# Treating Retinoblastoma

will discuss treatment options with you. It’s important to discuss all of the options as well as their possible side effects with your child’s doctors to help you make an informed decision.

If time allows, getting a second opinion from another doctor experienced with your child’s type of cancer is often a good idea. This can give you more information and help you feel more confident about the treatment plan you choose. If you aren’t sure where

symptoms or helping people feel better, many have not been proven to work. Some might even be harmful. Be sure to talk to your child's cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

- Complementary and Integrative Medicine

## Preparing for treatment

Before treatment, the doctors and other members of the team will help you, as a parent, understand the tests that will need to be done. The team’s social worker will also counsel you about the problems you and your child might have during and after treatments such as surgery, and might be able to help you find housing and financial aid if needed.

- When Your Child Has Cancer

## Help getting through cancer treatment

Your child's cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services can also be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help. For

# Surgery (Enucleation) for Retinoblastoma



Surgery is not needed for many retinoblastomas, especially for smaller tumors.

But if a tumor has grown large before it is found, vision in the eye might have already been lost, with no hope of getting it back. The usual treatment in this case is **enucleation**, an operation to remove the whole eye, plus part of the optic nerve attached to it.

## Possible risks and side effects

Enucleation might also be needed if the cancer is not cured using other treatments that were meant to try to save the eye.

This surgery is done while the child is under general anesthesia (in a deep sleep). During the same operation, an **orbital implant** is usually put in to take the place of the eyeball. The implant is made of silicone or hydroxyapatite (a substance similar to bone). It is attached to the muscles that moved the eye, so it should move the same way as the eye would have.

Your child will probably be able to leave the hospital the same day or the next day.

After several weeks, you can visit an **ocularist**, who will create an artificial eye for your child. This is a thin shell that fits over the orbital implant and under the eyelids, like a big contact lens. It will match the size and color of the remaining eye. Once it's in place, it will be very hard to tell it apart from the real eye.

When retinoblastoma occurs in both eyes, enucleation of both eyes would result in complete blindness. If neither eye has useful vision because of damage already caused Tf dald color if the cangar . 47 gs  caused

Last Revised: December 3, 2018

# Radiation Therapy for Retinoblastoma



This treatment uses high energy x-rays or particles to kill cancer cells. Radiation therapy is an effective treatment for some children with retinoblastoma. Compared with surgery, it has the advantage of possibly saving vision in the eye. But radiation therapy also has some disadvantages (see Possible side effects below).

Two types of radiation therapy can be used to treat children with retinoblastoma.

## External beam radiation therapy

External beam radiation therapy (EBRT) focuses radiation beams from a source outside the body on the cancer. This was once a common treatment for retinoblastoma. But because of the side effects it can cause, it is now most often used only for cancers that are not well-controlled with other treatments.

### How EBRT is done

Before treatments start, the radiation team takes careful measurements with imaging tests[1] such as MRI scans to determine the correct angles for aiming the radiation beams and the proper dose of radiation. This planning session is called **simulation**.

Radiation is usually given 5 days a week for several weeks. Each treatment is much like getting an x-ray, but the dose of radiation is much stronger. For each session, your child will lie on a special table while a machine delivers the radiation from precise angles.

The actual treatment each day lasts only a few minutes, but the setup time – getting your child into place for treatment – usually takes longer. The child's head is positioned in a custom-fitted mold that is similar to a cast used to treat broken bones. The treatment is not painful, but young children may be given medicine to make them sleep so they will stay still during treatment.

## Newer forms of EBRT

Many centers now use newer types of external radiation therapy, which can target the tumor more precisely. This lowers the doses that surrounding normal tissues get, which may help reduce side effects.

### *Intensity modulated radiation therapy (IMRT)*

IMRT lets doctors shape the radiation beams and aim them at the tumor from several angles, as well as adjust the intensity (strength) of the beams to limit the dose reaching the nearby normal tissues. This may let the doctor deliver a higher dose to the tumor, while reducing side effects. Many major hospitals and cancer centers now use IMRT.

### *Proton beam therapy*

Protons are positive parts of atoms. Unlike the x-rays used in standard radiation, which release energy both before and after they hit their target, protons cause little damage to tissues they pass through and then release their energy after traveling a certain distance. Proton beam radiation may be able to deliver the same level of radiation to the tumor while causing much less damage to nearby normal tissues.

Early results with proton beam therapy are promising, but it's still fairly new, and there is very little long-term data on its use for retinoblastoma. Only a limited number of centers offer proton beam therapy in the United States at this time.

