Moderately hypofractionated breast radiation therapy: is more evidence needed?

Authors' reply

We thank Gustavo Marta and Philip Poortmans for recognising the importance of our study. We agree that this trial has some limitations, which were discussed in the Article.[1] However, the 5-year cumulative incidence of locoregional recurrence of 8·3% was reasonable because of the inclusion of patients with stage III disease. We believe that some patients might benefit from three-dimensional (3D) techniques because of better target coverage and reduction of dose heterogeneity, but we do not expect much scope for decreasing locoregional recurrence. In one recent study[2] with 3D techniques and additional internal mammary node irradiation, a 5-year cumulative incidence of locoregional recurrence of 8·7% was reported in similar high-risk patients as in our study. However, in another similar study,[3] a lower 5-year cumulative incidence of locoregional recurrence of 0·53–2·52% was reported; however, only 222 (27·5%) of 807 patients had at least four positive nodes.

The hypofractionated schedule explored in our study delivered a higher biological equivalent dose than established schedules after breast conserving surgery. To date, studies investigating the optimal radiation dose for patients with different risk classifications or different radiation targets are scarce, and personalisation of radiotherapy dose for breast cancer requires more research. In conventional two-dimensional (2D) planned radiotherapy, the dose is prescribed to the isocenter, rather than the target volume. If the dose to the target volume is evaluated, the 2D plan does not cover the volume-defined target to the full prescription dose. This discrepancy should be considered for specific recommendations for dose prescription and developing dose–volume histogram criteria for plan evaluation of hypofractionated schedules when 3D techniques are used.

A major concern for generalisation of postmastectomy hypofractionated radiotherapy is the uncertainty surrounding the long-term toxicity of nodal irradiation. Most ongoing trials are designed to evaluate safety, rather than oncological outcomes, of hypofractionated radiotherapy, with arm oedema as the primary endpoint (NCT02700386, NCT03127995, NCT02958774, and NCT02384733). However, the biological effects of hypofractionated radiotherapy on late-reacting tissues in the nodal regions should not be different to those of the breast tissues. Because of the convincing evidence from our study[1] and many others, it appears that hypofractionation is a striking revolution in radiation oncology.[5] These practice-changing clinical trials could serve to improve cancer management globally, and not just in countries where global resources might be scare.

We declare no competing interests.

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