



BRACHYTHERAPY:

**THE PRECISE
ANSWER FOR
TACKLING
CERVICAL
CANCER**



Treatment options

There are several ways that cervical cancer can be treated. These include:^{1,2}

- **Radiation therapy—including Brachytherapy (interventional radiation therapy) and External beam radiation therapy (EBRT)**
- **Surgery**
- **Chemotherapy**

Sometimes just one of these methods is used to treat cervical cancer, but more commonly a patient will receive more than one type of treatment (e.g. brachytherapy and external beam radiation therapy plus chemotherapy).

The treatment or treatments that are most appropriate will depend on a number of factors, including how far the cancer has progressed. The table below provides a broad overview of the different treatments. Each treatment has advantages and disadvantages. These should be considered and discussed with your healthcare professional when choosing the most suitable treatment option for you.

Treatment^{1,2}

Brachytherapy (interventional radiation therapy)

Works by precisely targeting the cancerous tumor. The source of radiation is placed directly next to the tumor.

External beam radiation therapy (EBRT)

The source of radiation is directed at the tumor from outside the body through the skin.

Surgery (hysterectomy)

Removal of the cervix and the uterus (womb).

Chemotherapy

A course of chemotherapy may be recommended in addition to surgery and/or radiation therapy. Several pharmaceutical products are effective and your doctor will be able to advise the best one for you.

Grade of cancer

Early	Locally advanced	Advanced
✓	✓	✓
✓	✓	✓
✓	✓	
	✓	✓

Advantages and disadvantages of cervical cancer treatments

Each treatment has advantages and disadvantages. These should be considered and discussed with your healthcare professional when choosing the most suitable treatment option for you.

Treatment	Advantages	Disadvantages
Brachytherapy (interventional radiation therapy)	<ul style="list-style-type: none"> • Clinically proven to be highly effective.¹⁻⁴ • Reduced risk of unnecessary damage to surrounding healthy tissues and organs, which reduces the chance of side effects. • You can receive treatment on an outpatient basis. • Can be given in combination with other treatments (common for more advanced cancers).^{1,2} • Standard of care treatment for locally advanced cervical cancer in combination with external beam radiation therapy.^{1,2} 	<ul style="list-style-type: none"> • May need to stay in hospital for treatment in some cases
External beam radiation therapy (EBRT)	<ul style="list-style-type: none"> • Clinically proven to be highly effective.^{1,2} • You can receive treatment on an outpatient basis. • Can be given in combination with other treatments.² 	<ul style="list-style-type: none"> • Treatment course can be long (4–7 weeks) and includes repeat visits to hospital on a daily basis. • There is a risk of long-term side effects compared with brachytherapy, as the radiation has to pass through healthy tissues to reach the tumor.⁵
Surgery (hysterectomy)	<ul style="list-style-type: none"> • Clinically proven to be highly effective.^{1,2} • One-time procedure. • Can be given in combination with other treatments.^{1,2} 	<ul style="list-style-type: none"> • May require a hospital stay of up to 1 week.⁶ • Long recovery time (4–6 weeks).⁶
Chemotherapy	<ul style="list-style-type: none"> • Clinically proven to be highly effective.^{1,2} • Can be given in combination with other treatments.^{1,2} 	<ul style="list-style-type: none"> • The treatment course can be long (3–4 treatment week cycles, which are repeated at least 6 times). • Some side effects including hair loss and an increased risk of acquiring infections.⁷

What types of brachytherapy can be used for treatment of this cancer type?

Brachytherapy is a type of radiation therapy to treat cervical cancer. Depending on the tumor stage, it can be performed with intracavitary or combined intracavitary/interstitial technique.

Intracavitary/interstitial brachytherapy – when the tumor is big, a few needles are placed inside the tumor in addition to the applicator. Needles allow the radiation to kill the cancer cells in the whole tumor volume.

Modern brachytherapy uses Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) images to control the position of the tumor and the radioactive source. This type of brachytherapy is called image-guided or 3D brachytherapy, and it can be either intracavitary or interstitial.¹

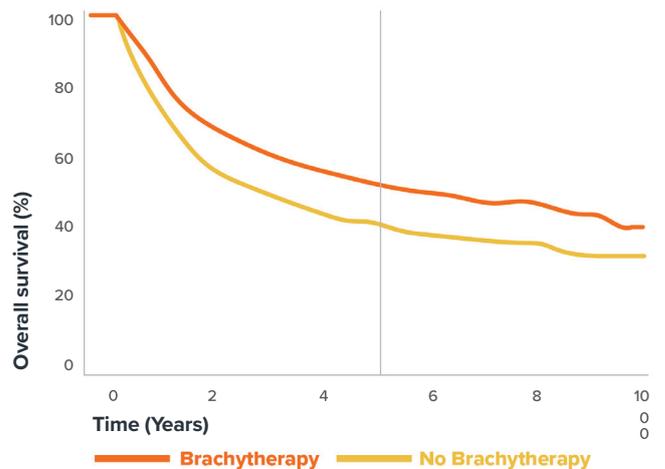




How effective is brachytherapy?

