SNMMI SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING
CLINICAL TRIALS NETWORK

JANUARY 2015

THE CLINICAL TRIALS NETWORK NEWSLETTER

Pathways

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Save the Date

PET in Prostate Cancer: A Focus on C-11 Choline

Val J. Lowe, MD and Eugene D. Kwon, MD

Val J. Lowe, MD

Eugene D. Kwon, MD

In the United States (US) and Western Europe, prostate cancer affects 1 in 6 men, making this cancer the most commonly-diagnosed non-cutaneous malignancy encountered in the male population. Nearly all men who die of prostate cancer each year (~35,000 annually) do so after either primary local or systemic therapy has failed. Based on the Surveillance, Epidemiology and End Results Program (SEER) data, it is predicted that approximately 100,000 men in the US will pursue subsequent therapy for prostate cancer relapse annually. Until recently, however, the lack of reliable and timely methods to identify sites of cancer relapse to formulate rational and effective treatment strategies has remained a major barrier to economizing and optimizing treatments for patients with recurrent disease. As such, improved imaging would be anticipated to have a seismic impact on this significant disease population.

PET imaging in prostate cancer is providing a reasonable option to identify the location of recurrence prostate cancer in this setting. PET imaging with choline and other prostate-specific PET drugs have shown impressive results in identifying the site of recurrent disease in this patient group. While conventional imaging technologies are sufficient for patients who are about to undergo definitive therapy for ostensibly localized prostate cancer, these conventional imaging technologies are insufficient for the detection of relapsing disease particularly at low PSA levels[1]. Data show that CT, MRI, and bone scan were unlikely to be useful to pinpoint sites of cancer recurrence in men with a low PSA. Importantly, it is often at these low PSA levels that critical decisions regarding further management of relapsing prostate cancer are made. Specifically, conventional imaging is least likely to be helpful in guiding subsequent management of patients with treatment failure, and overall sensitivity for conventional imaging modalities was disappointingly low at 11%, with a mean cut-off PSA of 23 ng/mL in these patients[2,3].

The efficacy of C-11 Choline PET in patients with biochemical recurrence of prostate cancer (BCR) was demonstrated in a retrospective study of 176 male patients who developed BCR after primary treatment failure of prostate cancer and underwent PET/CT scanning with C-11 Choline Injection at Mayo Clinic from 2007 to 2010[4]. BCR was defined as at least 2 separate prostate-specific antigen (PSA) measurements

Continued on page 2. See **C-11 Choline.**

C-11 Choline Continued from page 1.

acquired 3 months apart for radical prostatectomy patients, nadir plus 2 ng/mL for patients treated with radiation or primary cryoablation, or a steady rise in PSA for men treated with primary androgen deprivation therapy. All men had failed conventional imaging modalities for localization of recurrent prostate cancer. The doses administered in the retrospective study ranged from 10-20 mCi (370-740 MBq). Detection using C-11 Choline PET showed a sensitivity of 93% and a specificity of 76% when compared with a gold standard using biopsy and imaging for patients with all types of treatments. Sensitivity of 95% and specificity of 86% were observed when compared with a gold standard using biopsy and imaging for RRP patients only. The optimum PSA value for lesion detection was determined to be between 1.7 and 2.0 ng/mL to obtain a maximal clinical benefit. C-11 Choline PET markedly enhanced demarcation of relapsing prostate cancer sites (i.e., location and extent) in treatment-failure patients, leading to a 30% improvement over conventional imaging in defining optimal "next step" therapy for this substantive and complicated population of prostate cancer patients. Consistent with these data, several published reports show that C-11 Choline PET evaluation of patients with recurrent prostate cancer is advantageous[5,6]. Similar to these findings, early clinical trials with new PET drugs are now showing similar promise in detection of recurrent prostate cancer[7,8].

