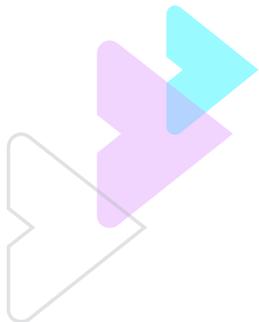
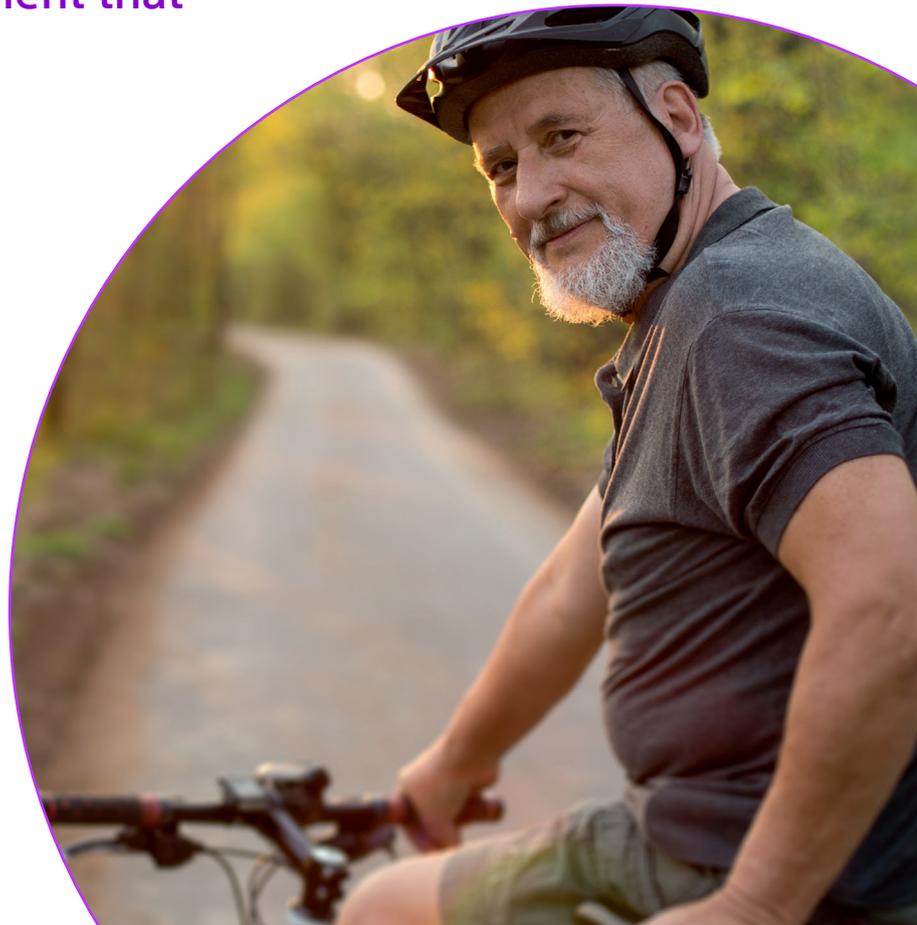




Prostate Cryotherapy

A clinically proven, minimally invasive,
radiation-free cancer treatment that
protects your quality of life.



Being diagnosed with prostate cancer is a time of concern for you and your loved ones, but medical advances mean that today, the chances of you beating your cancer are better than ever before. Your doctor will discuss with you the different treatments available. It is important that you research all the options and talk them over with your family to make sure you select the most appropriate one for you and your lifestyle.

This booklet is designed to help you in this process and provide you with more information on cryotherapy – a technique which uses extremely cold temperatures to kill cancer cells. Each year, thousands of prostate cancer patients choose cryotherapy because it is proven to cure cancer, avoids the need for radiation or surgical removal of the prostate, and offers quality-of-life benefits over surgery and other forms of treatment.

