Introduction to Stereotactic Radiation (Radiosurgery / SRS)

Stereotactic radiation, often referred to as stereotactic body radiation therapy (SBRT), stereotactic ablative radiotherapy (SABR) or stereotactic radiosurgery (SRS), is a form of radiation therapy that very precisely delivers a high dose of radiation to a tumor.

Stereotactic radiation differs from standard, conventional radiation (sometimes called IMRT or 3D conformal radiation), in that it involves fewer treatments (called "fractions"). Stereotactic radiation usually involves 1-5 treatments over 1-2 weeks, while conventional radiation involves daily treatments, 5 days a week typically over anywhere from 5-9 weeks, depending on the diagnosis. Stereotactic radiosurgery (SRS) is a form of stereotactic radiation that involves a single fraction and is generally reserved for treatment of lesions within the brain. Despite the connotation of the name, radiosurgery does not involve actual surgery, scalpels or cutting.

Although stereotactic radiation involves fewer fractions, the radiation dose delivered during each fraction is much higher than conventional radiation in order to achieve the same biological effect. Since the dose of radiation to that single point is high, the radiation oncologist must very precisely target the lesion's/tumor's location. In order to do this, stereotactic radiotherapy functions like a magnifying glass, delivering radiation from different angles to focus the radiation at one small point where the beams converge. The use of multiple unique beam angles limits dose to normal tissues as the beams enter and results in a very sharp radiation dose fall-off around the tumor. The sharp fall-off allows for decreased radiation dose to the surrounding normal tissue. In order for the radiation dose to adequately conform around the tumor, the size and shape of the tumor are important. Additionally, because high doses of radiation are used, the location of the tumor may impact whether SBRT is a viable treatment option. For example, SBRT may not be safe if a tumor is bordering or touching a critical, sensitive, normal structure. Due to the strict criteria for size, shape and location of the tumor, SBRT can only be used in select cases.

The biologic mechanism for killing cancer cells is different in stereotactic radiation and conventional radiation. Conventional radiation damages the DNA of cancer cells to prevent them from replicating and multiplying. By using different biologic mechanisms to cause cancer cell death, including DNA and blood vessel damage, stereotactic radiation is often used to treat cancers that have been considered to be less responsive to conventional radiation, such as melanoma, renal cell carcinoma and sarcoma. However, because SBRT is a relatively newer technology, the long term side effects of SBRT are not well known or understood.

Treatment Modalities

Conventional radiation treatment uses a general linear accelerator machine that produces high energy x-rays used to kill cancer cells. In stereotactic radiation, there are 3 main modalities or machines that deliver radiation: GammaKnife, CyberKnife, and a highly advanced Linear Accelerator. Let's look at these in more depth.

GammaKnife

The GammaKnife machine is exclusively used to treat brain tumors or benign brain conditions with stereotactic radiosurgery (1 treatment of stereotactic radiation). After an initial consultation with a radiation oncologist and neurosurgeon and review of all relevant brain MRI scans, the patient will be scheduled for the GammaKnife procedure. The procedure is performed as a 1-day outpatient treatment. Patients are usually given a calming medication and a head frame is attached to the skull using small screws with local anesthesia (numbing of the skin). This head frame allows the head to be positioned with sub-millimeter accuracy in the treatment machine, facilitating the precise delivery of the radiation in a single treatment. With the frame on, the patient undergoes an MRI scan to help the treating physicians visualize the tumor; the frame serves as a stable reference point for locating the tumor. The MRI is then used to plan the radiation treatment using specialized software. Because of its complexity, radiosurgery requires the participation of both neurosurgery and radiation oncology during treatment planning and delivery. The tumor and normal structures are outlined on the MRI and a treatment plan is constructed to avoid critical brain structures, while giving optimal dose to the tumor. While the physicians plan the treatment, the patient waits with the head frame...
attached. The waiting time varies, but can take a few hours depending on the complexity of the case and the number of patients scheduled for treatment. After the radiation plan is verified and approved, the patient is taken into the treatment room. The head frame is then attached to the treatment machine and radiation can be delivered with sub-millimeter accuracy. Treatment times vary considerably, from several minutes to more than one hour, and are dependent on the complexity of the plan, the number of tumors that need treatment and the age of the radiation source. The source for GammaKnife is cobalt-60. As the radioactivity of cobalt decays, the treatment time increases to deliver the same dose of radiation. After treatment is complete, the head frame is removed and the patient is discharged home.

