



## Cryotherapy

Cryotherapy uses imaging guidance, a needle-like applicator called a cryoprobe, and liquid nitrogen or argon gas to create intense cold to freeze and destroy diseased tissue, including cancer cells. It may be used to treat a variety of skin conditions as well as tumors within the liver, kidneys, bones, lungs and breasts.

Your doctor will instruct you on how to prepare, including any changes to your medication schedule. Tell your doctor if there's a possibility you are pregnant and discuss any recent illnesses, medical conditions, allergies and medications you're taking, including herbal supplements and aspirin. You may be advised to stop taking aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), or blood thinners several days prior to your procedure. Ask your doctor if you will need to be admitted overnight. Leave jewelry at home and wear loose, comfortable clothing. You may be asked to wear a gown. Plan to have someone drive you home.

## What is Cryotherapy?

Cryotherapy, also called cryosurgery, cryoablation, percutaneous cryotherapy or targeted cryoablation therapy, is a minimally invasive treatment that uses extreme cold to freeze and destroy diseased tissue, including cancer cells. Although cryotherapy and cryoablation can be used interchangeably, the term "cryosurgery" is best reserved for cryotherapy performed using an open, surgical approach.

During cryotherapy, liquid nitrogen or high pressure argon gas flows into a needle-like applicator (a cryoprobe) creating intense cold that is placed in contact with diseased tissue. Physicians use image-guidance techniques such as ultrasound, computed tomography (CT) or magnetic resonance (MR) to help guide the cryoprobes to treatment sites located inside the body.

## What are some common uses of the procedure?

Cryotherapy can be applied topically (on the skin surface), percutaneously, or surgically. Topical cryotherapy is used typically in the case of skin and eye lesions. When the lesion is situated below the skin surface, a needle-like therapy probe or applicator needs to be placed through the skin. Occasionally, a surgical incision is required.

Cryotherapy is used to treat:

- skin tumors.

- pre-cancerous skin moles.
- nodules.
- skin tags.
- unsightly freckles.
- retinoblastomas, a childhood cancer of the retina.
- prostate, liver, and cervical cancers, especially if surgical resection is not possible.

Cryotherapy is also being used to treat tumors in other parts of the body, such as the kidneys, bones (including the spine), lungs, and breasts (including benign breast lumps called fibroadenomas). Although further research is needed to determine its long term effectiveness, cryotherapy has been shown to be effective in selected patients.

## How should I prepare?

For skin treatment, some physicians recommend taking ibuprofen (400 mg) a half-hour before this procedure to relieve minor discomfort; others give a dose of antibiotics before cryotherapy as a way to guard against infection. For deeper treatments involving tumors, patients should avoid blood thinning medications for the recommended period of time before the treatment.

You should report to your doctor all medications that you are taking, including herbal supplements, and if you have any allergies, especially to local anesthetic medications, general anesthesia or to contrast materials containing iodine (sometimes referred to as "dye" or "x-ray dye"). Your physician may advise you to stop taking aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs) or blood thinners for a specified period of time before your procedure.

Women should always inform their physician and x-ray technologist if there is any possibility that they are pregnant. Many imaging tests are not performed during pregnancy so as not to expose the fetus to radiation. If an x-ray is necessary, precautions will be taken to minimize radiation exposure to the baby. See the Safety page for more information about pregnancy and x-rays.

Some physicians recommend a short, overnight hospital stay after cryotherapy of deep tumors. In the case of cryotherapy performed using a large, surgical incision (cryosurgery) a short hospitalization will be required. Percutaneous cryotherapy can be performed as an outpatient service, but may require a short, overnight hospital stay.

You should plan to have a relative or friend drive you home after your procedure.

You may be asked to wear a gown during the procedure.

## What does the equipment look like?

In this procedure, ultrasound, computed tomography (CT) or magnetic resonance (MR) imaging, a cotton swab or spray device, cryoprobe and bronchoscope may be used. For cryosurgery, laparoscopic surgery may be performed.

Ultrasound scanners consist of a console containing a computer and electronics, a video display screen and a transducer that is used to do the scanning. The transducer is a small hand-held device that resembles a microphone, attached to the scanner by a cord. Some exams may use different transducers (with different capabilities) during a single exam. The transducer sends out high-frequency sound waves (that the human ear cannot hear) into the body and then listens for the returning echoes from the tissues in the body. The principles are similar to sonar used by boats and submarines.

The ultrasound image is immediately visible on a video display screen that looks like a computer or television monitor. The image is created based on the amplitude (loudness), frequency (pitch) and time it takes for the ultrasound signal to return from the area within the patient that is being examined to the transducer (the device placed on the patient's skin to send and receive the returning sound waves), as well as the type of body structure and composition of body tissue through which the sound travels. A small amount of gel is put on the skin to allow the sound waves to travel from the transducer to the examined area within the body and then back again. Ultrasound is an excellent modality for some areas of the body while other areas, especially air-filled lungs, are poorly suited for ultrasound.