Results of a large study compared the treatment outcome of cervical cancer with or without brachytherapy.

It showed a clear advantage in the survival of patients at 5 years when brachytherapy is added to the treatment (54% with brachy vs 42% without brachy) (see picture 1).² It means that patients who received brachytherapy lived longer. This study was performed in the era before image-guided brachytherapy, so the survival rate was much lower than today. However, even adding conventional 2D brachytherapy, the survival rate was improved.



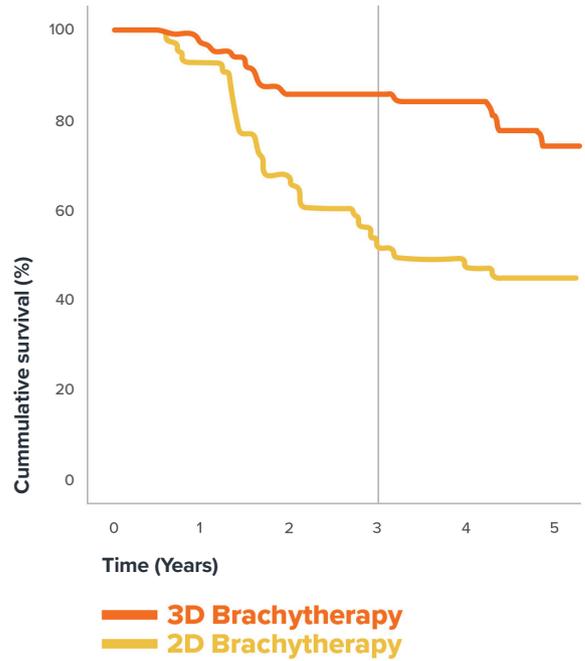
Picture 1

Overall survival in patients with cervical cancer treated with brachytherapy and without brachytherapy²

Image-guided brachytherapy makes the treatment more precise which further improves the survival rate. A study from the Netherlands showed a big difference in overall survival after image-guided brachytherapy compared with conventional 2D brachytherapy at 3 years (86% vs 51%) (see picture 2).³ It happens because brachytherapy under CT- or MRI-guidance is more precise. It targets the tumor but spares surrounding healthy tissues and organs.

Overall survival in patients with cervical cancer treated with conventional brachytherapy and image-guided brachytherapy³

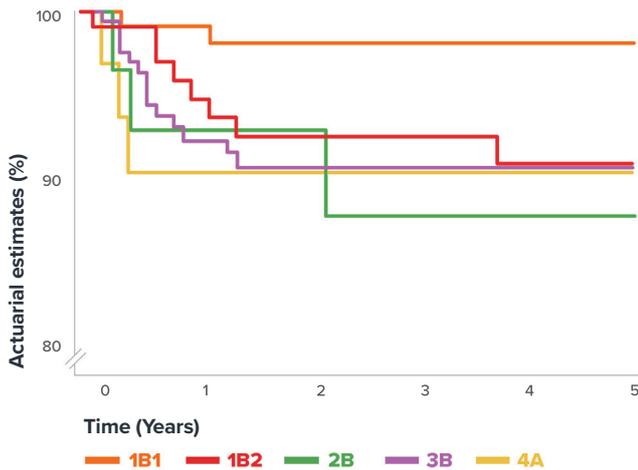
According to a multi-center international EMBRACE I study, which included 1341 patients with cervical cancer, MRI-guided brachytherapy ensured local control (the tumor didn't grow back after treatment) in 92% of patients through all stages at 5 years. In women with stage 1B1, the local control at 5 years was even higher—98% (see picture 3).⁴ It means that the earlier the diagnosis, the better results can be achieved—but, if MRI-guided brachytherapy is added into the treatment, it ensures very good treatment results at any tumor stage.



Picture 2

Local control in patients with cervical cancer (data from the EMBRACE I study)

Image-guided brachytherapy makes the treatment more precise, which further improves the survival rate. A study from the Netherlands showed a big difference in overall survival after image-guided brachytherapy, compared with conventional 2D brachytherapy at 3 years (86% vs 51%) (see picture 2).³ It happens because brachytherapy under CT- or MRI-guidance is more precise. It targets the tumor but spares surrounding healthy tissues and organs.



Picture 3

Advantages of brachytherapy

The advantages of brachytherapy vary depending on the patient, their priorities, and preferences. But, as a minimally invasive treatment method, the benefits of avoiding surgery are universal. These can include:

Quicker recovery time.