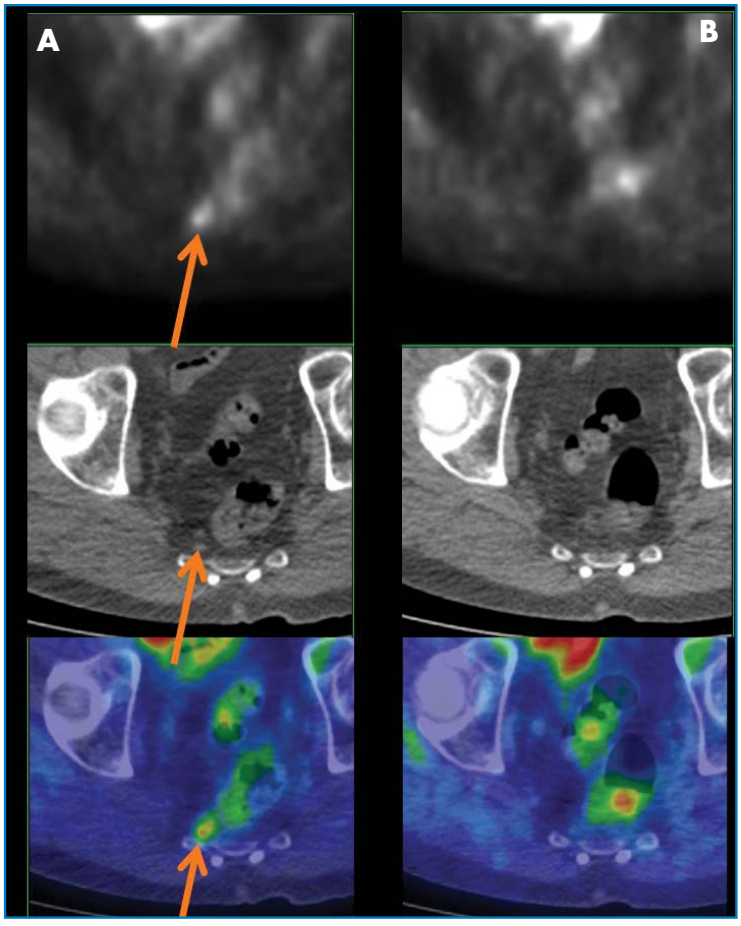


Figure 1. PET/CT (A) showing a choline avid 3mm right perirectal lymph node (arrows) as a site of disease (CT biopsy-proven) in a patient with prostate cancer recurrence (PSA 0.92) with two other small choline avid nodes (not shown) and a PET/CT 5 months later (B) after androgen deprivation therapy showing resolution of choline uptake (PSA < 0.01). Systemic therapy rather than prostate bed irradiation was chosen based on PET findings.

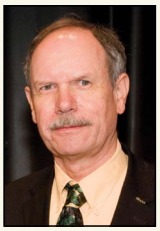
Continued on page 4. See **C-11 Choline.**

Message from the Co-Chairs: 2014 in Review

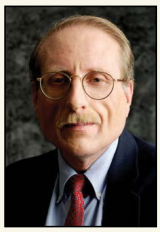
2014 was a busy year for CTN Leadership and its 6 Committees to meet the goals set forth in our Strategic Plan. To this end, we have worked with SNMMI leadership, industry and other imaging groups worldwide to provide tools and resources to promote faster, more cost-effective drug development and increase the availability and performance of molecular imaging radiopharmaceuticals for use in the clinic. The following is an abbreviated description of some of our accomplishments.

- CTN administration provided a significant role in the support of seven studies utilizing seven different investigative PET imaging agents.
- CTN played a pivotal role in the planning and set-up of the 3rd Theranostics World Congress on Gallium-68 and PRRT scheduled for March 2015. SNMMI is co-sponsoring this meeting with Johns Hopkins.
- Scanner Validation Committee developed a new chest phantom that contains the same number and sizes of lesions found in the NEMA NU-2 phantom. The committee is going to work with other groups (e.g., EARL/EANM) to help PET imaging achieve a better, more international level of standardization in clinical research.
- Site Education Committee developed a course for technologists that was presented as part of the SNMMI Technologist Section 2014 RoadShow. The committee also presented 5 live webinars, published an article in *Uptake* and began work on 2 JNMT articles.
- Utilizing contacts collected in its database, CTN assisted the National Institute of Biomedical Imaging and Bioengineering (NIBIB) with a national survey of radiochemists, physicians and scientists on the production of isotopes that are important in medical imaging, treatment, or diagnostics. The survey results reprioritized the input from the NIBIB to the DOE.

