Comparing Radical Prostatectomy and Brachytherapy for Localized Prostate Cancer

By Brian P. Quaranta, MD, Lawrence B. Marks, MD, and Mitchell S. Anscher, MD

Radical prostatectomy and ultrasound-guided transperineal brachytherapy are both commonly used for the treatment of localized prostate cancer. No randomized trials are available to compare these modalities. Therefore, the physician must rely on institutional reports of results to determine which therapy is most effective. While some investigators have concluded that both therapies are effective, others have concluded that radical prostatectomy should remain the gold standard for the treatment of this disease. This article reviews the major series available for both treatments and discusses the major controversies involved in making these comparisons. The data indicate that for low-risk disease, both treatments are effective, controlling disease in over 80% of the cases, with no evidence to support the use of one treatment over the other. Similarly, for intermediate-risk disease, the conclusion that one treatment is superior to the other cannot be drawn. Brachytherapy should be performed in conjunction with external-beam radiation therapy in this group of patients. For patients with high-risk disease, neither treatment consistently achieves biochemical control rates above 50%. Although radical prostatectomy and/or brachytherapy may play a role in the care of high-risk patients in the future, external-beam radiation therapy in combination with androgen deprivation has the best track record to date.

Radical prostatectomy and brachytherapy are two commonly employed methods of treating localized prostate cancer. Due to a lack of randomized trials, the selection of optimal treatment for these patients remains controversial. A wealth of single-institution data is available, but comparisons are difficult because of differences in patient selection and outcome end points. This has resulted in a frustrating situation for patients and physicians alike. A number of articles have attempted to interpret these data, and two different conclusions have emerged. Several authors have concluded that the available evidence indicates both treatments achieve approximately equal results and should be offered to patients with low-risk disease. Other physicians have concluded that in the absence of randomized trials, radical prostatectomy should be considered superior to brachytherapy and remain the standard of care. The primary reasons cited by these authors for continuing to regard radical prostatectomy as superior to brachytherapy are listed in Table 1. In this review, we will address the latest results of treatment with each modality and attempt to draw conclusions regarding their relative merits.

Results of Treatment Selection of Series

A Pubmed search was utilized in an attempt to identify all available series reporting results for transrectal ultrasound (TRUS)-guided interstitial low-dose-rate ("seed") brachytherapy and radical prostatectomy in the prostate-specific antigen (PSA) era. Updates published in abstract form were used when available. For the sake of comparison, only series that reported PSA-based outcomes were considered. Series were selected for analysis if they included data for at least 100 total patients.
Authors generally agree that an accurate comparison of treatment results can only be achieved if the patients compared have similar prognostic factors.\cite{1,3,8} Therefore, series are presented here only if they reported results according to standard pretreatment prognostic factors. The definitions of risk groups used are shown in Table 2.

### Table 2

#### Definition of Risk Groups for Localized Prostate Cancer

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Disease Stage</th>
<th>Gleason Score</th>
<th>Prostate-Specific Antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>T1–T2a</td>
<td>≤ 6</td>
<td>&lt; 10 ng/mL</td>
</tr>
<tr>
<td>Intermediate</td>
<td>T2b–T2c</td>
<td>7</td>
<td>10–20 ng/mL</td>
</tr>
<tr>
<td>High</td>
<td>≥ T3</td>
<td>≥ 8</td>
<td>&gt; 20 ng/mL</td>
</tr>
</tbody>
</table>

#### Risk Grouping in Memorial Sloan-Kettering Cancer Center and Seattle Papers

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Disease Stage</th>
<th>Gleason Score</th>
<th>Prostate-Specific Antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>≤ T2a</td>
<td>≤ 6</td>
<td>&lt; 10 ng/mL</td>
</tr>
<tr>
<td>Intermediate</td>
<td>One elevated risk factor: Gleason score ≥ 7, PSA ≥ 10 ng/mL, or stage ≥ T2a disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>Two elevated risk factors</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: In the standard risk groups, patients become intermediate or high risk based on any criteria that places them in that group; for example, a patient with stage T1c disease, a PSA of 6 ng/mL, and Gleason score of 9 would be a "high-risk" patient despite having only one high-risk feature. The Seattle group has published using a modification of the Memorial Sloan-Kettering Cancer Center system, which eliminates clinical stage from consideration.

