REFERENCES

1. Cai Z, Pignol JP, Chan C, Reilly RM. Cellular dosimetry of ^{111}In using Monte Carlo N-particle computer code: comparison with analytic methods and correlation with in vitro cytotoxicity. *J Nucl Med.* 2010;51:462–470.
2. Goddu SM, Howell RW, Rao DV. Cellular dosimetry: absorbed fractions for monoenergetic electron and alpha particle sources and S-values for radionuclides uniformly distributed in different cell compartments. *J Nucl Med.* 1994;35:303–316.
3. Goddu SM, Howell RW, Bouchet LG, Bolch WE, Rao DV. *MIRD Cellular S Values: Self-Absorbed Dose per Unit Cumulated Activity for Selected Radionuclides and Monoenergetic Electron and Alpha Particle Emitters Incorporated into Different Cell Compartments.* Reston, VA: Society of Nuclear Medicine; 1997:15, 87.
4. Agostinelli S, Allison J, Amako K, et al. GEANT4: a simulation toolkit. *Nucl Instrum Methods Phys Res A.* 2003;506:250–303.
5. Howell RW. Radiation spectra for Auger-electron emitting radionuclides: report no. 2 of AAPM Nuclear Medicine Task Group no. 6. *Med Phys.* 1992;19:1371–1383.

Robert Freudenberg*

Jorg Kotzerke

*Universitätsklinikum Carl Gustav Carus Dresden

Fetscherstrasse 74

Dresden, Germany, 01307

E-mail: robert.freudenberg@uniklinikum-dresden.de

DOI: 10.2967/jnumed.110.078832

REPLY: We thank Drs. Freudenberg and Kotzerke for their interest in our work on cellular dosimetry of ^{111}In using Monte Carlo N-particle (MCNP) code (1) and for bringing to our attention the Geant4 toolkit, an alternative and free Monte Carlo computation code. For a single-cell model using Geant4, they obtained S values that compared well with ours. Yoriyaz et al. analyzed the discrepancy in photon and electron absorbed fraction calculations using MCNP and Geant4 (2). They pointed out, on the one hand, that major sources of discrepancy come from the set of parameters chosen by simulation and the different cross-section libraries used by the codes. On the other hand, MCNP is much easier to use and install than Geant4. MCNP does not require programming from users, whereas users of Geant4 are expected to have extensive knowledge of C++ compiler and the computer system. Moreover, the universe card of MCNP is handy for defining the repeated structure and thus useful for calculating the S values for cell monolayer and cluster models (3). It would be interesting to examine the capability of calculating S values for these geometries using Geant4.

The low-energy model of Geant4 allows the simulation of electron transport down to 250 eV, whereas MCNP allows simulation down to only 1 keV. The electron penetration length in water is about 10 and 40 nm for 250-eV and 1-keV electrons, respectively (4). Both are far lower than the smallest dimension of a cell nucleus (2 μm) used in our calculations. The difference in electron cutoff energy for MCNP and Geant4 should not cause any significant discrepancy in calculation of cellular S values, as is supported by the comparable S values obtained using both MCNP and Geant4. We note that PENELOPE is able to perform electron-photon transport simulations down to energies on the order of few tens of electron-volts and has an advantage over MCNP and Geant4 in calculation of nanodosimetry (5).

Drs. Freudenberg and Kotzerke calculated the S values taking into account both electron and photon emission. Though we are able to calculate the photon contribution to cellular S values using

MCNP, only electrons were considered in the calculation in our study. The contribution of γ - and x-ray photons to the S values ($<2\%$ of electron contribution to the S value of nucleus to nucleus [$S_{N \rightarrow N}$]; $<5\%$ of the electron contribution to the S value of cell surface to nucleus [$S_{CS \rightarrow N}$] and cytoplasm to nucleus [$S_{Cy \rightarrow N}$]) was considered negligible and, therefore, ignored. Goddu et al. (6,7) also ignored the photon radiation in calculation of cellular S values.