Continued on page 5. See **Message from Co-Chairs.**



Michael Graham, PhD, MD



John Hoffman, MD

In the NEWS

Highlights of SNMMI–FDA Stakeholder Meeting

Sue Bunning and Caitlin Kubler
SNMMI HPRA

On October 27, 2014, the Society of Nuclear Medicine and Molecular Imaging (SNMMI) hosted a broad stakeholder meeting in Linthicum Heights, Md. The Society brought in more than 40 experts from the field of nuclear medicine and molecular imaging to discuss the current regulatory climate. Represented at the meeting were leaders from the U.S. Food and Drug Administration (FDA), Centers for Medicare and Medicaid Services (CMS), National Cancer Institute (NCI), National Institutes of Health (NIH), Nuclear Regulatory Commission (NRC), industry and specialty societies.

Dwaine Rieves, MD, who retired from FDA in 2013 and has extensive experience in drug and biological product development, diagnostic imaging drug development, and regulatory strategies, moderated the meeting and challenged the group to think about what possibilities may exist for the creation of new pathways to support increased approval of both new and non-proprietary radiotracers.

SNMMI Vice-President-Elect Sally Schwarz, MS, RPh, BCNP, spoke about the work of SNMMI's FDA Task Force (the group responsible for planning this meeting) to strategize on creating a more efficient and timely approval process. Brief presentations were also given by Louis Marzella, MD, PhD, FDA's director in the Center for Drug Evaluation and Research, Office of New Drugs; John McInnes, MD, JD, CMS' director in the Division of Outpatient Care; and Paula Jacobs, PhD, NCI's associate director in the Division of Cancer Treatment and Diagnosis.

Meeting participants split into four breakout groups and discussed market/commercialization barriers, strategies to improve the current approval process, possible new approval pathways and outcome measures for both the FDA and CMS. Participants felt that certain challenges in the current regulatory process exist due to varying definitions of efficacy and clinical benefit/utility between FDA and CMS. Individuals felt that clearly defining these terms would reduce ambiguity for all stakeholders involved in the drug development process.

The Society is developing a detailed white paper, scheduled to be released in the coming months that will present the outcomes from each breakout group discussion and identify action items, recommendations and strategies that SNMMI plans to implement in the future.

SNMMI 2015 MWM CTN HIGHLIGHTS

Joint CTN / PET COE Symposium: Thursday, January 22; 8am–4pm

The Clinical Trials Network (CTN) is excited to co-sponsor a full-day symposium with the PET Center of Excellence on **"Coverage with Evidence Development and Life after NOPR."** Participants will hear from the experts on how NOPR has affected billing for certain PET scans and the status of coverage with evidence development for amyloid imaging agents. Additionally, the nuances for coding and billing for PET imaging agents in clinical research to maximize reimbursement will be presented with time allotted to answer questions from the audience. The session provides vital information on topics that directly impact the clinician and their patients.

CTN Session for Technologists: Saturday, January 24; 8am - 12 noon

Continuing CTNs collaboration with the Technologist Section, **"Discovering Clinical Research and Taking Steps to Transitioning"** incorporates key courses from the CTN curriculum on clinical research principles and how to use them to transition from the clinical practice setting. If you are considering applying your nuclear medicine technology skills to a career in clinical research or to supplement your knowledge and enhance your current position – this is a session you must attend.

Clinical Trials Network 2015 WEBINAR SERIES

These one-hour webinars are presented 6 times during the year beginning in February. Purchase the entire 2015 package and save money!

FEBRUARY 19
Dynamic PET Imaging for Technologists

APRIL 16
Cheson Criteria for Lymphoma: Updates on Staging and Measuring Response to Therapy

JUNE 25
CT Basics for PET/CT in Clinical Research

AUGUST 20
Good Clinical Practice (GCP) Review for Imaging and Radiation Trials

OCTOBER 15
CTN Scanner Validation Data: What Does it Mean?

DECEMBER 10
Updated Coverage, Coding & Billing for PET Scans & Imaging Agents in Clinical Trials

Check out the CTN website for more information on these webinars and other educational offerings available in the SNMMI Learning Center.

C-11 Choline Continued from page 2.

In clinical practice, the vast majority of patients with suspected recurrent prostate cancer are assigned to treatment based on clinical algorithms that are predictive of disease location for high-risk patients when none can, in fact, be identified. On the basis of these recent PET data, it seems highly likely that incremental benefits in terms of lesion detection during restaging of patients prior to secondary therapy, as provided by PET, will prove meaningful in altering treatment assignment and potentially lead to improved outcome for these patients (Figures 1 and 2).

