assurance measures do not detect viral contamination, and there are currently no requirements for operator training on blood-borne pathogen contamination. Professional and regulatory organizations should provide explicit guidance on appropriate precautions for commonly prepared radiopharmaceuticals and should consider whether additional guidance is needed for all sterile pharmaceuticals prepared in pharmacies that handle blood.

In summary, the current guidelines cited by Hung do not adequately address the risk of blood contamination of pharmaceuticals in nuclear pharmacies. The introduction of blood products into nuclear pharmacies where sterile pharmaceuticals are prepared should be accompanied by aggressive efforts to ensure safe blood-handling practices and appropriate infection control. Pharmacists and technicians working in these settings should have a thorough understanding of precautions to prevent blood contamination and how these differ from the approach to bacterial or fungal contamination and growth. Increased awareness of the risks of blood-borne pathogens in nuclear pharmacies through enhanced training, education, and professional leadership is needed. Nuclear pharmacies that handle blood or any potentially infectious biologic material should adhere to higher standards to ensure product integrity and patient safety.

DISCLAIMER: The findings and conclusions in this letter are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

REFERENCES

1. Hung JC. Hepatitis C virus infections from contaminated ^{99m}Tc-sestamibi [letter]. *J Nucl Med.* 2007;48:847–848.
2. Patel PR, Larson AK, Castel AD, et al. Hepatitis C virus infections from a contaminated radiopharmaceutical used in myocardial perfusion studies. *JAMA.* 2006;296:2005–2011.
3. Hung JC. The potential impact of USP general chapter <797> on procedures and requirements for the preparation of sterile radiopharmaceuticals. *J Nucl Med.* 2004;45(6):21N–26N.
4. American Pharmacists Association web site. APhA comments on USP chapter 797. Available at: http://www.aphanet.org/AM/Template.cfm?Section=Home&CONTENTID=6704&TEMPLATE=/CM/ContentDisplay.cfm. Accessed August 21, 2007.
5. U.S. Pharmacopeia web site. <797> Pharmaceutical Compounding: Sterile Preparations. Available at: http://www.usp.org/pdf/EN/USPNF/PF797.pdf. Accessed August 21, 2007.

Priti R. Patel
Joseph F. Perz
Anthony E. Fiore
Centers for Disease Control and Prevention
Atlanta, Georgia

Amanda D. Castel
George Washington University School of Public Health and Health Services
Washington, DC

DOI: 10.2967/jnumed.107.045195

REPLY: It seems to me that the letter by Patel et al. failed to identify the specific cause for this hepatitis C virus (HCV) outbreak, and in fact the letter made the whole issue more confusing. If the pharmacist who radiolabeled WBCs on October 14, 2004, had to exit the "blood room" to the "main room" to measure the radioactivity of ^{111}In and ^{111}In-oxine–labeled white blood cells, the syringes containing these materials would have been capped during the dose measurement and brought back to the blood room after the measurement. Also, the letter indicated that these syringes would not be reused "because of their radioactive contents." Thus, the process and syringes should not be the causes for the HCV contamination. Patel et al. surmised that a contaminated vial or bag of saline or possibly a contaminated syringe was somehow moved from the blood room to the main room and somehow caused contamination only to vial 1 and not the other 5 vials of ^{99m}Tc-sestamibi, all of which were prepared 1 min apart by the same pharmacist in the same hood (*1*). Let us assume that contaminated saline vials/bags or syringes were carried inadvertently into the main room on the afternoon of October 14, 2004. Before the preparation of ^{99m}Tc-sestamibi (vials 1–6) in the early morning of October 15, 2004, the pharmacist would have discarded any contaminated supplies (e.g., unwrapped syringes or used saline vials or bags) left in the hood of the main room as per the statement (i.e., "No pharmacists reported improper disposal or reuse of contaminated equipment or supplies.") in the letter by Patel et al.

Even though 59 (82%) of 72 patients who were injected with ^{99m}Tc-sestamibi drawn from vials 2–6 were later tested for anti-HCV and all were negative (*1*), I think that it would be prudent to closely follow up the medical condition of the other 13 individuals who did not take part in this test because the exact cause for this catastrophic HCV contamination is still unclear. Have symptoms related to HCV, hepatitis B virus, or HIV (human immunodeficiency virus) developed in any of these 13 patients after the incident?

