

# Healthcare Professional Guide

## Brachytherapy:

*The precise answer for tackling prostate cancer*



Because life is for living

## Radiotherapy: a cornerstone of prostate cancer care

Prostate cancer is the most commonly diagnosed malignancy in Western men, and the incidence is rising. In the US for example, there were over 192,000 new cases of prostate cancer diagnosed in 2009,<sup>1</sup> while in Europe, figures for 2006 identified 350,000 new cases.<sup>2</sup> The advent of prostate-specific antigen (PSA) screening in the early 1990s in Western countries has contributed to this dramatic increase in diagnosis rates and the opportunity to successfully treat prostate cancer early.<sup>3</sup>

**Although mortality from prostate cancer remains considerable, effective treatment options mean many men can realize good cancer control and quality of life.** Innovation in prostate cancer treatment is therefore key to addressing the current and future needs of patient care.

In recent years, cancer treatment goals have shifted from **life preservation** to **cure** with the preservation of quality of life. **Radiotherapy plays an important role in prostate cancer management** and has witnessed remarkable progress during the last two decades. This results from scientific and technical advances in imaging modalities, computerized planning and delivery, and hardware. In addition to providing clinical efficacy and safety, radiotherapy offers choice, convenience and efficient use of healthcare resources. It thus remains a cornerstone of prostate cancer treatment, alongside surgery and hormone therapy.

## Brachytherapy: treating prostate cancer 'from the inside, out'

Radiotherapy can be basically divided into **external beam radiotherapy** (EBRT), and **internal radiotherapy**, frequently referred to as **brachytherapy**. Unlike EBRT, brachytherapy involves placing a radiation source internally, into the prostate.

This brochure provides an overview of the significant benefits of brachytherapy that make it an important and preferred treatment option for many men with prostate cancer.

### Benefits of brachytherapy in prostate cancer; delivering radiation from the 'inside, out':

- **Demonstrated efficacy:** Cancer control and long-term survival rates similar to EBRT and surgery.<sup>4</sup>
- **Precision:** Radiation dose delivered precisely to target tumor area and does not travel through healthy tissue.<sup>5,6</sup>
- **Minimized risk of side effects:** Surrounding healthy tissue is spared from unnecessary radiation or surgical trauma leading to reduced side effects and favorable functional outcomes profile in terms of urinary and erectile function compared to EBRT and surgery.<sup>6,7</sup>
- **Minimally invasive, short recovery time:** Avoids the need for extensive surgery, and with shorter recovery times associated with brachytherapy than with surgery.<sup>8,9</sup>
- **Convenience:** Significantly shorter treatment times of days compared to several weeks associated with EBRT, allowing patients to get back to their everyday life sooner.<sup>8,9</sup>
- **Cost-effective:** Favorable investment, maintenance and cost-effectiveness profile.<sup>10</sup>



# Treating prostate cancer

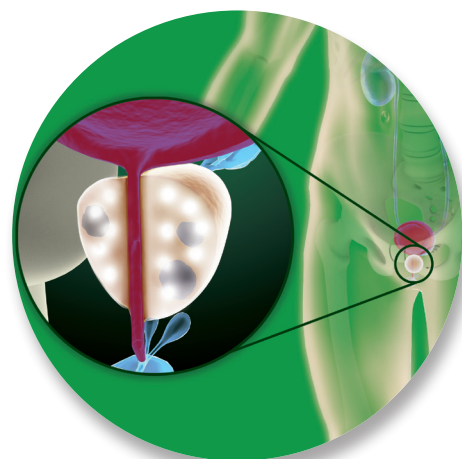
## Treatment options

The main treatment options for prostate cancer include **active surveillance, watchful waiting, surgery (radical prostatectomy) and radiotherapy (EBRT or brachytherapy).**