At the present time at Mayo Clinic, C-11 Choline PET is being used extensively in this group of patients, with 12 patients being scanned each day. Regulatory approvals (see "Biomarker Spotlight" article in this issue) have helped pave the way for clinical access to the test and would argue for more widespread adoption of PET imaging of recurrent prostate cancer in the future.

References:

1. Gomez P, Manoharan M, Kim SS and Soloway MS. Radionuclide bone scintigraphy in patients with biochemical recurrence after radical prostatectomy: when is it indicated? *BJU Int.* 2004;94:299-302.

2. Okotie OT, Aronson WJ, Wieder JA, Liao Y, Dorey F, De KJ and Freedland SJ. Predictors of metastatic disease in men with biochemical failure following radical prostatectomy. *J Urol.* 2004;171:2260-4.

3. Choueiri TK, Dreicer R, Paciorek A, Carroll PR and Konety B. A model that predicts the probability of positive imaging in prostate cancer cases with biochemical failure after initial definitive local therapy. *J Urol.* 2008;179:906-10;discussion 910.

4. Mitchell CR, Lowe VJ, Rangel LJ, Hung JC, Kwon ED, Karnes RJ. Operational characteristics of (11)C-choline positron emission tomography/computerized tomography for prostate cancer with biochemical recurrence after initial treatment. *J Urol.* Apr 2013;189(4):1308-1313.

5. Giovacchini G, Picchio M, Coradeschi E, Bettinardi V, Gianolli L, Scattoni V, et al. Predictive factors of [11C]choline PET/CT in patients with biochemical failure after radical prostatectomy. *Eur J Nucl Med Mol Imaging.* 2010: 37;301–9.

6. Cstellucci P, Fuccio C, Nanni C, Santi I, Rizzello A, Lodi F, et al. Influence of trigger PSA and PSA kinetics on 11C-choline PET/CT detection rate in patients with biochemical relapse after radical prostatectomy. *J Nucl Med.* 2009;50(9):1394-400.

7. Nanni C, Schiavina R, Brunocilla E, et al. 18F-FACBC compared with 11C-choline PET/CT in patients with biochemical relapse after radical prostatectomy: a prospective study in 28 patients. *Clinical genitourinary cancer.* Apr 2014;12(2):106-110.

8. Afshar-Oromieh A, Zechmann CM, Malcher A, et al. Comparison of PET imaging with a (68)Ga-labelled PSMA ligand and (18)F-choline-based PET/CT for the diagnosis of recurrent prostate cancer. *Eur J Nucl Med Mol Imaging.* Jan 2014;41(1):11-20.

Update Your Site in the CTN Database!

Review your site's information and keep it updated, especially if you are actively participating in clinical studies. If your site has not yet joined the CTN, please go to www.ctndatabase.org and complete the information to get started.

