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The Evolving World of Modern Radiation Oncology: Part One

Introduction to Radiation Oncology

Radiation oncology is a board certified medical specialty. Basically, radiation oncologists use a variety of types of **controlled** radiation to treat cancers and some benign tumors and unusual growths in the body. For a doctor to practice in this specialty in the United States, he or she will first attend college for 4 years, then graduate from a medical school, which is an additional 4 years of education. Then, after receiving a doctoral degree in medicine, an additional 5 years of clinical residency training in radiation oncology must be successfully completed before a doctor can practice in this specialty area of cancer medicine. **(4 + 4 + 5 = 13 years of formal study are required to be able to do this work.)** Radiation oncology training includes training in general cancer medicine, applied cancer radiology, medical physics (specifically the physics of radiation), and radiobiology (the study of how radiation kills cancer cells and affects normal tissues and cells. Until the 1990s, 50% or more of patients treated by radiation oncologists had incurable advanced cancers. These patients were treated for "palliation"--for symptom management-- not for cure.

Today, many cancers such as breast, prostate, cervix, and colorectal cancers, are discovered by screening tests. These cancers are now often diagnosed at earlier stages, and have better opportunity for cure. So today, most radiation oncology doctors have 60% or more of their patients being treated for cure, and only the minority of patients are considered to be palliative cases. Radiation oncology in 2007 is an exceedingly dynamic and complex medical specialty playing a crucial role in both curative and palliative cancer care. The tool box available to the radiation oncologist has enlarged dramatically in the past 25 years. We will look at the tools of the radiation oncologist in this discussion. Then over the rest of the month we will discuss some of the common cancers treated with radiation therapy. We will discuss radiation side-effects and some of the results of therapy.

The Tools of the Radiation Oncologist

1. **External Beam Radiation Therapy (EBRT):**

The linear accelerator remains the workhorse of the radiation oncologist. This large, versatile electrical machine can make and deliver 6 or more different energies of radiation. Most machines will produce two or three photon beams, which are deeply penetrating x-rays—with energy levels ranging from 4 MillionVolts (MV) to 35 MV. Additionally, most machines will also produce superficially penetrating high energy electrons, which are a form of atomic particle radiation. Electrons penetrate tissue to a specific depth, and the energy of the electron beam will determine that depth. For example, an electron beam with energy of 6 Million electron Volts (MeV) will deliver most of its energy in the most superficial inch of skin and tissue. A 15 MeV beam will be used to treat down to 1 ½- 2 inches. Most modern accelerators will produce 5 electron beams—ranging from 6 MeV to 21 MeV. Electrons are very useful as single therapy for superficial tumors such as skin cancers. When mixed with photons, electrons play a role

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in the treatment for head and neck cancers, breast cancers, skin cancers, and other relatively non-deep tissue cancers.

Treatment Planning

Today, all curative-goal external beam radiation is planned in a computer-based virtual 3-dimensional fashion, using special planning CAT scans and specialized radiation planning computer software. For complex planning, especially after a cancer has been surgically removed, the radiation oncologist can use the patient's pre-operative diagnostic studies--CAT, MRI, and/or PET scans--which have the accurate location of the tumor mass, and directly "fuse" or overlay those studies to the radiation planning CAT scans. These fusion studies enable planning to be done with enormous precision, and have eliminated the problems that used to be common in radiation planning—lack of accuracy in finding where the tumor used to be, the area we call the tumor bed. Radiation oncology training was lengthened a full year in the last decade so that trainees could learn how to better use the modern diagnostic studies such as MRI scans and PET scans.

In addition to being able to better locate the tumor and direct the radiation with greater accuracy for planning, the actual delivery of radiation from the linear accelerator has improved tremendously in the last 15 years. In 1990 the average curative radiation plan utilized 2 to 4 large x-ray beams that focused on a large volume of patient body. The tumor-containing area and surrounding tissues were treated, but a large volume of healthy normal tissues was also treated with high radiation doses. These normal tissues were occaisionally damaged, and that damage was called the "side-effects." Some immediate side-effects of radiotherapy were temporary (occurring during the actual treatment course). Other, more serious side effects occurred later on. These late or chronic effects evolved for years after the radiation was completed. It was because of these late side-effects that radiation doses had to be limited. Late effects such as marked scarring, soft tissue and bone break-down, organ shrinkage and even organ failure were reported. Radiation researchers studied these complications, determined what types and doses of radiation caused the complications, and developed guidelines for radiation safety. Research from the 1930s through the 1990s provided radiation oncologists with the knowledge of what techniques were safe and what radiation doses would be safe for any one part of the body. Because radiation side -effects were often pretty serious, radiation doses and cures were limited and radiation was delivered fairly conservatively.

3-Dimensional and Intensity Modulated Treatments:

Over the last 15 years, the development of computer-based planning has allowed the radiation oncologist to devise much better, but more complex radiation plans. **3-D Conformal Radiation** treatments were the first step in complex CAT scan-based planning. 3D conformal plans generally use multiple (4-8) beams that literally, "shape" the radiation to the area of the anatomy that requires treatment. Another innovation in EBRT delivery is **Intensity Modulated Radiation Therapy (IMRT)**. This very labor-intensive form of therapy improves further on the 3-D conformal approach, breaking each of 5 to 12 beams into 10 or more "beamlets" (so that the IMRT plan may actually have

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50 to 120 beamlets) that creates even more customized distributions of the radiation through the patient's anatomy. The most obvious result from all this research was less side effects.

