

cancers that are too extensive to remove surgically. In some circumstances, radiation therapy can be used alone, without surgery or chemotherapy.

The most common form of radiation therapy is external beam radiation therapy. With external beam radiation therapy, the patient lies on a table, and a beam or multiple beams are emitted from a machine known as a linear accelerator. The beams are directed to the tumor and surrounding tissues that may also contain cancer cells. The beams penetrate the skin, other tissues, and organs before reaching the tumor target. External beam radiation therapy is given daily during the week, Monday through Friday, typically for 6 to 7 weeks. Scheduling the radiation treatment this way allows for an effective dose of radiation during the week to kill cancer cells and allows the patient and normal cells to recover during the weekend from the effects of radiation. The treatment takes 5 to 10 minutes, depending on the type of linear accelerator used.

The typical dose of radiation given for most lung cancers ranges from 6000 to 7000 cGy (centigray), depending on the stage and whether or not chemotherapy is included. Such a high dose of radiation cannot be given all at once to a patient without lethal side effects. Therefore, the dose given per treatment is 180 to 200 cGy, which usually is well tolerated by patients. The unit centigray replaces the older term “rad” as a measure of radiation dose; 100 centigray is equal to 1 gray (Gy), which is equal to 1 Joule per kilogram of tissue (1 Joule = 1 Newton-meter).

Radiation Treatment Team

The delivery of radiation therapy requires several individual team members that play a crucial role in the successful treatment of patients. **Radiation oncologists** are medical doctors who have completed medical school and at least five years of residency training before joining the workforce. They are frequently certified by the American Board of Radiology (although they are not diagnostic radiologists). Radiation oncologists talk to, examine, and counsel patients for consultation, and design and direct the radiation treatment plan. Radiation oncologists are the physician specialists during a patient's radiation therapy who provide evaluation, simulation (discussed next), weekly treatment visits, and follow-up visits after completing treatment.

“Whenever you find yourself doubting how far you can go, just remember how far you have come. Remember everything you have faced, all the battles you have won, and all the fears you have overcome.
- Anonymous

Figure 1: A radiation oncologist confers with a medical physicist to develop a radiation treatment plan for a lung cancer patient.



Radiation oncology nurses provide detailed education to patients on the clinical aspects of radiation treatment. They provide counseling on managing any side effects of treatment and tips on how to decrease the intensity of side effects. They often are the team members who address patient concerns and communicate more serious issues to the radiation oncologist.

Dosimetrists help calculate and optimize the treatment plan designed by the radiation oncologist. They work to ensure that the intended dose of radiation prescribed by the radiation oncologist is delivered to the patient. They work closely with the radiation oncologist to determine the optimal angles, fields, and energy of radiation needed for a treatment plan.¹

Medical physicists perform scheduled quality assurance tests to ensure that linear accelerators are working properly. They work closely with radiation oncologists and dosimetrists to help design the radiation treatment plan. They often supervise the dosimetrist in making sure the treatment plan is feasible and tailored to the individual patient.

Radiation therapists operate the linear accelerators, place patients in the correct position, give the daily radiation treatments, and keep an accurate record of treatments given.¹ Other staff members are important to patients receiving lung radiation, including social workers, physical therapists, occupational therapists, dieticians, and respiratory therapists.

The delivery of radiation therapy requires several individual team members that play a crucial role in the successful treatment of patients.

Simulation

After the consultation with the radiation oncologist, and a decision has been made for a lung cancer patient to receive radiation therapy, the patient first must undergo simulation. Simulation is a procedure where a radiation oncologist and a simulation technician (usually a radiation therapist) place the patient in the exact position for treatment to ensure that the radiation hits the correct target consistently. The patient lies down on the back, usually with the arms placed above the head. There may be immobilization devices such as handlebars for the patient to hold onto above the head. Custom cradles may be molded to conform to the patient for lying in the same position for each treatment. Skin marks (which may be washed off) and permanent tattoos (pinpoint dots, no larger than a mole) are placed and lined up with laser pointers in the room to make sure the patient can lie in the same position each day. In some institutions, X-rays are taken after the patient's treatment position has been determined.

Figure 2: A CT scan of the neck and chest is done in the treatment position with all immobilization devices in place.



Some radiation therapy facilities will place a belt around the patient's abdomen to encourage the patient to take more shallow breaths during simulation and treatment. This is done to decrease the distance that the lung tumor may move up or down during breathing. Other techniques that help regulate the effect of breathing on tumor location include timed breath holding and the use of respiratory tracking (gating) systems that electronically follow the movement of the tumor (discussed in more detail below).²


Subsequently, a CT (computed tomography) scan of the neck and chest is done in the treatment position with all the immobilization devices in place (Figure 2). This CT scan will provide a computerized 3-dimensional digital virtual model of the patient's chest and internal organs. The radiation oncologist and dosimetrist use this model to design a patient's radiation treatment fields

on a planning computer equipped with radiation treatment planning software. This planning or simulation CT scan is different from the diagnostic CT scan used to help diagnose and stage lung cancer. Intravenous contrast is sometimes used at the discretion of the radiation oncologist designing the treatment fields, and this contrast can provide better detail about the extent of lung cancer. Planning CT scans for simulation typically take less time to obtain than diagnostic scans. Furthermore, planning CT scans are not read or interpreted by a diagnostic radiologist but are processed with treatment planning software to help design the treatment fields.

Some institutions use 4-dimensional CT, which is a planning CT scan that tracks how a patient's breathing cycle affects the location of the lung tumor (a technique known as respiratory gating).² The distance a tumor moves up, down, or sideways can be useful to the dosimetrist to determine the margin size around the tumor required for planning treatment.

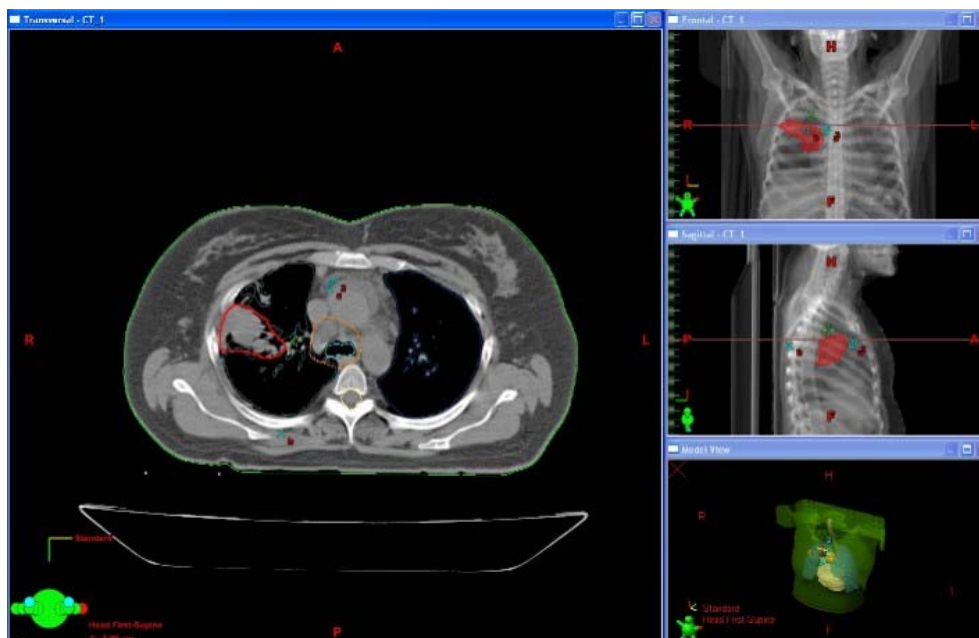
Treatment Planning

After the simulation is completed, the radiation oncologist, dosimetrist, and medical physicist develop a treatment plan. The simulation CT scan images are electronically sent to a computer with treatment planning software. The slices of the CT scan are reviewed, and the anatomic structures, such as the lungs, heart, and spinal cord, are outlined or contoured in different colors. The sum of the slices of these contours define the volume of the anatomic structures (Figure 3). The radiation oncologist, using information from positron emission tomography (PET) scans, diagnostic CT scans, and other reports will contour the actual tumor and lymph nodes involved with cancer. The volume of the actual tumor is called the gross tumor volume, and the gross tumor volume frequently is contoured in red.³ At some centers, the dosimetrist can take a PET scan (previously obtained to stage the tumor) and fuse this with the simulation CT scan. Because the lung tumor and regional lymph nodes light up brightly on the PET scan, fusion with the simulation CT scan can greatly help the radiation oncologist define the volume of cancer with more accuracy.