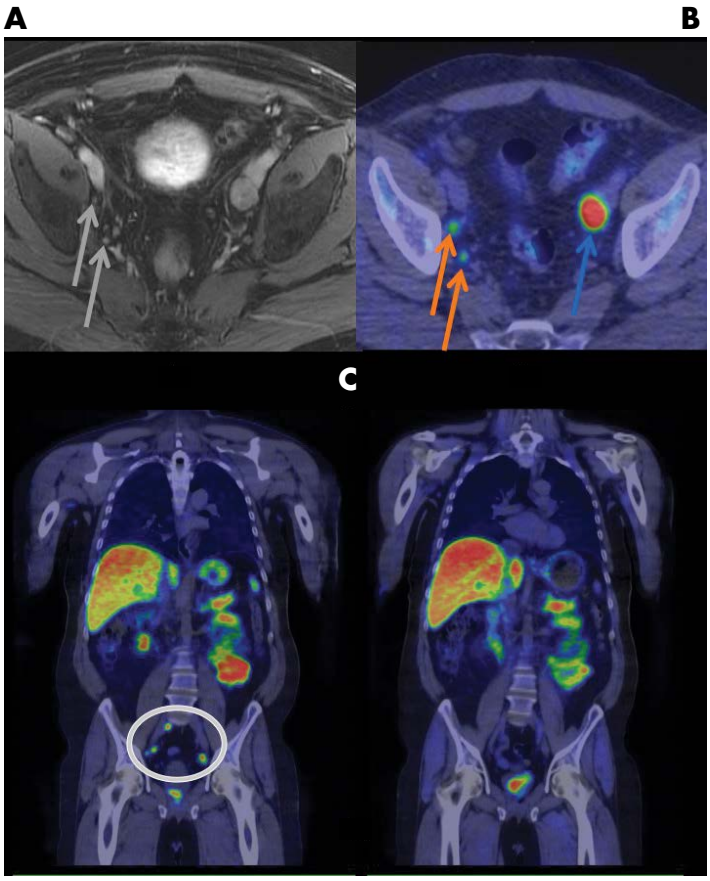


Figure 2. MRI (A) and choline PET/CT (B) in a patient with prostate cancer recurrence (PSA 3.3) show an enlarged left external iliac lymph node with choline uptake (blue arrow) and small right external iliac and internal iliac lymph nodes (grey arrows) with choline uptake (orange arrows). The small right nodes are only considered abnormal on choline PET/CT. PET showed more extensive disease than MRI. After treatment (C), all nodal disease (circle) shows resolution (right image) and the PSA is < 0.01.

CTN Numbers At-a-Glance

6 FLT manufacturers under the SNMMI-CTN IND

7 investigational radiopharmaceuticals under study

24 countries represented in the CTN database

411 sites registered in the CTN database

163 sites with validated PET/CT scanners

241 validated PET/CT scanners

Special FEATURE

SNMMI SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

THERANOSTICS World Congress Ga-68 & PRRT

JOHNS HOPKINS MEDICINE

3RD THERANOSTICS WORLD CONGRESS ON Ga-68 AND PRRT

The use of Gallium-68 (Ga-68) for molecular imaging of disease has seen a remarkable increase over the last several years. Applications for Ga-68 PET are emerging across a broad spectrum of diagnostic imaging challenges, including cancer, cardiovascular disease, infection and inflammation. The increase in enthusiasm for Ga-68 use can be ascribed to several factors, which promise an increasing role for Ga-68 as a tool for the design of compounds that have both diagnostic and therapeutic attributes, i.e., theranostics (Schultz M. *J Nucl Med.* April 2013; 54(4)659-660). The term THERANOSTICS epitomizes the inseparability of diagnosis and therapy, the pillars of medicine, and takes into account personalized management of disease for a specific patient.

In 2011, the "1st World Congress on Ga-68 and Peptide Receptor Radio Nuclide Therapy (PRRNT)" was held in Bad Berka, Germany. This congress offered a unique forum for high-level scientific discussions on recent developments in theranostics for neuroendocrine tumor (NET) patients and attracted over 400 participants from 53 countries representing all 5 continents. The success of this meeting led to the "2nd Congress on Ga-68, Molecular Imaging (PET/CT), Targeted Radionuclide Therapy and Dosimetry" in Chandigarh, India in 2013, which had over 500 attendees. During the 3-day meeting, more than 100 presentations and posters reflected advancements in using Ga-68 as a tracer for infection and inflammation as well as for receptor positive forms of breast and prostate cancer, in addition to its approved use as a tracer for NET patients.

Since the 1st World Congress, Ga-68 PET/CT imaging has grown tremendously and has been used to image NETs clinically in Europe and other countries—however, this has yet to be approved in the United States. To bring awareness to American physicians, scientists and the regulatory community on the importance and value of Ga-68 PET/CT imaging and to support efforts aimed at its approval, it was suggested that the next congress be held in the United States. After reviewing several options, congress leaders decided that the "3rd Theranostics World Congress on Ga-68 and PRRT" will take place on the Johns Hopkins medical campus in the United States in Baltimore, Md., March 12-14, 2015. SNMMI and Johns Hopkins are co-sponsoring the meeting, and CME credit is being sought for all sessions. In addition to planned talks given by a diverse group of renowned speakers, time will be allotted for original research presentations and poster sessions, as well as for viewing many trade exhibits.

AGENDA

With the potential of an approved agent available in the US in the near future, this conference is particularly useful to those who are new to Ga-68 PET radiopharmaceuticals. Presentations on clinical applications and patient advocacy observations are new to this congress, providing a unique perspective for all attendees. We hope to see you in Baltimore in 2015 for this cutting-edge meeting. Additional information can be found at www.snmmi.org/wcga68.