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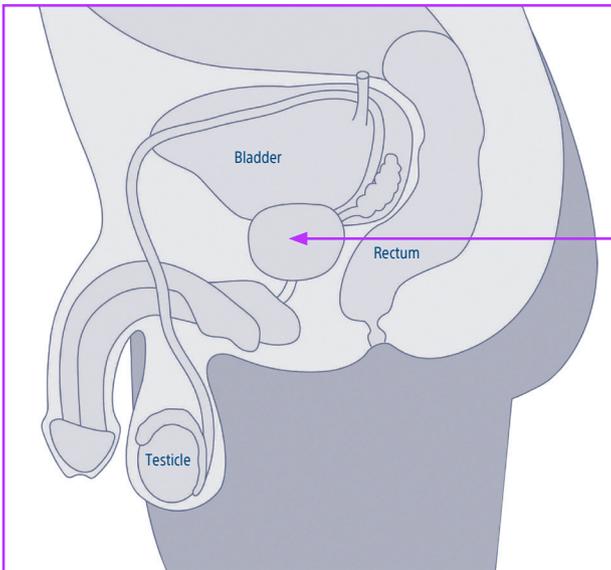
The prostate gland

The prostate is part of the male sex gland. The prostate opens into the urethra just below the bladder. During ejaculation it secretes an alkaline fluid that forms part of the semen.

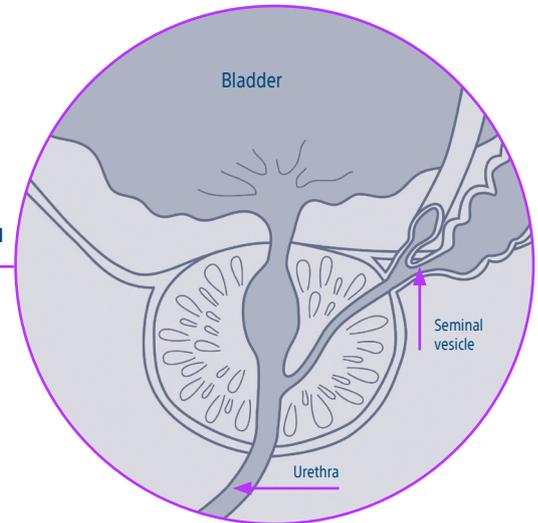
Cancer growing within the prostate may have the effect of disrupting the flow of urine as it can place pressure on the urethra that passes through the prostate. However, this problem may also be caused by benign prostatic hyperplasia or hypertrophy (BPH). BPH is a benign (non-cancerous) condition which affects many men as they get older. Since the prostate continues to grow after puberty, it may eventually apply pressure on the urethra, causing weak or interrupted urine flow.

BPH can also make emptying the bladder difficult, causing urgency and frequent visits to the bathroom. BPH is usually controlled by drugs or treated by a simple surgical procedure.

Like prostate cancer, BPH can also cause an elevation in PSA levels, which can be misleading. If a PSA test gives cause for concern, it is usually followed by a biopsy to clarify what is happening in the prostate and determine if prostate cancer or BPH is the cause. Prostate cancer is the most common form of cancer in men over the age of 60.



Prostate Gland





What is cryotherapy?

“ I am now three years post cryotherapy and my PSA remains low. I still manage to go on holidays and enjoy my quality of life. ”

What is cryotherapy?

Cryotherapy is a minimally invasive treatment (no incisions) that uses extremely cold temperatures to kill cancer tumors. Cryotherapy is widely used around the world and has over ten years' clinical experience to support its safety and effectiveness.¹ It is also recognized by both the American Urological Association and the European Association of Urology as a treatment for prostate cancer.

To treat a patient with cryotherapy, doctors create iceballs using compressed gas and specially designed thin probes which deliver the ice to the target area. These iceballs are very precisely shaped and positioned to freeze the prostate and destroy all of the cancerous tissue. The process is carefully controlled by your doctor who uses ultrasound imaging systems and temperature monitors to help ensure that the healthy tissue surrounding the prostate is not affected by the cold temperatures.