 *You are braver than you believe, and stronger than you seem,
and smarter than you think.*

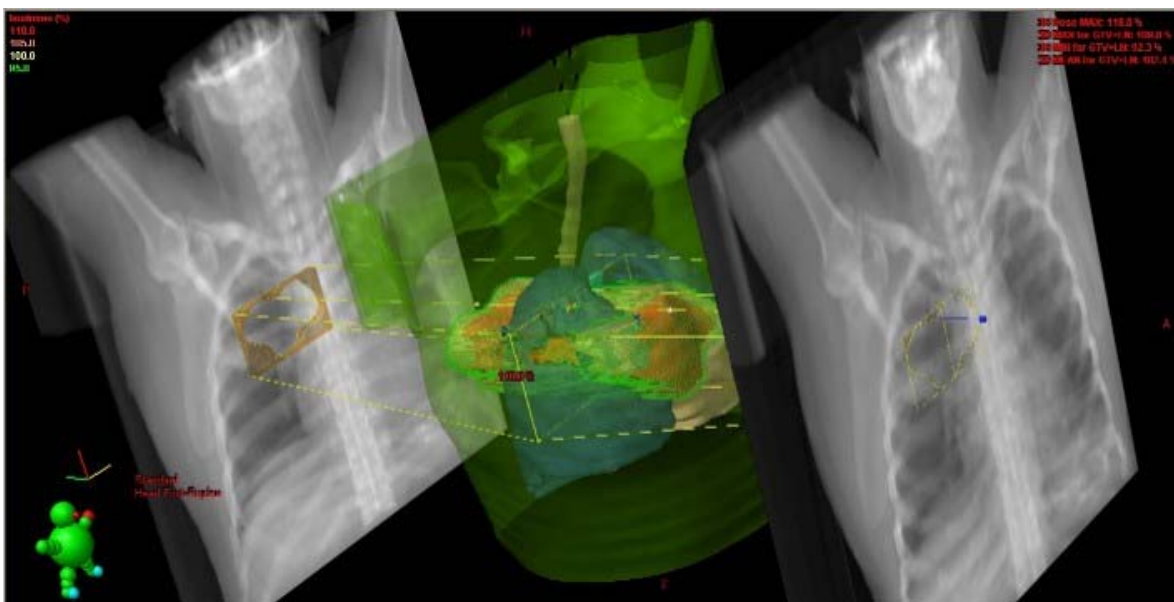
-Christopher Robin

Figure 3. Contours of Normal Organs and the Gross Tumor Volume



After the normal tissue volumes and gross tumor volume have been defined, the tumor is more clearly seen in relation to other organs. The dosimetrist or radiation oncologist set up portals or fields that encompass the gross tumor volume and the involved mediastinal lymph nodes. The mediastinum is a space in the middle of the chest that includes the esophagus, trachea, and large blood vessels above the heart; this space is rich in lymph nodes and lymph vessels, making it a common place for lung cancer to spread.³

Figure 4. Computer Generated Image of Chest Fields

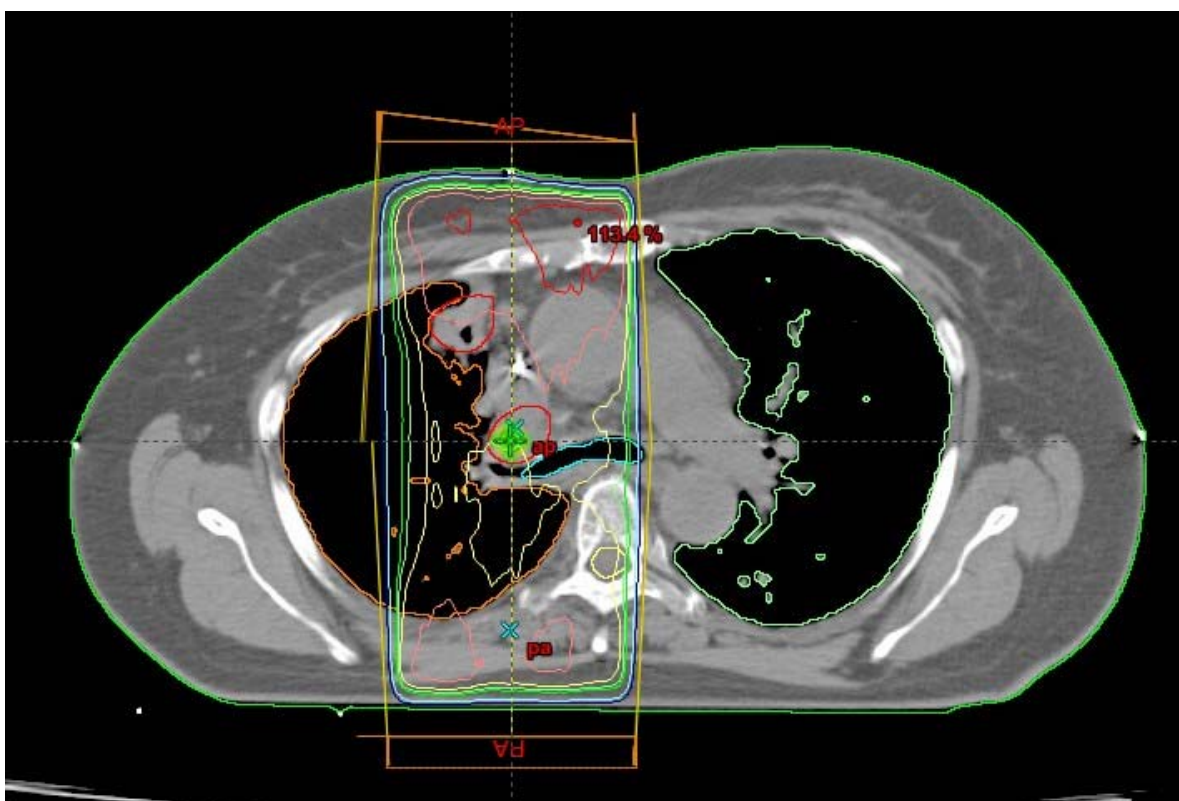


Three-Dimensional Conformal Radiation Therapy

The classic method used to treat lung cancer involves two fields: one field is oriented facing the patient's front chest (anteroposterior [AP]) and one field is oriented facing the patient's back (posteroanterior [PA]). The term AP/PA is used to describe this setup (Figure 4).