Thursday, March 12, 2015	Friday, March 13, 2015	Saturday, March 14, 2015
Generators, Post-Processing, and Synthesis Modules	Peptide Receptor Radiotherapy – Status Quo and Where to Go	State of the Art Management of NETs – Clinician and Patient Perspectives
Chelators and Labeling Chemistry for Theranostic Isotopes	Targeting Prostate Cancer: Imaging and Therapy	Imaging with Gallium – From D to T (Diagnosis to Therapy)
Theranostic Targeting Vectors	Established and Innovative Applications for Diagnosis and Therapy	How to Deliver Theranostics

REGISTER FOR THE
3rd Theranostics World Congress
at http://wcga68.org/registration

Message from Co-Chairs Continued from page 2.

- Two manuscripts on phantom comparisons, PET/CT scanner performance, and quantitative data analysis of over 400 scans obtained on over 230 unique scanners as part of the CTN Scanner Validation Program during its first 5 years were submitted to JNM for publication.
- CTN services were utilized by the Nuclear Medicine Clinical Trial Group, LLC (NMCTG) in oversight of 4 studies (4 different imaging agents) worldwide.

Moving forward into 2015, we anticipate that many of these activities will continue. As other opportunities arise, the CTN's efforts to standardize imaging and facilitate therapeutic drug and imaging agent development will expand to meet the demands of the community.

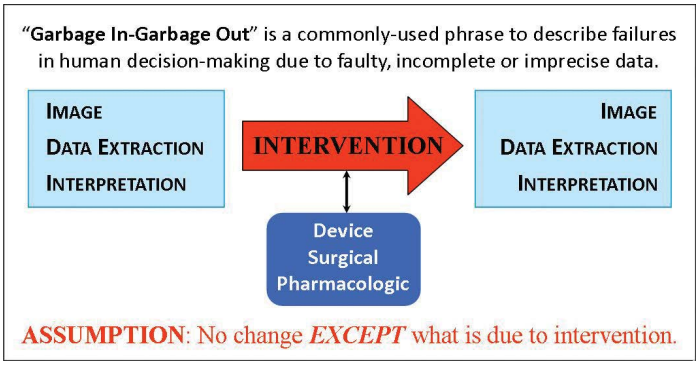
Tech **Talk**

GARBAGE IN-GARBAGE OUT

LisaAnn Trembath, CNMT, MSM, CCRA, FSNMTS

Study coordinators are often responsible for managing all clinical trial activity at a site, including interactions with other departments such as imaging. However, they are often NOT aware of what a PET scan actually is nor realize what is involved in patient preparation and scheduling these types of scans. Occasionally, I have been asked to provide training to study coordinators specifically on this topic, and one concept I stress is the age-old data principle of "garbage in-garbage out."

The principle behind imaging in clinical trials, especially for studies designed to monitor therapeutic effect, is that the only change between the first image and subsequent images should be the patient's physiologic response to the intervention. However, as many technologists know, other things impact a PET scan, and these can subsequently confound the actual data analysis. In FDG PET, for example, the uptake time for all study scans must be consistent. If uptake for a baseline scan is at 45 minutes but is 75 minutes for a post-treatment scan, there could be a quantitative change that has nothing to do with the actual study intervention.



Direct communication between the imaging department and a study coordinator is key to success. Following the tips below can help you assist a study coordinator in better understanding the nuances behind performing study PET scans.

1. Become involved with the study coordinator in the early stages of a trial. Technologists must know in advance if study PET parameters vary from routine clinical practice.
2. Request that the study coordinator notify the PET department scheduler about all clinical trial patients at the time of scheduling to plan for appropriate scan time. A 45-minute scan may actually take 3 hours depending on the imaging protocol.

Remember: Accuracy, consistency and careful planning help minimize the creation of "garbage" data and directly impacts patient care.