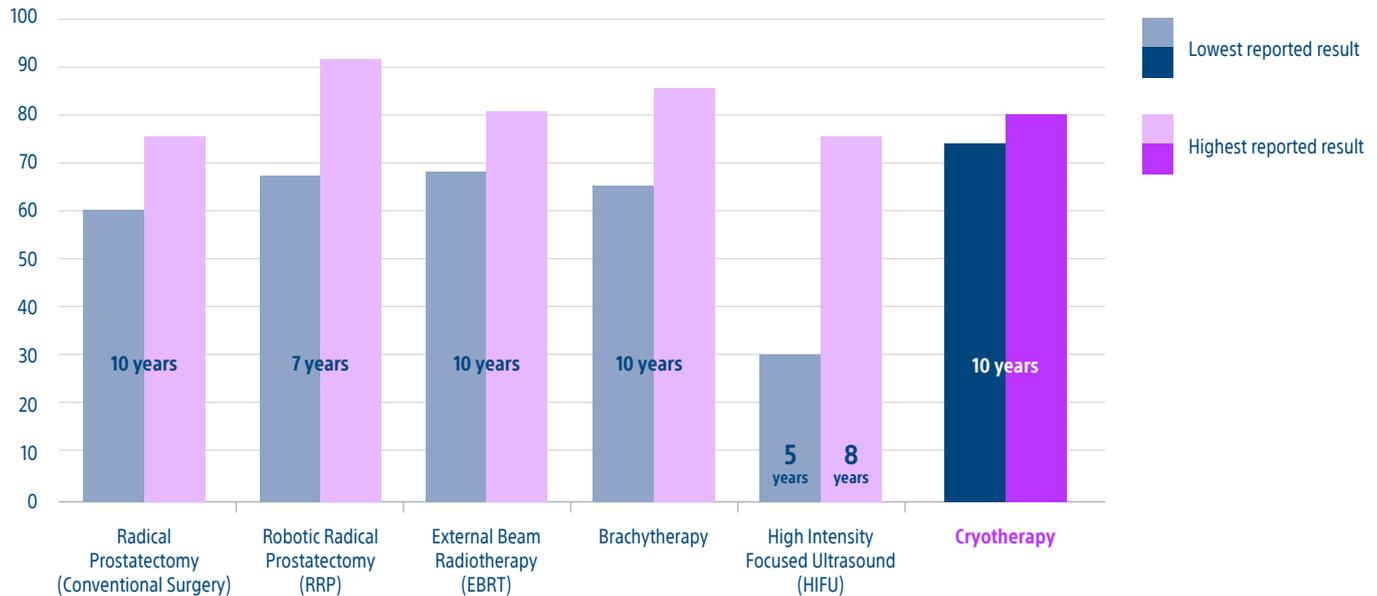
Will cryotherapy cure my cancer?

If your doctor considers you to be suitable for prostate cryotherapy, it is extremely likely that the procedure will cure your prostate cancer. The effectiveness of cancer therapies is measured in terms of the number of years patients enjoy being disease-free after treatment. The graph opposite shows the percentage of patients who are cancer-free a number of years after treatment.

It demonstrates that cryotherapy is at least as effective as any other therapy – including surgery – at giving patients a life free from cancer. Since prostate cancer treatments have similar survival rates, side effects and quality of life are important considerations when choosing your treatment.

Biochemical Disease-Free Survival (% Patients) after Treatment for Primary Prostate Cancer

A high number means more people were disease-free at time of follow up*



The graph shows disease-free survival for patients, as published in medical journals by their doctors. The follow-up period for established treatments, including cryotherapy, is ten years. Follow-up times for RRP and HIFU are shorter, because they are newer treatments and have less clinical experience.

Published results for low and intermediate-risk prostate cancer patients:

Radical Prostatectomy: European Association of Urology Guidelines on Prostate Cancer.
 RRP: Patel *et al.* BJU Int (2008).
 EBRT: Alicikus *et al.* Cancer (2010); Talcott *et al.* JAMA (2010); Koukourakis *et al.* Anticancer Research (2006).
 Brachytherapy: Machtens *et al.* World J Urol (2006).
 HIFU: Misraï *et al.* World J Urol (2008); Crouzet *et al.* Eur Urology (2010).
 Cryotherapy: Cohen *et al.* Urology (2008).



Benefits and risks

“Straightaway, I was able to resume normal life activities; this was important to me as my wife is disabled and I am her primary caregiver. I feel absolutely wonderful”

What are the benefits of cryotherapy?

Cryotherapy offers many advantages over other treatment options, including:

- **A minimally invasive** (no incisions), **curative** treatment
- **10-year clinical data**¹ supports safety and effectiveness in treating prostate cancer
- **Single treatment**, performed on outpatient basis or requiring just one overnight stay
- **Short hospital stay** reduces risk of hospital-acquired infection
- **Short recovery time** permits rapid return to everyday life
- **Lower risk of incontinence**² (leaking urine) than with any other therapy
- **May improve urinary** function in patients experiencing problems prior to cryotherapy^{3,4}
- **Minimal or no pain**