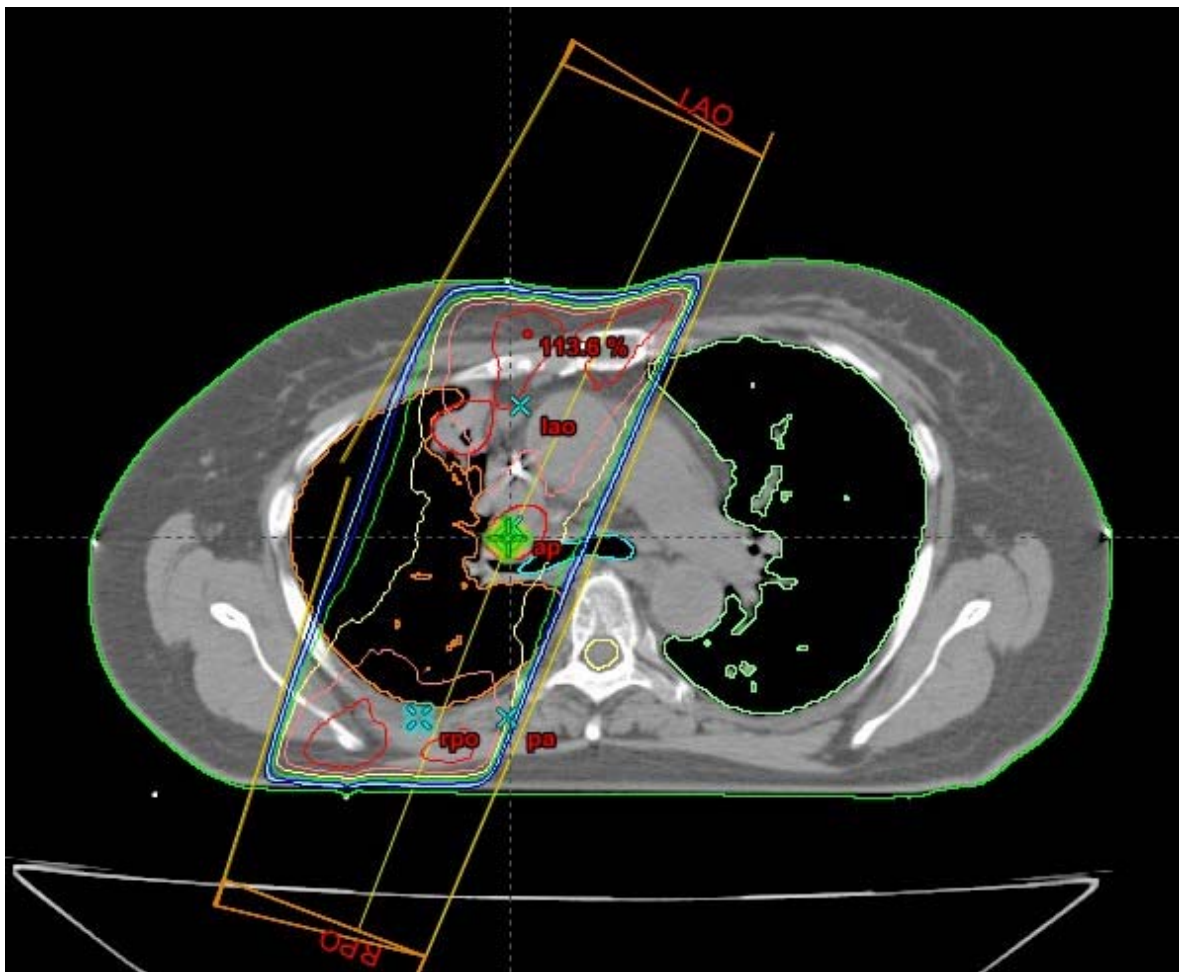
The initial AP/PA fields frequently include the spinal cord (Figure 5a). The spinal cord can usually tolerate 5000 cGy before the risk of spinal cord damage occurs. Radiation oncologists usually aim to keep the spinal dose below 4500 to 5000 cGy but may use a lower dose when chemotherapy is used concurrently with radiation. Most lung cancer treatments involve doses of 6000 to 6600 cGy, so the patient cannot be treated using AP/PA fields for the entire treatment. Therefore, the patient is treated using AP/PA fields to a dose between 4000 to 5000 cGy, and then the fields must be modified. As you can see from Figure 5a, the radiation dose is shaped more like a rectangle and results in some normal lung getting the similar doses as the tumor volume.

Figure 5a. Orientation of AP/PA Fields Including the Spinal Cord



The modified fields are called the off-cord boost. The typical method of designing an off-cord boost is to change the angle of the fields to oblique fields that are diagonal and avoid the spinal cord (Figure 5b). Attempts are made to include the involved lymph nodes with the gross tumor volume and safely avoid the spinal cord. However, if this is not possible, the off-cord boost may treat only the gross tumor volume. The inclusion of the involved lymph nodes in the off-cord boost can sometimes be done with the use of intensity modulated radiation therapy.

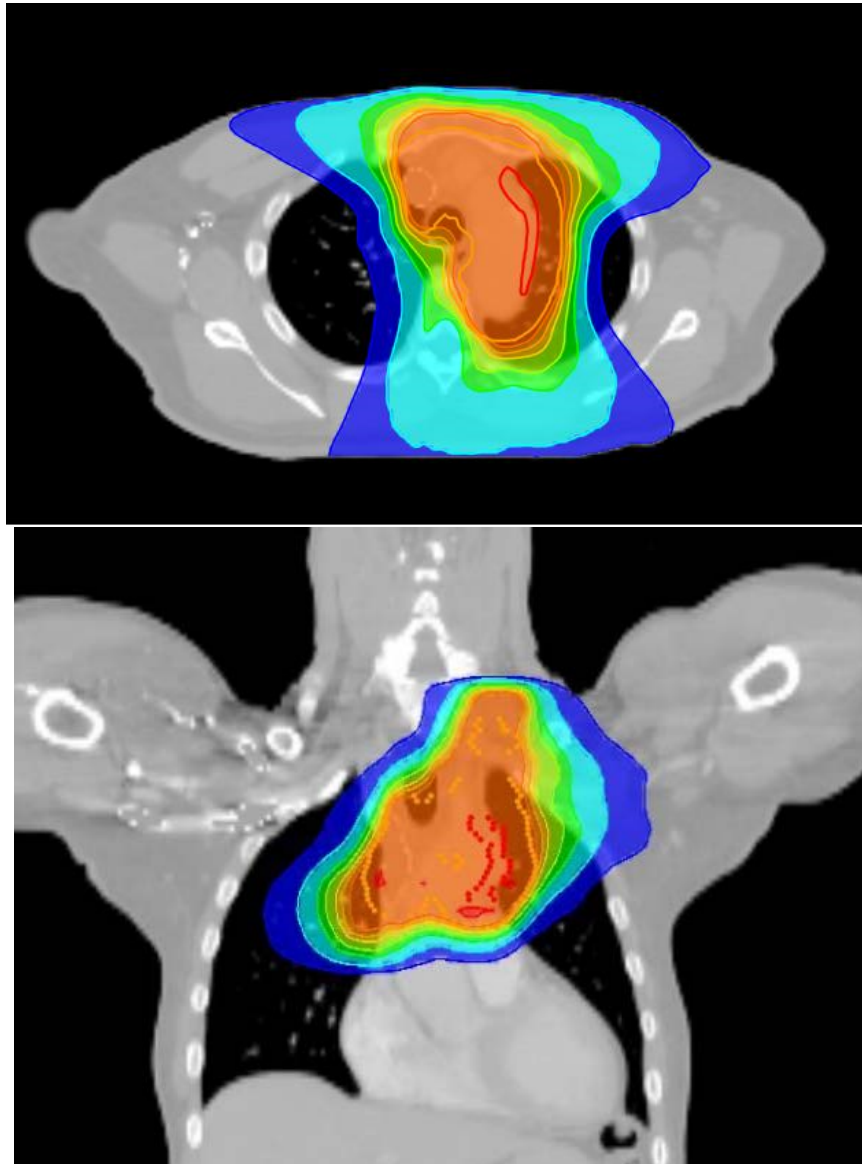
Figure 5b. Oblique Fields Angled to Avoid the Spinal Cord



Intensity Modulated Radiation Therapy

A technique known as intensity-modulated radiation therapy (IMRT), sometimes called tomotherapy, uses multiple beams or fields directed at the gross tumor volume and involved lymph nodes, and is becoming a recognized standard technique used to treat lung cancer. A 1.0 to 2.0 cm margin frequently is placed around the visible tumor to account for tumor movement (from breathing, setup variation, and patient motion). IMRT has been a popular method of treating lung cancers because the intensity of each beam directed at the tumor can be varied to where the sum of all the beams adds up to a dose cloud that better conforms to the shape of the tumor (Figure 6). Although IMRT allows a radiation oncologist to spare more normal lung and other normal tissues from the high dose meant for the tumor, it spreads low dose radiation to a larger area. Despite this, IMRT can dose to any organ and can limit the radiation dose to normal organs that do not need to be radiated. The technical aspects of IMRT are beyond the scope of this chapter, but a helpful website with information on IMRT can be found at <http://www.radiologyinfo.org/en/info.cfm?pg=imrt>.

