

Scintillator

July 2013

FROM THE PRESIDENT



Erica Cohen, DO, MPH, CCD

First and foremost, on behalf of the NMRO Board, I would like to express our appreciation to the ACNM Board for approving our international membership initiative! Membership in NMRO is now FREE to residents across the globe!

We have sent invitations to our colleagues in Europe, Asia, South America, and the Middle East. If this is your first issue of the Scintillator, hello and welcome! We are so glad to have you!

We have just wrapped up our Annual Networking Luncheon at the SNMMI Annual Meeting. Our topic this year was Government Relations and Politics with guest speakers Dr. Robert Henkin, Sue Bunning, and Dr. Erin Grady. Thank you to everyone who participated in our discussion. I am hopeful that everyone walked away with a better understanding of the socioeconomic issues that nuclear medicine is currently facing. I encourage everyone to get involved, whether it is nationally or in your hometown! We also hosted the first ever Residents & Young Professionals Networking Happy Hour! I hope everyone had a great time!

Be on the lookout for our next Virtual Journal Club which will be held in the late summer. We hope to have CME credit available for attending physicians who wish to join our discussion.

I want to take a moment to thank the outgoing Board of Directors for their hard work and dedication over the past year, and to welcome our new incoming Board Members! The NMRO has been extremely productive with an outstanding number of accomplishments over the past year. I am sure that our organization will continue to prosper in the year ahead!

Warm regards,
Erica Cohen, DO, MPH, CCD
NMRO President

GOVERNMENT CORNER

Erica Cohen, DO, MPH, CCD

Welcome to the newest addition to the Scintillator, The Government Corner! This recurring section will feature the latest news from the SNMMI-ACNM Joint Health Policy and Regulatory Affairs Committee in a simple, bullet point format, highlighting the issues that are most important to Residents and Young Professionals! More detailed information can always be found on the Committee's website by visiting www.snmmi.org and clicking on the "Government Relations" tab. Here are your top stories for Spring 2013:

- Basic nuclear medicine research has historically been funded by the Department of Energy. Prior to 2006, we received approximately \$34 million dollars. Funding has been progressively cut over the past 7 years down to \$5 million dollars. It has recently been proposed that funding be moved to the National Institute of Health Division of Biomedical Imaging and Bioengineering (NIBIB). Under the NIBIB, Nuclear Medicine research would no longer be "earmarked" and we could lose what little we have left. This was one of the major issues lobbied during SNMMI's Capitol Hill Day this April.
- The United States consumes approximately half of the world's supply of Mo-99, but has no domestic source of supply. Our two primary reactor sources in Canada and the Netherlands are nearly 50 years old and will be phased out of production beginning in 2016. Last year, Congress enacted the American Medical Isotopes Production Act, enabling domestic development of Mo-99 Facilities; however, we have yet to break ground. As part of a national security initiative, industry must also convert from highly enriched uranium (HEU) to lowly enriched uranium (LEU); this will likely be associated with increased cost, although at this point we are not certain how much. This was another major issue lobbied during Capitol Hill Day.
- As of April 1, 2013, all Medicare physician services were subjected to a 2% payment cut under budget sequestration. The sequester is expected to be in effect for 9 years unless Congress and the White House are able to reach a significant deficit reduction agreement that replaces it. It is believed that in the near future, physician reimbursements will move from fee-for-service to quality measures. So far, we do not have a clear definition of what "quality" looks like for imagers. The Patient Simulator (Phantom) Program is the first technique we are utilizing to assess quality of our cameras, technologists, and physicians. More information can be found on SNMMI's website by clicking the "Practice" tab.

SAVE THE DATE

SNMMI 2014 Mid-Winter
February 6-9, 2014
Palm Springs, California
www.snmmi.org/mwm2014

Call For Abstracts — 2014 Annual Meeting

The Program Committee of the American College of Nuclear Medicine invites the submission of original abstracts for the Annual Meeting, held in conjunction with the Mid-Winter Meeting, February 6 – 9, 2014 in Palm Springs, CA. Papers on all aspects of clinical and basic science in nuclear medicine, correlative imaging in radiology, nuclear cardiology and radiation oncology will be considered. The accepted presentations will be in oral and poster format.