PSA = prostate-specific antigen.

Finally, the importance of adequate length of follow-up has been demonstrated.\cite{3,9,10} Therefore, only series with a median follow-up greater than 3 years are presented. We have attempted to include the latest update of each series. In the case of groups that have published results numerous times, we have used their latest report that segregates the patients based on prognostic factors.

#### Biochemical Disease-Free Survival in Brachytherapy Series

Tables 3, 4, and 5 list the results of available brachytherapy series for patients with low-, intermediate-, and high-risk disease, respectively.\cite{1,2,11-22} Reports by Merrick,\cite{23,24} Singh,\cite{25} and Blank\cite{26} are not included because they had either fewer than 100 patients or less than 3 years median follow-up. Results published by Koutrouvelis are not shown because the implants were performed via a nonstandard technique.\cite{27} The results of all of the above series are consistent with, or superior to, the results presented in these tables. Finally, the 32-patient series from Dr. Holm\cite{28}-the first transperineal implants ever reported, last published in 1991-which reported poorer results, was also excluded. The majority of the series did not include any patients who underwent hormonal manipulation in order to rule out a possible confounding effect. Zelefsky et al\cite{11} did include 13% of patients who underwent androgen deprivation for a mean duration of 2 months. Patients in the Dattoli,\cite{22} Lederman,\cite{12} and Kollmeier\cite{13} papers received hormonal ablation in 30%, 16%, and 60% of the cases, respectively. D'Amico\cite{29} reported patients who received androgen deprivation separately, and they are not shown here. In all cases, hormonal ablation was of short duration (3 to 6 months). Of note, the series from Ragde et al\cite{14} clearly presents the worst published results for low-risk patients treated with brachytherapy. These were among the first transperineal implants performed in the United States (treated from 1987 to 1989), thus representing the learning curve for this group, as well as a "discovery curve" for this procedure,
during which time important refinements in technique and dosimetry were made. Improvement in technique, and therefore in results, should be expected with increasing experience, and this is demonstrated in a paper by Grimm et al.[15] These investigators compared their data from 1986 to 1987 with their data from 1988 to 1989, and demonstrated an improvement in long-term biochemical no evidence of disease (bNED) rate from 66% in the 1986 to 1987 cohort to 87% in the 1988 to 1989 cohort, despite very similar patient characteristics. Once each table was completed, a weighted average of bNED rates for each prognostic group was calculated using data from all of the included series. The percentage bNED at 5 years in each series was multiplied by the number of patients in that study, and these results were added together and then divided by the total number of patients in the risk group. The data from Sylvester et al[16] were not used in these calculations, as the number of patients in each risk group was not available.

