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## Adopting shorter radiation regimens: rules of engagement for sarcoma

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B Ashleigh Guadagnolo and colleagues<sup>1</sup> deserve high praise for conducting the largest prospective radiotherapy trial for patients with sarcoma since NCIC-SR2, which shows that hypofractionated preoperative radiotherapy delivered over 15 fractions results in rates of major wound complications similar to those seen with standard 25-fraction radiotherapy. These data also lend support to findings from earlier prospective trials of five-fraction regimens that also did not observe higher rates of wound complications than standard 25-fraction radiotherapy, suggesting that fractionation (when prescribing biologically similar doses) does not have a substantial effect on wound healing. We eagerly await longer-term outcomes.

It is intriguing, however, that Guadagnolo and colleagues have incorporated their single-institution phase 2 results into routine clinical practice (with appropriate patient counselling), especially given their statement that clinicians might not be amenable to adopting five-fraction regimens without randomised data. The adoption of the 15-fraction regimen in routine care prompts two questions. First, what is the standard of evidence for offering an alternative, more convenient fractionation scheme in a rare disease like sarcoma? Second, given comparable data (ie, single-institution, single-arm, and approximately 120 patients), would the authors offer the more convenient five-fraction regimen in routine practice?

Having led one of the larger prospective studies using a five-fraction regimen,<sup>2</sup> our group is invested in understanding the thresholds for adopting this regimen in routine practice. If one considers only published prospective studies designed to biologically mimic the effects of conventional 25-fraction regimens, five-fraction regimens have been utilised in 106 patients across three institutions.<sup>2-4</sup> Assuming data emerge with results that are similar to those seen with 25-fraction regimens, it would be difficult to advise patients to choose the more costly and inconvenient 15-fraction regimen over five fractions. Perioperative five-fraction regimens are no longer radical in radiation oncology; they are used in breast and prostate cancer. And if we adopt the 15-fraction regimen as a standard option on the basis of the authors' well executed single-arm, phase 2 study, then I would expect similar openness to adopting five-fraction regimens if similar data emerge.

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AK served as principal investigator of a prospective clinical trial of five-fraction preoperative radiotherapy for soft-tissue sarcoma of the trunk and extremities.

To be clear, we are not critiquing the authors' decision to adopt the 15-fraction regimen in routine practice, nor suggesting that changes in fractionation require a randomised trial. In fact, according to a survey completed by 47 sarcoma specialists, over 68% of specialists would adopt a five-fraction regimen on the basis of data from a multi-institutional, single-arm phase 2 study; only 17% of specialists would wait for a randomised trial.<sup>5</sup> We only seek to clarify the community standards for adopting new radiotherapy regimens for this rare disease to inform the design of future studies and facilitate patient-centred innovation.

## References

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