Research Essentials:
The IRB, RSC and RDRC– Their Role in Clinical Research

Excerpt from CTN Course #113

In 1974, U.S. National Research Act was adopted as a regulatory mechanism to supervise human research activities. It established the Institutional Review Board (IRB), whose overall responsibility was to oversee the protection of human subjects participating in research trials. The IRB is comprised of a diverse group of members involved in both scientific and non-scientific areas and possess professional competence necessary to review specific research activities. Once the study is approved, the IRB monitors activity throughout the duration of the trial, including surveillance of adverse events and review of proposed changes to the original research plan. The review ensures that:

- Procedures are appropriate for the proposed research
- Research methods are scientifically valid
- Risks to subjects are minimized and reasonable in relation to any anticipated benefits
- Informed consent is complete and appropriately obtained from subjects or their legal representatives

The Radiation Safety Committee (RSC) is the de facto expert in assessing risks, benefits and methods of radiation research. Most RSC charters provide empowering authority to review all uses of radiation. The RSC review differs from the IRB in that it is focused primarily on the following:

- Type and frequency of radiation use and route of administration
- Radiation dose per event and total dose per subject
- Appropriateness of the timing and spacing of events
- PI is an authorized user of radioactive materials
- Facility is licensed to perform procedures
- Is the study covered by a new drug application (NDA) or being done under an IND

If the research plan involves the use of a radioactive drug that is not FDA-approved nor listed on an IND, the Radioactive Drug Research Committee (RDRC) must first review the project. Many rules and regulations govern the RDRC and are described in full in the Code of Federal Regulations (21CFR361.1).

These committees have been established to ensure that the subject is protected at all times and that it is always the highest priority in any clinical trial.

BIOMARKER **SPOTLIGHT**

THE PATHWAY TO FINAL APPROVAL OF AN NDA FOR CHOLINE C-11 INJECTION

Joseph C. Hung, PhD, BCNP and Timothy R. DeGrado, PhD

In the mid 90s, Dr. Hara showed, in preliminary clinical studies, that brain tumors[1] and prostate cancer[2] avidly take up ^{11}C-choline with high tumor-background contrast. Subsequent clinical trials done in the early 2000s in Japan and Europe focused on the potential of ^{11}C-choline PET in the management of patients with recurrent prostate cancer (see this issue's Lead Article by Drs. Lowe and Kwon). At the Mayo Clinic, the use of ^{11}C-choline PET became an integral part of our prostate cancer imaging program.

The radiosynthesis of ^{11}C-choline is a straightforward ^{11}C-methylation of dimethylethanolamine (DME) in acetone, followed by solid-phase extraction isolation of ^{11}C-choline from DME using a carboxymethyl (CM) cartridge (Figure 1). The CM cartridge is washed with ethanol before elution of the product with sterile isotonic saline through a 0.2 µm sterilizing filter. The ^{11}C-choline product is found to be >99% radiochemically pure by cation-exchange radio-HPLC. All other standard CGMP quality control parameters must pass (with exception of sterility that requires 2 weeks) before doses are released for human use.

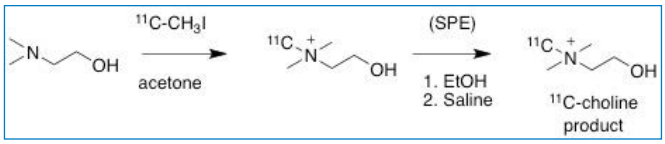


Figure 1. Synthetic scheme for ^{11}C-choline.

The publication of the final rule on CGMP for PET drugs on December 10, 2009 triggered the need to pursue NDA status for ^{11}C-choline so that we could continue to offer this vital imaging care for our prostate cancer patients. Although there was no commercial interest to the broader community due to its very short half-life (20 min) and non-proprietary nature, we moved forward on our own to obtain the required NDA. After multiple calls and emails with the FDA for guidance on the submission process, a formal meeting was held on February 8, 2011 to discuss our plan of action.

FDA representatives advised us to develop a more focused indication that reflected how ^{11}C-choline would be most effectively utilized in patients. They granted us a 505(b)(2) submission[3,4] that, for approval of an NDA, permits FDA to rely on data not developed by the applicant but, instead, through data already available in published literature. FDA cautioned us to carefully review the similarities and differences in the drug formulation used in literature studies and allowed us to address clinical pharmacology based on data from animal studies, non-radioactive injectable choline, and ^{18}F-choline.