## Possible side effects of EBRT

Some of the side effects of EBRT tend to go away after a short while and are usually not serious. Short-term problems might include effects on skin areas that receive radiation, which can range from mild sunburn-like changes and hair loss to more severe skin reactions.

More importantly, EBRT can damage nearby normal body tissues. This might eventually lead to cataracts (clouding of the lens of the eye) and damage to the retina or optic nerve, which could reduce vision. Radiation can also slow the growth of bones and other tissues near the eye, which can affect the way the area around the eye looks over time.

External radiation therapy can also increase the risk of developing a second cancer[2] in the area. This is especially important in children with the hereditary form of retinoblastoma, who are already at increased risk for developing other types of cancer.

Newer forms of radiation therapy, such as IMRT and proton beam therapy, target the tumor more precisely and spare more normal tissue. This may make some of these side effects less likely than in the past.

## Brachytherapy (plaque radiotherapy)

The use of brachytherapy, also known as **internal radiation therapy** or **episcleral plaque radiotherapy**, is limited to small tumors.

During brachytherapy, a small amount of radioactive material is placed on the outside of the part of the eyeball where the tumor is, and it stays there for several days. The radioactive material is put in a small carrier (known as a **plaque**), which is shaped like a very small bottle cap. The plaque is made of gold or lead to shield nearby tissues from the radiation. The radiation travels a very short distance, so most of it will be focused only on the tumor.

The plaque is sewn in place on the eyeball with tiny stitches during a short operation. It is then removed during a second operation several days later. Both operations are done while the child is under general anesthesia (in a deep sleep). The child typically stays in the hospital while the plaque is in place.

### Possible side effects of brachytherapy

Brachytherapy is less likely to cause side effects than external radiation. The main concern is damage to the retina or optic nerve, which can affect vision many months later. Recent advances in treatment may make this problem less likely. Brachytherapy has not been linked to an increased risk of developing a second cancer.

## More information about radiation therapy

To learn more about how radiation is used to treat cancer, see Radiation Therapy[3].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[4].

## Hyperlinks

1. www.cancer.org/cancer/types/retinoblastoma/detection-diagnosis-staging/how-

- Transpupillary thermal therapy (TTT)

Lasers are highly focused beams of light that can be used to heat and destroy body tissues. Different types of laser therapy can sometimes be used to treat small retinoblastoma tumors.

## Laser photocoagulation

Photocoagulation is a type of treatment that uses a laser beam aimed through the pupil (the dark spot in the front of the eye). The laser is focused on the blood vessels that surround and supply the tumor, destroying them by heating them. Photocoagulation is effective only for smaller tumors toward the back of the eye.

Your child will be under general anesthesia (in a deep sleep) during the treatment. The treatment is usually given 2 or 3 times, with about a month between treatments.

### Possible side effects

In some cases, laser therapy can damage the retina, which can lead to blind spots or temporarily cause the retina to detach from the back of the eyeball.

## Transpupillary thermal therapy (TTT)

For this treatment, also just called **thermotherapy**, the doctor uses a different type of laser than what's used in photocoagulation. This laser applies infrared light directly to the tumor to heat and kill the tumor cells. The temperatures aren't quite as high as those used in photocoagulation, so some of the blood vessels on the retina may be spared.

Thermotherapy can be used alone for very small tumors. For larger tumors, it can be used along with chemotherapy (called **thermochemotherapy**) or with radiation therapy (called **thermoradiotherapy**). Heat seems to help these other treatments work better.

The treatment is given while the child is asleep (under general anesthesia), usually for about 10 minutes at a time. Typically, 3 treatments about a month apart are needed to control each tumor. When used as part of thermochemotherapy, the heat is usually applied at a lower temperature over a slightly longer period of time, starting within a few hours after chemotherapy.

### Possible side effects

Thermotherapy can sometimes cause part of the iris (the colored part of the eye) to shrink. Other possible effects include clouding of part of the eye lens or damage to the retina, which might affect vision.

### References

Hurwitz RL, Shields CL, Shields JA, et al. Chapter 27: Retinoblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2016.

Kaufman PL, Kim J, Berry JL. Retinoblastoma: Treatment and outcome. UpToDate. Accessed www.uptodate.com/contents/retinoblastoma-treatment-and-outcome on September 25, 2018.

National Cancer Institute. Retinoblastoma Treatment (PDQ®). 2018. Accessed at www.cancer.gov/types/retinoblastoma/hp/retinoblastoma-treatment-pdq on September 25, 2018.