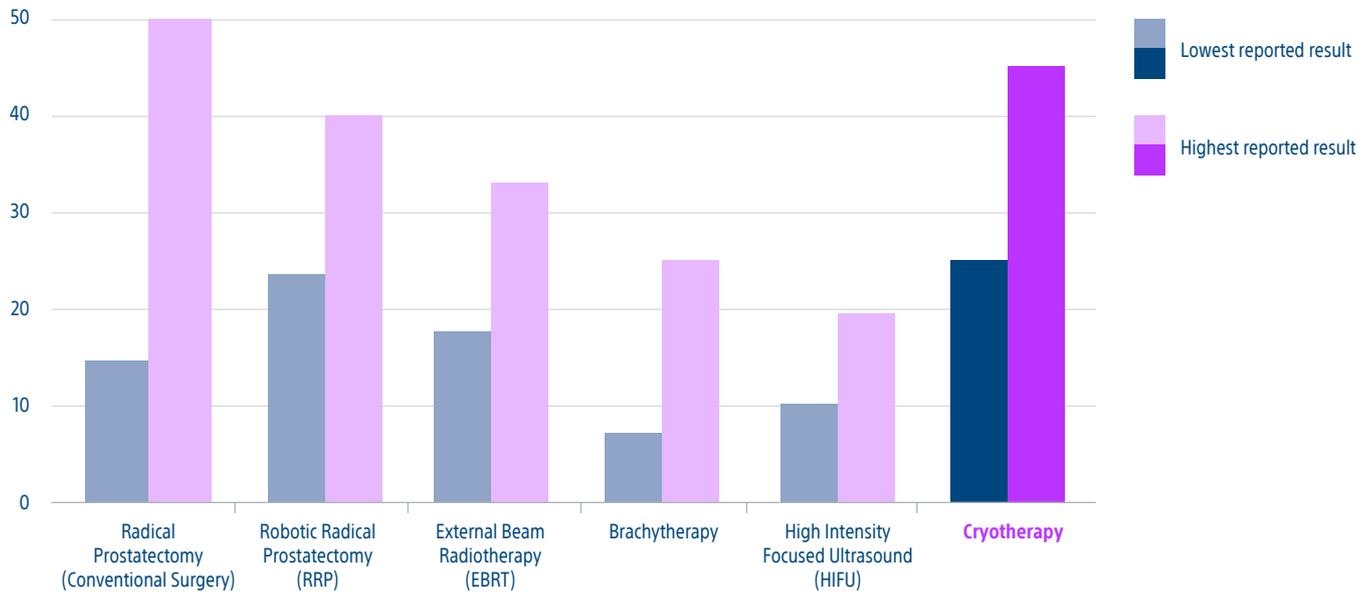
- **No need for radiation** or radioactive substances and risk of associated side effects (e.g. secondary cancer)
- **Low risk of rectal damage**² or irritation
- **Can be used when other treatments**, such as intensity modulated radiation therapy (IMRT), external beam radiotherapy (EBRT) and brachytherapy **have failed to cure prostate cancer**

What are the risks and side effects of cryotherapy?

Your doctor will advise you that any medical procedure has risks associated with it. However, cryotherapy avoids many of the risks and complications of other therapies. The potential side effects of curative prostate cancer treatments include incontinence (although the risk of this is very low with cryotherapy) and erectile problems. These are discussed in more detail later in this booklet.

Risk of Incontinence (%) after Treatment for Primary Prostate Cancer

A low risk means less likelihood of incontinence



1. Cohen *et al.* Urology (2008).
2. Langenhuijsen *et al.* European Urology (2009).
3. Kimura *et al.* Urology (2010).
4. Malcolm *et al.* J Urol (2010).

Published results for low and intermediate-risk prostate cancer patients:

Radical Prostatectomy: European Association of Urology Guidelines on Prostate Cancer.
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 Brachytherapy: Machtens *et al.* World J Urol (2006).
 HIFU: Warmuth *et al.* Eur Urology (2010).
 Cryotherapy: Langenhuijsen *et al.* European Urology (2009);
 Finley *et al.* Urol Clin N Am (2010).



Change in urinary symptoms

“ I go to bed every evening and sleep right through, I never need to get up during the night to go to the toilet, which is great! ”