Figure 6. Rendering of Doses in an IMRT Plan



Images courtesy of Steve Rhodes, M.S., R.T.(T), CMD

When the field designs have been completed, the dosimetrist will calculate how effective the fields may provide the radiation dose to the gross tumor volume. The dosimetrist will also calculate how much radiation the surrounding tissues are receiving, such as the spinal cord, heart, and lungs. If any of these tissues receive radiation beyond a maximum threshold, then the fields must be adjusted. The V20 is the volume of both lungs that receive ≥ 20 Gy (2000 cGy); dosimetrists attempt to keep the V20 below 30% because the risk of a serious side effect known as radiation pneumonitis increases dramatically if $V20 > 35\%$.⁴

After the treatment plan is completed, the patient returns to the radiation therapy department for a block check or verification procedure (Figure 7). The patient is placed on the actual treatment machine (linear accelerator) in the same position as in the simulation CT scanner. Radiographs are made and reviewed to make sure that the images match the images on the planning CT scan and are consistent with the CT based treatment plan. Many treatment centers perform a low energy CT

scan called a cone beam CT (CBCT) on the treatment table and overlay this CT with the planning CT scan to give a more precise confirmation of the accuracy of the field being treated and to enable any needed adjustments because of setup variations (see section on Quality Assurance).

Figure 7. A Block Check or Verification Before Starting Treatment



Treatment

Radiation treatment usually is started the day after the block check or verification. For most lung cancer patients, radiation is given every day from Monday to Friday, with weekends off, for approximately seven weeks. The patient is on the treatment table receiving radiation for 5 to 10 minutes (Figure 8) and usually is in the department for 30 minutes or less, to include arrival at the waiting room, changing into a gown, getting in the treatment position on the treatment table, and having the radiation therapist make any needed adjustments.

“Courage doesn’t always roar, sometimes it’s the quiet voice at the end of the day whispering, I will try again tomorrow.”

- Mary Anne Radmacher

Figure 8. A Patient on the Table of a Linear Accelerator Receiving Radiation Treatment



The patient will meet with the radiation oncologist once a week on a specified day to review how the patient is feeling. During these weekly visits, the patient can ask any questions that may not have been addressed during the consultation. The radiation oncologist will check to see if there are any side effects from the radiation treatment and may prescribe medication to help with these side effects.

Quality Assurance

Traditionally, an X-ray is taken every five treatments with a beam's eye view of the treatment fields. The radiation oncologist would compare this X-ray to images (digitally reconstructed radiographs, DRR's) generated from the planning CT scan with the treatment fields in place to ensure that the tumor is being targeted accurately. It is difficult to see actual organs in these films, with mainly bones serving as landmarks for the treatment fields. If the fields are off by more than 5 to 10 mm, the radiation oncologist will instruct the radiation therapist to make a shift in the direction(s) to offset the difference. This technique has largely been replaced by image-guided radiation therapy (IGRT) with onboard cone-beam computed tomography (CBCT) in which a low energy CT scan is done prior to every treatment and aligned to the treatment planning CT scan. This form of IGRT has become very popular and allows the radiation therapist to more realistically align the patient's daily anatomy to the treatment planning CT structures, instead of just bones.⁵ (Figure 9 and 10)

Figure 9: (Left) A digital reconstructed radiograph (DRR), reconstructed from the patient's planning simulation CT and (Right) a port film taken from the linear accelerator with the patient on the table. Note the port film is similar to a plain X-ray and lacks detail in soft tissues, so the physician relies on bones to determine the accuracy of the field.

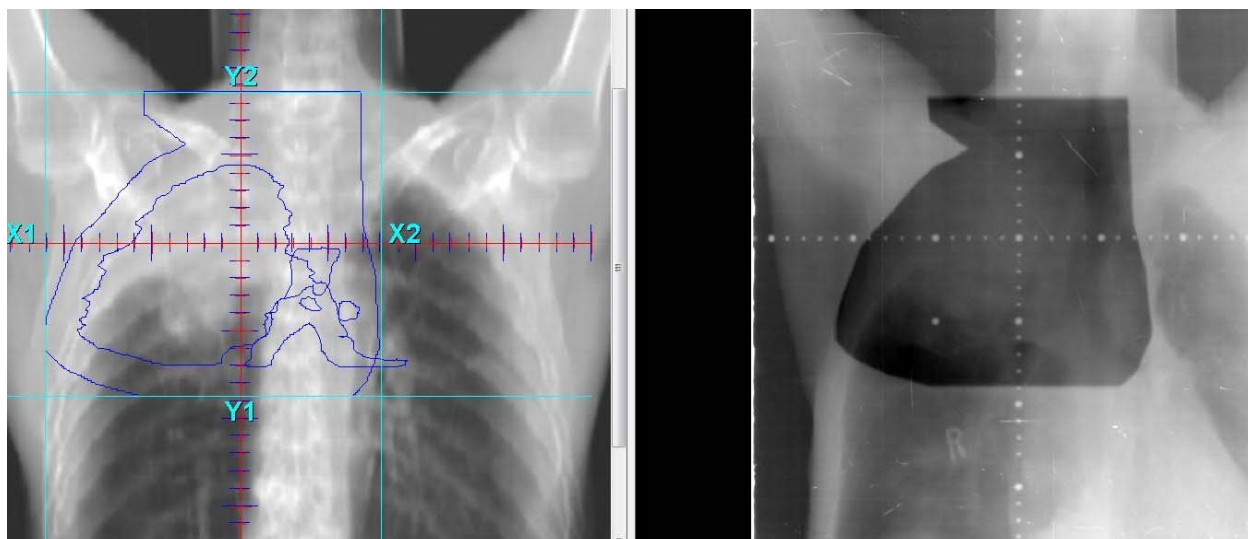
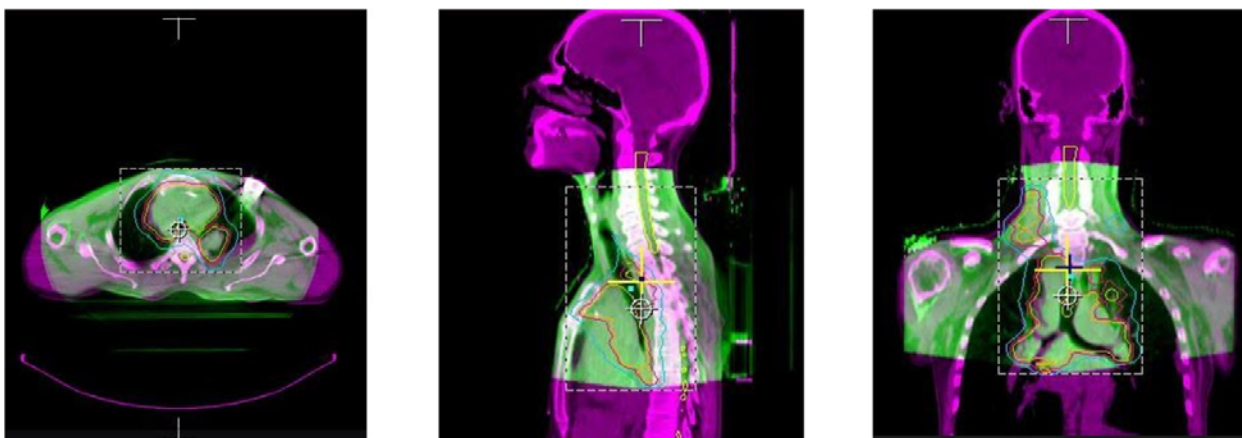


Figure 10: Modern image guided radiation therapy (IGRT) with the use of cone beam CT. The purple images are taken from the patient's planning simulation CT and the green images are the cone beam CT taken from the linear accelerator with the patient on the table. Note the increased detail and ability to see the organs and tumor in 3 different planes.



