dual Phase "washout" examinations because it does not show adequate differential washout from thyroid tissue relative to parathyroid tissue.[1,3]

III. Thyroid Scintigraphy and Uptake

Radiopharmaceuticals	^{123}I sodium iodide ^{99m}Tc sodium pertechnetate
Recommended Adult Administered Activity by Protocol[8,9] ^{123}I sodium iodide for Imaging and Uptake ^{99m}Tc sodium pertechnetate for Imaging ^{131}I sodium iodide for Uptake	 0.2-0.6 mCi (7.5-22 MBq) PO 2-10mCi (74-370 MBq) IV 0.004-0.01 mCi (0.15-0.37 MBq) PO
Performance Considerations[8,9]	^{123}I sodium iodide is preferred for routine use because of its lower radiation exposure to the thyroid compared to ^{131}I sodium iodide.
Maneuvers To Minimize Dose[8,9]	Screen the patient to avoid interfering materials that invalidate the examination: thyroid hormone, iodine containing foods and medications, iodinated contrast, and anti-thyroid medications.
Appropriateness Criteria[10,11]	**Thyroid nodules:** the appropriate choice of scintigraphy, ultrasound, and/or fine needle aspiration, varies with the clinical scenario.

IV. Scintigraphy for Differentiated Papillary and Follicular Thyroid Cancer

Radiopharmaceuticals	^{123}I sodium iodide ^{131}I sodium iodide
Recommended Adult Administered Activity by Protocol[8,12] ^{123}I sodium iodide ^{131}I sodium iodide	 0.4-5 mCi (15-185 MBq) PO 1-5 mCi (37-185 MBq) PO
Performance Considerations[8,12]	^{131}I sodium iodide yields higher radiation exposure than ^{123}I sodium iodide, but after thyroidectomy a patient's exposure from both tracers tends to be relatively low. Ensure adequate preparation with sufficient withdrawal of hormone replacement (TSH > 30mU/L) or administer thyrotropin (Thyrogen) per protocol. Maximize the diagnostic potential of the examination: 1. Screen the patient to avoid interfering materials that invalidate the examination: thyroid hormone, iodine containing foods and medications, iodinated contrast. 2. SPECT/CT may be useful to localize disease.
Appropriateness Criteria[11]	The appropriate use of radioiodine scintigraphy in patients who are post-thyroidectomy for newly-diagnosed differentiated thyroid carcinoma or are being followed after ablation is not universally agreed upon in all clinical scenarios. The evaluation of candidates for radioiodine scintigraphy should include a consideration of patient factors such as clinicopathologic stage and other risk factors including laboratory data and size of the remnant post-thyroidectomy.

V. Lung (V/Q) Scintigraphy

Radiopharmaceuticals	^{99m}Tc MAA (perfusion, Q) ^{99m}Tc DTPA (ventilation, V) ^{133}Xe (ventilation, V)
Recommended Adult Administered Activity[13,14] ^{99m}Tc MAA ^{99m}Tc DTPA ^{133}Xe	 1-5 mCi (37-185 MBq) IV 20-50 mCi (740-1850 MBq) in the nebulizer 5-30 mCi (185-1,110 MBq) inhaled as gas
Performance Considerations[14,16,17,18]	1. Administer lowest activity in prescribed range. Balance administered radiopharmaceutical activity versus image quality. 2. For MAA perfusion imaging, using less than 100,000 particles should be avoided in adults.
Maneuvers To Minimize Radiation Dose[13,14,15,16,17,18]	1. In a patient with suspected pulmonary embolism, chest radiography is an important initial examination as it may reveal alternative explanations for acute symptoms (e.g., pneumonia or pleural effusion). However, a normal chest radiograph cannot exclude pulmonary embolus. 2. If MAA perfusion imaging is performed before ventilation imaging, the lowest activity should be administered. If normal, ventilation imaging may be omitted, thereby lowering the effective radiation exposure; this protocol may be advantageous, particularly in the pregnant patient. However, disadvantages should be considered: even the lowest administered MAA activity contributes background activity to the subsequent ventilation images.
Appropriateness Criteria[15,16]	Guidelines have been developed for patients with suspected pulmonary embolism. 1. Chest radiography should be considered as an initial examination because it may suggest alternative diagnoses to explain the patient’s symptoms. 2. Doppler Ultrasound uses no radiation and may be helpful in patients with a high degree of suspicion of deep venous thrombosis (DVT) in the lower extremities, particularly in pregnant patients.