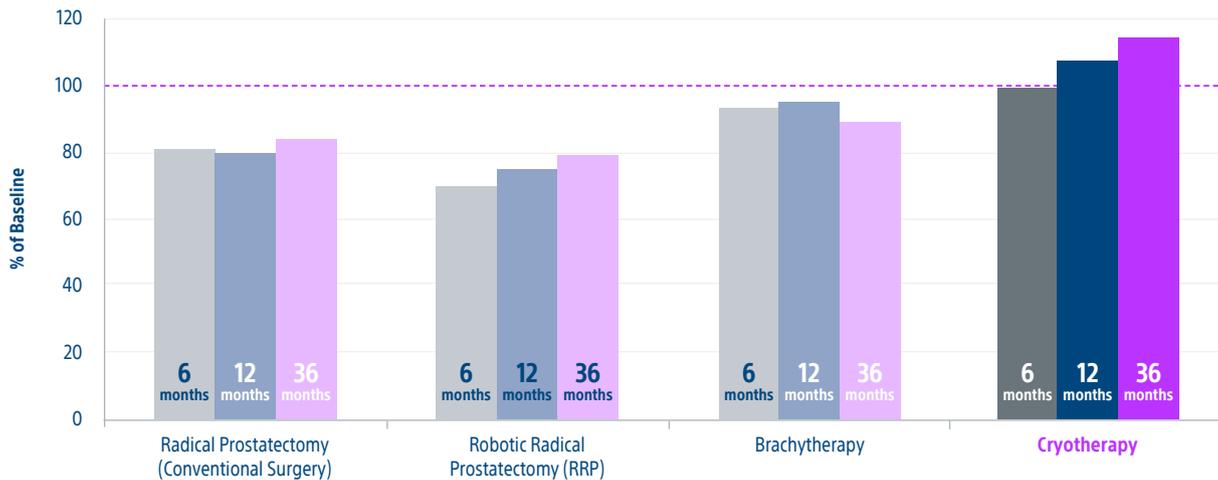
Over the years, I realize I need to urinate more than I used to, and I'm worried that my cancer treatment might make this worse.

Many prostate cancer patients find emptying (“voiding”) their bladder difficult. Even when they have the urge to urinate, they cannot do so effectively, and this means the need “to go” is typically only satisfied for a short period of time. Some patients also experience irritation when they urinate. These problems are referred to “urinary symptoms” by urologists and can be caused by a blockage to the outlet flow of urine.

A recent study¹ looked at how different prostate cancer therapies affect their patients' health-related quality of life (QOL). They identified urinary symptoms as one of the factors which has an impact on a patient's quality of life. Frequent visits to the bathroom during the day are inconvenient and can be embarrassing, while, at night, they lead to disturbed sleep patterns for the patient and spouse. Patients in the study were asked to give a score as to how much urinary symptoms

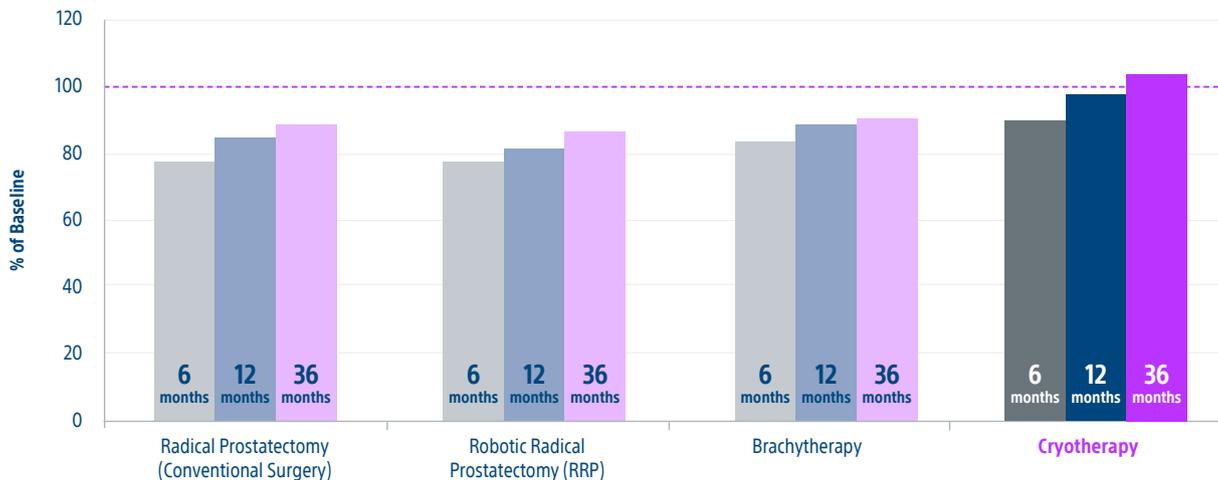
affected their quality of life **before** their prostate cancer treatment (which became their baseline score) and then they scored this again at regular intervals **after** their treatment. The study showed that **with surgery (conventional and robotic) and brachytherapy, urinary symptoms became more of a problem** for patients after their treatment. With the cryotherapy patients, urinary symptoms were a problem immediately following the procedure, but **patients recovered quickly**, reaching 97% of their pre-treatment/ baseline QOL score **within 12 months** of their treatment, and then going on to **exceed** their baseline score at 36 months. In other words, **their urinary symptoms improved after cryotherapy**. The doctors who conducted the study believe that this is due to the cryotherapy reducing the bladder obstruction and leading to a **subsequent improvement in the patients' quality of life**.