Now with less acute and late side-effects radiation oncologists began to see that they could give more radiation dose. Increasing the accuracy and the dose of radiation has provided better cancer control, better cure rates, and less risk. Today, radiation oncologists work to maximize the benefits of radiation, and also work with medical oncologists to use chemotherapy simultaneously with radiotherapy. For some cancers this combination of radiation and chemotherapy has cured more patients. But there are still side-effects-- the side-effects are not gone, but different.

The Lastest Innovations:

The latest innovation in the delivery of EBRT is delivering IMRT with ultimate precision using **Image Guided Radiation Therapy (IGRT**). Here, small digital CAT scan imaging processors are built onto the linear accelerator. Now on a daily basis the patient's anatomy can be evaluated and the radiation beams shifted appropriately to deliver intensity modulated radiation to within 1-3 mm (about 1/8 inch) accuracy.

In very large population centers innovative radiation machinery producing radioactive particles such as protons, neutrons, and other "heavy particle" radiation are available for specialty applications. New robotic machinery and electronic guidance therapy that uses live-time feedback loops to adjust the beams are currently commercially available. To date, most of these very expensive, physics labor-intensive modalities have yet to prove benefit over the more common and less glamorous linear accelerator.

The Evolving World of Modern Radiation Oncology: Part 2

In Part 1, we discussed the most common type of radition therapy used to fight cancer—external beam radiation therapy (EBRT). In EBRT the patient lies on a table under a large machine, a linear accelerator, and x-ray beams and electron beams deliver the radiation dose.
Here, we will discuss less common types of radiation that are also used by radiation oncologists:

Tools of the Radiation Oncologist (Continued)

1. BRACHYTHERAPY

Also known as "Implant" therapy, this specialized type of radiation utilizes a variety of "solid" radioactive materials, called radio-isotopes, to deliver therapeutic radiation. The radioisotopes come in an assortment of fairly small shapes-- pellets, seeds, needles, ribbons, etc. These little pieces of radiation are referred to as radioactive sources. Some of these sources are very high energy and are used for temporary placement into the patient's cancerous tissues. Other lower energy sources, can be placed permanently into the patient.

The selection of the type of surgical implantation and the specific radio-isotope to be used is determined by the radiation oncologist. For most implants the radiation doctor will work in an Operating Room with a surgeon. The surgeon will dissect the tissues to be implanted, aid in

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placement of the seed, needles, or hollow plastic sterile tubes (catheters), which are then used to actually hold the radioactive sources in place. Brachytherapy requires a high level of coordination between radiation and surgical specialists, medical physicists, and radiation safety specialists. Cancers in which brachytherapy has been particularly effective are prostate cancer, many gynecologic cancers, head and neck malignancies, and rare cancers of the extremities know as sarcomas.

2. Liquid/Pill forms of Radio-Isotope Therapy

In many communities these therapeutic radiation treatments are delivered by either radiation oncologists or diagnostic radiologists with specialty training in Nuclear Medicine. A variety of liquid radio-isotopes are used, usually but not always, in injectable form, to deliver radiation to specific organs in the body. For example, radioactive Samarium and Strontium molecules are injected into the veins. Both these molecules travel to the bone just like calcium. Once in the bones, these radioactive drugs deliver a localized radiation treatment directly into the bones. These treatments are used for prostate and breast cancer patients whose incurable cancer has spread throughout their bones. These drugs can provide tremendous pain relief for patients with this complication of advanced cancer.

Another commonly used isotope is Iodine-131, given in oral pill form to treat of thyroid cancer. In the healthy state, the thyroid gland takes up Iodine from our diet (especially from iodized salt). Certain thyroid cancers also continue to take up Iodine. So, a dose of special radioactive iodine, iodine-131 will carry its radiation right to the cancer cells and kill the cancer cells.

A truly innovative form of liquid radio-isotope therapy is known as radio-labeled monoclonal antibody therapy. While still in its infancy, this technology is truly one of the treatments of the Future. It uses special anti-tumor antibodies that are made in a laboratory. And like our immune system antibodies that help fight infections, these antibodies will attach to, and help kill cancer cells. Attached to each of the antibodies is single radioactive molecule. These antibodies with their attached radiation are injected through the veins and subsequently end up attached to the tumor cells. The radioactive molecule is thus brought in contact with the cancer cell and can deliver its radiation dose directly to the tumor cells—thus "sparing" normal tissues from high doses of radiation. So far, two radiolabeled antibodies are commercially available, both used for the
treatment of Non-Hodgkin's lymphomas. Many other radiolabeled monoclonal
antibodies are in the research pipeline.

Conclusions

Radiation has been used as a therapeutic modality for only the last century. In the last two decades, with the advent of computer-based imaging and planning, radiation oncology has become a really dynamic medical
specialty. The modern radiation oncologist is trained to play a crucial
role in the evaluation and therapeutic management of the cancer patient.

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Radiation oncologist will work with surgeons and medical oncologists to develop a modern cancer treatment program for each patient. Since there are so many different types of cancer, the radiation oncologist has a diverse set of radiation tools from which to select the best technique for each patient. The ability to fine-tune the various forms of radiation has made modern therapeutic radiation remarkably less toxic and easier to combine with surgery and chemotherapy. These innovations have in many cases, not only increased the cure, but improved the quality of life and life functions for patients with cancer.