### Biochemical Disease-Free Survival in Radical Prostatectomy Series

Tables 6, 7, and 8 present the available data from major series of radical prostatectomy for patients with low-, intermediate-, and high-risk features.[1,2,4,17,30-34] The series from the University of California, Los Angeles,[35] is not presented because it did not stratify results by pretreatment prognostic factors. Barry et al[36] did not report biochemical failure as an end point. Because several of these series do not report results stratified by risk group, but rather, by individual prognostic factors, the data for those series are presented for patients who had features characteristic of that group; ie, patients with a Gleason score of 7 are presented in the intermediate-risk table. It should be noted that this may have a slight negative effect on the outcome of patients in the low-risk table, because some of the subset of patients who had a PSA < 10 ng/mL would be expected to have a Gleason score of 7 or higher, and vice versa. Data for patients stratified according to their multifactor risk group is presented where available. The results from the University of Pennsylvania,[1] Baylor,[30] Cleveland Clinic,[32] William Beaumont Hospital,[30] and Urology Health Center[2] are derived from data published in papers that compared radical prostatectomy to radiation therapy. The Johns Hopkins group has published bNED rates for 5 and 10 years[31]; both are reported here, the 5-year rate to allow comparison to other series, and the 10-year rate to show
long-term results. Because many of the surgical series do not provide the number of patients in each prognostic group, a useful weighted average could not be calculated.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Author</th>
<th>Number of Patients</th>
<th>Median Follow-up</th>
<th>Failure Definition</th>
<th>Time Point</th>
<th>bNED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachytherapy alone</td>
<td>Shrank et al, 2002[3]</td>
<td>59</td>
<td>36 mo</td>
<td>PSA &gt;1.5 ng/mL and rising</td>
<td>5 yr</td>
<td>59%</td>
</tr>
<tr>
<td>D'Amico et al, 1998[1]</td>
<td>42</td>
<td>41 mo</td>
<td></td>
<td>ASTRo</td>
<td>2 yr</td>
<td>15%</td>
</tr>
<tr>
<td>Blasko et al, 2002[2]</td>
<td>20</td>
<td>41.5 mo</td>
<td></td>
<td></td>
<td>5 yr</td>
<td>65%</td>
</tr>
<tr>
<td>Brachman et al, 2000[11]</td>
<td>16</td>
<td>51 mo</td>
<td></td>
<td>ASTRo</td>
<td>5 yr</td>
<td>65%</td>
</tr>
<tr>
<td>Sikes et al, 2000[17]</td>
<td>39</td>
<td>58 mo</td>
<td></td>
<td>ASTRo or PSA nadir &gt;0.2 ng/mL</td>
<td>5 yr</td>
<td>65%</td>
</tr>
<tr>
<td>Kollmeier et al, 2000[18]</td>
<td>92</td>
<td>75 mo</td>
<td></td>
<td>ASTRo</td>
<td>8 yr</td>
<td>65%</td>
</tr>
<tr>
<td>Kock et al, 2000[19]</td>
<td>25</td>
<td>84 mo</td>
<td></td>
<td>ASTRo</td>
<td>5 yr</td>
<td>24%</td>
</tr>
</tbody>
</table>

**Comparisons of Brachytherapy and Radical Prostatectomy**

Surgeons from Johns Hopkins and Washington University have compared their surgical results to those of a single brachytherapy series for low-risk patients.[5,37] In both cases, the authors used the report of Ragde et al.[38] as the comparison series and concluded that radical prostatectomy was the superior therapy. An alternative conclusion is that these papers demonstrate the importance of the learning curve for procedure-based prostate cancer treatment. The significant improvement in results achieved by the Seattle group between 1986 to 1987 and 1988 to 1989 has been documented.[15] They attributed this to an improvement in their technique as they gained experience with the procedure. Interestingly, the Johns Hopkins radical prostatectomy experience has also been analyzed by era of treatment,[39] 1982-1988 vs 1989-1991, and a significant difference was found between the results for the two groups of patients. Thus, both the brachytherapy and surgery series demonstrated improvement in outcome over time. These results should not be surprising in light of the fact that both the Johns Hopkins University surgeons and Seattle radiation oncologists were pioneering new procedures. Figure 1 illustrates the results of Seattle era 1 and 2 as compared with Johns Hopkins era 1 and 2. This graph demonstrates that the magnitude of the improvement between eras was similar at both centers. Although the prostatectomy patients in the Johns Hopkins comparison paper came from era 2, many of the brachytherapy patients came from Seattle era 1. Thus the Johns Hopkins paper may be simply demonstrating the importance of experience in performing prostate cancer treatment.
Furthermore, since the above papers from Johns Hopkins and Washington University were published, multiple brachytherapy studies have emerged reporting results that are superior to the brachytherapy data used in their comparisons. In light of this new information, a reassessment of their conclusions is in order. A number of groups have published experiences comparing their own brachytherapy and radical prostatectomy data.[1,2,17,30] None of these authors concluded that radical prostatectomy was superior for patients with low-risk disease. In their study, D'Amico et al[1] concluded that prostatectomy was superior to brachytherapy as a single modality for intermediate- and high-risk disease. As the tables above indicate, the outcomes for patients in this study were generally inferior to other published results for both radical prostatectomy and brachytherapy. Additionally, the total sizes of the brachytherapy (n = 218) and radical prostatectomy (n = 402) series were small. In a paper by Sharkey et al,[2] a private practice urology group analyzed their experience with brachytherapy and radical prostatectomy. They concluded that there was no evidence that radical prostatectomy provided superior PSA recurrencefree results for any subgroup of patients. Interpretation of this study is limited by the small number of patients (n = 282) in the radical prostatectomy group, and by the short median follow-up (36 months). Stokes et al[17] compared results at a single institution for radical prostatectomy and brachytherapy. Numbers were small and brachytherapy results were generally poorer than those reported by other centers. No differences were found except for an improvement in outcome for high-risk patients with radical prostatectomy. Of note, patients in this study were considered for radiation only if they were not candidates for surgery. Vicini et al[30] published a retrospective review of large numbers of patients treated with radical prostatectomy, brachytherapy, and external-beam radiation therapy at nine different institutions. Grouping patients into nine different prognostic groups, they concluded that outcomes for all treatments for patients in the low- and intermediate- risk groups were "remarkably similar," and that outcomes for patients with high-risk disease were poor regardless of treatment chosen.

