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# Prostate Cancer

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Patient Information

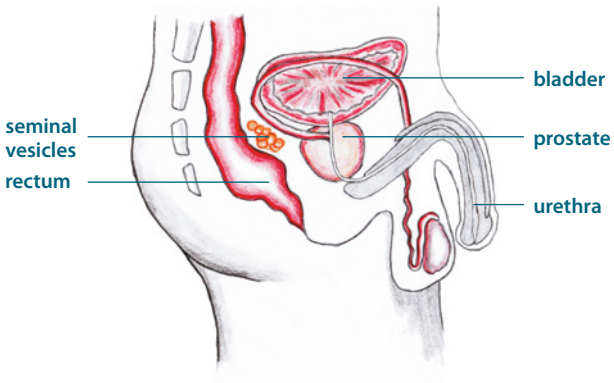


Eckert & Ziegler

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# Introduction

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Sagittal cut through the male abdomen

The prostate is a small gland in the male reproductive system. It is approximately the size of a walnut and is located right below the bladder with the urethra running right through it. The prostate produces the seminal fluid to transport the semen during ejaculation.

Cancer is a disease defined by uncontrollable cell growth and cell division. In some cases these cells form a small lump of tissue, a so called tumor. Tumors can either be benign (non-carcinomatous) or malignant (carcinomatous).

In many men age 45 and above, the prostate slowly starts growing. This growth is normally benign and known as prostatic hyperplasia. It can cause ailments such as frequent urination or a weak urinary stream but is usually not life threatening.

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In some cases tumors may turn out to be malignant and become invasive causing the destruction of healthy tissue. Symptoms which may indicate a malignant tumor are a weak urinary stream, interruptions, pain and bleeding during urination as well as the inability to urinate although they do not necessarily have to be associated with prostate cancer.

Prostate cancer is the second most frequent type of cancer in men worldwide.<sup>1</sup> If diagnosed and treated early on, prostate cancer can often be cured effectively. But prostate cancer often grows slowly over several years without causing any symptoms.

Early detection of prostate cancer is of utmost importance to allow a timely treatment and improve chances of healing the disease. As long as the cancer's presence is limited to the prostate, chances of a complete removal of the tumor and therefore curing the patient are high. But as soon as the tumor grows beyond the gland, treatment becomes more difficult.

Generally, men at a certain age are advised to undergo regular preventive examinations by an urologist. In Great Britain and Spain these yearly check-ups are recommended starting at age 50 if there are no known cases of prostate cancer in the family history. In Germany and France a yearly examination is suggested starting at age 45. For further information and enquiries please contact your primary care physician or urologist.

<sup>1</sup> GLOBOCAN 2020. WHO

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# Diagnosis

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Normally, multiple options from a range of possible examinations are combined to achieve a high diagnostic accuracy.

## Prostate-specific antigen (PSA) test

PSA is a protein which is produced by cells in the prostate. Its concentration in human blood is determined through a PSA test. The PSA level in healthy males is relatively low, while elevated levels are indicative of an abnormal situation in the prostate. A heightened concentration may not necessarily be a sign of prostate cancer but can also be the result of a benign growth in the prostate. In case of a suspicious PSA test result, it is recommended to follow up with additional examinations.

## Digital rectal exam (DRE)

During a DRE the prostate is examined with a finger through the rectum. For the exam the finger is inserted into the rectum using a disposable glove and a lubricant. Due to the prostate's proximity to the rectal wall, changes in the gland can then be felt if they reach a certain size and position. The DRE is often combined with a PSA test to avoid false negative or false positive examination results.

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## Imaging

Examination imaging has become better and better over the years. For transrectal ultrasound (TRUS), an ultrasound probe is inserted into the rectum. It provides precise images of the prostate and its surroundings. Increasingly, multiparametric MRI (mpMRI) of the prostate is also being used. It is a special form of MRI examination. Compared to conventional MRI, mpMRI offers greater accuracy in the detection of prostate cancer as it combines several parameters. All imaging procedures are painless for the patient.