VI. Radionuclide Infection Imaging

Radiopharmaceuticals	^{67}Ga citrate ^{111}In leukocytes ^{99m}Tc leukocytes
Recommended Adult Administered Activity[19.20.21.22.23] ^{67}Ga citrate ^{111}In leukocytes ^{99m}Tc leukocytes	 8-10 mCi (300-370 MBq) IV 0.3-0.5 mCi (11-19 MBq); up to 1 mCi (37 MBq) IV in large pts 5-20 mCi (185-740 MBq) IV
Performance Considerations[19,20,21,22,23]	Nuclear medicine offers a variety of examinations that detect and localize sites of infection. It is important to choose the radiopharmaceutical protocol that optimizes diagnostic efficacy. ^{67}Ga citrate has the highest radiation exposure, but may be advantageous for the diagnosis of discitis/spinal osteomyelitis (see below), tuberculosis and fungal infections, and chronic infections. ^{111}In leukocytes and ^{99m}Tc leukocytes have advantages and disadvantages. For example, ^{111}In leukocytes allow contemporaneous bone marrow (^{99m}Tc sulfur colloid) or bone (^{99m}Tc HDP/MDP) scans, while ^{99m}Tc leukocytes require a 48-hour delay. ^{99m}Tc leukocytes have the lowest patient radiation exposure and a photon energy optimal for gamma camera imaging, but radioactivity normally appears in the intestinal and urinary systems, which could limit diagnostic efficacy for infections in the abdomen. Patient radiation exposure should not be a primary determinant when choosing among these alternatives; the emphasis is choosing the examination with the highest diagnostic efficacy in that particular scenario.
Appropriateness Criteria[20,21]	Radionuclide infection imaging encompasses a wide variety of clinical scenarios and the corresponding appropriateness criteria for each particular scenario should be reviewed. In general: 1. Peripheral infections such as osteomyelitis: Often radiography is the initial examination of choice; the results determine the next imaging step. The imaging sequence is often impacted by whether or not the patient is able to undergo MRI. 2. Spinal Infections: The imaging sequence is often impacted by whether or not the patient is able to undergo MRI or CT. 3. Intra-abdominal/pelvic infections such as abscess: Often CT is the initial examination of choice; the results impact the next imaging step.

VII. Hepatobiliary Scintigraphy

Radiopharmaceuticals	^{99m}Tc iminodiacetic acids(disofenin, mebrofenin)
Recommended Adult Administered Activity[24,25]	3-5 mCi (111-185 MBq) IV Higher doses may be needed in hyperbilirubinemia.
Performance Considerations[24,25]	Mebrofenin may improve exam quality in patients with moderate to severe hepatic dysfunction because of its higher hepatic extraction. Minimize Sources of Error (False Positive Results) including: 1. Insufficient fasting (<2-4 hours) 2. Prolonged fasting (>24 hours including TPN). Sincalide protocols have been proposed in such patients. 3. Severe hepatic dysfunction 4. Prior cholecystectomy
Appropriateness Criteria[25,26, 27]	**Right upper quadrant pain:** In many clinical scenarios, abdominal ultrasound is the initial exam, because it does not use ionizing radiation, and it can provide morphological assessment, including the presence or absences gallstones and biliary ductal dilation. However, hepatobiliary scintigraphy often has a role due to its slightly higher sensitivity and specificity, particularly in problematic cases. **Jaundice:** Hepatobiliary Scintigraphy cannot distinguish intrahepatic cholestasis from mechanical biliary obstruction, which precludes routine use in the jaundiced patient. **Post-operative setting:** Identification of bile leak (e.g., after cholecystectomy, transplant, trauma).