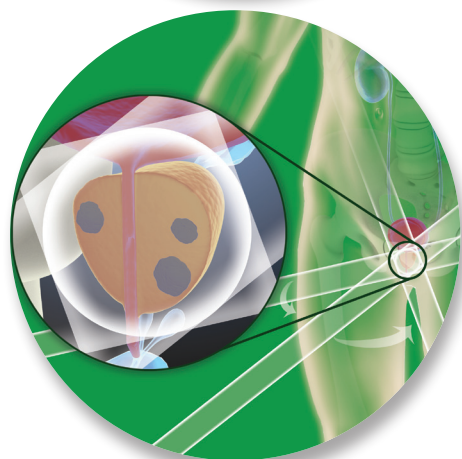
Two different brachytherapy techniques can be used: **low dose rate (LDR)** brachytherapy in which radioactive sources are permanently implanted into the prostate tissue and **high dose rate (HDR)** brachytherapy, in which the source is temporarily placed into the prostate tissue.

There is no one recommended 'standard' treatment for prostate cancer, as evidence suggests comparable efficacy between the different options.<sup>10</sup> Thus, other differences such as treatment-related side effects, impact on patients' quality of life and functional outcomes, patient convenience, patient preference and cost-effectiveness all become important considerations.

**Brachytherapy aims to put the patients' needs at the center of treatment planning and delivery without compromising on efficacy.**



Brachytherapy works 'from the inside, out'



External beam radiotherapy (EBRT) works 'from the outside, in'

## Tumor classification and risk status

Tumor characteristics, such as stage (clinical extent of the disease), Gleason score (assessment of biopsies) and PSA level, are all predictive of cancer outcomes. These measures are used to assign patients to risk groups (Table 1),<sup>3</sup> based on their prognosis, and help guide decisions on the best treatment option or combination for each patient.

Both LDR and HDR brachytherapy can be utilized as monotherapy or in combination with other treatments such as EBRT. LDR brachytherapy utilized as monotherapy is most effective in low- and intermediate-risk patients<sup>4,11</sup> and may also be used in combination with EBRT in intermediate-risk patients.<sup>8,11</sup> HDR brachytherapy has demonstrated excellent outcomes across all risk groups, notably in high-risk patients in combination with EBRT<sup>12</sup> or in low- and intermediate-risk patients as monotherapy.<sup>8</sup>

The various options that exist in brachytherapy treatment provide the opportunity to create highly individualized treatment plans depending on patients' needs.

Parameter	Low-risk	Intermediate-risk	High-risk
Tumor stage	T1–T2a	T2b–T2c <b>or</b>	T3a <b>or</b>
Gleason score	2–6	7 <b>or</b>	8–10 <b>or</b>
Pre-treatment prostate-specific antigen (PSA)	≤10 ng/mL	10–20 ng/mL	>20 ng/mL

**Table 1.** Prostate cancer risk groups  
(Adapted from NCCN Practice Guidelines in Oncology: Prostate Cancer, 2010)<sup>3</sup>

## Low dose rate (LDR) brachytherapy

### Features

LDR brachytherapy, also known as '**seed therapy**', involves the precise and **permanent** implantation of radioactive 'seeds' into the prostate using specially designed needles. These iodine 125 ( $^{125}\text{I}$ ) or palladium 103 ( $^{103}\text{P}$ ) sources deliver a high total dose of radiation (typically 125–145 Gy) at a very low dose rate (<40 cGy/h) over a period of weeks to months, until the seeds become inactive.<sup>8,11</sup>

### Indications

Currently, LDR **monotherapy** is considered the optimal treatment for patients with **low-risk** disease<sup>4,10</sup> but is also used in **intermediate-risk** patients with a favorable risk-factor profile.<sup>11</sup>

LDR brachytherapy is also used in combination with EBRT in intermediate-risk patients to deliver the increased doses required to treat those with a poorer risk profile, without the increased toxicity and side effects associated with using a higher dose of EBRT alone.<sup>8,11</sup>