A panel of physicians will judge the young investigator's posters, and the authors of the best submissions will be presented with their awards during a special banquet on Thursday evening. The presenter must be in attendance at the meeting to be eligible for an award. There will be three Best Essay Awards, each for \$500 and two Travel Grants each for \$750.

Abstracts must be submitted via e-mail to Delicia Hurdle at dhurdle@snmmi.org. The author's names' and affiliations should be included with the title of the abstract. For more information regarding the abstract submission guidelines and submission form, please visit the ACNM website at www.acnmonline.org

Submission Deadline: November 1, 2013

Parting Words to all Nuclear Medicine Residents: GET INVOLVED!

Karen Ayres, MD – NMRO Immediate Past President



Karen Ayres, MD

It has been an amazing two years on the NMRO board, first as president and then as immediate past president under Erica Cohen's strong leadership. Being involved in NMRO facilitated my transition from clinical pediatrics to nuclear medicine (with my ultimate goal being to practice pediatric imaging). In the imaging sciences, there is a much

stronger push to do research, present abstracts, and attend meetings. As president of the NMRO, I was able to attend several ACNM and SNMMI meetings. I met with the leaders in our field. I presented a poster at the Orlando winter meeting 2012, and I am currently working on an original research project. I really feel like a part of the world-wide nuclear medicine community, not just a resident in Nashville.

I am currently in a diagnostic radiology residency, but had I made the decision to look for a job in nuclear medicine, my work in the NMRO would have opened doors. The nuclear medicine job market is tight, and the best opportunities will go to the people who get involved and make themselves known. For that reason, I advise all incoming residents to SIGN UP for an NMRO committee and GET INVOLVED. You will be exposed to amazing education and research opportunities, and you will make connections that may lead to a job one day, so it's a win-win all around. There is a committee for everyone- education, IT, leadership, and editorial, to name a few. If you have any questions, contact any of the board members, including Erica Cohen (ericajill@gmail.com) or myself (karen.ayres@vanderbilt.edu).

If you are an upper level resident reading through this Scintillator, and there are new residents in your program who have not signed on yet, please forward them the email with the link to the Scintillator and tell them about ACNM and NMRO. And while you are at it, drop us a line with your interest in a committee or your own Scintillator submission!

News You Can Use: Lymphoseek...Lymphofound?

Anthony Fotenos, MD – NMRO Intern



Anthony Fotenos, MD

It's not just the grass sprouting this Spring. Between March and May, the FDA approved three new or expanded labels for radiopharmaceuticals of interest to nucs residents: Navidea's Lymphoseek (Tc-99m tilmanocept) on March 13, GE's AdreView (I-123 iobenguane) on March 20, and Bayer's Xofigo (Ra-223 dichloride) on May 15. We'll start with Lymphoseek, and future editions of this column will describe

AndrewView and Xofigo.

To quote from its label, "Lymphoseek is a radioactive diagnostic agent indicated for lymphatic mapping with a hand-held gamma counter to assist in the localization of lymph nodes draining a primary tumor site in patients with breast cancer or melanoma." [1] Lymphoseek is relevant to us in nucs because of our role in lymphoscintigraphy. For example, at my institution, nucs residents perform intradermal injections of Tc-99m sulfur colloid for single-photon imaging (lymphoscintigraphy) mostly to help guide surgical lymph node biopsies in patients with intermediate-risk melanoma. (At Johns Hopkins, lymphoscintigraphy is rarely performed for breast cancer patients). For me, then, Lymphoseek represents a potential alternative to intradermal Tc-99m sulfur colloid injections around primary sites of melanoma.