References

1. Donohoe KJ, Brown ML, Collier BD, et al. Procedure Guidelines for Skeletal Scintigraphy, version 3.0. Society of Nuclear Medicine and Molecular Imaging Practice Guidelines, 2003. (http://interactive.snm.org/docs/pg_ch34_0403.pdf)

2. Guidelines and Standards Committee of the ACR Commission on Nuclear Medicine in collaboration with the SPR. ACR-SPR Practice Guideline for the Performance of Adult and Pediatric Skeletal Scintigraphy (Bone Scan). American College of Radiology and Society of Pediatric Radiology, 2012. (http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Skeletal_Scintigraphy.pdf)

3. Roberts CC, Weissman BN, Appel M, et al. Expert Panel on Musculoskeletal Imaging. ACR Appropriateness Criteria® Metastatic Bone Disease (revised). American College of Radiology, 2012. (http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/MetastaticBoneDisease.pdf)

4. Expert Panel on Musculoskeletal Imaging. ACR Appropriateness Criteria® Musculoskeletal Imaging Criteria. American College of Radiology (ACR), 2008. (http://www.acr.org/Quality-Safety/Appropriateness-Criteria/Diagnostic/Musculoskeletal-Imaging)

5. Guidelines and Standards Committee of the ACR Commission on Nuclear Medicine in Collaboration with the SPR. ACR -SPR Practice Guideline for the Performance of Parathyroid Scintigraphy. American College of Radiology and Society of Pediatric Radiology, 2009. (http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Parathyroid_Scintigraphy.pdf)

6. Greenspan BS, Dillehay G, Intenzo C, et al. SNM Practice Guideline for Parathyroid Scintigraphy 4.0. J Nuc Med Tech, 2012; 40:2:1. (http://interactive.snm.org/docs/Parathyroid_Scintigraphy_V4_0_FINAL.pdf)

7. Hinde E, Ugar O, Fuster D, et al. 2009 EANM Parathyroid Guidelines. Eur J Nucl Med Mol Imaging, 2009; 36:1201–1216. (http://www.eanm.org/publications/guidelines/gl_parathyroid_2009.pdf)

8. Guidelines and Standards Committee of the Commission on Nuclear Medicine in collaboration with the SPR and SNM. ACR–SNM–SPR Practice Guideline for the Performance of Thyroid and Scintigraphy and Uptake Measurements. American College of Radiology, Society of Nuclear Medicine and Molecular Imaging, Society of Pediatric Radiology, 2009. (http://interactive.snm.org/docs/Thyroid_Scintigraphy.pdf)

9. Balon HR, Silberstein EB, Meier DA, et al. Society of Nuclear Medicine Procedure Guideline for Thyroid Scintigraphy V3.0. Society of Nuclear Medicine and Molecular Imaging, 2006. (http://interactive.snm.org/docs/Thyroid_Scintigraphy_V3.pdf)

10. Gharib H, Papini E, Paschke R, et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules. Endocr Pract, 2010; 16:468–475. (https://www.aace.com/files/thyroid-guidelines.pdf)

11. Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid, 2009; 19:1167–1214. http://thyca.org/DTCguidelines.pdf

12. Silberstein EB, Alavi A, Balon HR, et al. Society of Nuclear Medicine Procedure Guidelines for Scintigraphy for Differentiated Papillary and Follicular Thyroid Cancer. Society of Nuclear Medicine and Molecular Imaging, 2006. http://interactive.snm.org/docs/Scintigraphy%20for%20Differentiated%20Thyroid%20Cancer%20V3%200%20(9-25-06).pdf

13. Parker JA, Coleman RE, Grady E, et al. SNM Practice Guideline for Lung Scintigraphy 4.0. J Nucl Med Tech, 2012, 40:1:57-6 HTTP://INTERACTIVE.SNM.ORG/DOCS/LUNG_SCINTIGRAPHY_V4_FINAL.PDF

14. Guidelines and Standards Committee of the ACR Commission on Nuclear Medicine in collaboration with the SPR. ACR–SPR Practice Guideline for the Performance of Pulmonary Scintigraphy. American College of Radiology and Society of Pediatric Radiology, 2009. http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Pulmonary_Scintigraphy.pdf

15. Bettmann MA, Baginski SG, White RD, et al. Expert Panel on Cardiac Imaging. ACR Appropriateness Criteria® Acute Chest Pain – Suspected Pulmonary Embolism. American College of Radiology, 2011. http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/AcuteChestPainSuspectedPulmonaryEmbolism.pdf

16. Leung AN, Bull TM, Jaeschke R, et al. An Official American Thoracic Society/Society of Thoracic Radiology Clinical Practice Guideline: Evaluation of Suspected Pulmonary Embolism In Pregnancy. Am J Respir Crit Care Med, 2011, 184:1200-1208. http://www.thoracic.org/statements/resources/respiratory-disease-adults/evaluation-of-suspected-pulmonary-embolism-in-pregnancy.pdf