### Key benefits

- **Demonstrated efficacy:** Comparable efficacy to surgery and EBRT.<sup>12</sup> LDR monotherapy is considered a standard of care for low-risk patients.<sup>4</sup>
- **Precision:** Real-time intra-operative treatment planning and delivery in one step allows accurate dose delivery precisely to the target tissue. This results in reduced side effects and shorter treatment times.<sup>9</sup>
- **Minimized risk of side effects:** As radiation doses to surrounding healthy tissue are minimized, LDR brachytherapy is well tolerated with reduced side effects such as incontinence and erectile dysfunction, and better long-term quality of life compared to other treatments.<sup>7,13,14</sup>
- **Convenience:** Significantly shorter treatment time of 1 day compared to around 7 weeks with EBRT allowing patients to return to their normal life quicker, often returning to work the next day.<sup>3,9,12</sup> Compared to surgery, LDR brachytherapy offers shorter recovery times.<sup>10</sup>
- **Easy to use:** The integration of planning, imaging and delivery simplifies the treatment process.<sup>11,15</sup> Outcomes are reproducible and new robotic seed implantation techniques have improved the accuracy of seed placement.<sup>16,17</sup>

“Low dose rate brachytherapy for both low-risk and selected intermediate-risk cancers achieves exceptional cure rates. Even with dose escalation, it will be difficult for EBRT to match the proven track record of brachytherapy seen over the past decade.”<sup>19</sup>



LDR brachytherapy 'seeds'

## Efficacy

### *LDR brachytherapy: monotherapy*

**LDR monotherapy provides exceptional cancer control** and long-term survival rates in both low- and intermediate-risk patients, with comparable efficacy to EBRT and surgery.<sup>11,12</sup> LDR monotherapy is considered an **optimal choice for patients with low-risk disease**.<sup>4,10</sup>

Studies in Europe and the US have shown **cancer control rates of 87–94% at 10 years follow-up** in low-risk and 70–95% at 7 or more years follow-up in intermediate-risk patients.<sup>4</sup>

These treatment responses are maintained long-term, with excellent survival rates seen with more than 10 years of follow-up. Disease-specific and actuarial overall survival rates of 95% and 85% respectively, have been reported.<sup>18</sup>

LDR brachytherapy has demonstrated comparable efficacy to surgery and superior efficacy to EBRT. A matched-pair analysis reported control rates for low- and intermediate-risk patients of 95% for LDR brachytherapy compared to 85% for EBRT, with the rate falling to 75% for EBRT but remaining stable for LDR brachytherapy after 7 years.<sup>19</sup>

### *LDR brachytherapy: in combination with EBRT ('boost')*

LDR brachytherapy can also be used in combination with hormone therapy or EBRT, especially for those with a less favorable risk profile to achieve dose escalation without compromising side effect risk. Excellent long-term results have been reported with relapse-free survival rates for low- (86%) and intermediate-risk (80%) patients at 15 years follow-up.<sup>20</sup>

## Side effects and functional outcomes

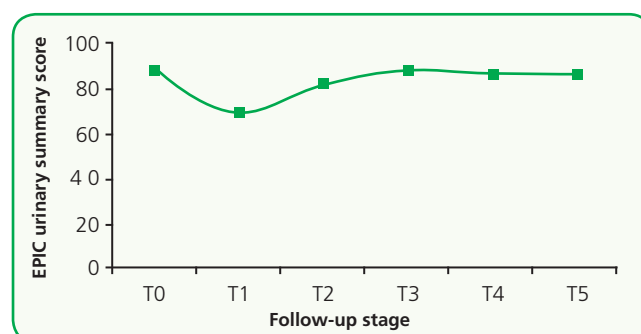
The precision of LDR brachytherapy minimizes radiation doses to surrounding, healthy tissues. **The reduced risk of side effects and improved functional outcomes and long-term quality of life compared to other treatment options, allows LDR brachytherapy patients to return to their everyday life quickly.**

**Urinary function:** Short-term urinary bother is reported in the first 6 months following LDR brachytherapy but return to pre-treatment levels within 1 year.<sup>7,21</sup> There is a **low risk of long-term urinary incontinence** with LDR brachytherapy (1%),<sup>13</sup> which is much lower than rates reported with surgery.<sup>22</sup>