<table>
<thead>
<tr>
<th>Author</th>
<th>Total Number of Patients</th>
<th>Median Follow-up</th>
<th>Failure Definition</th>
<th>Time Point</th>
<th>By PSA &lt; 10 ng/mL</th>
<th>By Gleason Score &lt; 7</th>
<th>By Stage ≤ T1c or T2a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vicini et al, 2002[30]</td>
<td>1,025 (493)</td>
<td>34 mo</td>
<td>Any detectable PSA</td>
<td>5 yr</td>
<td>97%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>Paulson et al, 2001[33]</td>
<td>1,242</td>
<td>37 mo</td>
<td>PSA &gt; 0.2 ng/mL 5 yr</td>
<td>4-8 ng/mL: 90% 6-24 ng/mL: 77%</td>
<td>98%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>Sharkey et al, 2002[2]</td>
<td>208 (117)</td>
<td>35 mo</td>
<td>PSA &gt; 0.2 ng/mL 5 yr</td>
<td>10 yr</td>
<td>92%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>D'Amico et al, 1995[1]</td>
<td>586 (282)</td>
<td>40 mo</td>
<td>ASTRO</td>
<td>7 yr</td>
<td>92%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>Catalano et al, 1999[9]</td>
<td>1,778</td>
<td>48 mo</td>
<td>PSA &gt; 0.2 ng/mL 5 yr</td>
<td>7 yr</td>
<td>97%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>Kupelian et al, 2008[32]</td>
<td>1,056 (526)</td>
<td>50 mo</td>
<td>PSA &gt; 0.2 ng/mL 5 yr</td>
<td>7 yr</td>
<td>88%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>Blute et al, 2004[35]</td>
<td>2,518</td>
<td>67 mo</td>
<td>&quot;Increased PSA&quot;  5 yr</td>
<td>10 yr</td>
<td>92%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>Han et al, 2001[31]</td>
<td>2,404</td>
<td>70 mo</td>
<td>PSA &gt; 0.2 ng/mL 5 yr</td>
<td>5 yr</td>
<td>95%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>Han et al, 2001[31]</td>
<td>2,404</td>
<td>70 mo</td>
<td>PSA &gt; 0.2 ng/mL 10 yr</td>
<td>10 yr</td>
<td>95%</td>
<td>Not available</td>
<td>Available</td>
</tr>
<tr>
<td>Stokoe, 2000[11]</td>
<td>222 (54)</td>
<td>78 mo</td>
<td>PSA &gt; 0.2 ng/mL after surgery or ≥ 3 ribs</td>
<td>5 yr</td>
<td>78%</td>
<td>Not available</td>
<td>Available</td>
</tr>
</tbody>
</table>

*When patients were stratified by risk group in this study, the single value reported is the result for patients in that risk group stratification. Sites and times are listed in order of increasing length of follow-up.
*When number of patients in a particular risk group was reported, the value is given in parenthesis.
*Estimated from published tables.
*Note that when patients with Gleason score > 7, and for intermediate-risk, are reported together with low-risk patients.