There is no doubt that higher standards should be established for the handling of radiolabeled blood cells to ensure product integrity and patient safety. However, we should carefully evaluate the suitability and practicality of any proposed standards so that their cost (e.g., the cost of significant changes in remodeling, monitoring, or staffing) does not force facilities (especially small or rural nuclear pharmacies/nuclear medicine laboratories) to discontinue providing products such as ^{111}In-oxine–labeled white blood cells to patients.

REFERENCE

1. Patel PR, Larson AK, Castel AD, et al. Hepatitis C virus infections from a contaminated radiopharmaceutical used in myocardial perfusion studies. *JAMA.* 2006;296:2005–2011.

Joseph C. Hung
Mayo Clinic
Rochester, Minnesota

DOI: 10.2967/jnumed.107.045393

Attenuation Correction for Stress and Rest PET ^{82}Rb Myocardial Perfusion Images

TO THE EDITOR: The July 2007 article by Gould et al. (*1*) reported a 40% false-positive rate for cardiac PET ^{82}Rb myocardial perfusion imaging with CT attenuation correction, using helical slow imaging (29 s) during free breathing and helical fast imaging (4 s) during a breath-hold at end expiration. Further, the authors suggested that correction with nonhelical, time-averaged

cine CT images eliminates artifactual defects in PET ^{82}Rb images. Our concern with the study is that it contrasts false-positive findings from cine CT with software alignment and false-positive findings from helical CT without software alignment. Because most manufacturers of PET/CT scanners have a software alignment tool to be used in conjunction with helical CT, we suggest that it is appropriate and important for Gould et al. to compare false-positive findings from software-aligned cine CT and false-positive findings from software-aligned helical CT (e.g., their slow helical CT scan). Table 5 of Gould et al. lists an artifact frequency for unshifted slow helical CT studies (27%, or 39/145) similar to that found for "conventional" PET ^{82}Rb studies (21%, or 252/1, 177) in an earlier publication by Dr. Gould's group (*2*), in which a ^{68}Ge rod source was used for the attenuation correction. After visual checking of the PET ^{82}Rb and attenuation images for misregistration, the misaligned conventional rod source studies were manually shifted using computer software (*2*). Moreover, even with cine CT, Gould et al. reported that 19% (22/114) of patient datasets were misaligned with PET and required software alignment (*1*). That is, the new paper (*1*) combined with the earlier publication (*2*) supports the conclusion that free-breathing helical CT and cine CT have nearly the same frequency of artifacts as does conventional PET. Significantly, all techniques required a software alignment solution.

In our institution, we have used a somewhat different approach on our 64-slice Biograph PET/CT scanner (Siemens). We acquire 3 very fast (2.7-s) helical CT scans during free breathing, 1 immediately before and 2 immediately after acquiring the stress PET ^{82}Rb images (*3*). The exposure, $CTDI_{vol}$, is 0.7 mGy in each scan. We have found that this protocol increases the probability of alignment between a PET ^{82}Rb image and an acquired CT image. Our protocol also includes 3 CT scans at rest for correction of the rest PET ^{82}Rb scan. Like Gould et al. (*1*), we have estimated visually the degree of PET/CT misalignment with this procedure using the PET/CT 3-dimensional fusion software of the manufacturer (*3*). We found no apparent misalignment between PET and at least 1 CT scan in 85% of studies at stress and 89% of studies at rest. The best-case misalignment was small, and appropriate for PET attenuation correction, in an additional 14% of the studies at stress and 11% of the studies at rest (*3*). In only a few cases (<1%) did we observe a large or severe PET misalignment with all 3 of the CT scans that then required computer software alignment. We have acquired 1,400 rest/stress PET/CT ^{82}Rb clinical studies with this protocol. The total $CTDI_{vol}$ is 4.2 mGy with our 6–CT scan protocol. Gould et al. quoted a radiation exposure of 5.7 mGy for their helical CT scan and a radiation dose of 10 mGy for cine CT. We are studying techniques to reduce the dose even further. These steps include reducing the x-ray voltage from 120 to 100 kVp and even to 80 kVp in very thin patients and reducing the number of CT scans, thus requiring a greater reliance on software alignment.