Change in Urinary Incontinence (% Return to Quality-of-Life Baseline) in Prostate Cancer Patients



Overall, the risk of incontinence is significantly lower with cryotherapy than with any other curative treatment, as shown by the graph on page 6. In addition, as explained opposite, many patients who suffer from incontinence before their treatment, see an improvement in symptoms after cryotherapy.^{1,2}

Change in Urinary Symptoms (% Return to Quality-of-Life Baseline) in Prostate Cancer Patients



1. Malcolm *et al.* J Urol (2010).
 2. Kimura *et al.* Urology (2010).



Change in urinary symptoms

“ I feel wonderful! After the procedure I had no pain and felt great. When my catheter was removed, my body adjusted and today, I feel normal – I need no pads. ”

Will I need to wear incontinence pads after the procedure?

The other urinary-related side effect of treatment for prostate cancer is incontinence (leaking urine). This is one of the most common side effects of treatment for prostate cancer. Many men need to wear and regularly change pads as a result of leaking urine; this is a significant hurdle for cancer patients in regaining a good quality of life after their treatment. It is particularly difficult for men who have previously enjoyed a full social life, outdoor sports and other activities.

The same study¹ that looked at urinary symptoms, also looked at urinary incontinence in terms of its impact on quality of life; the results are shown in the lower graph on page 8. Once again, the **cryotherapy group saw much better results than the other treatment groups** (including robotic radical prostatectomy).

The cryotherapy group recovered to 99% of their baseline score within six months and went on to improve upon their baseline score by an average of 13% over three years.

Glossary of terms

Ablation: The destruction of tissue by the application of extreme cold, heat or light (laser).

Anaesthesia: The loss of sensation and usually of consciousness artificially produced by the administration of one or more agents that block the passage of pain impulses along nerve pathways to the brain.

Benign prostatic hyperplasia/ hypertrophy (BPH): A non-cancerous condition that can affect PSA levels and cause enlargement of the prostate. This growth of the prostate can press on the urethra and cause urination and bladder problems (urinary symptoms).

Biopsy: The removal and examination of a sample of tissue for diagnostic purposes.

Brachytherapy: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near a tumor.

Cancer: A malignant and invasive growth or tumor.

Catheter: A tube inserted into the bladder to temporarily drain urine into a plastic bag. Depending upon your doctor's recommendation, a catheter is normally kept in place 1-2 weeks after prostate cryotherapy.

Cryotherapy: The destruction of tissue by the application of extremely cold temperatures.

Erectile dysfunction (ED): The loss of the ability to produce and/or sustain an erection. Often referred to as "impotence". In many cases, an erection can be achieved with assistance.

External Beam Radiation Therapy (EBRT): See Radiation therapy.

Fistula: An abnormal passage from a hollow organ to the body surface or from one organ to another.

Gleason score: A system of grading prostate cancer cells based on how they look under a microscope. Gleason scores range from 2 to 10 and indicate how likely it is that a tumor will spread.

Impotence: See Erectile dysfunction.

Incontinence: See Urinary incontinence.

Intensity-modulated radiation therapy (IMRT): See Radiation therapy.

Perineum: The area of skin between the scrotum and the anus through which the doctor inserts the ultra-thin cryotherapy probes. After the procedure, a dressing is applied and the tiny holes heal rapidly.

Percutaneous: Through the skin. In percutaneous kidney cryoablation, MRI, CT or ultrasound scanning allows the operator to clearly see the internal organs, and probes are passed directly through the skin into the kidney. Percutaneous procedures avoid the need to open up the abdomen with a large incision, as required with conventional surgery.

Prostate: A gland in the male reproductive system just below the bladder. The prostate surrounds part of the urethra, the canal that empties the bladder, and produces a fluid that forms part of semen.

Prostate cancer staging:

Stage I: The cells closely resemble normal cells and the gland feels normal to the examining finger.

Stage II: More of the prostate is involved and a lump can be felt within the gland.

