Dynamic PET/CT with ^{11}C-Acetate in Prostate Cancer

TO THE EDITOR: In the April 2012 issue of *The Journal of Nuclear Medicine,* Mena et al. (*1*) reported on PET/CT studies using ^{11}C-acetate in localized prostate cancer. This was an interesting article, in which our work from 2008 (*2*) was quoted several times.

The prostate acetate uptake curves shown in Figure 1 of their article are strikingly different from what we have demonstrated. We have never seen a biphasic pattern with a rapid decline after the initial peak. Aijun Sun, in her PhD thesis, (*3*) showed acetate time–activity curves just like ours, with a rapid increase that reached a plateau after 3 min. Therefore, the biphasic morphology in the prostate curves of Mena et al. is a reason for concern. Given the biphasic shape of the prostate time–activity curves, it is not surprising that Patlak graphical analysis did not fit, since the Patlak plot performs best for uptake curves reaching a plateau.

The prostate time–activity curves of Mena et al. peaked at around 5 min, and they attributed this finding to initial tumor perfusion and dispersion. This cause is unlikely, since the iliac vessels are near the prostate gland and peak within 1 min (*2,3*). Their Figure 1 depicts an input function (iliac curve) with a maximum standardized uptake value just above 10, which is similar to ours, at 10.5, after removing the partial-volume correction. The peak of prostate cancer in Figure 1 is approximately 70% of that of the input function, indicating that the perfusion is high (estimated at $>$1.5). We found the 3-compartment, 3-parameter model optimal for the prostate (*2*) and measured an average perfusion of 0.42 for primary prostate cancer, 0.21 for recurrent cancer, and 0.34 for benign prostatic hyperplasia. These values compare favorably with Sun's 0.3 (estimated) for recurrent prostate cancer (*3*). Normal prostate perfusion measured with nuclear magnetic resonance techniques yielded 0.23 for Lüdemann et al. (*4*) and 0.26 for Li and Metzger (*5*). (All perfusion units are in mL/min/g, assuming a specific mass of 1 g/cm^3 for prostate tissue.)

The relatively late appearance of the prostate peak in Figure 1 ($\sim$5 min), implies that acetate has a long residence time in prostate tissue, suggestive of a large distribution volume (estimated at $>$5 mL/g, compared with our 1.25 mL/g). What accounts for such a large apparent distribution volume?

To put this in a biologic perspective, the prostate cancer uptake curves of Figure 1 suggest a perfusion similar to that of the myocardium. Myocardial acetate kinetics measured in our laboratory showed a biphasic pattern with an early peak at 1–2 min, which can safely be interpreted as the tracer transit time through tissue. Thereafter, the myocardial time–activity curve demonstrated a continuous drop, without a plateau (*6*).

When the experiments of Mena et al. are compared with ours, there is a major difference in the acquisition protocol. Our acquisition consisted of a single dynamic scan of 21 min. Mena et al. used dynamic imaging for 6 min followed by 4 static scans. This mixing of dynamic and static imaging raises concern on whether technical factors could be responsible for the biphasic uptake curve of the prostate. Did the authors perform a phantom experiment to validate the combined dynamic and static protocol?

In summary, Mena et al. reported a biphasic shape for acetate uptake in the prostate—a pattern strikingly different from what others have found. The data of Mena et al. suggest values for prostate perfusion and distribution volume that are too high. This possibility is concerning and raises questions about technical issues.

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Christiaan Schiepers*
Sung-Cheng Huang
Magnus Dahlbom
**David Geffen School of Medicine*
University of California, Los Angeles
200 Med Pl., B-114
Los Angeles, CA 90095
E-mail: cschiepers@mednet.ucla.edu

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REPLY: We thank Schiepers et al. for their comments on our article (*1*). Schiepers et al.'s publication on a similar topic (*2*) did not show the biphasic pattern of ^{11}C-acetate uptake that we saw in some patients. In response, we reviewed all the time–activity curves generated for our subjects both for tumor and for benign prostatic hyperplasia in the prostate, blood pool, and muscle volumes of interest. The summary data plots of the time–activity curves for ^{11}C-acetate uptake, as shown in Figure 1 of our article, are an average representation across all subjects. Within these data, we found 2 classes of uptake curves, as shown in the plots in Figures 1A and 1B of our article. One class clearly demonstrated a biphasic pattern (e.g., subject 36), whereas the other demonstrated a simple, irreversible uptake pattern (e.g., subject 28) more consistent with Schiepers et al. When averaged together, the biphasic pattern emerges.

