0.05). Adequate prediction by the 6 hr image score may be more applicable than scores from other images due to the fact that in over one half of the patients, uptake quantified by a lumbar ROI (*1*) as well as uptake assessed by semiquantitative image scores peaked by 6 hr. The semiquantitative scores obtained by an experienced observer for images acquired 6 hr after infusion of ^{131}I-Lym-1 proved to be a good method to predict myelotoxicity in patients with non-Hodgkin's lymphoma and chronic lymphocytic leukemia. The method may have applications for myelotoxicity prediction in multicenter RIT trials in patients likely to have marrow (or skeletal) malignancy because it is readily implemented. The marrow scores were reproducible when determined by an experienced observer.

Accurate prediction of the degree of myelotoxicity to be expected after infusion of therapeutic amounts of radiopharmaceutical is important because it identifies patients in need of closer monitoring of blood counts and facilitates earlier administration of colony stimulating factors or other blood reconstitution methods. Although therapy images were studied here, the semiquantitative image score method can be used for tracer images as well (*14*) to predict myelotoxicity before administration of the therapeutic dose. In this instance, it would be essential to accumulate sufficient image counts.

CONCLUSION

A well-defined semiquantitative marrow image score generated by an experienced observer can be used to predict myelotoxicity from RIT in patients in whom marrow malignancy may exist. Other factors that need to be investigated to enhance the prediction of myelotoxicity include previous chemotherapy and radiation therapy.

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EDITORIAL

Predicting Myelotoxicity in Radioimmunotherapy: What Does Dosimetry Contribute?

Potential radiogenic damage to the hematopoietic bone marrow is the primary dose-limiting toxicity for systemic radionuclide therapy in general and radioimmunotherapy in particular. A variety of approaches have been pursued in an effort to establish a predictive dose-response relationship for myelotoxicity (*1–7*). Although such efforts are still in their infancy, a number of tentative conclusions have emerged. First, although no such correlations have been particularly impressive, absorbed dose yields a better correlation than administered activity. Second, marrow absorbed dose appears to be a marginally better predictor of myelotoxicity than whole-body absorbed dose. Third, in an "intermediate" absorbed-dose range, myelotoxicity has been unpredictable. As noted in Lim et al. (*8*), because of time and effort required to obtain patient-specific absorbed-dose estimates and their limited use to date in predicting myelotoxicity, the development of less rigorous (i.e., nondosimetric), but simpler, approaches to the prediction of myelotoxicity warrants evaluation.

Myelotoxicity is a classic nonstochastic (i.e., deterministic) effect, characterized by a sigmoidal, rather than by a linear, dose-response relationship (Fig. 1). Such a dose-response relationship is well-behaved only for a reasonably homogeneous population. With increasing heterogeneity of the irradiated population, the biological variability of responses may confound the derivation of a meaningful (i.e., predictive) dose-response relationship. As illustrated in Figure 2, fitting a single linear function to widely dispersed data from a heterogeneous population may result in a poorly fit dose-response function that is quantitatively unreliable for managing individual patients. With stratification of patients into clinically distinct subpopulations with separate dose-response functions (illustrated in Fig. 3 as a series of separate data sets and corresponding fitted curves), the goodness of fit and, therefore, the clinical utility of such functions should be greatly improved. This rather intuitive concept becomes significant in practice only when clinically evaluable criteria for such stratification can be identified and implemented. In radioimmunotherapy, the effect of prior cytotoxic therapy and/or disease involvement on the functional capacity and radiation sensitivity of the hematopoietic marrow now appears to be

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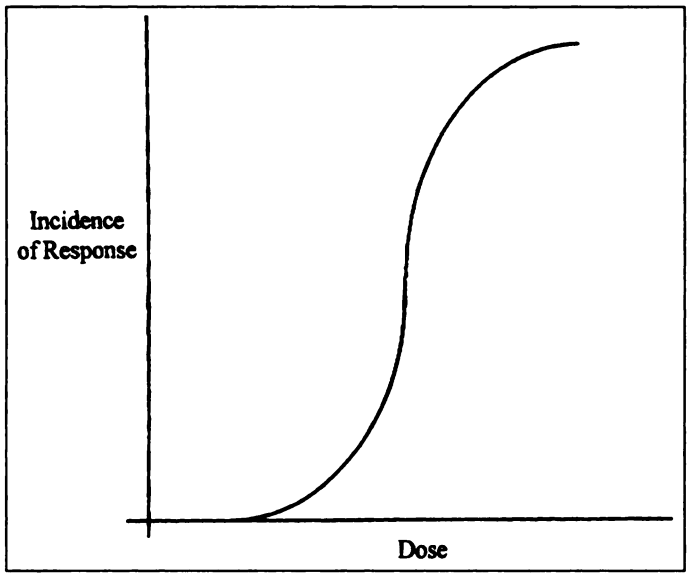

FIGURE 1. A sigmoidal dose-response curve characteristic of nonstochastic radiogenic effects.

