



## Review Article

# The declining utilization of brachytherapy for the treatment of prostate cancer: Can magnetic resonance imaging reverse the trend?

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**ABSTRACT**

The utilization of brachytherapy for the treatment of prostate cancer has fluctuated over the years. Whereas initial excitement led to rapid expansion of this modality, more recent data suggest that prostate brachytherapy is in decline. This article reviews previous and current trends in the utilization of prostate brachytherapy and postulates the potential impact of the integration of magnetic resonance imaging on this modality. © 2017 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

**Keywords:**

Prostate cancer; Brachytherapy; Magnetic resonance imaging

**Historical development of prostate brachytherapy**

X-rays and radioactivity have been used for cancer therapy ever since they were first discovered around the end of the 19th century. The earliest forms of prostate brachytherapy used intracavitary radium as a means to treat both benign and malignant diseases of the prostate (1). Thereafter, various other radionuclides and treatment techniques were applied, such as interstitial radon and radioactive gold, in colloidal and seed forms. Beginning in the 1960's, researchers at Memorial Sloan Kettering Cancer Center began depositing radioactive I-125 in the prostate via an open approach (1). Around the same time, researchers in France deposited afterloaded Ir-192 into the prostate, also using an open approach (1). These early techniques were not widely adopted; however, as they were labor intensive, associated with complications, and, moreover, were of limited efficacy for the locally advanced cases seen in the pre-PSA era.

Several developments helped to make brachytherapy more reproducible and effective. For one, the development of the template in the mid 1900's, led to improved implant quality by maintaining spacing between implanted needles

and sources. By the early 1970's, researchers used the template as means to deposit radioactive sources into the prostate via a less-invasive, transperineal approach, initially under fluoroscopic guidance (1). In the 1980's, researchers in Europe combined this technique with transrectal sonographic guidance, increasing the accuracy of real-time radiation source deposition (1). Eventually, ultrasound-guided permanent low-dose-rate prostate brachytherapy made its way to the United States at centers such as the Seattle Prostate Institute, where it was further refined. Around the same time, ultrasound-guided needle placement followed by high-dose-rate prostate brachytherapy techniques were developed, as well. Finally, the adoption of PSA screening leading to earlier diagnosis of prostate cancer likely indirectly assisted brachytherapy as this modality is felt to be most effective when prostate cancer is localized (versus extending beyond the prostate).

**Initial rise in the utilization of prostate brachytherapy**

The development of modern prostate brachytherapy techniques led to its rapid adoption in the United States and eventually led to it being recognized as a standard management option, along with surgery, external beam radiation, and active surveillance/observation, for localized prostate cancer (2). Several previous patterns of care studies demonstrated increased use of brachytherapy relative to other treatment modalities for the treatment of localized prostate cancer beginning in the 1980's and through the early 2000's (3–8). As an example, Jani et al. (8) identified 823,294 men diagnosed with localized prostate

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adenocarcinoma between 1973 and 2004 using the Surveillance, Epidemiology, and End Results (SEER) database and analyzed treatment modality by year of diagnosis. They found that radiation therapy (both external beam and brachytherapy) use steadily increased from 9.1% in 1973 to 26.0% in 2004. Moreover, during that time, brachytherapy as monotherapy increased from 0.0% to 29.6%, whereas external beam radiation correspondingly decreased from 99.3% to 59.3%. Also, combination external beam radiation and brachytherapy increased from 0.0% to 11.1%. The increase in brachytherapy use (either as monotherapy or in combination with external beam radiation) specifically began in the mid-1980s. Of note, whereas in earlier years, brachytherapy as monotherapy and combination external beam radiation and brachytherapy were roughly stable, after 2000, brachytherapy as monotherapy increased, whereas the combination therapy decreased. There were some slight differences in the time-trend curves which were analyzed according to grade and stage subsets.