Rodriguez-Galindo C, Orbach DB, VanderVeen D. Retinoblastoma. *Pediatr Clin North Am*. 2015;62(1):201-223.

Last Revised: December 3, 2018

# Cryotherapy for Retinoblastoma

In cryotherapy, the doctor uses a small metal probe that is cooled to very low temperatures, killing the retinoblastoma cells by freezing them. It is only effective for small tumors toward the front of the eye. It is not used routinely for children with several tumors.

The child will be in a deep sleep (under general anesthesia) during the treatment. After the child is asleep, the probe is placed on the outer surface of the eyeball next to the tumor, which is then frozen and thawed several times. Cryotherapy is usually given 2 or 3 times, with about a month between treatments.

### Possible side effects

Cryotherapy can cause the eye and eyelid to swell for a few days. As with laser therapy,

cryotherapy can damage the retina, which can lead to blind spots or temporarily cause the retina to detach from the back of the eyeball.

### References

Hurwitz RL, Shields CL, Shields JA, et al. Chapter 27: Retinoblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2016.

Kaufman PL, Kim J, Berry JL. Retinoblastoma: Treatment and outcome. UpToDate. Accessed www.uptodate.com/contents/retinoblastoma-treatment-and-outcome on September 25, 2018.

National Cancer Institute. Retinoblastoma Treatment (PDQ®). 2018. Accessed at www.cancer.gov/types/retinoblastoma/hp/retinoblastoma-treatment-pdq on September 25, 2018.

Rodriguez-Galindo C, Orbach DB, VanderVeen D. Retinoblastoma. *Pediatr Clin North Am*. 2015;62(1):201-223.

Last Revised: December 3, 2018

# Chemotherapy for Retinoblastoma



Chemotherapy (chemo) is the use of anti-cancer drugs to treat cancer. Chemo can be given in different ways to treat retinoblastoma.

## Systemic chemotherapy

Chemo drugs can be injected into a vein (IV) or given by mouth. These drugs enter the bloodstream and reach throughout the body. This is known as systemic chemotherapy.

Systemic chemo is given in cycles, with each treatment followed by a rest period to give the body time to recover. Each chemo cycle typically lasts for a few weeks, and the total length of treatment is often several months.

Some of the chemo drugs used to treat retinoblastoma include:

- Carboplatin
- Cisplatin
- Vincristine
- Etoposide
- Cyclophosphamide
- Topotecan
- Doxorubicin

Most often, 2 or 3 drugs are given at the same time. A standard combination is carboplatin, vincristine, and etoposide, although for very small tumors, only carboplatin and vincristine may be enough. Other drugs might be used if these are not effective.

## Intra-arterial chemotherapy

Sometimes instead of systemic chemotherapy, the chemo is injected directly into the ophthalmic artery, the main artery that supplies blood to the eye. In this newer technique, a very thin catheter (a long, hollow, flexible tube) is inserted into a large artery on the inner thigh and slowly threaded through the blood vessels all the way up into the ophthalmic artery. (This is done with the child asleep under general anesthesia.) The chemo is then infused into the artery. The drug used most often is melphalan, but other drugs such as carboplatin and topotecan can also be used. This process may then be repeated every few weeks, depending on how much the tumor shrink.9rg /GS4.08 Tm 0 0 0 rg

## Intravitreal chemotherapy

In this newer approach, a tiny needle is used to inject a chemo drug (typically melphalan or topotecan) directly into the vitreous humor, the jelly-like substance inside the eye. This is sometimes used (along with systemic or intra-arterial chemo) to treat tumors that

- Diarrhea or constipation
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

Most of these side effects go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce

- Detachment of the retina from the back of the eye
- Bleeding inside the eye
- Weakening of the muscles that move the eye
- Drooped eyelid
- Loss of eyelashes

Possible long-term side effects are not yet clear, as this technique is still fairly new. Treatment might affect the small blood vessels in and around the eye, although it's not yet known if this might affect vision as the child gets older. This approach also exposes the child to some radiation, because real time x-rays are used to help guide the catheter into place. It's not yet clear if (or how much) this might raise cancer risk later in life.

**Intravitreal chemo:** As with intra-arterial chemo, the side effects from this newer technique seem to be limited to the eye and nearby areas. Each treatment might damage the retina slightly, which might affect vision.

In the past, there was concern that placing a needle into the eye to give the chemo might open a small hole that could allow tumor cells to spread outside of the eye. However, studies have found that this risk is very low, and doctors now use techniques that lower this risk even further.