**Table:** Results of Major Radical Prostatectomy Series for Patients With Low-Risk Features

The Baylor results with radical prostatectomy for intermediate- and high-risk patients, included in the Vicini paper, are the best published. This is partially accounted for by the fact that the data were presented by breaking down the patients into nine prognostic groups rather than three. Therefore, each of the patients presented here as intermediate-risk had only one of the three factors in the intermediate-risk range, making them a slightly better prognostic group than the "standard" intermediate-risk group defined in Table 2. Similarly, approximately 50% of the high-risk group presented here consists of patients who would otherwise qualify as intermediate risk. While stratifying patients into as many groups as possible may enhance our ability to provide accurate prognostic information, it does make comparisons among different series more difficult.
These studies represent a step in the right direction. As their results mature, the data will become more valuable. The argument that there is insufficient long-term follow-up of brachytherapy series[5] is no longer appropriate. The 1980s witnessed the development of the nerve-sparing radical prostatectomy, TRUS-guided brachytherapy, three-dimensional conformal external-beam radiation therapy, and the use of PSA as a tool to select patients for therapy and follow and evaluate treatment outcomes. These innovations have necessitated that evaluations of the efficacy of the various prostate cancer treatments must essentially "start over" in the PSA era, and therefore, the major series shown here have roughly similar durations of follow-up. In Tables 3 through 8, the average follow-up per patient was 53.7 months for the brachytherapy patients and 57.5 months for the surgery patients. The series published by Kollmeier,[13] Dattoli,[22] Kwok,[18] and the Seattle Group[14,15] all have mean long-term follow-up equal to or longer than the longest mean follow-up for a surgical series published in the PSA era. All of the brachytherapy series demonstrate a flattening of the survival curves with time (Figure 2), indicating that few very late failures should be expected.[14,15,18,22] While the numbers of available patients are still smaller than those in the major surgery series, the above tables describe results for 4,106 patients treated with brachytherapy. It is undoubtedly true that longer followup will allow us to make more informed decisions; however, this argument applies equally to both types of treatment.
The Problem of Defining Failure

The comparison of surgery vs brachytherapy series is complicated by differences in the definition of failure. This topic has been discussed in depth elsewhere.[3,6,7,40-42]