Radiation Therapy for Different Stages

Stage I and II Non-Small Cell Lung Cancer

Surgery, usually a lobectomy, is the typical treatment for Stage I and II non-small cell lung cancer. However, not all patients have surgery, either because of a personal preference to avoid surgery or because of medical conditions, such as severe emphysema or heart disease, that increase the risk of surgery and anesthesia. If surgery cannot be done for stage I or II non-small cell lung cancer, radiation therapy is a good alternative.

Conventional Radiation

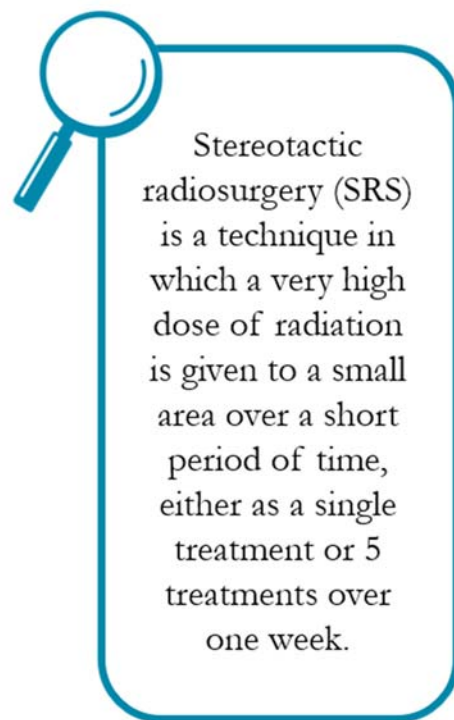
In centers that do not have access to stereotactic radiation techniques, conventional radiation therapy for stage I and II non-small cell lung cancer is still an accepted treatment. Conventional radiation for lung cancer gives a total dose of 6600 to 7000 cGy to the lung tumor volume, in doses of 180 to 200 cGy per day over seven weeks. Stage I and II non-small cell lung cancers have not spread to the lymph nodes in the middle of the chest between the lungs (mediastinum), so only the lung tumor is treated, making the amount of tissue radiated much smaller.⁶

Many patients cannot commit to a 7-week course of daily radiation therapy, especially if they must travel long distances to reach a radiation treatment facility. In these cases, effective doses of radiation can be given over a shorter period if larger doses are given per treatment, a technique called hypofractionation. However, larger doses per treatment may result in more long-term tissue scarring, especially in long term survivors. Therefore, to minimize the effect of lung scarring caused by hypofractionation, radiation must be limited to a much smaller volume of tissue. For fragile patients who are too sick to come for treatment for seven weeks, hypofractionation with 4800 cGy in fractions of 400 cGy over 12 treatments (2 weeks and 2 days) has been used successfully.⁷

Stereotactic Body Radiation Therapy

Stereotactic radiosurgery (SRS) is a technique in which a very high dose of radiation is given to a small area over a short period of time, either as a single treatment or five treatments over one week. The term SRS has always been used to describe this technique for brain tumors.

Radiosurgery, contrary to what the term implies, is not surgery and does not involve any incision or cutting by the radiation oncologist, but the high dose of radiation results in the killing of the tumor as if it was surgically removed. The high precision of the multiple beams used in stereotactic radiosurgery results in the margins around the gross tumor volume being much smaller (0.5 cm to 1.0 cm) than with typical radiation therapy techniques (Figure 11). Gamma Knife, CyberKnife, and linear accelerator-based SRS (Tomotherapy, VMAT, and Rapid Arc) are examples of proprietary methods of delivering SRS. Gamma Knife is only used for SRS to brain lesions.



Stereotactic radiosurgery for tumors *outside of the brain* is known as stereotactic body radiation therapy (SBRT), stereotactic ablative radiotherapy (SABR), or extracranial radioablation (ECRA). SBRT is the most common term to describe any type of stereotactic radiosurgical technique to treat tumors in the spine, lung, liver, pancreas, adrenal glands, or lymph nodes—anything outside the brain. This method is widely used for patients with stage I or II non-small cell lung cancer (who are either too frail for surgery or do not want surgery), with comparable or better outcomes when compared with the conventional radiation therapy techniques described above.^{6,8} Dose schedules in

stereotactic body radiation therapy includes either a total dose of 6000 cGy given in 3 treatments of 2000 cGy over a period of 2 weeks, a total dose of 4800 cGy given in 4 treatments of 1200 cGy, or a total dose of 5000 cGy given in 5 treatments of 1000 cGy daily over 1 week. A patient may be treated with SBRT for non-small cell lung cancer if the lung tumor is ≤ 5 cm in greatest diameter and peripheral to the mediastinum (more to the side of the chest rather than the middle).⁹ CyberKnife and linear accelerator based SRS (Tomotherapy, VMAT, and Rapid Arc), are examples of proprietary methods of delivering SBRT. Gamma Knife is not used in SBRT because it is only used for brain tumors.