Stage III: The tumor has spread through the prostate wall and the lump can be felt on the surface of the gland.

Stage IV: The tumor has invaded nearby tissue.

Prostatectomy: Surgical removal of the prostate.

PSA: Prostate specific antigen, a protein produced by the prostate.

PSA test: The PSA test measures levels in the blood and is used to help detect prostate cancer as well as to monitor the results of treatment. Elevated PSA may be an indicator of prostate cancer.

Radiation therapy (Radiotherapy): Uses high-energy radiation to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external beam or intensity modulated radiation therapy) or from materials placed inside the body (internal radiation therapy, implant radiation, or brachytherapy).

Radical prostatectomy: The surgical removal of the entire prostate gland, the seminal vesicles and nearby tissue.

Rectum: The short tube located at the end of the large intestine, which connects the intestine to the anus.

Robotic radical prostatectomy: Instead of directly moving the instruments, the surgeon uses a computer console to manipulate the instruments attached to multiple robot arms. The computer translates the surgeon's movements, which are then carried out on the patient by the robot.

Stage: The extent of a cancer. See also Prostate cancer staging.

Transrectal ultrasound (TRUS): The use of sound waves to create a picture of the prostate on a screen to help examine the condition of the prostate and guide insertion of the cryotherapy probes.

Urethra: The tube that carries urine from the bladder to the outside of the body.

Urinary incontinence: Involuntary loss of urine associated with a sudden strong urge to urinate.

Urinary symptoms: Problems associated with obstruction to flow of urine, usually caused by BPH.



Frequently asked questions

“

Radiotherapy had affected that, I was already impotent so that was not a key concern for me. There is more to life.

Only recently, we buried a younger guy – mid-50s – with prostate cancer.

It's better to be alive. ”

Will cryotherapy impact my sex life?

Your doctor may have explained to you that all curative treatments for prostate cancer can affect a man's ability to obtain and maintain an erection. This risk can seem daunting, but it is important to remember that there have been significant advances in medication and other aids to help men whose natural ability to obtain an erection is lost or reduced. This condition – called impotence or erectile dysfunction (ED) – is very common among middle-aged men (including those who have not had prostate cancer) and today there is lots of help available to ensure they are still able to lead a fulfilling sex life. After cryotherapy, many patients have had success regaining erections through what is called penile rehabilitation, which combines medication (e.g. Viagra®) and a vacuum device.

With penile rehabilitation, close to 50% of men were able to regain potency after one year.¹ The graph opposite shows the relative risks of impotence with different prostate cancer treatments, as shown by a variety of studies.