Joseph C. Hung, PhD, BCNP

Timothy R. DeGrado, PhD

A waiver request for the user fees[5] was submitted to the FDA two months prior to the NDA submission and was eventually granted by the FDA. In the waiver approval letter, the FDA's Division of Medical Imaging Products stated "the visualization of recurrent cancer is a clinically important imaging claim", "… an accurate imaging test to detect local disease recurrence in patients who have undergone extensive therapy [RP, RT] is an important medical tool." As such, a *Priority Review* classification was issued to our application for Choline C-11 Injection (the drug name used in our NDA submission), and we eventually received the formal FDA approval notice on September 12, 2012 (Figure 2).

Patent Data

There are no unexpired patents for this product in the Orange Book Database.

EXCLUSIVITY DATA

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration
N203155	001	NCE	Sep 12, 2017
N203155	001	W	Sep 12, 2017

Figure 2. Patent and exclusivity data of Choline C-11 Injection as posted on the FDA Orange Book[6]. N203155 = NDA number of Choline C-11 Injection; NCE = new chemical entity; W = withdrawal. According to 21 CFR 314.108(b)(2), if a drug product contains a NCE, no person may submit a 505(b)(2) application or ANDA for a drug product contains the same active moiety for a period of 5 years[7]. We indicated to FDA that we would like to disclaim this exclusivity right as we have indicated in the very beginning of our NDA process that we waived any market exclusivity rights to this PET drug.

References:

1. Hara T, Kosaka N, Shinoura N, Kondo T. PET imaging of brain tumor with [methyl-^{11}C]choline. *J Nucl Med* 1997; 38:842-847.
2. Hara T, Kosaka N, Kishi H. PET imaging of prostate cancer using carbon-11-choline. *J Nucl Med* 1998; 39:990-995.
3. Section 505(b)(2), FD&C Act Chapter V: Drugs and Devices. Available at: http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/fdcactchaptervdrugsanddevices/default.htm. Silver Spring, MD: Food and Drug Administration. Accessed October 28, 2014.

Continued on page 8. See **Biomarker Spotlight.**

What's **Happening**

JNM Accepts CTN Phantom Data Manuscript

Since its inception in 2008, the CTN PET/CT Phantom Program has collected over 400 sets of phantom data from more than 230 unique scanners located at imaging sites around the world using its oncology clinical simulator phantom. The scanners include most commercially-available PET/CT systems from the three main vendors, ranging from the older, basic models to the most current state-of-the-art systems. Results from the acquired data was the basis for a manuscript recently accepted for publication in the JNM with a planned publication date of January 2015. This article, *"Quantitative PET/CT Scanner Performance Characterization Based upon the CTN Oncology Clinical Simulator Phantom"* by John Sunderland, describes the quantitative variability observed in multicenter clinical trials and discusses methods to help minimize this variability. Additional manuscripts from this rich data set are under development.

Biomarker Spotlight Continued from page 7.

4. Guidance for Industry: Applications Covered by 505(b)(2). Available at: http://www.fda.gov/downloads/Drugs/Guidances/ucm079345.pdf. Silver Spring, MD: Food and Drug Administration; 1999. Accessed October 28, 2014.

5. Guidance for Industry: User Fee Waivers, Reductions, and Refunds for Drug and Biological products. Silver Spring, MD: Food and Drug Administration, 2011. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079298.pdf. Accessed October 28, 2014.

6. Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations – Choline C 11 Injection. Available at: http://www.accessdata.fda.gov/scripts/cder/ob/docs/patexclnew.cfm?Appl_No=203155&Product_No=001&table1=OB_Rx. Accessed October 29, 2014.

7. Food and Drug Administration. Title 21 Code of Federal Regulations 314.108(b0(2) New drug product exclusivity. Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.108. Accessed October 28, 2014.

Save the **Dates**

SNMMI 2015 Mid-Winter Meeting
January 22 – 25, 2015 • San Antonio, TX

AACR-SNMMI Joint Conference on Molecular Imaging in Cancer Biology and Therapy
February 11 – 14, 2015 • San Diego, CA

3rd Theranostics World Congress on Ga-68 and PRRT
March 12 – 14, 2015 • Baltimore, MD

AACR Annual Meeting 2015
April 18 – 22, 2015 • Philadelphia, PA

2015 ASCO Annual Meeting
May 29 – June 2, 2015 • Chicago, IL

SNMMI 2015 Annual Meeting
June 6 – 10, 2015 • Baltimore, MD

DIA 2015 51st Annual Meeting
June 14 – 18, 2015 • Washington, DC

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