

Book Reviews

Quality Assessment and Improvement for Dose-Response Models. Some Effects of Study Weaknesses on Study Findings. "C'est Magnifique?" AAPM Report No. 43. Biological Effects Committee Task Group 1. Donald E. Herbert, principal author. 372 pp. Medical Physics Publishing Corp., Madison, Wisconsin. Price: \$25.00.

C'est magnifique, mais ce n'est pas la guerre.

So remarked General P. Bosquet in 1857, on observing the innovative deployment of Lord Raglan's light cavalry brigade at Balaklava. And, as indicated in the Report's title, this quotation does indeed characterize the current literature on radiobiological modeling reviewed in AAPM Report No. 43. Loosely translated in this context, the quotation reads: "It looks great, but it ain't science!"

Report 43 is the culmination of many years of investigation of the radiobiological literature by Task Group 1 of AAPM's Biological Effects Committee, consisting of Donald E. Herbert (Chairperson and principal author of the Report), Arnold Feldman, Engikolai Krishnan, Colin Orton, Jacques Osvadia, Bhudatt Padival, Timothy Schultzeis, Prakash Shrivastava, Alfred Smith, Marilyn Stovall, and Lionel Cohen (Consultant). What Task Group 1 did was to critically evaluate 40 authoritative studies of models of radiation dose response for certain endpoints: radiation toxicity, mutagenesis, tumorigenesis, and lethality. They closely examined the empirical evidence and theoretical arguments—concepts, data, methods, and criteria—which were presented in these studies, and concluded that what is required is a "sea-change" in the statistical practices employed in the construction, testing, and deployment of radiobiological models.

Task Group 1 did not come into this enterprise as unbiased observers—after all, an unbiased mind is an empty mind! They knew that there were fundamental problems with current radiobiological modeling, and they took a general approach toward dealing with these problems, seeking to answer four questions: 1. What do we believe? 2. Why do we believe it? 3. Should we believe it? 4. What shall we do now? The result has been a highly unorthodox presentation which starts with consideration of the philosophy of science. Such an approach does seem to be necessary, in order to effect the required sea-change in our ways of thinking, given the failure of more traditional formats to do so. (For example, that of AAPM Monograph No. 13, *Multiple Regression Analysis: Applications*

in the Health Sciences, edited by D. Herbert and R. Myers, 1986.) Quite deliberately, Report 43 tries both to inform and to persuade, rather than being a dispassionate scientific treatise.

The heart of Report 43 is its long (115 pp.) Sec. 7, which presents the statistical methods required for correct modeling of radiobiological data. But it "presents" this vital information as an advocate of the new methods ("new," at least, to much of the radiobiological literature). First, in Sec. 7, there is detailed mathematical explanation of these statistical methods, and then, most importantly, these methods are applied in understanding Barw in the 40 studies reviewed. (Full secondary analyses of 34 of these studies are given elsewhere, in what Report 43 refers to as its Annexes.) Many of the Report's 173 figures are in Sec. 7, and in themselves all these figures constitute a highly useful "teaching file," as the Report points out. Add to Sec. 7 the secondary analyses presented in Secs. 16 and 17, as self-contained attachments to the main body of the Report, and you have an immensely valuable introduction to how to do your dose-response modeling right! (The importance of this cannot be overstated.)

Given these fundamental problems with current radiobiological modeling, what should be done now? This is the fourth general question which Task Group 1 sought to answer, and in Sec. 14 they recommended four ways to go forward. First, we should use classical meta-analysis, combining results from a number of related studies of a common hypothesis to arrive at conclusions (e.g., rejection of the hypothesis) that could not be achieved otherwise because of various weaknesses (such as small sample sizes) in the component studies; furthermore, we should continue to perform secondary analyses of the data upon which published results are based, to validate these results. Second, Task Group 1 suggest using certain mixture methods for discriminating between the linear quadratic and target theory models of cell survival. Their third recommendation is to use a recently developed class of Bayesian statistical methods—Bayesian hierarchical meta-analysis—for interspecies extrapolation of radiation dose-response data (the "mouse-to-human" problem). Finally, Task Group 1 suggest using multivariate probit analysis for both clinical and animal studies of the joint occurrence of characteristic radiation responses in normal and tumor tissues. Appendix II continues further, proposing a somewhat different perspective on radiation "tolerance" for use in statistically adequate models.

An unexpected, but most welcome, aspect of Report 43 is its presentation of con-

cise quotations on the philosophy of science. This is actually done in considerable depth, both in separate subsections and in introducing many subsections, as is appropriate to effect a sea-change in our approach to science. We certainly tend to accept the usual way of doing things ("normal science"), until "paradoxes" (outcomes which "should not" have occurred) shake up our complacency. But why wait for the paradoxes to occur? Better to understand clearly how one approaches scientific research, what pitfalls lie lurking. For example, given two sets of data for similar situations, taken at different times, our tendency is to construct a model from the first set of data and use this model to explain the second set of data. But what if we had taken the second set of data first? Would we not perhaps have constructed a qualitatively different model, and tried to fit the first set of data to this model? If our methods for data acquisition and analysis might lead to two different models, then we have not really deduced the model from the data. This problem evidently has occurred in current radiobiological modeling, but any domain of science is susceptible to it.

Task Group 1's Report 43 is of incalculable importance for rectifying the fundamental problems in current dose-response modeling, and for investigators in this field, there is no excuse for not reading it carefully and following its lead. There are, however, some minor problems with the presentation of this material. First, the already dense reading may be slowed down by occasional use of obscure words ("anest"?)—be sure to have your dictionary handy when you are in the philosophy-of-science parts! The Report could have been made more readable by using headings for sections and subsections in a larger (and perhaps different) typeface, and starting sections on new pages. (In fact, until page 94 there are not even blank lines between sections!) Finally, there is the sexist language which occasionally crops into Report 43, with the use of the male pronoun to describe people in general. Even when repeating a historical quotation, it is possible to avoid doing this, such as by replacing "men" with "[women and] men." Medical physics, like our society in general, is overwhelmingly dominated by men, but is it not time for a "sea-change" in this regard?

Reviewed by David Jette

Dr. Jette is Executive Director of the Lawrence H. Lund Institute of Medical Physics in Seattle, and Professor of Medical Physics at Rush University in Chicago.

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Claude Leroy, Pier-giorgio Rancoita



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