Letters to the Editor

Potential of Palladium-109-Labeled Antimelanoma Monoclonal Antibody for Tumor Therapy

TO THE EDITOR: In a recent article in the Journal, Fawwaz et al. (*1*) demonstrated successful coupling of palladium-109 (^{109}Pd) to 225.28S, a monoclonal antibody reactive with a high-molecular-weight antigen associated with melanoma. In in vivo localization experiments they showed preferential ^{109}Pd MoAb accumulation in the tumor relative to other tissues, although liver and particularly kidney doses were relatively high (*1*). I congratulate them on their important work, but must take issue with their unreferenced statement that: "Although the concentration of ^{109}Pd-labeled anti-melanoma monoclonal antibody in kidney and liver also were high, these tissues are relatively radioresistant and can withstand much greater radiation doses than the more radiosensitive tumor."

Malignant melanomas are "classically radioresistant" tumors (*2*). In fact, in the early days of radiation therapy, Paterson stated that if radiation kills the tumor, it was probably not the ordinary malignant melanoma (*3*). Although I do not have specific information on the Colo 38 cell line's radiosensitivity, most melanomas are only relatively radiation sensitive at best, and there is a great deal of variability in their response to radiation therapy (*4*). With conventional fractionation, radiation therapy of melanomas produced only a 57% response rate for all sites in one large series (*5*). Response rates are somewhat higher when larger individual fraction sizes are used (*6*), although total doses of 2000–4000 rad are suggested for the therapeutic course (*7*).

Despite Fawwaz et al.'s statement to the contrary, the liver is generally regarded as a very radiosensitive organ (*8*). With 300 rad/fraction, tolerance of the whole liver to radiation is felt to be 1800–2400 rad. Radiation hepatitis frequently will occur following higher doses with similar fractionation (*9*). This, of course, can be fatal.

Similarly, the kidney has long been recognized as a radiosensitive organ that can limit radiation doses to abdominal tumors (*10,11*). In unilaterally nephrectomized mice, which then underwent an unfractionated localized radiation dose to their remaining kidney, Phillips and co-workers showed an LD 50 (at 16 mo postradiation) of just 1278 rad, with deaths due to renal failure. Although survival after higher, more fractionated doses was possible, these data confirm that the kidney is quite radiosensitive. Interestingly, damage to the kidneys appeared to progress with time in this study, implying that adequate repair of radiation damage was not ongoing (*12*). Although bone marrow doses aren't included, these may also be limiting factors in therapy with radiolabeled antibody (*13*).

Obviously, extrapolations from external beam to internally administered radiotherapies such as radiolabeled antibodies are only that, however relative radiosensitivity relationships are likely to persist. From these data it is difficult to reach the conclusion that the liver and kidneys "can withstand much greater radiation doses than the more radiosensitive tumor." It is important to recognize this relative radiation sensitivity of the liver and kidneys, and relative radiation insensitivity of many melanomas to avoid radiation-induced injury, should therapies with agents such as ^{109}Pd MoAb be undertaken in humans.

I agree with the authors that if, through improvements in labeling and purification, active antibody binding percentages can be increased to significantly more than 40%, then these potential dosimetric problems may become less important.

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REPLY: We welcome the comments of Dr. Wahl, whose note of caution is appropriate and important. Clinically, with the use of appropriately fractionated doses, hepatic and renal tissue tolerate doses of ~2000 rad (*1*,*2*). The response of melanoma to radiation is variable (*3*); some tumors respond favorably to doses as low as 1400 rad while others demonstrate resistance to doses as high as 6000 rad. The reason for this discrepancy is not clear; it may be related to tumor size (hypoxia), degree of dose fractionation, or individual cell sensitivity to radiation. Obviously, hepatic and renal problems are less important in patients with relatively radiosensitive tumors.

We agree with Dr. Wahl on the importance of recognizing the *relative* radiation sensitivity of the liver and kidney, and we stressed the need for improved methods of labeling and/or purification to lower the radiation dose to these organs. Until this is accomplished, the palladium-109-labeled antibodies reported in the manuscript would be of value only in treating the patient with a radiosensitive melanoma. The results, however, do demonstrate the feasibility of this approach for radiotherapy. A similar labeling approach should be able to be used to produce antibodies against other tumors with greater sensitivity to radiation and greater margins of safety with respect to hepatic and renal radiation exposure.

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Selection of Energy Windows for the NEMA Standard Specifications

TO THE EDITOR: Over the last several years our group at the University of Washington has had the opportunity to conduct a variety of test procedures on a large number of scintillation cameras. More recently, in conjunction with a portable computer system being developed for the National Center for Devices and Radiological Health (FDA contract #223-80-6004), we have applied the National Electrical Manufacturers Association (NEMA) standard specification procedures (*1*) to over 30 scintillation cameras. After analyzing the data obtained from these cameras, we are convinced that the current recommended pulse height analyzer window setting of 20% (or the proposed change to a 15% window setting that is under consideration) does not reflect optimal performance of any given camera. We have noticed a wide range of energy resolution in the cameras we have measured and while testing some of the cameras, we repeated the NEMA standard specifications with a full width at half maximum (FWHM) energy window. Selecting a FWHM window is based both on the early work in rectilinear scanners which indicated that a FWHM window presented a good compromise between sensitivity and scatter rejection and on the notion that a FWHM energy window results in all cameras accepting approximately the same percentage of the unscattered photopeak events. A camera with a better energy resolution can certainly be operated with a narrower window providing better scatter rejection and essentially no loss in image information. A 20% energy window becomes even less appealing when measuring a modern scintillation camera since many of the instruments currently in production provide energy resolution on the order of 10% at FWHM. Therefore, we suggest changing the pulse height analyzer window setting in the NEMA standard test procedures to the FWHM in order to provide a more objective measurement of the imaging performance of modern scintillation cameras.

Reference

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Brain Scan: A Useful Tool in Detection of Neurosyphilis

TO THE EDITOR: Recent statistics from the Centers for Disease Control, Atlanta, reflect an increase in cases of primary syphilis, the incidence having risen by more than 25% between 1979 and 1981 (*1*). In Finland, since 1966, the annual incidence of early syphilis has been a steady increase at about four cases per 100,000 (*2*). Because of the extensive preventive measures and the use of antibiotics (*3*), clinical neurosyphilis is seldom seen today. As a result, atypical forms become more common and physicians have forgotten that the disease still exists (*2*). Acute meningovascular syphilis constitute 1-2% of cases of symptomatic neurosyphilis (*1*). Angiographic and computerized tomographic (CT) findings have already been described (*1*,*3-9*). To our knowledge, scintigraphic changes of menin-