EDITORIAL

The BJR and progress in radiobiological modelling

R G DALE, PhD, FIPEM, FInstP, FRCR (Hon)

Radiation Physics & Radiobiology, Imperial College Healthcare NHS Trust, London W6 8RF, UK

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Exactly 21 years ago this journal published an extensive article by Professor Jack Fowler [1], which examined the role of the linear-quadratic (LQ) radiobiological model in stratifying radiotherapy fractionation schedules. At that time the LQ model was already well-established, but its fuller and more practical usefulness was still unfolding.

Fowler's 1989 paper introduced the concept of biologically effective dose (BED) as an overall "one-number" measure of the biological effectiveness of a radiotherapy schedule on a given tissue. With BED, Fowler extended the earlier concept of extrapolated response dose (ERD) [2] (in particular, by introducing allowance for tumour repopulation effects during treatment). He used it to demonstrate the value of modelling in making choices between different radiotherapy treatments. This article has been particularly well cited.

In this edition of the *BJR*, Fowler revisits the role of BED and, in a wide-ranging review [3] (which includes many references to the role played by the *BJR*) examines how quantitative radiobiology has helped progress the design and analysis of new schedules. This includes those that do not involve conventional low-LET external beam delivery. In particular, Fowler identifies how even simple modelling has proved capable of separating out the relative influence of the factors that govern radiotherapy in a wide variety of clinical circumstances.

Two points are especially noteworthy. Firstly, the interval between the two articles serves as a reminder that useful scientific developments frequently have a long lead-in time before they become widely accepted. That some progress is being made can be seen in the fact that Part I FRCR examinations in clinical oncology now routinely include LQ-related questions. Secondly, as Fowler pointed out in 1989 and does so again here, although the LQ model itself remains an over-simplified description of the events which govern radiotherapy

response, its strength stems from its ability to identify potentially dangerous treatments that are best avoided. Given the complexity of many modern radiotherapy techniques and how rapidly advances are being made, this is a particularly valuable asset.

While it may appear that radiobiological modelling is in a healthy state, there are some concerns. One worry is that BED, instead of being considered as the fulcrum measure of the radiobiological impact of any given schedule, is sometimes confused with EQD2, the "equivalent total dose which, when delivered in 2 Gy fractions of photon irradiation, produces the same biological effect". This confusion between "biologically effective" and "biologically equivalent" doses is easy to understand, given the similarity between the names and the fact that both are expressed in physical dose units (Gy). However, frequent misuse of BED has the capacity to create new problems and to undermine progress [4]. For some of the newer radiotherapy techniques, for example those using technologically advanced beam delivery patterns, high LET radiations or biologically targeted radionuclides, it is perhaps questionable whether the concept of "2 Gy photon equivalence" has much relevance in these areas. If this is the case, the argument for judging all schedules in terms of "biological doses" (BEDs) is strengthened.

On account of this, Fowler [3] proposes that consideration be given to introducing a unit that is unique to BED. Such an idea was first put forward in embryonic form in 2009 [5], the suggestion then being made specifically by the nuclear medicine community to help establish easier comparison between the results of targeted radionuclide therapy with those seen with conventional external beam therapy. But, as Fowler points out [3], the establishment of a dedicated unit for BED would have wider benefit and impact, not least because it would help to remove some wider confusion. The suggested name for the BED unit is the barendsen (symbol Bd), in recognition of the seminal work of Professor GW Barendsen [3–5]. The process of considering a unit for expressing deterministic effects in radiation oncology is likely to be a protracted process (it will

Address correspondence to: R G Dale, Radiation Physics & Radiobiology, Imperial College NHS Trust, London W6 8RF. E-mail: r.dale@imperial.ac.uk

require international agreement on concepts, quantities and units), but the need has been established.

The message emerging from Fowler's latest article is that *properly applied* radiobiological principles can positively guide the introduction of technological and fractionation advances in radiotherapy. However, it is also noteworthy that Fowler reflects on the fact that only in retirement did he have the time to give this topic his full attention.

Given Fowler's eminence in the field, this must surely be the strongest of indications that this important and expanding field now justifies the serious attention of a new generation of oncologists and scientists who can contribute ideas and advance them. This is something the *BJR* wishes to continue to encourage and support.

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