Radiation Therapy for the Brain

Introduction to Brain Tumors:

There are many types of brain tumors and tragically, they occur in all age groups. Brain tumors are particularly common in children, and are the most common "solid" tumor of childhood, with only leukemia (a "liquid" tumor of the blood) being more frequent. The most common tests used to diagnose brain tumors are MRI scans of the brain and CAT scans of brain. The largest variety of types of brain tumors arise in the pediatric group. Adults, in general, are affected with just 2 or 3 basic types of tumors, known as astrocytomas or gliomas.

Symptoms of Brain Tumors:

Headaches, nausea and vomiting, seizures, stroke-like symptoms with loss of function of part of the body—including speech, behavior, change in personality, paralysis, numbness of part of the face or body.

Surgical Treatment:

Radiation therapy plays a role in the management of the majority of types of brain tumors. The initial treatment for most tumors that arise from brain tissues (also called primary brain tumors) is a surgical biopsy and, when possible, removal of the tumor. Brain surgeons (neurosurgeons) are often must limit how much surgery they perform because of the precious nature of brain tissue. Because removal of brain tissue is limited, radiation therapy is then used after surgery to eliminate tumor cells that are left behind. Other common brain tumors are cancers that spread to the brain from other parts of the body (also called secondary brain tumors or brain metastases). The cancers that tend to spread to the brain are lung cancers and breast cancers, most commonly, but any type of cancer may spread into the brain, especially after the cancer has spread through the rest of the body. When brain metastases occur, often many small tumors evident spread throughout the brain.

Radiotherapy for Brain tumors:

The types, doses, and amount of brain tissue that is irradiated varies with the type of tumor. For metastasis to the brain a common treatment is therapy to the whole brain. In the setting of widespread cancer, these treatments are palliative—that is not curative—and the goal is to relieve the patient's symptoms. Whole brain irradiation is delivered over a one to 4 week time course. The course of treatment varies with the cancer type, and the state of health of the

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patient. For some patients with only one or two metastatic brain lesions, and who have no other active cancer in their body, more aggressive treatment is available, including surgery to remove the lesions, and highly focused, intense radiation called stereotactic brain irradiation.

Primary brain tumors are usually treated with partial brain irradiation. Care is taken by the radiation oncologist to limit how much healthy brain receives high dose radiation. Unlike metastases, most primary brain tumors are treated with curative goals and techniques. The radiation doctor will use the pre-operative MRI scans to map out the area that needs to be irradiated. The particular type of brain tumor, especially in children, determines the dose of radiation that is used, as well as the extent of brain that needs to be treated. Most courses of curative brain irradiation will be between 4 and 7 weeks of daily treatment.

Side-effects of brain irradiation:

Since the radiation has to pass through the skin of the scalp to get to the brain, the skin is an innocent bystander with respect to side-effects. The most common side-effect of scalp irradiation is loss of the hair. If the whole brain is being treated, then hair loss of the entire scalp occurs. With partial brain irradiation, there will be a more patchy hair loss. Regrowth of the hair depends on the dose of radiation that the skin receives. For most patients, the hair falls out approximately 3 weeks after the start of radiation, and tends to grow back 3 to 6 months after the completion of radiation. Other skin side effects are a sun-burn like reaction of the scalp.

The brain is usually quite symptomatic from the tumor, and if surgery has been performed, from the surgical procedure. Most patients with brain tumors will have a certain degree of brain swelling, which causes headache, nausea, vomiting, and seizures. These patients will be on high doses of a steroid drug, known as dexamethasone to reduce this swelling.

When radiation is started, 2-3 weeks after surgery, it may cause some additional brain swelling, and the radiation oncologist will adjust the medications appropriately. In general, brain swelling and fatigue are the only side-effects of brain radiotherapy during the course of treatment.

The Sleepy Syndrome

After the completion of brain irradiation, especially is patients who are cured, there are potential side-effects that can occur. In most children who receive brain irradiation, and in a minority of adults, a very peculiar side effect know as the “Somnolence (or Sleepy) Syndrome” may occur about 1 month after radiation to the brain is over. This syndrome is benign, in that it is temporary and causes no permanent brain damage.

However, for parents of a child who has just gone through brain surgery and a course of irradiation, the Sleepy Syndrome is very distressing. The patient becomes very sleepy, and for about 3-4 weeks, that is all they want to do—sleep. The sleepy syndrome results from an inflammatory reaction in the neurons of the brain. After the brain has recovered from the syndrome, the symptoms do not reoccur.

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For most adults who have had brain radiotherapy, there is a steady recovery of energy and function. Since the adult brain is fully grown, most adults will not experience any further brain dysfunction after treatments are completed.
Children, on the other hand, because their brains are still growing, are at risk for delayed radiation effects of slowing of the intellectual capacity over time. The degree of the impairment depends on the age of the child at the time of radiotherapy, with very young children much more susceptible than are teenagers. In the last 10-15 years pediatric brain tumor specialists have found certain chemotherapy drugs that will slow down the growth of several types of brain tumors in children. By putting the youngest children on these drugs, often for years, the brain will be allowed to mature before radiation becomes absolutely necessary.