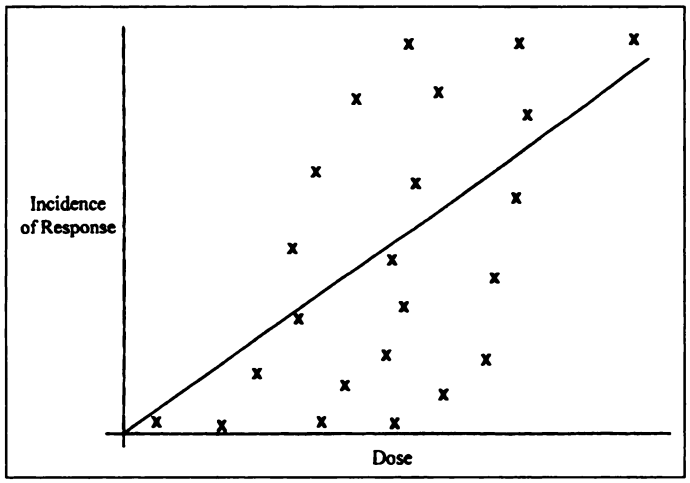

FIGURE 2. A linear fit of hypothetical dose-response data from a heterogeneous population, illustrating the response heterogeneity of such a population and the notably poor fit of a linear function to such widely dispersed data. At any given dose, note the wide dispersion of the response incidence and the large deviations of the data from the linear fit, indicating that such a fit is not reliable in predicting myelotoxicity in individual patients.

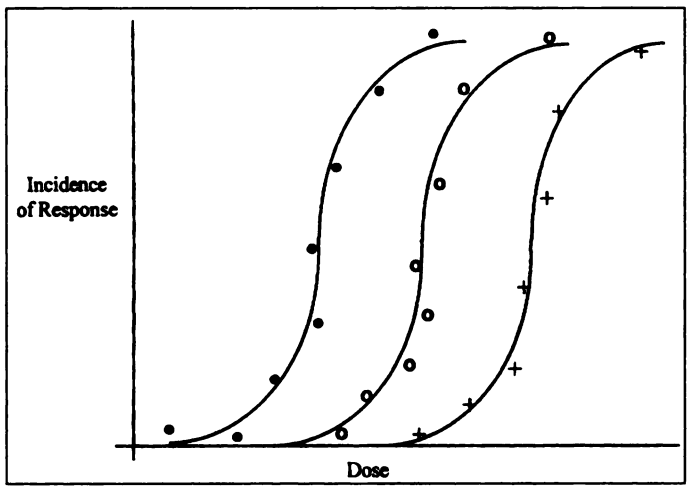

FIGURE 3. Separate sigmoidal fits of the same hypothetical dose-response data in Figure 3 but stratified into three separate datasets corresponding to each of three distinct subpopulations within the overall population.

a particularly important criterion for such stratification (*6–7*).

Lim et al. (*8*) have used qualitative or semiquantitative approaches to treatment planning for radioimmunotherapy, that is, to the prediction of radiogenic myelotoxicity. The tacit implication of such empirical techniques, however, is that the generally poor correlation between myelotoxicity and marrow absorbed dose in radioimmunotherapy is due to the intractability of marrow dosimetry. Unfortunately, qualitative or semiquantitative techniques contribute little to our understanding of radiogenic myelotoxicity and associated dose-response relationships. While absolute quantitation may not be practical or even necessary in the clinic, abandoning marrow radiation dosimetry in radioimmunotherapy is premature. Indeed, mounting clinical evidence suggests that it is the heterogeneity of patients [particularly with respect to prior cytotoxic chemotherapy (*6–7*)], and not the intractability or impracticality of marrow radiation dosimetry, that undermines the derivation and the clinical utility of predictive dose-response relationships for myelotoxicity.

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