**CyberKnife**

The CyberKnife machine is a linear accelerator placed on a robotic arm that can treat all sites of the body with one or multiple fractions. The robotic arm and robotic table enable the CyberKnife to treat tumors from more directions and angles than a general linear accelerator in order to minimize exposure to normal tissues. The unique advanced technology of CyberKnife also allows it to track or follow tumors in real-time, overcoming movement and further reducing normal tissue exposure. Tumor tracking is performed in two different ways. The first mechanism for tracking uses image detectors in the ceiling and floor to image the patient multiple times every minute, accounting for millimeter shifts of the patient's body during treatment. The second mechanism accounts for respiratory movement of the tumor in real-time by continuously tracking the patient's breathing cycle with LED detectors.

While the procedure for CyberKnife treatment is similar to the procedure for conventional radiation, there are some key differences. During an initial consultation and prior to the CAT Scan (CT) simulation, the radiation oncologist will determine the need for placement of fiducial markers (metal markers). Fiducial markers assist the Cyberknife technology with tumor tracking during treatment. The fiducial markers remain permanently in the body and are placed via a procedure similar to a biopsy. An Interventional Radiologist in the Radiology Department often performs this minimally invasive procedure.

After initial consultation and fiducial marker placement, the patient will undergo pre-treatment imaging with a CT simulation, which is performed days to weeks prior to the first treatment. While similar to the procedure for conventional radiation treatment, small ink tattoo marks (which are usually used for patient alignment during treatment) may not be required. On the day of simulation, the patient may need to be placed on the CyberKnife table to determine the appropriate positioning and to ensure that the Cyberknife technology will be able to track the tumor. An immobilization device, such as a head and neck mask or Vac-lock bag (see below), may be used. Depending on the site and the type of tumor, the radiation oncologist may require additional imaging, such as an MRI or PET scan to help assist the treatment planning process.

After the simulation, Cyberknife treatment planning generally takes days to weeks. After the number of treatments and radiation dose are determined, the patient is scheduled for treatment. Treatments may be daily or 2-3 times a week. The length of each treatment varies from several minutes to more than 1 hour.

**Advanced Linear Accelerator (Linac-based SBRT)**

Conventional radiation therapy is delivered with a general linear accelerator (also called a linac). Today, more advanced linear accelerators are being produced that have the capability of delivering stereotactic radiation therapy by delivering radiation using numerous angles. Examples of this advanced technology include RapidArc and Tomotherapy. Linac-based SBRT can treat most body sites, most commonly lung and liver. While linac-based SBRT cannot track respiratory motion in real time, tumor motion from breathing is accounted for during the CT simulation and treatment planning.

The procedure for stereotactic radiation treatment using an advanced linear accelerator is similar to the procedure for conventional radiation treatment. A CT simulation is performed using a 4-dimensional simulation to account for breathing motion. Tattoos are placed during the simulation to assist with patient positioning and alignment during treatment. Like CyberKnife, the procedure may require placement of fiducial markers before the simulation and the use of immobilization devices during the simulation and treatment. In this case, the fiducial markers assist with patient alignment on the machine rather than tumor motion tracking. Depending on the site and the type of tumor, the radiation oncologist may require additional imaging, such as an MRI or PET scan to help assist the treatment planning process.

After the simulation, treatment planning generally takes days to weeks. After the number of treatments and radiation dose are determined, the patient is scheduled for treatment. Treatments may be daily or 2-3 times a week. As opposed to GammaKnife and CyberKnife, the length of each treatment with linac-based SBRT is shorter, generally several minutes. However, the

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patient's position needs to be aligned and verified, which takes time and may require the patient to be on the table for about an hour in some cases.

**Disease Sites in Which Stereotactic Radiation is Used**

The lung and the brain are the two most common and well-established sites treated with stereotactic radiation. Multiple, well-conducted, prospective studies have been performed to demonstrate and validate the effectiveness and safety of stereotactic radiation in the brain and lung. Other increasingly common sites are the abdomen (liver, pancreas, kidney), spine and prostate. Usually, SBRT is used only to treat 1-2 areas of disease; however, studies are underway examining whether SBRT may be useful for patients with more areas of known disease.