Why might I want to try Lymphoseek? Molecular design is its top selling point (see figure). Compared to sulfur colloid, a non-binding agent phagocytosed by monocytes and introduced in 1963 for liver and spleen imaging, Lymphoseek specifically binds to the CD206 receptor of monocytes and has a smaller molecular diameter. From these differences, reasonable hypotheses follow: Lymphoseek should travel faster to primarily draining nodes, yet stay in them longer, compared to sulfur colloid. Data from phase I and II studies support these hypotheses, and, notably, Lymphoseek is FDA-approved for injection as briefly as 15 minutes before intraoperative mapping [2-3]. By comparison, surgeons typically have to wait at least 1-2 hours between injection and mapping when using sulfur colloid [4]. Lymphoseek's rapid lymphatic transit may lead to

Continued on page 4. See News You Can Use.

Physics Corner: Quality Control

Not the most “scintillating” topic, but one everyone should be familiar with. There are many types of quality control, but here we will discuss CLAG for dose calibrators: constancy, linearity, accuracy, and geometry. Constancy and calibration (similar to accuracy) are tests performed for survey meters. If you remember the word CLAG, you will remember the frequency which these tests should be performed. C, L, A, and G are checked in order of decreasing frequency: daily, quarterly, annually, and at installation of a device, respectively. (All CLAG should be checked at installation, following repairs, and after a device is moved, with the exception that geometry does not have to be checked after a device is moved.)

Constancy: To ensure that the calibrator readings are constant from day to day, a long-lived nuclide such as Cs-137 (half life of 30 years) is measured daily and should be within 10% of the expected dose considering decay.

Linearity: To ensure that the calibrator is as accurate for low activities as it is for medium and high activities, linearity is checked quarterly. One method is to measure the maximum activity that a department might use, such as 200 mCi Tc-99m, and measure it at various intervals over the next 4 days as it decays. A less time-consuming method is to measure a dose unshielded and then again with lead sleeves of varying thickness that reduce the activity and simulate lower doses.

Accuracy: To ensure that a calibrator gives accurate readings, two long-lived nuclide sources, such as Cs-137 (half life of 30 years) and Co-57 (half life of 270 days), are measured repeatedly in the calibrator. The averaged readings are compared to values issued by the National Institute of Standards and Technology and should be within 10% of the expected activity. For a survey meter, the test is referred to as calibration. Readings are taken from the two sources at incremental distances, and they must be within 20% of the expected measurement.

Geometry: To ensure that the volume and shape of a dose within the calibrator do not affect the readings, a small amount of activity is placed at the bottom of a container and progressively diluted, for example with water. Or, a sample can be measured in different containers such as vials, syringes, etc. All measurements should be within 10%.

Have you checked your constancy today?

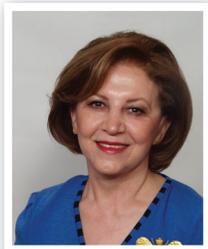
Powsner, R. and Powsner, E. Essential Nuclear Medicine Physics, second edition. Blackwell Publishing, MA, 2006, pp. 136-138.



Karen Ayres, MD

ACNM Corner

Simin Dadparvar, MD, FACNM



Simin Dadparvar, MD, FACNM

This year, the American College of Nuclear Medicine celebrates its 41st year of establishment. Four decades ago, two new organizations were established to fulfill the practical functions of nuclear medicine: The American College of Nuclear Medicine was established to support the education of nuclear radiologists in 1972, and the American College of Nuclear Physicians was established in 1974 to support physicians & scientists in nuclear medicine through advocacy, socioeconomics, and government relations. On September 1, 2009, the colleges joined their efforts to promote best practices in nuclear medicine and molecular imaging before legislative and regulatory bodies, other medical organizations, the media, and the general public.

About a decade ago, the need for establishment of a resident organization was identified and the organization was established through the dedication of ACNM leadership, residents, and fellows in nuclear medicine across the country. Over the years, many talented and dedicated individuals have joined the leadership of the residents and created great programs such as mentorship, lectures,

job placement, knowledge bowl, virtual journal clubs, board review questionnaire, the newsletter and more...