## Biopsy

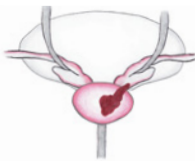
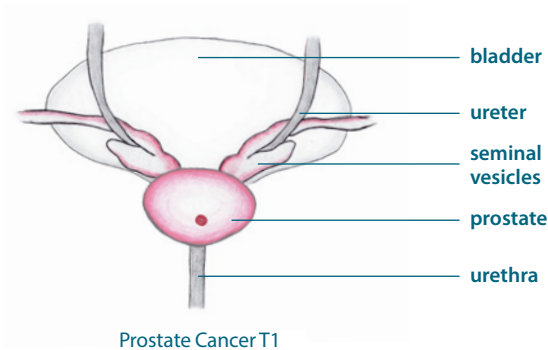
If PSA test and/or DRE resulted in a recommendation for further examinations (and maybe after mpMRI of the prostate), according to the current guidelines, usually a prostate punch biopsy is performed. Access is either transperineal (ultrasound-controlled TRUS and/or MRI fusion biopsy) or transrectal (ultrasound-controlled TRUS). The tissue samples taken during the biopsy (biopsy specimen) are analysed under a microscope in the laboratory by specialists known as pathologists. Your doctor usually tells you when to expect the results.

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# Classification

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In order to plan the treatment and select the appropriate therapy, the tumor is classified according to internationally accepted criteria. In addition to the “grading” after biopsy (malignancy of the tissue), the anatomical spread is assessed for classification (“staging”). This is done according to the TNM-system (tumor, node, metastasis). T indicates the size and spread of the primary tumor, N the absence or presence of local or neighbouring lymph node metastasis and M the presence of distant metastasis. After classification, your doctor will discuss the possible treatment alternatives with you.<sup>2,3,4</sup>



	Low Risk	Intermediate Risk	High Risk
Stage	T1 – T2	T2b – T2c	T3a
	and		or
Gleason Score	≤ 6	7	≥ 8
	and		or
PSA	< 10 ng/mL	< 20 ng/mL	> 20 ng/mL
<b>Favorable Intermediate</b>		<b>Unfavorable Intermediate</b>	
1 intermediate risk factor		2 – 3 intermediate risk factors	
and		and/or	
Gleason Score 7 (3+4)		Gleason Score 7 (4+3)	
and		and/or	
< 50% positive biopsies		> 50% positive biopsies	

<sup>2</sup> S3-Guideline Prostate Carcinoma. German Guideline Program in Oncology. Version 6.0. May 2021

<sup>3</sup> EAU-Guideline 2024

<sup>4</sup> NCCN-Guideline 2024

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## Treatment Options

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Modern medicine offers a variety of methods for the treatment of localized prostate cancer. The treatment may involve just a single form of therapy (monotherapy) or a combination of multiple treatment options. The individual decision regarding the treatment plan is based on the classification of the tumor, the doctor's medical assessment and the patient's general health as well as his personal wishes. Based on the results of your preliminary examination, your doctor will discuss the ideal course of action with you.

### Active surveillance of the tumours development

This method involves regular examinations and is used for patients with low risk diagnoses and seniors with weak constitutions to initially avoid a surgical or hormonal intervention. If the resulting findings become worse, a therapy may be initiated.

### Radical prostatectomy

In a radical prostatectomy, the prostate is surgically removed alongside the seminal vesicles and organ specific lymph nodes. This method is used for low, intermediate and high risk tumors and is always carried out as an inpatient treatment.

### External beam radiation therapy (EBRT)

In EBRT, a machine is used to deliver radiation from outside the body into the tumor. Cancer cells are more



vulnerable to radiation than healthy cells and are therefore destroyed while healthy tissue is more likely to survive. According to the individual treatment plan, the patient is treated over a longer period of time, often in several sessions per week. Since during EBRT healthy tissue is also exposed to radiation, patients may suffer from a range of side effects. These may include fatigue, diarrhea, stomach issues and intestinal discomfort.

## Brachytherapy

During brachytherapy radiation is delivered to the tumor from inside the body. This can be done using HDR-brachytherapy (High-Dose-Rate; also known as afterloading) or LDR-brachytherapy (Low-Dose-Rate).

## LDR-Brachytherapy / seed implantation

“Brachy” (=“short”) refers to the short distance between the radioactive source and the tumor tissue. During this form of therapy, small, radioactive sources called Seeds are permanently implanted into or next to the tumor. This way a high radiation dose can be delivered to the tumor while reducing damage to healthy tissue.

The implanted Seeds are radioactive Iodine-125 sources with a length of 4.5 mm and a diameter of 0.8 mm. Each Seed delivers a specific radiation dose to the surrounding tissue. Calculation on a case-by-case basis allows precise placement of the Seeds for maximum safety and efficiency. The whole prostate can be covered by the desired radiation dose to successfully destroy the tumorous cells. This method especially limits the damage to tissue adjacent to the gland, urethra, bladder and rectum since the radiation focus is limited to a small area around the Seeds. This makes permanent brachytherapy one of the most tissue-preserving treatment options for early-stage prostate cancer. In contrast to the nerve-preserving radical prostatectomy, this treatment can very easily include areas surrounding the prostate, enabling a significant improvement of chances to cure the disease.