Some notes on Stereotactic Brain Irradiation:

This specialized type of radiation generally gives one very intensive treatment to a very small part of the brain. This therapy is used for patients will a limited number of brain metastases (1-4), very small primary brain tumors in very critical parts of the brain that cannot be removed surgically, and some benign brain conditions. The benign lesion are several. One is a condition known as trigeminal neuralgia, which is a very painful disease in which a large nerve that supplies sensation to the face sends out inappropriate severe pain signals. Stereotactic radiation can directly target this nerve and eliminate the pain signal fibers. Another condition that benefits from stereotactic treatment is Arterio-venous Malformations (AVM). AVMs are very abnormal collections of blood vessels that form in the brain, and very often hemorrhage, causing devastating strokes. Stereotactic irradiation can cause these blood vessels to scar down, decreasing the need for surgery especially in parts of the brain that are difficult to access with surgery. Stereotactic irradiation has very few side effects in patients who are selected carefully and treated by a team of specialists who use this therapy with some frequency.

Results Of Therapy

Compared to the past, today a vast majority of children with brain tumors are cured with modern treatment. Unfortunately, the most common brain tumor of adulthood, known as high grade astrocytoma. Still remains a highly aggressive, lethal cancer. The good new is tht brain tumors remain an area of very intense research, with lots of hopeful discoveries in the works.

In the next discussion, we will move south, and discuss the much more common cancers of the head and neck area.

Radiation Therapies of the Mouth, Tongue, and Throat (i.e. Head and Neck Cancers) Part 1

Introduction

Cancers of the soft, moist skin-like lining of the mouth, tongue, and throat are collectively known as Head and Neck Cancers. These cancers, generally, are diseases of adults. The lining tissue of these structures is a skin-like tissue known as the squamous mucosa. The term mucosa indicates that these tissues are “moist” in that they contain glands that secrete mucous and saliva.

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Because the tissue type is squamous type, the common cancers of this part of the anatomy are known as squamous carcinomas, or squamous cancers. There are a few other types of cancers of the head and neck, such as salivary gland carcinomas, but these are relatively rare compared to the squamous carcinomas. Therefore, we will restrict our discussion to the common squamous cancers.

Causes of Head and Neck Cancers: TOBACCO Squamous tumors of the head and neck are, in general, caused by lifestyle behaviors—habits, specifically, using tobacco and alcohol. Tobacco, in all its forms is the most serious cause of these cancers. Tobacco is a cancer-causing agent, a carcinogen, for squamous tumors of the head and neck. When an individual smokes or chews tobacco a total of 40 different chemicals in the smoke or chew act as toxins on the mouth and throat lining cells! Years of exposure to these toxins ultimately give rise to the formation of the cancers. The addition of alcohol to these carcinogenic
(cancer-causing) chemicals just speeds up the process. In the last few years we have also learned that the Human Papilloma Virus (HPV), the same carcinogenic virus that causes squamous cancer of the female cervix (a gynecologic cancer), also causes certain specific types of squamous cancer of the back of the mouth!! However, today the most common cause of head and neck cancers remains TOBACCO.

The type of tobacco use can determine the location of the growth of the cancer. For example, pipe smokers are more likely to get cancers of the lip and front of the mouth. Cigar smokers tend to get cancers in the floor of the mouth, the hollow, under the tongue, where their spittle pools. Tobacco chewers are more likely to get cancers of the mouth, the gums, under the tongue, and in the cheek pouches, where the chewer tucks his chew.
Cigarette smokers can get cancers anywhere the smoke can go. So, we see smokers developing cancers in their nasal passageways, mouth, tongue, throat, and voice box. Because the lung airways and the esophagus are also lined with squamous tissues, cigarette smokers also have very high risks of developing squamous carcinoma of the lung and esophagus as well. So, just as we see the risk of lung cancer dropping when people quit smoking, we see the risk of head and neck cancers also drop when smokers or chewers of tobacco quit.

The symptoms of Head and Neck Cancers:
A sore or ulcer in the mouth or tongue that won't heal. Pain in the jaw, throat, or ear. Pain with chewing or swallowing; difficulty swallowing.
Hoarseness, or change in quality and characteristics of the voice.
Swellings in the neck—a lump or lumps that may or may not be painful.
Rarely do we see patients presenting with bleeding from the mouth or throat.
Frequently, especially with throat cancers, the patient may have an irritative cough, and occasionally, the tumor may get so large that the tumor blocks off the wind pipe, causing choking.

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In the next section, we will look closer at treatment, side-effects from treatment, and goals of treatment.

Radiation Therapies of the Mouth, Tongue, and Throat (i.e. Head and Neck Cancers) Part 2

Previously, we discussed the types and causes of cancers of the Head and Neck region. Now we will look more closely at treatment, side-effects and cure.

Treatment for Head and Neck Cancers:

This part of the anatomy is very complex, and the treatments vary from site to site. In general, unless the cancer is very small and limited, surgery, radiation, and chemotherapy are required to some degree for most of these tumors. Head and neck cancers are extremely aggressive and are highly lethal. The treatment has to be equally aggressive in order to have an opportunity for cure. Surgery is used very selectively because surgical removal of some of the head and neck anatomy—especially the voice box and the tongue—causes devastating physical loss of function and psychological adjustment problems. Surgery, such as an emergency tracheotomy (a surgical hole in the windpipe to allow breathing), can provide life saving intervention to a patient who is strangling to death from his cancer. Most surgery is not done as an emergency, but rather is a planned, highly technical cancer procedure designed to remove as much cancer as possible.

Today, following successful surgery, or as an alternative to surgery, high dose radiotherapy is used for the majority of head and neck cancers. In order to make the radiation even more effective for really large cancers additional drug therapies are given at the same time. The simultaneous use of chemotherapy and other drugs called tumor growth inhibitors can improve the cure rates by 10-20 %. This enhanced cure is truly important, particularly when the oncology doctors are trying to save not only the patient's life, but their voice, or their ability to swallow.