As the field of molecular imaging is growing in the world, ACNM is reaching out to the international community to bring more members to strengthen the field in the U.S. and around the globe. The mentorship program assists residents in research, publications, networking, and employment opportunities, access to publication in the Clinical Journal of Nuclear Medicine and beyond. There are several leadership opportunities by serving on the NMRO board. All residents have the opportunity to join ACNM as full members upon completion of their training.

Full membership of the college has many advantages. Full membership provides an advantage for networking, employment, publication in the Clinical Journal of Nuclear Medicine, and most importantly, fellowship in the college. Many outstanding members with leadership skills have had the chance to serve on the ACNM board and give back to the community.

I urge you to become an ACNM resident member as a part of NMRO, and upon completion of your training, to join as a full member. As the field of nuclear medicine and molecular imaging is growing, ACNM can provide global communications among the physicians and scientists around the world.

News You Can Use continued from page 2.

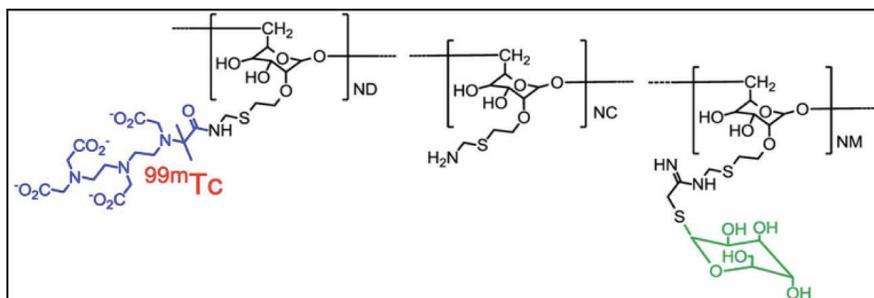


Figure. Lymphoseek molecular structure. Black represents the dextran backbone, blue represents DTPA units to which Tc-99m is attached, and green represents mannose moieties for attachment to the CD206 receptor of monocytes in lymph nodes.

its approval for new cancer types in the future. For example, preliminary results from an ongoing Phase III trial in patients with head and neck cancer, which requires intraoperative injection, suggest nodal mapping with Lymphoseek may reduce the morbidity currently associated with pathologically negative total neck dissections [5].

What about Lymphoseek's clinical efficacy in patients with breast cancer and melanoma, the currently approved indications? In a word, Lymphoseek is better than isosulfan blue dye. In particular, the FDA's approval decision hinged on two Phase III trials published in 2013, one in patients with melanoma [6] and the other in patients with breast cancer [7]. If you only have time to read one reference, I recommend the latter by Wallace and colleagues [7]. Their report describes how 148 breast cancer patients undergoing lymph node mapping were injected with Lymphoseek and then, intraoperatively, with isosulfan blue. The primary endpoint was concordance with dye: of 209 lymph nodes stained blue, 207 also concentrated Lymphoseek (99% concordance). More importantly, of 33 pathology-positive lymph nodes, 94% were detected by Lymphoseek compared to only 76% by dye, a significant and clinically meaningful difference. Analogous outcomes in the Phase III melanoma trial, involving 154 patients, were 99% concordance and 100% pathology detection with Lymphoseek, compared to 80% with dye.

Some readers may question why Navidea, Lymphoseek's owner, did not try its agent against sulfur colloid when seeking FDA approval. Study authors describe at least two reasons, and both strike me as valid. First, the FDA did not approve sulfur colloid for lymph node mapping in patients with breast cancer and melanoma until 2012, whereas isosulfan blue has been approved for these indications since 1981, with a large literature supporting its use as

a reference standard. Second, both sulfur colloid and Lymphoseek share a common radionuclide, Tc-99m, so comparing the two radiopharmaceuticals would almost certainly require a less elegant between-subject design. Finally, without a pathological gold standard based on complete nodal dissections, it's hard to imagine any study design of clinical efficacy demonstrating definite superiority, yet it would likely be unethical to subject breast and melanoma patients to this gold standard today.