**Gastrointestinal function:** Rates of gastrointestinal toxicity after LDR brachytherapy are low (5–8%) and greatly reduced compared to EBRT.<sup>12,19</sup>

**Sexual function:** Lower risk of erectile dysfunction is seen with LDR brachytherapy than after surgery.<sup>7,22</sup>

**Quality of life:** In common with EBRT and surgery, adverse effects on urinary and sexual function are reported for LDR brachytherapy during the first few months. Quality of life scores return close to baseline levels 6–12 months after LDR treatment and remain stable (Figure 1).<sup>21</sup> In contrast, surgery is associated with worse sexual functioning and urinary incontinence, while EBRT is associated with worse sexual functioning and poorer bowel function.<sup>7</sup> Furthermore, at 6 years follow-up, there was no negative impact of LDR treatment on quality of life reported on urinary, bowel and sexual outcomes as well as social and psychological functioning and well-being.<sup>14</sup>



**Figure 1.** Low risk of long-term urinary incontinence with LDR brachytherapy<sup>21</sup> †

# High dose rate (HDR) brachytherapy

## Features

In HDR brachytherapy, a high dose rate iridium 192 (<sup>192</sup>Ir) source is **temporarily** placed in the prostate tissue using specialized needles to deliver a high treatment dose over a short period. Each dose period session takes about 60–90 minutes to administer and this is then repeated 2–4 times over 1–2 days to deliver the total treatment dose required.<sup>8</sup> The number of treatment sessions depends on a number of factors, including the stage of the prostate cancer and what other treatment modalities are used, e.g., combination with EBRT.

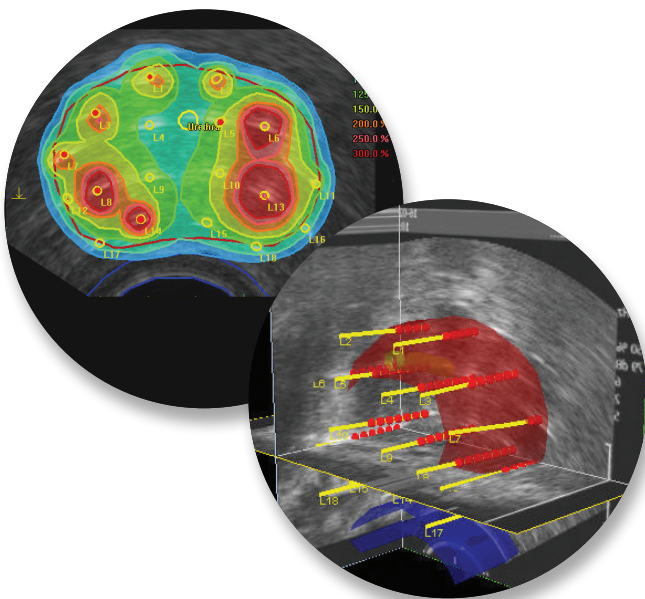
## Indications

HDR brachytherapy is primarily and most extensively used in combination with EBRT to deliver increased treatment doses – ‘**boost**’ brachytherapy. HDR boost brachytherapy is favored in **intermediate- and high-risk** patients, as it provides the dose escalation essential for control of locally advanced disease without the increased toxicity and side effects that can be associated with higher EBRT dosing.<sup>12</sup>

HDR **monotherapy** is now also a useful treatment option in both **intermediate- and low-risk** patients.<sup>8</sup> It has been found that the high dose rate delivery of HDR monotherapy may be more biologically efficient than EBRT or LDR brachytherapy due to the distribution of radiation and shortened treatment time, preventing repopulation of prostate cancer cells.<sup>4</sup>