Radiation Therapy

Radiation therapy to the head and neck is extremely complex, and generally has a great deal of side-effects. The complex organs of speaking, chewing, swallowing, and facial movement and expression have a very rich nerve supply, especially the nerves of sensation. Thus, when these organs develop radiation side-effects, the nervous system perceives these side-effects very intensely, and this is perceived as pain.

Also, these organs have several different functions, and each of these functions can be altered by the radiation. For example, the tongue is used to form words, help with swallowing, and to perceive taste. When the tongue requires radiation, each of these functions will be affected. The entire squamous mucosa is protected by a liquid barrier of saliva and mucous, produced by 4 major salivary glands, and hundreds of microscopic minor salivary glands. These glands are particularly sensitive to radiation, and after just one dose of radiation, these glands can completely shut down production of their important secretions.

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Most head and neck cancers require 6-8 weeks of radiation therapy.

Side-Effects:
The side-effects can, as noted above, start after the first day, with dry mouth causing immediate change in taste. Then in the second week of treatment the specific mucosal surfaces hit with the radiation will become very tender. If chemotherapy is given simultaneously, all of these side effects are greatly enhanced. In week three, the tissues being treated develop ulcers and sloughing of the lining. This reaction, known as mucositis, is very similar to the reaction the mouth has to burning from very hot liquids. However, when you burn your mouth with liquids or food, the mouth very quickly repairs the burn in 24-48 hours. When radiation is delivered, this reaction does not heal until the radiation is fully completed. So, most patients develop very painful sores in the parts of the mouth and throat that are being treated. This pain can be so severe that the patient will require narcotic pain medication, special numbing mouth rinses, and drastic changes in the types of food and liquid that can be swallowed. For some patients, this severe reaction is so predictable that the radiation doctor has the patient get a surgical feeding tube placed into their stomach before even starting the radiation therapy. Then, when the mouth or throat pain starts, the patient can receive nutrition through the tube, and will not need to "use" their natural anatomy to take nutrition.
Luckily, all of these painful problems will recover when the cancer treatments are completed. Recovery can take 1-6 months depending on the specific case.

The Salivary Glands and Modern Interventions Unfortunately, the recovery of the salivary glands is never complete. In the past, many patients had permanent dry mouth and loss of taste after a course of curative radiation treatments. A great deal of research has gone into tackling this long-term side-effect. Today, radiation oncologists can use a special drug, Amifostine, which protects the salivary glands and helps them to recover function faster and better. Also, a very complex form of radiation, known as Intensity Modulated Radiation Therapy (IMRT) has been developed. IMRT allows the oncologist to "sculpt" the radiation doses around the major salivary glands, so that these glands get much less dose than they did in the past. The lower doses will then cause less permanent damage. IMRT is extremely labor-intensive for the radiation oncologist and the radiation physics and technical teams. Thus, IMRT is very expensive, and requires special positioning devices, such as head and shoulder immobilization masks that will not let the patient move during the radiation treatment. IMRT treatments may take as long as 25-45 minutes each day.
Less complicated non-IMRT treatments require the patient to hold still on the treatment table for only 10-15 minutes each day. Another recent "breakthrough" is the use of the drug, cetuximab, with radiation. This drug targets small growth factors on the cancer cells. The main side-effect of cetuximab is a very dramatic skin rash. So, patients who get cetuximab and radiation have fairly severe skin reactions on their faces and neck.
However, the cure rates are increased quite dramatically when this drug is used. And luckily, the rash and skin reaction will clear up in the month after treatment is completed.

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Conclusions:
So, radiation therapy for head and neck cancers sounds like a nightmare!!
It is. It is probably the most difficult type of radiation therapy delivery (the only other part of the body that has such a hard time are the delicate squamous tissues of the genitals and the bottom of the rectum, known as the anus). So why do we do this to our patients?

In the past, when people developed these cancers, very extensive surgeries were used that removed parts of the face, the jaws, the tongue, the throat, and the voice box. People were not only severely disfigured, but were never able to swallow, chew, or talk after some of these procedures. Despite the aggressive nature of the surgeries, 3 out of 4 patients with big head and neck cancers still died of the cancer. Modern radiation therapy has drastically improved the outcome. Today, we see 90% of early voice box cancers are cured with radiation. In 60-80% of more advanced throat cancers, we can permanently preserve the voice box. Removal of the tongue, jaw bones, and facial structures is rarely done today because we have better non-surgical therapy. With new innovations in radiation oncology we can preserve this important organs and structures and get recovery of saliva and taste. Not only are more patients alive, but alive and functioning better.

Radiation Oncology of the Organs of the Chest: Part 1

The Lungs & Esophagus

First, the Numbers:
Two of the most common cancers in our society arise in or on the chest.
Lung cancers are diagnosed in 213,000 men and women in the US each year.
Breast cancers are diagnosed in 180,000 women and almost 3,000 men each year. There are some very rare forms of cancer that can grow on the chest structures, but the only other fairly common tumor is cancer of the esophagus, the swallowing tube, which occurs at a rate of 15,600 cases each year.