## More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see Chemotherapy[5]M 0 0 d(5)Tj 0 Ts 0 g /F2 12 Tf 0 0 0 rg /GS61g 0 0R55 55t.68 2 5 Ts (M 0 0 d(5)T

6. www.cancer.org/cancer/managing-cancer/side-effects.html

**References**

Hurwitz RL, Shields CL, Shields JA, et al. Chapter 27: Retinoblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2016.

Kaufman PL, Kim J, Berry JL. Retinoblastoma: Treatment and outcome. UpToDate. Accessed www.uptodate.com/contents/retinoblastoma-treatment-and-outcome on September 25, 2018.

National Cancer Institute. Retinoblastoma Treatment (PDQ®). 2018. Accessed at www.cancer.gov/types/retinoblastoma/hp/retinoblastoma-treatment-pdq on September 25, 2018.

Rodriguez-Galindo C, Orbach DB, VanderVeen D. Retinoblastoma. *Pediatr Clin North Am*. 2015;62(1):201-223.

Smith SJ, Smith BD. Evaluating the risk of extraocular tumour spread following intravitreal injection therapy for retinoblastoma: A systematic review. *Br J Ophthalmol*. 2013;97(10):1231-1236.

Smith SJ, Smith BD, Mohney BG. Ocular side effects following intravitreal injection therapy for retinoblastoma: A systematic review. *Br J Ophthalmol*. 2014; 98(3): 292-297.

Last Revised: December 3, 2018

# Treatment of Retinoblastoma, Based on Extent of the Disease

- If the eye can see and probably can be saved

If your child has retinoblastoma, a number of factors can affect the treatment options your child's doctor recommends. Some of these include:

- The size and location of the tumor(s)
- Whether the cancer is just in one eye or both
- The chance for saving vision in the eye(s)
- Whether the cancer has spread outside the eye

Many of these factors are taken into account as part of the stage[1] of the cancer.

If the retinoblastoma is **only in one eye**, treatment depends on whether vision in the eye can be saved.

If the retinoblastoma is in **both eyes**, doctors will try to save at least one eye if at all possible so that the child maintains some vision.

Many children will get several types of treatment. Treatment might be needed for months or even years.

mighy

No matter which types of treatment are used, it's very important that they are given by experts at centers experienced in treating these tumors.

## If the eye can see and probably can be saved

(known as **intra-arterial chemotherapy**) instead of systemic chemotherapy. If the cancer has spread widely inside the eye, chemo might also be injected directly into the eye (known as **intravitreal chemotherapy**). Usually a few treatments are needed, each given a few weeks apart.

Depending on how much the tumor shrinks and where it is in the eye, different focal treatments can then be applied, usually starting after the first or second cycle of chemotherapy. Treatment options might include brachytherapy (plaque radiotherapy), cryotherapy, or laser therapy (photocoagulation or thermotherapy). External radiation therapy might also be given, but if so, it's usually delayed until the end of chemotherapy.

If the combination of these treatments doesn't control the disease, the eye might need to be removed.

## If the eye cannot see or cannot be saved

If there is no vision in the eye, if the tumor is so advanced within the eye that there is no hope of cure by other means, or if there is painful glaucoma (increased pressure inside the eye), then the eye is removed and an orbital implant is placed in the socket.

**If the cancer affects only one eye**, no other treatments may be needed. But sometimes, after looking at the removed eye under the microscope, the doctors find that some retinoblastoma cells might have escaped the eye, which means the cancer might come back later in other parts of the body. These children may be given chemotherapy, possibly along with radiation therapy to the area around the eye, to try to lower this risk.

**In some instances where there are large tumors in b toGS759 0 s may  ippa2s re ft7 hs to the ar**

radiation, and in some cases surgery.

If the cancer has spread only to the orbit (the area around the eye), treatment with chemotherapy, surgical removal (enucleation) of the eye, and radiation therapy to the orbit is often successful.

If the cancer has spread outside the orbit to distant parts of the body such as the liver or the bones and bone marrow, the chances of a cure using standard chemotherapy and

National Cancer Institute. Retinoblastoma Treatment (PDQ®). 2018. Accessed at www.cancer.gov/types/retinoblastoma/hp/retinoblastoma-treatment-pdq on September 25, 2018.

Rodriguez-Galindo C, Orbach DB, VanderVeen D. Retinoblastoma. *Pediatr Clin North Am*. 2015;62(1):201-223.