

***Institute for Clinical and Economic Review
Scoping Committee and Evidence Review Group for:***

***Brachytherapy/Proton Beam Therapy for Clinically Localized, Low-Risk
Prostate Cancer***

***Scoping Committee Call Summary
January 30, 2008***

Present:

ICER: Steve Pearson, Dan Ollendorf, Mary Lou Quinlan

Affiliated Researcher: Pamela McMahon

Scoping Committee: Wade Aubry, John Ayanian, Peter Bach, Mike Barry, Bill Corwin, Michele DiPalo, Wendy Everett, Dennis Falkenstein, Scott Gazelle, Marthe Gold, Lou Hochheiser, Nora Janjan, Peter Juhn, Phil Kantoff, Andre Konski, Armin Langenegger, Marcel Marc, Newell McElwee, Lisa Prosser, Jim Sabin, Manny Subramanian, Steve Teutsch, Sean Tunis, Bhadrasain Vikram, Milt Weinstein

Absent:

Affiliated Researchers: Julia Hayes, Joe Ladapo

Scoping Committee: Marc Berger, John J. Coen, Ted Ganiats, Jerry Kassirer, David Meltzer, Martin Sanda, Fiona Wilmot

Meeting Summary

Assessment-Specific

- With respect to our planned focus for proton beam therapy on dosing levels of 75-80 Gy, in daily fractions of 1.8-1.9 Gy:
 - Some in the group felt that fractions of 2 Gy or higher be considered, as some centers are dosing at this rate; others felt that our proposed range was appropriate, given that we will not be able to account for all variants of relative biological effectiveness (RBE), and that there are little to no data on fraction sizes higher than 2
 - There was a suggestion to include intensity-modulated proton therapy (IMPT) in our review, although it was acknowledged that is not yet common practice to deliver protons using this method in the US

- With respect to our planned focus for brachytherapy on permanent, low-dose-rate brachytherapy, with general anesthesia and use of iodine or palladium:
 - There was a suggestion that spinal anesthesia and use of cesium be considered, as these variants are standard practice in at least some centers.
 - Exclusion of high-dose-rate brachytherapy was also questioned by some, although there was a lack of consensus as to whether this procedure is used with any volume in low-risk patients
- The group was in agreement that some stratification and/or adjustment for patient age would be critical. Other suggested risk factors for consideration included comorbidities (e.g., hypertension, diabetes), use of anticoagulants, and prostate size.
- There was general discussion around our proposed use of 3D-CRT as the universal referent comparator (as was done in the previous IMRT assessment). The group felt strongly that comparisons should be made with IMRT at this point, as it has now supplanted 3D-CRT as the standard of care.
- With respect to outcomes of interest, it was suggested that the focus of our review be on survival and patient-reported outcomes, and not on so-called surrogate endpoints (e.g., biochemical disease-free survival). In addition, both short- and long-term toxicities of treatment were felt to be of importance.
- In correlation to the above, caution was urged in analyses of higher radiation doses (i.e., 75-80 Gy), as it was felt that such doses increase toxicity without any survival benefit. Consideration of lower doses was suggested, at least for alternative analyses of comparative effectiveness and cost-effectiveness.
- With respect to salvage therapy, there was a suggestion that the mix of salvage options might differ by initial treatment; for example surgery might be an option for failed brachytherapy, but not for failed proton therapy.
- The group was in agreement that the potential for secondary malignancy from radiation should be examined. The potential for hip fracture from proton therapy was also discussed; if this is to be analyzed, it was suggested that data on bone mineral density be obtained to evaluate background fracture risk in men.
- With respect to costs, it was suggested that some estimate of fixed cost be included in the proton beam estimate, given the high cost of constructing such facilities. The relative merit of using the typical Medicare reimbursement range for

proton beam (\$50,000-\$60,000) was debated, as there appears to be at least anecdotal evidence that private insurers are paying 2-3 times this amount for a course of proton beam therapy.

- Regarding our intent to use a societal perspective in these analyses, it was suggested that time in therapy, productivity, caregiver burden, and symptoms during therapy were important issues to consider in our analysis.

General

- It was mentioned that information on potential biases and conflicts of interest will be requested of all Scoping Committee members at a later date.
- Recruitment of patient representatives to the Scoping Committee is ongoing; we hope to have patients on the Committee by the next conference call.
- The next set of activities will involve the creation of separate sub-committees to inform the systematic review and decision-analytic model components respectively.