Figure 11. A Rendering of Dose and Beams in a SBRT Plan

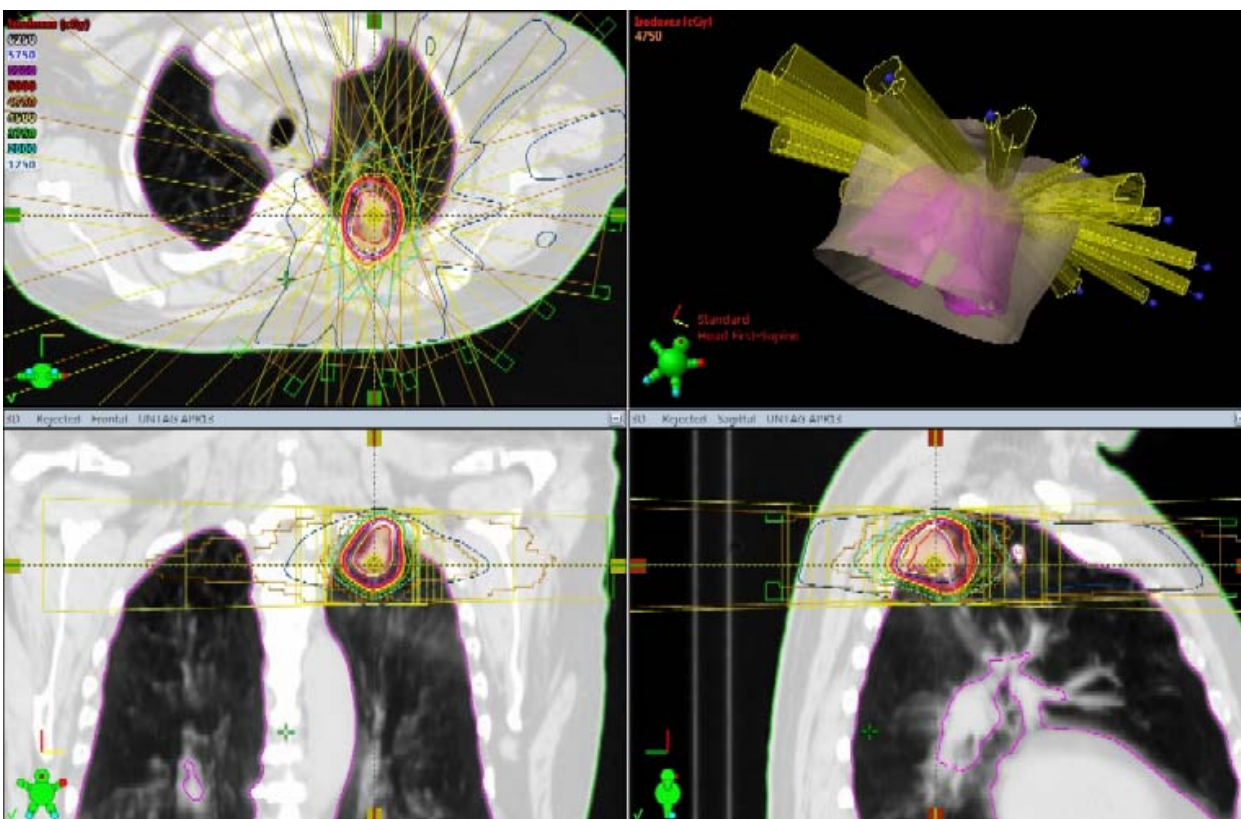


Image courtesy of Steve Rhodes, M.S., R.T.(T), CMD

Stage III Non-Small Cell Lung Cancer

Most cases of stage IIIA and IIIB non-small cell lung cancer are inoperable (except for some cases of stage IIIA cancer) because of the extent of disease. For patients with inoperable stage IIIA and stage IIIB non-small cell lung cancer, recommendations for treatment in the National Comprehensive Cancer Network include concurrent chemotherapy and chest radiation therapy. The first doses of chemotherapy and radiation therapy are given on the same day. Depending on the drug selected, the chemotherapy is given at varying intervals, but radiation therapy is given daily. The typical dose of radiation therapy, when given with chemotherapy, is 6000 to 7000 cGy given in 180 to 200 cGy fractions over seven weeks.¹⁰ The typical intravenous chemotherapy regimens given in combination with radiation therapy are: (1) cisplatin (days 1, 8, 29, and 36) and etoposide

(days 1 to 5 and 29 to 33); (2) cisplatin (weeks 1 and 4) and vinblastine (weekly); or (3) weekly carboplatin and paclitaxel.¹⁰

For stage III non-small cell lung cancer that is marginally or borderline operable, measures can be taken to increase the potential for success with surgery. This can include giving chemotherapy or chemotherapy with radiation therapy before surgery to decrease the size of the lung mass and mediastinal lymph nodes. If radiation is given with chemotherapy with the intention of doing surgery later, the radiation dose is only 4500 cGy, and the patient has another CT scan with or without a positron emission tomography (PET) scan to evaluate response. If the tumor appears operable, then surgery is done. However, if the lung cancer remains inoperable, then the patient would be given further radiation for a total dose of 6300 cGy with chemotherapy, similar to other patients with inoperable non-small cell lung cancer.¹⁰

In some cases, in which surgery is done for a stage I or II non-small cell lung cancer, postoperative evaluation of the mediastinal lymph nodes that had been sampled during surgery may show these nodes to be positive for cancer. In this situation, the stage of non-small cell lung cancer is revised to stage III. For this patient, surgery alone is not sufficient treatment, and the patient will require chemotherapy and radiation.¹¹

If there is a suspicion that there is cancer remaining in the patient after surgery, demonstrated by a positive margin of resection (meaning there are cancer cells at the edge where the surgeon had excised the tumor), then radiation therapy (usually to a dose of 5000 cGy) is given with concurrent chemotherapy. If the surgery was complete with clear margins of resection (a ring of normal tissue surrounds the tumor), then the chemotherapy and radiation are given separately; typically, chemotherapy is given initially, followed by radiation therapy to a dose of 5000 cGy.¹⁰

Stage IV Non-Small Cell Lung Cancer

In stage IV non-small cell lung cancer, cancer has spread to the opposite lung, metastasized to a different organ (such as the liver, brain, or bones), or produced fluid containing cancer cells within the space surrounding the lung (a condition known as a malignant pleural effusion). The primary treatment for patients with stage IV non-small cell lung cancer is chemotherapy. The various drugs used in stage IV non-small cell lung cancer are discussed in more detail in the chapter on chemotherapy for non-small cell lung cancer. See Chapter 2: *Systemic Therapy for Non-Small Cell Lung Cancer*.

Radiation therapy to the lung does not improve the lifespan of a patient with stage IV non-small cell lung cancer and is not routinely used in these cases. However, if a patient with stage IV cancer has a large lung mass that is causing chest pain, facial/neck/arm swelling, difficulty swallowing, or shortness of breath (known as superior vena cava syndrome), radiation therapy to the lung mass may be given, typically in doses from 3000 cGy (10 treatments of 300 cGy fractions over two weeks) to 5000 cGy (20 treatments of 250 cGy fractions over four weeks).¹²⁻¹³

Palliative Radiation Therapy for Sites of Metastases in Stage IV Non-Small Cell Lung Cancer

Stage IV lung cancers may frequently spread or metastasize to the brain. When metastases occur in multiple sites of the brain (usually more than five tumors), radiation therapy frequently is given to the entire brain to shrink the existing tumors and prevent new brain metastases from forming. The most common dose given for whole-brain radiation therapy is 3000 cGy (10 treatments of 300 cGy fractions over 2 weeks), although patients with a good performance status with estimated survival of more than 6 months can receive 3750 cGy (15 treatments of 250 cGy over 3 weeks), as a more "gentle" treatment that may result in less cognitive side effects, although there is no clinical trial data to support this. Side effects of whole-brain radiation therapy (WBRT) include fatigue, drowsiness, alteration in taste/smell, hair loss, and scalp itchiness. The primary long-term effect of WBRT is short term memory loss. WBRT in adults does not cause personality changes, Alzheimer's disease, or mental retardation. Typically, an engineer or accountant will have more difficulty doing math in their heads and will have to write things down. Although not widely used, memantine, a drug FDA approved to treat Alzheimer's dementia, has been shown to reduce the rate of decline in memory, executive function, and processing speed in patients receiving WBRT.¹⁴

If a patient has ≤ 3 brain metastases and all the lesions are ≤ 3 cm in diameter, the patient may have surgery to remove the metastases, followed by whole-brain radiation to prevent new tumors from forming,¹⁵ or followed by stereotactic radiosurgery (SRS) to the resection cavities (the "hole" left after tumor removal). The patient could also be treated with upfront stereotactic radiosurgery (SRS). Stereotactic radiosurgery for brain metastases has the advantage of allowing for less brain radiation, but the disadvantage that new brain metastases could form in areas that were not radiated. Nevertheless, with regular MRI brain imaging done every 3 to 4 months, patients can be monitored for any new brain metastases. SRS is becoming the preferred form of radiation therapy over WBRT for those with "limited" brain metastases (typically ≤ 5 , although this standard is changing).¹⁶ (Figure 12)

“Everything can be taken from a man but one thing: the last of human freedoms - to choose one's attitude in any given set of circumstances, to choose one's own way.