The natural end point for any cancer therapy is overall survival. However, because prostate cancer is a disease that (1) has a long natural history, and (2) affects primarily elderly patients, overall survival differences are difficult to detect without very large studies conducted over long periods of time. Therefore, surrogate end points have been sought, and PSA recurrence ("biochemical failure") has been widely regarded as the most useful. Biochemical failure in radical prostatectomy patients is typically defined as any detectable PSA, since all prostate tissue is surgically removed. In contrast, successful radiation treatments may not kill all viable noncancerous prostate cells, and thus, the PSA level declines gradually over many months. A "bounce" or "spike" phenomenon has also been demonstrated.[43] There may often be persistently detectable PSA that nevertheless does not herald a clinical failure.[41] These characteristics of PSA behavior after radiation therapy created interest in an American Society for Therapeutic Radiology and Oncology (ASTRO) consensus statement, generated in 1997, to define PSA failure after radiation therapy.[44] The ASTRO definition of treatment failure is "three consecutive rises in PSA separated by at least 3 months." When this definition is met, the date of failure is defined as the midpoint between the PSA nadir and the time of the first rising PSA value. It should be noted that this definition was generated using data from patients treated with external-beam radiation therapy only. Nevertheless, in the absence of a consensus definition of failure for patients treated with brachytherapy, the ASTRO definition has been commonly employed in the brachytherapy literature. The value of the ASTRO definition in predicting outcome in patients treated with external-beam irradiation has been demonstrated.[45,46] Other groups have suggested that while the definition is a valuable starting point, improvements could be made.[42,47] Several authors have suggested that the ASTRO definition causes an artificial increase in bNED rates due to the effects of backdating and early censoring.[7,40] The Hopkins group analyzed their radical prostatectomy patients and demonstrated significant improvements in the bNED rate at all time points when using the ASTRO definition.[7]
Amling et al, in a similar study, noted that the ASTRO definition lowered the short-term bNED rate but raised the long-term bNED rate, underestimating late failures.[40] Recently, Horwitz et al analyzed patients treated with radiotherapy and similarly concluded that the elimination of backdating reduced the long-term bNED rate.[48] In contrast, another study has found that early censoring did not significantly affect bNED rates in patients treated with brachytherapy.[42] and Ragde et al reported no significant change in outcomes when using a failure definition of PSA > 0.5 ng/mL vs the ASTRO definition.[14] A recent paper by Kuban et al examined the utility of over 100 definitions of biochemical failure when applied to a large group of patients treated with external-beam radiation therapy.[41] The sensitivity and specificity of each in predicting eventual clinical failure was examined. The ASTRO definition was one of the most accurate. These authors also concurred with findings that backdating caused earlier bNED rates to appear lower and long-term bNED rates to appear higher than they would without backdating. This effect is important to note when examining the curves in Figure 2 because it may artificially flatten the long-term bNED curves. They also looked at the effect of applying surgical definitions of failure to patients treated with radiation therapy. They found that while these definitions resulted in excellent sensitivity (PSA > 0.2 ng/mL = 91% sensitivity; PSA > 0.5 ng/mL = 90% sensitivity), they also were extremely nonspecific (PSA > 0.2 ng/mL = 9% specificity; PSA > 0.5 ng/mL = 26% specificity). The vast majority of patients declared biochemical failures by these surgical definitions never experienced clinical failures. Therefore, surgical definitions of failure are simply not clinically valid when evaluating the success of radiation treatments. It appears reasonable to conclude that the nonstandard definitions for failure make comparing these treatments difficult, and the ASTRO definition may artificially increase
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long-term bNED rates (at the expense of decreased short-term bNED rates). A reanalysis of bNED data for brachytherapy using criteria that do not employ backdating may be useful. Several brachytherapists have attempted to address these issues. The Seattle investigators have employed a two-rise definition of failure in their large series with results that remain comparable or superior to those of the radical prostatectomy series. Additionally, Dattoli[22] and Critz[19] have both reported their findings with a PSA > 0.2 ng/mL definition of failure, showing results that (stratified per risk group) are comparable or superior to the radical prostatectomy series. D’Amico et al[1] employed the ASTRO definition for the radical prostatectomy patients in their paper, and the results achieved do not appear to be better than the results for brachytherapy in Tables 6 through 8.

The behavior of PSA after radiation therapy demands a different type of failure definition than that typically used for surgery. The ASTRO criteria are imperfect but provide a basis for standardized comparisons between series. It is an unfortunate truth that differences in failure definitions complicate comparisons of these two modalities. Nevertheless, the comparisons must be made. More accurate comparisons may be possible when improvements to the ASTRO definition are made and implemented; they may also be facilitated if surgical series are published using the ASTRO definition.

Comparison of Side Effects
The incidence of common side effects from radical prostatectomy[49] and brachytherapy[50,51] have been reviewed recently, and the reader is referred to these sources for in-depth treatment of this issue. In summary, comparing morbidities between these two procedures is even more complicated than comparing recurrence-free survival, due to variability in definitions and data collection (physician vs patient reporting) as well as patient- selection factors. However, some conclusions can be drawn:

