Seed implant brachytherapy for prostate cancer

Kudos to Juanita Crook and colleagues for attempting to wrestle some scientific sense into recommendations for seed implant brachytherapy for prostate cancer.[1]

Unfortunately, there are no data from randomized trials on which to base a comparison of brachytherapy with prostatectomy and external beam radiotherapy for early-stage prostate cancer. The literature in the era of prostate-specific antigen (PSA) screening is too immature to allow one to accurately comment on disease-specific survival, with most studies having a follow-up period of 3–4 years after surgery, radiotherapy or brachytherapy.

Although results are promising for brachytherapy as monotherapy for patients at low risk (T1 or T2a tumour, Gleason score of 6 or lower and serum PSA level of 10 μg/L or less), we should remain skeptical about the durability of these results, just as we should be skeptical about the results of surgical and external radiotherapy series in the era of PSA screening.

It is even more difficult to make a recommendation concerning brachytherapy for patients at intermediate risk (T2b tumour, Gleason score of 7 or lower and serum PSA level of 10–20 μg/L). Very few such patients are included in the studies quoted by Crook and colleagues, and continuing evolution of the seed implantation technique is likely to affect outcomes for patients at intermediate risk even more dramatically than for those at low risk. In addition, because the intermediate-risk group encompasses a broad range of patients, any recommendation for the entire group is likely to be an oversimplification. A recent study showed that some patients with one intermediate risk factor do as well with brachytherapy alone as patients in the low-risk group described by Crook and colleagues.[2]

In my opinion, the authors' statement that "brachytherapy should be offered only to selected patients with favourable disease (T1c or T2a tumour, Gleason score of 6 or lower and serum PSA of 10 μg/L or less)" is too strongly worded for the evidence upon which it is based. It would be more appropriate if the word "only" were left out.

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Juanita Crook and colleagues have provided a timely review of the use of brachytherapy in men with prostate cancer.[1] We agree that permanent interstitial implants as monotherapy should be reserved for those with early-stage, localized prostate cancer. However, commentator Curtis Nickel was skeptical about the use of brachytherapy in such patients.[2] We challenge the assertion that these patients represent a "small minority" of men found to have prostate cancer. In fact, with the advent of prostate-specific antigen screening, men are being diagnosed at a younger age with disease at an earlier stage than previously.[3,4] On the basis of the available 10-year data, brachytherapy is an effective intervention for early-stage prostate cancer and is no longer considered experimental therapy.

It is unclear why Nickel characterizes the rates of side effects as "disturbing." The most common one, irritative urinary symptoms, is generally self-limited. Impotence rates compare

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favourably with those following radical prostatectomy. This is part of the reason that patients are keen on being treated with brachytherapy. With the introduction of sophisticated technologies to further enhance the precision of the seed implant procedure, such approaches offer even greater promise for improved success rates, lower rates of side effects and an enhanced quality of life.[5]

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[Two of the authors of the research article respond:]

We appreciate Ross Halperin's insightful comments on our review of the evidence for brachytherapy in clinically localized prostate cancer.[1] He is absolutely correct that there is a lack of level 1 evidence from a properly conducted randomized clinical trial. We hope that the soon-to-be-open cooperative randomized trial from the American College of Surgeons Oncology Group (trial Z0070) and the National Cancer Institute of Canada (trial PR10) comparing radical prostatectomy and permanent seed brachytherapy will eventually provide the evidence that is currently lacking. This cooperative trial has been named SPIRIT (Surgical Prostatectomy v. Interstitial Radiation Intervention Trial). Interestingly, the patients who will participate in this large multicentre randomized trial are exactly the same type of patients for whom we suggested that brachytherapy was suitable as monotherapy (with favourable, low-risk T1c or T2a tumours, a Gleason score of 6 or lower and a serum prostate-specific antigen level of 10 μg/L or less).

Patients at intermediate risk (those with a Gleason score of 7 or a serum prostate-specific antigen level greater than 10 μg/L but less than 20 μg/L) are not a homogeneous group for whom one can make a single recommendation. The evidence suggesting the prognostic factors that will subdivide this group is still very young. As the data mature, recommendations can be revisited and altered appropriately.

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Who should foot the bill for continuing review of research?

Charles Weijer addressed the important issue of continuing review of research approved by research ethics boards in a recent commentary[1] on an article by Jane McCusker and colleagues.[2] Resources must be found when already-overburdened research ethics boards are asked to undertake new activities; higher personnel costs are the most important factor. Where, one might ask, should this money come from?

Weijer suggests that "research ethics boards may choose to pay for continuing review by charging for such activities." The burden of the cost for continuing monitoring should not rest with the research ethics board, but rather with the institution itself. In fact, the case can easily be made that the research ethics board should not even be involved in the collection of protocol fees because of a possible conflict. What if not enough money is raised from protocol review? Many protocols being reviewed have no budgets. Should personnel be fired and continuing monitoring stopped? Clearly not.

Research ethics boards serve a vital function and must be supported adequately to protect research participants. The public expects this. Contracts from pharmaceutical companies already serve as a source of revenue for institutions' administrations, and protocol review fees provide additional revenue. Research cannot take place without research ethics boards. Institutions must shoulder their responsibilities.

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[The author responds:]

I would like to thank Jack Mendelson and Franca Cantini for giving