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# Seed Implantation

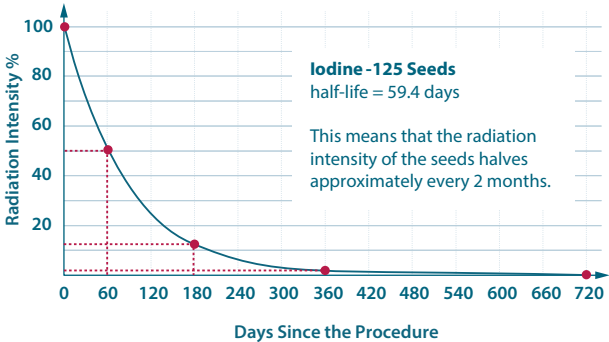
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## Procedure of a seed implantation

- The patient is anaesthetized. An ultrasound probe is inserted rectally.
- Based on the ultrasound image a treatment planning system then calculates the necessary number of Seeds as well their exact position in the prostate. This guarantees optimal distribution of the radiation and minimal damage to surrounding tissue and organs at risk.
- The attending doctor inserts the implantation needles into the prostate and places the Seeds through it. Positioning of the Seeds is simultaneously monitored using ultrasound and potentially fluoroscopy. The precise placement is crucial to administer the recommended prescription dose of 145 Gy throughout the diseased tissue and a certain safety margin. The complete procedure takes about 50 to 70 minutes.
- After the procedure the patient typically leaves the clinic and is able to return to his daily routine after a couple of days.
- Iodine-125 has a very short half-life and therefore just radiates for a limited amount of time. Its relatively low energy levels limit the radiation risk outside of the body to a very low level.

- The intensity of possible side effects has been part of numerous scientific studies over the years. They show that the negative effects associated with LDR brachytherapy are very moderate.<sup>5,6</sup> A large amount of clinical data also proves the effectiveness<sup>7,8</sup> of this treatment.

### Seed Radiation Over Time



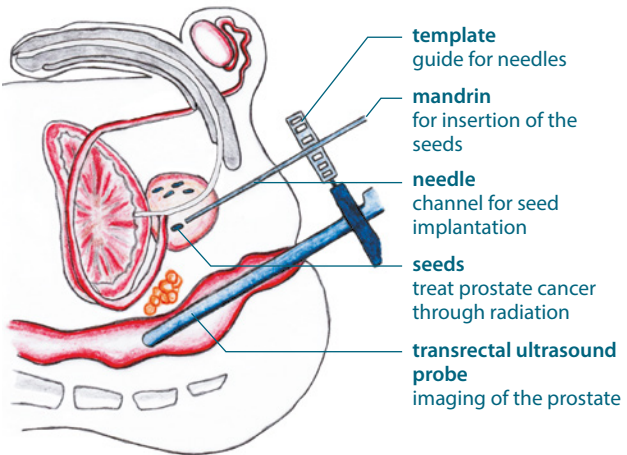
<sup>5</sup> Viktorin-Baier et al., Long-term oncological and functional follow-up in low-dose-rate brachytherapy for prostate cancer: results from the prospective nationwide Swiss registry. 2020

<sup>6</sup> Pons-Llanas et al., Impact of real-time, dose-escalated permanent seed implant brachytherapy in intermediate-risk prostate cancer. 2020

<sup>7</sup> Zimmermann et al., Five-year effectiveness of low-dose-rate brachytherapy: comparisons with nomogram predictions in patients with non-metastatic prostate cancer presenting significant control of intra- and periprostatic disease. 2018

<sup>8</sup> Jaques et al., Brachytherapy for favorable prognostic prostate cancer in men up to 60 years of age: Long term follow-up. 2024

# Seed Implantation



Sagittal cut through the male abdomen during Seed implantation

## Treatment characteristics

Prostate Seed implantations are especially well suited for patients with prostate cancer in early stages. In monotherapy, the tumor should be limited to the prostate and should fulfill the following diagnostic criteria:

<b>Gleason Score</b>	< 7
<b>PSA</b>	< 10
<b>Stage</b>	T2a or lower, N=0, M=0
<b>Prostate Volume</b>	< 50 cm <sup>3</sup>
<b>Urinary Flow Rate</b>	Maximum Flow Rate >15 mL/s

If your parameters deviate from these, a combination therapy with EBRT with/without hormone therapy (ADT = androgen deprivation therapy) may be an option for you.