REFERENCES

1. Cai Z, Pignol JP, Chan C, Reilly RM. Cellular dosimetry of ^{111}In using Monte Carlo N-particle computer code: comparison with analytic methods and correlation with in vitro cytotoxicity. *J Nucl Med.* 2010;51:462–470.
2. Yoriyaz H, Moralles M, Siqueira PDD, Guimarães CD, Cintra FB, dos Santos A. Physical models, cross sections, and numerical approximations used in MCNP and GEANT4 Monte Carlo codes for photon and electron absorbed fraction calculation. *Med Phys.* 2009;36:5198–5213.
3. Briesmeister JF for the X-5 Monte Carlo Team. *MCNP—A General Monte Carlo N-Particle Transport Code, Version 5.* Los Alamos, NM: Los Alamos National Laboratory; 2003. UR-03-1987.
4. Meesungnoen J, Jay-Gerin JP, Filali-Mouhim A, Mankhetkorn S. Low-energy electron penetration range in liquid water. *Radiat Res.* 2002;158:657–660.
5. Bernal MA, Liendo JA. An investigation on the capabilities of the PENELOPE MC code in nanodosimetry. *Med Phys.* 2009;36:620–625.
6. Goddu SM, Howell RW, Rao DV. Cellular dosimetry: absorbed fractions for monoenergetic electron and alpha particle sources and S-values for radionuclides uniformly distributed in different cell compartments. *J Nucl Med.* 1994;35:303–316.
7. Goddu SM, Howell RW, Bouchet LG, Bolch WE, Rao DV. *MIRD Cellular S Values: Self-Absorbed Dose per Unit Cumulated Activity for Selected Radionuclides and Monoenergetic Electron and Alpha Particle Emitters Incorporated into Different Cell Compartments.* Reston, VA: Society of Nuclear Medicine; 1997:15, 87.

Zhongli Cai

Jean-Philippe Pignol

Conrad Chan

Raymond M. Reilly*

*University of Toronto

144 College St.

Toronto, Ontario, Canada, M5S 3M2

E-mail: raymond.reilly@utoronto.ca

DOI: 10.2967/jnumed.110.079129

PET/CT Colonography

TO THE EDITOR: We read with interest the article by Taylor et al. on combined CT colonography and PET using a nonlaxative preparation (1). It is nice to see others pursuing further this technically feasible examination on which we originally reported (2). There are a few points of interest that have prompted this letter: First, we found it remarkable that the mean volume of CO_2 insufflated was 3.1 L with a maximum of 4.1 L! Our own examinations averaged 33 L with a maximum of 65 L and had no reported side effects. Our mean room time was longer, however (77 min). Unlike their technique, we did not systematically turn down the CO_2 pressure to 15 mm Hg after achieving patient tolerance because we believed that reabsorption of CO_2 is so rapid that reducing the pressure would reduce colonic distension. It is hard to understand the difference in volumes between our 2 studies, and

we wonder if the authors could comment. Second, as the authors correctly state, the increased specificity supposedly offered by PET assumes that the lack of focal ^{18}F -FDG uptake always indicates lack of a true lesion (which the authors disproved, like others, in their own paper). Therefore, in this study with few lesions overall, the true meaning of this increased specificity seems to remain a bit questionable. Third, we wonder if the reported level and frequency of discomfort at colonoscopy might be attributable to the type of sedation administered (midazolam and pethidine). Types of sedation vary worldwide and may not even be used in some centers (3,4). In the United States, propofol (Diprivan; AstraZeneca), a deep-sedative hypnotic, is being used more often. Patients seem to achieve greater comfort and less recollection of pain. One wonders if this would have changed the balance of preference. Fourth, it is hard to extrapolate Figure 7 from results in Figure 6. It seems that about the same number of patients rates each examination “well” or “fairly well” and yet most chose PET/CT colonography as more acceptable and as more desirable to undergo again. One wonders if there was some sort of recall bias or whether the entire equation comes down to the colonic preparation involved rather than the actual test itself. Do the authors have any sense for what part the preparation played in the rating? That is, is there a statistical way to separate out this component? Also 13 patients did not even return the questionnaire. Could they all have been utterly disgusted with both examinations? Fifth and finally, one disadvantage to which the authors allude but do not address is that if this minimal-preparation technique were to be implemented, patients who have a positive finding would have to undergo a full preparation for colonoscopy. In our study, patients went directly to colonoscopy. However, if in fact the negative predictive value of such a test in this population were shown to be high, patients could avoid a full preparation and a colonoscopy altogether—the obvious advantage.