- Viktor E. Frankel

Figure 12. A Rendering of Dose and Beams in a SRS Plan

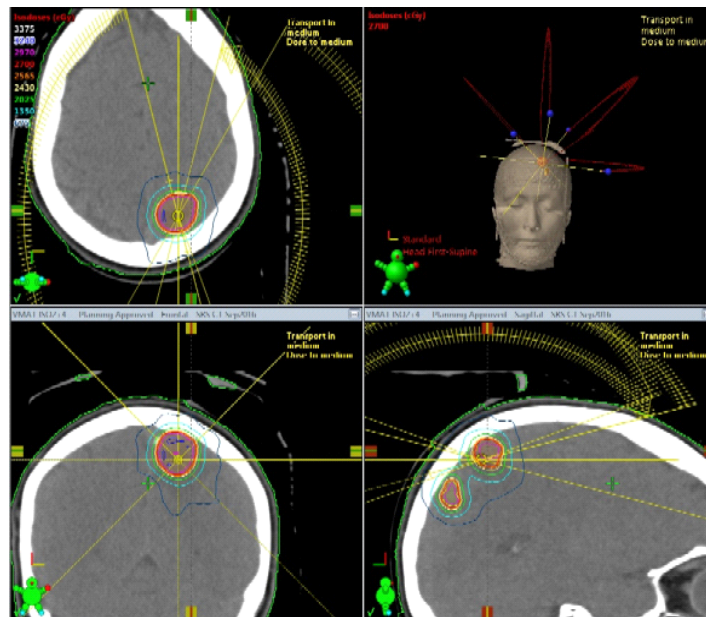
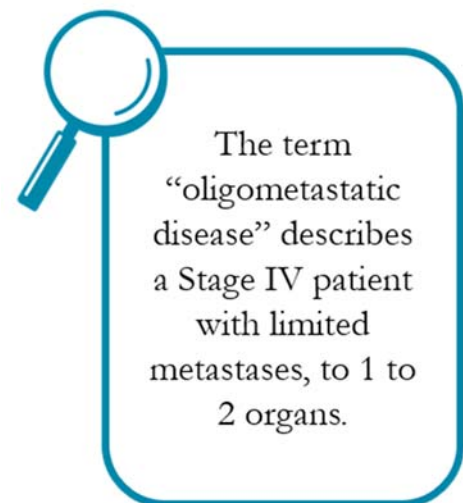


Image courtesy of Steve Rhodes, M.S., R.T.(T), CMD

When lung cancer spreads to the vertebrae, patients may experience severe back pain. Growing cancer could compress the spinal cord and cause paralysis. These metastases can be removed surgically, especially if there is only one metastatic lesion. In this case, radiation therapy is given 1 to 2 weeks after surgery to prevent cancer from recurring in the spine.¹⁷ If metastases are too extensive to remove surgically, radiation therapy alone is used, most commonly at a dose of 3000 cGy (10 treatments of 300 cGy fractions over two weeks). In cases where a previously treated vertebral body metastasis comes back, stereotactic body radiation therapy (SBRT) can be used to better avoid previously treated tissue and concentrate radiation to the areas involved by cancer, using techniques similar to SRS of the brain.

Lung cancer can also spread to the liver, adrenal glands, and bones. When this occurs while the patient is receiving systemic therapy (chemotherapy, biologic therapy, with or without immunotherapy), this is a sign that the cancer has become resistant to the drug(s). Radiation therapy (either conventional radiation or SBRT) can be used to treat these areas if surgery is not an option. Palliative radiation is effective in reducing or eliminating pain in patients where cancer has spread to any bone (ribs, hips, vertebra, etc.).

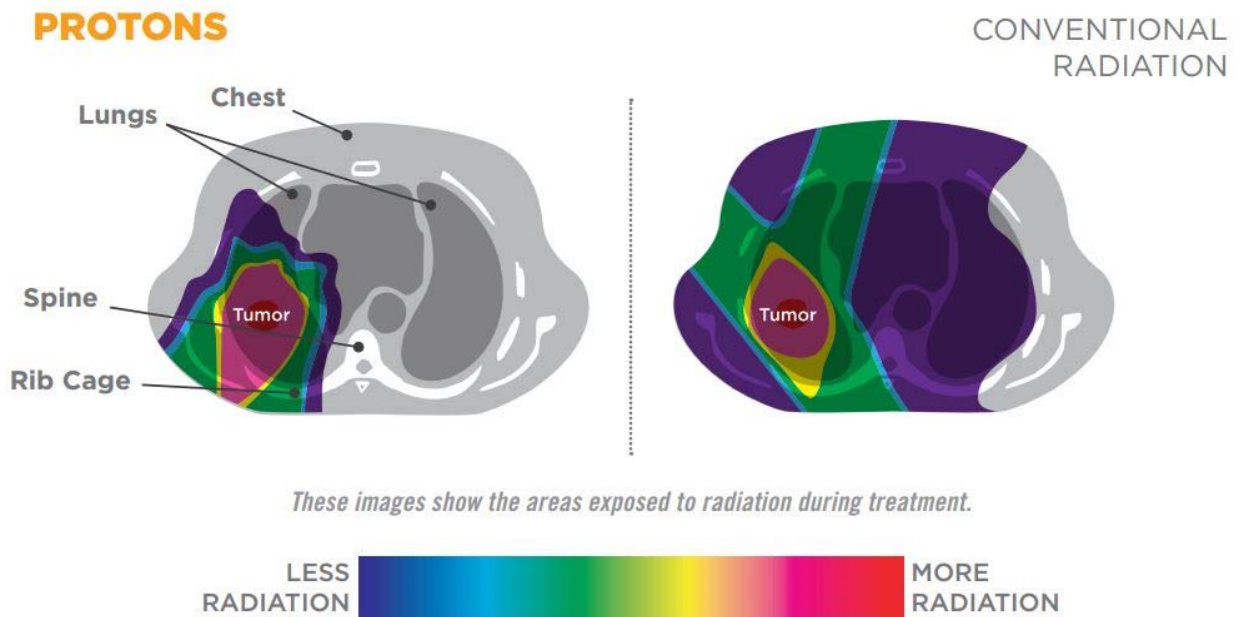
The term “oligometastatic disease” describes a Stage IV patient with limited metastases, to 1 to 2 organs. In the past, these patients were still treated with just systemic therapy, but research has shown that for patients with fewer than three metastatic tumors, and stable (not progressing) disease, radiation therapy to these affected areas improves survival (17 months) compared to getting systemic therapy alone (10 to 12 months).¹⁸



Alternate Forms of Radiation Therapy for Non-Small Cell Lung Cancer

Proton beam therapy is a form of external beam radiation therapy that uses protons (usually from a hydrogen atom) instead of x-rays. Proton beams do not have any exit dose beyond the target tumor. Therefore, the radiation from proton beams is deposited only along the path of the beam to the tumor, and no radiation is given behind the tumor, so the patient receives less radiation to nearby normal tissue. Proton beam therapy is available only in slightly over 20 centers in the United States and is used in unique situations, such as in children with brain or spinal tumors where it is critical to protect as much normal tissue from radiation.¹ In lung cancer, proton beam therapy is especially useful in patients who have previously been treated with conventional radiation therapy and need repeat treatment to the same area. (Figure 13).

Figure 13. A Rendering of Dose in a Proton Plan Versus a 3-D Conformal Plan



Graphic courtesy of Provision Center for Proton Therapy in Knoxville, TN | ProvisionProton.com

With brachytherapy, the radioactive sources are placed in or just next to the tumor. High dose rate brachytherapy involves the accurate placement of a powerful radiation source, usually iridium-192, into the tumor for several minutes through a tube called a catheter.¹ Endobronchial brachytherapy involves the placement of a catheter into a lung bronchus or bronchiole where there is a tumor. The iridium-192 source is placed into the catheter where it remains for a few minutes, exposing a small area of the lung to a high dose of radiation. Endobronchial high dose rate brachytherapy is useful for treating pain, shortness of breath, cough, and hemoptysis (coughing up of blood).¹⁹

Side Effects of Lung Radiation Therapy

Acute side effects occur when a patient is receiving lung radiation therapy with or without chemotherapy. These include redness and irritation of the skin overlying the radiation treatment portals; inflammation of the esophagus (esophagitis) causing heartburn or a feeling that something is stuck in the throat; irritation of the lung causing a dry cough; inflammation of the sac surrounding the heart causing chest pain (pericarditis); electric shock sensations in the low back or legs when bending the neck (Lhermitte sign); and generalized fatigue. These acute side effects typically resolve two weeks after completing chest radiation therapy.