Less time spent in the hospital or no admission to the hospital.

Potential saving of healthy tissues and organs.

Reduced risk of postoperative infections.

Advantages in comparison with EBRT are related to time needed to deliver the treatment, reduction in exposure to organs at risk and, consequently, a reduction in side effects.

We should not bias brachy to EBRT in the treatment of patients with cervical cancer because they are complementary. Brachytherapy is a part of treatment protocol for these patients, which includes chemotherapy, EBRT and brachytherapy. Although brachytherapy has advantages over EBRT, EBRT has other advantages like large irradiation volume covering lymph nodes and parametrium, which make it possible to treat lymph node metastases and the whole tumor volume.

The doctor should choose the **best treatment combination** for the patient according to the tumor stage and other conditions

Side effects of brachytherapy

All treatments for cervical cancer carry a risk of side effects.

Radiation therapy is generally associated with side effects. These side effects are well known and most do not depend on the type of radiation therapy. However, brachytherapy is associated with sparing surrounding healthy tissue from unnecessary radiation, with the potential for fewer side effects than alternatives such as external beam radiation therapy.

People respond to treatments in different ways. The type of side effects that may be experienced depends on a number of factors, such as the stage of the cervical cancer and whether there are any compounding health problems. The majority of brachytherapy patients receive a multimodality treatment with other treatments such as surgery, EBRT and chemotherapy. This makes it very difficult to distinguish between side effects from brachytherapy, side effects caused by other treatments and disease related symptoms and complications.

Side effects that have been reported in literature in association with brachytherapy treatment of gynecological cancers and could be related to the use of brachytherapy are:¹⁻⁶

- **Non-specific toxicities such as fatigue, insomnia and hot flashes.**
- **Skin toxicities such as radiation dermatitis and telangiectasia.**
- **Gastrointestinal toxicities such as nausea, diarrhea, constipation, intestinal fistula, proctitis, rectal ulcers and rectovaginal fistula.**
- **Urinary toxicities such as urinary frequency/urgency, incontinence, cystitis, chronic recurrent urinary tract infection, bladder fistula.**
- **Vaginal toxicities such as vaginal dryness, vaginal stenosis, mucositis.**
- **Other toxicities such as pain, bleeding, fibrosis, abscess, lower limb edema and/or secondary cancer.**

It should be noted that many patients show comparable symptoms as manifestations of their disease. Although the frequency of severe complications is low and a causal relationship with brachytherapy is often not clear, lowering the radiation dose or lowering the number of fractions could be an alternative to reduce the risk of severe complications.

Most side effects go away soon after treatment is finished. Progress from 3D-based imaging and treatment planning for cervical cancer brachytherapy significantly reduced side effects.¹⁻⁶



Can I just have brachytherapy alone to treat my cervical cancer?

Usually, brachytherapy is a part of the treatment protocol which includes EBRT and chemotherapy. Your doctor will discuss your treatment options with you.

I've never heard of brachytherapy, how do I know if it's any good?

Brachytherapy has been used to effectively treat cancer for over 100 years. It is very effective and is recognized as the standard treatment in combination with external beam radiation therapy for cervical cancer in many countries.

If the cancer comes back, can I choose to have brachytherapy again?

Yes, this is possible. Brachytherapy can be used in case of cancer recurrence. Your doctor will recommend the most appropriate treatment or a treatment combination.

Will I lose my hair during the radiation therapy course?

It would be unusual for you to lose your hair during brachytherapy. Hair loss is more likely during a course of chemotherapy.

How long do I have to stay in the hospital, how many treatments will I receive?

How long you stay in the hospital really depends on the tumor stage and which type of brachytherapy is used—intracavitary or combined intracavitary/interstitial. The most common situation is when brachytherapy is used after a course of EBRT. There are different protocols which include 3 or 4 brachytherapy treatments. Patients leave the hospital after the procedure or spend a night in the hospital to get two procedures.

Will the brachytherapy procedure hurt?

No. Brachytherapy is usually performed under anesthesia.

How I will know that brachytherapy has worked?

Your doctor will usually perform a follow-up at 6, 9, 12, 18, 24, 30, 36, 48 and 60 months after treatment. The follow-up can include gynecological examination, blood test, MRI and CT examination, questions about side effects and quality of life. The results of the follow-up will tell if the treatment was effective.