The Concept of Organ Preservation
For all three of these cancers, radiation oncology plays a very significant role in the cure, in the relief of symptoms from the tumors, and in the preservation of these organs. By “organ preservation” we mean using less surgery and more radiation therapy and chemotherapy so that an entire organ no longer needs to be removed surgically. In lung, breast, and esophageal cancers, organ preservation is extremely important. For example, most people with lung cancer also have severe lung disease such as emphysema or chronic bronchitis (together, these two lung diseases are known as Chronic Obstructive Pulmonary Disease or COPD). Patients with COPD and lung cancer cannot safely undergo surgical removal of large parts of the lung containing the lung cancer. Thus, non-surgical treatment with radiation is used, and this will allow the patient to keep more useful lung tissue. Similarly, when the esophagus is taken out surgically for the treatment of esophageal cancer, the ability to swallow food is compromised. Surgeons removing

the cancerous esophagus will have to pull the stomach up into the chest and sew it to the low neck.

Esophagus-sparing radiation therapy leaves the esophagus intact, and swallowing will remain much more natural. Finally, the removal of the breast with a surgery known as mastectomy is very disfiguring for women.
The ability to offer women with breast cancer breast preserving treatment has made breast cancer a much less terrifying diagnosis for women.

Let's look a little more closely at lung cancer and esophageal cancer here, and how radiation oncology is used for treatment. Breast cancer will be discussed in the next lecture.

1. LUNG CANCER:
Lung cancer remains the most lethal cancer for both men and women in the U.S. Today, the overall cure rate for lung cancer remains a dismal 10-15% because these cancers are diagnoses usually after they are already large and have spread. Very small lung cancers are more curable, but are rarely discovered. These small lung cancers are usually found accidentally when other tests are done (such as a work-up for heart disease or emphysema).
Surgical removal of the very early lung cancer can provide a cure rate of 75%. Tragically the majority of lung cancer patients will have large, incurable tumors. Modern treatment has been able to double the length of time that patients live, as well as improves the quality of the patients' lives by improving breathing, decreasing chest pain and cough, and decreasing coughing up blood. Still today, cigarette smoking causes the vast majority of lung cancers!! So lung cancer is one of the truly preventable cancers.

Symptoms of Lung Cancers:
Unexplained weight loss and fatigue. Change in cough. Increased or new cough. Coughing up blood. Chest or chest wall pain. Increasing shortness of breath. Rarely, patients will develop swollen lymph nodes in their neck, and rarely, a swollen head with dizziness. New bone pain. May have some difficulty swallowing.

Treatment:
Radiation therapy is used to treat most lung cancers. Today, radiation is usually delivered with simultaneous chemotherapy. This combination is more effective than either treatment alone, but there are side effects to both types of treatment. The combination of treatments also makes the side effects of both more intense.

The main symptomatic effect from chest radiation for lung cancer is known as radiation esophagitis. The esophagus, the food swallowing tube, runs through the middle of the chest. Lung cancers usually start out in the lung tissue, but spread quickly to the lymph nodes in the center of the chest. These lymph nodes run right along the esophagus. So, when radiation is given for the lung cancer, the doctor also has to treat these lymph nodes, and the esophagus (an innocent bystander) gets hit. Usually in the 3rd week of a 6-7 week course of lung cancer

radiotherapy, the side effects become noticeable. Radiation esophagus starts with the patient developing a sensation of something stuck in his throat, behind the breastbone. This mild sensation then develops into pain with swallowing. For patients getting chemotherapy and radiation, this pain can be very severe, and will limit swallowing dramatically. Most patients will lose 10 or more lbs.
during this time. Luckily, radiation esophagitis is a temporary effect, and it usually recovers completely within a month of completing treatment.

Radiation dermatitis is a red, irritated skin reaction that occurs also after 3 to 4 weeks of radiation. Often the radiation doctor can use a "skin sparing" type of radiation to limit this reaction. Skin sparing ensures that the skin gets much less dose than the cancer. Today, most lung cancer patients have only mild sunburn like reaction on the skin of their chest. Like sunburn, the skin will tan and peel a bit. Within 2-3 weeks from completing radiation the skin will recover.

RADIATION PNEUMONITIS
Following the completion of lung cancer radiation therapy, the majority of patients will make a good recovery, and they will experience just improvement in their shortness of breath, bleeding, coughing, and pain from the lung cancer. However, a few patients can get an inflammation of the
section(s) of lung that was hit with the radiation. This inflammation is called radiation pneumonitis, because the patient will have symptoms similar to a pneumonia infection. This is not an infection, and antibiotics will not cure it. For the small number of lung cancer patients that develop radiation pneumonitis, the symptoms of a dry cough, low-grade fever, and new shortness of breath can be treated with anti-inflammatory cortisone.

Today, with CT-based planning, the radiation oncologist is able to limit the amount of lung tissue that is put at risk for this inflammation.
So we see less radiation pneumonitis. Radiation doctors are better able to select the type of radiation, and can custom design the dose and volume of lung irradiated. Despite precautions, some lung cancer patients who have emphysema, or COPD, before they developed lung cancer, will have real risk if they develop any form of pneumonia, even radiation –caused pneumonia. The radiation doctor will work with the patient's pulmonary (breathing) specialist to get the COPD patient's lungs as healthy as possible, both before and after radiotherapy.

2. CANCER OF THE ESOPHAGUS
Causes:
Esophageal cancer is much less common than lung cancer. Like lung cancer, it can be caused by the use of tobacco, and is increased when a smoker also drinks alcohol. So, like lung cancer, some cases of esophageal cancer can
be prevented!! Other people who suffer from acid reflux disease have a
higher risk of esophagus cancer. Acid-reflux disease is a variety of conditions that allow stomach acid to back up into the esophagus. The chronic acid exposure makes the esophageal

lining cell mutate into a pre-cancerous condition known as Barrett's esophagitis. If Barrett's esophagitis and heart burn are not treated, over a period of years that mutation turns into real cancer. So, if people who have chronic heartburn see a gastroenterologist for evaluation, these conditions can be diagnosed early. Many medications are now available that will turn off the excess stomach acid production. So here again, these potential cases of esophageal cancer could be prevented.