## Key benefits

- **Demonstrated efficacy:** Excellent efficacy and disease outcomes which are comparable to surgery and EBRT.<sup>8,23,24</sup>
- **Precision:** Sophisticated software and imaging combined with a treatment delivery device known as an ‘afterloader’ provide accurate source delivery, while sparing surrounding healthy tissue from unnecessary radiation. This approach maximises efficacy, achieving reproducible results, with minimal side effects thus improving patient outcomes. Recent studies have suggested that the targeted precision and sparing of healthy organs such as the bladder and bowel achieved with HDR brachytherapy is superior to that with intensity-modulated radiation therapy (IMRT) or tomotherapy.<sup>5,6</sup>
- **Minimized risk of side effects:** Due to its targeted approach, HDR brachytherapy is well tolerated with reduced side effects such as incontinence and erectile dysfunction compared to other treatments such as EBRT and surgery.<sup>6,23,25,26</sup>
- **Convenience:** Significantly shorter treatment time of 1–2 days compared to around 7 weeks with EBRT, and reduced recovery times compared to surgery. HDR brachytherapy results in less interference in patients’ daily lives and allows a quicker return to normality.<sup>26–28</sup>
- **Easy to use:** The integration of planning, imaging and delivery simplifies the treatment process.<sup>11,15</sup>



HDR brachytherapy 3D imaging and dose distribution

## Efficacy

### *HDR brachytherapy: in combination with EBRT ('boost')*

HDR boost brachytherapy is an important treatment option for many patients with excellent efficacy and disease outcomes. Results are comparable to treatment with EBRT monotherapy as **efficient dose escalation can be achieved without an increased risk of side effects**.

Studies in low- and intermediate-risk patients have demonstrated **5–10 year relapse-free survival rates of 93–100% and 82–100%**, respectively.<sup>8</sup> For high-risk patients, rates have proved more variable, typically ranging from 60–80%, although rates of over 90% have been reported.<sup>8</sup>

Disease specific outcomes such as local recurrence (7–11%) and cause-specific survival (96–98%) have also reinforced HDR boost brachytherapy as an optimal treatment option for patients with localized disease.<sup>8</sup>

Dose escalation with HDR boost brachytherapy has demonstrated better efficacy compared to EBRT alone with relapse-free survival of 5.1 years reported versus 4.3 years, respectively.<sup>24</sup>

### *HDR brachytherapy: monotherapy*

Recent years have seen clinical studies showing the potential effectiveness of HDR monotherapy for many patients.

Impressive **relapse free rates of 89–100%** are reported in low- and intermediate-risk patients with local control and cause specific survival of 100% at 3–5 years follow-up.<sup>8</sup>

Importantly, these rates are similar to findings with surgery, EBRT, LDR monotherapy, and HDR boost brachytherapy.<sup>29</sup>

## Side effects and functional outcomes

HDR brachytherapy provides increased dose escalation and excellent treatment outcomes but **with a reduced risk of side effects compared to other treatment options, all of which increases its patient acceptability**.

**Urinary function:** HDR brachytherapy has similar **low rates of urinary dysfunction** as LDR brachytherapy (5–6%), with comparison studies even indicating fewer effects on urinary symptoms.<sup>23,25</sup> Furthermore, surgery is associated with a greater risk of long-term incontinence than HDR brachytherapy.<sup>22</sup>

**Gastrointestinal function:** Rates of gastrointestinal toxicity are generally low after HDR brachytherapy (4–8%), with lower reported incidence of acute rectal pain than LDR brachytherapy.<sup>23,25,28</sup>

**Sexual function:** HDR brachytherapy has shown **improved rates of sexual function** post treatment than with surgery and even LDR brachytherapy. This may become a distinct advantage for HDR brachytherapy as the potential of reduced sexual functioning for many men is particularly distressing.<sup>23,25</sup>

**Quality of life:** There is currently a lack of health-related quality of life studies comparing HDR brachytherapy with other approaches. One long-term study has reported **excellent quality of life levels**, similar to patients with prostate cancer before therapy, after treatment with HDR brachytherapy in combination with EBRT.<sup>30</sup>

The lower rates of urinary and gastrointestinal symptoms compared with LDR brachytherapy point towards an even lower impact on patients' lives after HDR treatment.<sup>23,26</sup>

## LDR and HDR brachytherapy

### Patient acceptability

Brachytherapy's mode of action 'from the inside, out' enables delivery of high treatment doses to very precise areas that kill tumor cells over a short time period. This allows for **much shorter overall treatment times** and recovery periods than with EBRT or surgery, respectively, which in turn facilitates flexibility in the design of brachytherapy treatment plans that can be more readily tailored to patients' individual needs.

