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Functional Imaging to Differentiate Pulmonary Carcinoids

TO THE EDITOR: We read with great interest the article by Kayani et al. (*1*). They evaluated 11 cases of typical carcinoids, 2 of atypical carcinoids, 1 of small cell neuroendocrine tumor, 1 of large cell neuroendocrine tumor, 2 of diffuse idiopathic pulmonary neuroendocrine hyperplasia, and 1 of adenocarcinoma with neuroendocrine differentiation using ^{18}F-FDG PET/CT and ^{68}Ga-DOTATATE PET/CT. They reported that, compared with typical carcinoids, atypical and other less differentiated carcinoids revealed significantly higher uptake on ^{18}F-FDG PET/CT scans ($P = 0.005$) and significantly lower uptake on ^{68}Ga-DOTATATE PET/CT scans ($P = 0.002$).

We observed an interesting finding by evaluating the ratios of maximum standardized uptake value (SUVmax) on ^{68}Ga-DOTATATE PET/CT to SUVmax on ^{18}F-FDG PET/CT scans. The ratios range from 1.2 to 19.5 in typical carcinoids (median SUVmax, 7.3) but from 0.1 to 1.1 in other less differentiated carcinoids (median SUVmax, 0.16). This difference in the ratios of typical versus atypical and other less differentiated carcinoids is statistically significant. The *P* value is 0.002 (Mann–Whitney test for nonparametric data, 2-tailed). Thus, the ratio of SUVmax on ^{68}Ga-DOTATOC PET/CT and ^{18}F-FDG PET/CT may also be of help in predicting the histopathologic variety of the carcinoid tumor and may have an equally high accuracy. A larger study is indicated to validate this observation and to objectively determine a cutoff value for the possible differentiation.

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REPLY: We thank the authors for their interest in our article (*1*). The authors state that the standardized uptake value ratios of ^{68}Ga-DOTATATE PET/CT to ^{18}F-FDG PET/CT can differentiate well-differentiated from less differentiated carcinoids and predict the histopathologic variety of the carcinoids. However, caution should be exercised. Occasionally, well-differentiated and poorly differentiated cell populations exist within the same tumor mass, and predicting histology on the basis of ^{68}Ga-DOTATATE PET/CT–to–^{18}F-FDG PET/CT ratios would not be appropriate.

REFERENCE

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Cellular Dosimetry Using the Geant4 Monte Carlo Toolkit

TO THE EDITOR: Cai et al. (*1*) reported Monte Carlo calculations to estimate cellular doses using ^{111}In in different cell configurations. Therefore, the authors used the Monte Carlo N-particle (MCNP) code and compared their results with values provided by Goddu et al. (*2,3*) for a single-cell model. Their results were within 66.2%–153.4% of the results of Goddu et al.

We performed similar simulations for a single-cell model using the Geant4 tool kit (*4*). Using the low-energy extensions, Geant4 is able to simulate electron–photon interactions down to 250 eV. The Geant4 source code is freely available and can be downloaded from the official Geant4 collaboration Web site (www.geant4.org). According to cellular experiments in our laboratory, we considered ^{99m}Tc, ^{123}I, and ^{111}In. Emission spectra were taken from Howell (*5*); unlike Cai et al., we used electron and photon emissions. Decay sites were assumed to be homogeneously distributed inside the nucleus or cytoplasm or on the cell surface; dose deposition was considered only in the nucleus for different cell and nucleus radii. For each run, 10^7 particles were simulated to give at least 10,000 hits in the nucleus.

Our results corresponded well to the S values given by the authors in their Table 1. For a single cell, S values S(N←N) are 0.3%–3% higher, S(N←Cy) deviates from −1.3% to 10.1%, and S(N←CS) deviates from −5.1% to 7.4% (N, Cy, and CS are nucleus, cytoplasm, and cell surface, respectively).

Furthermore, Cai et al. calculated S values for cell clusters and cell monolayers. These values are important when cells in those configurations were irradiated. Thus far, we have examined clonogenic cell survival, whereby cells can be considered as single cells. Hence, we do not calculate S values for clusters or monolayers. Nevertheless, the compliance between the results of Cai et al. (*1*), Goddu et al. (*2*), and our simulations show the feasibility of using Monte Carlo methods to assess absorbed doses in cellular dimensions. In contrast to MCNP, Geant4 is free and is available on the Web.

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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.

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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