Symptoms of Esophageal Cancer:
Difficulty swallowing—may be painful or not. May be worse for solids, but will also eventually worsen with drinking too. The patient may get marked coughing (choking) with swallowing. Most people may report worsening of heartburn. Most will tell their doctors that they have lost a significant amount of weight in the prior few months.

Treatment:
For patients who are lucky enough to have very small esophageal tumors, with no spread to the lymph nodes of the central chest, surgery by itself can be highly curative.
But, just like lung cancer, most patients with esophageal cancer, in the US, will have very advanced cancers when they are diagnosed. In the setting of very poor health, very advanced cancer, surgery will not be considered. So, radiation and chemotherapy play very big roles in the treatment of this disease.

The first goal of treatment is to get the patient swallowing more effectively, so that their nutrition improves. Unfortunately, as the patient gets to the 3rd week of the 6-7 week course of radiation, they develop RADIATION ESOPHAGITIS (see discussion above).
Luckily, the esophagitis does go away within a month of completing treatment. And for the vast majority of esophageal cancer patients, they will be able to swallow naturally again.

Other Side effects:
Esophageal cancer patient also develop a risk of radiation pneumonitis, because the radiation has to pass through the lungs to hit the esophagus.
Modern conformal treatment has lowered this risk tremendously. People, who develop esophagus cancer because they were smokers, also have a high rate of lung disease, like COPD. So the smoker's risk of pneumonitis is higher.

Results/ Prevention:
Today, like lung cancer, the majority of patients with esophageal cancer will not be cured. Here again, preventing this cancer killer is the best intervention of all. If we could get smokers to stop smoking and decrease alcohol intake we would have less esophagus cancer. If more patients with acid reflux disease told their doctors about their heartburn, we could place them on the right medications and prevent even more cancers.

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In the next lecture, we will examine the other common chest cancer, BREAST CANCER.

Radiation Oncology of the Organs of the Chest: Part 2

The Breast

First, The Numbers
Breast cancers are diagnosed in 180,000 women and almost 3,000 men each year. Another 20,000 women will be diagnosed with pre-malignant breast tumors known as Ductal Carcinoma in Situ (DCIS) of the breast. In general, the premalignant DCIS tumors will require very similar surgery and radiation treatments as the actual cancers. DCIS does not require chemotherapy, but many true cancers will also require such drug treatment.

The Concept of Organ Preservation
Radiation oncology plays a very significant role in the cure, in the relief of symptoms from advanced tumors, and in the preservation of the female breast. By "organ preservation" we mean using less surgery and more radiation therapy and chemotherapy so that an entire organ no longer needs
to be removed surgically. Finally, the removal of the breast with a
surgery known as mastectomy is very disfiguring for women. {My apologies to the 3000 fellows, who develop breast cancer, but there is no real need to preserve the male breast tissues, so mastectomy is the preferred surgery for these rare male cancers.} The ability to offer women with breast cancer and pre-malignant DCIS breast preserving treatment has made breast cancer a much less terrifying diagnosis for women.

Breast Cancer:
Breast cancer is the most common cancer of women. However, still today lung cancer kills more women in the U.S each year!! So, in comparison, breast cancer is more treatable, and more curable than lung cancer. The use of screening mammograms has shifted breast cancer into more curable sizes of disease. A mammogram can perceive a breast cancer smaller than a grain of rice. In the time before mammography, a breast lump discovered by actually feeling the lump, was usually an inch or more in size at the time of discovery. Smaller tumors lead to larger cures!! The risk that an average lady in our society will get a breast cancer over the length of her lifetime is one in every 8 women (about a 10-12% risk).

When Ductal Carcinoma in situ (premalignant breast tumor) is treated effectively, the risk of a lady dying from breast cancer is only 1-2 %.
Early stage 1 breast cancer (up to an inch in size) has an 85-9r% cure rate; stage 2 (1 to 2 inches in size) has a 75-85% cure. Stage 3 cancers, are bigger than an inch, or have lots of spread to the lymph nodes under the arm, have much less change for cure (<75 %); and stage 4 cancers (very advances, or have already spread) are not curable, but therapy can prolong quality life by YEARS!!

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Heredity of Breast Cancers:
The discovery of the breast cancer related genes, BRCA-1 and BRCA-2 in the early 1990s has shown us that about 15% of breast cancer4s are due to known genetic mutations. In families that have these mutations, the average risk that a woman will develop breast cancer over the course of her lifetime is 60%. In BRCA-2 families, even the men are at higher risk for breast cancer.

Other families that have frequent breast cancers have been tested for BRCA 1 & 2, but do not have this genetic abnormality. We say that these families have a genetic predisposition to breast cancer. Women in these families do have a higher risk of developing breast cancer, but science cannot always explain why.

Today, 85% of breast cancers remain unexplained, or "sporadic". There is an enormous amount of research going on in this area. The future holds a lot of hope for families and women with breast cancer.