As brachytherapy does not require daily hospital visits, it is much more **convenient for patients** – particularly working and elderly patients, and those who live considerable distances from treatment centres.<sup>31</sup> Less frequent outpatient visits also supports **greater adherence to the treatment plan**, ensuring that the total dose is delivered.

The impact of the favorable tolerability of brachytherapy on patient acceptability is evident from a recent survey where 40% of those receiving LDR brachytherapy indicated side-effect profile as their motivation for choosing that therapy, compared with 1.2% of patients selecting surgery. Furthermore, given the choice, 81% of patients who had LDR brachytherapy said they would choose to have the same procedure again, compared with 72% who would choose surgery again.<sup>32</sup>

**Overall, patient-centred brachytherapy means less interference in patient's daily lives, allowing a quicker return to normal life.**

### The cost-effective choice

The reduced treatment times associated with both LDR and HDR brachytherapy and the possibility of outpatient treatment provide real and significant **cost-saving benefits to patients and healthcare providers** and reduce pressure on resources.

#### Treatment costs

The Institute for Clinical and Economic Review (ICER) in the US recently considered the comparative value of surgery, brachytherapy, IMRT and proton therapy in low-risk prostate cancer. Brachytherapy was considered a 'high value' alternative, as lifetime treatment costs were almost \$3,000 less than for surgery (Table 2).<sup>10</sup>

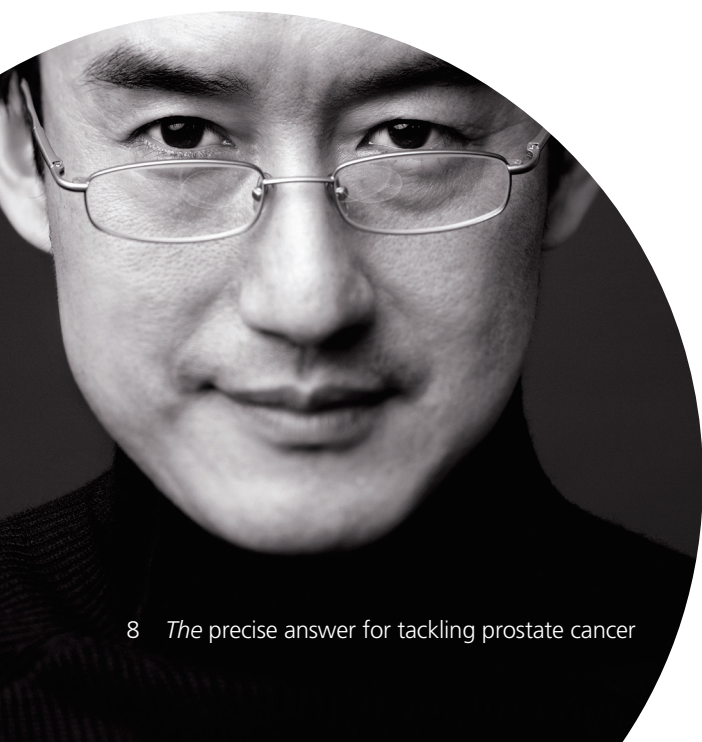
	QALYs	Incremental QALYs	Cost (\$)	Cost/QALY(\$)
Brachytherapy	8.12	0.30	25,484	< Ref.
Active surveillance	8.97	1.15	30,422	1,803
Radical prostatectomy	7.82	Ref.	28,348	Ref.
Intensity-modulated radiation therapy	8.09	0.27	37,861	35,223
Proton beam	7.97	0.15	53,828	169,867

**Table 2.** Lower costs/QALY for brachytherapy compared to other treatments in 65-year old men with low-risk prostate cancer (Adapted from ICER, 2010)<sup>10</sup>

All incremental costs and QALYs calculated relative to radical prostatectomy; QALY: quality-adjusted life years

#### Set up

Compared with the substantial investment required for IMRT and proton beam therapy, **infrastructure and running costs for brachytherapy are much more modest.** HDR brachytherapy also maximizes the use of existing resources as most radiotherapy centres already possess an HDR afterloading machine for other indications, such as breast or cervical cancer. This can ultimately result in further efficiencies and costs savings within centres.