### More recent declining utilization of prostate brachytherapy

Since the development of modern prostate brachytherapy techniques in the 1980's and 1990's, there has been development of newer surgical and external beam radiation techniques. Moreover, active surveillance/observation plays an increasing role in the management of localized prostate cancer. As such, our group decided to evaluate more recent trends in prostate brachytherapy (9). We analyzed 182,183 men diagnosed with localized prostate adenocarcinoma between 2004 and 2009 using the SEER database. Of these, 75,434 were treated non-surgically, with radiation therapy and were the main focus of our analysis. We found that, among these patients, external beam radiation use nadired at 55.5% in 2005 and, thereafter, increased to 62.0% by 2009. Brachytherapy use (including monotherapy and combination brachytherapy with external beam radiation) correspondingly peaked at 44.5% in 2005 and decreased to 38.0% by 2009. The difference in the utilization of external beam radiation vs brachytherapy grew from 11.6% in 2004 to 24.0% in 2009. When analyzed individually, brachytherapy monotherapy decreased from 30.4% in 2004 to 25.6% in 2009, whereas combination external beam radiation plus brachytherapy initially increased from 13.8% in 2004 to 15.4% in 2005 and, thereafter, decreased to 12.3% in 2009. We noted significant variation in the decline of brachytherapy utilization by race (greater decline among Whites), median county income (greater decline among patients from poorer counties), NCCN risk categorization (greater decline among patients with low-risk disease), and by SEER Registry. Multivariable analysis found that younger age, White race, being unmarried, higher median county income, lower NCCN risk category, and SEER registry were independent predictors of brachytherapy as

treatment choice. Moreover, after accounting for all patient and tumor characteristics, multivariable analysis demonstrated decreasing utilization of brachytherapy with increasing year of diagnosis (OR for BT = 0.920, 95% CI: 0.911–0.929,  $p < 0.001$ ).

Shortly after publication of our manuscript, Martin et al. (10) were able to independently verify our findings of decreasing utilization of prostate brachytherapy using another national cancer data set. They identified 1,547,941 patients diagnosed with localized prostate cancer between 1998 and 2010 using the National Cancer Data Base (NCDB). When looking at all patients diagnosed with prostate cancer, they noted that brachytherapy monotherapy reached a peak of 16.9% in 2002, and then steadily declined to a low of 8% in 2010. In the NCDB, brachytherapy as a boost was not differentiated from other radiation therapy until 2003; however, the authors did note a steady decline of combination external beam radiation and brachytherapy from 5.4% in 2003 to 2.5% in 2010. The authors noted that the steepest decline of prostate monotherapy utilization was among patients with low-risk disease, whereas combination external beam radiation and brachytherapy declined most rapidly among patients with intermediate risk disease. Interestingly, the percent decline in prostate brachytherapy utilization was more marked among academic/research programs as compared with community programs and unknown facility types. Of particular note, the rate of surgery increased from 46.1% in 1998 to 59.1% in 2010 among all patients during the years studied.

Of note, it remains unknown whether the above trends are specific to low-dose-rate or high-dose-rate prostate brachytherapy, or both. Neither the SEER nor NCDB data sets reliably differentiate between the two modalities. That said, as per a recent comparative effectiveness study performed using the SEER-Medicare data set, which included patients diagnosed between 1998 and 2007, it would seem that LDR accounts for most prostate brachytherapy procedures in the United States (87% of all prostate brachytherapy cases, 95% of brachytherapy monotherapy cases, and 78% of combination brachytherapy and external beam cases in their data set) (11). Therefore, it is likely that these trends are representative of LDR brachytherapy, at a minimum.

What is the cause of this declining utilization of prostate brachytherapy? Unfortunately, determining the cause of the changing utilization of cancer therapy is difficult to do using population-based data sets, such as the SEER database and NCDB, alone. Nonetheless, we believe that the declining utilization of prostate brachytherapy is likely multifactorial. For one, the decline in the utilization of brachytherapy coincides with recent advances in surgery (laparoscopic and robotic techniques) and external beam radiation (principally intensity modulated radiation therapy but also stereotactic body radiotherapy [SBRT] and proton therapy) (12). These novel techniques are associated with higher reimbursement rates relative to brachytherapy, which likely drives their increasing utilization along with

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