The CT scanner is typically a large, box-like machine with a hole, or short tunnel, in the center. You will lie on a narrow examination table that slides into and out of this tunnel. Rotating around you, the x-ray tube and electronic x-ray detectors are located opposite each other in a ring, called a gantry. The computer workstation that processes the imaging information is located in a separate control room, where the technologist operates the scanner and monitors your examination in direct visual contact and usually with the ability to hear and talk to you with the use of a speaker and microphone.

The traditional MRI unit is a large cylinder-shaped tube surrounded by a circular magnet. You will lie on a moveable examination table that slides into the center of the magnet.

Some MRI units, called short-bore systems, are designed so that the magnet does not completely surround you. Some newer MRI machines have a larger diameter bore which can be more comfortable for larger size patients or patients with claustrophobia. Other MRI machines are open on the sides (open MRI). Open units are especially helpful for examining larger patients or those with claustrophobia. Newer open MRI units provide very high quality images for many types of exams. Older open MRI units may not provide this same image quality. Certain types of exams cannot be performed using open MRI. For more information, consult your radiologist.

The computer workstation that processes the imaging information is located in a separate room from the scanner.

Cryotherapy to treat tissue located outside the body uses a cotton swab or spray device.

Cryotherapy to treat tissue located inside the body requires image guidance and a cryotherapy applicator or cryoprobe, a thin wand-like device with a handle or trigger or a series of small needles. The cryoprobe is connected via tubing to a source of nitrogen or argon. Most cryotherapy units use argon gas and are approved by the U.S. Food and Drug Administration (FDA).

A bronchoscope, a thin, lighted tube used to examine the inside of the trachea and bronchi, or the air passages that lead into the lungs, may also be used.

The cryotherapy system is generally housed in the procedure room. It has a computer that can be used to control the flow of the cooling agent, which is typically stored in nearby gas tanks.

Other equipment that may be used during the procedure includes an intravenous line (IV), ultrasound machine and devices that monitor your heart beat and blood pressure.

## How does the procedure work?

Cryotherapy uses nitrogen or argon gas to create extremely cold temperatures to destroy diseased tissue. To destroy diseased tissue located outside the body, liquid nitrogen is applied directly with a cotton swab or spray device. For tumors located below the skin surface and deep in the body, the physician will use image-guidance to insert one or more applicators, or cryoprobes, through the skin to the site of the diseased tissue and then deliver the liquid nitrogen or argon gas.

Living tissue, healthy or diseased, cannot withstand extremely cold conditions and will die from:

- ice formation in the fluid outside cells, which results in cellular dehydration.
- ice formation within the cell. At approximately  $-40^{\circ}\text{C}$  ( $-40^{\circ}\text{F}$ ) or less, intracellular lethal-ice crystals begin to form and will destroy almost any cell.
- bursting from both swelling caused by ice expansion inside the cell or shrinking caused by water exiting the cell.
- loss of blood supply. Cells die when their blood supply is choked off by ice forming within small tumor blood vessels, causing clotting. Since the average blood-clotting time is approximately 10 minutes, the extreme cold is maintained for at least 10-15 minutes, if not longer, to assure that lethal-ice temperatures have been reached. Direct observation of the ablation temperature is possible with some apparatuses.

Because cryotherapy consists of a series of steps that lead to cell death, tumors are repeatedly frozen and thawed; typically, two or more freeze-thaw cycles are used.

Once the cells are destroyed, the white blood cells of the immune system work to clear out the dead tissue.

## How is the procedure performed?

Percutaneous image-guided procedures such as cryotherapy are most often performed by a specially trained interventional radiologist in an interventional radiology suite or occasionally in the operating room.

This procedure is often done on an outpatient basis. However, some patients may require admission following the procedure. Please consult with your physician as to whether or not you will be admitted.

You will be positioned on the examining table.

If topical cryotherapy is performed, your physician will apply liquid nitrogen to the area with a cotton swab or spray device.

For tumors deep inside the body that can be approached through the skin, your physician will perform a percutaneous procedure and insert thin, needle-size applicators or cryoprobes.

You may be connected to monitors that track your heart rate, blood pressure and pulse during the procedure.

A nurse or technologist will insert an intravenous (IV) line into a vein in your hand or arm so that sedative medication can be given intravenously. Moderate sedation may be used. As an alternative, you may receive general anesthesia.

The area where the applicators or cryoprobe are to be inserted will be shaved, sterilized and covered with a sterile drape.

A very small skin incision is made at the site.

Using imaging guidance, the physician will insert one or more applicators or cryoprobes through the skin to the site of the diseased tissue. Once the applicators or cryoprobe(s) are in place, the liquid nitrogen or argon gas is delivered. Aside from the cryoprobe(s), nothing else enters the body. An "ice ball" is created by a rapid decrease in the temperature at the tip of the probe. This causes all water in the area around the tip of the probe to freeze. Imaging is used to guide the placement of the applicators, and monitor the freezing process. The "ice ball" can be visualized using ultrasound, CT or MRI.