(1) The incidence of erectile dysfunction after radical prostatectomy varies tremendously, with very
high impotence rates in series reporting on multicenter or population-based results (59%,[52] 89%,[53] 80%,[54]) and lower rates from single institutions with high volume (14%,[3] 33%,[55]). High potency rates occur only after nerve-sparing procedures, for which not all patients qualify.[49] Reportedly erectile dysfunction rates after brachytherapy are low, ranging from 14% to 38% in patients fully potent prior to implant.[50] However, it must be noted that large population-based studies using patient-reported data (such as that reported by Stanford et al.[52]) are not available for brachytherapy. It is conceivable that outcomes from low-volume practices may be worse than those reported for high-volume institutions, in a manner similar to that shown for the radical prostatectomy. (3) Sildenafil (Viagra) is effective for patients treated with brachytherapy, with reported response rates of 62%,[56] and 88%.[57] For postprostatectomy patients, sildenafil may be quite effective in patients who are able to undergo a bilateral nerve-sparing prostatectomy (80% response rate), but has essentially no effect otherwise (0% response rate).[58] (4) Incontinence rates after radical prostatectomy vary from 0% to 6% for "severe" incontinence and 4% to 33% for stress incontinence, showing a similar disparity between high-volume centers and population-based studies.[49] Recent research confirms that high-volume centers have lower complication rates.[59] Rates of bladder neck contracture vary from 0.5% to 20.5%.[49] (5) Mild incontinence rates after brachytherapy range from 0% to 22%.[50] However, in series reporting on 300 or more patients, the rates range from 0% to 6.6%, indicating that patient volume and operator experience may affect the results. An early report of very high rates of incontinence (85%) after transurethral resection of the prostate (TURP)[60] has been contradicted by a recent report in similar patients (0%).[61] Reported rates of TURP being necessary to relieve obstructive symptoms after brachytherapy range from 0% to 8.7%.[50] (6) Rectal toxicity in patients treated with brachytherapy is generally mild, and severe toxicity is rare.[50] Rectal toxicity is very rare (0.5%) after retropubic prostatectomy.[49] However, a recent study of perineal prostatectomy demonstrated a 5.5% rectal injury rate, with a 1% incidence of stool fistula and a 0.7% chance of requiring a colostomy.[62] A study from Duke demonstrated a 2.9% incidence of stool leakage 12 months after perineal prostatectomy in patients who previously denied stool leakage.[63] In general, both procedures have a low rate of severe rectal complications.

Discussion Is prostate brachytherapy an acceptable treatment for localized prostate cancer? Or should radical prostatectomy remain the "gold standard?" To answer this question effectively, it must be asked separately for patients in each prognostic group. Low-Risk Disease