Bottom line: Lymphoseek will almost certainly be more convenient for patient scheduling and more expensive than sulfur colloid (~\$300 compared to ~\$100 per patient administration). In addition, retrospective meta-analysis [8] and early-phase studies suggest the clinical efficacy of Lymphoseek is almost certainly not worse, and possibly slightly better, than sulfur colloid. Lastly, there is this tantalizing line buried deep in the results of the Phase III breast cancer study: "Even though local analgesics were not used in conjunction with administration of Lymphoseek, only 2 of 154 patients reported injection site pain or slight breast pain." As one resident all too familiar with the howls of patients undergoing sulfur colloid injections, I integrate the totality of this evidence and conclude that Lymphoseek is a welcome addition to the market for lymph node mapping. Speaking personally, I'd love to give it a try.

References:

1. <http://goo.gl/kCCcc>
2. <http://goo.gl/RZ7QJ>
3. <http://goo.gl/vU2i1>
4. <http://goo.gl/EA87x>
5. <http://goo.gl/78pDd>
6. <http://goo.gl/M6nQp>
7. <http://goo.gl/28XwG>
8. <http://goo.gl/96Tk5>

President Biography

Erica Cohen, DO, MPH, CCD



Erica Cohen, DO, MPH, CCD

I was born in Ft. Lauderdale, FL and lived in the nearby suburbs until entering college at the University of Florida in Gainesville. I majored in Biology and minored in Business Administration. After finishing my degree in a short three years, I moved back to South Florida to attend medical school at Nova Southeastern University College of Osteopathic Medicine, where I also earned a Masters in Public Health as part of a dual-degree program. During my fourth-year elective radiology rotations, I visited Chicago for the first time and found it to be an amazingly fun and beautiful city. I felt drawn to nuclear medicine as the specialty that radiology residents knew the least about, and so I pursued a residency in nuclear medicine directly out of medical school. After finishing a very challenging year as a surgical intern, I have loved

and appreciated the past two years that I have spent in the nuclear medicine department at Loyola University Medical Center.

Over the past year, I have been honored with the Robert Henkin Government Fellowship, ACNM/SNMMI Best Abstract Award, and the Sino-American Exchange Program. I have also spent the past two years representing the ACNM as a delegate to the Young Professionals Section of the American Medical Association. None of this would have been possible without the support of NMRO and the ACNM. I am so thankful to these organizations and to my mentors for giving me these amazing opportunities to represent the interests of Nuclear Medicine Residents and help guide us towards a "scintillating" future. Entering my final year of residency is very bittersweet, and three years serving the NMRO has been the cherry on top. I highly encourage all residents to be active within the NMRO and all young professionals to be active within the ACNM!

Parathyroid Scintigraphy

MJ Johnston, MD



MJ Johnston, MD

Case A.

SUBJECTIVE: 66-year-old G2P2 lady, 16y post-menopausal and not using hormonal therapy, presented for evaluation of chemical suspicion for parathyroid adenoma. No prior imaging was available for review. Her past medical history was significant for a non-typified Breast Cancer, which had been treated with bilateral

mastectomy with cosmetic prosthetic placement, in the distant past.

TECHNIQUE: 26 mCi Technetium 99m sestamibi was injected pIV. 15 minutes later and 2 hours later, SPECT and planar imaging of the neck and upper thorax was performed (“nose to below aortic arch”). Coincident with the 2 hour delayed imaging; a CT of the same area was performed for attenuation correction and anatomic localization of both time points.

LABS: PTHintact: 136 (12-88)nl & Ca: 11.4 (8.6-10.2)nl & TSH:nl & BUN/Cr:nl

FINDINGS: 15 minute delayed planar and SPECT/CT images (not shown) of the neck and upper thorax demonstrated appropriate physiologic activity within the soft tissues, myocardium, parotid glands, a left submandibular gland (right has been surgically removed), and within a 2cm left axillary lymph node. 2 hours delayed planar and SPECT/CT MIP (figure 1) and axial fusion (figure 2) images demonstrated no evidence of focal activity within the neck and upper thorax to suggest the presence of a parathyroid adenoma. Faint activity was persistent within the left axillary adenopathy.