**Brain**

Stereotactic radiation to the brain is a well-established, effective, safe treatment with evidence from large, prospective studies that started accruing patients in the early 1990s. Stereotactic radiation to the brain is commonly used to treat patients with cancers that have spread to the brain (metastases), primary brain tumors (like meningioma) in difficult locations for surgery, and patients with benign conditions such as acoustic neuroma, arteriovenous malformation (AVM) and trigeminal neuralgia. While GammaKnife if most commonly used, Cyberknife or linac-based SBRT can also be used to treat the brain with stereotactic radiation.

Patients with brain metastases need to be carefully selected for radiosurgery, and must have small tumors that are few in number, cause minimal neurologic symptoms and carry a relatively good prognosis. Studies have demonstrated that stereotactic radiation can help these patients live longer. Stereotactic radiation to the brain may be recommended as the sole treatment for brain metastases, as follow-up treatment after surgical resection, or in combination with low-dose whole brain radiotherapy, which uses conventional radiation therapy to the whole brain (usually in 10 treatments over 2 weeks). In addition to controlling the known cancer cells in the brain, whole brain radiotherapy decreases the risk of developing new brain metastases. Stereotactic radiation to the brain only targets the known and visible areas of metastasis.

In the short-term after stereotactic radiation to the brain, the patient can experience mild swelling in the area that was treated. This side effect can manifest in different ways, but generally is associated with worsening headache, nausea or vomiting. If a patient experiences these symptoms, he/she should call the doctor, as steroid medication may be needed. A longer-term side effect of stereotactic radiation to the brain is a condition called "radiation necrosis," which manifests as worsening neurologic symptoms due to the radiation and which may require surgery. It is often difficult for doctors to distinguish between radiation necrosis and a recurrence of the tumor.

**Lung**

Stereotactic radiation to the lung is usually recommended in patients with early stage lung cancer who cannot undergo surgery, mostly due to other medical issues; increasingly, stereotactic radiation is being offered as an alternative to surgery in operable patients. Multiple studies have demonstrated that stereotactic radiation can completely eradicate the lung tumor and prevent more than 90% of these lung cancers from coming back. Surgery is still the standard of care for early stage lung cancer, but SBRT is preferred if a patient is unable to tolerate surgery. Additional studies are underway to directly compare stereotactic radiation to surgery in early stage lung cancer who could undergo surgery.

Patients with other cancers that have spread to the lung may be candidates for SBRT to the lung metastases. To benefit from SBRT in these situations, patients need to have few, small lung tumors with a limited amount of cancer elsewhere in the body. Patients are carefully selected and commonly include patients with head and neck cancer, colorectal cancer or sarcoma.

Patients who receive SBRT to the lung typically receive 3-5 treatments, with either CyberKnife or Linac-based SBRT. Location and size of tumors are very important with stereotactic radiation to the lung, as tumors in the wrong location can put patients at increased risk for serious side effects. For example, if a tumor is very close to the trachea (windpipe), patients can experience damage to these areas.

**Spine**

Cancer that has spread to the bones and vertebrae can cause significant pain and can press on the spinal cord, resulting in weakness, numbness and in severe cases, paralysis. Radiation to the spine is effective at slowing the progression of the
cancer to decrease pain and prevent paralysis. In some circumstances, stereotactic radiation to the spine can be used. Stereotactic radiation to the spine has been studied and demonstrated to decrease pain levels and decrease the risk that the tumor in the spine will come back or grow further.

**Abdomen/Pelvis**

Stereotactic radiation to organs in the abdomen is becoming more common, particularly with SBRT to the liver for treating liver metastases. A few studies have demonstrated safety and the ability to prevent > 90% of the tumors in the liver from coming back. The use of stereotactic radiation for pancreatic cancer, kidney cancer (renal cell carcinoma), hepatocellular carcinoma, and prostate cancer is also being studied at multiple institutions. Patients who receive SBRT to the abdomen/pelvis typically receive 3-5 treatments with either CyberKnife or Linac-based SBRT. Again, patients need to be carefully selected, as proximity to the intestine and other critical organs can potentially result in significant side effects, such as damage to the bowel or intestine.

**Re-irradiation**

Stereotactic radiation is a unique modality that is sometimes used in the setting of re-irradiation. If a patient's tumor comes back in an area that was previously treated with radiation, that patient is usually unable to receive another full course of radiation therapy. Because SBRT uses multiple beam angles that allow for decreased radiation dose to the surrounding normal tissue, SBRT can sometimes be used to treat these tumors that have come back. These situations, however, are always complex and only very select cases are appropriate for re-irradiation with SBRT.