EDITORIAL

Radiation Oncology Clinical Trial Design: An Opportunity to Evaluate Value

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Costs of cancer care continue to rise in the United States at an unsustainable pace.¹ Beyond novel systemic therapies, radiation oncology represents an area of growing cost, primarily because of increased utilization of advanced technologies and techniques.²,³ These techniques are routinely prospectively studied before clinical use, but cost effectiveness and determination of value often is not. We assert that this window is not prioritized sufficiently, neglecting the chance for the specialty to lead the development of value-driven, evidence-based therapies.

Value can be defined as the return in outcomes (recurrence, survival, toxicity) achieved for dollars spent. There are different ways to assess value. Radiation trials investigating changes in fractionation (eg, hypofractionation in breast/prostate cancer) that have shown equal effectiveness could evaluate reductions in reimbursement to demonstrate value. However, many new technologies and techniques will increase costs, and looking at reimbursement without accounting for improved outcomes is misleading. Here, value can be assessed using incremental cost effectiveness ratios (ICERs), a statistic that measures the difference in cost of two techniques divided by the difference in effect, often reported as cost/quality-adjusted life-year. Finally, time-driven activity-based costing (TDABC) uses the cost of equipment/individuals and the time required for a process to derive the total cost of an activity. TDABC has been used increasingly, including in radiation oncology, to evaluate cost and value.⁴

To incorporate value into trial design, radiation oncologists must first recognize that the juice is indeed worth the squeeze—incorporating economic details into trials and understanding that this is worthwhile. More specifically, the design of protocols could be improved, moving beyond P value—defined significance to include endpoints that, if achieved, are predicted to place a treatment within the realm of cost effectiveness.⁵ A trial evaluating a new technology compared with standard of care would include, as part of protocol design, an evaluation of cost effectiveness if the trial’s primary endpoint was met. If the new technique increases cost, a cost-effectiveness analysis would be prespecified, using the primary endpoint along with costs and utilities to provide the ICER for a given outcome. If the cost-effectiveness value was not met, options would include alternative endpoints, evaluating cost effectiveness among subsets, redefining ICER thresholds for cost effectiveness, or reassessing at a later time point to assess potential downstream cost savings. Additionally, institutions would, via blinded surveys of manpower/infrastructure, provide data to allow for TDABC models. Finally, data that can be directly correlated with health utilities can be collected to improve models; for example, patients with events such as neurocognitive decline or local or distant failure should be queried before and after such an event. Together, this would allow for cost effectiveness to be evaluated, such that patients, providers, and payers can assess value through different lenses. With

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such complexity, it would be necessary to add a health economist to focus on the economic assessments in the trial and cost-effective publications after the primary analysis, regardless of outcome.

This vision is complex, and barriers exist. With limited budgets, the increased expertise and costs associated are a challenge. Industry is not often motivated to fund concepts that focus on value, particularly with new devices or drugs for which incorporation of such analyses may limit reimbursement or revenue. Collection of cost data is novel, but survey response rates are low and many institutions consider this information proprietary and may not provide it without encouragement and safety measures. Prospective cost-effectiveness studies face challenges including unrecognized costs of care during follow-up that may limit the completeness of long-term cost evaluations. Furthermore, cost assessments are complicated because costs can be highly skewed with large variances requiring even greater sample sizes and longer follow-up than otherwise needed, further increasing trial costs.

Examples of such an approach are available. NRG 1308 is an outstanding trial that assesses the cost effectiveness of protons as a secondary endpoint (via Medicare reimbursement and utilization surveys). This trial also prospectively uses the EQ-5D to determine utilities. This is a major step forward. Future trials, rather than determining costs by using arbitrary reimbursement rates, could survey institutions for a more robust estimation of direct costs of technology and by adding prospective TDABC analyses for professional efforts. Use of such techniques could ensure that reimbursement is reflective of the true costs of technology, construction, maintenance, safety, and delivery. In addition, because the survival difference between protons and photons will likely be small or nil, cost effectiveness could be the primary endpoint. Currently, national funding organizations prefer “hard” endpoints (even if unlikely to be clinically helpful) rather than a “soft” endpoint such as “cost effectiveness” even though the latter is the key question. We would like to see this perspective change on a national level—good science is indeed possible with cost effectiveness as an endpoint.

The rationale for this change is that it is the right and honest path forward for our patients, who deserve to receive effective value-oriented treatment, in light of the financial toxicity of cancer treatment. Second, payers will be more likely to adopt therapies that are economically viable. Third, in the face of alternative payment models, cost effectiveness reduces the chance that radiation therapy will be “cut out” in favor of inferior but less expensive therapies and allow for potential increased use of cost-effective radiation approaches. Finally, radiation oncology, as a field, is small enough to rapidly become a light on a hill—an example for all of health care in the quest for cost-effective technologies.

In summary, it is time to take radiation oncology trials to the next level by placing emphasis on a robust prospective assessment of the economic impact of new techniques and to incorporate this into primary trial design rather than as an afterthought. Radiation oncologists must then act upon the results of such studies; data demonstrate that we have failed to do so in the past (eg, use of single-fraction palliative radiation therapy). This may be something that alternative payment models address moving forward. This should not be seen as a discouragement of new concepts, but as a way to balance considerations of clinical benefit and financial toxicity.

References

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