IMPRESSION: There was no suspicion for parathyroid adenoma. The focal radiotracer deposition in the left axillary lymph node was reported as concerning for disease recurrence.

FOLLOW UP: The Left Axillary Lymph node was biopsied and

found to be benign sclerosing intra-ductal papilloma. Pathology recommended “excision of this lesion is recommended.” The patient underwent surgical resection of the node.

Case B.

SUBJECTIVE: 80 year-old lady found to have hypercalcemia and hyperparathyroidism on routine blood work. She has no other significant history and her renal function is appropriate.

TECHNIQUE: Similar to above, using 26.5mCi.

LABS: PTH, intact: 161 (12-88)nl & Ca: 10.7 (8.6-10.2)nl & TSH:nl & BUN/Cr:nl

FINDINGS: 15 minute delayed planar, SPECT/CT, and 2 hour delayed images of the neck and upper thorax demonstrated appropriate physiologic activity within the soft tissues, myocardium, submandibular, and parotid glands.

Additionally, 15 minute delayed MIP image (figure 3, left) demonstrates radiotracer deposition within the left and right thyroid bed regions. There is focal deposition in the superior left region and the inferior left region. No ectopic foci were identified. 2 hour delayed MIP image (figure 3, right) demonstrates focal persistence of radiotracer within what appears to be; 1. a right upper lobe intra thyroidal parathyroid adenoma, 2. a left upper lobe intra thyroidal parathyroid adenoma, 3. a right sided/inferior parathyroid adenoma which is likely in or very close to the tracheoesophageal groove.

IMPRESSION: (Note: this was the actual impression, it turns out to have been accurate but not precise) “Likely parathyroid adenomas within the upper poles of the right and left thyroid tissue proper, as well as an inferior, slightly right-sided, parathyroid adenoma, at or near the TE groove.”

Continued on page 6. See Parathyroid Scintigraphy.

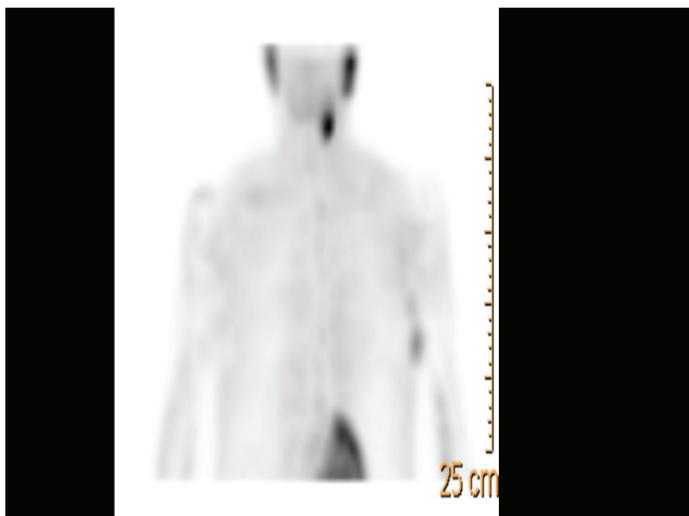


Figure 1

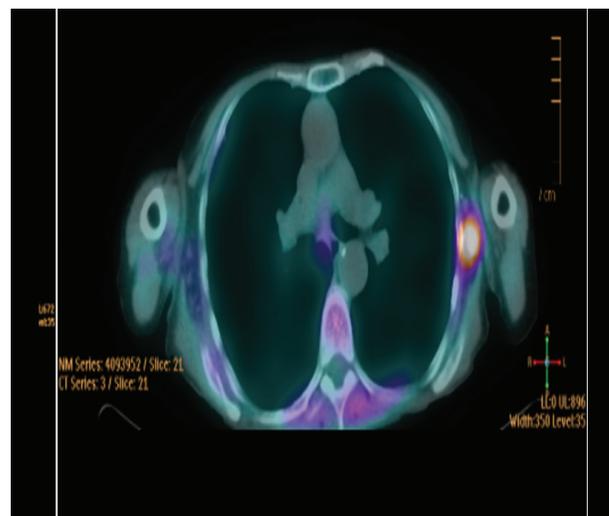


Figure 2

Parathyroid Scintigraphy. continued from page 5.