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Seed implantation is an effective treatment for prostate cancer which is tolerated well by the majority of patients.<sup>1</sup> Compared to other treatment options, the following advantages can be recognized:

- The single, well-tolerated and minimally invasive procedure facilitates a faster physical recovery and allows mobility on the day after the implantation, encouraging a quick return to your daily routine.
- Only a brief stay in the hospital is required or the operation often is carried out in outpatient care
- Short treatment times (one treatment unit with a total duration of approx. 50 – 70 minutes for implantation)
- Precise dosing for high dose in the prostate with low radiation exposure to adjacent organs for better preservation of urinary continence, erectile function, and bowel function

LDR brachytherapy is recommended as a treatment option in the guidelines of various associations:

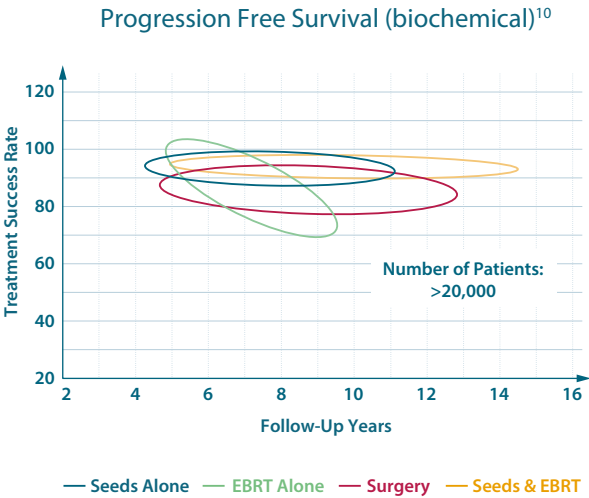
- European Society for Urology
- National Comprehensive Cancer Network
- German Society for Urology
- European Society for Radiotherapy and Oncology

<sup>1</sup> GLOBOCAN 2020. WHO

# Seed Implantation

## Studies

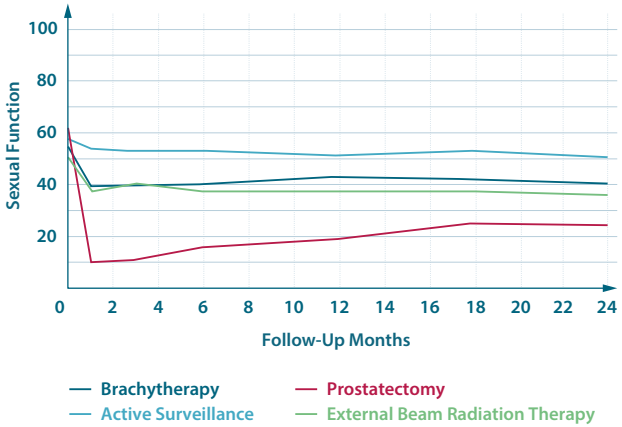
Based on the PSA progression, survival without tumor growth could be demonstrated for a large majority of treated patients. The results of the study presented suggest that brachytherapy is superior<sup>9</sup> to other therapeutic options in terms of successful treatment of the tumor.



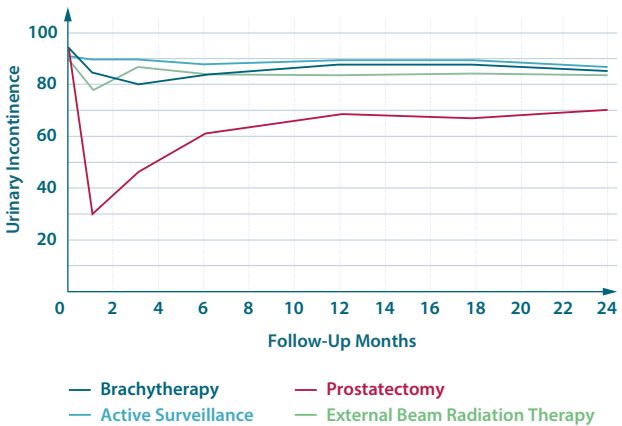
<sup>9</sup> Grimm et al., Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate or high risk prostate cancer treatment by radical therapy: Results from the Prostate Cancer Results Study Group.

<sup>10</sup> [www.prostatecancerfree.org/compare-prostate-cancer-treatments-low-risk](http://www.prostatecancerfree.org/compare-prostate-cancer-treatments-low-risk)

## Sexual Function<sup>11</sup>



## Continence<sup>11</sup>



<sup>11</sup> Chien et al., Health-related quality of life outcomes from a contemporary prostate cancer registry in a large diverse population.

**This patient information was provided by:**

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