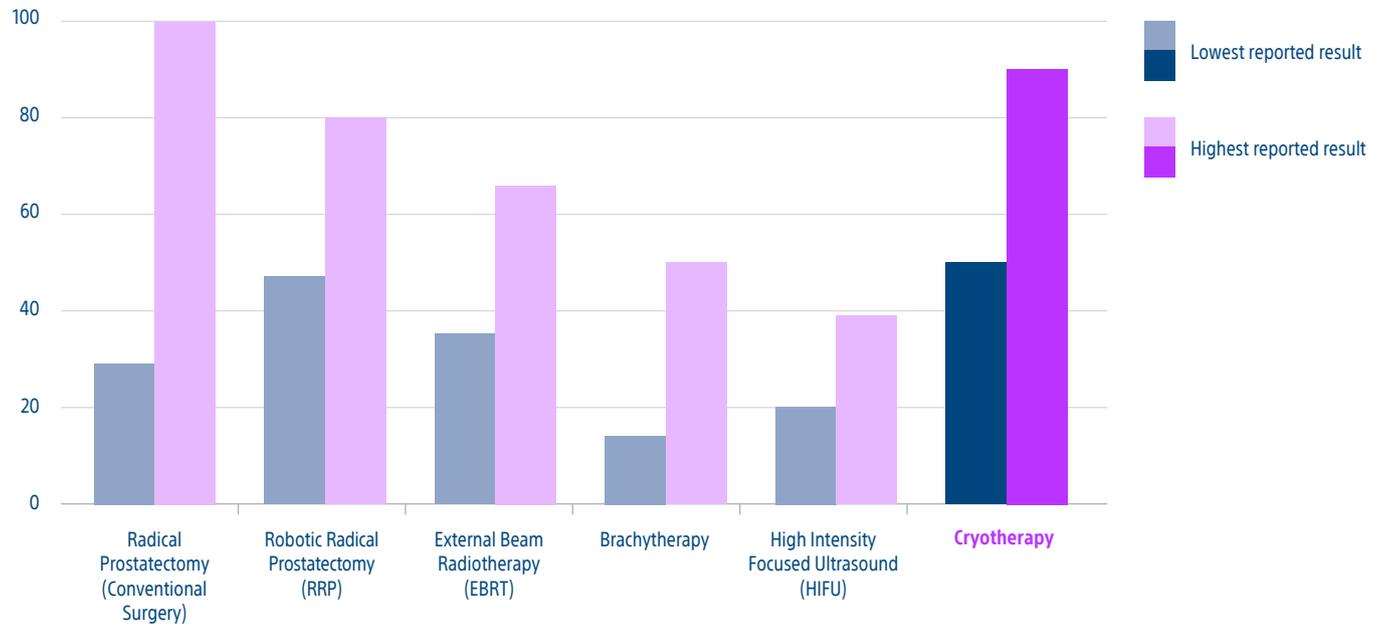
“

If I had to say which treatment would be top of my list, it would be cryotherapy.

I have a good quality of life, and there is a good chance I could have the treatment again, if necessary. ”

Risk of Impotence (%) after Treatment for Primary Prostate Cancer

A low risk means less likelihood of impotence



Published results for low and intermediate-risk prostate cancer patients:

Radical Prostatectomy: European Association of Urology Guidelines on Prostate Cancer.
 RRP: Patel *et al.* BJU Int (2008).
 EBRT: Talcott *et al.* JAMA (2010); Koukourakis *et al.* Anticancer Research (2006).
 Brachytherapy: Machtens *et al.* World J Urol (2006).
 HIFU: Warmuth *et al.* Eur Urology (2010).
 Cryotherapy: Langenhuijsen *et al.* European Urology (2009);
 Finley *et al.* Urol Clin N Am (2010).



Frequently asked questions

“

*I feel fantastic, really I feel great.
I am going to the gym and keeping
very active.* ”

I heard cryotherapy is an experimental therapy – is that true?

No. Cryotherapy is recognized by both the American Urological Association and the European Association of Urology as a treatment for prostate cancer and has over ten years' clinical data to support its safety and effectiveness.¹ In the USA, cryotherapy has FDA clearance and is covered by Medicare and most insurance companies.

Am I suitable for cryotherapy?

While your doctor can help determine if you are a good candidate, prostate cryotherapy is used to treat all stages and all types of localized prostate cancer (cancer which has not spread outside the prostate). Prostate cryotherapy is also used to treat patients who have failed radiation therapy.



Frequently asked questions

How long does the procedure take?

A prostate cryotherapy procedure usually takes between 90 minutes (1½ hours) and 120 minutes (2 hours).

How long will I need to be in hospital?

Prostate cryotherapy can be performed on an outpatient basis. This means that you do not need to stay in hospital for more than a few hours after your treatment, and no overnight stay is required. Sometimes one overnight stay is preferred, but this is dependent on local arrangements or the individual case.

How will I feel after the procedure?

You may feel some slight discomfort immediately after the procedure, but you will be given pain medication for this and it will improve very quickly. You will have a drainage catheter left in place for a few days until you are able to urinate. You will be shown how to manage the catheter before you return home. Most patients feel a great sense of relief that their cancer has been treated and some feel quite emotional as a result of this.

How long before I can return to work?

Your doctor will advise you on the time you should plan to take off. Because cryotherapy does not involve open surgery, most patients are able to return to work and an active lifestyle once they no longer need their catheter – typically a week or less.

What about other activities, such as sports?

Your doctor will advise you on when it is appropriate to resume active hobbies and sports, but usually this will be a week or two after your procedure.



“ Prostate Cancer Patient Comments

If you have the right treatment at the right time, you can live a perfectly normal life. Early diagnosis is important.

The more you know about prostate cancer treatment options, the better prepared you will be to choose the best prostate cancer treatment with the help of your doctor.

When the cancer came back after radiation, I had cryotherapy. Looking back, if I had been offered cryotherapy instead of radiotherapy, that would have been my first choice.

I had radiotherapy for five weeks, every working day, and the round trip was two hours per day (ten hours per week). I felt so sick I wanted to pack it in before the treatment was complete. For two-and-a half months, I had no quality of life.

If prostate cancer is caught in the early stages, cryotherapy becomes an option for most men.

I liked the idea of cryotherapy as it was less invasive, and if the cancer should return at a later date, the treatment can safely be repeated. This is a great comfort to me and my family.



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