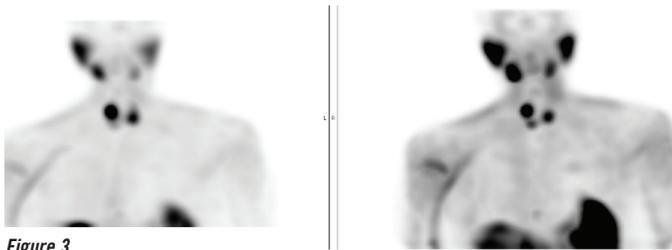


Figure 3

FOLLOW UP: She underwent surgical resection of the concerning foci. Post-excision pathology revealed (figure 4);

1. Right thyroid: follicular adenoma, multinodular goiter, no parathyroid tissue.
2. Right inferior parathyroid: hypercellular and enlarged parathyroid
3. Left Thyroid: Papillary Carcinoma and multinodular goiter.
4. Left inferior parathyroid: enlarged and hypercellular parathyroid.

Discussion: Breast cancer recurrence detected on sestamibi parathyroid scintigraphy has been previously reported (1). Papillary thyroid cancer detected on sestamibi parathyroid scintigraphy has been previously reported (2). As sestamibi uptake is a reflection of mitochondrial activity and concentration, sestamibi scan is a somewhat sensitive study, yet not rather specific. When a prior medical history is non-contributory, the dilemma is more confusing. As in the second case, a broad differential may be considered in the impression, rather than listing the most likely diagnosis---clearly a

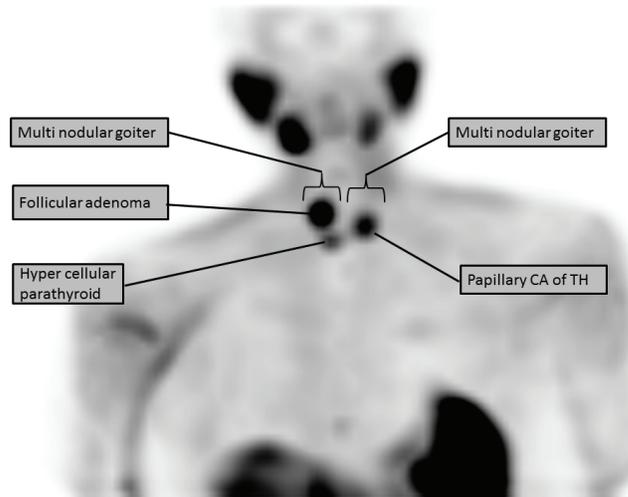


Figure 4

matter of personal and institutional choice---as long as we are aware of the choice and intentionally doing it.

References:

1. Conrad GR, Sloan, DA, Sinha P: Detection of late chest wall recurrence of breast carcinoma during Tc-99m Sestamibi parathyroid scintigraphy. *Clin Nucl Med* 28:408-9, 2003.
2. Spieth ME, Mulligan GM, Nguyen T, etal: Incidental thyroid cancer on parathyroid imaging. *Clin Nucl Med* 27:658-9, 2002.

Who Makes Your Moly??

Erica Cohen, DO, MPH, CCD

Unscramble the 5 Nuclear Reactor Sites and the proposed site for the US Reactor

F P R G N Q W C F F H K U N D
 A S T E C E U Z F E X N E I W
 K C S D N A L R E H T E N S M
 D T I S F F H J U M H J O N C
 A Q R R J R O Y U D D C E O I
 B D X Q F S A I M G W R Y C Z
 Q U R Z J A G N O O W I C S Z
 V X Y R X L H H C O D D C I P
 T M T V E U N T O E C F Q W I
 R X K B J Q F J U C A N A D A
 I R M Q S F C H I O O T F K S
 F R T V T P R E J A S X K K A
 Z F D S I Y T R E Q L L Q G U
 I O Y J P A B S R M U M V Z O
 R Z R L M R Q U A N V H P T J