## Leading innovation in radiotherapy

The latest real-time, image-guided planning and delivery technology enables brachytherapy to deliver high-precision, targeted radiotherapy.

Advanced 3D imaging and planning allows accurate visualization of the tumor and surrounding tissues to design a personalized, targeted radiotherapy plan. Real-time intra-operative planning and delivery procedures ensure accurate radioactive source positioning and refinement of the treatment plan during the procedure as the position of each implant (HDR brachytherapy) or needle delivering the seeds (LDR brachytherapy) is fed back to the planning programme. Such accuracy ensures minimal radiation exposure to surrounding healthy tissues and improved patient outcomes compared to both established and other modern treatment modalities.<sup>5,6,8,9,33</sup>

**LDR brachytherapy has demonstrated better long-term health-related quality of life outcomes in terms of urinary and sexual function compared to modern forms of surgical techniques such as robotic-assisted laparoscopic prostatectomy, as well as cryotherapy and open prostatectomy.**<sup>33</sup>

Recent studies have also suggested that the targeted precision of HDR brachytherapy, offering improved dose distribution, better dosimetric selectivity and sparing of 'organs at risk' such as the bladder, urethra and bowel and the subsequent **reduced risk of side effects is superior to that achieved with newer, more expensive technologies such as IMRT or tomotherapy** (an advanced form of continuous helical IMRT).<sup>5,6</sup>

“Adaptive image-guided prostate... brachytherapy ....[has] set benchmarks exploiting the full potential of advanced radiotherapy with very promising clinical results.”<sup>15</sup>

## Key benefits of advanced LDR and HDR brachytherapy technology

- 'One-step' treatment planning and delivery option; reduced treatment times compared to EBRT.
- Sophisticated imaging and highly accurate source placement provides better tumor targeting; reduced side effects compared to surgery and EBRT.
- Modern imaging techniques allow for 'real-time' dosing and placement adjustment during treatment; increased precision.
- Lower set-up and maintenance costs than modern EBRT; more cost-effective.



Brachytherapy: one-step planning and treatment delivery

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**For further information on brachytherapy for prostate cancer, consult the following resources:**

**Speak to colleagues who have successfully integrated brachytherapy into their practice**

**ESTRO** (European Society for Therapeutic Radiology and Oncology)  
[www.estro.org](http://www.estro.org)

**ASTRO** (American Society for Therapeutic Radiology and Oncology)  
[www.astro.org](http://www.astro.org)

**GEC-ESTRO** (Groupe Européen de Curiethérapie and the European Society for Therapeutic Radiology and Oncology)  
[www.estro.org/about/Pages/GEC-ESTRO.aspx](http://www.estro.org/about/Pages/GEC-ESTRO.aspx)

**ABS** (American Brachytherapy Society)  
[www.americanbrachytherapy.org](http://www.americanbrachytherapy.org)

**NCCN** (National Comprehensive Cancer Network)  
[www.nccn.org](http://www.nccn.org)



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## Brachytherapy:

*The precise answer for tackling prostate cancer*

Reasons to consider brachytherapy in prostate cancer management

- Demonstrated efficacy
- Precision radiotherapy
- Minimized toxicity
- Patient-centered
- Cost-effective
- State-of-the-art

Because life is for living

For more information please visit  
[www.brachyacademy.com](http://www.brachyacademy.com)

A global educational initiative of Elekta  
[www.elekta.com](http://www.elekta.com)