Intermediate to long-term followup data are available on more than 2,000 patients with low-risk disease, treated with brachytherapy with or without external-beam irradiation at a variety of academic and community practices (Table 3). In nearly all of these series, the bNED rate was higher than 80%, with most series approaching or exceeding 90%. While no randomized trials have compared the usefulness of adding external-beam radiation therapy for these patients, retrospective data do not support its use. The available data do not support the assertion that radical prostatectomy provides superior results for low-risk patients (Tables 3 and 6). Excellent results are achieved with both modalities. Widespread understanding and acceptance of these data have led to the adoption of brachytherapy (as monotherapy) as an accepted primary treatment option by the National Comprehensive Cancer Network (NCCN).
Intermediate-Risk Disease
For intermediate-risk patients, the proper role of brachytherapy is less clear. Intermediate to long-term follow-up is available on more than 1,100 patients (Table 4). In the series reporting on brachytherapy boost after external-beam radiation therapy, the data have uniformly reported bNED rates ≥ 75%. However, for patients treated with brachytherapy only, reported results have ranged from as high as 82% to as low as 34%. Proposed reasons for these variations have included differences in treatment margin size, dosimetric and source factors, and brachytherapist experience. However, the ambiguity of these data has led the American Brachytherapy Society to conclude that the addition of external-beam radiation therapy to brachytherapy should be considered in these patients, and the NCCN recommends brachytherapy only in combination with external-beam irradiation in this risk group. A phase III trial by the Radiation Therapy Oncology Group, RTOG 232, which is randomizing intermediate-risk patients to brachytherapy or brachytherapy plus external-beam irradiation, will attempt to answer this question. Results of radical prostatectomy do not appear to be superior to those of brachytherapy for intermediate-risk patients (Tables 4 and 7). Long-term control rates range from 35% to 65%, roughly 15% to 25% lower than those achieved with brachytherapy plus external-beam irradiation. Even if wide room for interpretation is allowed given the above discussion on failure definitions and so forth, it seems unlikely that surgery represents superior treatment for this patient group. High-Risk Disease
Outcomes for high-risk patients unfortunately are poor for either modality. For brachytherapy, data are available for just over 400 patients, and the results differ widely from series to series. Three series report good long-term results,[13,19,20] but in general, control rates are 50% or less. Surgical outcomes appear similar, ranging from 26% to 48%, with the series from Kupelian reporting better results (62%) because intermediate-and high-risk patients were grouped together.[32] For both modalities, the results are uniformly worse than those achieved in the European Organization for Research and Treatment of Cancer (EORTC) trial of external-beam radiation therapy plus androgen deprivation (see Table 9).[64] The NCCN therefore gives a category 1 recommendation (uniform consensus based on high-level evidence) for use of external-beam irradiation plus androgen deprivation in these patients, with radical prostatectomy to be reserved only for select patients. The American Brachytherapy Society currently recommends brachytherapy in these patients only as a boost to external-beam irradiation. Conclusions
The available evidence supports both brachytherapy and radical prostatectomy as effective treatments for low-risk prostate cancer. Patients should be made aware of their options and allowed to choose accordingly. Among intermediate-risk patients, the results are suboptimal for both treatments: the best results appear to be from the external-beam radiation therapy-plus-seeds series, but that cannot be said definitively due to the limitations of this type of comparison. Surgery and brachytherapy should both be considered. For high-risk patients, the results in all series are poor. External-beam irradiation with androgen deprivation should be the most common choice. For patients in this group, protocols attempting to optimize the modalities of surgery, radiation therapy, and chemo/hormonal therapy-and possibly combining these-should be developed. Most patients are attracted to brachytherapy because it is perceived as being associated with very low morbidity. Developing evidence suggests that this is not necessarily the case. While the comparison is extremely difficult to make, postbrachytherapy impotence rates (at least in experienced hands) do appear to be lower in general than for surgery. Urinary morbidity is different between the two procedures: Surgery appears to have more long-term incontinence, whereas brachytherapy can cause problems with urinary retention, frequency, and dysuria during the months after the procedure. No strong evidence exists that overall urinary morbidity is significantly decreased for brachytherapy patients. Long-term significant rectal toxicity is rare after either treatment but probably slightly higher with brachytherapy. All authors have concluded that data from randomized trials would help clarify the relative effectiveness of these treatments. However, it has proven difficult to execute these studies due to inherent biases among physicians and patient refusal to be randomized. The American College of Surgeons Oncology Group and Canadian National Cancer Institute are currently conducting a randomized trial of radical prostatectomy vs brachytherapy for low-risk patients but have found accrual to be difficult.[65] At best, it will be years before helpful data are available. That said, we must use whatever information we do have available to make the best decisions. While the published experience with radical prostatectomy is somewhat longer and larger, ample data now exist for a realistic assessment of the effectiveness of brachytherapy. Thoughts on the ‘Gold Standard’
It is relevant in this context to note the conditions under which radical prostatectomy became regarded as the “gold standard.” No randomized trials established its superiority over external-beam irradiation-and possibly combining these-should be developed.
Comparing Radical Prostatectomy and Brachytherapy for Localized Prostate Cancer

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Radiation therapy or watchful waiting; demand for the procedure was driven by patient desire for cure and enthusiasm about improved morbidity. In time, it became accepted on the basis of good results from institutional series. It was not until 2002, 21 years after Dr. Walsh pioneered the nerve-sparing prostatectomy, that the first randomized trial demonstrated a cause-specific survival benefit for this procedure as compared to watchful waiting.[66] Its superiority to external-beam radiation therapy has never been demonstrated in a randomized trial. Brachytherapy has become popular under very similar conditions. In the continued absence of randomized trials, the same criteria should be applicable to brachytherapy that were applied to radical prostatectomy. With favorable results now published from multiple centers, prostate brachytherapy appears to be at least equivalent in outcome to radical prostatectomy for all risk groups. The "gold standard" no longer applies.

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