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Cooperberg, Matthew R

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INVITED COMMENTARY

Expanding Utilization of Intensity-Modulated Radiotherapy for Prostate Cancer

Soaring Costs, Dubious Benefits

Prostate cancer in the United States is characterized by a unique epidemiology: a prevalence unrivaled by any other visceral malignant neoplasm among men and a prolonged natural history often measurable in decades rather than years. Early detection and aggressive management of higher-risk prostate cancer explain a substantial proportion of the more than 40% drop in prostate cancer mortality rates observed since the 1990s.¹ The price of this remarkable success, however, has been high rates of avoidable overtreatment of both newly diagnosed and recurrent prostate cancer, with excessive attendant morbidity and cost. Reflecting both screening of asymptomatic men and increasingly intensive surveillance (eg, with ultrasensitive prostate-specific antigen [PSA] tests, more extensive biopsies, and growing use of advanced imaging) of those treated, men are receiving both primary and salvage treatments at younger ages and earlier in the natural history of the disease. Reducing the potential morbidity of these treatments remains one of the central goals of prostate cancer clinical research.

The recent evolution of management options for localized prostate cancer largely reflects the advent of 2 technologies: robot-assisted laparoscopic surgery and intensity-modulated radiotherapy (IMRT). The promulgation of these 2 treatment platforms for prostate cancer has been in many respects parallel: both have been marketed aggressively and widely adopted based on relatively limited and sometimes contradictory data. The growth of IMRT has been particularly explosive: IMRT accounted for 0.15% of external-beam radiotherapy treatments in 2000 and 95.9% in 2008.² In general, IMRT is associated with lower toxicity than conventional 3D conformal radiotherapy (CRT), although the benefits are fairly modest, and at least one analysis² found greater sexual dysfunction after IMRT than after CRT.

External-beam radiation also may be combined with brachytherapy, and following radical prostatectomy—whether open or robot-assisted—it may be administered to men with high-risk pathology and/or persistent or recurrent PSA as adjuvant or salvage therapy. Recent trials generally support a greater role for postoperative radiotherapy, and utilization of this combination of surgery with radiotherapy may be expected to increase, particularly for men with higher-risk disease.³ Although at least some evidence exists to support the use of IMRT over CRT for primary monotherapy of prostate cancer, data for its use in these other contexts are essentially absent. For combination brachytherapy with external radiation, IMRT utilization nearly quadrupled in 3 years—from 8.5% in 2002 to 31.1% in 2005, with no published studies suggesting a benefit in this setting.

Goldin et al⁴ used Medicare data to examine trends and outcomes for radiation given as adjuvant or salvage therapy after prostatectomy. The authors found that here, as in other settings, IMRT has rapidly overtaken CRT as the dominant radiation modality, rising from zero cases in 2000 to 82.1% of cases in 2009. Once again, there were no observed benefits—in terms of either cancer control or any quality-of-life domain—observed for IMRT vs CRT.

Important caveats to this analysis should be noted. Aside from the fact that Medicare only enrolls men older than 65 years, the Centers for Medicare & Medicaid Services data files only include men in Medicare fee-for-service. Indeed, more than 61% of the potential sample was excluded either for the availability of less than 1 year of preradiotherapy claims data and/or for discontinuous fee-for-service enrollment. How representative the remaining men are of the broader population of men with prostate cancer is unclear because there are likely important differences between those enrolling in managed care plans and those choosing to remain in fee-for-service. As more Medicare participants en-

roll in managed care plans, even transiently, incomplete data will become a growing problem with Medicare analyses in general.

The analysis by Goldin et al also did not include short-term morbidity, which may be an important source of distress for treated men. More important, although administrative claims data have been repeatedly used to measure the effects of various treatments on patient well-being, such data in fact constitute a relatively weak surrogate for patient-reported outcomes assessed via validated questionnaires, which are the criterion standard indicators of quality of life. However, to date there are no such data regarding the issue of IMRT vs CRT in the postoperative setting—and data are sparse in general in the setting of postsurgical radiotherapy. Despite these limitations, this study by Goldin et al is a commendable one, extending this research group's prior work on evolving trends in the use of advanced radiotherapy in a new, important direction.

The authors only briefly address issues of cost and reimbursement that are integral to any understanding of the rapid adoption of IMRT. Indeed, a critical difference between the recent evolution of surgery and that of radiation is that most payers pay no more for robot-assisted prostatectomy than for open surgery; the additional costs associated with the robot-assisted approach are largely borne by hospitals. On the other hand, IMRT is reimbursed at a high premium compared with CRT—and an exceptional one compared with surgery or brachytherapy. In fact, from a payer perspective, IMRT is rarely cost-effective for most patients compared with these alternatives.⁵

The disconnect between data and reimbursement is not unique to IMRT. Proton beam therapy is twice again as expensive as IMRT, and unlike IMRT, no study has been published demonstrating any clinical benefit for proton beam therapy of prostate cancer in any context. In fact, 2 recent studies^{2,6} have shown proton beam outcomes to be indistinguishable from or inferior to IMRT outcomes. Yet proton therapy facilities continue to be built at a rapid rate and extraordinary cost, hoping to capture a growing share of the prostate cancer treatment market.

Clear comparisons also may be drawn to the parallel dissemination of robot-assisted laparoscopy, which also proceeded far ahead of any evidence showing its superiority. However, 2 important differences must be considered. First, as noted, the financial incentive to providers for robot assistance rather than open surgery is negligible compared with the premium paid for IMRT or proton-beam therapy compared with conventional CRT.⁷ Second, although prospective trials are lacking and population-based studies have not shown benefits for robotic procedures in terms of long-term outcomes, multiple comparative series⁸—albeit of variable methodologic quality—have now been published suggesting that at least in high-volume centers, robot-assisted surgery can yield superior outcomes to the open approach. Comparable data do not exist for IMRT given postoperatively or together with

brachytherapy or for proton beam treatment directed to the prostate in any context.

Prostate cancer care must be driven to be more cost-effective as well as more effective, yet our reimbursement system continues to reward technological arms races rather than an increased focus on outcomes assessment and improvement. Therefore, prostate cancer care remains preference sensitive—driven by various non-evidence-based motivations of clinicians and patients in the absence of clear comparative effectiveness data—and supply sensitive, with utilization rates of interventions correlating with extent of availability of those services.⁹ Prostate cancer outcomes must be tracked systematically—in all types of practice settings, following all forms of management—using validated patient-reported outcomes measures. However, until reimbursement incentives are rationalized with patient-centered outcomes, we will likely see continued dissemination of treatments, which drain dwindling resources and which offer negligible improvements in the outcomes that actually matter to the patients whose interests the system purports to serve.

Matthew R. Cooperberg, MD, MPH

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Author Affiliations: Departments of Urology and Epidemiology and Biostatistics, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, San Francisco.

Correspondence: Dr Cooperberg, Departments of Urology and Epidemiology and Biostatistics, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, 1600 Divisadero St, A-624, PO Box 1695, San Francisco, CA 94143 (mcooperberg@urology.ucsf.edu).

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