With regards to the skin reaction over the skin of the chest corresponding to the treatment portals, the intensity of the reaction is typically increased when chemotherapy is given during the radiation treatment. The skin over the back (posterior chest) tends to be more affected than the front (anterior chest). Patients can get a sunburn-like reaction with a painful burning sensation that can progress to skin peeling (often called desquamation). Although the skin effects are well tolerated by most patients, a small number of patients can develop severe redness and skin peeling and require daily wound care. Fortunately, such severe skin reactions are not frequent. The skin heals fairly quickly after completing radiation, and most redness and peeling resolve in 4 to 6 weeks. By the 3-month mark, there may be a tan corresponding to the radiation treatment fields. Permanent skin scarring occasionally occurs in those with more severe skin reactions during treatment.

Subacute side effects occur 1 to 6 months after completing radiation therapy. These side effects are less frequent and may include radiation pneumonitis, which is inflammation of the lung that causes chest pain, fever, and cough.²⁰ As mentioned above in the section on treatment planning, radiation pneumonitis infrequently occurs, especially when the V20 (volume of both lungs receiving ≥ 20 Gy or 2000 cGy) is no more than 35%. Your radiation oncologist, dosimetrist, and physicist work hard to ensure that the least amount of radiation possible goes to normal lung without sacrificing coverage of the lung tumor. Treatment of radiation pneumonitis includes corticosteroids such as prednisone or dexamethasone.

Another rare subacute side effect is pericardial effusion in which fluid accumulates in the pericardium (the sac surrounding the heart), causing tamponade (pressure on the heart) with symptoms such as neck vein distention, shortness of breath, and a rapid heart rate. Pericardial effusions may resolve spontaneously, but in some cases, treatment may include needle aspiration to drain the excess fluid or diuretics.

Long-term side effects of lung radiation therapy include pulmonary fibrosis (permanent scarring of the radiated lung tissue), esophageal fibrosis and stricture (scarring and narrowing of the esophagus that causes difficulty swallowing and treated with esophageal dilation), constrictive pericarditis (shrinkage of the sac surrounding the heart, that may require surgical removal), and damage to the heart muscle and blood vessels that may increase the risk of heart failure and heart attack. These long-term side effects have become less common because modern radiation therapy techniques have resulted in better sparing of normal tissues and organs.

The authors wish to thank Steve Rhodes, BS RT(T) CMD, Debra Monaco, CMD, RT (R) (T), Barbara Agrimson, CMD BS RT (R)(T), and Paul H. Cooper, Phys, CMD for submitting some of the treatment planning images used in this chapter.



Questions to Ask Your Doctor about Radiation Treatment

- Why do I need radiation therapy?
- What is my treatment regimen and how long will it last?
- Can I continue my usual work and exercise schedule?
- Can I miss a few treatments?
- What are the side effects?

Notes

References

1. American Society for Radiation Oncology. Radiation Therapy for Cancer. Fairfax, VA: American Society for Radiation Oncology, 2009.
2. Zhang J, Xu GX, Shi C, et al. Development of a geometry-based respiratory motion-simulating patient model for radiation treatment dosimetry. *J Appl Clin Med Phys*. 2008;9(1):2700.
3. Kong FM, Ritter T, Quint DJ, et al. Consideration of Dose Limits for Organs at Risk of Thoracic Radiotherapy: Atlas for Lung, Proximal Bronchial Tree, Esophagus, Spinal Cord, Ribs, and Brachial Plexus. *Int J Radiat Oncol Biol Phys*. 2010 Oct 7. [Epub ahead of print].
4. Graham MV, Purdy JA, Emami B, et al. Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non-small cell lung cancer (NSCLC). *Int J Radiat Oncol Biol Phys*. 1999;45(2):323-9.
5. Nabavizadeh N, Elliott DA, Chen Y, et al. Image Guided Radiation Therapy (IGRT) Practice Patterns and IGRT's Impact on Workflow and Treatment Planning: Results from a National Survey of American Society for Radiation Oncology Members. *Int J Radiat Oncol Biol Phys*. 2016 Mar 15;94(4):850-7.
6. Chang JY, Bradley JD, Govindan R, et al. Inoperable Non-Small Cell Lung Cancer -Definitive Radiotherapy for Stage I/II. In: Halperin EC, Perez CA, Brady LW, eds. *Principles and Practice of Radiation Oncology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:1086-7.
7. Slotman BJ, Antonisse IE, Njo KH. Limited field irradiation in early stage (T1-2N0) non-small cell lung cancer. *Radiother Oncol*. 1996; 41:41-4.
8. Timmerman RD, Paulus R, Galvin J, et al. Stereotactic Body Radiation Therapy for Medically Inoperable Early-stage Lung Cancer Patients: Analysis of RTOG 0236. *Int J Radiat Oncol Biol Phys*. 2009; 75(3S):S3.
9. Timmerman R, McGarry R, Yiannoutsos C, et al. Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer. *J Clin Oncol*. 2006;24(30):4833-9.
10. Jabbari S, Hansen EK, Haas-Kogan DA. Non-small Cell Lung Cancer. In: *Handbook of Evidence-Based Radiation Oncology*, 2nd Ed. New York, NY: Springer; 2010:221-247.
11. Douillard JY, Rosell R, De Lena M, et al. Impact of postoperative radiation therapy on survival in patients with complete resection and stage I, II, or IIIA non-small-cell lung cancer treated with adjuvant chemotherapy: the adjuvant Navelbine International Trialist Association (ANITA) Randomized Trial. *Int J Radiat Oncol Biol Phys*. 2008;72(3):695-701.
12. Hayman JA, Abrahamse PH, Lakhani I, et al. Use of palliative radiotherapy among patients with metastatic non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2007;69(4):1001-7.
13. Tsuji SY, Wara WM. Palliation and Benign Conditions. In: *Handbook of Evidence-Based Radiation Oncology*. New York, NY: Springer; 1994:675-690.
14. Brown PD, Pugh S, Laack NN, et al. Memantine for the prevention of cognitive dysfunction in patients receiving whole-brain radiotherapy: a randomized, double-blind, placebo-controlled trial. *Neuro Oncol*. 2013 Oct;15(10):1429-37.
15. Patchell RA, Tibbs PA, Regine WF, et al. Postoperative radiotherapy in the treatment of single metastases to the brain: a randomized trial. *JAMA*. 1998;280(17):1485-9.
16. Yamamoto M, Serizawa T, Higuchi Y, et al. A Multi-institutional Prospective Observational Study of Stereotactic Radiosurgery for Patients with Multiple Brain Metastases (JLGK0901 Study Update): Irradiation-related Complications and Long-term Maintenance of Mini-Mental State Examination Scores. *Int J Radiat Oncol Biol Phys*. 2017 Sep 1;99(1):31-40.
17. Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet*. 2005;366(9486):643-8.
18. Gomez, D., Tang, C., Zhang, J. et al, Local consolidative therapy (LCT) improves overall survival (OS) compared to maintenance therapy/observation in oligometastatic non-small cell lung cancer (NSCLC): final results of a multicenter, randomized, controlled phase 2 trial. *Int J Radiat Oncol Biol Phys*. 2018; 102:1604

19. Nag S, Scruggs GR. Clinical Aspects and Applications of High-Dose-Rate Brachytherapy. In: Halperin EC, Perez CA, Brady LW, eds. *Principles and Practice of Radiation Oncology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:560-582.
20. Chang JY, Bradley JD, Govindan R, Komaki R. Toxicity of Normal Tissue. In: Halperin EC, Perez CA, Brady LW, eds. *Principles and Practice of Radiation Oncology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:1102-4.