and rib morbidity in patients given fewer fractions (p<0·0001). Although the 4·25 Gy dose is higher than the highest dose per fraction (3·3 Gy) reported by Owen and colleagues,[1] these results[5] are a salutary caution to the premature use of regimens with shorter and higher doses per fraction and to the importance of long-term follow-up in randomised trials of dose and fractionation.

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I declare no conflicts of interest.

1 Owen JR, Ashton A, Bliss JM, et al. Effect of radiotherapy fraction size on tumour control in patients with early-stage breast cancer after local tumour excision: long-term results of a randomised trial. *Lancet Oncol* 2006; **7:** 467–71.
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4 Whelan T, MacKenzie R, Julian J, et al. Randomised trial of breast irradiation schedules after lumpectomy for women with lymph node-negative breast cancer. *J Natl Cancer Inst* 2002; **94:** 1143–50.
5 Rodger A, Jack WJL, Kerr G. A change in postmastectomy radiotherapy fractionation: an audit of tumour control, acute and late morbidity. *The Breast* 1996; **5:** 244–50.

Authors' reply

Dr Kunkler is correct to assume that clinical and pathological risk factors tabulated in an earlier paper are balanced between randomised arms of the trial.[1] With respect to radiotherapy boost allocation and regimen, Drs Munshi and Kunkler need not be concerned about interpretation of trial outcome. In the earlier article reporting late adverse effects, we stated that if the clinician felt it was appropriate and the patient consented, a subrandomisation to boost versus no boost was done in patients with complete microscopic tumour resection. Otherwise, an elective boost was given. Similar to surgical excision margins and adjuvant systemic therapy, the boost is a randomly distributed variable. Stratification ensured that the distribution of patients in the boost categories was virtually identical in the three randomised groups (table 1). There was no evidence of an interaction between the effect of fractionation schedule and boost on the risk of local relapse (p=0·95), as shown by the results of Cox proportional hazards regression analysis stratified by boost (table 2). The 13-fraction regimen was delivered in the same overall treatment time (5 weeks) as the 25-fraction control schedule, so we can reassure Kunkler that there is no source of bias here. In addition, Munshi should understand that it is not possible to compute an equivalent schedule based on seven fraction sizes of 3·0 Gy or 3·3 Gy and α/β values of 1·8 Gy and 6·0 Gy. The size or number of fractions would have to change, and this would confound the randomisation.

Kunkler argues for several decades of follow-up before judging the relative effects of different fractionation regimens, but relations between randomised schedules are unlikely to change qualitatively beyond the 10 years for adverse effects and the 16 years for tumour control that we reported. Where cardiac morbidity and mortality are concerned, the priority is to exclude the heart from the treatment volume altogether; this can usually be achieved by adjustments of arm position or breathing technique. As Munshi states, the breast is a compound tissue, but comprehensive clinical and photographic assessments yield a great many relevant dose-response data. Our report of late adverse effects

	Crude hazard ratio (95% CI)	
	Boost	No boost
50 Gy	1	1
42·9 Gy	0·88 (0·53–1·46)	0·80 (0·39–1·63)
39 Gy	1·38 (0·88–2·16)	1·24 (0·65–2·35)

Table 2: **Survival analysis of local relapse according to fractionation schedule and breast boost**

	Randomised fractionation schedule			
	50 Gy (n=470)	42·9 Gy (n=466)	39 Gy (n=474)	Total (n=1410)
Randomly assigned to no boost	120 (26%)	118 (25%)	121 (26%)	359 (25%)
Randomly assigned to boost	122 (26%)	119 (26%)	123 (26%)	364 (26%)
Non-randomised boost	228 (49%)	229 (49%)	230 (49%)	687 (49%)

Table 1: **Breast boost in 1410 patients according to randomised fractionation schedule**

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shows that change in breast appearance and palpable induration are highly sensitive to randomised dose.[1] The irradiated breast looking and feeling the same as the contralateral breast 10 years after treatment is a valid outcome for patients. The associations between external assessments and patients' self-assessments of symptoms and quality of life are under study in the current UK START Trial.

Finally, Kunkler urges caution on the basis of his own department's use of 42·5 Gy in ten fractions over 4 weeks. Given the α/β value of 3·0 Gy for late adverse effects, by calculation of the biological equivalent dose, his schedule is equivalent to 61·6 Gy in 2·0 Gy fractions, a dose expected to generate a high incidence of late normal-tissue injuries. Kunkler should not blame the fraction size; eight fractions of 4·25 Gy (total 34 Gy) would have reproduced the late adverse effects of 50 Gy in 2·0 Gy fractions in the breast. The sensitivity of late normal-tissue endpoints to changes in fraction size is well established, and means that a large total dose reduction is needed when the fraction size is increased. Whether appropriate adjustments represent an advantage relative to standard regimens depends on the differential fractionation sensitivity of breast cancer versus late effects. This association has also been clear for many years, but the outcome of our trial provides the first useful numerical estimate of this property for breast cancer. The trial has sufficient power, as reflected in the 95% CI for the estimate, to support the hypothesis that the fractionation sensitivity of breast cancer is similar to that of late effects.

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We declare no conflicts of interest.

1 Yarnold J, Ashton A, Bliss J, et al. Fractionation sensitivity and dose response of late adverse effects in the breast after radiotherapy for early breast cancer: long-term results of a randomised trial. *Radiother Oncol* 2005; **75:** 9–17.

Case Reports and *Clinical Pictures* in *The Lancet Oncology*

Following the introduction of original research in 2005, *The Lancet Oncology* has decided to phase out the publication of *Case Reports* and *Clinical Pictures*, because we believe their value within the journal has diminished. Therefore, from Sept 1, 2006, submission of these article types will no longer be permitted. This reduction in the number of article categories will enable us to increase the amount of content in other existing sections of the journal.

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Erratum

Owen R, Ashton A, Bliss JM, et al. Effect of radiotherapy fraction size on tumour control in patients with early-stage breast cancer after local tumour excision: long-term results of a randomised trial. Lancet Oncol 2006; **7:** 467–71. In this Article, the last sentence of the 5th paragraph in the "Procedures" section (p 469) should have read: "The proportion of patients who received a boost was almost identical in all three treatment groups: 350 (75%) patients for 50 Gy, 348 (75%) for 42.9 Gy, and 353 (75%) for 39 Gy."