17. Bajc M, Neilly JB, Miniati M, et al. EANM guidelines for ventilation/perfusion Scintigraphy Part 1. Pulmonary Imaging with Ventilation/Perfusion Single Photon Emission Tomography. Eur J Nucl Med Mol Imaging, 2009, 36:1356–1370. http://www.eanm.org/publications/guidelines/gl_pulm_embolism_part1.pdf

18. Bajc M, Neilly JB, Miniati M, et al. EANM Guidelines for Ventilation/Perfusion Scintigraphy Part 2. Algorithms and Clinical Considerations for Diagnosis of Pulmonary Emboli with V/PSPECT and MDCT. Eur J Nucl Med Mol Imaging, 2009, 36:1528–1538. http://www.eanm.org/publications/guidelines/gl_pulm_embolism_part2.pdf

19. Guidelines and Standards Committee of the ACR Commission on Nuclear Medicine in collaboration with the SPR and the SNM. ACR–SNM–SPR Practice Guideline for the Performance of Scintigraphy for Inflammation and Infection. American College of Radiology, Society of Nuclear Medicine and Molecular Imaging, Society

of Pediatric Radiology, 2009. ACR–SNM–SPR Practice Guideline for the Performance of Scintigraphy for Inflammation and Infection

20. Palestro CJ, Brown ML, Forstrom LA, et al. Society of Nuclear Medicine Procedure Guideline for 111In-Leukocyte Scintigraphy for Suspected Infection/Inflammation Version 3.0. Society of Nuclear Medicine and Molecular Imaging, 2004. http://interactive.snm.org/docs/Leukocyte_v3.pdf

21. Palestro CJ, Brown ML, Forstrom LA, et al. Society of Nuclear Medicine Procedure Guideline for 99mTc-Exametazime (HMPAO)-Labeled Leukocyte Scintigraphy for Suspected Infection/Inflammation Version 3.0. Society of Nuclear Medicine and Molecular Imaging, 2004. http://interactive.snm.org/docs/HMPAO_v3.pdf

22. Roca M, de Vries EFJ, Jamar F, et al. Guidelines for the Labeling of Leucocytes with 111In-oxine. Eur J Nucl Med Mol Imaging 2010; 37:835–841. http://www.eanm.org/publications/guidelines/1_EJNMMI_InfInf_GL_WBCLabelling_111In_04_2010.pdf

23. Roca M, de Vries EFJ, Jamar F, et al. Guidelines for the Labeling of Leucocytes with 99mTc-HMPAO. Eur J Nucl Med Mol Imaging, 2010; 37:842–84. http://www.eanm.org/publications/guidelines/2_EJNMMI_InfInf_GL_WBCLabelling_99mTc_04_2010.pdf

24. Tulchinsky M, Ciak BW, Delbeke D, et al. SNM Practice Guideline for Hepatobiliary Scintigraphy 4.0. J Nuc Med Tech, 2010; 38:4:210-218. http://interactive.snm.org/docs/Hepatobiliary_Scintigraphy_V4.0b.pdf

25. Guidelines and Standards Committees of the Commissions on Nuclear Medicine and Pediatric Radiology in collaboration with the SPR. ACR–SPR Practice Guidelines for the Performance of Hepatobiliary Scintigraphy. American College of Radiology and Society of Pediatric Radiology, 2008. http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Hepatobiliary_Scintigraphy.pdf

26. Katz DS, Rose MP, Blake MA, et al. Expert Panel on Gastrointestinal Imaging. ACR Appropriateness Criteria® Right Upper Quadrant Pain. American College of Radiology, 2010. http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/RightUpperQuadrantPain.pdf

27. Lalani T, Couto CA, Rose MP, et al. Expert Panel on Gastrointestinal Imaging. ACR Appropriateness Criteria® Jaundice. American College of Radiology, 2010. http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/Jaundice.pdf

28. Davis PC, Wippold FJ, Cornelius, RS, et al. Expert Panel on Neurologic Imaging. ACR Appropriateness Criteria® Low Back Pain. American College of Radiology, 2011. http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/LowBackPain.pdf