REFERENCES

1. Taylor SA, Bomanji JB, Manpanzure L, et al. Nonlaxative PET/CT colonography: feasibility, acceptability, and pilot performance in patients at higher risk of colonic neoplasia. *J Nucl Med*. 2010;51:854–861.
2. Gollub MJ, Akhurst T, Markowitz AJ, et al. Combined CT colonography and ^{18}F -FDG PET of colon polyps: potential technique for selective detection of cancer and precancerous lesions. *AJR*. 2007;188:130–138.
3. Takahashi Y, Tanaka H, Mitsuyo K, et al. Sedation-free colonoscopy. *Dis Colon Rectum*. 2005;48:855–859.
4. Ylinen ER, Vehvilainen-Julkunen K, Pietila AN, et al. Medication-free colonoscopy: factors related to pain and its assessment. *J Adv Nurs*. 2009;65:2597–2607.

Marc J Gollub*

Tim Akhurst

*Memorial Sloan-Kettering Cancer Center
1275 York Ave., Room C276F
New York, NY 10065
E-mail: gollubm@mskcc.org

DOI: 10.2967/jnumed.110.079632

REPLY: We thank Drs. Gollub and Akhurst for their interest in our article (1) and acknowledge their work in this field.

We agree with their comment about the large volumes of CO_2 insufflated. In the article, we report the volume of carbon dioxide insufflated in the supine position (3.1 L; range, 2.2–4.1 L) before

the supine CT acquisition and then the additional mean volume of gas insufflated just before the prone scan acquisition (based on assessment of the prone scout scan). We reported the volume in this manner to give readers a practical guide as to how we performed the technique—the total volume of gas insufflated over the whole hour is of less relevance. As to this total volume of carbon dioxide, we agree this volume can be very large because of absorption of the gas during the procedure. By reducing the pressure to 15 mm Hg, we obtained total volumes that were a little smaller than those experienced by Dr. Gollub but were in the range of 10–40 L.

The increase in specificity afforded by PET in our study does rely on the assumption that significant pathology would be PET-avid, which we agree is not always the case. Reporting of colonic neoplasia during CT colonography is rarely a yes/no phenomenon. Readers take many factors into consideration when deciding whether to call a lesion real or not: for example, morphology, lesion movement, attenuation homogeneity, general state of bowel preparation, and distension. ^{18}F -FDG avidity or otherwise of the lesion is an additional factor that may aid the radiologist, and in our feasibility study we found that false-positives were reduced. It is perhaps more intuitive that PET would increase sensitivity in nonlaxative studies. We did not find this to be so, but as we discuss, we used an experienced reader to report the CT colonography component of the examination. It would seem likely that ^{18}F -FDG avidity would improve the sensitivity of less experienced CT colonography readers, somewhat akin to computer-aided-detection software, and further work on this possibility is under way.

A difference in sedation techniques may in part explain some of the patient discomfort during colonoscopy that we reported. Of course, heavy-sedation regimes are not without risk, particularly in older patients. In a recent study investigating the use of propofol and remifentanyl during colonoscopy, oxygen saturation dropped to less than 90% in 5 of 25 patients, who required bag mask ventilation (2). Our endoscopists carefully titrated the amount of administered analgesia and sedation against patients' feeling of discomfort during colonoscopy to maximize both patient comfort and safety.

It is reassuring that patients generally tolerated both colonoscopy and PET/CT colonography reasonably well, and although we can only speculate on the views of questionnaire nonresponders, it would perhaps seem unlikely they were “disgusted”! It is absolutely correct that when assigning an overall preference between 2 tests, patients weigh many factors, not just the physical experience of the test itself. We believed that the convenience of bowel preparation for PET/CT colonography was a major factor, but there are many other facets more difficult to quantify, such as test environment, staff attitudes, posttest care, feedback of results, patients' assumptions on test performance, and fear of complications. We know, for example, that patients often assume that new, expensive imaging technologies must be “better” than conventional tests (3). Although quantitative questionnaires do have the benefit of speed and simplicity, in reality detailed qualitative studies are required to tease out which factors most influence patients' test preferences, and even then, these factors often differ widely between individuals.

To justify the use of nonlaxative PET/CT colonography as a first-line test in the investigation of older patients, a high positive predictive value is essential, as Drs. Gollub and Akhurst correctly state, because patients with reported pathology must undergo invasive colonoscopy with bowel preparation. However, the test must also be sensitive (low false-negative rate) and so have a