treatment (b) is likely to be less than that of treatment (a), the associated tumour BED value being lower by around 15–25%. Since tumour control probability (TCP) is likely to be strongly influenced by relatively small changes in BED [6], especially when the existing TCP is neither very high nor very low [7, 8], the observed clinical results are consistent with those predicted by simple modelling. Similarly, the concerns of Fentiman and colleagues regarding the likelihood of increased normal tissue toxicity with implant alone are probably unfounded, as evidenced by the tabular data for the two lower α/β values. In practice, it is likely that, provided the iridium-192 dose-rate were not increased, the total dose in treatment (b) could be increased to 60 Gy, or possibly more, without compromising late-normal toxicity.

The purpose of this communication is not to criticise the work of Fentiman and associates, whose article clearly highlights the clinical dilemmas involved in introducing alternatives to long-standing and well-tried treatments. Rather, it is to highlight two facets of radiobiological modelling which can be valuable in the design of clinical trials in radiation oncology. These are:

(i) That modelling has a place in comparing the results of potential alternative treatments and provides indirect evidence that the commonly assumed modelling parameters may often be sufficient for such purposes. The validity of this approach has previously been highlighted elsewhere [9].

(ii) Potentially closer matches can be achieved between the two arms of a particular trial with prospective modelling. Not only does closer matching help guard against the possibility that patients in one arm may be unnecessarily disadvantaged, it also means that the subsequent comparison of the results from two radiobiologically matched arms can help establish finer tolerances on the likely range of the biological parameters involved. In this context, the use of radiobiological modelling should always be considered a prerequisite in the design of clinical trials [8] and ethical committees should have evidence that the radiobiological aspects have at least been considered before approving clinical trials in radiation oncology.

Perhaps it is timely to propose that future published results of clinical trials in radiation oncology should include abbreviated summaries of the tumour and normal tissue Beds associated with the various trial arms, in much the same way as has already been achieved in relation to including standardised statistical summaries.

1. Fentiman IS, Poole C, Tong D, *et al.* Inadequacy of iridium implant as sole radiation treatment for operable breast cancer. *Eur J Cancer* 1996, **32A**, 608–611.
2. Barendsen GW. Dose fractionation, dose rate and iso-effect relationships for normal tissue responses. *Int J Radiat Oncol Biol Physics* 1982, **8**, 1981–1997.
3. Dale RG. The application of the linear-quadratic dose-effect equation to fractionated and protracted radiotherapy. *Br J Radiol* 1985, **58**, 515–528.
4. Joiner MC. The linear-quadratic approach to fractionation. In Steel GG, ed. *Basic Clinical Radiobiology*. Edward Arnold, 1993, 55–64.
5. Thames HD, Hendry JH. *Fractionation in Radiotherapy*. London, Taylor and Francis, 1987.
6. Kallman P, Agren A, Brahme A. Tumour and normal tissue responses to fractionated non-uniform dose deliver. *Int J Radiat Biol* 1992, **62**, 249–162.
7. Dale RG, Sinclair JA. A proposed Figure of Merit for the radiobiological assessment of unscheduled treatment interruptions. *Br J Radiol* 1994, **67**, 1001–1007.
8. Jones B, Dale RG. The reduction of tumour control with increasing overall time: mathematical considerations. *Br J Radiol* 1996, **69**, 830–838.
9. Fowler JF. The linear-quadratic formula and progress in fractionated radiotherapy. *Br J Radiol* 1989, **62**, 679–694.

European Journal of Cancer, Vol. 33, No. 10, pp. 1708, 1997

Printed in Great Britain
0959-8049/97 $17.00+0.00

PII: S0959-8049(97)00189-5

Response from I.S. Fentiman and D. Tong

I.S. Fentiman[1] and D. Tong[2]

[1]Departments of Clinical Oncology; and [2]Radiotherapy, Guy's Hospital, London SE1 9RT, U.K.

DALE AND associates provide a possible explanation for the unsatisfactory outcome of our pilot study. We must first correct one inaccuracy. The standard technique which was in use at our unit was that used in EORTC 10801 [1]. This comprised insertion of a single or double plane flexible implant at the time of surgery. The implant was afterloaded the following day with iridium^{192} wires to deliver 20 Gy over approximately 48 h. This was followed by external beam radiotherapy rather than being preceded by it.

At the time that we were contemplating the high dose study, all our experience had been limited to flexible implants delivering a boost to a relatively small volume. Because of the change to a rigid implant occupying a larger volume we were anxious not to overdose the patient. A small pilot of rigid implants had resulted in occasional skin necrosis, infection around implant sites, serious oozing and occasional impaired wound healing. We were also concerned that patients would not tolerate breast compression immediately after surgery if a higher dose was given.

The aim was to achieve gross clearance of tumour and use the rigid implant to irradiate the involved quadrant. We were not implanting intact tumours, but were carrying out the implant at a time of wound healing after tumorectomy and axillary clearance. There was breast oedema associated with this which lead to pressure necrosis in some cases. We consulted with other colleagues at the time of study design and reached a consensus as to the most likely dosage to achieve tumour control without undue morbidity. With hindsight, the dosage was inappropriate but the use of higher doses would undoubtedly have led to greater local morbidity.

1. van Dongen JA, Bartelink H, Fentiman ES, *et al.* Factors influencing local relapse and survival and results of salvage treatment after breast conserving therapy in operable breast cancer: EORTC 10801 trial comparing breast conservation with mastectomy in TNM Stage I and II breast cancer. *Eur J Cancer* 1992, **28**, 801–804.

Correspondence to I.S. Fentiman
Received 24 Mar. 1997; accepted 8 Apr. 1997.