Some tumors require multiple applicators to freeze completely. For prostate cancer, six to eight applicators are inserted through the perineum (the tissue between the rectum and the scrotum and penis) using ultrasound guidance.

At the end of the procedure, the applicator(s) are removed and pressure will be applied to stop any bleeding. The opening in the skin is covered with a bandage. Typically, no sutures are needed.

Your intravenous line will be removed.

The entire procedure is usually completed within one to three hours.

## **What will I experience during and after the procedure?**

Devices to monitor your heart rate and blood pressure will be attached to your body.

You will feel a slight pin prick when the needle is inserted into your vein for the intravenous line (IV) and when the local anesthetic is injected. Most of the sensation is at the skin incision site, which is numbed using local anesthetic. You may feel pressure when the catheter is inserted into the vein or artery.

If you receive a general anesthetic, you will be unconscious for the entire procedure, and you will be monitored by an anesthesiologist.

If the procedure is done with sedation, the intravenous (IV) sedative will make you feel relaxed, sleepy and comfortable for the procedure. You may or may not remain awake, depending on how deeply you are sedated.

You may experience discomfort from having to be still during the procedure.

Following percutaneous cryotherapy, you should be able to resume your usual activities within one to

three days.

If you have had open cryosurgery, you should be able to resume your usual activities within seven to 10 days. You should avoid lifting heavy objects for at least 72 hours. Consult your physician as to when you can resume your usual activities.

## Who interprets the results and how do I get them?

The interventional radiologist or physician treating you will determine the results of the procedure and will send a report to your referring physician, who will share the results with you.

Your interventional radiologist may recommend a follow-up visit after your procedure or treatment is complete.

The visit may include a physical check-up, imaging procedure(s) and blood or other lab tests. During your follow-up visit, you may discuss with your doctor any changes or side effects you have experienced since your procedure or treatment.

## What are the benefits vs. risks?

### Benefits

- When an open surgical approach is taken, the recovery time following cryosurgery of kidney or liver tumors may be less than for open, surgical removal of the tumor.
- For percutaneous cryotherapy, the patient may stay overnight or be released several hours after the procedure. Overnight stays for pain control are usually not needed.
- Percutaneous cryotherapy is less traumatic than open surgery since only a small incision is needed to pass the probe through the skin, which limits damage to healthy tissue. Consequently, percutaneous cryotherapy is less costly and results in fewer side effects than open surgery. A patient usually can resume activities of daily living 24 hours after the procedure, if not sooner. However, caution about heavy lifting may extend for several days after abdominal treatment.
- For treatment of fibroadenomas, cryotherapy causes minimal scar tissue and no apparent post-treatment calcifications.

### Risks

- Like any percutaneous procedure, bleeding may result—both from the puncture and the freezing of tissues such as the liver, kidney or lung.
- Damage to normal structures may occur. During liver cryotherapy, the bile ducts may be injured. During kidney cryotherapy, the ureter or collecting system may be damaged. The rectum may be damaged during prostate cryotherapy. Any treatment of the abdomen may result in damage to the bowel and cause a hole in the bowel, which may release bowel contents into the abdomen that can lead to potential life-threatening infection.
- If freezing occurs near the diaphragm, fluid can accumulate in the space around the lungs.

- If the procedure is in or near the lung, the lung may collapse.
- Nerve damage may result. Completely frozen nerves can cause motor weakness or numbness in the area supplied by the nerves.
- Complications related to medications, including anesthesia, administered during the procedure may occur.
- Women should always inform their physician or x-ray technologist if there is any possibility that they are pregnant. See the Safety page for more information about pregnancy and x-rays.
- This procedure may involve exposure to x-rays. However, radiation risk is not a major concern when compared to the benefits of the procedure. See the Safety page for more information about radiation dose from interventional procedures.

Specific possible complications related to the cryotherapy of prostate cancer:

- Permanent impotence since nerves controlling sexual potency are commonly involved in the freezing process. However, nerves can regenerate, resolving the problem in some patients.
- While the patient is under anesthesia, a bladder tube is positioned to drain urine until the swelling of the bladder neck—as a result of the procedure—resolves.
- May cause urethral sloughing; that is, blocking of the urine stream with dead tissue. Sloughing is reduced by keeping the urethra warm with sterile water circulating continuously through a catheter placed in the urethra during the procedure.

## What are the limitations of Cryotherapy?

Cryotherapy is an alternative cancer treatment when surgical removal of a tumor may be difficult or, for some patients, impossible. But its long-term effectiveness is still being examined. Currently, little published data deal with the long-term results of percutaneous cryotherapy but long-term follow-up for prostate cancer suggests cancer-control rates are similar to surgery or radiation therapy.

Cryotherapy is considered a localized therapy. It can only treat disease at a single site. It cannot treat cancer that has spread to other parts of the body. Because physicians treat the tumors they see on radiologic images, microscopic cancer may be missed.

Although its use in the bone, kidney, liver and lung is promising, percutaneous cryotherapy research is ongoing to determine longer term clinical outcomes.

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