Treatment options

1. ESMO guidelines. Available at: [https://www.annalsofncology.org/article/S0923-7534\(19\)42148-0/fulltext](https://www.annalsofncology.org/article/S0923-7534(19)42148-0/fulltext) Accessed June 2021
2. ASTRO guidelines. Available at: <https://www.practicalradonc.org/cms/10.1016/j.prro.2020.04.002/attachment/b3495c02-3020-4944-9248-122057abef3b/mmc1.pdf> Accessed June 2021
3. Han K et al. Int J Radiat Oncol Biol Phys. 2013 Sep 1;87(1):111-9. Available at: [https://www.redjournal.org/article/S0360-3016\(13\)00595-6/fulltext](https://www.redjournal.org/article/S0360-3016(13)00595-6/fulltext) Accessed June 2021
4. Sturdza A et al. Radiother Oncol. 2016 Sep;120(3):428-33. Available at: [https://www.thegreenjournal.com/article/S0167-8140\(16\)31018-0/fulltext](https://www.thegreenjournal.com/article/S0167-8140(16)31018-0/fulltext) Accessed June 2021
5. Georg D et al. Int J Radiat Oncol Biol Phys. 2008 Jul 1;71(4):1272-8. Available at: [https://www.redjournal.org/article/S0360-3016\(08\)00510-5/fulltext](https://www.redjournal.org/article/S0360-3016(08)00510-5/fulltext) Accessed June 2021
6. National Cancer Institute. Available at: <http://www.cancer.gov/cancertopics/pdq/treatment/cervical/HealthProfessional/page4>. Accessed June 2021
7. Cancer Research UK. Available at: <https://www.cancerresearchuk.org/about-cancer/cervical-cancer/treatment/chemotherapy-treatment> Accessed June 2021

Brachytherapy

1. Banerjee R et al. Int J Womens Health. 2014 Sep;6:555-64. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4045176/pdf/ijwh-6-555.pdf> Accessed June 2021
2. Han K et al. Int J Radiat Oncol Biol Phys. 2013 Sep 1;87(1):111-9. Available at: [https://www.redjournal.org/article/S0360-3016\(13\)00595-6/fulltext](https://www.redjournal.org/article/S0360-3016(13)00595-6/fulltext) Accessed June 2021
3. Rijkmans EC et al. Gyn Oncol. 2014 Aug 26;135(2):231-8. Available at: [https://www.gynecologiconcology-online.net/article/S0090-8258\(14\)01280-3/fulltext](https://www.gynecologiconcology-online.net/article/S0090-8258(14)01280-3/fulltext) Accessed June 2021
4. Poetter R et al. The Lancet Oncol. 2021 April 1;22(4):538-47. Available at: [https://doi.org/10.1016/S1470-2045\(20\)30753-1](https://doi.org/10.1016/S1470-2045(20)30753-1) Accessed June 2021

Side effects of brachytherapy

1. Spampinato S et al. Radiother Oncol. 2021 Feb 2 (in press). Available at: [https://www.thegreenjournal.com/article/S0167-8140\(21\)00020-7/fulltext](https://www.thegreenjournal.com/article/S0167-8140(21)00020-7/fulltext) Accessed June 2021
2. Smet S et al. Radiother Oncol. 2018 Apr 4;127(3):440-8. Available at: [https://www.thegreenjournal.com/article/S0167-8140\(18\)30141-5/fulltext](https://www.thegreenjournal.com/article/S0167-8140(18)30141-5/fulltext) Accessed June 2021
3. Kirchheiner K et al. Radiother Oncol. 2016 Jan 9;118(1):160-6. Available at: [https://www.thegreenjournal.com/article/S0167-8140\(16\)00002-5/fulltext](https://www.thegreenjournal.com/article/S0167-8140(16)00002-5/fulltext) Accessed June 2021
4. Jensen N et al. Radiother Oncol. 2018 Jun 4;127(3):431-9. Available at: [https://www.thegreenjournal.com/article/S0167-8140\(18\)30275-5/fulltext](https://www.thegreenjournal.com/article/S0167-8140(18)30275-5/fulltext) Accessed June 2021
5. Fokdal L et al. Radiother Oncol. 2018 May 18;127(3):423-30. Available at: [https://www.thegreenjournal.com/article/S0167-8140\(18\)30242-1/pdf](https://www.thegreenjournal.com/article/S0167-8140(18)30242-1/pdf) Accessed June 2021
6. Mazon R et al. Radiother Oncol. 2016 Jul 7;120(3):412-19. Available at: [https://www.thegreenjournal.com/article/S0167-8140\(16\)31154-9/fulltext](https://www.thegreenjournal.com/article/S0167-8140(16)31154-9/fulltext) Accessed June 2021
7. Najjari Jamal D et al. Radiother Oncol. 2018 Apr 6;127(3):449-55. Available at: [https://www.thegreenjournal.com/article/S0167-8140\(18\)30170-1/fulltext](https://www.thegreenjournal.com/article/S0167-8140(18)30170-1/fulltext) Accessed June 2021