In summary, the slow helical non–breath-hold CT approach originally proposed by Brunken et al. (*4*) produces a frequency of misalignment-related artifacts that is similar to the frequency reported for cine CT (*1*) and conventional PET (*2*). Gould et al. (*1*) did not provide the false-positive rate for software-shifted non–breath-hold helical CT, and this omission represents a major limitation of the paper. PET and CT alignment can be achieved with a fast helical multi–CT scan protocol that limits the need for software alignment tools to a small percentage of studies, while using an even lower radiation dose (*3*).

REFERENCES

1. Gould KL, Pan T, Loghin C, Johnson NP, Guha A, Sdringola S. Frequent diagnostic errors in cardiac PET/CT due to misregistration of CT attenuation and emission PET images: a definitive analysis of causes, consequences, and corrections. *J Nucl Med.* 2007;48:1112–1121.
2. Loghin C, Sdringola S, Gould KL. Common artifacts in PET myocardial perfusion images due to attenuation-emission misregistration: clinical significance, causes, and solutions. *J Nucl Med.* 2004;45:1029–1039.
3. Streeter J, Eisner R, Hamill J, Nelson M, Patterson R. Attenuation correction of stress PET Rb82 with ultrafast CT images [abstract]. *J Nucl Med.* 2007;48(suppl 2):446P.
4. Brunken RC, DiFilippo FP, Bybel B, Neumann DR, Kaczur T, White RD. Clinical evaluation of cardiac PET attenuation correction using "fast" and "slow" CT images [abstract]. *J Nucl Med.* 2004;45(suppl):120P.

Robert L. Eisner
Randolph E. Patterson
Emory Crawford Long Hospital
Atlanta, Georgia

DOI: 10.2967/jnumed.107.045468

REPLY: In their letter to the editor, Eisner and Patterson make 3 criticisms that they call "major limitations" to our report on attenuation–emission misregistration in cardiac PET/CT (*1*), as follows: First, the frequency of attenuation–emission artifacts in PET/CT is similar using slow helical CT during breathing, using a rotating rod during breathing, and using cine CT during breathing, all without manual shifting for final optimal coregistration. In our report, this "baseline" frequency of misregistration was corrected by manual coregistration of attenuation and emission scans for the rotating rod (*2*) and cine CT attenuation data (*1*). Second, in their protocol, 1 of 3 sequential fast helical CT scans were acquired during breathing without shifting to achieve coregistration. Artifacts were small or, in 85% of cases, absent, and only more severe artifacts were corrected by shift software. Third, the radiation dose for PET/CT is too high and needs to be reduced.

Our paper in *The Journal of Nuclear Medicine* validated a PET/CT protocol that eliminates all misregistration artifacts, thereby providing a definitive, quantitative, standalone noninvasive guide for the management of coronary artery disease. To our knowledge, the paper was the first large, systematic clinical report defining and solving this problem in PET/CT and having significant implications.

The vehemence of their terming their criticisms as "major limitations" is puzzling for several reasons. Basically, Eisner and Patterson agree that attenuation–emission misregistration is a real problem in cardiac PET, a problem not widely addressed clinically until our first reports in *The Journal of Nuclear Medicine* (*1,2*). Contrary to the emphasis in their letter, the frequency of misregistration artifacts with cine CT attenuation correction (*1*) without manual shifting should be and is similar to that with the rotating rod (*2*) because both acquire attenuation data that are averaged over the breathing cycle. The data would be inconsistent otherwise. However, breathing during slow helical CT distorts the attenuation data such that manual shifting to achieve coregistration fails to eliminate the corresponding artifacts, as our data show (*1*). Despite averaging of attenuation correction during breathing using either a rotating rod or cine CT, misregistration still occurs, requiring manual shifting to optimize coregistration in all patients.

A careful paper from Bacharach's laboratory (*3*) on quantitative PET demonstrates that the degree of attenuation varies substantially with respiration even when cardiac borders are coregistered.