Dr. Schiepers was correct in pointing out the complexity of our imaging protocol. As opposed to Dr. Schiepers' imaging method, which included the prostate throughout the duration of the scan, our imaging protocol included both the prostate and the lower abdomen so as to detect potential metastatic disease. This protocol required that we move the patient back and forth between the 2 scanning positions, first scanning the pelvis and then the lower abdomen, each for 2 min at a time. This technique can create subtle misalignments and other quantitation issues due to altered decay corrections and the inability of the reconstruction software to reproduce accurate SUVs. However, the latter issue is minor and is related mostly to rounding-off errors in entering the injection time.

The most challenging part of the imaging protocol was that the first 6 min of the scan were acquired in list mode; thus, we reconstructed the data in time frames, with the last time frame truncating the time–activity curve at 6 min. The prostate was then moved out of the field of view for the first lower-abdomen scan and then back into the field of view for the next 2-min scan at about 12–15 min after injection. The use of these time frames necessarily causes a sampling gap between 6 min and 12–15 min that would help confirm either a true biphasic pattern or an artifact due to the complicated nature of the imaging protocol. Another potential issue is that the dose used (1,480 MBq) was substantially higher than that used in the Schiepers study (370 MBq), thus causing potential SUV nonlinearities at early acquisition times.

To determine whether there were high rate effects or whether the complicated imaging protocol would lead to an artificial biphasic uptake curve, during the review of the time–activity data, fresh volumes of interest were drawn on hot-spot lesions in the prostate and in muscle tissue as a reference. If an artificial biphasic uptake pattern had been generated by either the high activity or the imaging protocol, it should have shown up in both prostate lesion and muscle tissue time–activity curves. Neither subject 36 nor subject 28 showed a biphasic pattern in the muscle time–activity curve, thus raising the possibility that the biphasic pattern is real and reflects actual metabolic differences among prostate cancers that may be of importance.

Regardless of the presence or absence of this biphasic pattern in the time–activity curve, the main conclusion of our paper remains the same: ^{11}C-acetate does not do a very good job in distinguishing between malignant tumors and BPH lesions. Because this is the major determinant of whether an imaging tool for localized prostate cancer succeeds, ^{11}C-acetate would not seem to pass this test.

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Stephen Adler
Karen Kurdziel*
Liza Lindenberg
Peter Choyke
Esther Mena
**National Cancer Institute*
10 Center Dr., Room B3B403
Bethesda, MD 20892
E-mail: kurdziek@mail.nih.gov

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The Timing of Pregnancy Testing in ^{131}I Therapy

TO THE EDITOR: In the publication of the SNMMI guideline on ^{131}I therapy (*1*), there appears a recommendation for a pregnancy test to be performed within 24 h of the administration of ^{131}I for women of reproductive age who cannot provide written documentation of a hysterectomy or bilateral salpingo-oophorectomy.

Some readers have raised the concern that if the pregnancy test is obtained some hours before the suggested 24-h limit and a false-negative result ensues, they would be liable for a lawsuit. We must emphasize that a guideline is not a regulation and has no force of law.

It is simply a fact that pregnancy tests are negative until implantation of the embryo, which occurs 7–10 d after fertilization. Therefore, a test performed 48 h before therapy will miss more pregnancies than one performed at 24 h or on the same day, and it seems unreasonable to take that chance.

At the University of Cincinnati Medical Center, we draw blood for a β–human chorionic gonadotropin study on the day of therapy, the results of which will be returned in 30 min. Meanwhile, the nuclear pharmacy will not deliver the prescribed activity for 90–120 min, so no one is inconvenienced, and the patient is protected to the best of our ability from being treated while pregnant.

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Edward B. Silberstein
University of Cincinnati Medical Center
234 Goodman St.
Room G026, Mont Reid Pavilion
Cincinnati, OH 45219
E-mail: edward.silberstein@uchealth.com

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