Symptoms of Breast Cancers:
Most breast tumors have NO symptoms. Ideally, we want to find a new premalignant tumor or cancer before the patient has any awareness of its presence in her breast. Tumors over ½ inch in size may be discovered on self-examination of the breast. Bigger cancers may have a lump in the breast, or a lump in the armpit. A few breast cancers will cause some discharge, even bloody, from the nipple. Other cancers may distort the shape of the breast or nipple.
Rarely, breast cancers can involve the skin of the breast. So a doctor should examine any persistent rash on the nipple. A very aggressive type of breast cancer, called "inflammatory" breast cancer causes the breast to become red and swollen—so it looks inflamed.
Because our society now talks about breast cancer, fewer women come in with really advanced cancers today than did in up through the 1990s.
Occasionally, a lady will have a cancer that causes an ulcer in the skin of the breast. These malignant ulcers are a sign of advanced disease and may be painful.

Today, we don't have one single intervention that will actually prevent breast cancer for the lifetime of a woman. So, getting annual mammograms after the age of 40 is the best
Treatment:

Surgery is used to treat most breast cancers. When possible, surgeons try
to offer safe breast saving surgery as an alternative to mastectomy. There are some breast cancers, which cannot be safely treated with "lumpectomy"
removal of the breast tumor and a rim of normal breast tissue around the tumor. After a lumpectomy most patient will then require some form of radiation therapy to ensure that cancer does not grow back in that breast.

Situations where breast preservation surgery is not safe:

1. Multiple cancers are present in one breast, or extensive cancer involving much of the breast (these changes may be seen on the mammogram, on an MRI scan of the breast, or at the time of a lumpectomy.

2. Very large cancers (over 2 inches in size), especially when the cancer is in a small breast.

3. Women with very rare serious auto-immune diseases, called collagen vascular disease (lupus and scleroderma, particularly), have skin that does not tolerate therapeutic doses of radiation 4. Radiation therapy cannot be given during pregnancy.

5. Inflammatory breast cancers, and really advanced cancers involving the skin.

6. Young women (in their 20s and 30s) with the BRCA 1 or 2 mutations.

For women with the above situations, mastectomy is still the preferred type of surgery.

Chemotherapy, or drug therapies are used for a large number of breast cancer patients. The discussion of which patient s need chemotherapy, which need hormone therapy, and which need other types of drug therapy is a topic that could be a full month's discussion by itself.

Types of Radiation For Breast Cancer:
1. Partial Breast Radiotherapy: This is still an experimental treatment, and is offered in the research setting to women with breast cancers that are small, and have non- aggressive biologic behavior.
a. Brachytherapy: At the time of a lumpectomy surgery, the surgeon places a hollow tube into the lumpectomy cavity in the breast tissue. Then a series of 10 treatments (2 each day for 5 days) using a powerful radioactive seed is given. An alternative version uses a series of hollow tubes to hole the radioactive seed in place.
b. External, conformal partial breast radiotherapy: Uses the linear accelerator to focus a high dose treatment to the lumpectomy bed, sparing the rest of the breast from radiation.

2. Whole breast radiotherapy: This is the standard of care for all forms of breast cancers after lumpectomy. Here, the patient is treated with the linear accelerator. Most women will receive 5 weeks of daily radiation to their whole breast. Then, a smaller radiation electron beam will be used to deliver 1 to 1 ½ weeks of "boost" radiation to the lumpectomy site.

3. Additive radiation to the chest wall after mastectomy. Women who required mastectomy because they had advanced cancers will benefit from radiation to the chest wall and the node areas in the underarm and low neck.
Called post -mastectomy radiation, these treatments help to prevent these aggressive cancers from growing back on the skin or in the chest wall. By preventing these "local" recurrences, post-mastectomy irradiation also gives these people a better chance of cure. Men with breast cancer do have mastectomies, and most will require post-mastectomy radiation therapy.

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Post-mastectomy radiation is generally 5 ½- 6 ½ weeks in length.

Side Effects of Radiation to the Breast or Chest wall:
Radiation dermatitis is a red, irritated skin reaction that occurs also after 3 to 4 weeks of radiation. Often the radiation doctor can use a "skin sparing" type of radiation. Skin sparing ensures that the skin gets muck less dose than the cancer. Today, most breast cancer patients treated for breast preservation have only mild sunburn like reaction on the skin of their breast. Like sunburn, the skin will tan and peel a bit. Within 2-3 weeks from completing radiation the skin has recovered.

Patients with more advanced cancer that require mastectomy do have a certain risk that the breast cancer could grow back in the skin of their chest wall (or in the skin of their "reconstructed" breast). For these patients, the skin is treated more aggressively. "Skin-sparing techniques may not be used, and the skin will have a more sever reaction with some blistering.
The skin is very resilient, and for most people, this skin reaction recovers completely in 3-4 weeks. This more intense reaction is painful, and requires pain medication, special ointments, and skin care.

Other side effects from radiation that are commonly seen are; some fatigue, a mild drop in the book counts, and a slight change in texture of the skin of the treated breast. Today, with modern CAT scan based planning, serious lung and heart side effects are not seen.

Women who undergo brachytherapy may experience some other rare late side effects such as a dense scarring of the tissues in a very limited area near the implants. These effects are being studied, and to date, seem to be very uncommon.

One final note for cigarette smokers: Women who smoke through their breast cancer treatments and afterwards do seem to have a higher risk of lung cancer in lung under the treated breast or chest wall, when compared to women who smoke and never get radiation therapy. However, non-smoking breast cancer patients do not have any increase in lung cancer risk from these necessary treatments.

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